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Emergency Medicine, Critical Care, and Anesthesia

PART VII

Chapter 77

Emergency Medical Services for Children

Charles G. Macias, Katherine E. Remick, and Steven E. Krug

The overwhelming majority of the 27 million children who present annually for emergency care in the United States are seen at community-based general emergency departments (EDs). Visits to children's hospital EDs account for just 10% of initial ED encounters. Additionally, across emergency medical services, children account for approximately 10% of all transports. This distribution suggests that the greatest opportunity to optimize care for acutely ill or injured pediatric patients, on a population basis, occurs broadly as part of a systems-based approach to emergency services, an approach that incorporates the unique needs of children at every level. Conceptually, emergency medical services for children are characterized by an integrated, continuum-of-care model (Fig. 77.1). The model is designed such that patient care flows seamlessly from the primary care medical home through transport and on to hospital-based definitive care. It includes the following five principal domains of activity:

1. Prevention, both primary and secondary
2. Out-of-hospital care, both emergency response and prehospital transport
3. Hospital-based care: ED and inpatient, including critical care
4. Interfacility transport, as necessary, for definitive or pediatric medical and surgical subspecialty care (see Chapter 77.1)
5. Rehabilitation

Fig. 77.1 The emergency medical services for children (EMSC) continuum of care. Seriously ill and injured children interface with a large number of healthcare personnel as they move through the EMSC system.

The federal **Emergency Medical Services for Children (EMSC)** program of the Health Resources and Services Administration Maternal and Child Health Bureau has stewarded improvements in the care of children in the context of the continuum-of-care model. The programmatic mission of the EMSC program is as follows:

- To ensure U.S. emergency care systems across the continuum of care are pediatric-ready, meaning pediatric-specific needs are incorporated into every aspect of patient care, including patient safety practices, equipment and supplies, competency requirements, policies and procedures, quality improvement efforts, and administrative oversight and coordination of care.
- To ensure access to high-quality emergency medical care for ill or injured children and adolescents of all ages regardless of geographic location.
- To ensure that pediatric services are well integrated into an emergency medical services (EMS) system and backed by optimal resources.
- To ensure that the entire spectrum of emergency services—including primary prevention of illness and injury, acute care, and rehabilitation—is provided to infants, children, and adolescents at a level equal to that of adults.

PRIMARY CARE PHYSICIAN AND OFFICE PREPAREDNESS

The primary care physician (PCP) has multiple important roles in the EMS system. Through anticipatory guidance, the PCP can help shape the attitudes, knowledge, and behaviors of parent and child, with the primary goal of preventing acute medical events, such as injury and exacerbations of illness. The point-of-care initiation for many acute problems is often the PCP office. From the standpoint of personnel, equipment, training, and protocols, the PCP office setting must be adequately prepared to initially manage acute and emergency exacerbations of common pediatric conditions, such as respiratory distress and seizures. Furthermore, on rare occasion, the PCP office environment may be confronted with a child in clinical extremis who requires resuscitation and stabilization. It is therefore incumbent on the PCP not only to ensure access to EMS, that is, 911 system activation, but also to ensure that there is adequate equipment and supplies and on-site cognitive and psychomotor skill preparation to deal with such an emergency. **Office preparedness** requires training and continuing education for staff members, protocols for emergency interventions, ready availability of appropriate resuscitation drugs and equipment, and knowledge of local EMS resources and ED capabilities. PCPs can also play a pivotal role in informing and advocating for pediatric emergency and disaster readiness for families (especially those of children and youth with special healthcare needs) and in local EMS agencies, schools and childcare programs, and community hospitals. In all communities, the medical home plays a vital role in promoting family readiness for emergencies and disasters.

Staff Training and Continuing Education

It is a reasonable expectation that all office staff, including receptionists and medical assistants, be trained in cardiopulmonary resuscitation (CPR) with recertification maintained every 2 years. Nurses and physicians should also have training in a systematic approach to pediatric resuscitation that optimizes performance of high-quality CPR. Core knowledge may be obtained through standardized courses in **advanced life support (ALS)** offered by national medical associations and professional organizations. Frequent practice and timely

recertification are important for knowledge retention and skill maintenance. Examples include the Pediatric Advanced Life Support (PALS) and Pediatric Emergency Assessment, Recognition and Stabilization (PEARS) courses sponsored by the American Heart Association (AHA), the Advanced Pediatric Life Support (APLS) course sponsored by the American Academy of Pediatrics (AAP) and American College of Emergency Physicians (ACEP), and the Emergency Nurses Pediatric Course (ENPC) sponsored by the Emergency Nurses Association (ENA).

Protocols

Standardized protocols for telephone triage of seriously ill or injured children are essential. When a child's clinical status is guarded and prehospital care is available, ambulance transport in the care of trained personnel is always preferable to transport by other means (e.g., private vehicle). This obviates the potentially serious medical consequences of relying on distraught, often untrained, parents who lack essential equipment and supplies to provide even **basic life support (BLS)** measures to an unstable child during transport. Practitioners can work with their regional pediatric emergency care resource center (e.g., children's hospital, academic medical center, trauma center) to develop and maintain written protocols for office-based management of a range of conditions, including anaphylaxis, cardiopulmonary arrest, head trauma, ingestions, shock, status asthmaticus, status epilepticus, extremity injuries, and upper airway obstruction. Regular practice using mock code scenarios improves office-based practitioner and staff performance and self-efficacy in managing these problems.

Resuscitation Equipment

Availability of necessary equipment is a vital part of an emergency response. Every physician's office should have essential resuscitation equipment and medications packaged in a weight-based pediatric resuscitation cart or kit (Table 77.1). This cart or kit should be checked on a regular basis and kept in an accessible location known to all office staff. Outdated medication, a laryngoscope with a failed light source, or an empty oxygen tank represents a potential catastrophe in a resuscitation scenario. Such an incident can be easily avoided if an equipment checklist and regular maintenance schedule are implemented. A pediatric kit that includes posters to reinforce clinical management and procedures, a drug-dosing formulary, and a color-coded length-based resuscitation tape specifying weight and emergency equipment size are invaluable in avoiding critical therapeutic errors during resuscitation.

To facilitate emergency response when a child needs rapid intervention in the office, all personnel should have designated roles. Organizing a "rapid response team" within the office ensures that necessary equipment is made available to the physician in charge, an appropriate medical record detailing all interventions and the child's response is generated, and the 911 call for EMS response or a critical care transport team is made in a timely fashion. Regular practice for these infrequent events will promote timely response when needed.

Transport

Once efforts to stabilize the child have begun, a decision must be made on how best to transport a child to a facility capable of providing definitive care. If a child requires airway or cardiovascular support, has an altered mental state or unstable vital signs, or has significant potential to deteriorate en route, it is not appropriate to send the child via privately owned vehicle, regardless of proximity to a hospital. Even when an ambulance is called, it is the PCP's responsibility to initiate essential life support measures and to attempt to stabilize the child before transport.

In metropolitan centers with numerous public and private ambulance agencies, the PCP must be knowledgeable about the scope of service provided by each. The availability of BLS vs ALS services, the configuration of the transport team, and pediatric expertise vary greatly among agencies and across jurisdictions. BLS services provide basic support of airway, breathing, and circulation, whereas ALS units are capable of providing resuscitation drugs and procedural interventions as well. Some communities may have only BLS services available, whereas others may have a two-tiered system, providing both BLS and ALS. It may be appropriate to consider medical air transport when definitive or specialized care is not available within the community or when ground transport times are prolonged. In that case, initial transport via ground to an appropriate helicopter landing zone or a local hospital for interval stabilization may be undertaken, pending arrival

Table 77.1 Recommended Drugs and Equipment for Pediatric Office Emergencies

DRUGS/EQUIPMENT	PRIORITY
DRUGS	
Oxygen	E
Albuterol for inhalation	E
Epinephrine (1:1,000 [1 mg/mL])	E
Activated charcoal	S
Antibiotics	S
Anticonvulsants (diazepam/lorazepam)	S
Corticosteroids (parenteral/oral)	S
Dextrose (25%)	S
Diphenhydramine (parenteral, 50 mg/mL)	S
Epinephrine (1:10,000 [0.1 mg/mL])	S
Atropine sulfate (0.1 mg/mL)	S
Naloxone (0.4 mg/mL)	S
Sodium bicarbonate (4.2%)	S
INTRAVENOUS FLUIDS	
Normal saline (0.9 NS) *or* lactated Ringer solution (500-mL bags)	S
5% dextrose, 0.45 NS (500-mL bags)	S
EQUIPMENT FOR AIRWAY MANAGEMENT	
Oxygen and delivery system	E
Bag-valve-mask (450 mL and 1,000 mL)	E
Clear oxygen masks, breather and non-rebreather, with reservoirs (infant, child, adult)	E
Suction device, tonsil tip, bulb syringe	E
Nebulizer (or metered-dose inhaler with spacer/mask)	E
Oropharyngeal airways (sizes 00-5)	E
Pulse oximeter	E
Nasopharyngeal airways (sizes 12-30F)	S
Magill forceps (pediatric, adult)	S
Suction catheters (sizes 5-16F and Yankauer suction tip)	S
Nasogastric tubes (sizes 6-14F)	S
Laryngoscope handle (pediatric, adult) with extra batteries, bulbs	S
Laryngoscope blades (straight 0-2; curved 2-3)	S
Endotracheal tubes (uncuffed 2.5-5.5; cuffed 6.0-8.0)	S
Stylets (pediatric, adult)	S
Esophageal intubation detector or end-tidal carbon dioxide detector	S
EQUIPMENT FOR VASCULAR ACCESS AND FLUID MANAGEMENT	
Butterfly needles (19-25 gauge)	S
Catheter-over-needle device (14-24 gauge)	S
Arm boards, tape, tourniquet	S
Intraosseous needles (16 and 18 gauge)	S
Intravenous tubing, micro-drip	S
MISCELLANEOUS EQUIPMENT AND SUPPLIES	
Color-coded tape or preprinted drug doses	E
Cardiac arrest board/backboard	E
Sphygmomanometer (infant, child, adult, thigh cuffs)	E
Splints, sterile dressings	E
Automated external defibrillator with pediatric capabilities	S
Spot glucose test	S
Stiff neck collars (small/large)	S
Heating source (overhead warmer/infrared lamp)	S

E, essential; S, strongly suggested.

From Frush K, American Academy of Pediatrics, Committee on Pediatric Emergency Medicine. Policy statement-preparation for emergencies in the offices of pediatricians and pediatric primary care providers. *Pediatrics*. 2007;120:200-212. Reaffirmed in *Pediatrics*. 2011;128:e748.

of the air transport team. Independent of whether a child is to be transported by air or ground, copies of the pertinent medical records and any imaging or laboratory studies should be sent with the patient and a call made to the physician at the receiving facility to alert them to the referral and any treatments administered. Such notification is not merely a courtesy; direct physician-to-physician communication is essential for optimal care quality and to ensure adequate transmission of patient care information, to allow mobilization of necessary resources in the ED, and to redirect the transport if the emergency physician believes that the child would be more optimally treated at an alternative facility.

PEDIATRIC PREHOSPITAL CARE

Prehospital care refers to emergency assistance rendered by trained emergency medical personnel before a child reaches a treating medical facility. The goals of prehospital care are to further minimize systemic insult or injury through a series of well-defined and appropriate interventions and serve as the first link in high-quality emergency care. Prehospital emergency care services embrace patient safety, family-centered care, and timely and effective interventions as core tenets. Most U.S. communities have a formalized EMS system; the organizational structure and nature of emergency medical response depend greatly on local demographics and population base. EMS may be provided by volunteers or career professionals working in a fire department–based or independent third-service response system. All EMS and fire-based agencies have an identified medical director who defines provider competencies and scope of practice. Key points to recognize in negotiation of the juncture between the community physician and the local EMS system include access to the system, provider capability, and destination determination.

Access to the EMS System

Virtually all Americans have access to the 911 telephone service that provides direct access to a dispatcher who coordinates police, fire, and EMS responses. Many communities have a next-generation 911 system, in which the location of the caller is automatically provided to the call taker and/or dispatcher regardless of landline or mobile device use, permitting emergency response even if the caller, such as a young child, cannot give an address. Next-generation 911 also provides text-messaging capabilities. The extent of medical training for call takers and dispatchers varies among communities, as do the protocols by which they assign an emergency response level (BLS vs ALS). Many dispatch centers have adopted the Medical Priority Dispatch System (MPDS) to use standardized protocols and prearrival/postdispatch instructions. MPDS requires emergency medical dispatchers to ask a series of questions that determine the appropriate level of priority and EMS response. In some smaller communities, no coordinated dispatch exists, and emergency medical calls are handled by the local law enforcement agency or fire department. When activating the 911 system, the physician must make clear to the dispatcher the nature of the medical emergency and the condition of the child.

Provider Capability

There are many levels of training for prehospital EMS providers, ranging from individuals capable of providing only first aid to those trained and licensed to provide ALS. All EMS personnel, whether basic **emergency medical technicians (EMTs)** or paramedics, receive some initial training in pediatric emergencies; however, in most programs the dedicated time allotted to pediatric emergencies is minimal. Furthermore, state requirements vary for pediatric continuing education, and exposure to critically ill or injured children in the prehospital setting is infrequent, even in urban settings. PCPs should recognize that prehospital providers may need additional consultation or support, especially when managing children with uncommon medical conditions. PCPs can support maintenance of pediatric knowledge by EMS providers by serving as or working closely with an identified pediatric emergency care coordinator (PECC) within the EMS agency to fully integrate the needs of children into every aspect of system-based care: policies, protocols, quality improvement, patient safety, family-centered care, staff competencies, and equipment and supplies. Although children represent a minority population in the prehospital setting, the joint policy statement, *Pediatric Readiness in Emergency Medical Services Systems,* provides a comprehensive overview of how EMS systems can address the needs of children throughout all aspects of care. The identification of a PECC and physical demonstration of pediatric-specific skills represent two of the reference standards that the federal EMSC program has adopted as performance measures for state-level operational readiness to care for children in an EMS system.

First responders may be law enforcement officers or firefighters, who are dispatched to provide emergency medical assistance, or bystanders. Public safety personnel have a minimum of 40 hours of training in first aid and CPR. Their role is to provide rapid response and stabilization pending the arrival of more highly trained personnel. In some smaller communities, this may be the only prehospital emergency medical response available.

In the United States the bulk of emergency medical response is provided by EMTs, who may be volunteers or paid professionals. Basic EMTs may staff an ambulance after undergoing a training program of approximately 100 hours. They are licensed to provide BLS services but may receive further training in some jurisdictions to expand their scope of practice to include intravenous catheter placement and fluid administration, management of airway adjuncts, and use of an automated external defibrillator (AED).

Paramedics, or EMT-Ps, represent the highest level of EMT response, with medical training and supervised field experience of at least 1,000 hours. Paramedic skills include advanced airway management, including endotracheal intubation; placement of peripheral vascular or intraosseous lines; intravenous administration of drugs and blood products; administration of nebulized aerosols; needle and finger thoracostomy; and cardioversion, cardiac pacing, and manual defibrillation. These professionals provide ALS services, functioning out of an ambulance equipped as a mobile intensive care unit (ICU). The joint position statement *Recommended Essential Equipment for Basic Life Support and Advanced Life Support Ground Ambulances 2020* published by the AAP, ACEP, American College of Surgeons Committee on Trauma, EMSC Innovation and Improvement Center, ENA, National Association of EMS Physicians, and National Association of EMS Officials outlines national standards for essential equipment, medications, and supplies necessary to provide BLS and ALS care across the age spectrum.

Both basic EMTs and paramedics function under the delegated licensing authority of a supervisory EMS medical director. This physician oversight of prehospital practice is broadly characterized under the umbrella term *medical control.* **Direct**, or **online**, **medical control** refers to medical direction either at the scene or in real time via voice or video transmission. **Indirect**, or **offline**, **medical control** refers to the administration of medical direction before and after the provision of care (i.e., clinical protocols). Offline activities, such as provider education and training, protocol development, and medical leadership of quality assurance/quality improvement programs, represent areas in need of greater pediatric input. Whether in the presence or absence of a PECC, a pediatric advisory committee may provide additional pediatric knowledge and expertise. Evaluation and tracking of pediatric performance is critical to ensuring high-quality care for children in a community. The National EMS Information System (NEMSIS) serves as a registry for standardized EMS data collection. EMS agency participation in NEMSIS-compliant data submission is one of the federal EMSC performance measures. The National EMS Quality Alliance (NEMQA) and the National EMS Model Clinical Guidelines complement the NEMSIS program by providing evidence-derived pediatric quality measures for adoption in any EMS agency. As a measure of the degree to which EMSC permanence is being established in state EMS systems, the federal EMSC program has required demonstration of the presence of an EMSC advisory committee at the state level. These advisory bodies are well positioned to support EMS agencies in their pediatric readiness and provide a forum for the active engagement of pediatric care experts at a system level.

Destination Determination

The destination to which a pediatric patient is transported may be defined by parental preference, provider preference, or jurisdictional protocol, which is typically predicated on field assessment and, in the case of trauma, mechanism of injury. The 2021 National Guidelines for the Field Triage of Injured Patients relies on injury patterns, physiologic criteria, mechanism of injury, and other special considerations (e.g., suspicion for child maltreatment). Based on these criteria, EMS providers determine the optimal trauma center destination in the setting of injury. In communities served by an organized trauma system that incorporates pediatric designation based on objectively verified hospital capabilities (i.e., pediatric readiness), seriously injured children may be triaged by protocol to the highest-level pediatric-capable trauma center reachable within a reasonable amount of time. Other communities have established state or regional emergency care systems that use pediatric readiness criteria to recognize EDs appropriate for pediatric patients. A high level of pediatric readiness in both medical and trauma centers is linked to decreased mortality in critically ill and injured children. The mantra is to deliver the child to the *right care in the right time,* even if it requires bypassing closer hospitals.

Regionalization in the context of EMS is defined as a geographically organized system of services that ensures access to care at a level appropriate to patient needs while maintaining efficient use of available resources. This system concept is especially germane in the care of children, given the relative scarcity of facilities and their associated providers that are capable of managing the full range and scope of pediatric conditions (Fig. 77.2). Regionalized systems of care coordinated with emergency medical dispatch, field triage, and EMS transport have demonstrated efficacy in improving outcomes for pediatric medical and trauma patients. The existence of statewide or regional standardized systems that formally recognize hospitals able to stabilize and/or manage pediatric medical and traumatic emergencies is a federal EMSC performance measure against which operational capacity to provide optimal pediatric emergency care in the United States is currently being evaluated. Over 15 states now offer pediatric medical facility recognition programs. For the majority, hospital participation in these programs is voluntary. EMSC state partnership programs in the respective jurisdiction can provide further guidance on the application process and requirements for participation. Similarly, several state trauma systems now integrate elements of pediatric readiness into trauma center designation. Moreover, beginning in 2023, the American College of Surgeons (ACS) Committee on Trauma requires all ACS-verified trauma centers to adhere to specific pediatric readiness criteria.

In communities that do not have a hospital with the equipment and personnel resources to provide definitive pediatric inpatient care, **interfacility transport** of a child to a regional pediatric center should be undertaken after initial stabilization (see Chapter 77.1). In the end, all emergency care facilities must stand ready to provide care to ill and injured children of all ages.

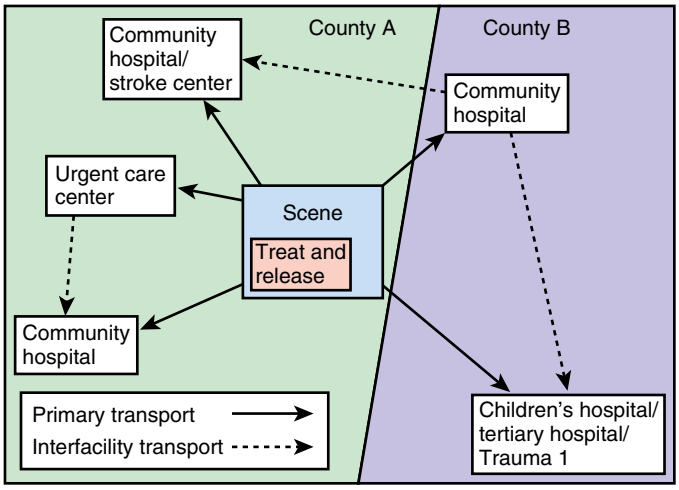

Fig. 77.2 Transport options within a coordinated, regionalized emergency medical services system model. The objective is to ensure access to definitive care at a level appropriate to meet patient needs. *Solid arrows,* Primary transport; *dashed arrows,* interfacility transport. *(Adapted from Institute of Medicine, Committee on the Future of Emergency Care in the U.S. Health System.* Hospital-Based Emergency Care: At the Breaking Point. *Washington, DC: National Academies Press; 2006.)*

THE EMERGENCY DEPARTMENT

The ability of EDs to respond to critically ill and injured children depends on all aspects of pediatric readiness: administrative oversight, staff competencies, pediatric-specific policies and procedures, patient and medication safety, quality improvement, and equipment and supplies. Training, awareness, and experience of the staff as well as access to support services, pediatricians, and medical and surgical subspecialists also play a key role. The majority of children who require emergency care are evaluated in community EDs. Emergency care staff, including physicians, nurses, and advanced practice providers, may have variable degrees of pediatric training and experience. Although children account for approximately 25% of all ED visits, only a fraction of these encounters represents true emergencies. Because the volume of critical pediatric cases is low, emergency physicians and nurses working in lower-volume EDs often have limited opportunity to reinforce and sustain their knowledge and skills in the assessment and stabilization of severely ill or injured children. Indeed, nearly 70% of U.S. EDs provide care for <15 children per day. General pediatricians from the community or pediatric hospitalists may be consulted when a seriously ill or injured child presents to the ED, and they should have a structured approach to the initial evaluation and treatment of an unstable child of any age, regardless of the underlying diagnosis. Telemedicine and e-health may serve as a mechanism to provide better connectivity between patients, primary care, EDs, and tertiary/quaternary institutions. *Early recognition of life-threatening abnormalities in oxygenation, ventilation, perfusion, and central nervous system function and rapid intervention to correct those abnormalities are key to successful resuscitation and stabilization of the pediatric patient.*

The **National Pediatric Readiness Project (NPRP)** is a national quality improvement initiative started by the federal EMSC program, AAP, ACEP, and ENA to ensure high-quality emergency care for all children. The effort began in 2013 with a national assessment of pediatric readiness in U.S. EDs (as measured by compliance with published guidelines). Initial results demonstrated a high level of engagement in pediatric readiness but notable gaps in the ability of U.S. EDs to meet the needs of children: 48% of EDs had a physician PECC; 59% of EDs had a nurse PECC; 46% of EDs included pediatric-specific needs in quality improvement efforts; and 47% had a disaster plan that addressed the needs of children. Higher readiness levels are seen in larger-volume EDs and in EDs with physician and nurse PECCs and/or quality improvement plans that included children. Since then, numerous efforts, including national quality improvement collaboratives, have targeted key areas of readiness. A second NPRP assessment was completed in 2021, and national efforts continue to promote widespread adoption of pediatric readiness within U.S. EDs. In 2019, the National Prehospital Pediatric Readiness Project launched with similar efforts focused on ensuring high-quality prehospital emergency care for children. Table 77.2 lists essential policies, procedures, and protocols specifically addressing the needs of children in the ED. ED staff and other stakeholders can access pediatric readiness checklists and toolkits and identify opportunities to participate in pediatric readiness efforts on the website of the EMSC Innovation and Improvement Center, https://emscimprovement.center/. Given the link between pediatric readiness and increased survival for critically ill and injured children, baseline readiness standards must be met by all EDs and EMS agencies to ensure that children receive the best emergency care possible.

The way the family supports the child during a crisis, and consequently how the family is supported by the local EMS agency and in the ED when caring for the child, are critical to patient recovery,

Table 77.2 Guidelines for Pediatric-Specific Policies, Procedures, and Protocols for the Emergency Department (ED)

- Illness and injury triage
- Pediatric patient assessment and reassessment
- Documentation of pediatric vital signs, abnormal vital signs, and actions to be taken for abnormal vital signs
- Identification and notification of the responsible provider of abnormal vital signs (age or weight based)
- Immunization assessment and management of the underimmunized patient
- Sedation and analgesia for procedures, including medical imaging
- Consent (including situations in which a parent is not immediately available)
- Social and mental health issues
- Physical or chemical restraint of patients
- Child maltreatment (physical and sexual abuse, sexual assault, and neglect) mandated reporting criteria, requirements, and processes
- Death of the child in the ED
- Do-not-resuscitate orders
- Lack of a medical home
- Children with special healthcare needs
- Family-centered care, including:
  1. Involving families in patient care decision-making and in medication safety processes
  2. Family and guardian presence during all aspects of emergency care, including resuscitation
  3. Education of the patient, family, and regular caregivers
  4. Discharge planning and instruction
  5. Bereavement counseling
- Communication with patient's medical home or primary healthcare provider
- Telehealth and telecommunications
- Medical imaging policies that address age- or weight-appropriate dosing for children receiving studies that impart ionizing radiation, consistent with ALARA (as low as reasonably achievable) principles
- All-hazard disaster preparedness plan that addresses the following pediatric issues:
  1. Availability of medications, vaccines, equipment, and appropriately trained providers for children in disasters
  2. Pediatric surge capacity for both injured and noninjured children
  3. Decontamination, isolation, and quarantine of families and children of all ages
  4. Minimization of parent-child separation and includes system tracking of pediatric patients, allowing for the timely reunification of separated children with their families
  5. Access to specific medical and mental health therapies, as well as social services, for children in the event of a disaster
  6. Disaster drills, which should include a pediatric mass casualty incident at least every 2 years
  7. Care of children with special healthcare needs
  8. A plan that includes evacuation of pediatric units and pediatric critical care and specialty units
- Evidence-based clinical pathways, order sets, or decision support tools
- Written interfacility transfer procedure and agreements that include the following components:
  1. Defined process for initiation of transfer, including the roles and responsibilities of the referring facility and referral center (including responsibilities for requesting transfer, method of transport, and communication)
  2. Transport plan to deliver children safely (including the use of child passenger restraint devices) and in a timely manner to the appropriate facility capable of providing definitive care
  3. Process for selecting the appropriate care facility for pediatric specialty services not available at the hospital
  4. Process for selecting the appropriately staffed transport service to match the patient's acuity level (i.e., level of care required and equipment needed for transport) and appropriate for children with special healthcare needs
  5. Process for patient transfer (including obtaining informed consent)
  6. Plan for transfer of critical patient information (i.e., medical record, imaging, copy of signed transport consent), as well as personal belongings and provision of directions and referral institution information to family
  7. Process for return transfer of the pediatric patient to the referring facility as appropriate
  8. Integration with telehealth/telecommunications processes and mobile integrated health/community paramedicine as appropriate

Adapted from Remick K, Gausche-Hill M, Joseph MM, Brown K, Snow SK, Wright JL; American Academy of Pediatrics Committee on Pediatric Emergency Medicine and Section on Surgery; American College of Emergency Physicians Pediatric Emergency Medicine Committee; Emergency Nurses Association Pediatric Committee. Pediatric readiness in the emergency department. *Pediatrics*. 2018;142(5):e20182459.

family satisfaction, and mitigation of behavioral and mental health impact. Commitment to patient- and family-centered care in the ED ensures that the patient and family experience guides the practice of culturally sensitive care and promotes patient dignity, comfort, and autonomy. In both the ED and EMS settings, particular issues, such as family presence, deserve specific attention. Surveys of parents have indicated that most want to be with their child during invasive procedures and even during resuscitation. Allowing their presence has been shown to reduce parental and patient anxiety and does not interfere with procedure performance. Patient- and family-centered care practices are also strongly associated with improved care quality and patient safety.

Disaster Preparedness

Throughout a public health emergency or catastrophic event, natural or human-made, several unique factors place children at disproportionate, increased risk. Combined with other factors, global climate change has promoted increased frequency and severity of weather-related disasters. During an average workday, an estimated 69 million U.S. children are separated from their families in schools and childcare centers, where mass casualty events can easily occur. This separation adds the further challenge of safe and timely reunification of children with family during or after an incident. Furthermore, in the event of a biologic, chemical, or radio-nuclear attack, unique anatomic, developmental, and physiologic features make children especially vulnerable to absorption, ingestion, or inhalation of toxic agents and related morbidity and mortality (see Chapter 763).

Pediatric planning considerations include training of first responders and other care providers, patient triage, decontamination, surge capacity and capabilities, medical countermeasures (medications, vaccines, equipment, supplies), evacuation, transport, sheltering, and family reunification. The community plays a significant role in preparedness and is inclusive of schools, school nurses, faith-based organizations, and other community entities.

All levels of the healthcare system must be prepared for disaster-driven surges in patient care needs. Surge capacity refers to the ability to evaluate and care for a markedly increased volume of patients—one that challenges or exceeds normal variations in operating capacity. Surge capability refers to the ability to provide specialized medical services for unique patient populations, such as children, that may not be routinely available under normal operating conditions. Surges may require alternative care processes and additional resources to meet the demand for services. Critical surges may require consideration of contingency plans that typically require activation of alternative care standards. Surges that exceed the additional capacity of contingency plans may require implementation of crisis care standards as a means to increase capacity beyond levels that exceed normal daily operations. During a public health emergency, surge requirements may extend beyond direct patient care to include tasks such as laboratory screening or epidemiologic investigations. All levels of the healthcare system may be challenged to increase their capabilities, providing medical services for patient populations, such as children, that may not be routinely available. As an example, the community hospital that routinely transfers higher-acuity ill or injured children or children with medical

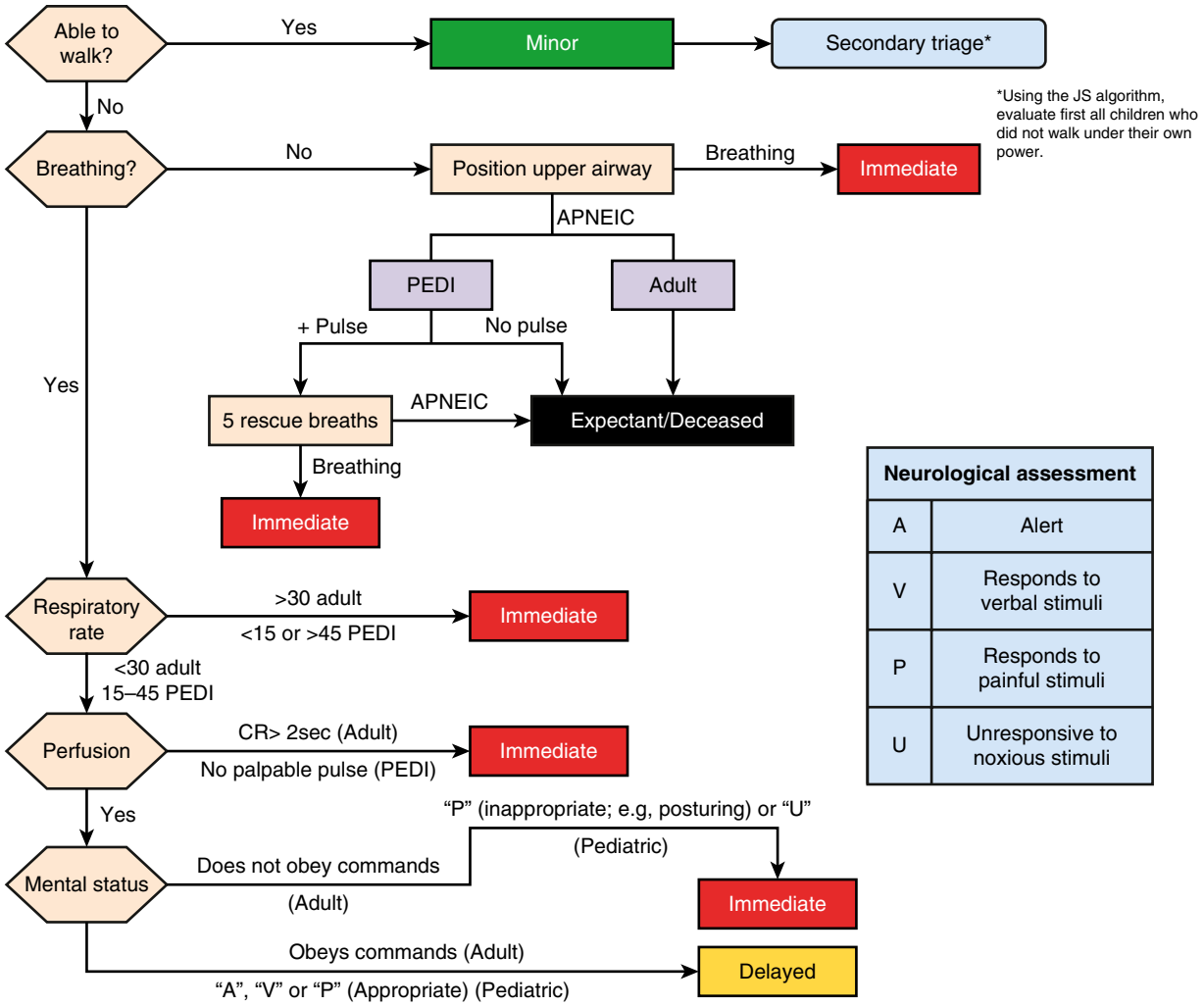

Fig. 77.3 Combined START/Jump START triage algorithm. (*Copyright 2002, Lou Romig, MD.*)

complexity to a pediatric tertiary center may be unable to do so during a disaster. Mechanisms for remote consultation and support of pediatric care, leveraging community pediatricians and tertiary pediatric subspecialists via telemedicine, should be considered.

Beyond acute medical treatment needs, pediatric planning must also consider the typically broad mental and behavioral health impact disasters have on children and families. Mental and behavioral health concerns commonly represent the largest impact of disasters on children and adolescents. Pediatric plans must also be in place for locations where children congregate, such as schools and childcare; these plans must be aligned with local jurisdiction planning and communicated to families.

Community practice and healthcare system readiness and resiliency begin with *personal and family readiness planning* engaged by healthcare providers and support staff; these efforts should also include attention to provider wellness.

The AAP's Children and Disasters website* (https://www.aap.org/en/community/aap-councils/council-on-disaster-preparedness-and-recovery-codpr/) contains toolkits, checklists, and other resources pertinent to pediatric readiness within the community, schools, the medical home, and hospitals; educational materials are also available for families. Reliable information and excellent disaster readiness resources are also located on the websites of the EMSC Innovation and Improvement Center and U.S. Department of Health and Human Services (HHS) and Assistant Secretary for Preparedness and Response (ASPR) Eastern Great Lakes Pediatric Disaster Center of Excellence (https://emscimprovement.center), U.S. Centers for Disease Control and Prevention (https://emergency.cdc.gov), U.S. Department of Health and Human Services (https://www.phe.gov/preparedness/Pages/default.aspx), U.S. HHS ASPR Technical Resources, Assistance Center, and Information Exchange (TRACIE) (https://asprtracie.hhs.gov/), U.S. Federal Emergency Management Agency (https://www.fema.gov), HHS ASPR Western Regional Alliance for Pediatric Emergency Management (WRAPEM) (https://www.wrap-em.org/index.php/resources-edocman-public), and HHS HRS Pediatric Network (PPN) (https://pedspandemicnetwork.org/).

Triage in Disaster Pediatric Medical Care

Mass causality events (hurricanes, bombings, gas leaks, bus or plane crashes, earthquakes, mass shootings, fires, others) require *scene-based* assessment, assignment, and tagging (Figs. 77.3 and 77.4). Assessment must be rapid (~30 seconds) and includes breathing, circulation, and mental status. These parameters are incorporated in the **START** (simple triage and rapid treatment) triage tool for adolescent and adults and the **Jump START** assessment for 0- to 14-year-old children. The combined algorithm is noted in Figure 77.3. The "jump" in Jump START relates to one difference between pediatric and adult approaches wherein children are given a rescue breath if they remain apneic with a pulse after positioning the airway (see Fig. 77.3). Triage categories are color coded (see Fig. 77.4) at the site of the disaster based on risk. **Red** – immediate life-threatening injury; **Yellow** – potentially stable for a short period; **Green** – minor injury, walking wounded; **Black** – dead or not expected to survive.

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* https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/Children-and-Disasters/Pages/default.aspx.

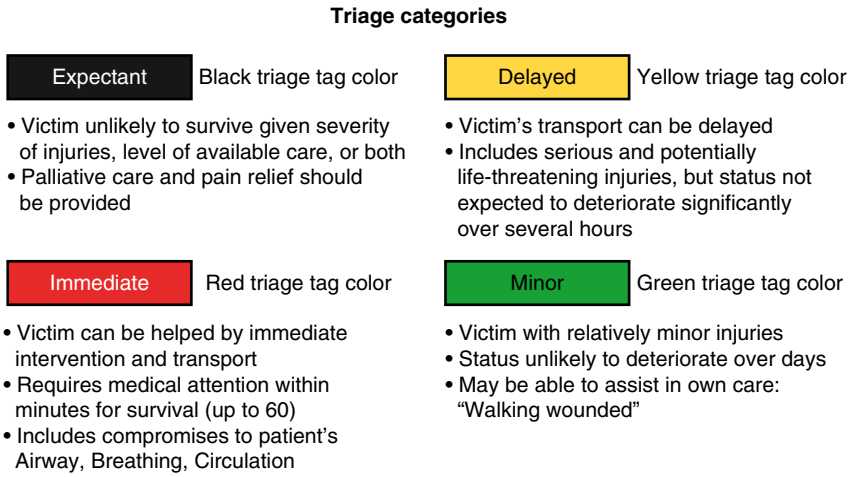

Fig. 77.4 Triage categories. (*From US Department of Health and Human Services: https://chemm.hhs.gov/startpediatric.htm.*)

77.1 Interfacility Transport of the Seriously Ill or Injured Pediatric Patient

*Corina Noje, Mary Beth Howard, and Bruce L. Klein**

Patients often seek treatment at facilities that lack sufficient expertise to treat their conditions, necessitating transfer to more appropriate specialty centers. This is especially pronounced in pediatrics. Emergency medical services (EMS) providers or parents usually take children to local emergency departments (EDs) first, where their conditions and physiologic stabilities are assessed. Although bringing a child directly to the local ED may be proper logistically, community-based local EDs can be less than ideal for pediatric emergencies. Children have been reported to account for about 20% of all ED visits, but not all EDs have the necessary supplies for pediatric emergencies. Also, general EDs are less likely to have pediatric expertise or policies in place for the care of children. Outcomes for critically ill children treated in pediatric intensive care units (PICUs) are better than for those treated in adult ICUs. When pediatric critical care is required, transport to a regional PICU is indicated. In addition, often the type of subspecialty care needed (e.g., pediatric orthopedics) is available only at the pediatric center.

Pediatric transport medicine consists of the interfacility transfer of infants, children, and adolescents from community facilities to pediatric centers that can provide the needed level of expertise. Transport is performed by professionals proficient in pediatric transport using age-equipped ground, rotorcraft, or fixed-wing ambulances. Pediatric transport medicine is a multidisciplinary field comprising pediatric critical care and pediatric emergency medicine (PEM) physicians (and, sometimes for newborn infants, neonatologists); nurses, respiratory therapists, and paramedics with advanced training for pediatric transport; and communications specialists. The goal is to deliver quality pediatric care to the region's children, while optimizing the use of regional resources. For the individual child, the aim is to stabilize and, when appropriate, begin treating as soon as possible—that is, at the local ED and during transport, well before arrival at the referral center.

Models for pediatric transport services vary depending on the needs and available resources in a geographic region, but all should have certain basic components: a network of community hospitals and regional pediatric centers; an established communications and dispatch system that easily facilitates transfer to the pediatric center; ground and/or air ambulances; medical and nursing leadership from pediatric critical care or PEM (or neonatology); experienced pediatric **medical control physicians (MCPs)**; a multidisciplinary team of pediatric transport professionals specially trained and equipped to provide the appropriate level of care required during transport; operational and clinical policies and procedures that guarantee safe, state-of-the-art, and timely pediatric critical care transport; and a database for quality and performance assessment.

COMMUNICATIONS AND DISPATCH CENTER

Communications are one of the most vital components of a regional transport system. Treating a critically ill or injured child is generally an uncommon event for most community physicians. Therefore they need to know *whom, how,* and *when* to call for assistance in the stabilization and transfer of a pediatric patient. The communications and dispatch center provides a single telephone number for such calls.

The communications and dispatch center coordinates communications among the outlying facility, receiving unit, MCP, transport team, and other consultants. This center may be part of a hospital unit (e.g., ED, PICU), self-contained in a single institution (e.g., emergency communications and information center), or based off-site as a freestanding center coordinating communications and dispatch for multiple transport programs.

Staffing varies depending on the type of center. On-duty nurses or physicians may receive calls at unit-based models with low volumes. In contrast, dedicated communications specialists usually staff self-contained or freestanding centers, which tend to be busier. The communications specialist has numerous responsibilities, including answering the referring physician's call promptly; documenting essential patient demographic information; arranging for immediate consultation with the MCP; dispatching the transport team to the referring facility expeditiously; updating the referring facility with any changes in the arrival time; and coordinating medical control and other necessary transport-related calls. The transport team must be able to contact the receiving and referring facilities immediately, when necessary. Furthermore, with advances in technology and wireless communication systems, **telemedicine**—either *interactive* (synchronous) or *store and forward* (asynchronous)—is being used during pediatric transport, and certain programs have incorporated it into their routine transport operations.

MEDICAL CONTROL PHYSICIAN

The MCP is involved in the clinical care and safe transport of the patient from the time of referral through arrival at the receiving hospital unit. The MCP's oversight increases once the transport team arrives at the referring facility. The MCP should have expertise in pediatric critical care or PEM (or sometimes neonatology). Besides having the knowledge required to stabilize a critically ill or injured child, the MCP must be familiar with the transport environment; the transport team members' resources and capabilities; the program's policies and procedures; and the region's geography, medical resources, and regulations regarding interhospital transport. The MCP must possess good interpersonal and communication skills and must be able to maintain

* Adapted initially from Dr. Lorry R. Frankel's chapter in the 18th edition of this book. We also want to thank Dr. Beth Edgerton, who co-authored a prior version of this chapter.

collegiality with the referring hospital's staff during a potentially difficult and stressful situation.

Once a transport call is received, the MCP must be immediately available to confer with the referring physician. Although the MCP may have other responsibilities, these transport responsibilities take priority in order to avoid undue delays when transferring a critically ill child. Often the MCP recommends further testing or therapeutic interventions that can be delivered by the referring hospital before the transport team arrives. The MCP may seek additional guidance from other specialists, as necessary. Because the child's condition may change rapidly, the MCP must remain ready to give additional advice. All conversations and recommendations regarding the care of the patient should be documented. Some centers record these conversations.

After discussion with the referring physician—and when warranted, with the transport staff—the MCP determines the best team composition and vehicle for transport. The MCP usually does not accompany the team but remains available to supervise care. With advances in video conferencing capabilities, there has been increased use of telemedicine in the pediatric transport medical direction process. For some acutely ill patients or those requiring visual diagnoses, telemedicine has been reported to improve disposition at the receiving hospital, potentially leading to improved clinical outcomes.

TRANSPORT TEAM

Transport team composition varies greatly among programs—and sometimes within an individual program. The team's composition is based on a variety of factors, including the child's age; the severity of the illness or injury; the distance to the referring facility; the transport vehicle used; the team members' advanced practice scope and abilities; the referrer's insistence that a physician be present; the program's historical professional makeup; and the region's staffing regulations. The pediatric transport workforce may include physicians, advanced practice providers, nurses, respiratory therapists, and paramedics who have expertise in pediatric critical care, PEM, or neonatology (in some cases), as well as advanced education and training in those cognitive and procedural areas important for pediatric critical care transport. Physician trainees—usually fellows and, less often, residents—may also participate in transport in some capacity. There is a lower incidence of transport-related morbidity for critically ill and injured children transported by pediatric specialty teams than for those transported by generalist teams. Nevertheless, in-transit critical events occur in ~10% of pediatric critical care transports.

Various scoring systems that can help guide team composition and/or mode of transport have been developed to aid in transport planning. A team member's training, experience, and skill in treating critically ill patients are more important considerations than that team member's professional degree. Team members must understand basic pediatric pathophysiology and collectively must be able to assess and monitor a critically ill or injured child; manage the airway and provide respiratory support; obtain vascular access; perform point-of-care testing; and administer fluids and medications (including infusions) typically used in pediatric critical care transport. They must be familiar with the physiologic alterations and practical difficulties of the transport environment and, importantly, must be comfortable working in an out-of-hospital setting. Physicians are less often deployed on transport teams in part because of the advanced training that other healthcare professionals on the transport team receive.

The transport team should have a designated team leader who, in addition to the team leader's many other responsibilities, interacts with the MCP during the transport. Once the team arrives at the referring facility, the team should reassess the child's condition, review all the pertinent diagnostic studies and therapies, and discuss the situation with the referring staff and parents. If the patient's condition has changed significantly, the team leader may need to contact the MCP for additional advice. Otherwise, the team leader should generally notify the MCP before starting to bring the child to the receiving facility. Any care delivered by the team during transport should be documented, and copies of all medical records—including laboratory data, radiographs, and scans—should accompany the child to the pediatric center. The receiving unit must be updated before arrival so it can finalize preparations for the patient.

GROUND VS AIR AMBULANCE

Transport vehicle options include ground, rotorcraft, and fixed-wing ambulances. Vehicle selection depends on the child's emergency needs, transport team's capabilities, any out-of-ordinary staffing or equipment requirements (e.g., extracorporeal membrane oxygenation, inhaled nitric oxide, heliox), referring facility's abilities, distance, terrain, traffic patterns, ground or air ambulance availability, helicopter landing pad or airport access, weather conditions, and expense.

The transport vehicle must be equipped with electrical power, oxygen, and suction and must have sufficient space for the equipment and supplies that the team brings along—stretcher or isolette, monitor, ventilator, oxygen tank(s), medication pack(s), infusion pumps, and more. Compared with helicopters, ambulances typically are more spacious and able to carry more weight, so they can accommodate larger teams and more equipment. Another advantage of ground ambulance transport is the ability to stop en route if the patient's condition deteriorates; this may facilitate the performance of certain interventions or procedures, such as intubation.

An airplane may be able to fly to an area when distance (>150 miles), altitude, or weather precludes helicopter use. However, the use of an airplane necessitates several ambulance transfers, with their attendant delays and additional risks. There also are delays when the plane must fly from a remote base to the program's jurisdiction.

TRANSPORT PHYSIOLOGY

When possible, the transport team tries to provide the same care during transport as the patient would receive in the specialty center. This can be difficult, however, because of limitations in personnel, equipment, and space, as well as other environmental challenges.

The team and child are subjected to variable intensities of background noise and vibration while traveling in the vehicle cabin. **Noise** can impair the team's ability to auscultate breath sounds and heart sounds or accurately measure the blood pressure manually—another reason for monitoring vital signs mechanically and relying on other assessment modalities, such as the level of mentation, skin color, and capillary refill. For rotor transports in particular, the crew and patient should wear helmets or headphones (or another wearable noise attenuator) to mitigate noise. **Motion** and **vibration** are additional transport hazards and can lead to increased metabolic rate, shortness of breath, and fatigue in the patient, as well as motion sickness in the patient and staff.

On fixed-wing or certain rotary-wing transports, the patient may suffer adverse physiologic effects from **altitude**. With increasing altitude, the barometric (atmospheric) pressure decreases, and gas expands to occupy a greater volume due to the decreased pressure exerted on it. Therefore, as barometric pressure drops with altitude, the partial pressures of inspired oxygen (Pio_2) and, consequently, arterial oxygen (Pao_2) decrease, as does the arterial oxygen-hemoglobin saturation (Spo_2). For example, at 8,000 feet—an elevation at which unpressurized airplanes may fly, as well as the effective cabin altitude for many pressurized airplanes flying at 35,000-40,000 feet—the barometric pressure, Pio_2, Pao_2, and Spo_2 fall to 565 mm Hg, 118 mm Hg, 61 mm Hg, and 93%, respectively. In comparison, the barometric pressure, Pio_2, Pao_2, and Spo_2 are 760 mm Hg, 159 mm Hg, 95 mm Hg, and 100% at sea level. Although healthy individuals usually tolerate these changes well, patients with respiratory insufficiency, pulmonary hypertension, significant blood loss, or shock may decompensate and should receive supplemental oxygen and/or have the cabin pressurized at sea level.

Gases expand up to 10% at the few thousand feet where helicopters typically fly, and approximately 30–40% at 8,000 feet. Gases within the body itself also expand as the altitude increases. The degree of gas expansion must be considered during transport via air of any patient with pneumocephalus, pneumothorax, bowel obstruction, or another condition involving entrapped gas. Before transport, a pneumothorax should generally be decompressed and a nasogastric tube inserted for ileus.

SAFETY

Safety is of paramount importance and mandates constant vigilance by everyone involved. Accident rates for pediatric air and ground transport have been estimated at approximately 1 in 1,000 transports. The team should routinely attend pilot briefs and perform safety inspections of the vehicles and equipment, aided by checklists. When in doubt, the MCP should solicit input from the staff about whether to transport via air or ground ambulance or to employ lights and sirens, decisions that cannot be taken lightly. The pilot's or driver's judgment as to the safety of proceeding during inclement weather or with a mechanical problem must not be overruled.

Organizations such as the Federal Aviation Administration (FAA) and the National Transportation Safety Board (NTSB) play a role in ensuring safe interfacility transport. The **Commission on Accreditation of Medical Transport Systems (CAMTS)** is an independent, peer-review organization established in 1990 in response to the number of air medical accidents in the 1980s. CAMTS, through voluntary participation, audits and accredits fixed-wing, rotary-wing, and ground interfacility medical transport services.

FAMILY-CENTERED CARE

Family-centered care represents a philosophy that respects the important role that family members play in a child's care. It recognizes family members and healthcare providers as partners in caring for the child. Family presence during transport is beneficial because it provides support to both children and parents in stressful situations and assists healthcare providers in delivering care to patients with complex and chronic medical problems.

As care is transitioned from the referring hospital, it is the transport team's responsibility to maintain culturally sensitive, family-centered care. The team meets with family members to explain the transport process, help obtain consent, and discuss anticipated management. When possible, the transport team should attempt to accommodate a family member's presence onboard. However, the family member and child may need to be separated when the child is critically ill and rapid transport is essential, or in case of space or weight limitations in the air or ground ambulance. In these situations, it is important that family members have a clear understanding of how the child will be cared for during the separation.

REFERRING HOSPITAL RESPONSIBILITIES

Transfer of a child to another facility requires written documentation by the referring physician of the need and reasons for transfer, including a statement that the risks and benefits, as well as any alternatives, have been discussed with the parents. Informed consent should be obtained from the parent/legal guardian before transfer.

Federal law under the Emergency Medical Treatment and Active Labor Act (EMTALA), part of the Consolidated Omnibus Budget Reconciliation Act (COBRA), imposes specific requirements that a patient presenting to an ED be given a medical screening examination without regard for ability to pay. If on examination an emergency medical condition is found, the hospital is required to stabilize the patient or to transfer the patient to another facility if unable to stabilize the patient (or if requested by the patient in writing after being informed of the risks). The primary requirement is that the referring physician must certify that the medical risks of transfer are outweighed by its potential benefits. The receiving hospital must agree to accept the patient if it has the space and staff to provide the necessary level of care. The transferring hospital is responsible for arranging for the transfer and ensuring that it is performed by qualified medical personnel with appropriate equipment. The transferring hospital must also send copies of the patient's medical records and test results, even those that become available after the transfer is complete.

Some referring hospitals have entered into transfer agreements with specialty centers to facilitate the smooth and safe transfer of pediatric patients. Having prepared forms for all the purposes noted earlier also aids in the transfer process.

Each hospital needs to review its facility's guidelines; if established guidelines do not exist, the Emergency Medical Services for Children National Resource Center in partnership with the Emergency Nurses Association and the Society of Trauma Nurses has developed the "Interfacility Transfer Tool Kit for the Pediatric Patient" (available at: https://emscimprovement.center/education-and-resources/toolkits/interfacility-transfer-toolbox/). This tool kit includes the essentials for comprehensively and safely transferring the pediatric patient to the most appropriate level of care in a timely manner.

EDUCATIONAL OUTREACH

Besides safe and rapid transport, regional pediatric transport programs (and their specialty centers) have an obligation to provide educational opportunities to community healthcare providers so that these providers can acquire the necessary skills to evaluate and stabilize a critically ill or injured child until the transport team arrives. These learning activities may include transport case reviews; lectures on pediatric acute care topics; resuscitation and related programs such as the Pediatric Advanced Life Support (PALS) course, Advanced Pediatric Life Support (APLS) course, Pediatric Education for Prehospital Professionals (PEPP) course, and S.T.A.B.L.E. (sugar and safe care, temperature, airway, blood pressure, lab work, emotional support) program; and rotations through the specialty center's pediatric ED and PICU. These activities also help cement relationships with the referring facility's staff.

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77.2 Risk Adjustment and Outcomes Measurement of Pediatric Emergency Medical Services

Anna K. Weiss

Health services research has demonstrated wide variation in implementation of equitable, evidence-based care for pediatric patients in U.S. hospitals, a reality that can negatively affect the health of children and youth (see Chapter 2). The complexities of delivering high-quality, evidence-based care are magnified in the emergency department (ED), where patients are often in crisis, patient-physician interactions are brief, and the variety and volume of complaints and diagnoses are immense. In the context of this frenetic environment, practitioners can only assess their local system relative to recognized benchmarks and standards of care if there are clear guidelines for measurement of performance. However, no two places of practice are the same, and a single ED may differ significantly from a theoretical "best practice" standard. To reflect this, practitioners seeking to make local improvements must assess not only raw outcomes (e.g., throughput times, mortality, patient satisfaction) but must also adjust for severity of illness, case mix, and risk of morbidity.

OUTCOME MEASURES IN EMERGENCY MEDICAL SERVICES FOR CHILDREN

To ensure delivery of equitable, evidence-based care in the ED, pediatric emergency medical systems must support the use of national standards for emergency care performance measurement. The *Donabedian structure-process-outcome model* provides a framework for most contemporary quality measurement and improvement activities. In this framework, **structural** elements provide indirect quality-of-care measures related to a physical setting and resources (e.g., available staff, equipment, and supplies). **Process** indicators provide a measure of the quality of care and services by evaluating the method or process by which care is delivered, including both technical and interpersonal components. **Outcome** elements describe valued results related to lengthening life, relieving pain, reducing disabilities, and satisfying the consumer.

A true *outcome-based* approach to **performance improvement** describes observable measures such as mortality, risk of organ system failure, and disability. An alternative approach is a *resource-based* outcome measure with a definition that is relative to the level of care required. Children who are more ill generally require more resources; therefore resource use across groups of patients reflects relative **severity of illness** within the groups, provided clinicians have a similar approach to practice. Examples of resource-based outcomes include need for hospital admission (ED disposition), ED length of stay, costs, and diagnostic and therapeutic interventions performed in the ED. Although this approach provides a measurement of clinical activity, when used in a vacuum it does not indicate whether the patient receiving the therapeutic interventions or resources actually needed them (i.e., data may also reflect physician behavior and/or [lack of] experience). Therefore some other assessment is needed that incorporates information on *how sick* the patient is or their specific diagnosis.

Table 77.3 provides a list of performance measures for pediatric ED care developed by the **Emergency Medical Services for Children Innovation and Improvement Center** supported by the Health Resources and Services Administration of the U.S. Department of Health and Human Services.

RISK ADJUSTMENT

The purpose of measuring outcomes in the ED is to evaluate **performance**—offering EDs and other components of the healthcare system the opportunity to make meaningful improvements over time using benchmarks within and between units. When making comparisons over time, one must ensure that patient-related attributes (e.g., age, preexisting conditions, severity of illness) have not changed; otherwise, one may be looking at changes in demography and case mix rather than at true change in performance. To ensure fair and meaningful measurement across time, **risk adjustment** is necessary to *level the playing field*. As an example, illness severity typifies the concept of *risk*—the higher the severity, the higher the risk of a given outcome. Without risk adjustment, EDs with sicker patients may appear to have poorer outcomes.

Risk Adjustment Tools in the ED

Although other risk adjustment scoring systems—such as the PRISM score for pediatric critical care—use mortality and morbidity as primary outcomes, this approach is not appropriate for the ED setting. Across U.S. EDs, pediatric mortality is low, and a patient's presenting physiology may reflect interventions performed in the prehospital setting. Similarly, eventual morbidity and/or mortality may reflect what happens in the PICU or during hospital ward care.

Table 77.3 Stakeholder-Endorsed Performance Measures for Pediatric Emergency Care

- Measuring weight in kilograms for patients <18 years of age
- Presence of a method to identify age-based abnormal pediatric vital signs
- Pediatric equipment in the ED
- Presence of on-site pediatric coordinator(s)
- Parent/caregiver understanding of discharge instructions
- Door to provider time
- Total length of stay
- Reducing pain in children with acute fractures
- Children with minor head trauma receiving a head CT scan
- Protocol for suspected child abuse in place
- Systemic corticosteroids in asthma patients with acute exacerbation
- Evidence-based guideline for bronchiolitis
- Reducing antibiotic use in children with viral illnesses
- Return visits within 48 hours resulting in admission
- Medication error rates

ACEP, American College of Emergency Physicians; AAP, American Academy of Pediatrics; ENA, Emergency Nurses' Association; GCS, Glasgow Coma Score; CT, computed tomography.

In the ED, the choice of a risk adjustment tool depends on ED-specific outcomes of interest. Two general risk adjustment tools have been developed specifically for PEM, the second-generation Pediatric Risk of Admission (PRISA II) score and the Revised Pediatric Emergency Assessment Tool (RePEAT).

Pediatric Risk of Admission II

PRISA II uses components of acute and chronic medical history as well as acute physiology to determine the probability of hospitalization. The outcome measure of interest is *mandatory hospital admission* (admissions using therapies that are best delivered in the inpatient setting). Table 77.4 lists the patient-related attributes contributing to the PRISA II risk adjustment score. Analytic models, including the PRISA II score, have good **calibration** (how well the probabilities predicted from the model correlated with the observed outcomes in the population) and **discrimination** (the ability to categorize subjects correctly into the categories of interest) with respect to mandatory hospital admission. Construct validity of the PRISA II score has been demonstrated by measuring rates of the secondary outcomes: mandatory admission, PICU admission, and mortality. As the probability of hospital admission rises, the proportion of patients with these increasing care requirements also increases. This finding supports the use of the PRISA II score as a measure of illness severity. PRISA II has also been used to demonstrate racial/ethnic differences in severity-adjusted hospitalization rates, as well as variation in hospitalization rates between teaching and nonteaching hospitals.

Revised Pediatric Emergency Assessment Tool

RePEAT uses a limited set of data collected at the time of ED triage to model severity of illness as reflected by the level of care provided in the ED—for example, routine assessment (clinical examination only ± nonprescription medicine) vs specific ED care (ED diagnostics and/or therapeutics) vs hospital admission. In this model, it is assumed that patients needing a higher level of care have a higher severity of illness. Table 77.5 lists the patient-related attributes contributing to

Table 77.4 Elements of the PRISA II Score

- Age
- Injury severity
- Temperature
- Referral status (e.g., self-referral vs referral from physician's office or from another ED)
- Presence of:
  - Abdominal pain in an adolescent
  - Immunodeficiency
  - Indwelling medical device
  - Controller asthma medication
  - Decreased mental status
  - Low systolic blood pressure (<70 neonates and infants; <83 children; <100 adolescents)
  - High diastolic blood pressure (>59 neonates and infants; >70 children; >90 adolescents)
  - Low serum bicarbonate value (<20 mEq/L)
  - High potassium value (>4.9 mEq/L)
  - High blood urea nitrogen value (>80 mg/dL)
  - High white blood cell count (>20,000/mm^3)
  - Oxygen therapy other than during inhaled bronchodilator treatments
  - Low bicarbonate and high potassium values

Table 77.5 Elements of the RePEAT Score

- Age
- Chief complaint
- Triage category
- Current use of prescription medications
- Arrival via EMS (ground/air)
- Heart rate (relative to age-based norms)
- Respiratory rate (relative to age-based norms)
- Temperature

the RePEAT risk adjustment score. Analytic models such as RePEAT have good calibration and discrimination with respect to predicting ED care and hospital admission. Furthermore, analytic models that compare costs and length of stay between EDs are improved by adjusting for severity of illness using the RePEAT score. RePEAT is a reasonable objective marker of severity of illness that could be used in the administrative process comparing outcomes between EDs. With implementation of scoring systems such as PRISA II and RePEAT, U.S. EDs can benchmark the care that they provide to children and make meaningful improvements to ensure that this care is equitable and evidence-based.

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77.3 Principles Applicable to the Developing World

David M. Walker and Victorio R. Tolentino Jr.

The maturity of pediatric emergency medicine (PEM) in any given area depends on the healthcare priorities and resources of that geographic or physical setting. The places in which emergency care takes place range from the community (especially for those with no access to organized medical care) to state-of-the-art pediatric emergency departments (EDs), typically in larger population centers. The scope ranges from the care of the individual patient to the management of populations of children involved in large-scale disasters. Barriers to quality care vary in each situation and in each part of the world, with the implication for the PEM practitioner that the care provided must be relevant to the local context of healthcare.

CONTINUUM-OF-CARE MODEL

This Emergency Medical Services for Children (EMSC) framework can also be applied to discussion of emergency care for children on a global level (see Chapter 77). Although medical infrastructure in some parts of the developing world may not be consistent or well organized, or has been weakened by civil strife, natural disasters, or economic loss, the EMSC framework can still apply generally to individual healthcare systems.

Prevention

Infectious Diseases

International child health has focused mainly on reducing the incidence of preventable childhood illnesses, primarily through immunization initiatives. Enormous advances have been realized in measles, neonatal tetanus, and polio; wild-type smallpox was eradicated in 1978. Although there are advocates for providing primary care interventions (e.g., vaccinations) in the ED, the role of the PEM practitioner in this area of prevention has been limited.

Injuries

Injuries are a leading cause of childhood morbidity and mortality. Unintentional injuries constitute 90% of injury mortality to children 5-19 years old and are the cause of 9% of the world's mortality (see Chapter 14). Intentional injuries, which remain underrecognized and underreported, make a smaller but significant contribution. Unintentional injuries cause more than 2,000 childhood deaths daily, or 950,000 annually worldwide. The burden of these deaths is borne disproportionately by children in middle- and lower-income countries, where >95% of all injury-related deaths occur. For each of these deaths, many more children are permanently disabled, and an even larger number are treated and released without permanent sequelae.

Traffic-related injuries, burns, and drowning are the main causes of injury-related mortality in children. The World Health Organization (WHO) and United Nations Children's Fund (UNICEF) have outlined several proven injury prevention strategies of which child health practitioners in the global community must be aware. Although these strategies have proved effective, the data are based on U.S. research and may not be generalizable to other countries.

Out-of-Hospital Care

Out-of-hospital care comprises access to emergency services, prehospital care, and interfacility transport of patients. Morbidity and mortality arise from delayed or limited access to emergency care, lack of prehospital care, transport without proper monitoring or trained personnel, or delayed transport to a higher level of care. Safe transport of seriously ill children is a neglected global health issue. An emergency response system must address the following links in the patient's care: a communication system with prompt activation of emergency medical services (EMS), the correct assessment and initial treatment of the patient, and the rapid transport to definitive care.

Access to Care

When a child is injured or ill, a parent or caretaker must be able to access help and activate EMS. In the majority of low- and middle-income countries, no universal emergency numbers have been established, requiring access by direct dialing to an ambulance, if such private services exist. In countries that have a universal emergency number, barriers remain related to absence of phones in some households, unclear addresses in rural areas, and insufficient reach of the emergency system.

In most low- and middle-income countries, the family must bring the ill or injured child to the health facility for stabilization and treatment. For this to occur, families must also overcome financial and geographic barriers, which can result in delayed presentation for care. This delay predictably increases the likelihood of associated complications and decreases the likelihood of full recovery and survival.

Prehospital Care

In regions with maturing EMS systems, there must be adequately trained personnel to stabilize and transport the child to a medical facility. The quality and level of training of such prehospital personnel vary among countries and within regions of the same country. In urban areas, there is a greater concentration of medical care and therefore a greater opportunity to have strong prehospital training. In most of Asia and sub-Saharan Africa, trained personnel are used primarily to transfer patients between health facilities, not from the initial site of illness or injury. In most high-income countries, medical services are dispatched to the patient.

Around the world, the effort to establish standardized approaches to prehospital care exists primarily in the form of courses to educate EMS and hospital personnel in the emergency management of patients. The WHO manuals *Prehospital Trauma Care Systems* and *Guidelines for Essential Trauma Care* focus on guidelines for prehospital and trauma care systems that are affordable and sustainable. The American Academy of Pediatrics (AAP) course "Pediatric Education for Prehospital Professionals" is a dynamic, modularized teaching tool designed to provide specific pediatric prehospital education that can be adapted to any EMS system. Table 77.6 describes additional prehospital resources.

Although most middle- and high-income countries have a system of trained EMS workers, lower-income countries lack this advanced tier of emergency care. In these countries, commercial drivers, volunteers, and willing bystanders provide the first line of care. Training a cadre of first responders can rely on existing networks of aid or can be drawn from specific populations, such as students, soldiers, or public servants. Training needs to emphasize basic lifesaving and limb-saving interventions, including how to stop bleeding and support breathing, access advanced care, and splint broken limbs. In Ghana, for example, taxi drivers participated in a first-aid course that relied heavily on demonstration and practice rather than knowledge transfer through didactic sessions. Taxi drivers were selected because they already provided much of the transport for injured patients. Two years after the course, external evaluators favorably rated the quality

Table 77.6 Pediatric Emergency Care Resources

PREHOSPITAL CARE

Emergency Pediatric Care
Course developed by the National Association of Emergency Medical Technicians (NAEMT) focused on field treatment of sick and injured children. Course is open to physicians, nurses, EMTs, and paramedics.
Website: https://www.naemt.org/education/epc

Pediatric Trauma Life Support for Prehospital Care Providers
An 8-hour pediatric prehospital course sponsored by the global organization International Trauma Life Support (ITLS)
Website: https://www.itrauma.org/education/itls-pediatric/

Pediatric Education for Prehospital Professionals (PEPP)
Curriculum designed specifically to teach prehospital professionals how to assess and manage ill or injured children.
Website: https://www.peppsite.com/

HOSPITAL CARE

Pocket Book of Hospital Care for Children: Second Edition
WHO publication providing guidelines for the management of common illnesses in resource-limited settings; incorporates both the Emergency Triage Assessment and Treatment (ETAT) and Integrated Management of Childhood Illness (IMCI) guidelines.
Website: https://www.who.int/publications/i/item/978-92-4-154837-3

African Federation of Emergency Medicine (AFEM) Handbook of Acute and Emergency Care
Management strategies organized according to low-, moderate-, and full-resource settings.
Website: https://afem.africa/project/afem-handbook-of-acute-and-emergency-care/

African Federation of Emergency Medicine (AFEM) Rapid Approach Protocols for Children
Open-access clinical protocols for common presenting problems in children. Includes differential diagnoses and recommendations on initial investigations.
Website: https://www.dropbox.com/sh/cwhcl3eu8vrvwqu/AAA-MSDs9u3Y0SIgwU1R3hFxa?dl=0

African Federation of Emergency Medicine (AFEM) Tier 1 Paediatric Emergency Medicine Curriculum
Open-access curriculum targeted to nurses, EMS personnel, pharmacists, and other providers who care for acutely ill and injured children. Organized into modules by clinical presentation or disease processes.
Website: https://www.dropbox.com/sh/pgv8zd5y6z1elvo/AAA_df2fUj1bSzABbjZFjSgfa?dl=0

Standards of Care for Children in Emergency Departments, Version 3.0
Open-access document from the International Federation of Emergency Medicine that proposes worldwide standards for pediatric emergency care.
Website: https://www.ifem.cc/standards_of_care_for_children_in_emergency_departments_v3_2019

African Emergency Nursing Curriculum
Open-access educational framework for emergency nursing practice in resource-limited settings. Developed by the African Federation of Emergency Nurses.
Website: http://afem.co.za/wp-content/uploads/2017/10/AFEM-African-Emergency-Nursing-Curriculum.pdf

HUMANITARIAN EMERGENCIES

Manual for the Health Care of Children in Humanitarian Emergencies
WHO publication that provides comprehensive guidance on childcare in emergencies; includes information on care of traumatic injuries and mental health emergencies.
Website: https://www.who.int/publications/i/item/9789241596879

Pediatric Disaster Care Centers of Excellence (United States)
Coalition of medical centers and government agencies established to guide the delivery of pediatric healthcare services in a disaster.
Website: https://emscimprovement.center/domains/preparedness/asprcoe/

MENTAL HEALTH EMERGENCIES

The Mental Health & Psychosocial Support Network
A hosted online practice network organized around crowdsourcing of mental health and psychosocial support resources for use in emergencies and ongoing humanitarian crises in the developing world.
Website: https://mhpss.net/

Save the Children Psychological First Aid Training
Practitioner training manual dedicated to the provision of psychological first aid to children exposed to trauma.
Website: https://resourcecentre.savethechildren.net/document-collections/save-children-psychological-first-aid-training

Psychological First Aid: Guide for Field Workers
Open-access training manual from the WHO for those who may respond to large-scale crises.
Website: https://www.who.int/publications/i/item/9789241548205

ACCESS TO ACADEMIC PUBLICATIONS RELEVANT TO PEM

PEMdatabase.org
A website devoted to pediatric emergency medicine (PEM). Contains links to conferences, evidence-based medicine reviews, research networks, and professional organizations.
Website: www.pemdatabase.org

HINARI Access to Research for Health Programme
Program established by WHO and others to enable developing countries to gain access to one of the world's largest collections of biomedical and health literature.
Website: https://partnership.who.int/hinari

ORGANIZATIONS INVOLVED IN GLOBAL PEM ACTIVITIES

American College of Emergency Physicians (ACEP) Ambassador Program
Provides the names of U.S.-boarded emergency medicine physicians who can provide advice and information on issues pertaining to the progress and status of emergency medicine in their assigned countries.
Website: https://www.acep.org/intl/ambassador-program/

U.S. Agency for International Development (USAID)
Government agency providing U.S. economic and humanitarian assistance worldwide.
Website: https://www.usaid.gov/global-health/health-areas/maternal-and-child-health/technical-areas/child-health

Child Health and Development Unit, World Health Organization (WHO)
United Nations agency dedicated to child health.
Website: https://www.who.int/teams/maternal-newborn-child-adolescent-health-and-ageing/child-health

United Nations Children's Fund (UNICEF)
Organization dedicated to providing lifesaving assistance to children affected by disasters and to protecting their rights in any circumstances; formerly United Nations International Children's Emergency Fund.
Website: www.unicef.org

Safe Kids Worldwide
International nonprofit organization dedicated to preventing unintentional childhood injury.
Website: www.safekids.org

of their care compared with untrained drivers. In rural areas, such first responders become vital in providing emergency interventions when more definitive care is distant. Thus a system of trained first responders forms the foundation of an effective prehospital system.

In the French model, a physician, often an emergency medicine specialist, will review calls for acuity and can dispatch a physician-led team by ambulance to go to the patient's home to assess, stabilize, and initiate treatment. This Franco-German system is used in other countries, including many in Latin America and Europe. There are no clear data on the cost-effectiveness and patient outcomes associated with delivery of patients to the nearest facility vs bringing hospital resources to the patient.

Methods of Transport

In many low-income countries, there is no reliable means of transport. Health centers may only have one vehicle for transport to a

higher-level facility. This vehicle may also be used for outreach primary care services, such as offering immunizations and collecting drugs and equipment from a central supply location, and sometimes, improperly for personal reasons by local officials or politicians. In large cities, taxis and auto rickshaws are frequently used because they are rapidly available, well disseminated, and able to pass around traffic jams. Where organized prehospital systems exist, different types of vehicles are adapted for emergency transportation. The WHO recommends identifying transport vehicles in advance, choosing vehicles that can be repaired and maintained locally, and equipping the vehicles according to recognized standards. The provision of available and appropriately staffed and equipped transport vehicles is crucial to the realization of recommended emergency care plans.

Hospital-Based Care

Once a child has reached a medical facility for the care of an injury or illness, adequate emergency services should be available. In many countries the ED serves only as a triage area where patients are distinguished by their likely disease process and directed for admission to the corresponding unit within the hospital. Strengthening emergency services includes seeing the ED as a unit where definitive treatment can be provided to the ill and injured child. Critically ill children must receive not only prompt care but also correct care. Such expedience and accuracy are ensured by implementation of an effective triage system, moving the sickest patients to immediate care and standardizing the initial care of emergency conditions.

Triage

Too often, children presenting to EDs are treated on a first-come first-served basis in an approach that creates long waiting times for critically ill children, a contributor to unnecessary mortality. Medical facilities should adopt an efficient and effective triage system to respond rapidly to the needs of patients and to assign the appropriate amount of resources. The WHO has developed a course entitled **Emergency Triage Assessment and Treatment (ETAT)**. This course teaches emergency, priority, or nonurgent signs and how to provide emergency treatment for life-threatening conditions. ETAT emphasizes the evaluation of a patient's ABCD status to identify emergency situations—the patency of the airway (A), the quality of breathing (B), the quality of circulation and presence of coma or convulsions (C), and the presence of severe dehydration (D).

One of the benefits of the ETAT guidelines is that they can be adapted to centers with limited resources and are applicable to areas with high morbidity and mortality from meningitis, dehydration, malaria, respiratory illness, and malnutrition. Another benefit is that the care algorithms are based on limited diagnostic studies, that is, hemoglobin measurement, blood smear for malaria, and bedside blood glucose testing. Widely accepted triage assessment guidelines are teachable to emergency care staff, and their adoption can provide better organization within a healthcare center. At the Queen Elizabeth Central Hospital in Blantyre, Malawi, for example, the institution of triage and rapid treatment in its emergency care center led to a 50% decrease in the mortality of children within 24 hours of presentation to the hospital, with a further 50% decrease as implementation and practice of triaging patients have continued.

Beyond triage, education on overall emergency center organization is a low-resource intervention that can reduce some of the obstacles to quality care delivery. Additionally, the arrangement of short-stay areas (hydration and infusion rooms) within or near the ED can lessen the burden on inpatient units.

Pediatric-Specific Emergency Centers

Anecdotally, most countries have developed at least one pediatric-capable center, usually as part of an academic medical center. The emergency services in these centers are variable, but certainly can be a starting point from which to build overall improvement in pediatric emergency care.

Practitioners

Throughout the world, nurses, paramedics, nonphysician clinicians, and nonspecialist physicians deliver most of the care to acutely ill or injured children. The majority of sick children attend local clinics or district or central hospitals, where financial and human resources are not always matched to the potential acuity of presenting patient complaints. Nominal supervision is provided to staff attending these patients. Pediatric EDs located in tertiary hospitals are often staffed by training physicians with little or no supervision from faculty, who themselves may have limited exposure to or training in pediatric emergencies. General hospitals lack dedicated pediatric staff; guidelines as to which patients should be moved to a higher level of care are often not standardized and depend on local influences and/or cultural beliefs about health and illness.

Clinical Guidelines

The **Integrated Management of Childhood Illnesses (IMCI)** guidelines were developed by the WHO and UNICEF to provide assistance in the initial triage and management of the presenting signs and symptoms of the major killers of children <5 years old in first-level health facilities (e.g., clinics, health centers, outpatient departments of hospitals). The flow charts within each chapter of the IMCI manuals allow easy accessibility to materials that can enhance education and outreach to less experienced health workers.

Evaluations in various countries of the implementation of IMCI guidelines have shown improvements in health worker performance and quality of care, as well as decreases in delay in treatment and mortality of the under-5 population. These guidelines also dramatically reduce the cost of healthcare. The WHO website provides all the necessary implementation tools, including course manuals and evaluation tools.

The International Federation of Emergency Medicine developed Standards of Care for Children in Emergency Departments to improve emergency care globally. These standards are not just aimed at dedicated EDs, but at any setting where emergency care takes place, regardless of the providers or the resources available. At the same time, however, the existence of the standards allows sites to advocate for improved resources dedicated to expertise in the various aspects of providing quality emergency care for children. The standards address design of care spaces, child- and family-centered care, assessment of ill and injured children, staff training and competencies, quality and safety, and disaster response.

Trauma

Morbidity and mortality from trauma are among the most prevalent problems for children worldwide. Trauma care presents the challenge of sequential, often simple, interventions that must be performed in a timely manner to limit the severity of the outcome. However, with lack of specific training, signs and symptoms of pediatric trauma may go unrecognized or may be underappreciated. Trauma courses such as Advanced Trauma Life Support (ATLS) are educational tools that can be disseminated to improve the quality of care at emergency centers worldwide. For low-resource settings, the WHO has developed the Integrated Management for Emergency and Essential Surgical Care toolkit, which provides clear directions and reasoning for the initial care of injured patients. Not expressly addressed in the ATLS course is specific concern about child abuse as the cause of trauma. This is an area of pediatric care that many countries do not yet address comprehensively in their medical training, their law enforcement, or their judicial systems. The epidemiologic need for reliable trauma registries is great, as is the need to identify personnel with trauma management skill sets and dedicated trauma centers to serve as higher-level referral sites.

Equipment

Pediatric emergency equipment guidelines are available for a variety of settings where acutely ill and injured children would present. Although these equipment guidelines may represent minimum supplies to treat

the widest variety of pediatric emergencies, the roles of substitution and improvisation often provide for the equivalent function of recommended supplies.

Inpatient Services

After the initial stabilization, children requiring ongoing care are admitted to the hospital. The quality of inpatient services varies greatly depending on institutional and provider experience, comfort with pediatric conditions, and the resources available to treat them. The WHO has produced the *Pocket Book of Hospital Care for Children,* which is based on IMCI guidelines and focuses on inpatient management of high-morbidity/high-mortality illnesses common in developing countries.

Mental Health Emergencies

The recognition of mental health conditions among the pediatric population is continuing to evolve. It is estimated that about 15% of children globally suffer from anxiety, depression, or other mental health challenges. The prevalence of mental health problems is likely higher, as much of the existing data comes from Europe and North America, whereas a majority of children live in middle- and lower-income regions of the world.

Mental health capacity varies by country and is reflective of cultural beliefs about mental health and the priority and funding that local governments have allocated to address these concerns. It is widely accepted that the current global mental health infrastructure fails to meet the existing demands of the world's population. These concerns are amplified in the developing world and disproportionately affect children whose lives are often touched by emotional and social trauma (e.g., poverty, natural disasters, armed conflict).

Increasingly, children are presenting to emergency settings in crisis. In many developing countries, mental health services are concentrated in urban settings and lacking in rural areas. Where there is no shortage of medical personnel, expertise in child psychiatry corresponds with the local development of this specialty. In areas with no formal mental health system, care is provided by an informal network of family members, faith healers, or community leaders who do not have formal medical training. It is essential that children presenting for mental health evaluation receive a comprehensive examination, as certain psychiatric presentations can be rooted in infectious diseases conditions or inadequate nutrition, which are prevalent in some developing world contexts.

The WHO has provided examples of best practice in the acute treatment of mental health conditions in *Hospital-Based Mental Health Services: Promoting Person-Centered and Rights-Based Approaches*. This document is available as a section of the *Guidance and Technical Packages on Community Mental Health Services* available on the WHO website. Although the publication does not include examples of pediatric-specific care, the document is meant to be tailored to the local context and can be adapted to the needs of children.

Telemedicine

Telemedicine technology is one way to overcome provider shortages or geographic challenges that can affect the care of acutely ill and injured children. Patients and families can potentially access basic emergency care through video-based platforms. The responding provider can use established triage techniques to help determine the severity of illness and the need for consultation at a healthcare center; they can also recommend basic first aid as needed.

Access to real-time lectures, case discussions, and conferences, led by experts in PEM, can increase the capacity of those in limited-resource settings to provide care for pediatric emergency patients. These educational offerings can also provide a forum for a bilateral exchange of ideas and perspectives. Expert consultations via real-time telemedicine programs or a store-and-forward process, in which the request for consultation is recorded and sent to an expert who can reply typically over email, can be used. Additionally, within a given region, telemedicine can link the referring hospital to the receiving hospital in order to collaborate on decisions about management and the need for transfer.

The success of telemedicine collaborations depends on a variety of factors, including availability of easy-to-use technology and reliable internet access.

HUMANITARIAN DISASTERS

Children are a vulnerable population who experience disproportionate suffering during humanitarian emergencies, either natural (earthquakes, tsunamis, hurricanes, floods, droughts) or manmade (armed conflicts, terrorist attacks). The under-5 population is especially susceptible to infectious diseases, malnutrition, and trauma after disasters.

The WHO *Manual for the Health Care of Children in Humanitarian Emergencies* is based on IMCI guidelines and addresses the emergency care of children in disaster situations where hospital facilities and resources are not immediately available. It goes beyond the IMCI guidelines by discussing initial assessment and management of trauma, burns, poisonings, neonatal illness, and psychosocial problems, which are considered high priority in acute care settings.

Exchange and Dissemination of Information

The WHO established the internet-based **HINARI** Access to Research for Health Programme in 2002 to provide institutions in low-resource countries free or reduced-cost access to medical literature. Registration for the program is required. Eligibility is based on national economic or development criteria.

Another valuable tool is the website pemdatabase.org. This nonproprietary site was started as an online resource for PEM practitioners. It contains links to PEM abstracts and articles, evidence-based reviews, pediatric resuscitation websites, and relevant journals, as well as PEM conferences and professional organizations.

In countries where internet access continues to be a barrier, resources for education and research may be limited to out-of-date textbooks and journals.

Visit Elsevier eBooks+ at eBooks.Health.Elsevier.com for Bibliography.

Chapter 78

Triage of the Acutely Ill Child

Anna K. Weiss and Frances B. Balamuth

Identifying the acutely ill child in the ambulatory setting is a challenge. Children presenting to pediatricians' offices, urgent care practices, and emergency departments (EDs) may have a range of illnesses from simple viral infections to life-threatening emergencies. Although most children in this setting will have a benign course of illness, it is incumbent on the pediatric practitioner to discern quickly and accurately which children are likely to deteriorate from potentially serious or life-threatening disease. When assessing an acutely ill child, practitioners must remember that the early signs of severe illness may be subtle. There are about five pediatric triage system tools that assess the severity of illness and thus the degree of needed interventions. One example is presented in Table 78.1.

ASSESSMENT OF VITAL SIGNS

Assessment of vital signs is critical in all pediatric visits for acute illness, including temperature, heart rate, respiratory rate, and blood pressure. Normal vital signs vary with age. Although there have been increasing efforts to build evidence-based vital sign cutoffs for different age-groups, most institutions use nonempirically derived cutoffs such as those in Pediatric Advanced Life Support (PALS). **Tachycardia** is common in children presenting for acute care and can result from benign (fever, pain, dehydration) to life-threatening (septic shock, hemorrhage, multisystem inflammatory system in children [MIS-C], dysrhythmia, heart failure, hyperthyroidism) conditions. An abnormal heart rate should prompt a full history and physical examination, as described later, and careful *reassessment* (often multiple times) after the presumed cause is identified and treated. Most children will improve after initiation of simple interventions such as antipyretics or analgesia. Tachycardia that persists after fever, pain, and dehydration have been treated *must* be evaluated further, particularly if the child appears ill or has a deficit in perfusion or altered mental state.

Tachypnea is also common among ill children and has many causes, including fever, respiratory conditions (bronchiolitis, asthma, pneumonia), cardiac disease (heart failure), and metabolic acidosis (shock, poisoning, diabetic ketoacidosis). Like tachycardia, tachypnea often resolves with antipyretics in febrile children and should be reassessed to ensure resolution once fever has been managed. In cases where bronchiolitis and asthma have been ruled out, persistent tachypnea and fever can be a sign of pneumonia, even in the absence of focal lung findings on examination. Consider evaluation for metabolic acidosis in cases of significant tachypnea without apparent pulmonary or cardiac causes. **Apnea** is a sign of respiratory failure and should be *treated emergently with bag-valve-mask ventilation and immediate ED evaluation.*

Hypotension is rare in children and, when present, it is a sign of critical illness. Children with hypotension should be evaluated in an ED. Hypotension is evidence of decompensated circulatory shock and can result from severe dehydration, sepsis, hemorrhage, neurogenic spinal shock, anaphylaxis, or cardiogenic shock.

Pulse oximetry (oxygen-hemoglobin saturation, Spo_2) should be assessed in children with respiratory or cardiac illness/compromise and in children with underlying abnormalities of oxygenation. Healthy children have Spo_2 >95%. The practitioner should consider evaluating for any underlying respiratory or cardiac causes in children with Spo_2 <93–95%. For children with underlying abnormalities, the child's baseline Spo_2 should be assessed and alterations from that baseline should be investigated further.

The combination of bradycardia, hypertension, and altered breathing known as **Cushing triad** can be a sign of life-threatening increased intracranial pressure (ICP) and should be evaluated in an ED. Anisocoria and a sixth cranial nerve palsy are other signs of increased ICP. **Toxidromes** should also be considered in children with abnormal combinations of vital signs (see Chapter 94).

HISTORY

A thorough history is paramount to identifying patients whose condition will require prompt intervention. Obtaining an accurate history from young patients is challenging, particularly with preverbal or anxious children who are unable or unwilling to localize the source of their discomfort. In such instances, parents or caretakers often provide the most important information, and their perceptions of the child's course of illness must be carefully considered. Pediatricians should be guided by the patient's chief complaint to ask *open-ended questions* that help distinguish between benign and potentially life-threatening disease entities. The most common complaints leading to acute care visits among children include fever, headache and altered mental status, trauma, abdominal pain and vomiting, respiratory distress, and chest pain. Table 78.2 describes signs and symptoms and risk factors that should prompt immediate transfer to an ED or, if already in the ED, initiation of rapid intervention.

Fever is the most common reason for a sick-child visit. Most cases of fever are the result of self-limited viral infection. However, pediatricians need to be aware of the age-dependent potential for serious bacterial or viral infections, such as urinary tract infection (UTI), sepsis, meningitis, pneumonia, acute abdominal infection, and osteoarticular infection.

During the first 2 months of life, the neonate is at risk for sepsis caused by pathogens that are uncommon in older children. These organisms include group B streptococcus, *Escherichia coli, Listeria monocytogenes,* and herpes simplex virus (HSV). In neonates, the history must include maternal obstetric information and the patient's birth history. Risk factors for sepsis include untreated maternal group B streptococcus colonization, prematurity, chorioamnionitis, and prolonged rupture of membranes. If there is a maternal history of sexually transmitted infections (STIs) during the pregnancy, the differential diagnosis must be expanded to include infection with those pathogens. Septic infants can present with lethargy, poor feeding, grunting respirations, and cool or mottled extremities in addition to fever (or hypothermia). Febrile infants in the first 1 to 2 months of life should be evaluated broadly for infection, including sampling blood, urine, and, in some cases, cerebrospinal fluid (CSF) (see Chapter 220).

When the infant matures beyond 2 months of age and receives their first set of vaccinations, serious bacterial infections become less common. Evaluation to rule out serious infection is an important part of treating the febrile older child. Children with fever should have a full set of vital signs, history, and physical examination to ensure that critical illness is absent and to identify any focal source. Red flags for **septic shock** include hypotension, poor perfusion, altered mental status, or the presence of purpuric or erythrodermic rash. Red flags for **meningitis** include severe headache, meningismus, and altered mental state. The presence of any of these signs should prompt emergency evaluation in the ED or rapid treatment if the patient is already in the ED.

Additional focal findings to consider include evaluation for acute otitis media, pharyngitis, pneumonia, abdominal infections (bacterial enteritis, appendicitis), skin and soft tissue infections, septic arthritis, and osteomyelitis. Occult UTI should be considered if three of the following risk factors are present: age <1 year, fever >39°C, fever >48 hours, and no focal source of fever. Pneumonia should be considered in the presence of tachypnea, hypoxia, or focal findings on chest examination. Bacteremia is rare in the post–pneumococcal and *Haemophilus influenzae* vaccine era but should be considered if staphylococcal infection or meningococcemia is suspected and in unvaccinated children or children with signs of septic shock. In addition to infection, inflammatory conditions to consider include juvenile idiopathic arthritis (JIA), macrophage activating syndrome (MAS), Kawasaki disease (KD), and MIS-C. The diagnosis of KD, MIS-C, or MAS should be considered if

Table 78.1 Definition of Emergency Severity Index for Children

LEVEL 1	LEVEL 2	LEVEL 3	LEVEL 4	LEVEL 5
Cardiac arrest Respiratory arrest Severe respiratory distress SpO_2 <90 Critically injured and unresponsive trauma patient Severe respiratory distress with agonal or Gasping-type respirations Severe bradycardia or tachycardia with signs of Hypoperfusion Hypotension with signs of hypoperfusion Trauma patient who needs resuscitation Anaphylactic reaction Baby who is flaccid Hypoglycemia with a change in mental status	Seizures Sepsis, severe dehydration Diabetic ketoacidosis Child abuse, burns Head trauma Vitamins/iron or other overdoses/ingestions Infant less than 28 days of age with a fever of 38°C (100.4°F) or greater 1-3 mo of age with a fever of 38°C (100.4°F) or greater may be considered up to II Vital signs not stable	Multiple resources needed 3 mo to 3 yr of age T >39°C (102.2°F)	Single resource needed	Only history, physical exam required

From Wang L, Zhou H, Zhu JF. Application of emergency severity index in pediatric emergency department. *World J Emerg Med.* 2011;2(4):279-282, Table 1, p. 280.

the patient meets the diagnostic criteria for that illness, although some patients may have an atypical or incomplete presentation (see Chapters 207 and 208).

For patients presenting in an **altered mental state**, the pediatrician should inquire about symptoms such as fever or headache. Screening questions should explore feeding changes, medications in the household, ill contacts, and the possibility of trauma. Parents will often describe a febrile child as lethargic, but further questioning will reveal a tired-appearing child who interacts appropriately when no longer febrile. The child who appears ill only when febrile must be differentiated from the lethargic patient who presents with suspected sepsis or meningitis and from the child whose altered behavior is secondary to an intracranial emergency or seizure. Infants with meningitis, sepsis, or cardiac defects may have a history of irritability, inconsolability, poor feeding, grunting breathing, seizures, poor urine output, and/or color changes such as pallor, mottling, or cyanosis. Patients with poisoning or inborn error of metabolism can also present with lethargy, poor feeding, unusual odors, seizures, and vomiting. **Nonaccidental trauma** should always be considered in a lethargic infant, particularly in the absence of additional signs or symptoms. In infants and young toddlers, rapidly growing head circumference or bulging anterior fontanel may signal increased ICP. Older children may present with altered mental state as a result of meningitis/encephalitis, trauma, or ingestions. School-age children and adolescents with meningitis may have a history of fever and neck pain; other associated symptoms may include rash, headache, photophobia, or vomiting. Children with ingestions can present with other abnormal neurologic symptoms, such as ataxia, slurred speech, and seizures, or with characteristic constellations of vital sign changes and other physical findings consistent with certain toxidromes.

In patients with **headache**, ask questions about the chronicity of the headache and any accompanying symptoms. Headaches that occur upon arising in the morning, that are worse when lying flat, or that are accompanied by vomiting are concerning for increased ICP. Similarly, headache accompanied by focal neurologic deficit(s) should be referred to an ED for urgent head imaging. Although migraine headaches in teenagers are similar in presentation to those in adults (unilateral, throbbing, accompanied by an aura), pediatric practitioners should be aware that migraines in prepubertal children may have a nonclassic presentation; may be bilateral; and may not be accompanied by aura, photophobia, or phonophobia.

Parents may interpret a variety of symptoms as **respiratory distress**, and care must be taken to distinguish normal and benign respiratory patterns from true respiratory distress. Tachypnea secondary to fever is a common source of parental anxiety, and parents of newborn infants are sometimes alarmed by the presence of periodic breathing. Parents should be questioned about their child's other symptoms, such as fever, limitation of neck movement, drooling, choking, and the presence of stridor or wheezing. A history of apnea or cyanosis warrants further investigation. Practitioners should also remember that tachypnea in a child without evidence of true respiratory distress may be evidence of compensation for shock or metabolic acidosis, both of which will require rapid treatment. Although wheezing is often secondary to bronchospasm, it can also be caused by cardiac disease or congenital airway anomalies such as vascular rings. Parents may interpret **stridor** as noisy breathing or wheezing. Stridor is most frequently caused by upper airway obstruction such as croup. However, anatomic abnormalities such as laryngeal webs, laryngomalacia, subglottic stenosis, and paralyzed vocal cords also cause stridor. Toddlers who present with breathing difficulty after a coughing or choking episode should be evaluated for **foreign body aspiration**. In these cases, practitioners must ask about the possibility of button-battery ingestion, as this constitutes a true medical emergency that warrants immediate endoscopic removal or transfer to a facility that can perform the procedure. In toxic-appearing children with stridor, the pediatrician should consider epiglottitis, bacterial tracheitis, or a rapidly expanding retropharyngeal abscess. The incidence of epiglottitis has greatly declined with the advent of the *H. influenzae* type b (Hib) vaccine, but it remains a possibility in the unimmunized or partially immunized patient. Children with retropharyngeal abscesses may also present with drooling and limitation of neck movement (especially hyperextension) after a recent upper respiratory infection or penetrating mouth injury.

Abdominal pain is a common complaint in the ambulatory setting and can herald either acute intraabdominal or pelvic pathology, or it can be a subtler sign of systemic illness. Both relatively benign (e.g., streptococcal infection, UTI, pneumonia) and severe abdominal (e.g., appendicitis) or systemic (e.g., diabetic ketoacidosis, MIS-C) illness can present with abdominal pain, and questions to the patient and parent should include whether there is an extraabdominal source of discomfort. Questions should include details about pain onset and location; presence of accompanying symptoms, such

Table 78.2 History and Examination Findings that Should Prompt Immediate Intervention and/or Transfer to Emergency Department

HISTORY AND EXAM FINDINGS	RISK FACTORS
RED FLAGS FOR RESPIRATORY FAILURE	
Tachycardia	Tracheostomy
Tachypnea	Ventilator dependence
Cyanosis	History of critical airway
Apnea	
Brief resolved unexplained event (BRUE) with cyanosis or change in tone	
Suspected button-battery ingestion	
Foreign body aspiration with respiratory distress	
Sitting up, leaning forward, drooling	
Respiratory distress with hypoxemia	
Altered mental status	
RED FLAGS FOR CIRCULATORY FAILURE	
Tachycardia	Oncology (or other immunosuppressed) patients
Tachypnea	Bone marrow or solid organ transplants
Cyanosis	Sickle cell (or otherwise asplenic) patients
Cold extremities, poor pulses	Infants <60 days old
Apnea	Unrepaired or repaired congenital heart disease with change from baseline pulse oximetry
Petechial or purpuric rashes	Bleeding disorder with trauma
Erythroderma	
Peritonitis	
Bilious emesis	
Post-tonsillectomy or post-adenoidectomy with bleeding	
Extremity trauma with neurovascular deficits	
RED FLAGS FOR NEUROLOGIC FAILURE	
Tachycardia	Ventriculoperitoneal shunt
Bradycardia-hypertension	Diabetes or metabolic disease with altered mental status
Double vision	Hypoxic-ischemic encephalopathy
Ptosis	Clotting disorder with neurologic change(s)
Unequal pupils	Drug ingestion
Apnea	
Frequent or prolonged seizure(s)	
Focal neurologic deficit(s)	
Acute onset of severe headache	
Suicidal or homicidal ideation	
Psychosis	

Adapted from Farah MM, Tay Y, Lavelle J. A general approach to ill and injured children. In: Shaw KN, Bachur RG, eds. *Fleischer and Ludwig's Textbook of Pediatric Emergency Medicine*, 8th ed. Philadelphia: Lippincott, Williams & Wilkins; 2020.

as fever and abdominal distention; and changes in feeding, urination, and stooling patterns. Care should be taken to elicit a history of peritonitis or obstruction, including worsening pain with abrupt movements and persistent or bilious vomiting.

In neonates, a tender abdomen with or without bilious emesis should raise concern for the presence of a small bowel obstruction (e.g., volvulus). These infants appear ill and may have a history of decreased stooling. Pediatricians should be wary of neonates with abdominal tenderness and bloody stools, as 10% of cases of necrotizing enterocolitis occur in term infants. Infants with milk protein intolerance can also present with bloody stools, but these infants appear well and do not have abdominal tenderness. In older patients the differential diagnosis for emergency causes of abdominal pain expands to include intussusception and appendicitis. Patients with intussusception present in a variety of ways, ranging from colicky abdominal pain but otherwise well between episodes to being lethargic or in shock. The diagnosis of appendicitis in the child younger than 3 years is extremely difficult because children in this age-group cannot localize pain well. In adolescent females with abdominal pain, practitioners must obtain a menstrual and sexual history, as acute lower abdominal pain may be caused by adnexal pathology, including ovarian torsion or ectopic pregnancy.

For patients with **vomiting**, pediatricians should ask if they have experienced bilious or blood-stained emesis, abdominal distention or constipation, weight changes, and diarrhea or bloody stools. An infant with bilious emesis and abdominal distention may have intestinal obstruction (as with midgut volvulus or Hirschsprung disease), whereas an infant who appears immediately hungry after nonbilious projectile vomiting may have pyloric stenosis. In an older child, vomiting may be caused by peritonitis or obstruction and by systemic illnesses, including diabetic ketoacidosis, ingestion, or trauma. Patients with headache and vomiting raise the concern for increased ICP and should be questioned about neurologic changes, meningismus, and fever.

Practitioners should also obtain a thorough account of the child's **past medical history**. It is important to be aware of any underlying chronic problems that might predispose the child to recurring infections or a serious acute illness. Children with sickle cell anemia, indwelling central venous access devices, or immune compromise are at increased risk for bacteremia and sepsis. Similarly, children with prior surgery, including ventriculoperitoneal shunt placement or intraabdominal procedures, can develop complications from their previous surgeries.

PHYSICAL EXAMINATION

Observation is important when evaluating the acutely ill child. Most observational data that the pediatrician gathers should focus on assessing the child's response to stimuli. Does the child awaken easily? Does the child smile and interact with the parent or with the examiner? Evaluating these responses requires knowledge of normal child development and an understanding of the manner in which normal responses are elicited, depending on the child's age.

During the physical examination, the pediatric practitioner seeks evidence of illness. The portions of the exam that require the child to be most cooperative are completed first. Initially, it is best to seat the child on the parent's lap; the older child may be seated on the examination table. It is also important to assess the child's willingness to move, as well as ease of movement. It is reassuring to see the child moving about on the parent's lap with ease and without discomfort. *Vital signs are often overlooked but are invaluable in assessing ill children.* The presence of tachycardia out of proportion to fever and the presence of tachypnea and blood pressure abnormalities raise the suspicion for more serious illness. The respiratory evaluation includes determining respiratory rate; noting the presence or absence of hypoxia by Spo_2; and noting any evidence of inspiratory stridor, expiratory wheezing, grunting, coughing, or increased work of breathing (e.g., retractions, nasal flaring, accessory muscle use). The **skin** should be carefully examined for rashes. Frequently, viral infections cause an exanthem, and many of these eruptions are diagnostic, such as the reticulated rash and slapped-cheek appearance of parvovirus infections and the stereotypical appearance of hand-foot-and-mouth disease caused by coxsackieviruses, as well as measles, chickenpox, and roseola. The skin examination may also yield evidence of more serious infections, including petechiae and purpura associated with bacteremia and erythroderma associated with a toxin-producing systemic infection. Cutaneous perfusion should be assessed by warmth and capillary refill time. The extremities may then be evaluated not only for ease of movement but also for the presence of swelling, warmth, tenderness, or alterations in perfusion. Such abnormalities may indicate focal infections (e.g., cellulitis, bone/joint infection) or vascular changes (e.g., arterial or venous thromboembolus).

When an infant is seated and least perturbed, the examiner should assess the anterior fontanel to determine whether it is depressed, flat, or bulging. While the child is calm and cooperative, the **eyes** should be examined to identify features that might indicate an infectious or neurologic process. Often, viral infections result in watery discharge or redness of the bulbar conjunctivae. Bacterial infection, if superficial,

results in purulent drainage; if the infection is more deep-seated, tenderness, swelling, and redness of the tissues surrounding the eye may be present, as well as proptosis, altered visual acuity, and impaired extraocular movements. Abnormalities in pupillary response, extraocular movements, or ptosis may also be indicators of cranial nerve abnormalities and, if new, are indications for head imaging.

During this initial portion of the physical examination, when the child is most comfortable (and therefore most likely to be quiet), the **heart and lungs** are auscultated. It is important to assess the adequacy of air entry into the lungs; the equality of breath sounds; and any evidence of adventitial breath sounds, especially wheezes, rales, or rhonchi. The coarse sound of air moving through a congested nasal passage is frequently transmitted to the lungs. The examiner can become attuned to these coarse sounds by placing the stethoscope near the child's nose and then compensating for this sound as the chest is auscultated. The cardiac examination is next; findings such as pericardial friction rubs, loud murmurs, irregular rhythms, gallop rhythm, and distant heart sounds may indicate cardiac inflammation or infection. In the neonate, murmurs may herald congenital heart disease, especially in the presence of cyanosis, unequal extremity pulses, or a differential in upper- vs lower-extremity blood pressures. A complete cardiac exam should also look for displacement of the point of maximal impulse (PMI) and the presence of jugular venous distention or facial plethora.

The components of the physical examination that are more bothersome to the child are completed last. This is best done with the patient on the examination table. Initially, the **neck** is examined to assess for areas of swelling, redness, or tenderness, as may be seen in cervical adenitis. Resistance to neck movement should prompt evaluation for signs of meningeal irritation or retropharyngeal abscess. During examination of the **abdomen**, the diaper—if present—is removed. The abdomen is inspected for distention. Auscultation is performed to assess adequacy of bowel sounds, followed by palpation. Every attempt should be made to quiet a fussing child during this part of the exam; if this is not possible, practitioners should note that increased crying as the abdomen is palpated may indicate tenderness, especially if this finding is focally reproducible. In addition to focal tenderness, palpation may elicit involuntary guarding or rebound tenderness (including tenderness to percussion); these findings indicate peritoneal irritation, as may be seen in appendicitis. During palpation of the abdomen, practitioners should look for signs of hepatomegaly or splenomegaly. When palpating the bottom-most edge of the liver or spleen, examiners should begin in the pelvis and work upward toward the ribs, because severe organomegaly can be missed if the examiner begins palpating in the mid-abdomen. The **inguinal area and genitals** are then examined. One should assess the inguinal area for hernias. Care should be taken to examine the testicles of males with abdominal pain; testicular trauma, testicular torsion, and epididymitis all may present with abdominal discomfort. A unilateral swollen or painful testicle with an absent cremasteric reflex on the affected side is concerning for testicular torsion and should be referred for emergent ultrasound and urologic consultation. After the genital exam, the child is then placed in the prone position, and abnormalities of the **back** are sought. The spine and costovertebral angle areas are percussed to elicit any tenderness; such findings may be indicative of vertebral osteomyelitis or diskitis and pyelonephritis, respectively.

Examining the **ears and throat** completes the physical examination. These are usually the most bothersome parts of the examination for the child, and parents frequently can be helpful in minimizing head movement. During the oropharyngeal examination, it is important to document the presence of enanthems; these may be seen in many infectious processes, such as stomatitis caused by herpes or enteroviruses. This portion of the examination is also important in documenting inflammation or exudates on the tonsils, which may indicate viral or bacterial infection. Findings such as trismus or unilateral tonsillar swelling are concerning for peritonsillar abscess and for infections in the parapharyngeal and retropharyngeal spaces; such cases should be referred for specialist ear, nose, and throat evaluation and potential imaging of the neck.

Repeating portions of the assessment may be indicated. If the child cried continuously during the initial clinical evaluation, the examiner may not be certain whether the crying was caused by the high fever, stranger anxiety, or pain or is indicative of a serious or localizing illness. Constant crying also makes portions of the physical examination, such as auscultation of the chest, more difficult. Before a repeat assessment is performed, efforts to make the child as comfortable as possible are indicated. In young infants, **persistent irritability**, even when the examiner is absent from the room, is concerning for meningitis, encephalitis, or other causes of meningeal irritation (e.g., intracranial injury from nonaccidental trauma). When faced with a truly inconsolable infant, practitioners should have a low threshold to obtain head imaging and/or perform lumbar puncture, as the clinical scenario dictates.

MANAGEMENT

Most patients who present to the pediatrician's office with an acute illness will not require acute stabilization. However, the pediatrician needs to be prepared to evaluate and begin resuscitation for the seriously ill or unstable child. Outpatient pediatric offices and urgent care facilities should be stocked with appropriate equipment necessary to stabilize an acutely ill child. Maintenance of that equipment and ongoing training of the office staff in its use are required, and every effort should be made to ensure that pediatric clinicians are PALS certified (see Chapter 79).

The evaluation of the potentially unstable child must begin with assessment of the ABCs—airway, breathing, and circulation. When assessing the **airway**, chest rise should be evaluated and evidence of increased work of breathing sought. The examiner should ensure that the trachea is midline and should listen carefully for evidence of air exchange at the level of the extrathoracic airway. If the airway is patent and no signs of obstruction are present, the patient is allowed to assume a position of comfort. If the child shows signs of airway obstruction, repositioning of the head with the chin-lift maneuver may alleviate the obstruction. An oral or nasal airway may be necessary in patients in whom airway patency cannot be maintained. These devices are not well tolerated in conscious patients because they may induce gagging or vomiting; instead, they are most often used to facilitate effective bag-valve-mask ventilation in semiconscious or unconscious children. Once airway patency has been established, the adequacy of **breathing** should be evaluated. Slow respiratory rates or cyanosis may signal impending respiratory failure. If the airway is patent but the child's respiratory effort is inadequate, positive pressure ventilation via bag-valve-mask support should be initiated. Oxygen should be administered to all seriously ill or hypoxic children via nasal cannula or face mask. Auscultation of the lung fields should assess for air entry, symmetry of breath sounds, and presence of adventitious breath sounds such as crackles or wheezes. Bronchodilator therapy can be initiated to alleviate bronchospasm. Racemic epinephrine is indicated for stridor at rest in a patient with upper airway obstruction (e.g., croup). Once airway and breathing have been addressed, **circulation** must be evaluated. Symptoms of *shock* include tachycardia, cool extremities, delayed capillary refill time, mottled or pale skin, and effortless tachypnea. In children, hypotension is a late finding in shock and indicates that significant decompensation has already taken place. Vascular access is necessary for volume resuscitation in patients with impaired circulation, and an intraosseous line should be considered early if there is any difficulty in obtaining vascular access for a patient requiring resuscitation. Each time an intervention is performed, the clinician should **reassess the patient** to determine whether interventions have been successful and whether additional care is needed.

DISPOSITION

Most children evaluated for acute illness in the office or urgent care setting can be managed on an **outpatient** basis. These patients should have a reassuring physical examination, stable vital signs, and an adequate follow-up plan before being sent home. A mildly dehydrated

patient can be discharged home for a trial of oral rehydration. Patients with respiratory illness who exhibit signs of mild respiratory distress may be monitored at home, with a repeat examination scheduled the next day. Depending on the child's condition, the comfort of the parents, and the relationship of the family with the physician, telephone follow-up may be all that is necessary. When no specific diagnosis has been established at the first outpatient visit, a follow-up examination may yield the diagnosis and can provide reassurance for both the caregiver and the practitioner that a child's severity of illness has not progressed.

However, if it is deemed that the child needs a higher level of care, it is the pediatrician's responsibility to decide what method of transfer is appropriate. Physicians may be reluctant to call for help because of a misperception that emergency 911 services should be activated only for ongoing resuscitation. Emergency medical services (EMS) transport should be initiated for any child who is physiologically unstable (e.g., with severe respiratory distress, hypoxia, signs of shock, or altered mental state). If the family's ability to adhere promptly to a recommendation for ED evaluation is in question, this patient also should be transported by EMS. Some physicians and families may defer calling EMS because of the perception that a parent can reach the hospital faster by private motor vehicle. Although rapidity of transport should be considered, the need for further interventions during transport and the risk of clinical decompensation are other important factors in the decision to activate EMS. Ultimately, the legal responsibility for choosing an appropriate level of transport for a patient lies with the referring physician until responsibility of care is officially transferred to another medical provider.

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Chapter 79

Pediatric Cardiorespiratory Emergencies and Resuscitation

Ryan W. Morgan and Alexis A. Topjian

Children in the community and those in the hospital are at risk for a variety of injuries and life-threatening disease processes that lead to cardiac or respiratory compromise, which require prompt evaluation and intervention.

ASSESSMENT AND EVALUATION OF CHILDREN WITH CARDIORESPIRATORY EMERGENCIES

The first response to a pediatric emergency of any cause is a rapid and systematic **general assessment** of the scene and the child to identify immediate threats to the child, care providers, and others. If an emergency is identified, the emergency response system (emergency medical services [EMS]) should be activated immediately. Care providers should then proceed through **primary**, **secondary**, and **tertiary** assessments as allowed by the child's condition, safety of the scene, and resources available. This standardized approach organizes what might otherwise be a confusing or chaotic situation and ensures that key elements of assessment and treatment are not omitted. If at any point during these assessments the provider identifies a life-threatening problem, progression through the systematic assessment is paused and targeted lifesaving interventions are prioritized. Further assessments and interventions should be delayed until other providers arrive to assist or until the life-threatening condition is successfully treated or stabilized.

General Assessment

Upon arrival at the scene of a critically ill or injured child or upon the child's presentation for medical care, a provider's first task is a quick survey of the scene itself. Is the rescuer or child in imminent danger because of circumstances at the scene (e.g., fire, high-voltage electricity)? If so, can the child be safely extricated to a safe location for assessment and treatment? Can the child be safely moved with the appropriate precautions (e.g., cervical spine protection) if indicated? A rescuer is expected to proceed only if these important safety conditions have been met so that they do not jeopardize their own safety.

Once the provider's and child's safety have been ensured, the provider performs a rapid **visual survey** of the child, assessing the child's **general appearance** and **cardiopulmonary function**. This action should only take a few seconds and includes assessment of (1) general appearance, determining color, tone, alertness, and responsiveness; (2) adequacy of breathing, distinguishing between normal, comfortable respirations versus respiratory distress or apnea; and (3) adequacy of circulation, identifying cyanosis, pallor, or mottling. If a child is found unresponsive or becomes unresponsive during the provider's assessment, the provider should stimulate the patient and assess the patient's response to voice. If there is no response, the provider should assess for breathing. If the child is breathing but ineffectively, rescue breathing should be started. If the child is not breathing or has agonal respirations, the provider should initiate cardiopulmonary resuscitation (CPR) and follow Basic Life Support (BLS) pediatric cardiac arrest algorithms for one rescuer or two or more rescuers (Figs. 79.1 and 79.2).

Primary Assessment

Once the emergency response system has been activated and the child is determined not to require CPR, the provider should proceed with a primary assessment that includes a brief, hands-on evaluation of cardiopulmonary and neurologic function. This assessment includes a limited physical examination, evaluation of vital signs, and measurement of pulse oximetry if available. The American Heart Association (AHA), in its Pediatric Advanced Life Support (PALS) curriculum, supports the structured format of **airway, breathing, circulation, disability, exposure (ABCDE)**. *The goal of the primary assessment is to obtain a focused, systems-based assessment of the child's injuries or abnormalities so that resuscitative efforts can be rapidly targeted to these areas;* if the provider identifies a life-threatening abnormality, further evaluation is postponed until appropriate corrective action has been taken.

The exam and vital sign data can be interpreted only if the provider has a thorough understanding of normal values. In pediatrics, normal respiratory rate, heart rate, and blood pressure have age-specific norms (Table 79.1). These ranges can be difficult to remember, especially if used infrequently, and providers should therefore maintain ready access to these normal ranges. Hypotension is defined as blood pressure less than the fifth percentile for age. This is considered a systolic blood pressure of <60 mm Hg for neonates up to 28 days, <70 mm Hg for infants from 1 month to 1 year, <70+ (age in years ×2) mm Hg for children 1-10 years, and <90 mm Hg for children older than 10 years of age.

Airway and Breathing

The most common precipitating event for cardiac instability in infants and children is respiratory failure (the inability to adequately oxygenate or ventilate). Therefore *rapid assessment for respiratory failure and immediate restoration of adequate ventilation and oxygenation remain the first priorities in the resuscitation of a child.* Using a systematic approach, the provider should first assess whether the child's airway is patent and maintainable. A **patent** airway is unobstructed, allowing normal respiration without noise or effort. A **maintainable** airway is one that is either already patent or can be made patent with a simple maneuver. To assess airway patency, the provider should look for breathing movements in the child's chest and abdomen, listen for breath sounds, and feel for the movement of air at the child's mouth and nose. Abnormal breathing sounds (e.g., snoring or stridor), increased work of breathing,

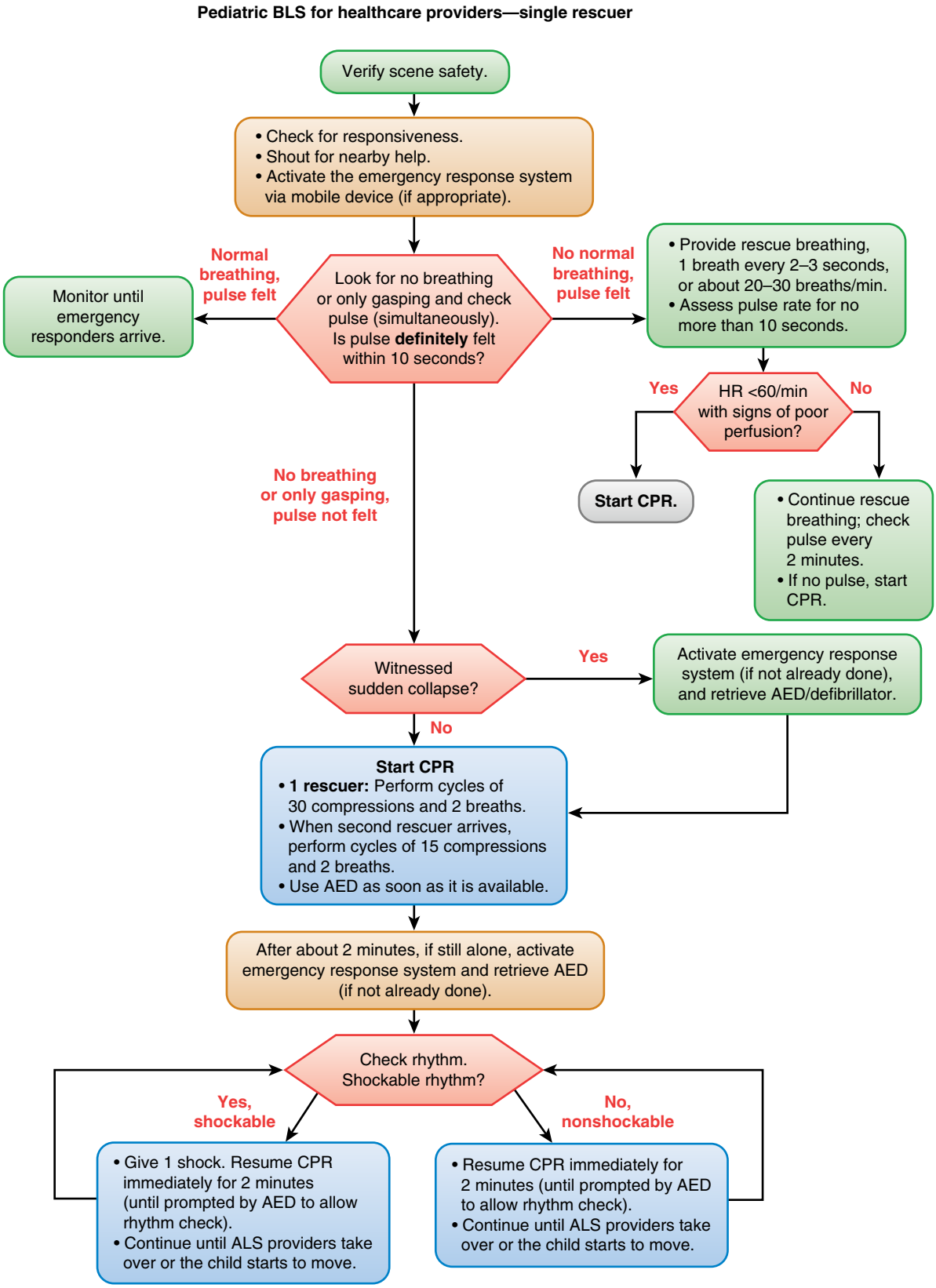

Fig. 79.1 Basic Life Support (BLS) algorithm for healthcare providers: Pediatric cardiac arrest algorithm for the single rescuer—2020 update. AED, Automated external defibrillator; ALS, advanced life support; CPR, cardiopulmonary resuscitation. (*From Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142[16 Suppl 2]:S469-S523.*)

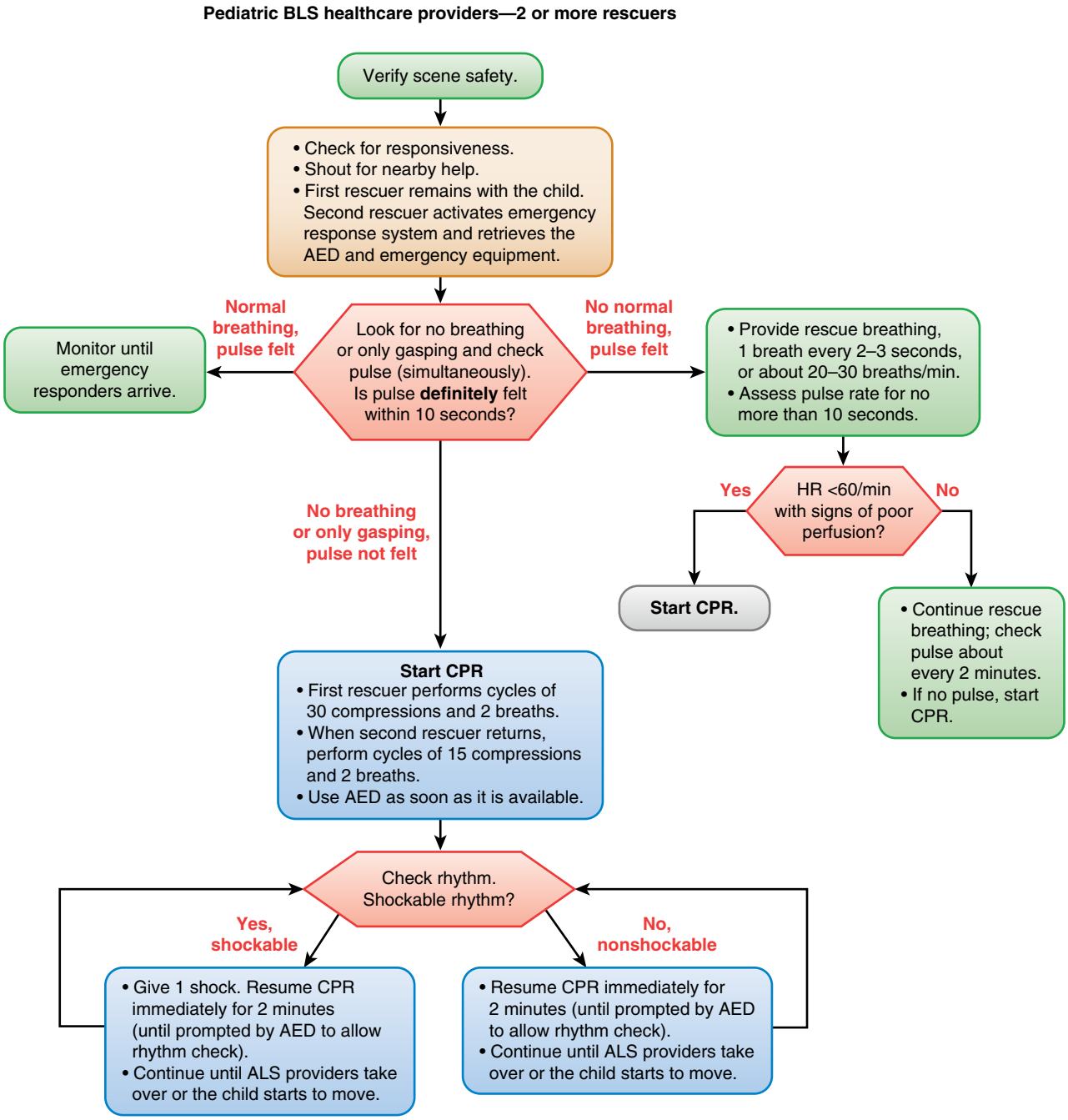

Fig. 79.2 Basic Life Support (BLS) algorithm for healthcare providers: Pediatric cardiac arrest algorithm for two or more rescuers—2020 update. AED, Automated external defibrillator; ALS, advanced life support; CPR, cardiopulmonary resuscitation. (*From Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142[16 Suppl 2]:S469-S523.*)

and apnea are all findings potentially consistent with airway obstruction. If there is evidence of obstruction, the provider should start with repositioning and "head-tilt, chin-lift" if neck injury is not suspected or a jaw thrust if neck injury is a concern (Fig. 79.3). Suctioning of the airway or placement of adjunct airway devices such as a nasopharyngeal airway should be considered based on the exam findings and the likely etiologies of airway obstruction. Maneuvers to relieve the obstruction should be instituted before the provider proceeds to evaluate the child's breathing.

Assessment of breathing includes evaluation of the child's respiratory rate, respiratory effort, breath sounds, and peripheral oxygen saturation via pulse oximetry. Normal breathing appears comfortable, is quiet, and occurs at an age-appropriate rate. Abnormal respiratory rates include apnea and rates that are either abnormally slow (bradypnea) or fast (tachypnea). *Bradypnea and irregular respiratory patterns (such as gasping or agonal respirations) require urgent attention because they are often signs of impending respiratory failure, apnea, or cardiorespiratory arrest.* Signs of increased respiratory effort include nasal flaring, grunting, chest or neck muscle retractions, head bobbing, and seesaw respirations. Hypoxemia, measured by pulse oximetry, often accompanies parenchymal lung disease, apnea, or airway obstruction. However, providers should keep in mind that adequate perfusion is required to produce a reliable peripheral oxygen saturation measurement. Central cyanosis is a sign of severe hypoxemia and indicates an emergent need for oxygen supplementation and respiratory support.

Table 79.1 Normal Vital Signs According to Age

AGE	HEART RATE (beats/min)	BLOOD PRESSURE† (mm Hg)	RESPIRATORY RATE+ (breaths/min)
Premature	120-205*	60-76/31-45	40-70
Neonate	100-205*	67-84/35-53	35-55
Infant	100-180	72-104/37-56	30-53
Toddler	98-140	86-106/42-63	22-37
Preschooler	80-120	89-112/46-72	20-29
School-age child	75-118	97-120/57-80	18-25
Adolescent	60-100	110-131/64-83	12-20

*In sleep, heart rates may be significantly lower, but if perfusion is maintained, no intervention is required.
†A blood pressure cuff should cover approximately two-thirds of the arm; too small a cuff yields spuriously high pressure readings, and too large a cuff yields spuriously low pressure readings. Values are systolic/diastolic and assume 50th percentile for height for children 1 year and older.
+The respiratory rate is expected to increase in the presence of fever and stress.
‡Approximately equal to postconception age in weeks (may add 5 mm Hg).
Modified from Hazinski MF. Children are different. In Hazinski MF, ed. *Nursing Care of the Critically Ill Child,* 3rd ed. Philadelphia: Mosby; 2013:1-18.

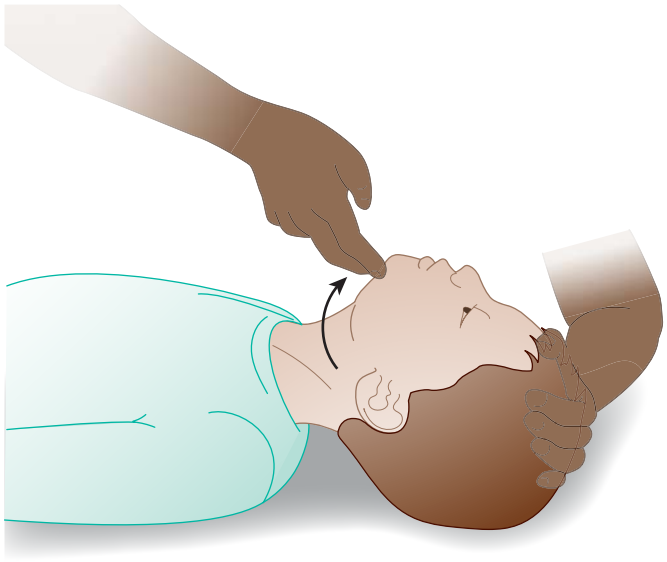

Fig. 79.3 Opening the airway with the head-tilt/chin-lift maneuver. One hand is used to tilt the head, extending the neck. The index finger of the rescuer's other hand lifts the mandible outward by lifting the chin.

Table 79.2 AVPU Neurologic Assessment

A	The child is awake, alert, and appropriately responsive to caregivers and stimuli.
V	The child responds only to voice such as calling the child's name or speaking loudly.
P	The child responds only to painful stimuli, such as sternal rub or pinching the trapezius.
U	The child is unresponsive to all stimuli.

A, Alert; V, verbal; P, pain; U, unresponsive.
From Ralston M, Hazinski MF, Zaritsky AL, et al., eds. *Pediatric Advanced Life Support Course Guide and PALS Provider Manual*. Dallas: American Heart Association; 2007.

Table 79.3 Modified Pediatric Glasgow Coma Scale

≥2 YEARS		<2 YEARS	
EYE OPENING			
Spontaneous	4	Spontaneous	4
To sound	3	To sound	3
To pressure	2	To pressure	2
None	1	None	1
VERBAL RESPONSE			
Oriented; words/phrases normal for chronological age	5	Babbles, coos; words/phrases normal for chronological age	5
Confused; some words/phrases not normal for chronological age	4	Some words/phrases not normal for chronological age	4
Words	3	Inconsolable crying	3
Sounds	2	Sounds	2
None	1	None	1
MOTOR RESPONSE			
Obeys commands	6	Normal spontaneous movement	6
Localizes pain	5	Rapidly withdraws extremity to stimulation	5
Normal flexion	4	Normal flexion	4
Abnormal flexion	3	Abnormal flexion	3
Extension	2	Extension	2
None	1	None	1

Adapted from Kirschen MP, Snyder M, Smith K, et al. Inter-rater reliability between critical care nurses performing a pediatric modification to the Glasgow Coma Scale. *Pediatr Crit Care Med.* 2019;20(7):660-666.

Circulation

Cardiovascular function is assessed by evaluation of skin color and temperature, heart rate, heart rhythm, presence and quality of pulses, capillary refill time, and blood pressure. In nonhospital settings, much of this important information can be obtained without measuring the blood pressure; lack of blood pressure data should not prevent the provider from determining adequacy of circulation or implementing lifesaving support. Mottling, pallor, delayed capillary refill, cyanosis, weak pulses, and cool extremities are all signs of diminished perfusion and compromised cardiac output. **Tachycardia** is the earliest and most common sign of shock but lacks both sensitivity and specificity and should be correlated with other components of the exam, such as weakness, threadiness, or absence of pulses. An age-specific approach to heart rate assessment will yield the most reliable interpretation. **Bradycardia** can be normal in athletic children but should be assessed in the context of the child's perfusion, blood pressure, mental status, and oxygen saturation, as it can be a sign of impending cardiac arrest.

Disability

In the setting of a pediatric emergency, *disability* refers to a child's neurologic function in terms of the level of consciousness and cortical function. Standard evaluation of a child's neurologic condition can be done quickly with an assessment of pupillary response to light (if one is available) and use of either of the standard scores used in children: the Alert, Verbal, Pain, Unresponsive (AVPU) Pediatric Response Scale and the Glasgow Coma Scale (GCS) (Tables 79.2 and 79.3). The

Table 79.4 Pupillary Responses

DILATED (MYDRIASIS)	PINPOINT (MIOSIS)
Bilateral Anticholinergic agents (systemic, topical) Sympathomimetic agents Serotonin syndrome Botulism Brain death (fixed, nonreactive usually midposition)	Bilateral Opiates Organophosphates Barbiturates Pontine lesions
Unilateral Third nerve compression with uncal herniation	Unilateral Horner syndrome

causes of decreased level of consciousness in children are numerous and include conditions as diverse as respiratory failure with hypoxia or hypercarbia, hypoglycemia, poisonings or drug overdose, trauma, seizures, infection, and shock. *Most often, an acutely ill or injured child has an altered level of consciousness because of respiratory compromise, circulatory compromise, or both.* Any child with a depressed level of consciousness should be immediately assessed for abnormalities in cardiorespiratory status.

Alert, Verbal, Pain, Unresponsive (AVPU) Pediatric Response Scale: The AVPU scoring system is used to determine a child's level of consciousness and cerebral cortex function (see Table 79.2). Unlike the GCS, the AVPU scale is not developmentally dependent—a child does not have to understand spoken language or follow commands, merely respond to a stimulus. The child is scored according to the amount of stimulus required to obtain a response, from *alert* (no stimulus; the child is already awake and interactive) to *unresponsive* (child does not respond to any stimulus).

Glasgow Coma Scale (GCS): Although it has not been systematically validated as a prognostic scoring system for infants and young children, the GCS is frequently employed to describe level of consciousness and neurologic status. It has value as a way to communicate mental status to other providers and when used serially to detect improvement or deterioration. The GCS has three components: eyes, verbal, and motor. Individual scores for eye opening, verbal response, and motor response are added together, with a maximum of 15 points (see Table 79.3). There are numerous versions of the pediatric GCS, but most importantly, the pediatric GCS accounts for differences in development and the inability for children <2 years of age to follow commands and talk. Patients who have severe head injury with a GCS score ≤8 require aggressive management, generally including securement of the airway with endotracheal intubation and breathing with mechanical ventilation and, if indicated, placement of an intracranial pressure monitoring device.

The Full Outline of Unresponsiveness (FOUR) score is a neurologic assessment that incorporates brainstem reflex components and is associated with outcomes; it is commonly used in the intensive care unit setting (Table 82.1).

The pupillary response can give insight to causes of altered mental status. Pinpoint pupils can be due to many conditions, including narcotic ingestion, and dilated *asymmetric* pupils (anisocoria) can be caused by uncal herniation (Table 79.4 and Fig. 79.4). If a patient has a normal mental status, other causes of pupillary dilation and asymmetry should be considered.

Lesion/process associated with coma	Pupils	Comment
Metabolic		Normal
Bilateral hypothalamic		Small but reactive
Uncal herniation		Ipsilateral "blown," unreactive pupil, ptosis
Tectal		Midposition and unreactive to light
Midbrain		Dilated and unreactive
Pontine		Pinpoint but reactive
Brain death		Midposition to large, unreactive

Fig. 79.4 Pupils in comatose patients. (*From Balcer LJ: Pupillary disorders. In Liu G, Volpe L, Galetta S (eds): Liu, Volpe, and Galetta's Neuro-Ophthalmology: Diagnosis and Management, 3rd ed. Philadelphia: Elsevier, 2018. Fig 13.32.*)

Exposure

Exposure is the final component of the pediatric primary assessment. This component of the exam is reached only after the child's airway, breathing, circulation, and disability have been assessed and reasonably stabilized. In this setting, *exposure* stands for the dual responsibility of the provider both to expose the child to assess for previously unidentified injures and to consider prolonged exposure in a cold environment as a possible cause of hypothermia and cardiopulmonary instability. The provider should undress the child (as is feasible and reasonable) to perform a physical exam, assessing for burns, bruising, bleeding, joint laxity, and fractures. If possible, the provider should assess the child's temperature. All maneuvers should be performed with careful maintenance of cervical spine precautions when indicated.

Secondary and Tertiary Assessment

Secondary Assessment

For healthcare providers in community or outpatient settings, transfer of care of a child to emergency or hospital personnel may occur before a full secondary assessment is possible. However, before the child is removed from the scene and separated from witnesses or family, a brief history should be obtained for medical providers at the accepting facility. The components of a secondary assessment include a **focused history** and **focused physical examination**.

The history should be targeted to information that could explain cardiorespiratory or neurologic dysfunction and should take the form of a **SAMPLE history**: signs/symptoms; allergies; medications; past medical history; timing of last meal; and events leading to this situation. Medical personnel not engaged in resuscitative efforts can be dispatched to elicit history from witnesses or relatives. The physical examination during the secondary assessment is a thorough head-to-toe exam, although the severity of the child's illness or injury could necessitate curtailing portions of the exam or postponing nonessential elements until a later time.

Tertiary Assessment

The tertiary assessment occurs in a hospital setting, where ancillary laboratory and radiographic assessments contribute to a thorough understanding of the child's condition. A basic blood chemistry profile, complete blood count, liver function tests, coagulation studies, and arterial blood gas analyses provide estimates of renal function, acid-base balance, cardiorespiratory function, and presence or absence of shock. Chest radiographs can be useful to evaluate both the heart and

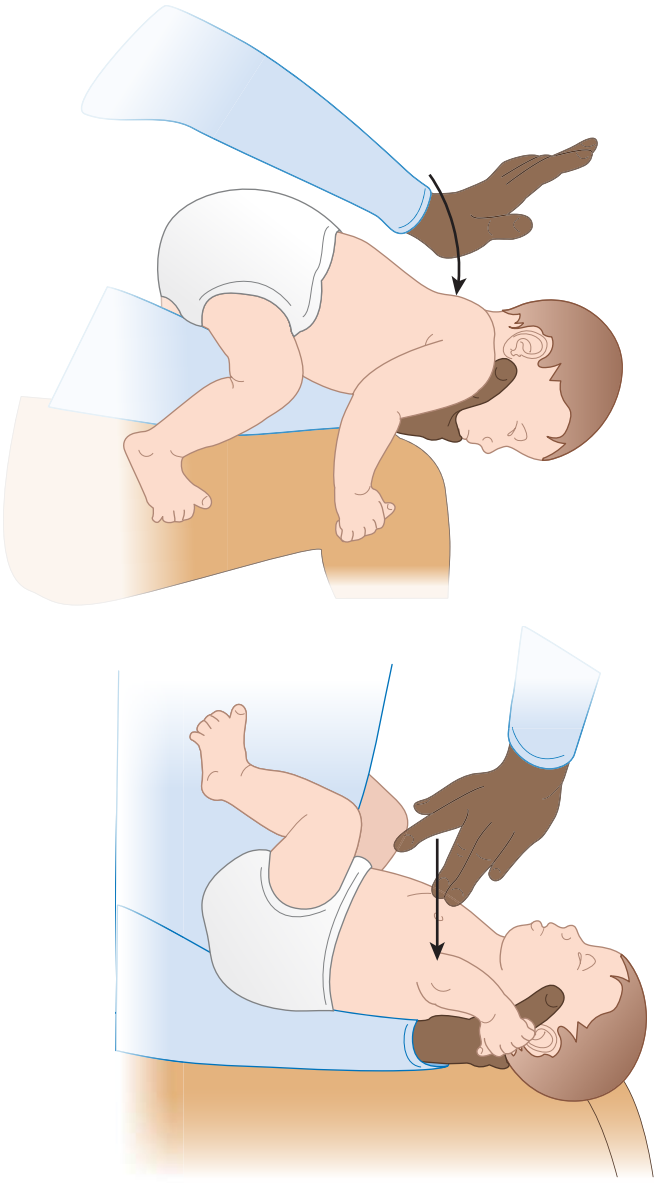

Fig. 79.5 Back blows *(top)* and chest thrusts *(bottom)* to relieve foreign body airway obstruction in the infant.

Fig. 79.6 Abdominal thrusts with the conscious victim standing or sitting.

lungs, although more detailed assessment of cardiac function can be performed with echocardiography.

RECOGNITION AND TREATMENT OF RESPIRATORY DISTRESS AND FAILURE

The goals of initial management of respiratory distress or failure are to rapidly stabilize the child's airway and breathing and to identify the cause of the problem so that further therapeutic efforts can be appropriately directed.

Airway Obstruction Due to Foreign Body

Children under 5 years of age are particularly susceptible to foreign body aspiration and choking. Liquids are the most common cause of choking in infants, whereas small objects and food (e.g., grapes, nuts, hot dogs, candy) are the most common source of foreign bodies in the airways of toddlers and older children. A history consistent with foreign body aspiration is considered diagnostic. Any child in the proper setting with the sudden onset of choking, stridor, or wheezing should be considered to have a foreign body aspiration until proven otherwise. Unfortunately, this classic history is not always present in all cases of foreign body aspiration.

Airway obstruction is treated with a sequential approach starting with the head-tilt/chin-lift maneuver to open and support the airway, followed by inspection for a foreign body, and finger-sweep clearance or suctioning if one is visualized. *Blind suctioning or finger sweeps of the mouth are not recommended.* A conscious child suspected of having a partial foreign body obstruction should be permitted to cough spontaneously until coughing is no longer effective, respiratory distress and stridor increase, or the child becomes unconscious. They can be allowed to find a comfortable position to facilitate air entry.

For *conscious infants,* providers should administer five back blows and then five chest thrusts (Fig. 79.5). After each cycle of back blows and chest thrusts, the child's mouth should be visually inspected for the presence of the foreign body. If identified within finger's reach, it should be removed with a gentle finger sweep. If no foreign body is visualized and the child is conscious, repeat back blows and chest thrusts. Do not blindly sweep for objects if they are not visible, as this can push the object farther into the airway.

For *conscious children* older than 1 year, providers should give a series of five abdominal thrusts **(Heimlich maneuver)** with the child standing or sitting (Fig. 79.6). After the abdominal thrusts, the airway is examined for a foreign body, which should be removed if visualized. If no foreign body is seen, abdominal thrusts should be repeated. For both infants and children, the sequence is repeated until the object is expelled or the patient loses consciousness, at which time CPR with ventilations should be initiated.

If the child becomes *unconscious,* the child should be gently placed on the ground in a supine position and ventilations should be initiated; compressions should also be started if the child is pulseless. The airway should be inspected for a foreign body at the time of ventilations.

Airway Obstruction or Narrowing from Other Causes

Airway obstruction can also be caused by airway narrowing in both the upper and lower airways. Upper airway obstruction refers to narrowing of the extrathoracic portion of the airway, including the oropharynx, larynx, epiglottitis, and trachea. In the upper airways, narrowing is most often caused by airway edema (e.g., croup or anaphylaxis) or epiglottic edema (e.g., epiglottitis) and often manifests with stridor. Stridor, in cases of extrathoracic airway obstruction, is a high-pitched sound heard on inspiration. When airway obstruction is intrathoracic, stridor can be biphasic, heard during both inspiration and expiration. Lower airway obstruction affects all intrathoracic airways, notably the bronchi and bronchioles. **Bronchiolitis** and acute **asthma** exacerbations are the major causes of intrathoracic airway obstruction in children, causing lower airway narrowing through a combination of airway swelling, mucus production, and circumferential smooth muscle constriction of smaller airways.

The approach to upper airway obstruction is dictated by both the underlying condition and the clinical severity of the problem. In cases of mild upper airway obstruction, the child has minimally increased work of breathing (evidenced by tachypnea and absent to mild retractions). Stridor, if present at all, should be audible with only coughing or activity. Children with these findings can often be supported with supplemental oxygen as needed. In cases with moderate obstruction, in which the child has more significant work of breathing or more pronounced stridor, nebulized **racemic epinephrine** and oral or intravenous (IV) **dexamethasone** can be added, particularly for **croup** (i.e., laryngotracheobronchitis) (see Chapter 434). **Heliox** (combined helium-oxygen therapy) administration may also be considered. Children with severe upper airway obstruction have marked intercostal retractions, prominent stridor, and decreased air entry on auscultation of the lung fields. They can also be hypoxemic, dyspneic, and either agitated or somnolent. A child in severe distress that does not rapidly respond to therapies may require endotracheal intubation to overcome the area of obstruction. Clinicians need to carefully observe patients, as impending respiratory failure may be initially confused with improvement. Stridor becomes quieter and retractions less prominent when a child's respiratory effort begins to diminish. This can either be the result of improvement or progressive respiratory failure with less air entry. The child in respiratory failure may have poor air movement on auscultation and decreased level of consciousness from hypercarbia, hypoxia, or both. When **anaphylaxis** is suspected as the cause for upper airway edema, providers should administer an intramuscular dose of epinephrine as needed (see Chapter 190). Racemic epinephrine can also help decrease localized airway edema. **Epiglottitis** often presents with a muffled voice, drooling, and difficulty swallowing. Epiglottitis is a medical emergency for which the initial focus should be on alerting otolaryngology and/or anesthesiology experts to be immediately present while keeping the patient calm. These patients usually need to have their airway secured in an operating room with contingency planning for emergency surgical airway placement. No matter the cause, any child with upper airway obstruction and impending respiratory failure should be prepared to undergo endotracheal intubation and respiratory support. Prompt notification of providers trained in advanced airway management is essential.

In cases of lower airway obstruction, therapies are targeted to both relieve the obstruction and reduce the child's work of breathing. For asthma, **inhaled bronchodilators**, such as albuterol, augmented by oral or IV **corticosteroids**, remain the mainstay of therapy in mild to moderate acute distress. Children with more significant obstruction appear dyspneic, with tachypnea, retractions, forced expiration, and audible wheezing or reduced breath sounds. In these cases, the addition of an anticholinergic agent, such as nebulized ipratropium bromide, or a smooth muscle relaxant, such as magnesium sulfate, may provide further relief, although the evidence for these measures remains controversial (see Chapter 185). Supplemental oxygen and IV fluid hydration can be useful adjuncts. Infants and young children with bronchiolitis often present with tachypnea. Patients with moderate to severe disease may have retractions, nasal flaring, or grunting and can be hypoxemic. These patients often do not respond to bronchodilators. Supportive care with chest physiotherapy to support mucous clearance and noninvasive positive pressure ventilation support can be used as these patients recover from this lower airway viral disease process.

Fig. 79.7 Rescue breathing in an infant. The rescuer's mouth covers the infant's nose and mouth, creating a seal. One hand performs the head-tilt while the other hand lifts the infant's jaw.

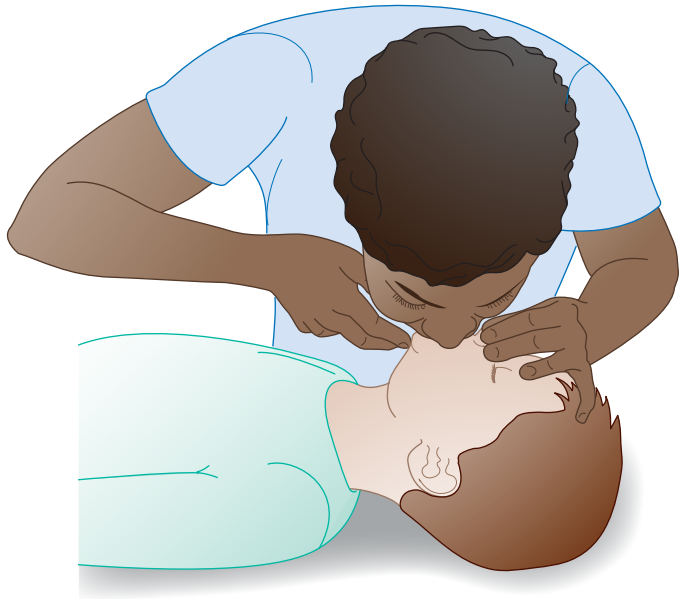

Fig. 79.8 Rescue breathing in a child. The rescuer's mouth covers the child's mouth, creating a mouth-to-mouth seal. One hand maintains the head-tilt; the thumb and forefinger of the same hand are used to pinch the child's nose. The other hand lifts the child's jaw.

Impending respiratory failure in children with lower airway obstruction can be insidious. When diagnosed early in a school-age child who is cooperative, respiratory failure can potentially be averted through judicious use of noninvasive support, including heated, high-flow nasal cannula (HFNC) therapy, continuous positive airway pressure (CPAP), or bilevel positive airway pressure (BiPAP). Endotracheal intubation should be performed only by skilled providers, preferably in a hospital setting, because there is a high risk of cardiorespiratory compromise in patients with lower airway obstruction during the procedure.

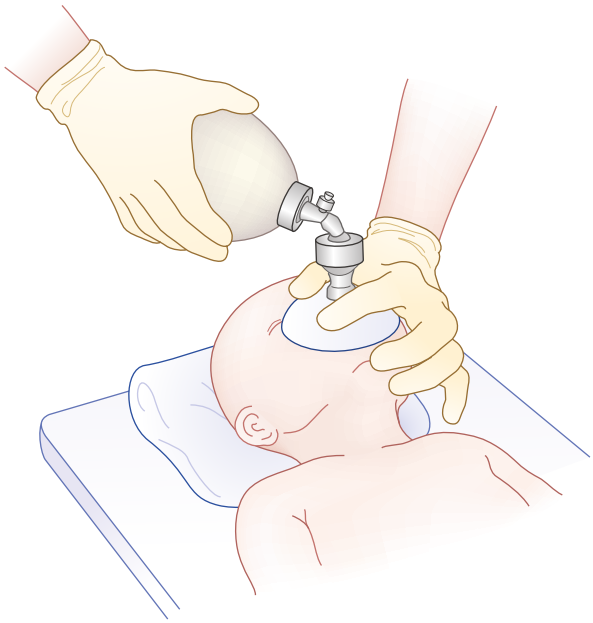

Fig. 79.9 "C-E" grip to secure a mask to a child's face with appropriate seal.

Parenchymal Lung Disease

Parenchymal lung disease includes a heterogeneous list of conditions, such as pneumonia, pediatric acute respiratory distress syndrome (PARDS), pneumonitis, bronchiolitis, bronchopulmonary dysplasia, cystic fibrosis, and pulmonary edema. The commonalities of these conditions are their effects on the small airways and alveoli, including inflammation and exudation leading to consolidation of lung tissue, decreased gas exchange, and increased work of breathing. Clinical management of these conditions includes specific treatment as indicated (e.g., antibiotics for bacterial pneumonia) and supportive care with oxygen, noninvasive respiratory support (e.g., HFNC, CPAP, or BiPAP), or invasive mechanical ventilation. The severity of work of breathing and degree of oxygenation or ventilation failure determine the degree of respiratory support needed and should be expected to evolve with time.

Airway and Breathing Management

Rescue Breathing

If a child is unconscious and not breathing effectively or apneic, **rescue breathing** should be provided. The provider should open the airway with the head-tilt/chin-lift maneuver and attempt mouth-to-mouth ventilation (Figs. 79.7 and 79.8). In trauma patients with suspected cervical spine injuries, a jaw thrust should be performed without the head-tilt maneuver. If ventilation is unsuccessful, the airway is repositioned, and ventilation should be attempted again.

Bag-Mask Ventilation

Ventilation with a bag-mask apparatus can be as effective as endotracheal intubation and safer when the provider is inexperienced with intubation. Bag-mask ventilation (BMV) requires training to ensure that the provider is competent to select the correct mask size, open the child's airway, form a tight seal between the mask and the child's face, deliver effective ventilation, and assess the effectiveness of ventilations. An appropriately sized mask is one that fits over the child's mouth and nose but does not extend below the chin or over the eyes. An adequate seal is best achieved through a combination "C-E" grip on the mask, in which the thumb and index finger form the letter "C" on top of the mask, holding the mask onto the child's face, and the remaining three fingers form an "E" grip under the child's mandible, holding the jaw forward without pressing on the soft tissues and extending the head up toward the mask. Using this method, the care provider can secure the mask to the child's face with one hand and use the other hand to compress the ventilation bag (Fig. 79.9).

The provider may have to move the head and neck through a range of positions to find the one that best maintains airway patency with adequate chest rise. In infants and young children, optimal ventilation is often provided when the child's head is in the neutral sniffing position without hyperextension of the head. Poor chest rise or persistent hypoxemia indicate inadequate ventilation. In this setting, the care provider should recheck the mask's seal on the child's face, reposition the child's head, and consider suctioning the airway. If these maneuvers do not restore ventilation, the provider should consider placement of a nasopharyngeal or oral airway. The inability to ventilate a patient with positive pressure after the previous measures is an emergency requiring expert consultation while preparing for endotracheal intubation.

Endotracheal Intubation

A child generally requires intubation when at least one of these conditions exists: (1) the child is unable to maintain airway patency or protect against aspiration (as occurs in settings of neurologic compromise such as seizures or traumatic brain injury); (2) the child is failing to maintain adequate oxygenation despite supplemental oxygen or noninvasive therapies; (3) the child cannot be adequately ventilated with evidence of elevated blood carbon dioxide levels and an unsafe acid-base balance; (4) sedation and/or paralysis is required for a procedure; (5) the need to decrease metabolic demand by sedating the patient to support extrapulmonary organs (e.g., septic shock or heart failure) is present; and (6) providers anticipate a deteriorating course that will eventually lead to any of the first five conditions. It should be noted that in centers experienced in noninvasive respiratory support, a trial of HFNC, CPAP, or BiPAP may be indicated based on the specific clinical scenario.

There are few *absolute contraindications* to tracheal intubation, but experts generally agree that in settings of known complete airway obstruction (e.g., severe subglottic stenosis), endotracheal intubation should be avoided, and emergency cricothyroidotomy or tracheostomy performed instead. It is important to assess a patient's airway before initiating endotracheal intubation. Any history of a difficult airway (difficult to intubate) or critical airway (unable to bag-mask ventilate) should prompt further investigation and expert consultation. Both history and physical exam features such as limited mouth opening, limited neck mobility, or micrognathia should raise concern for further assessment. Another important consideration is to ensure that providers maintain appropriate cervical spine (C-spine) protection during the intubation procedure when neck or spinal cord injury is suspected.

A critical phase of the intubation procedure is the preprocedural preparation, when the provider ensures all the equipment and staff needed for safe intubation are present and functioning. An easy pneumonic for this is **SOAP MM**: *suction* (Yankauer suction catheter attached to wall suction); *oxygen* (both preoxygenation of the patient and devices needed to deliver oxygen, such as a bag-mask); *airway* (appropriately sized endotracheal tube and laryngoscope as well as adjunct airway devices); *people* (all those needed during and immediately after the procedure, including respiratory therapists and nurses); *monitor* (pulse oximetry, ECG, blood pressure, capnography); and *medications* (sedation and often neuromuscular blockade to facilitate intubation). A simple formula for selecting the appropriately sized endotracheal tube (ETT) is:

$$\text{Uncuffed ETT size (in mm)} = \left(\frac{\text{age in years}}{4}\right) + 4$$

Cuffed ETTs should generally be 0.5 mm smaller. Providers should always have a range of ETTs available, given the heterogeneity of patients and airway size. The use of cuffed ETTs is recommended in most pediatric populations, as it may decrease the need for ETT changes caused by difficulty ventilating and may decrease the risk of aspiration.

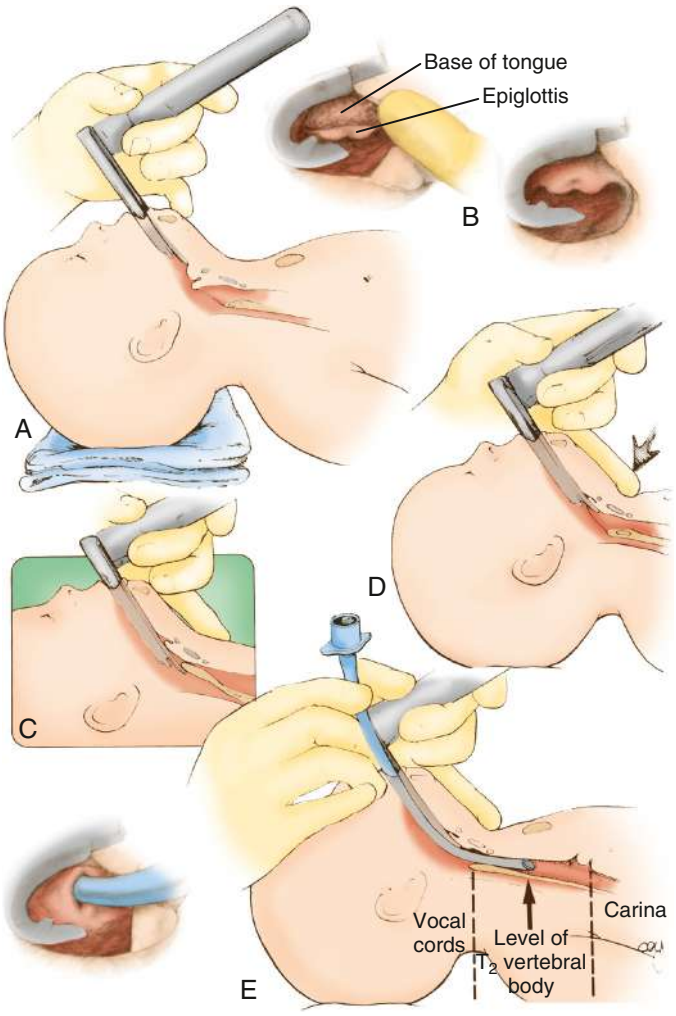

Fig. 79.10 A-E, Tracheal intubation technique. (*From Fleisher G, Ludwig S. Textbook of Pediatric Emergency Medicine, Baltimore: Williams & Wilkins;1983:1250.*)

Analgesia is recommended to reduce metabolic stress, discomfort, and anxiety during intubation. Pretreatment with a sedative, an analgesic, or an anesthetic or dissociative medication and potentially a neuromuscular relaxing agent (paralytic agent) is recommended unless the situation is emergent (e.g., cardiac arrest) and the administration of drugs would cause an unacceptable delay. Neuromuscular blocking agents should generally be avoided in patients who cannot be bag-mask ventilated because if the patient cannot be successfully intubated and cannot be bag-mask ventilated, they may progress to cardiopulmonary arrest.

Because many intubations in critically ill children are emergency procedures, providers should be prepared to rapidly intubate (Fig. 79.10). Rapid sequence intubation (RSI)—the process of intubating with a sedative (etomidate, ketamine, propofol) and neuromuscular blockade (rocuronium, succinylcholine) preintubation medications (order of administration not important)—is not always feasible in critically patients because BMV is necessary to maintain oxygenation and ventilation due to severe lung disease or intracranial hypertension. The routine use of cricoid pressure is not recommended because it does not decrease the risk of regurgitation of stomach contents, and it can impede effective BMV and airway visualization. Although there is a risk of regurgitation and aspiration, supporting the patient during induction and supporting rapid intubation is critical to minimize the risk to the patient.

Once the patient is intubated, proper ETT placement should be assessed by auscultation of breath sounds, observation of symmetric chest rise, and analysis of exhaled carbon dioxide (CO_2) by a colorimetric device or a capnographic device that quantifies CO_2 elimination. Chest radiography should be obtained to confirm appropriate tube position. Clinicians should assess ETT cuff pressures to minimize the risk of airway trauma.

RECOGNITION AND MANAGEMENT OF SHOCK

Shock occurs when oxygen and nutrient delivery to the tissues is inadequate to meet metabolic demands (see Chapter 85). A diagnosis of shock does not require the presence of hypotension. It is important for providers to recognize that **shock can occur with hypertension, normotension, or hypotension**. In early *compensated* shock, blood pressure is maintained, and oxygen delivery is mostly preserved through compensatory mechanisms such as tachycardia, increased systemic vascular resistance, or increased cardiac contractility. When compensatory mechanisms fail or are inadequate, the patient progresses to *decompensated* shock, which is defined by hypotension and organ dysfunction. If shock is not rapidly identified and treated, it can progress to multisystem organ dysfunction, cardiac arrest, and death.

Shock is also often described according to the underlying pathophysiology, which dictates the appropriate therapeutic response. **Hypovolemic shock** is the most common type of shock in children worldwide, usually related to fluid losses from severe diarrhea. Hemorrhagic shock is a specific type of hypovolemic shock after trauma or other causes of bleeding. **Distributive shock** occurs because of pathogenic dilation of the body's blood vessels and is often accompanied by relative intravascular hypovolemia due to capillary leak and "third-spacing" of intravascular fluids into the extravascular compartment. The most common causes of distributive shock are sepsis, anaphylaxis, and burn injuries, in which release of inflammatory cytokines causes massive capillary leak of fluid and proteins, leading to low oncotic pressure and intravascular volume. In the setting of myocardial dysfunction, a child has tissue hypoperfusion from **cardiogenic shock**. Common causes of cardiogenic shock are myocarditis, cardiomyopathy, and congenital heart disease, often in the postoperative setting. Severe sepsis and septic shock are often accompanied by myocardial dysfunction, and children with septic shock thus frequently manifest components of hypovolemic, distributive, and cardiogenic shock. **Obstructive shock** occurs when cardiac output is lowered by obstruction of blood flow to the body, as occurs with pericardial tamponade, tension pneumothorax, or massive pulmonary embolism. **Dissociative shock** manifests with normal cardiac and volume status but poor oxygen delivery due to severe anemia and carbon monoxide or cyanide poisoning.

The evaluation of a child in shock should proceed based on the primary, secondary, and tertiary assessments. Initial resuscitation should include the administration of crystalloid fluids in 10-20 mL/kg aliquots up to 60 mL/kg in the first hour if hypotension is present while paying close attention for signs of volume overload. If shock persists, volume overload is evident, or myocardial dysfunction is suspected, vasoactive infusions (e.g., epinephrine, norepinephrine) should be initiated. In hospital settings, catecholamine-dependent shock should trigger providers to consider placing a central venous catheter for stable venous access and an arterial line for continuous blood pressure monitoring. Laboratory assessment should include studies of renal and liver function; acid-base balance, including the presence of lactic acidosis, hypoxemia, and/or hypercapnia; and evidence of coagulopathy or disseminated intravascular coagulation to assess for signs of end-organ dysfunction and response to treatment. Assessment of peripheral perfusion, mental status, and urine output are also important to monitor. Treatment of the various etiologies of shock is noted in Chapter 85.

RECOGNITION AND TREATMENT OF ARRHYTHMIAS

In the advanced life support setting, arrhythmias are most usefully classified according to the observed heart rate (i.e., bradycardia or tachycardia) and the presence of cardiopulmonary compromise (e.g., altered mental status, hypotension, signs of shock). If the primary survey identifies a child with an abnormal heart rate and altered mental

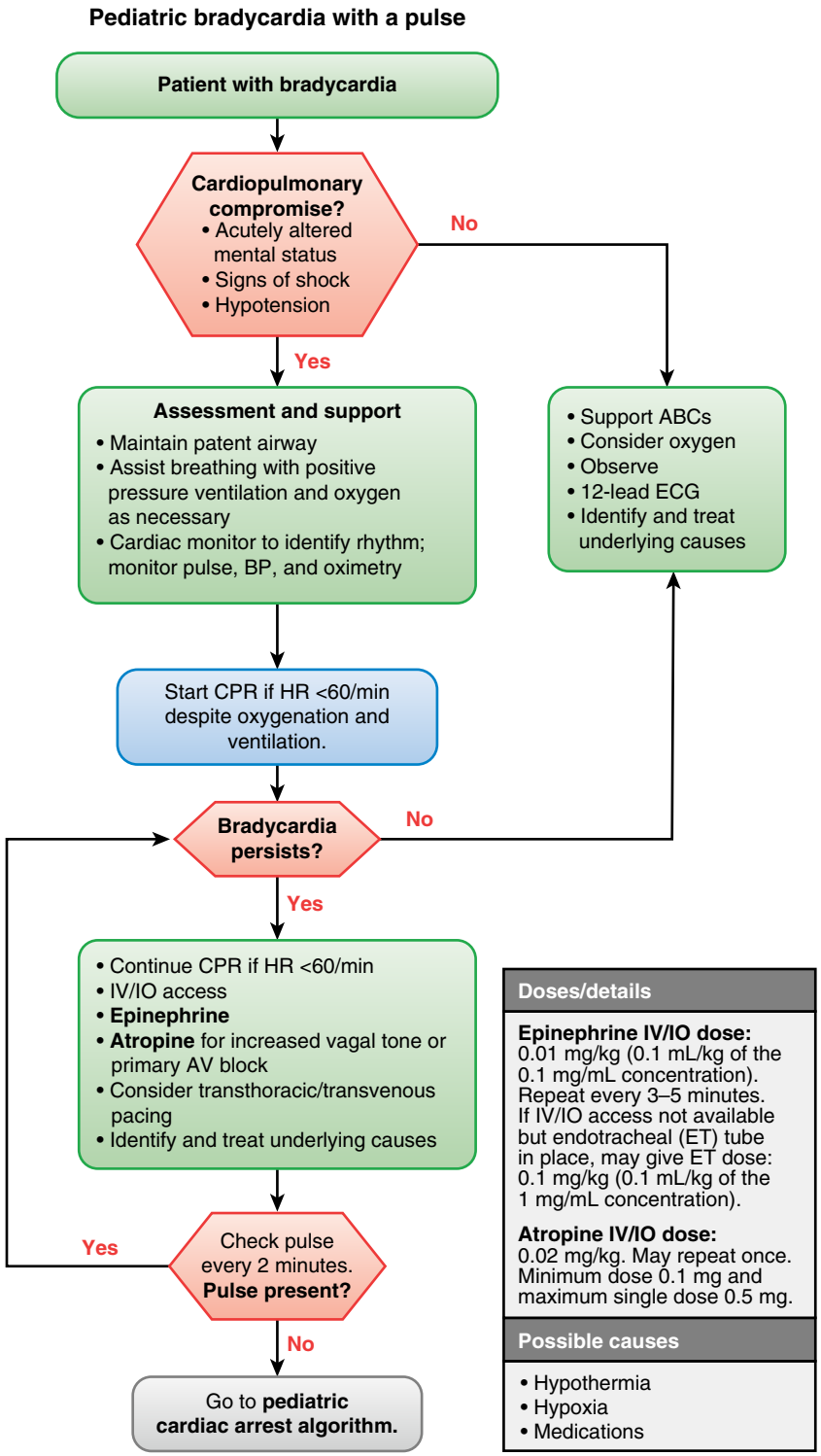

Fig. 79.11 Pediatric advanced life support: Bradycardia with a pulse algorithm. ABCs, Airway, breathing, and circulation; AV, atrioventricular (conductor); ECG, electrocardiogram; HR, heart rate; IO/IV, intraosseous/intravenous. (*From Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142[16 Suppl 2]:S469-S523.*)

status or other signs of shock or hypotension, the rhythm is inadequate no matter its rate.

Bradyarrhythmias

By definition, a child is *bradycardic* when the heart rate is slower than the normal range for age (see Table 79.1). Sinus bradycardia can be a harmless incidental finding in an otherwise healthy person and is not usually associated with cardiac compromise. A clinically significant bradycardia occurs when the heart rate is slow and there are signs of systemic hypoperfusion (i.e., pallor, altered mental status, hypotension, acidosis). Symptomatic bradycardia occurs most often in the setting of hypoxemia but can also be caused by hypoglycemia, hypocalcemia, other electrolyte abnormalities, hypothermia, heart block, and intracranial hypertension. Bradyarrhythmias are often the most common *prearrest* rhythms in young children.

Initial management of symptomatic bradycardia includes support or opening of the airway and confirming or establishing adequate oxygenation and ventilation (Fig. 79.11). After adequate oxygenation and ventilation have been confirmed, the child should be reassessed for continued bradycardia and poor perfusion. If cardiac

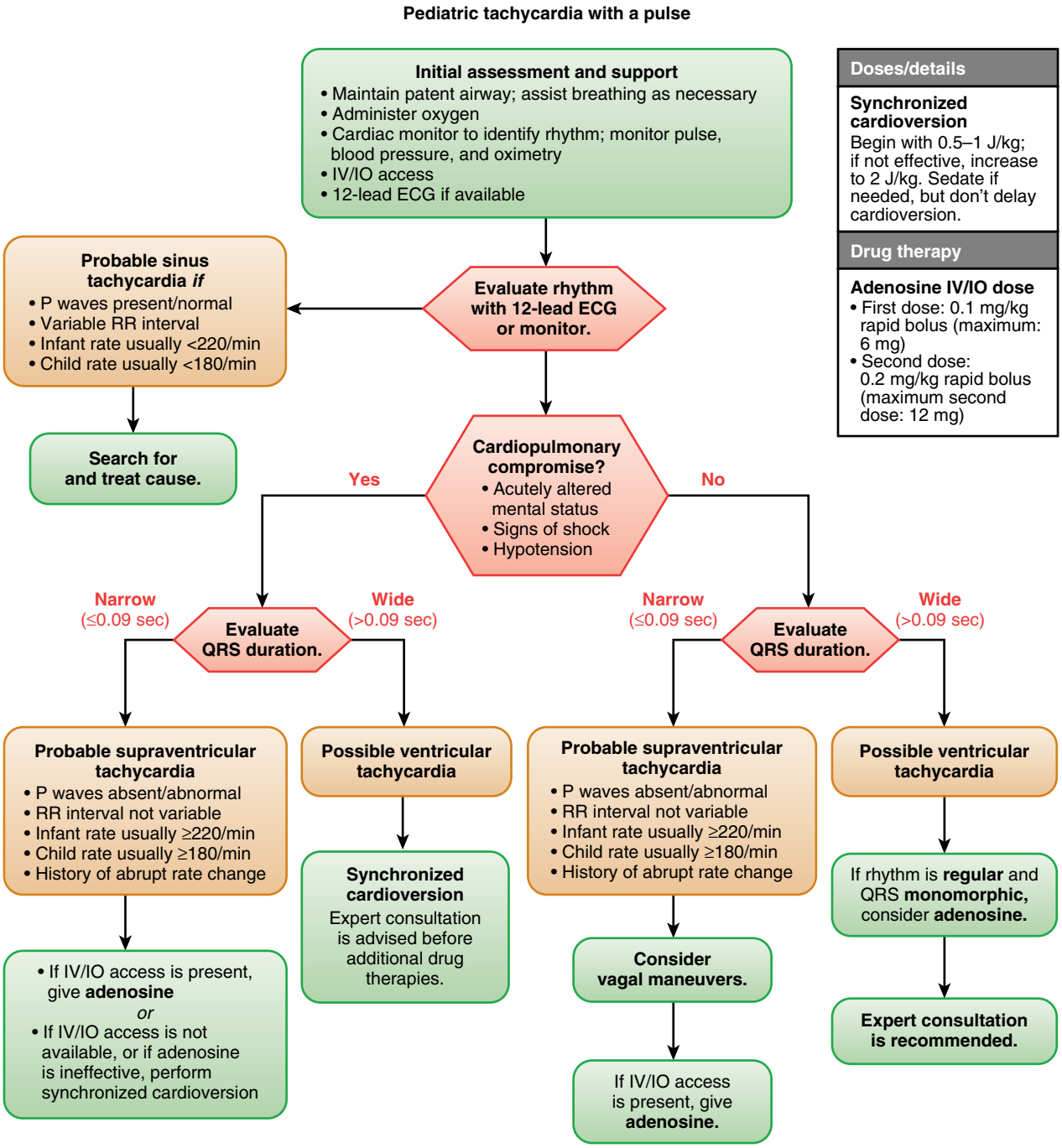

Fig. 79.12 Pediatric advanced life support: Tachycardia with a pulse algorithm. AV, Atrioventricular (conductor); ECG, electrocardiogram; HR, heart rate; IO/IV, intraosseous/intravenous. (*From Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142[16 Suppl 2]:S469-S523.*)

compromise was solely the result of respiratory insufficiency, support of the child's airway and breathing may have been sufficient to restore normal hemodynamics. If respiratory support does not quickly correct the perfusion abnormalities, further care is based on the quality of perfusion and degree of bradycardia. *A heart rate <60 beats/min with cardiopulmonary compromise is an indication to begin CPR,* including the administration of epinephrine. If increased vagal tone or primary atrioventricular block is suspected, atropine can be administered. For cases of refractory bradycardia, cardiac pacing should be considered (see Fig. 79.11).

Tachyarrhythmias

Tachyarrhythmias represent a wide variety of rhythm disturbances of atrial and ventricular origin (see Chapter 484). Sinus tachycardia is a normal physiologic response to the body's need for increased cardiac output or oxygen delivery, as occurs with fever, exercise, or stress. It can also occur in more pathologic states, such as hypovolemia, anemia, pain, anxiety, thyrotoxicosis, and shock. Non–sinus tachyarrhythmias that do not originate in the sinus node are often categorized as either *narrow complex rhythms* (i.e., originating in the atrium, such as supraventricular tachycardia or atrial flutter) or *wide*

Table 79.5 Medications for Pediatric Resuscitation and Arrhythmias

MEDICATION	DOSE	REMARKS
Adenosine	0.1 mg/kg (max dose: 6 mg) Repeat: 0.2 mg/kg (max dose: 12 mg)	Monitor ECG Rapid IV/IO bolus with flush
Amiodarone	5 mg/kg IV/IO; repeat 5 mg/kg doses up to 15 mg/kg Max dose: 300 mg	Monitor ECG and blood pressure, as it can cause hypotension Give over 20-60 min (can give via IV push for patients in cardiac arrest) Use caution when administering with other drugs that prolong QT interval (consider expert consultation)
Atropine	IV/IO: 0.02 mg/kg Minimum dose: 0.1 mg for bradycardia treatment Max dose: • Child: 0.5 mg • Adolescent: 1 mg Repeat once if needed ETT* 0.04-0.06 mg/kg Max dose: 2 mg	Higher doses may be used with organophosphate poisoning ETT dosing only if no IV/IO access
Calcium chloride (10%) Calcium gluconate	20 mg/kg IV/IO 50-100 mg/kg Max dose: 2 g	Administer slowly; fast push can cause heart block/asystole Use only with documented hypocalcemia
Dextrose	0.5-1 g/kg IV/IO • D10W: 5-10 mL/kg • D25W: 2-4 mL/kg • D50W: 1-2 mL/kg	Recheck serial blood sugars after administration, as hypoglycemia can recur
Epinephrine	IV/IO: 0.01 mg/kg (0.1 mL/kg of the 0.1 mg/mL concentration) Max dose: 1 mg ETT*: 0.1 mg/kg (0.1 mL/kg of the 1 mg/mL concentration) Max dose: 2.5 mg	May repeat every 3-5 min as needed Only give via ETT if no IV/IO access
Lidocaine	IV/IO: 1 mg/kg bolus Max dose: 100 mg Infusion: 20-50 µg/kg/min ETT*: 2-3 mg/kg	Repeat bolus dose if infusion is initiated >15 min after initial bolus
Magnesium sulfate	25-50 mg/kg IV/IO Max dose: 2 g	Can cause hypotension Administer over 10-20 min; faster in torsades de pointes
Naloxone	IV/IO/IM/SQ: 0.1 mg/kg for full reversal Max dose 2 mg IN: 4 mg spray; may repeat q2-3min ETT*: 2-3 times IV dose	Use lower doses in patients with opioid-induced respiratory depression from therapeutic opioid dosing (0.001-0.005 mg/kg) May need to redose every 2-3 minutes, as half-life is shorter than most narcotics ETT if IV/IO routine not available
Sodium bicarbonate	1 mEq/kg IV/IO	Administer slowly; ensure adequate ventilation

*Flush with 5 mL of normal saline and follow with 5 ventilations.
D5W, 5% Dextrose in water; IO, intraosseous; IV, intravenous; ETT, endotracheal tube; IM, intramuscular; IN, intranasal.

complex rhythms (i.e., rhythms of ventricular origin, such as ventricular tachycardia).

The initial management of tachycardia should include assessment for cardiopulmonary compromise (Fig. 79.12). If the patient has evidence of cardiopulmonary compromise (i.e., hypotension, altered mental status, or other signs of shock), further treatment is based on whether the QRS complex of the ECG is narrow (≤0.09 sec) or wide (>0.09 sec). For narrow complex tachycardia, providers must distinguish between sinus tachycardia and supraventricular tachycardia (SVT). In **sinus tachycardia**, the history and onset are consistent with a known cause of tachycardia, such as fever or dehydration. Sinus tachycardia usually has some degree of rate variability, and p-waves are consistently present on the ECG and are of normal morphology and axis. Treatment is then geared toward identifying and treating the cause of sinus tachycardia. In **SVT**, onset is often abrupt without prodrome, and p-waves are absent or have a nonsinus ECG axis. When SVT is associated with cardiopulmonary compromise, providers should rapidly move to convert the child's heart rhythm back to sinus rhythm. If the child already has IV access, adenosine should be administered (Table 79.5). Adenosine has an extremely short half-life, so administration through an IV close to the heart (e.g., upper extremity) is best. Adenosine should be administered with a three-way stopcock inline so that it can be given and immediately flushed into the circulation. If the child does not have IV access or adenosine does not successfully convert the heart rhythm back to sinus rhythm, then **synchronized cardioversion** (0.5-1.0 joule [J]/kg) should be performed. For wide-complex tachycardia (i.e., **ventricular tachycardia [VT]**) with a pulse and evidence of cardiopulmonary compromise, synchronized cardioversion should be performed.

For patients with tachycardia without cardiopulmonary compromise, the rhythm assessment proceeds in the same fashion, but treatment potentially differs. Vagal maneuvers can be considered for SVT in the stable patient, followed by administration of adenosine and obtaining expert consultation. Wide-complex tachyarrhythmias without cardiovascular compromise should also trigger expert consultation before administration of antiarrhythmic medications. If the rhythm is monomorphic, adenosine can be given, as some stable wide-complex tachycardias are SVT with aberrant conduction and thus have a wide QRS complex. Patients should be continually reassessed for development of cardiovascular compromise.

CARDIAC ARREST AND CARDIOPULMONARY RESUSCITATION

Overview

Cardiac arrest occurs when the heart fails as an effective pump and blood flow ceases. Outwardly, the patient in cardiac arrest presents as unresponsive and apneic with no palpable pulse. Internally, the cessation of cardiac output and oxygen delivery causes progressive tissue ischemia and organ failure. If not rapidly reversed, cardiac arrest leads to progressive deterioration in brain, heart, and other organ function, such that resuscitation and recovery are no longer possible. Cardiac arrest outcomes in children have improved as a result of improvements in the recognition of deteriorating patients and delivery of high-quality CPR. Prehospital and hospital providers should understand that pediatric cardiac arrest is an intervenable process for which favorable outcomes are common. Early recognition and rapid treatment with high-quality CPR can be lifesaving.

Prevention of Cardiac Arrest

Out-of-hospital cardiac arrest (OHCA) occurs due to a variety of causes, including sudden infant death syndrome (SIDS), drowning, foreign body aspiration, poisoning or drug overdose, and trauma. Sudden cardiac arrest due to arrhythmias or cardiac disease do occur (usually in adolescents and those with preexisting congenital heart disease) and should be recognized and promptly treated, but most pediatric OHCAs have an underlying respiratory etiology. Preventive measures such as "back to sleep" for infants to lower the risk of SIDS (see Chapter 423), child supervision around bodies of water, and minimizing access to high-risk choking foods substantially decrease the incidence of cardiac arrest. Recognition of the child with respiratory distress or impending respiratory failure and delivery of appropriate care, as outlined earlier, is the most common and practical means of preventing pediatric OHCA.

In hospitalized children, cardiac arrest is most often the result of the progression or worsening of an underlying respiratory, cardiac, or neuromuscular disease process. Most pediatric in-hospital cardiac arrests (IHCAs) occur in the setting of progressive respiratory failure or shock. Recognition of deteriorating patients, transfer to monitored settings (i.e., intensive care units), and institution of appropriate directed and supportive therapies are effective means of preventing IHCA or ensuring that if it does occur, care is delivered in a well-equipped and prepared setting.

Recognition of Cardiac Arrest

Cardiac arrest is recognized from general assessment and primary survey findings consistent with a pale or cyanotic child who is unresponsive, apneic, and pulseless. Even experienced providers have a relatively high error rate when asked to determine presence or absence of pulse in a child. Therefore lay rescuers should begin CPR immediately for any patient without signs of life. Healthcare providers can palpate for a pulse for up to 10 seconds but should provide CPR unless a pulse is definitively felt.

Although initial responders should focus on signs of lifelessness when determining if a patient requires CPR, recognition and understanding of cardiac arrest rhythms is also important for providers. Most pediatric cardiac arrest rhythms are "nonshockable" (i.e., asystole, pulseless electrical activity [PEA], or bradycardia with cardiopulmonary compromise). It is important pediatric providers recognize that bradycardia with cardiopulmonary compromise that does not swiftly resolve with ventilation and oxygenation should be treated with CPR. "Shockable" rhythms (ventricular fibrillation [VF] and pulseless VT) account for a relatively small proportion of pediatric OHCAs or IHCAs. However, these rhythms can occur as a secondary rhythm later in arrest. Because these rhythms require prompt defibrillation in addition to high-quality CPR, it is important to recognize and be prepared to treat VF or pulseless VT when present.

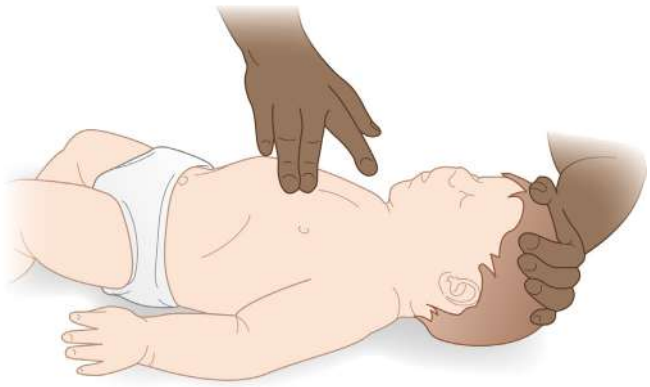

Fig. 79.13 Hand position for infant CPR for the single provider. The two-finger technique.

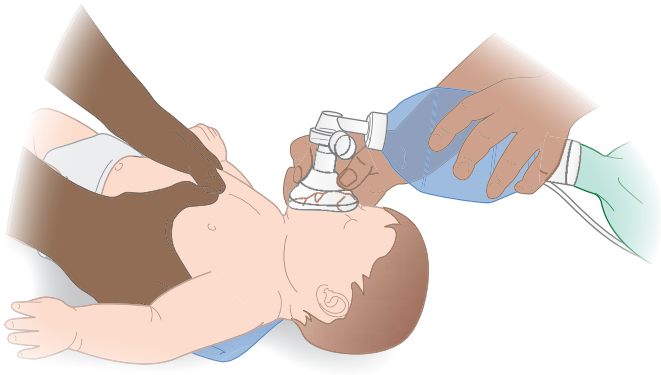

Fig. 79.14 Hand position for infant CPR for two providers. The 2-thumb-encircling hands technique.

Basic Life Support

The AHA Pediatric BLS algorithms for both single- and two-rescuer scenarios are depicted in Figures 79.1 and 79.2. Upon recognition of cardiac arrest, rescuers should begin CPR with both chest compressions and rescue breaths. Single rescuers who witness a sudden collapse should activate the emergency response system and retrieve an automated electronic defibrillator (AED) or defibrillator, if immediately available, before starting compressions, as many of these children have shockable rhythms. For single rescuers treating children in cardiac arrest without a witnessed sudden collapse, CPR should begin immediately with cycles of 30 compressions followed by two rescuer breaths for at least 2 minutes. An AED should be applied, and automated directions followed as soon as it is available. When two or more rescuers are present, one rescuer should be responsible for activating the emergency response system and retrieving an AED while the other rescuer(s) begins CPR. When both rescuers are providing CPR for an infant or prepubescent child, cycles of 15 compressions followed by two ventilations should be provided. Adolescents should receive cycles of 30 compressions and two ventilations regardless of the number of rescuers.

Components of High-Quality Cardiopulmonary Resuscitation

The goal of CPR is to provide temporary blood flow and oxygen delivery to the body during cardiac arrest. High-quality CPR that meets established goals and metrics optimizes this blood flow and is associated with improved outcomes from cardiac arrest. **Components of high-quality CPR include optimal hand positioning, appropriate chest compression rate, adequate chest compression depth, allowing for full chest recoil, minimization of interruptions, and appropriate ventilation rate.**

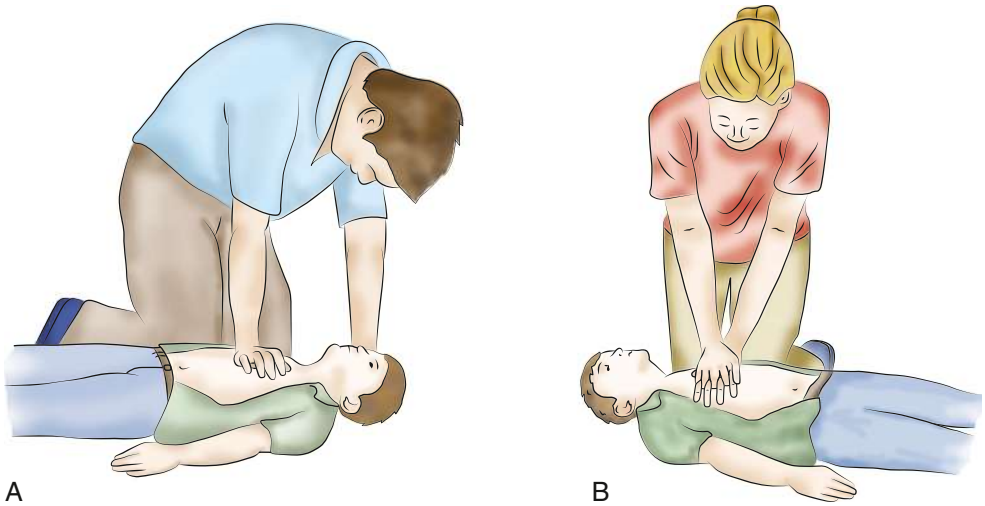

Fig. 79.15 Hand position for child CPR. A, One-handed chest compressions in a child. B, Two-handed chest compressions in a child or adult.

Hand positioning and CPR technique: Chest compressions in infants <1 year old performed by a single provider may be performed by placing two fingers or two thumbs just below the intramammary line (Fig. 79.13). When two providers are present, the two-thumb-encircling hands technique (Fig. 79.14) is recommended unless the rescuer cannot physically encircle the victim's chest, in which case two fingers can be used. If goal depths cannot be reached with these techniques, it is reasonable to use the heel of one hand for chest compressions. For children >1 year old, the care provider should perform chest compressions over the lower half of the sternum with the heel of one hand, or with two hands as used for adult resuscitation (Fig. 79.15). In all cases, care should be taken to avoid compression of the xiphoid and the ribs. When feasible, a backboard should be placed under the child's back and the hospital bed should be placed into "CPR mode" when applicable to maximize the effectiveness of compressions.

Chest compression mechanics: Chest compressions should be provided at a rate of **100-120 compressions per minute**. The goal chest compression depth for infants and children is at least **one-third the anterior-posterior diameter of the chest**, which is approximately 4 cm (1.5 inches) in infants and 5 cm (2 inches) in children. For children who have reached puberty, the adult depth of 5-6 cm can be used. Rescuers should avoid leaning and **allow the chest to fully recoil** after each compression in order to facilitate venous return to the heart. Resuscitation teams should seek to **minimize the duration and frequency of chest compression interruptions** during CPR. These chest compression mechanics can be measured during CPR through CPR quality-monitoring defibrillators, which are now widely used.

Advanced Life Support

The AHA PALS algorithm for cardiac arrest is depicted in Figure 79.16. Chest compressions should be delivered as detailed earlier. Ventilation is a key component of pediatric CPR because most patients have concomitant respiratory failure. For children without an advanced airway in place, chest compressions are paused to allow for the delivery of ventilations via mask with the compression-to-ventilation ratios discussed previously. For children with an advanced airway at the time of arrest, ventilations should be provided asynchronously (i.e., without interrupting chest compressions) at a rate of 20-30 breaths/minute. Providers should avoid overventilation during CPR, as this may increase intrathoracic pressure and decrease venous return to the heart.

Epinephrine is administered during CPR to increase systemic vascular resistance and coronary perfusion pressure in order to restore spontaneous circulation. Epinephrine should be administered intravenously or intraosseously (IO), though it can be administered via ETT if IV or IO access is not available (see Table 79.5). **The first dose of epinephrine should be given within 5 minutes of the onset of cardiac arrest and repeated every 3-5 minutes** until return of spontaneous circulation (ROSC) is achieved. Pulse and rhythm checks should be performed approximately every 2 minutes but should not last more than 10 seconds.

CPR quality can also be gauged by monitoring the patient's physiologic response to resuscitation. End-tidal carbon dioxide, which reflects pulmonary blood flow, can be an indicator of the adequacy of chest compressions. Diastolic blood pressure, measured via an arterial line, is used as a surrogate of coronary perfusion pressure, and values are therefore correlated with the likelihood of ROSC. Either of these tools can be used during CPR by practitioners appropriately trained in the nuances of their interpretation.

Defibrillation and Antiarrhythmic Medications

For those children with VF or pulseless VT, emergency defibrillation is indicated (see Fig. 79.16). Defibrillator pads should be applied to the bare chest during CPR regardless of initial rhythm, as these rhythms can develop later during cardiac arrest. Lay providers should follow the verbal instructions given by the AED. Ideally, the AED used for children <8 years of age should deliver an attenuated adult dose or should be designed for children; if neither of these options is available, a standard adult AED should be used. Healthcare providers should use either an AED or a manual defibrillator. An **initial defibrillation should be provided at a dose of 2 J/kg** with subsequent dosing per the PALS algorithm. CPR should be promptly resumed after each defibrillation attempt, with additional rhythm assessments and defibrillation attempts every 2 minutes while a shockable rhythm persists. Either amiodarone or lidocaine can be given as an antiarrhythmic for shock-refractory VF or VT (see Table 79.5).

Identification and Treatment of Underlying Causes of Cardiac Arrest

Pediatric cardiac arrest can occur because of a discrete and clear event (e.g., drowning), due to the progression of underlying disease processes (e.g., refractory hypoxemic respiratory failure), or for reasons that are unclear to the resuscitation team at the time of the arrest. In addition to providing high-quality CPR, reversing the underlying cause of cardiac arrest is critical in order to restore and maintain spontaneous circulation. Focused evaluation of likely etiologies based on the patient's history, risk factors, physical exam, and other findings often reveals addressable cause. Additionally, providers should systematically address common and correctable causes of cardiac arrest (e.g., the "Hs and Ts"; Table 79.6).

Duration of CPR

Unsurprisingly, children who receive prolonged CPR have worse outcomes than those who require brief CPR. However, previous assertions

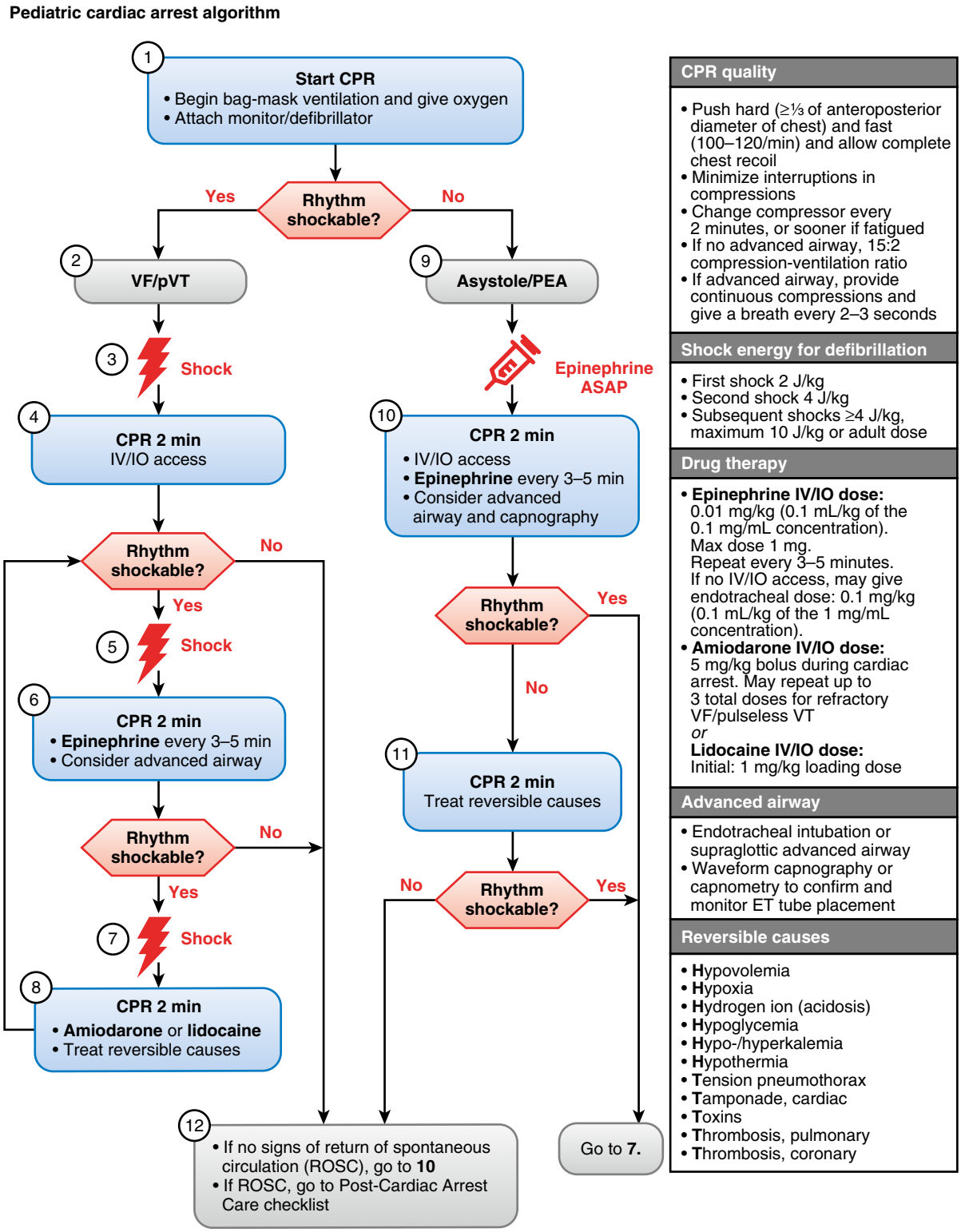

Fig. 79.16 Pediatric advanced life support cardiac arrest algorithm. CPR, Cardiopulmonary resuscitation; IO/IV, intraosseous/intravenous; PEA, pulseless electrical activity; VF/VT, ventricular fibrillation/tachycardia. (*From Topjian AA, Raymond TT, Atkins D, et al. Part 4: Pediatric Basic and Advanced Life Support: 2020 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation. 2020;142[16 Suppl 2]:S469-S523.*)

that CPR >20 minutes in duration was futile have been disproven. More than 15% of children who received >35 minutes of CPR for IHCA survived to hospital discharge in one large registry study. Therefore decisions regarding futility and when to cease resuscitation efforts should take into account patient factors, goals of care, arrest etiology and characteristics, and a host of other factors, rather than CPR duration alone.

Extracorporeal Membrane Oxygenation and Extracorporeal Cardiopulmonary Resuscitation

Extracorporeal membrane oxygenation (ECMO) is a modified form of cardiopulmonary bypass that can be employed in children with severe cardiac or respiratory failure. Blood is removed from a large central vein, carried through tubing to an oxygenator for gas

Table 79.6 Potentially Reversible Causes of Cardiac Arrest

CONDITION	COMMON CLINICAL SETTINGS	TREATMENT
THE H'S		
Hypovolemia	Dehydration, hemorrhage, major burns, diabetes, gastrointestinal losses, shock, and trauma	Administer fluids For hemorrhage, administer packed red blood cells and other blood products
Hypoxemia	Upper airway obstruction (croup, anaphylaxis, foreign body) Lower airway obstruction (asthma, bronchiolitis) Parenchymal lung disease (pneumonia) Restrictive lung disease (pleural effusion)	Provide supplemental oxygen Confirm endotracheal tube placement and chest rise
Hydrogen ion (acidosis)	Preexisting acidosis, diabetes, diarrhea, drugs and toxins, prolonged resuscitation, renal disease, and shock	Reassess the adequacy of cardiopulmonary resuscitation, oxygenation, and ventilation; reconfirm endotracheal tube placement Ensure adequate ventilation and avoid concomitant respiratory acidosis Administer IV fluids May consider bicarbonate administration with documented severe acidosis
Hypoglycemia	Starvation, toxin, diabetes medications, metabolic disease	Administer dextrose (glucagon if dextrose not available) Discontinue causative medications
Hyperkalemia	Metabolic acidosis, excessive administration of potassium, renal failure, drugs and toxins, vigorous exercise, hemolysis, rhabdomyolysis, tumor lysis syndrome, and clinically significant tissue injury	Stop potassium-containing fluids Stabilize cardiac membrane: calcium Treat acidosis: sodium bicarbonate Shift potassium intracellularly: sodium bicarbonate, insulin (with glucose to prevent hypoglycemia), and albuterol Promote potassium excretion: loop diuretics, Kayexalate Removal of potassium: dialysis
Hypokalemia	Diabetes, diuretic use, drugs and toxins, profound gastrointestinal losses	If profound hypokalemia is accompanied by cardiac arrest, initiate urgent IV potassium replacement
Hypothermia	Alcohol abuse, burns, central nervous system disease, debilitated patient, drowning, drugs and toxins, endocrine disease, history of exposure, homelessness, extensive skin disease, spinal cord disease, and trauma	If hypothermia is severe (temperature <30°C [86°F]), defibrillation may be ineffective; initiate active internal rewarming with cardiopulmonary support; can consider extracorporeal rewarming If hypothermia is moderate (temperature 30-34°C [86-93.2°F]), actively rewarm during CPR
THE T'S		
Tension pneumothorax	Procedural complication, mechanical ventilation complication, pulmonary disease with "air leak" (including asthma, chronic obstructive pulmonary disease, and necrotizing pneumonia), thoracentesis, and trauma	Needle decompression followed by chest tube insertion or primary chest tube insertion
Cardiac tamponade	Hemorrhage, malignancy, pericarditis, trauma, cardiac surgery, post–myocardial infarction	Administer fluids to increase cardiac preload (temporizing only); obtain bedside echocardiogram, if available Perform pericardiocentesis; immediate surgical intervention is appropriate if pericardiocentesis is unhelpful but cardiac tamponade is known or highly suspected
Toxins	Alcohol abuse, behavioral or metabolic presentation, classic toxicologic syndrome, psychiatric disease, depressed mental status of unclear etiology, medications in the home, history of depression/suicidality	Supportive care and toxin-directed therapies in consultation with a toxicologist
Thrombosis, pulmonary	Hospitalized patient, recent surgical procedure, peripartum, known risk factors for venous thromboembolism, history of venous thromboembolism, or prearrest presentation consistent with a diagnosis of acute pulmonary embolism, recent immobility or fractures	Administer fluids; augment with vasoactive medications as necessary Consider pulmonary vasodilators (e.g., inhaled nitric oxide) Consider systemic or site-directed thrombolytic therapy Consider mechanical thrombectomy Consider ECMO
Thrombosis, coronary	Known risk factors for myocardial infarction (congenital heart disease, family history of sudden cardiac death)	Consider fibrinolytic therapy Consider percutaneous coronary intervention

Adapted from Kleinman ME, Chameides L, Schexnayder SM, et al. Part 14: Pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18 Suppl 3):S876-S908.

exchange, and then returned to the body via either a vein (venovenous or VV-ECMO) or an artery (venoarterial or VA-ECMO). VV-ECMO is typically used in patients with refractory respiratory failure who require ECMO for gas exchange but continue to rely on their native cardiac function for cardiac output. VA-ECMO is used for patients with shock or cardiac failure, with or without concomitant respiratory failure, with the ECMO pump and circuit augmenting or replacing native cardiac output. The processes of determining ECMO candidacy, performing ECMO cannulation, maintaining ECMO circuit integrity, and caring for critically ill children on ECMO are

Table 79.7 Medications to Maintain Cardiac Output and for Postarrest Stabilization*

MEDICATION	DOSE RANGE	COMMENT
Dobutamine	2-20 µg/kg/min IV/IO	Inotrope, chronotrope, vasodilator
Dopamine	2-20 µg/kg/min IV/IO	Inotrope, chronotrope, vasodilator at low doses, vasoconstrictor at high doses
Epinephrine	0.01-1 µg/kg/min IV/IO	Inotrope, chronotrope, vasodilator at low doses, vasoconstrictor at medium and high doses
Milrinone	50 µg/kg IV/IO over 10-60 min then 0.25-0.75 µg/kg/min	Inodilator, lusitrope, vasodilator
Norepinephrine	0.01-1 µg/kg/min	Vasopressor; weak inotrope

*Alternative formula for calculating an infusion: Infusion rate (mL/hr) = [weight (kg) × dose (µg/kg/min) × 60 (min/hr)]/concentration µg/mL).
Data from Kleinman ME, Brennan EE, Goldberger ZD, et al. Part 5: Adult Basic Life Support and Cardiopulmonary Resuscitation Quality: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2015;132(18 Suppl 2):S414-S435.

complex; ECMO is thus performed only at centers with appropriate expertise and equipment.

Extracorporeal support can be employed as a rescue therapy for refractory cardiac arrest. Extracorporeal CPR (ECPR), which involves cannulating and placing a patient on VA-ECMO while CPR is in progress, has been successfully used in children. Its efficacy has been best demonstrated in hospitalized children with underlying cardiac disease; AHA guidelines therefore state that it can be considered for children "with cardiac diagnoses who have IHCA in settings with existing ECMO protocols, expertise, and equipment." In addition, ECPR has been employed in patients with noncardiac etiologies of cardiopulmonary arrest who are not responding to standard resuscitation protocols.

Post–Cardiac Arrest Care

After resuscitation from cardiac arrest, patients are at risk for developing **post-cardiac arrest syndrome (PCAS)**. PCAS is composed of post–cardiac arrest brain injury, myocardial dysfunction, systemic ischemia-reperfusion response, and persistence of preexisting pathophysiology and can last for days to weeks after the cardiac arrest. Primary brain injury occurs due to hypoxia and ischemia during the no-flow (pre-CPR) and low-flow (during CPR) periods. Secondary brain injury occurs during the postarrest period. Signs and symptoms of brain injury are encephalopathy, seizures, cerebral edema, and autonomic dysfunction. Myocardial dysfunction can present as hypotension, depressed left or right ventricular systolic or diastolic function, arrhythmias, or pulmonary edema. The systemic ischemia-reperfusion response is a "sepsis-like" syndrome and has clinical findings of hyperglycemia, coagulopathy, hypovolemia, fever, and multisystem organ dysfunction. These three components combined with the precipitant that caused the arrest (e.g., septic shock or PARDS) result in varied severity of PCAS ranging from minimal symptoms, with patients returning quickly to their neurologic baseline, to severe multisystem organ failure with high risk of repeat cardiac arrest.

To address this clinical spectrum, it is important to be deliberate and vigilant in caring for the postarrest patient. Thus close postarrest observation in an intensive care unit, where the child can receive ongoing multiorgan system assessments and support, is critical. To prevent secondary brain injury, which occurs during the postarrest period, clinicians should monitor for, prevent, and treat PCAS. Hypotension is common and can lead to organ hypoperfusion. Clinicians should frequently monitor blood pressure and should do so continuously with an arterial catheter if appropriate resources are available. IV fluids and vasoactive agents such as epinephrine or norepinephrine should be used to maintain a blood pressure greater than the fifth percentile for age. Clinicians should be proactive and not wait for hypotension to occur. Rather, they should be prepared with fluids, vasoactive infusions, and clearly defined postarrest blood pressure targets. Continuous arterial blood pressure monitoring can help the provider determine the need for, and response to, inotropic and chronotropic medications (Table 79.7).

Hyperoxia (Pao_2 >300) and hypoxemia after cardiac arrest should be prevented because both can worsen secondary brain injury. Clinicians should wean supplemental oxygen after ROSC, targeting a saturation of 94–99%. In most cases, weaning supplemental oxygen when patients are saturating 100% is not harmful. For patients with hypoxemia, clinicians may need to try alternative ventilator strategies if supplemental oxygen is insufficient to achieve a saturation above 94% or higher.

Fever is common after cardiac arrest and may worsen secondary brain injury. **Targeted temperature management (TTM)** is performed with an active temperature control device and should be used for children postarrest who do not return to their neurologic baseline. Because there is no difference in survival or neurologic outcomes between patients who receive TTM 33°C (32-34°C [89.6-91.4°F]) and patients who receive TTM 36.8°C (98.2°F) (36-37.5°C [96.8-99.5°F]), either can be selected. Patients should have continuous core temperature monitoring and receive sedation and analgesics to prevent discomfort. If shivering occurs, patients should be treated with a sedative or neuromuscular blockade. Hyperthermia must be avoided.

Seizures are common after cardiac arrest and often are nonconvulsive and therefore can only be detected on an EEG. It is unclear if treatment improves outcomes; however, antiseizure medications can be administered for convulsive and nonconvulsive seizures.

Most care is supportive, but close monitoring for organ injury that can be treated (e.g., coagulopathy or adrenal insufficiency) or that may require modification of therapies (e.g., medication dose adjusting in patients with acute kidney injury) should be considered. Survivors of cardiac arrest can have long-standing neurologic, cognitive, physical, and quality-of-life deficits. Clinicians should refer children for ongoing evaluation and assessments.

Communication with the patient's family is an essential element of postarrest care, as it is for the care of any acutely ill or injured child. The family should be thoroughly briefed on the elements of the resuscitation performed, the child's condition, and ongoing medical concerns, uncertainties, or issues. The provider should be available to answer the family's questions, clarify information, and provide comfort. Other support staff, including social workers and chaplains, should be contacted, as the family wishes, to provide additional support and comfort. For situations in which the resuscitation is ongoing, it is recommended that the provider make every effort possible to have the family present at the bedside, if they wish. Family presence during CPR or other emergency resuscitative efforts, even if the child dies, is associated with a more positive medical experience than if they are excluded. In situations where the child is critically ill but stable, the family should be brought to the bedside as soon as the healthcare team deems it safe and appropriate (see Chapter 8).

PROCEDURES

Vascular Access

Venous Access

Veins suitable for cannulation are numerous, but there is considerable anatomic variation from patient to patient. In the upper extremities, the *median antecubital vein,* located in the antecubital fossa, is often the largest and easiest to access. Many veins on the dorsum of the hand are also suitable for cannulation because they are often large and easily located, and their cannulation is generally well tolerated. The *cephalic vein* is usually cannulated at the wrist, along the forearm, or at the elbow. The *median vein* of the forearm is also suitable as it lies along a flat surface of the forearm. In the lower extremity, the *great saphenous vein,* located just anterior to the medial malleolus, is accessible in most patients. The dorsum of the foot usually has a large vein in the midline, passing across the ankle joint, but catheters are difficult to maintain in

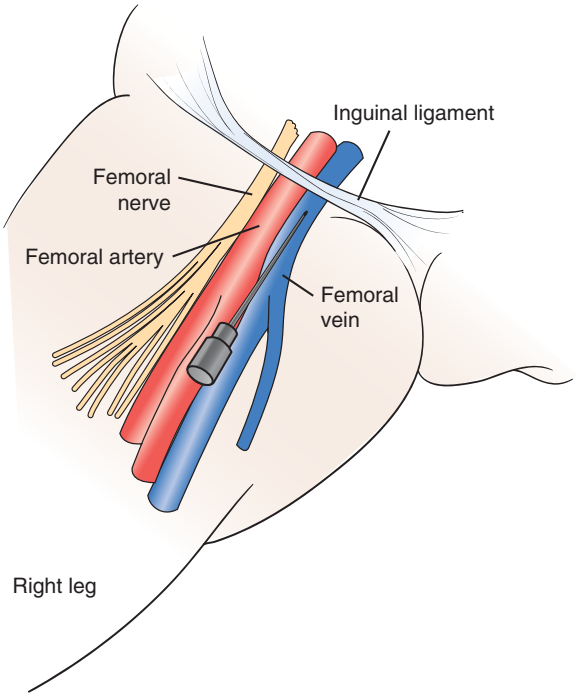

Fig. 79.17 Approach to the femoral vein. The patient is flat and supine, with the thigh slightly abducted and externally rotated. The introducer needle enters the skin 1-2 cm distal to the inguinal ligament and 0.5-1 cm medial to the pulse of the femoral artery. Remember the lateral to medial mnemonic NAVEL for nerve, artery, vein, empty space, and lymphatics. (*From Edwards LR, Malone MP, Prodham P, Schexnayder SM. Pediatric vascular access and centeses. In: Zimmerman JJ, Rotta AT, eds. Fuhrman & Zimmerman's Pediatric Critical Care, 6th ed. Philadelphia: Elsevier; 2022: Fig. 14.6, p. 102.*)

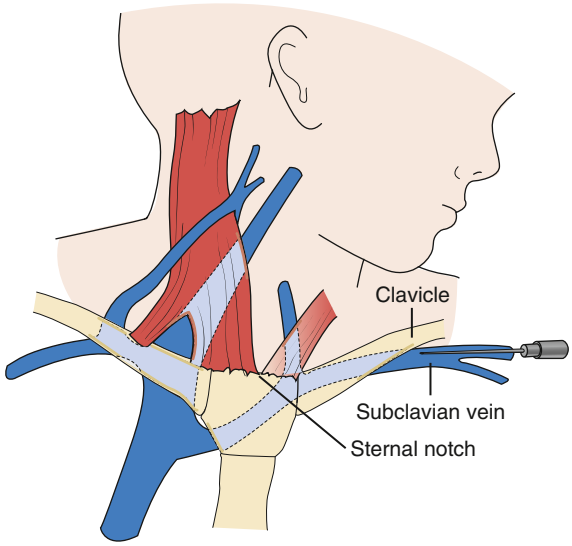

Fig. 79.19 Approach to the subclavian vein. The patient is supine, in slight Trendelenburg position, with a small roll along the spine between the shoulders. The needle enters the skin at the junction of the lateral and middle thirds of the inferior clavicle and is directed toward the suprasternal notch, passing along the inferior edge of the clavicle. (*From Edwards LR, Malone MP, Prodham P, Schexnayder SM. Pediatric vascular access and centeses. In: Zimmerman JJ, Rotta AT, eds. Fuhrman & Zimmerman's Pediatric Critical Care, 6th ed. Philadelphia: Elsevier: 2022: Fig. 14.5, p. 102.*)

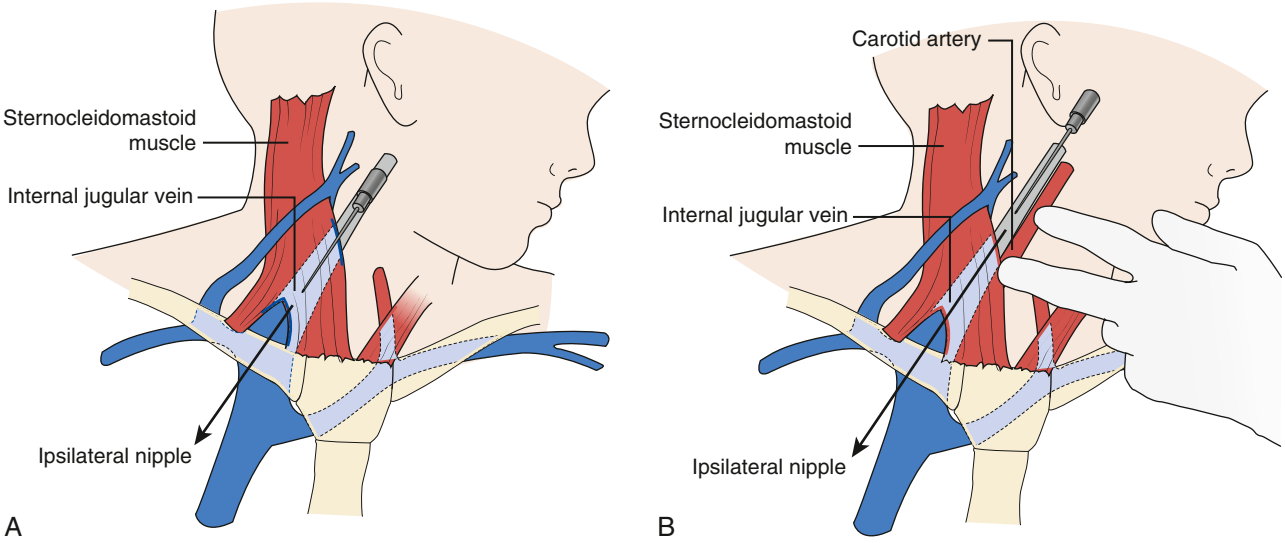

Fig. 79.18 Approaches to the internal jugular vein. The patient is supine, in slight Trendelenburg position, with the neck extended over a shoulder roll and the head rotated to the contralateral side. **A,** Middle approach: The introducer needle enters the skin at a 30-degree angle at the apex of the triangle formed by the heads of the sternocleidomastoid muscle and clavicle, directing it toward the ipsilateral nipple. **B,** Anterior approach: The carotid pulse is palpated and may be slightly retracted medially. The introducer needle enters along the anterior margin of the sternocleidomastoid, about halfway between the suprasternal notch and mastoid process, while being directed toward the ipsilateral nipple. (*Modified from Edwards LR, Malone MP, Prodham P, Schexnayder SM. Pediatric vascular access and centeses. In: Zimmerman JJ, Rotta AT, eds. Fuhrman & Zimmerman's Pediatric Critical Care, 6th ed. Philadelphia: Elsevier; 2022: Fig. 14.4, p. 101.*)

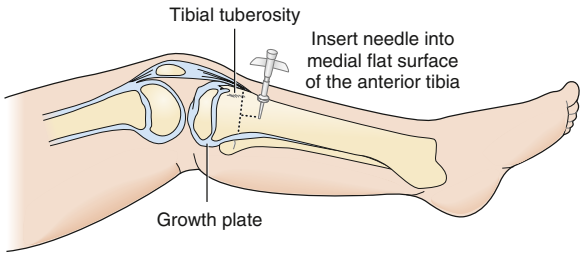

Fig 79.20 Insertion of the intraosseous needle into the anterior tibia. *(From Edwards LR, Malone MP, Prodham P, Schexnayder SM. Pediatric vascular access and centeses. In: Zimmerman JJ, Rotta AT, eds. Fuhrman & Zimmerman's Pediatric Critical Care, 6th ed. Philadelphia: Elsevier; 2022: Fig. 14.2, p. 95.)*

this vein because dorsiflexion tends to dislodge them. A second large vein on the lateral side of the foot, running in the horizontal plane, usually 1-2 cm dorsal to the lower margin of the foot, is preferable. The most notable scalp veins are the *superficial temporal* (just anterior to the ear) and *posterior auricular* (just behind the ear).

Deeper and larger central veins can provide more reliable access for medications, nutritive solutions, and blood sampling than peripheral venous lines. Placement of central access should be considered in the patient with difficult peripheral access where IVs may be challenging to obtain or may last for brief periods with increased risk of infiltration; when a patient is critically ill requiring numerous medications and needs stable access; when a patient requires IV vasoactive medications for more than a brief period; if long-term medications need to be administered in the hospital or at home; or if administered agents are vascular irritants (IV nutrition, electrolyte infusions, certain antibiotics). Central veins may be reached by percutaneous cannulation or surgical exposure. In infants and young children, the *femoral vein* or *internal jugular vein* are often the easiest to access and cannulate, but the subclavian veins may also be used (Figs. 79.17, 79.18, and 79.19). Peripherally inserted central catheters (PICCs) can be placed for longer-term access through the upper or lower extremity to administer medications or IV nutrition and can be used at home. With the expansion of bedside ultrasound availability and expertise, central venous catheters should be placed under ultrasound guidance to improve first-pass success and minimize the risk of complications.

Intraosseous Access

IO needles (for intramedullary venous plexus access) are specialized, rigid, large-bore needles. IO cannulation is recommended for patients in whom IV access proves difficult or unattainable in an emergent setting, even in older children. If venous access is not available within approximately 1 minute in a child with cardiopulmonary arrest, an IO needle should be placed in the anterior proximal tibia (with care taken to avoid traversing the epiphyseal plate) or other approved site. The needle should penetrate the anterior layer of compact bone, and its tip is advanced into the spongy interior of the bone (Fig. 79.20). Commercially available IO kits frequently include drills that mitigate the complications of needle placement associated with manual placement. All medications, blood products, and fluids may be administered through the IO route, including medications required for emergency resuscitation. Laboratory values can be sampled, although a complete blood count will be unreliable. Complications are uncommon but may include osteomyelitis with prolonged infusions, tibial fracture, and infiltration of fluids with dislodgement.

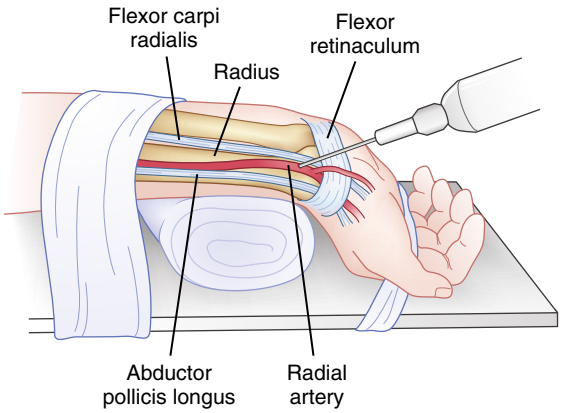

Fig. 79.21 Radial artery anatomy and cannulation.

Arterial Access

Arterial access is indicated when care providers need frequent blood sampling, particularly to assess adequacy of oxygenation, ventilation, or acid-base balance, or continuous blood pressure monitoring. The *radial artery,* the most commonly cannulated artery, lies on the lateral side of the anterior wrist, just medial to the styloid process of the radius (Fig. 79.21). The *ulnar artery,* just lateral to the tendon of the flexor carpi ulnaris, is used less often because of its proximity to the ulnar nerve. Useful sites in the lower extremity, particularly in neonates and infants, are the *dorsalis pedis artery,* on the dorsum of the foot between the tendons of the tibialis anterior and the extensor hallucis longus, and the *posterior tibial artery,* posterior to the medial malleolus. Arterial catheters require special care for insertion and subsequent management. Clinicians should monitor for signs of decreased perfusion distal to catheter placement.

NONVASCULAR EMERGENCY PROCEDURES

Thoracentesis and Chest Tube Placement

Thoracentesis is the placement of a needle or catheter into the pleural space to evacuate fluid, blood, or air. Most insertions are performed in one of the intercostal spaces between the fourth and sixth ribs in the plane of the midaxillary line. After appropriate systemic and local anesthesia/sedation, a needle (and later the chest tube) that enters the pleural space should penetrate the intercostal space by passing over the superior edge of the lower rib, because there are larger vessels along the inferior edge of the rib. Ideally, the chest tube should lie *anterior* in the pleural space for air accumulation and *posterior* for fluid accumulation. A radiograph must be obtained to verify chest tube placement and evacuation of the pleural space.

Pericardiocentesis

When fluid, blood, or gas accumulates in the pericardial sac, the heart may become compressed and may be unable to fill/empty with normal volumes of blood, leading to diminished cardiac output (i.e., pericardial tamponade with obstructive shock). The cardinal signs of such a restrictive pericardial effusion are tachycardia and hypotension, generally with a narrowed pulse pressure. Pericardiocentesis includes needle aspiration of the pericardial sac, often followed by the placement of a catheter for continuous drainage. As with thoracentesis, chest radiography should be done to confirm catheter location and to evaluate for any complications, such as pneumothorax or hemothorax. Pericardiocentesis may be performed with echocardiography.

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Chapter 80

Acute Care of Multiple Trauma

Courtney W. Mangus, Howard I. Pryor II, and Bruce L. Klein

EPIDEMIOLOGY

Injury is a leading cause of death and disability in children throughout the world (see Chapter 14). Deaths represent only a small fraction of the total trauma burden. Approximately 140,000 children were treated in U.S. trauma centers in 2016 for serious injury. Many survivors of trauma have permanent or temporary functional limitations. Motor vehicle–related injuries and falls rank among the top 15 causes of disability-adjusted life years in children worldwide. In childhood, blunt trauma predominates, accounting for the majority of injuries. In adolescence, penetrating trauma increases in frequency, accounting for approximately 13% of injuries, and penetrating trauma secondary to a firearm is associated with a high case fatality rate of 11%.

REGIONALIZATION AND TRAUMA TEAMS

Morbidity and mortality rates have decreased in geographic regions with comprehensive, coordinated trauma systems. Treatment at designated trauma centers is associated with decreased mortality. At the scene of injury, paramedics should administer necessary advanced life support and perform **triage** (Fig. 80.1). It is usually preferable to bypass local hospitals and rapidly transport a seriously injured child directly to a pediatric trauma center (or a trauma center with pediatric commitment). *Children have lower mortality rates, lower complication rates, and fewer operative interventions after severe blunt trauma when they are treated in designated pediatric trauma centers or in hospitals with pediatric intensive care units.*

When the receiving emergency department (ED) is notified before the child's arrival, the trauma team should be mobilized in advance. Each member has defined tasks. A senior surgeon (surgical coordinator) or an emergency physician leads the team. Team compositions vary somewhat from hospital to hospital; Figure 80.2 shows the model used at the Johns Hopkins Hospital Bloomberg Children's Center (Baltimore, MD). Consultants, especially neurosurgeons and orthopedic surgeons, must be promptly available, and the operating room staff should be alerted.

Physiologic status and mechanism of injury are used for field triage and to determine whether to activate the trauma team. More importance should be placed on physiologic compromise and less on mechanism of injury. Scoring scales such as the Abbreviated Injury Scale (AIS), Injury Severity Score (ISS), Pediatric Trauma Score (Table 80.1), and Revised Trauma Score use these parameters to predict patient outcome. The AIS and ISS are used together. First, the AIS is used to numerically score injuries—as 1 minor, 2 moderate, 3 serious, 4 severe, 5 critical, or 6 probably lethal—in each of six ISS body regions: head/neck, face, thorax, abdomen and pelvic contents, extremities/bony pelvis, and external. The ISS is the sum of the squares of the highest three AIS region scores.

ATLS: SYSTEMATIC EVALUATION OF THE INJURED PATIENT

The American College of Surgeons (ACS) endorses a systematic approach to trauma patients known as **Advanced Trauma Life Support** (ATLS). ATLS is accepted as the standard of care for the initial assessment of injured patients and is used internationally. The approach is centered on a standardized patient evaluation that prioritizes identification and management of injuries in a specific order that addresses their immediate risk to life. ATLS principles are detailed here and include performance of the primary survey with initial adjuncts followed by the secondary survey.

PRIMARY SURVEY

During the primary survey, the trauma team quickly assesses and treats life-threatening injuries (see also Chapter 79). The principal causes of death shortly after trauma are airway obstruction, respiratory insufficiency, shock from hemorrhage, and central nervous system (CNS) injury. The primary survey addresses the **ABCDEs**: Airway, Breathing, Circulation, Disability/Neurologic Deficit, and Exposure of the patient and control of the Environment.

Airway

Optimizing oxygenation and ventilation, while protecting the cervical spine (C-spine) from potential further injury, is of paramount importance. Airway obstruction manifests as snoring, gurgling, hoarseness, stridor, and/or diminished breath sounds even with apparently good respiratory effort. Children are more likely than adults to have airway obstruction because of their smaller oral and nasal cavities, proportionately larger tongues, more tonsillar and adenoidal tissue, higher and more anterior glottic opening, and narrower larynx and trachea. Obstruction is common in patients with severe head injuries, partly because of decreased muscle tone, which allows the tongue to fall posteriorly and occlude the airway. With trauma, obstruction can also result from fractures of the mandible or facial bones, secretions such as blood or vomit, crush injuries of the larynx or trachea, and foreign body aspiration.

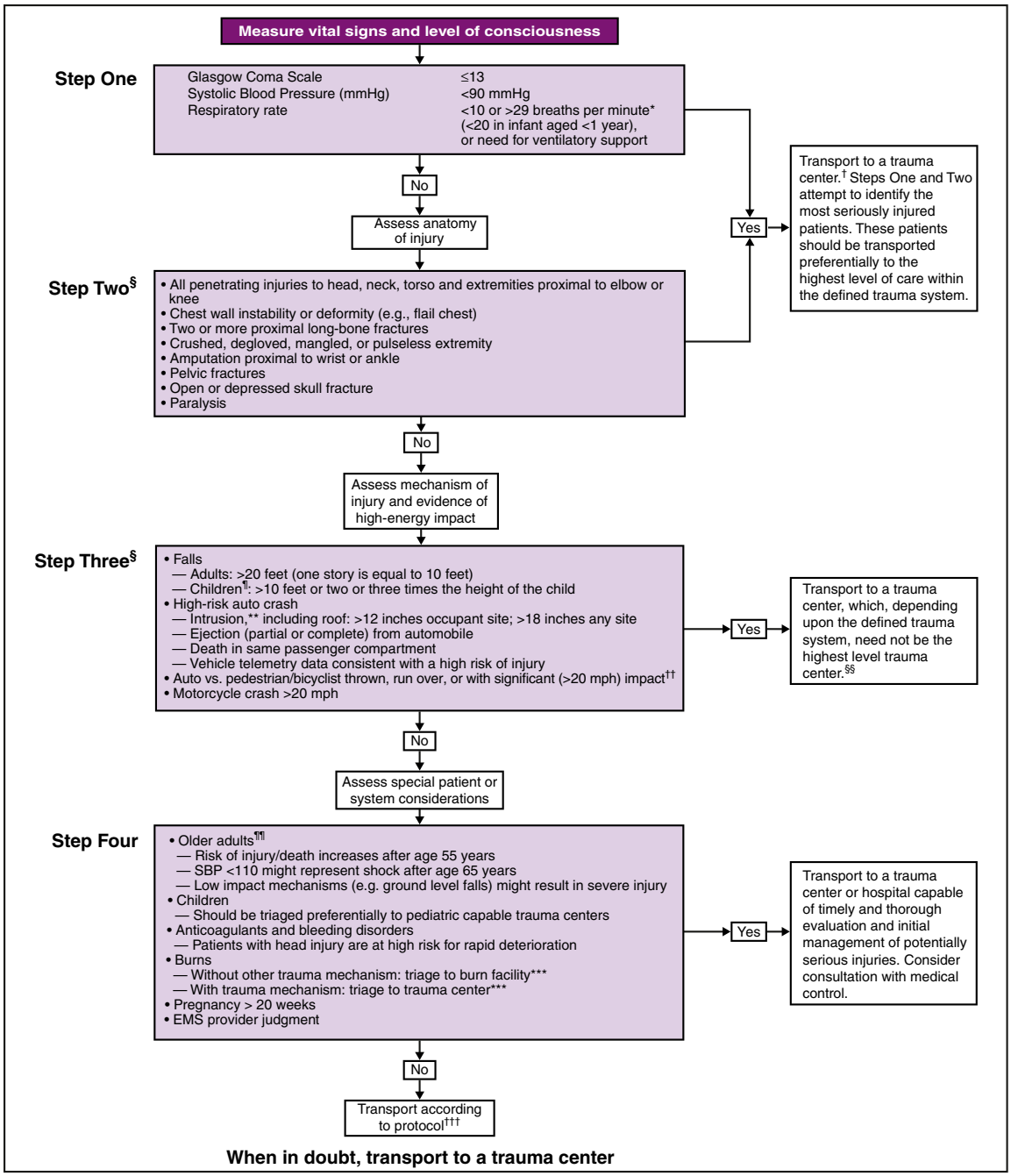
If it is necessary to open the airway, a jaw thrust without head tilt is recommended. This procedure minimizes cervical spine motion. In an unconscious child, an oropharyngeal airway may be inserted to prevent posterior displacement of the mandibular tissues. A semiconscious child will gag with an oropharyngeal airway but may tolerate a nasopharyngeal airway. A nasopharyngeal airway is contraindicated when there is significant nasal trauma or possibility of cribriform plate fracture. If these maneuvers plus suctioning do not clear the airway, oral endotracheal intubation is indicated. When endotracheal intubation proves difficult, a laryngeal mask airway can be used as a temporary alternative. A laryngeal mask airway consists of a tube with an inflatable cuff that rests above the larynx and thus does not require placement of the tube into the trachea. Other extraglottic devices that can be blindly inserted in a difficult airway scenario include the Combitube and King laryngeal airway tube; these devices are considered temporary and should be exchanged for a definitive airway as soon as possible. Video-assisted laryngoscopy or the use of a bougie can also be particularly helpful in the management of a difficult airway. Emergency cricothyrotomy is needed in <1% of trauma victims.

Breathing

The physician assesses breathing by counting the respiratory rate; visualizing chest wall motion for symmetry, expansion, and accessory muscle use; and auscultating breath sounds in both axillae. Pulse oximetry and continuous waveform capnography monitoring should also be used; however, they may be less reliable in patients with shock. If ventilation is inadequate, bag-valve-mask ventilation with 100% oxygen must be initiated immediately, followed by endotracheal intubation. End-expiratory carbon dioxide (CO_2) detectors or capnography help verify accurate tube placement.

Head trauma is the most common cause of respiratory insufficiency. An unconscious child with severe head injury may have a variety of breathing abnormalities, including Cheyne-Stokes respiration, slow irregular breaths, and apnea. A child with significant neurologic impairment will require endotracheal intubation and mechanical ventilation.

Although less common than a pulmonary contusion, tension pneumothorax and massive hemothorax are immediately life threatening (Tables 80.2 and 80.3). A **tension pneumothorax** occurs when air accumulates under pressure in the pleural space. The adjacent lung is compacted; the mediastinum is pushed toward the opposite hemithorax; and the heart, great vessels, and contralateral lung are compressed



* The upper limit of respiratory rate in infants is >29 breaths per minute to maintain a higher level of overtriage for infants.
† Trauma centers are designated Level I-IV. A Level I center has the greatest amount of resources and personnel for care of the injured patient and provides regional leadership in education, research, and prevention programs. A Level II facility offers similar resources to a Level I facility, possibly differing only in continuous availability of certain subspecialties or sufficient prevention, education, and research activities for Level I designation; Level II facilities are not required to be resident or fellow education centers. A Level III center is capable of assessment, resuscitation, and emergency surgery, with severely injured patients being transferred to a Level I or II facility. A Level IV trauma center is capable of providing 24-hour physician coverage, resuscitation, and stabilization to injured patients before transfer to a facility that provides a higher level of trauma care.
§ Any injury noted in Step Two or mechanism identified in Step Three triggers a "yes" response.
¶ Age <15 years.
** Intrusion refers to interior compartment intrusion, as opposed to deformation which refers to exterior damage.
†† Includes pedestrians or bicyclists thrown or run over by a motor vehicle or those with estimated impact >20 mph with a motor vehicle.
§§ Local or regional protocols should be used to determine the most appropriate level of trauma center within the defined trauma system; need not be the highest-level trauma center.
¶¶ Age >55 years.
*** Patients with both burns and concomitant trauma for whom the burn injury poses the greatest risk for morbidity and mortality should be transferred to a burn center. If the nonburn trauma presents a greater immediate risk, the patient may be stabilized in a trauma center and then transferred to a burn center.
††† Patients who do not meet any of the triage criteria in Steps One through Four should be transported to the most appropriate medical facility as outlined in local EMS protocols.

Fig. 80.1 Algorithm showing guidelines for field triage of injured patients—United States, 2011. (*From Guidelines for Field Triage of Injured Patients: Recommendations of the National Expert Panel on Field Triage. MMWR. 2012;61:6.*)

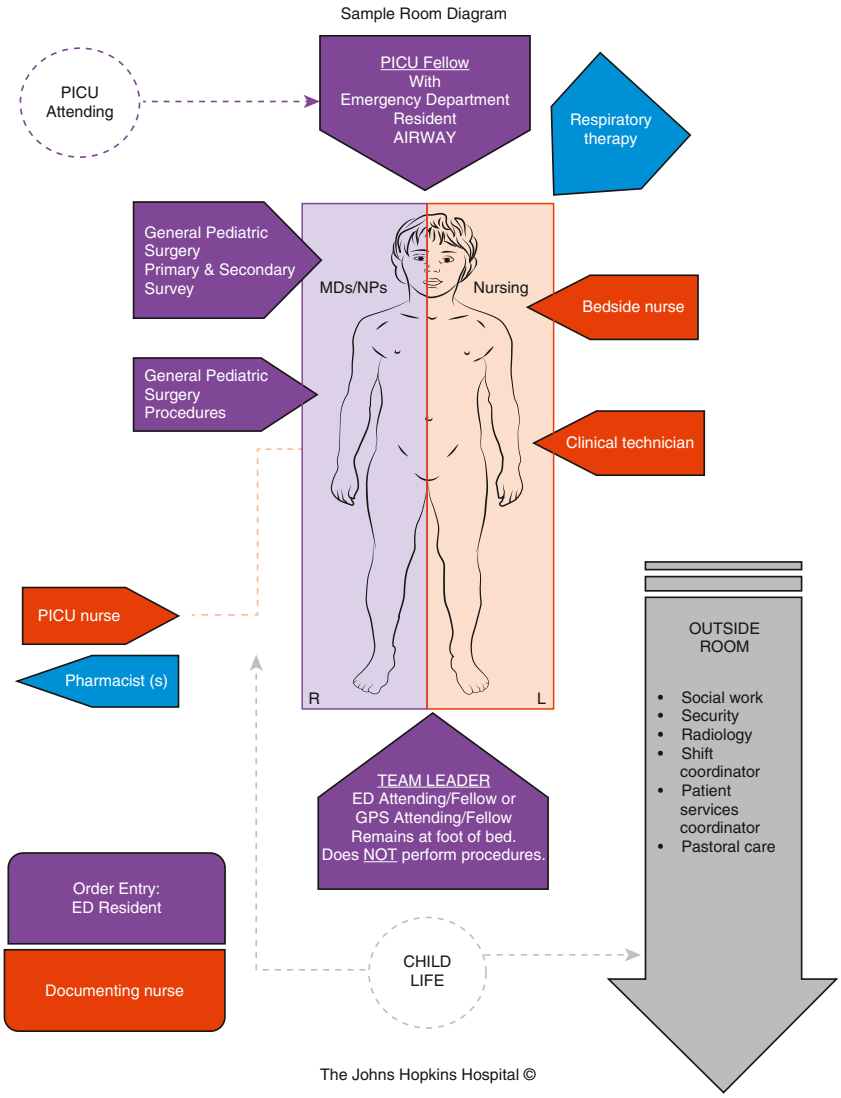


Fig. 80.2 Staff in the ED trauma bay at Johns Hopkins Hospital Bloomberg Children's Center. ED, Emergency department; NP, nurse practitioner; GPS, general pediatric surgery; PICU, pediatric intensive care unit. (*Courtesy The Johns Hopkins Hospital, Baltimore, Maryland.*)

Table 80.1 Pediatric Trauma Score*

COMPONENT	+2	+1	−1
Size	≥20 kg	10-20 kg	<10 kg
Airway	Normal	Maintainable	Unmaintainable
Systolic BP	≥90 mm Hg	50-90 mm Hg	<50 mm Hg
CNS	Awake	Obtunded/ LOC	Coma/ decerebrate
Open wound	None	Minor	Major/penetrating
Skeletal	None	Closed fracture	Open/multiple fractures
Sum total points			

*Children with a Pediatric Trauma Score ≤6 are at increased risk of mortality and morbidity.
BP, Blood pressure; CNS, central nervous system; LOC, loss of consciousness.
From Tepas JJ 3rd, Mollitt DL, Talbert JL, et al. The Pediatric Trauma Score as a predictor of injury severity in the injured child. *J Pediatr Surg.* 1987;22:14-18, Table 1, p. 15.

(see Chapter 461). Both ventilation and cardiac output are impaired. Characteristic findings include cyanosis, tachypnea, retractions, asymmetric chest rise, contralateral tracheal deviation, diminished breath sounds on the ipsilateral (more than contralateral) side, and signs of shock. When suspected, a tension pneumothorax should be treated before obtaining chest radiographs. Needle thoracentesis, followed by thoracostomy tube insertion, is diagnostic and lifesaving. **Hemothorax** results from injury to the intercostal vessels, lungs, heart, or great vessels. When ventilation is adequate, volume resuscitation should begin before evacuation, because a large volume of blood may drain through the chest tube, resulting in shock.

Circulation

Signs of **shock** include tachycardia; weak pulse; delayed capillary refill; altered mental status; and cool, mottled, or pale skin (see Chapter 85). The most common type of shock in trauma is *hypovolemic shock* caused by hemorrhage. Cardiac tamponade, which is a form of *obstructive shock,* occurs when blood or fluid accumulates in the pericardium. It may be suspected clinically with the classic findings of jugular venous distension, muffled heart sounds, and low blood pressure—collectively known as **Beck's triad**. Cardiac tamponade may be definitively diagnosed by ultrasound during a **focused assessment with sonography in**

Table 80.2 Differential Diagnosis of Immediately Life-Threatening Cardiopulmonary Injuries

	TENSION PNEUMOTHORAX	MASSIVE HEMOTHORAX	CARDIAC TAMPONADE
Breath sounds	Ipsilaterally decreased more than contralaterally	Ipsilaterally decreased	Normal
Percussion note	Hyperresonant	Dull	Normal
Tracheal location	Contralaterally shifted	Midline or shifted	Midline
Neck veins	Distended	Flat	Distended
Heart tones	Normal	Normal	Muffled

Modified from Cooper A, Foltin GL. Thoracic trauma. In: Barkin RM, ed. *Pediatric Emergency Medicine*, 2nd ed. St Louis: Mosby; 1997:325.

Table 80.3 Life-Threatening Chest Injuries

TENSION PNEUMOTHORAX
One-way valve leak from the lung parenchyma or tracheobronchial tree
Lung collapse with mediastinal and tracheal shift to the side opposite the leak
Compromises venous return and decreases ventilation of the other lung
Clinically, manifests as respiratory distress, unilateral absence of breath sounds, tracheal deviation, distended neck veins, tympany to percussion of the involved side, and cyanosis
Relieve first with needle aspiration, then with chest tube drainage

OPEN PNEUMOTHORAX (SUCKING CHEST WOUND)
Effect on ventilation depends on size

MAJOR FLAIL CHEST
Usually caused by blunt injury resulting in multiple rib fractures
Loss of bone stability of the thoracic cage
Major disruption of synchronous chest wall motion
Mechanical ventilation and positive end-expiratory pressure required

MASSIVE HEMOTHORAX
Must be drained with a large-bore tube
Initiate drainage only with concurrent vascular volume replacement

CARDIAC TAMPONADE
Beck's triad:
1. Decreased or muffled heart sounds
2. Jugular venous distention
3. Hypotension (with narrow pulse pressure)

Must be drained

Modified from Krug SE. The acutely ill or injured child. In: Behrman RE, Kliegman RM, eds. *Nelson Essentials of Pediatrics*, 4th ed. Philadelphia: Saunders; 2002:97.

trauma (FAST) examination or echocardiography. Cardiac tamponade is best managed by thoracotomy or pericardial window, although pericardiocentesis may be a necessary temporizing maneuver (see Table 80.3).

Early in shock, blood pressure remains normal because of compensatory increases in heart rate and peripheral vascular resistance (Table 80.4). Some individuals can lose up to 30% of blood volume before blood pressure declines. Notably, 25% of blood volume equals 20 mL/kg, which is only 200 mL in a 10-kg child. Loss of >40% of blood volume causes severe hypotension that, if prolonged, may be irreversible. Direct pressure should be applied to control external hemorrhage. When direct pressure does not control hemorrhage, a tourniquet should be applied to a proximal pressure point. Blind clamping of bleeding vessels, which risks damaging adjacent structures, is not advisable.

Cannulating a larger vein, such as an antecubital vein, is usually the quickest way to achieve intravenous (IV) access (see Chapter 79). A short, large-bore catheter offers less resistance to flow, allowing for more rapid fluid administration. Ideally, a second catheter should be placed within the first few minutes of resuscitation in a severely injured child. If IV access is not rapidly obtainable, an intraosseous (IO) needle should be inserted; all medications and fluids can be administered intraosseously (see Chapter 79). Other alternatives are central venous access using the Seldinger technique (e.g., in the femoral vein) and, rarely, surgical cutdown (e.g., in the saphenous vein). Ultrasonography may be employed to safely facilitate both peripheral IV placement and central venous catheter placement.

Traditionally, fluids are administered aggressively early in hemorrhagic shock to reverse and prevent further clinical deterioration. Isotonic crystalloid solution, such as lactated Ringer's or normal saline (20 mL/kg), should be infused rapidly. When necessary, repeated crystalloid boluses may be given. Most children are stabilized with administration of crystalloid solution alone; however, if the patient remains in shock after boluses totaling 40 mL/kg of crystalloid, packed red blood cells should be transfused. Massive transfusion protocols (including fresh-frozen plasma) should be initiated early to prevent coagulopathy, and tranexamic acid (TXA) should be considered. When shock persists despite these measures, exploratory surgery to stop internal hemorrhage is usually indicated. Emerging literature suggests modern trauma techniques for adults, including permissive hypotension, hemostatic resuscitation, and damage control surgery, confer similar benefits in children.

Disability/Neurologic Deficit

Neurologic status is briefly assessed by determining the level of consciousness and evaluating pupil size and reactivity. The level of consciousness can be classified using the mnemonic **AVPU**: Alert, responsive to Verbal commands, responsive to Painful stimuli, or Unresponsive. A **Glasgow Coma Scale** (GCS) or Pediatric GCS score (see Chapters 79 and 82) should be assigned to every child with significant head trauma or neurologic impairment. This scale assesses eye opening and motor and verbal responses. In the Pediatric GCS, the verbal score is modified for age. The GCS helps categorize neurologic disability, and serial measurements identify improvement or deterioration over time. Patients with GCS ≤8 should undergo endotracheal intubation and supportive mechanical ventilation. Importantly, the patient's pupil size/reactivity and ability to move extremities should be quickly assessed before administration of anticholinergics, sedatives, and paralytics in preparation for intubation.

The majority of pediatric blunt trauma deaths are accounted for by head injuries. Primary direct cerebral injury occurs within seconds of the event and is irreversible. Secondary injury is caused by subsequent anoxia or ischemia. *The goal is to minimize secondary injury by ensuring adequate oxygenation, ventilation, and perfusion and by maintaining normal cerebral perfusion pressure.* Focal hemorrhagic lesions (e.g., epidural or subdural hematomas) are less common but may require immediate neurosurgical intervention (Fig. 80.3).

Signs of increased intracranial pressure (ICP), including progressive neurologic deterioration and evidence of transtentorial herniation, must be treated immediately (see Chapter 82). Hyperventilation lowers the arterial partial pressure of carbon dioxide ($Paco_2$), resulting in cerebral vasoconstriction, reduced cerebral blood flow, and decreased

Table 80.4 Systemic Responses to Blood Loss in Pediatric Patients

SYSTEM	MILD BLOOD LOSS (<30%)	MODERATE BLOOD LOSS (30–45%)	SEVERE BLOOD LOSS (>45%)
Cardiovascular	Increased heart rate; weak, thready peripheral pulses; normal systolic blood pressure; normal pulse pressure	Markedly increased heart rate; weak, thready central pulses; peripheral pulses absent; low normal systolic blood pressure; narrowed pulse pressure	Tachycardia followed by bradycardia; central pulses very weak or absent; peripheral pulses absent; hypotension; narrowed pulse pressure (or undetectable diastolic blood pressure)
Central nervous	Anxiety; irritability; confusion	Lethargy; dulled response to pain	Coma
Skin	Cool, mottled; capillary refill prolonged	Cyanotic; capillary refill markedly prolonged	Pale and cold
Urine output	Low to very low	Minimal	None

Adapted from American College of Surgeons Committee on Trauma. *Advanced Trauma Life Support: Student Course Manual,* 10th ed. Chicago: American College of Surgeons; 2018:196.

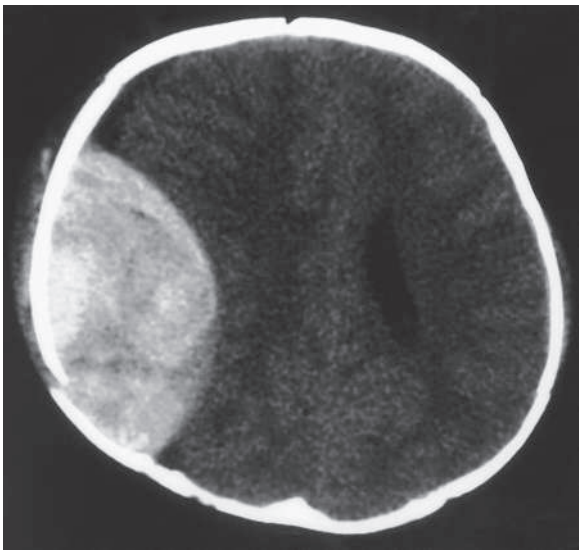


Fig. 80.3 Epidural hematoma. CT head scan from 7-mo-old female who, according to the history provided, did not wake up for her nightly feeding and began vomiting in the morning. The mother's friend reported that the infant had fallen from a chair the previous day. The CT scan shows a large epidural hematoma on the right and marked shift of the midline from right to left. The right lateral ventricle is compressed as a result of the mass effect, and the left lateral ventricle is slightly prominent. The infant underwent emergency surgical evacuation of the epidural hematoma and recovered uneventfully. (*From O'Neill JA Jr. Principles of Pediatric Surgery, 2nd ed. St Louis: Mosby; 2003:191.*)

ICP. Brief hyperventilation, targeting an end-tidal CO_2 goal of 30-35 mm Hg, remains an immediate option for patients with acute increases in ICP. Prophylactic hyperventilation, or vigorous or prolonged hyperventilation, is not recommended, because the consequent vasoconstriction may excessively decrease cerebral perfusion and oxygenation. Mannitol and hypertonic saline lower ICP and may improve survival. Because mannitol induces an osmotic diuresis, it can exacerbate hypovolemia and must be used cautiously. Hypertonic saline may be a more useful agent for control of increased ICP in patients with severe head injury. Neurosurgical consultation is mandatory and will dictate further management, including ICP monitoring and emergent neurosurgical interventions.

Exposure and Environmental Control

Full exposure of the patient occurs during the primary survey. Using trauma shears, all clothing should be removed to reveal any injuries. Cutting clothing is fastest and minimizes unnecessary patient movement. Children often arrive in the ED mildly hypothermic because of their higher body surface area–to–mass ratios. They can be warmed with use of radiant heat and heated IV fluids, as necessary. After a thorough physical exam, the patient should be covered with warmed blankets with close monitoring of body temperature.

Initial Adjuncts

While the primary survey is being performed, the patient will simultaneously be placed on a cardiac monitor, vitals obtained, and vascular access established. Fluid resuscitation can be initiated as soon as access is established. Initial laboratory work generally includes a complete blood count, electrolytes, blood urea nitrogen, creatinine, liver function tests, lipase, lactate, blood gas, coagulation studies, type and cross match, and urinalysis. Per ATLS, portable (single, anterior-posterior view) radiographs of the chest and pelvis should be obtained to screen for life-threatening injury and identify potential causes of hemorrhage (e.g., pelvic fracture, hemothorax, great vessel injury as suggested by a widened mediastinum). Finally, a FAST exam should be performed at the bedside to assess for the presence of free fluid (blood) and guide resuscitation.

FAST Exam

The FAST exam and extended FAST (eFAST) are other adjuncts to the initial trauma survey. This bedside ultrasound can be performed by any trained member of the trauma team to assess for the presence of blood or free fluid in the intraperitoneal, pericardial, or pleural space. The exam assesses four windows: the right upper quadrant abdominal view, the left upper quadrant abdominal view, the suprapubic view, and the subxiphoid cardiac view. The eFAST adds additional views of bilateral lungs to assess for the absence of lung sliding, which is indicative of a pneumothorax. In addition to detection of hemoperitoneum, the eFAST can identify findings that may require emergent management in an unstable patient—such as a pneumothorax requiring needle decompression or a large pericardial effusion requiring pericardiocentesis.

Although the FAST examination helps detect hemoperitoneum, the variably low sensitivity of this test in children suggests that it should not be used alone to exclude intraabdominal injury in patients with a moderate to high pretest probability for injury (e.g., a patient with elevated serum lipase or transaminases). A positive FAST exam for hemoperitoneum requires further investigation. The FAST exam is most clinically useful in patients who have blunt trauma and are hemodynamically unstable or in patients who require immediate operative intervention for nonabdominal injuries, because in these cases the performance of a CT scan will delay emergency surgery.

SECONDARY SURVEY

During the secondary survey, the trauma team completes a thorough, head-to-toe physical examination to assess for additional injuries. In critically ill or hemodynamically unstable patients, emergent interventions may delay the secondary survey until the patient has been stabilized.

Head Trauma

Initial management of traumatic brain injuries is discussed earlier. The secondary survey of the head should identify and document injuries,

including scalp hematomas and lacerations. The skull and face should be carefully palpated to assess for possible fractures. Findings suggestive of basilar skull fractures include bruising around the eyes ("raccoon eyes"), bruising over the mastoid process (Battle sign), and blood behind the tympanic membrane (hemotympanum). The eyes should be assessed for conjunctival hemorrhages, hyphemas, and corneal injuries. Limitation in extraocular movements may suggest orbital fractures with muscle entrapment. The nares should be inspected for bleeding and presence of a nasal septal hematoma, which must be evacuated urgently to prevent permanent disfigurement. The mouth should be assessed for injuries to the tongue, teeth, gums, palate, and oropharynx; normal jaw mobility should be ensured. Patients with suspected head or facial injuries will typically undergo CT of the head, orbits, and/or maxillofacial region.

Spinal Trauma

Spinal Immobilization

Initially, spinal injury should be suspected in any child sustaining multiple blunt trauma. To prevent further spinal injury, paramedics have traditionally been taught to immobilize the C-spine in neutral position with a stiff collar, head blocks, and tape or cloth placed across the forehead. To immobilize the rest of the spine, the child is typically placed on a rigid backboard, and straps or tape are placed across the torso and thighs to restrain them. Care should be taken to continue spinal immobilization during initial evaluation and resuscitation until spinal injury can be excluded (see Chapter 81).

C-Spine Trauma

Cervical spine injuries occur in <3% of children with blunt trauma—with the risk being substantially higher in those with GCS scores ≤8—but they are associated with significant mortality and morbidity (see Chapter 81). Bony injuries occur mainly from C1 to C4 in children younger than 8 years. In older children, they occur equally in the upper and lower cervical spine. The mortality rate is significantly higher in patients with upper C-spine injuries, and ~30% of all patients with C-spine injuries have permanent neurologic deficits.

Evaluation

Evaluation begins with a detailed history and neurologic examination. Identifying the mechanism of injury helps in estimating the likelihood of a spinal injury. Both the patient and the paramedic should be asked whether any neurologic symptoms or signs, such as weakness or abnormal sensation, were present before arrival in the ED. The spine should then be examined while maintaining immobilization. If no other distracting injuries are present (e.g., a displaced femur fracture), the collar can be carefully removed by one provider while a second provider manually stabilizes the neck. The C-spine should be palpated to assess for tenderness or step-offs. If the patient has neck pain, has neurologic symptoms, or is unable to participate in the exam, the collar should be replaced immediately. To assess the thoracic and lumbar spine, multiple providers are required to log-roll the patient and maintain spinal immobilization. A third provider will palpate the spine, assess for cutaneous injuries, and evaluate rectal tone. Before rolling the patient back to the supine position, the backboard must be removed to prevent further injury or patient discomfort.

Whenever the history, physical examination, or mechanism of injury suggests a spinal injury, imaging must be obtained after initial resuscitation. Depending on clinical suspicion, mechanism of injury, and the patient's symptoms and physiologic status, the provider may elect either radiography, CT, or MRI as the initial imaging modality.

The **National Emergency X-Radiography Utilization Study (NEXUS)** cervical spine rule helps identify low-risk patients who may not require radiographs (Table 80.5). The standard series of plain radiographs includes lateral, anteroposterior (AP), and odontoid views. Some centers use C-spine CT as the primary diagnostic tool, particularly in patients with abnormal GCS scores or significant injury mechanisms, recognizing that CT is more sensitive in detecting bony injury than plain radiographs. CT is also helpful if an odontoid fracture is suspected, because young children typically do not cooperate enough to obtain an open-mouth (odontoid) radiographic view. Use of cervical spine CT scan must be balanced with the knowledge that CT exposes thyroid tissue to 90-200 times the amount of radiation from plain films.

Table 80.5 National Emergency X-Radiography Utilization Study (NEXUS) to Rule Out Cervical Spine Injury After Blunt Trauma

If ***NONE*** *of the following is present, the patient is at very low risk for clinically significant cervical spine injury:*

- Midline cervical tenderness
- Evidence of intoxication
- Altered level of alertness
- Focal neurologic deficit
- Distracting painful injury

Data from Hoffman JR, Mower WR, Wolfson AB, et al. Validity of a set of clinical criteria to rule out injury to the cervical spine in patients with blunt trauma. *N Engl J Med.* 2000;343:94-99; and Viccellio P, Simon H, Pressman BD, et al. A prospective multicenter study of cervical spine injury in children. *Pediatrics.* 2001;108:e20.

SCIWORA

In a child with neurologic symptoms and normal findings on C-spine plain radiographs and CT scan, **spinal cord injury without radiographic abnormalities (SCIWORA)** must be considered. MRI of the spine is indicated in a child with suspected SCIWORA and in the evaluation of children who remain obtunded.

Thoracic Trauma

Pulmonary contusions occur frequently in young children with blunt chest trauma. A child's chest wall is relatively pliable; therefore less force is absorbed by the rib cage and more is transmitted to the lungs. Respiratory distress may be noted initially or may develop during the first 24 hours after injury.

Rib fractures result from significant external force. They are noted in patients with more severe injuries and are associated with a higher mortality rate. Flail chest, which is caused by multiple rib fractures, is rare in children. Table 80.6 lists indications for operative management in thoracic trauma. (See Table 80.2 for the differential diagnosis of immediately life-threatening cardiopulmonary injuries.) Thoracic trauma can be investigated via chest radiograph or CT, depending on the patient's symptoms, physical exam findings, mechanism of injury, and index of suspicion for injury.

Abdominal Trauma

Liver and spleen contusions, hematomas, and lacerations account for the majority of intraabdominal injuries from blunt trauma. The kidneys, pancreas, and duodenum are relatively spared because of their retroperitoneal location. Pancreatic and duodenal injuries are more common after a bicycle handlebar impact or a direct blow to the abdomen.

Although a thorough examination for intraabdominal injuries is essential, achieving it often proves difficult. Misleading findings can result from gastric distention after crying or in an uncooperative toddler. Calm reassurance, distraction, and gentle, persistent palpation help with the examination. Important findings include distention, bruises, and tenderness. Specific symptoms and signs give insight into the mechanism of injury and the potential for particular injuries. Pain in the left shoulder may signify splenic trauma. A lap belt mark across the abdomen raises concern for bowel or mesentery injury. The presence of certain other injuries, such as lumbar spinal fractures and femur fractures, increases the likelihood of intraabdominal injury.

An abdominal (and pelvic) CT scan with IV contrast medium enhancement rapidly identifies structural abnormalities and is the preferred study in a stable child. A negative abdominal CT scan has been shown to have a negative predictive value (NPV) of 99.6%. It has excellent sensitivity and specificity for splenic (Fig. 80.4), hepatic (Fig. 80.5), and renal injuries, but is less sensitive for diaphragmatic, pancreatic, or intestinal injuries. Small amounts of free fluid or air or a mesenteric

Table 80.6 Indications for Operation in Thoracic Trauma

THORACOTOMY IMMEDIATELY OR SHORTLY AFTER INJURY
Massive continuing pneumothorax or large air leak from tracheobronchial injury (cannot expand lung and ventilate)
Cardiac tamponade
Open pneumothorax
Esophageal injury
Aortic or other vascular injury
Acute rupture of the diaphragm
DELAYED THORACOTOMY OR THORACOSCOPY
Chronic rupture of the diaphragm
Clotted hemothorax
Persistent chylothorax
Traumatic intracardiac defects
Evacuation of large foreign bodies
Chronic atelectasis from traumatic bronchial stenosis

Modified from O'Neill JA Jr. *Principles of Pediatric Surgery,* 2nd ed. St Louis: Mosby; 2003:157.

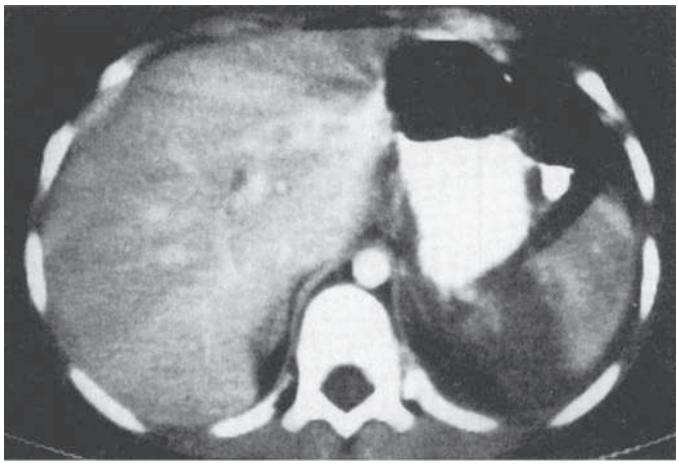


Fig. 80.4 Splenic rupture. CT scan with intravenous and gastrointestinal contrast enhancement shows an isolated splenic rupture that resulted from blunt trauma. This injury responded to nonoperative management, as do most splenic injuries. (*From O'Neill JA Jr. Principles of Pediatric Surgery, 2nd ed. St Louis: Mosby; 2003:166.*)

hematoma may be the only sign of an intestinal injury. Administration of an oral contrast agent is not routinely recommended for all abdominal CT scans, but it sometimes aids in identifying an intestinal, especially a duodenal, injury.

Nonoperative treatment has become standard for hemodynamically stable children with splenic, hepatic, and renal injuries from blunt trauma. The majority of such children can be treated nonsurgically. In addition to avoiding perioperative complications, nonoperative treatment decreases the need for blood transfusions and shortens hospital stay. When laparotomy is indicated, splenic repair is preferable to splenectomy.

Pelvic Trauma

Pelvic fractures in children are much less common than in adults, occurring in approximately 4% of children with more severe blunt trauma. Pelvic fractures are typically caused by high forces (e.g., high-speed motor vehicle crashes or pedestrian impacts) and are often associated with intraabdominal and/or vascular injuries. The pelvis itself

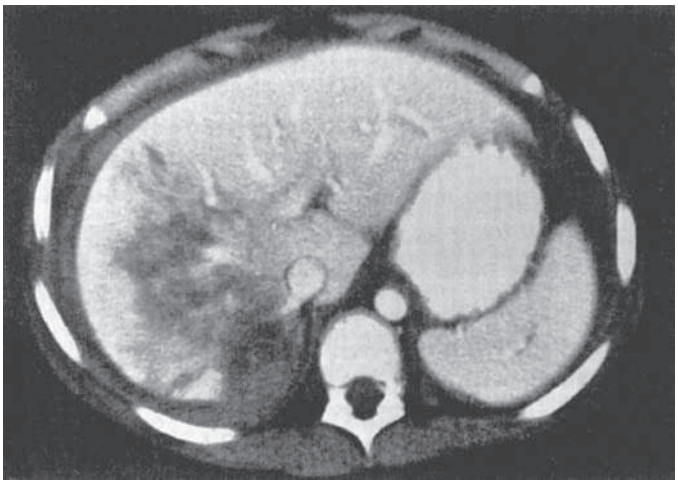


Fig. 80.5 Liver injury. CT scan performed after severe blunt injury of the abdomen shows a bursting injury of the liver. The patient was stable, and no operative intervention was required. The decision to perform surgery should be based on the patient's physiologic stability. (*From O'Neill JA Jr. Principles of Pediatric Surgery, 2nd ed. St Louis: Mosby; 2003:168.*)

forms a ring, and high-force impacts can lead to disruption of this ring. When the ring is disrupted in more than one location, such as the symphysis pubis and the sacroiliac joint, the ring can become unstable and displaced, potentially injuring large pelvic vessels and leading to massive blood loss. Catheter-directed embolization to control bleeding, performed by an interventional radiologist, may be required.

The pelvis should be assessed for stability by means of compression-distraction maneuvers. If instability is noted, immediate external fixation with a pelvis-stabilizing device or a sheet should be applied and orthopedic consultation sought. A trauma patient with a potential pelvic fracture should receive an AP pelvic radiograph in the trauma bay followed by a CT scan if there is still suspicion of injury. Children *without* a high-risk clinical finding (e.g., GCS <14; abdominal pain or tenderness; pelvic tenderness, laceration, ecchymosis, or abrasion; gross hematuria or >20 red blood cells/high-power field on urinalysis; or femur fracture) or a high-risk mechanism of injury (e.g., unrestrained motor vehicle collision, motor vehicle collision with ejection, motor vehicle collision rollover, auto vs pedestrian, or auto vs bicycle), however, are unlikely to have pelvic fractures.

Genitourinary Trauma

The perineum should be inspected and the stability of the bones of the pelvis assessed. Urethral injuries are more common in males. Findings suggestive of urethral injury include scrotal or labial ecchymosis, blood at the urethral meatus, gross hematuria, and a superiorly positioned prostate on rectal examination (in an adolescent male). Certain pelvic fractures also increase the risk for potential genitourinary injury. Any of these findings is a contraindication to urethral catheter insertion and warrants consultation with a urologist. Retrograde urethrocystogram and CT scan of the pelvis and abdomen are used to determine the extent of injury.

Extremity Trauma

Thorough examination of the extremities is essential because extremity fractures are among the most frequently overlooked injuries in children with multiple traumas. All limbs should be inspected for deformity, swelling, and bruises; palpated for tenderness; and assessed for active and passive range of motion, sensory function, and perfusion.

Before radiographs are obtained, suspected fractures and dislocations should be immobilized and an analgesic administered. Splinting a femur fracture helps alleviate pain and may decrease blood loss. An orthopedic surgeon should be consulted immediately to evaluate children with compartment syndrome, neurovascular compromise, open fracture, or traumatic amputations.

An acute extremity compartment syndrome is a surgical emergency usually associated with extremity fractures (e.g., tibia, supracondylar humerus, distal radius) but has also been noted after thermal and electric injuries, rhabdomyolysis, coagulopathies, or nephrotic syndrome. Manifestations include pain out of proportion to the injury, pain with passive stretching of the muscles, poor distal pulses, pallor, paresthesia, and weakness. In children, escalating pain not relieved by pain medications, anxiety, and agitation are additional features. If needed, compartmental pressure should be measured (normal is 8 mm Hg in adults, 10-15 mm Hg in children). Absolute pressure ≥30 mm Hg is one indication for fasciotomy. Another indication for fasciotomy is a diastolic blood pressure minus compartment pressure <30 mm Hg.

Advanced Imaging

After completion of the primary survey, diagnostic adjuncts, and secondary survey, most stable trauma patients will require advanced imaging with CT or additional plain radiographs. As detailed earlier, injury mechanism, patient history, and clinical exam findings will help determine the specific imaging to be obtained. Additionally, clinical prediction rules have been developed to identify those at low risk of injury for whom specific imaging studies may not be necessary. The NEXUS C-spine rule is a sensitive, easily applicable rule that was validated for adults and children, although there were fewer young patients studied (see Table 80.5). Several clinical prediction rules have been developed to identify children at low risk of traumatic brain injury in whom head CT can be safely avoided (Table 80.7). Another clinical prediction rule has been developed to identify children at very low risk of clinically important intraabdominal injuries after blunt trauma (Table 80.8). Although this rule has an NPV of 99.9%, it needs to be externally validated before widespread implementation. One benefit of standardizing the evaluation of patients with major trauma is that fewer decisions need to be made on an individual basis, possibly expediting ED management.

DISPOSITION

Disposition from the ED trauma bay is determined by several factors. Patients who are critically unstable with suspected internal hemorrhage are emergently transferred to the operating room (OR) for exploratory surgery before advanced imaging. Up to 30% of children evaluated for trauma require hospitalization. Of the children admitted for trauma, 30% have operative injuries identified on the physical exam or advanced imaging and undergo surgery during that hospitalization. Of those requiring surgery, 25% will require surgery within 24 hours of admission, and of that group, 57% require emergent intervention. Nonoperative patients who are critically injured will ultimately benefit from continued management in an ICU capable of caring for children and in a facility with the necessary surgical subspecialists.

PSYCHOLOGIC AND SOCIAL SUPPORT

Serious multisystem trauma may result in significant long-term psychologic and social difficulties for the child and family, particularly when there is a major head injury. Like adults, children are at risk for depressive symptoms and posttraumatic stress disorder. Caregivers face persistent stress and have been noted to have more psychologic symptoms. Psychologic and social support, during the resuscitation period and afterward, is extremely important. Parents often prefer to be offered the choice to be present during resuscitations. A member of the resuscitation team should be made responsible for answering the family's questions and supporting them in the trauma room.

Table 80.7 Prediction Rule for Identification of Children at Very Low Risk of Clinically Important Brain Injuries After Head Trauma

*Children <2 yr old are at very low risk of clinically important traumatic brain injury if they have **NONE** of the following:*
Severe mechanism of injury
History of LOC >5 sec
GCS ≤14 or other signs of altered mental status
Not acting normally per parent
Palpable skull fracture
Occipital/parietal/temporal scalp hematoma
*Children 2-18 yr old are at very low risk of clinically important traumatic brain injury if they have **NONE** of the following:*
Severe mechanism of injury
History of LOC
History of vomiting
GCS ≤14 or other signs of altered mental status
Severe headache in the ED
Signs of basilar skull fracture

LOC, Loss of consciousness; GCS, Glasgow Coma Scale score; ED, emergency department.

Modified from Kuppermann N, Holmes JF, Dayan PS, et al. Identification of children at very low risk of clinically-important brain injuries after head trauma: A prospective cohort study. *Lancet.* 2009;374:1160-1170.

Table 80.8 Prediction Rule for Identification of Children at Very Low Risk of Clinically Important Intraabdominal Injuries After Blunt Trauma

*If **NONE** of the following is present, the patient is at very low risk for clinically significant intraabdominal injury:*
Glasgow Coma Scale score <14
Vomiting
Evidence of thoracic wall trauma
Decreased breath sounds
Evidence of abdominal wall trauma or seatbelt sign
Abdominal pain
Abdominal tenderness

Modified from Holmes JF, Lillis K, Monroe D, et al. Identifying children at very low risk of clinically important blunt abdominal injuries. *Ann Emerg Med.* 2013;62:107-116, e2.

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Chapter 81

Spinal Cord Injuries in Children

Katie P. Fehnel and Mark R. Proctor

See also Chapter 751.

Compared with adults, spine and spinal cord injuries are rare in children, particularly young children, because of both anatomic differences and etiologies of injury. The main mechanisms of injury to the spine are motor vehicle crashes, falls, sports, and violence, which affect young children less often (see Chapter 80).

Several anatomic differences affect the pediatric spine. The head of a young child is larger relative to body mass than in adults, and the neck muscles are still underdeveloped, which places the fulcrum of movement higher in the spine. Therefore children <9 years old have a higher percentage of injuries in the upper cervical spine (C-spine) than do older children and adults. The spine of a small child also is very mobile, with pliable bones and ligaments, so fractures of the spine are exceedingly rare. However, this increased mobility is not always a positive feature. Transfer of energy leading to spinal distortion may not affect the structural integrity of the bones and ligaments of the spine but can still lead to significant injuries of the spinal cord. This phenomenon of **spinal cord injury without radiographic abnormalities (SCIWORA)** is more common in children than in adults (see Chapter 80). The term is relatively outdated, because almost all injuries are detectable by MRI, but is still clinically useful when referring to spinal cord injuries evaluated by plain radiographs or CT. There seem to be two distinct forms of SCIWORA. The **infantile** form involves severe injury of the cervical or thoracic spinal cord; these patients have a poor chance of complete recovery. In older children and adolescents, SCIWORA is more likely to be a less severe injury, with a high likelihood of complete recovery over time. The **adolescent** form, also called *transient neurapraxia,* is assumed to be a spinal cord concussion or mild contusion, as opposed to the severe spinal cord injury related to the mobility of the spine in small children.

Although the mechanisms of spinal cord injury in children include birth trauma, falls, and child abuse, the major cause of morbidity and mortality across all ages remains **motor vehicle injuries**. Adolescents incur spinal cord injuries with epidemiology similar to that of adults, including significant male predominance and a high likelihood of fracture dislocations of the lower cervical spine or thoracolumbar region. In infants and children <5 years old, fractures and mechanical disruption of spinal elements are more likely to occur in the upper cervical spine between the occiput and C3. Certain conditions predispose to C-spine injury (Table 81.1).

Table 81.1 Conditions that Predispose Patients to a Cervical Spine Injury

CATEGORY	CONDITIONS
Abnormal development of the cervical spine	Trisomy 21 Larsen syndrome Mucopolysaccharidosis IV/Morquio syndrome Klippel-Feil syndrome Achondroplasia Chiari malformation Syringomyelia
Abnormal bone and soft tissue	Marfan syndrome Ehlers-Danlos syndrome Osteogenesis imperfecta
Arthritis	Ankylosing spondylitis Rheumatoid arthritis
History of cervical spine injury or surgery	

Modified from McCollum M, Guse S. Neck trauma: Cervical spine, seatbelt sign and penetrating palate injuries. *Emerg Med Clin N Am.* 2021;39:573-588, Table 1, p. 574.

CLINICAL MANIFESTATIONS

One in three patients with significant trauma to the spine and spinal cord will have a concomitant severe head injury, which makes early diagnosis challenging. For these patients, clinical evaluation may be difficult. Patients with a potential spine injury need to be maintained in a protective environment, such as a collar, until the spine can be cleared by clinical and/or radiographic means. A careful neurologic examination is necessary for infants with suspected spinal cord injuries. Complete spinal cord injury will lead to **spinal shock** with early areflexia (see Chapter 751). Severe C-spine injuries will usually lead to paradoxical respiration in patients who are breathing spontaneously. **Paradoxical respiration** occurs when the diaphragm, which is innervated by the phrenic nerves with contributions from C3, C4, and C5, is functioning normally, but the intercostal musculature innervated by the thoracic spinal cord is paralyzed. In this situation, inspiration fails to expand the chest wall but distends the abdomen. Other complications during the acute (2-48 hours) phase include autonomic dysfunction (bradyarrhythmias and tachyarrhythmias, orthostatic hypotension, hypertension), temperature instability, thromboembolism, dysphagia, and bowel/bladder dysfunction.

The *mildest* injury to the spinal cord is **transient quadriparesis** evident for seconds or minutes with complete recovery in 24 hours. This injury follows a concussion of the cord and is most frequently seen in adolescent athletes. If their imaging is normal, these children can generally return to normal activities after a period of rest from days to weeks, depending on the initial severity, similar to cerebral concussion management.

Significant spinal cord injury in the cervical region is characterized by flaccid quadriparesis, loss of sphincter function, and a sensory level corresponding to the level of injury. An injury at the high cervical level (C1-C2) can cause respiratory arrest and death in the absence of ventilatory support. Injuries in the thoracic region are generally the result of fracture dislocations. They may produce paraplegia when at T10 or above or the **conus medullaris syndrome** if at the T12-L1 level. This includes a loss of urinary and rectal sphincter control, flaccid weakness, and sensory disturbances of the legs. A **central cord lesion** may result from contusion and hemorrhage in the center of the spinal cord (Fig. 81.1). It typically involves the upper extremities to a greater degree than the legs because the motor fibers to the cervical and thoracic region are more centrally located in the spinal cord. There are lower motor neuron signs in the upper extremities and upper motor neuron signs in the legs, bladder dysfunction, and loss of sensation caudal to the lesion. There may be considerable recovery, particularly in the lower extremities, although sequelae are common (see Chapter 751).

CLEARING THE CERVICAL SPINE IN CHILDREN

The management of children after major trauma is challenging. For older children, the clearance is similar to a lucid adult, and the National Emergency X-Radiography Utilization Study (NEXUS) criteria are appropriate (see Chapter 80, Table 80.5). Clearing the cervical spine in younger and uncooperative children involves similar issues as in adults with an altered level of consciousness

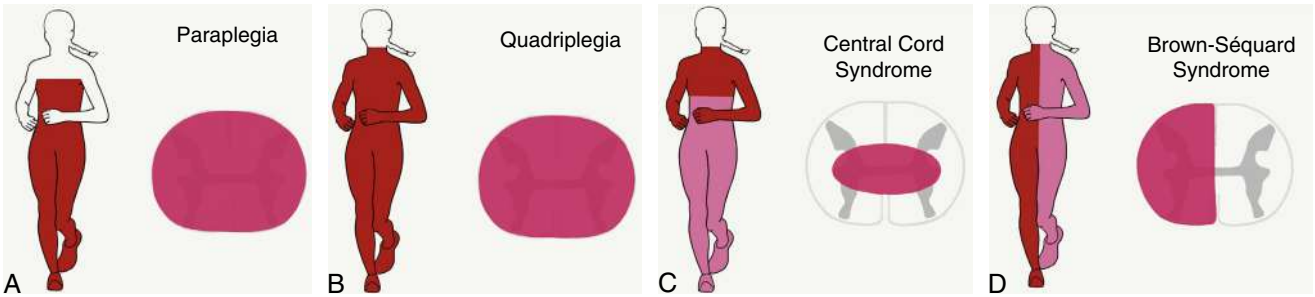

Fig 81.1 Patterns of spinal cord injury. Note the contrast between these syndromes and peripheral nerve/radicular injuries based on the distribution of motor and/or sensory loss beyond the affected extremity. *Paraplegia* (A) and *quadriplegia* (B): Complete loss of motor and sensory function below the level of injury resulting in loss of function of the legs only or arms and legs, respectively. *Central cord syndrome* (C): Injury of the central spinal cord resulting in functional greater impact of arm motor function than legs. Sensory deficits in this injury are variable. *Brown-Séquard syndrome* (D): Injury to one-half of the spinal cord resulting in ipsilateral motor weakness with contralateral sensory loss below the level of the lesion. (*From Jea A, Belal A, Zaazoue MA, Martin J. Cervical spine injury in children and adolescents. Pediatr Clin N Am. 2021;68:875-894: Fig. 11, p. 886.*)

Table 81.2 Risk Factors that Preclude Clinical Clearance of the C-Spine

HISTORY	PHYSICAL EXAMINATION
Child or parent reports persistent neck pain, abnormal head posture, or difficulty with neck movement	Visible known substantial injury to chest, abdomen, or pelvis (injury that is life-threatening, warrants surgical intervention or inpatient admission)
History of focal sensory abnormality or motor deficit	GCS of <14
High-risk injury*	Torticollis/abnormal head position
	Posterior midline neck tenderness
	Limited cervical range of motion
	Inability to maintain focus due to other injuries

*Diving, high speed motor vehicle crash, bike crash, motorized all-terrain vehicle.
GCS, Glasgow Coma Scale.
Modified from McCollum M, Guse S. Neck trauma: Cervical spine, seatbelt sign and penetrating palate injuries. *Emerg Med Clin N Am.* 2021;39:573-588, Table 2, p. 575.

(Table 81.2). Small children generally have a difficult-to-assess physical examination, and it is difficult to determine if they have cervical pain. Plain radiography remains a mainstay for assessing the spine because it is easy to obtain. There has been increasing emphasis on MRI for evaluation of potential C-spine instability, but in small children MRI requires sedation and in most centers the presence of an anesthesiologist (Fig. 81.2). CT scan is another important study with high sensitivity and specificity, but the risk of radiation exposure must be considered.

In addition to C-spine injury, neck trauma may also produce a radiculopathy or neuropathy (Table 81.3).

TREATMENT

The cervical spine should be immobilized in the field by the emergency medical technicians. In cases of acute spinal cord injury, weak data suggest acute infusion of a bolus of high-dose (30 mg/kg) methylprednisolone, followed by a 23-hour infusion (5.4 mg/kg/hr). The data for this treatment are controversial; the current neurosurgical guidelines for management of adult spine trauma do not recommend methylprednisolone; corticosteroids have not been specifically tested in children. *As such, many centers no longer use them routinely.*

Fig. 81.2 T2-weighted MRI performed the day after the accident showed cervical spinal cord swelling combined with high signal intensity (C1-C3) *(arrow)* and dislocation of C5-C6 *(arrowhead)*. (*From Inoue K, Kumada T, Fujii T, Kimura N. Progressive cervical spinal cord atrophy after a traffic accident. J Pediatr. 2017;180:287: Fig. 1, p. 287.*)

Maintenance of euvolemia and normotension is important, and vasopressors might be needed if the sympathetic nervous system has been compromised.

Surgical management of spinal injuries must be tailored to the patient's age but can be a crucial step in management. Any compression of the spinal cord must be surgically relieved to afford the best chance of a favorable outcome. In addition, spinal cord injury can be worsened by instability, so surgical stabilization can prevent further injury (Fig. 81.3). In general, younger children have a higher healing capacity for bones and ligaments, and external immobilization might be considered for injuries that require surgery in older children and adults. However, some injuries are highly unstable and always require surgery. **Occipitocervical dislocation** is one such highly unstable injury, and early surgery with fusion from the occiput to C2 or C3 should be performed, even in very young children. Fixation of the subaxial spine must be tailored to the size of the pedicles and other osseous structures of the developing axial skeleton.

Table 81.3 History and Examination Features Allowing for Discrimination of Myelopathy, Radiculopathy, and Peripheral Neuropathy

FINDING	PERIPHERAL NEUROPATHY	RADICULOPATHY	MYELOPATHY
Pain • Quality • Location	"Electric" Radiates either proximally or distally from injury site	Sharp, aching Radiates distally from the neck	Typically painless
Weakness	Variable, usually present	Variable, usually present	Variable, may be present
Sensory loss	Sharply demarcated borders	Indistinct borders	Indistinct borders, typically extends beyond single extremity
Tone/reflexes	Decreased	Decreased	Increased

From Jea A, Belal A, Zaazoue MA, Martin J. Cervical spine injury in children and adolescents. *Pediatr Clin N Am.* 2021;68:875-894, Table 4, p. 883.

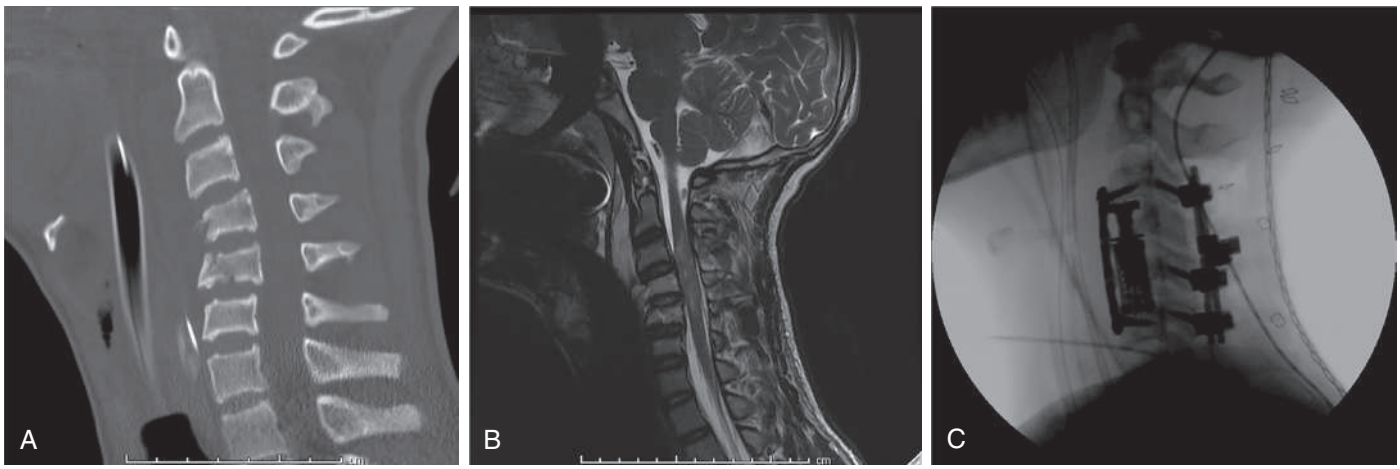

Fig. 81.3 A 15-year-old hockey player suffered acute paraplegia after his head struck the boards during a hockey game. **A,** CT scan shows compression fractures of C4 and C5. **B,** MRI shows severe spinal cord contusion. **C,** Because of the need to decompress the spinal cord and stabilize the spine, anterior and posterior surgery was performed. No meaningful recovery was obtained.

PREVENTION

The most important aspect of the care of spinal cord injuries in children is injury prevention. Use of appropriate child restraints in automobiles is the most important precaution. In older children and adolescents, rules against "spear tackling" in American football and the *Feet First, First Time* aimed at adolescents diving into swimming pools and natural water areas are important ways to help prevent severe cervical spinal cord injuries. Safe driving practices, such as using safety belts, avoiding distracted driving, and following the speed limit, can have substantial beneficial effects on injury rates.

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Chapter 82

Neurologic Emergencies and Stabilization

Patrick M. Kochanek and Michael J. Bell

NEUROCRITICAL CARE PRINCIPLES

The brain has high metabolic demands, which are further increased during growth and development. Preservation of nutrient supply to the brain is the mainstay of care for children with evolving brain injuries. *Intracranial dynamics* describes the physics of the interactions of the contents—brain parenchyma, blood (arterial, venous, capillary), and cerebrospinal fluid (CSF)—within the cranium. Normally, brain parenchyma accounts for up to 85% of the contents of the cranial vault, and the remaining portion is divided between CSF and blood. The brain resides in a relatively rigid cranial vault, and cranial compliance decreases with age as the skull ossification centers gradually replace cartilage with bone. The **intracranial pressure (ICP)** is derived from the volume of its components and the bony compliance. The **perfusion pressure** of the brain (cerebral perfusion pressure [CPP]) is equal to the pressure of blood entering the cranium (mean arterial pressure [MAP]) minus the ICP, in most cases.

Increases in intracranial volume can result from swelling, masses, or increases in blood and CSF volumes. As these volumes increase, compensatory mechanisms prevent increases in ICP by (1) decreasing CSF volume (CSF is displaced into the spinal canal or absorbed by arachnoid villi), (2) decreasing cerebral blood volume (venous blood return to the thorax is augmented), and/or (3) increasing cranial volume (sutures pathologically expand or bone is remodeled). Once compensatory mechanisms are exhausted (the increase in cranial volume is too large), small increases in volume lead to clinically meaningful increases in ICP or intracranial hypertension (Fig. 82.1). As ICP continues to increase, brain ischemia can occur as CPP falls. Further increases in ICP can ultimately displace the brain downward into the foramen magnum—a process called **cerebral herniation**, which can become irreversible in minutes and may lead to severe disability or death; Figure 82.2 notes other sites of brain herniation.

Oxygen and glucose are required by brain cells for normal functioning, and these nutrients must be constantly supplied by cerebral blood flow (CBF). Normally, CBF is constant over a wide range of blood pressures (blood pressure autoregulation of CBF) via actions mainly within

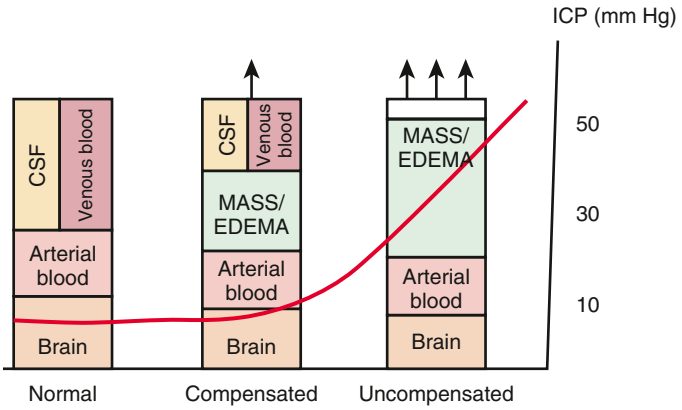

Fig. 82.1 The Munro-Kellie doctrine describes intracranial dynamics in the setting of an expanding mass lesion (i.e., hemorrhage, tumor) or brain edema. In the normal state, the brain parenchyma, arterial blood, CSF, and venous blood occupy the cranial vault at a low pressure, generally <10 mm Hg. With an expanding mass lesion or brain edema, initially there is a compensated state as a result of reduced CSF and venous blood volumes, and ICP remains low. Further expansion of the lesion, however, leads to an uncompensated state when compensatory mechanisms are exhausted and intracranial hypertension results.

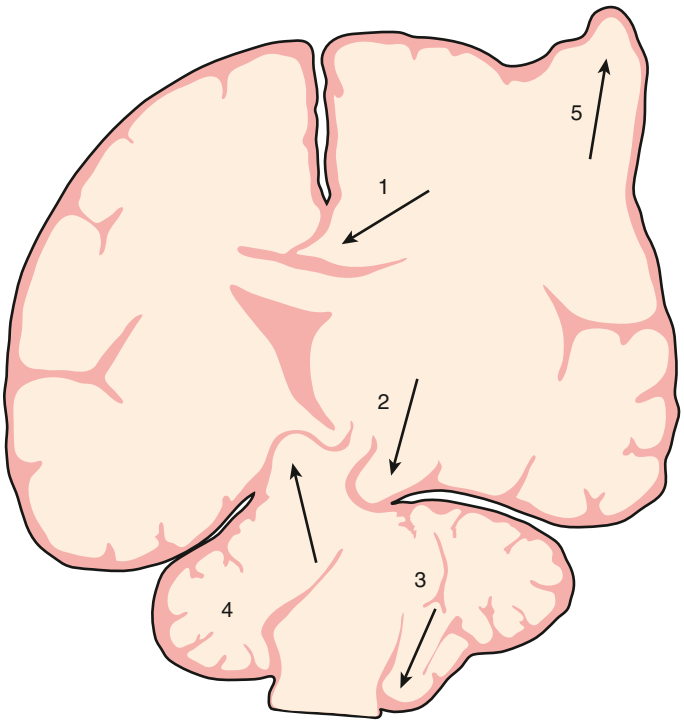

Fig. 82.2 Different forms of brain herniation. *1*, Cingulate. *2*, Uncal. *3*, Cerebellar tonsillar. *4*, Upward cerebellar. *5*, Transcalvarial. *(From Fishman RA. Cerebrospinal Fluid in Diseases of the Nervous System. Philadelphia: Saunders; 1980.)*

the cerebral arterioles. Cerebral arterioles are maximally dilated at lower blood pressures and maximally constricted at higher pressures so that CBF does not vary during normal fluctuations (Fig. 82.3). Above the upper limit of autoregulation, breakthrough dilation occurs that, if severe, can produce hypertensive encephalopathy. Acid-base balance of the CSF (often reflected by acute changes in arterial partial pressure of carbon dioxide [$Paco_2$]), body/brain temperature, glucose utilization,

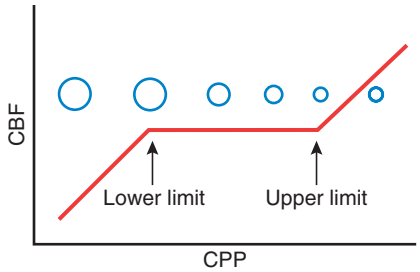

Fig. 82.3 Schematic of the relationship between CBF and CPP. The diameter of a representative cerebral arteriole is also shown across the center of the *y* axis to facilitate understanding of the vascular response across CPP that underlies blood pressure autoregulation of CBF. CPP is generally defined as the mean arterial pressure (MAP) minus the ICP. At normal values for ICP, this generally represents MAP. Thus, normally, CBF is kept constant between the lower limit and upper limit of autoregulation; in normal adults, these values are ≈50 mm Hg and 150 mm Hg, respectively. In children, the upper limit of autoregulation is likely proportionally lower than the adult value relative to normal MAP for age. However, according to the work of Vavilala et al. (2003), lower limit values are surprisingly similar in infants and older children. Thus infants and young children may have less reserve for adequate CPP. See text for details.

blood viscosity, and other vasoactive mediators (i.e., adenosine, nitric oxide, prostanoids) can also affect the cerebral vasculature.

Knowledge of these concepts is instrumental to preventing secondary brain injury. Increases in CSF pH that occur because of inadvertent hyperventilation (decreased $Paco_2$) can produce cerebral ischemia. Hyperthermia-mediated increases in cerebral metabolic demands may damage vulnerable brain regions after injury. Hypoglycemia can produce neuronal death when CBF fails to compensate. Prolonged seizures can lead to permanent injuries if hypoxemia occurs from loss of airway control.

Attention to detail and constant reassessment are paramount in managing children with critical neurologic insults. Among the most valuable tools for serial, objective assessments of neurologic condition is the **Glasgow Coma Scale (GCS)** (Table 82.1 and see Table 79.3). Originally developed to assess level of consciousness after traumatic brain injury (TBI) in adults, the GCS is also valuable in pediatrics. Modifications to the GCS have been made for nonverbal children and are available for infants and toddlers (see Table 79.3 in Chapter 79). Serial assessments of the GCS score along with a focused neurologic examination are invaluable to detect injuries before permanent damage occurs in the vulnerable brain. The **FOUR (full outline of unresponsiveness) score** (see Table 82.1) is a modification of the GCS, which eliminates the patient's verbal response but adds functional assessments of the brainstem (pupil, corneal, and cough reflexes) and respiratory pattern.

The most-studied monitoring device in clinical practice is the **ICP monitor**. Monitoring is accomplished by a catheter inserted either into the cerebral ventricle (externalized ventricular drain) or into brain parenchyma (parenchymal transducer). ICP-directed therapies are standard of care in TBI and are used in other conditions, such as intracranial hemorrhage, Reye syndrome, and some cases of encephalopathy, meningitis, and encephalitis. Other devices being used include catheters that measure brain tissue oxygen concentration, external probes that noninvasively assess brain oxygenation by absorbance of near-infrared light (near-infrared spectroscopy [NIRS]), monitors of brain electrical activity (continuous electroencephalography [EEG] or somatosensory, visual, or auditory evoked potentials), and CBF monitors (transcranial Doppler, xenon CT, perfusion MRI, or tissue probes). In the severe TBI guidelines, brain tissue oxygen concentration monitoring received level III support and thus may be considered as an adjunct to ICP-directed therapy.

Table 82.1 Commonly Used Coma Scores

GLASGOW COMA SCALE

Eye Opening
1 = does not open eyes
2 = opens eyes in response to noxious stimuli
3 = opens eyes in response to voice
4 = opens eyes spontaneously

Verbal Output
1 = makes no sounds
2 = makes incomprehensible sounds
3 = utters inappropriate words
4 = confused and disoriented
5 = speaks normally and oriented

Motor Response (Best)
1 = makes no movements
2 = extension to painful stimuli
3 = abnormal flexion to painful stimuli
4 = flexion/withdrawal to painful stimuli
5 = localized to painful stimuli
6 = obeys commands

FULL OUTLINE OF UNRESPONSIVENESS (FOUR) SCORE

Eye Response
4 = eyelids open or opened, tracking, or blinking to command
3 = eyelids open but not tracking
2 = eyelids closed but open to loud voice
1 = eyelids closed but open to pain
0 = eyelids remain closed with pain

Motor Response
4 = thumbs-up, fist, or peace sign
3 = localizing to pain
2 = flexion response to pain
1 = extension response to pain
0 = no response to pain or generalized myoclonus status

Brainstem Reflexes
4 = pupil and corneal reflexes present
3 = one pupil wide and fixed
2 = pupil or corneal reflexes absent
1 = pupil and corneal reflexes absent
0 = absent pupil, corneal, and cough reflex

Respiration
4 = not intubated, regular breathing pattern
3 = not intubated, Cheyne-Stokes breathing pattern
2 = not intubated, irregular breathing
1 = breathes above ventilatory rate
0 = breathes at ventilator rate or apnea

From Edlow JA, Rabinstein A, Traub SJ, Wijdicks EFM. Diagnosis of reversible causes of coma. *Lancet.* 2014;384:2064-2076.

TRAUMATIC BRAIN INJURY

Etiology

Mechanisms of TBI include motor vehicle crashes, falls, assaults, and abusive head trauma. Most TBIs in children are from closed-head injuries.

Epidemiology

TBI is an important pediatric public health problem, with over 800,000 emergency department visits, 23,000 hospitalizations, and over 2,500 deaths in children annually in the United States. It is also 1 of the top 10 causes of years lost to disability throughout infancy, childhood, and adolescence.

Pathology

Epidural, subdural, and parenchymal intracranial hemorrhages can result. Injury to gray or white matter is also commonly seen and includes focal cerebral contusions, diffuse cerebral swelling, axonal injury, and injury to the cerebellum or brainstem. Patients with severe TBI often have multiple findings; diffuse and potentially delayed cerebral swelling is common.

Pathogenesis

TBI results in primary and secondary injury. Primary injury from the impact produces irreversible tissue disruption. In contrast, two types of secondary injury are targets of neurointensive care. First, some of the ultimate damage seen in the injured brain evolves over hours or days, and the underlying mechanisms involved (including edema, apoptosis, programmed necrosis, and secondary axotomy) are therapeutic targets. Second, the injured brain is vulnerable to additional insults because injury disrupts normal autoregulatory defense mechanisms; disruption of autoregulation of CBF can lead to ischemia from hypotension that would otherwise be tolerated by the uninjured brain.

Clinical Manifestations

The hallmark of **severe TBI** is coma **(GCS score 3-8)**. Coma is often seen immediately after the injury and is sustained. In some cases, such as with an epidural hematoma, a child may be initially alert on presentation but may deteriorate after a period of hours. A similar picture can be seen in children with diffuse swelling in whom a *talk-and-die* scenario has been described. Clinicians should also not be lulled into underappreciating the potential for deterioration of a child with **moderate TBI (GCS score 9-12)** with a significant contusion, because progressive swelling can potentially lead to devastating complications. In the comatose child with severe TBI, the second key clinical manifestation is the development of *intracranial hypertension*. The development of increased ICP with impending herniation may be heralded by new-onset or worsening headache, depressed level of consciousness, vital sign changes (hypertension, bradycardia, irregular respirations), and signs of sixth (lateral rectus palsy) or third (anisocoria [dilated pupil], ptosis, down-and-out position of globe as a result of rectus muscle palsies) cranial nerve compression. Increased ICP is managed with continuous ICP monitoring, as well as monitoring for clinical signs of increased ICP or impending herniation. The development of brain swelling is progressive. Significantly raised ICP (>20 mm Hg) can occur early after severe TBI, but peak ICP generally is seen at 48-72 hours. Need for ICP-directed therapy may persist for longer than a week. A few children have coma without increased ICP resulting from axonal injury or brainstem injury. *In addition to head trauma, it is critical to identify potential cervical spine injury* (see Chapter 81).

Laboratory Findings

Cranial CT should be obtained immediately after resuscitation and cardiopulmonary stabilization (Figs. 82.4-82.10). In some cases, MRI can be diagnostic (Fig. 82.11). An approach to CT scanning is noted in Figure 82.12. Generally, other laboratory findings are normal in isolated TBI, although occasionally coagulopathy or the development of the syndrome of inappropriate antidiuretic hormone (SIADH) secretion or cerebral salt wasting (CSW) is seen. In the setting of TBI with polytrauma, other injuries can result in laboratory and/or radiographic abnormalities, and a **full trauma survey** is important in all patients with severe TBI (see Chapter 80).

Diagnosis and Differential Diagnosis

In severe TBI, the diagnosis is generally obvious from the history and clinical presentation. Occasionally, TBI severity can be overestimated because of concurrent alcohol or drug intoxication. The diagnosis of TBI can be problematic in cases of abusive head trauma or after an anoxic event such as drowning or smoke inhalation.

Treatment

Infants and children with severe or moderate TBI (GCS score 3-8 or 9-12, respectively) receive intensive care unit (ICU) monitoring. Evidence-based guidelines for the management of severe TBI have been published (Fig. 82.13 and Fig. 82.14). This approach to ICP-directed therapy is also reasonable for other conditions in which ICP is monitored. Care involves a multidisciplinary team comprising pediatric caregivers from neurologic surgery, critical care medicine, surgery, and rehabilitation, among other services, and is directed at

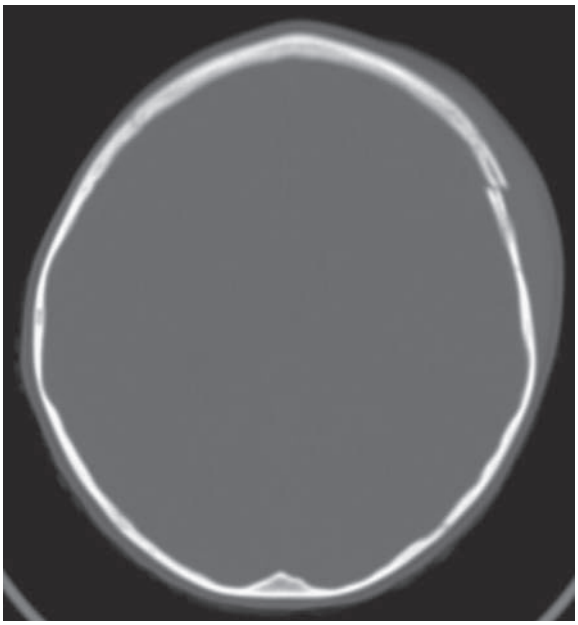

Fig. 82.4 Skull fracture. Mildly displaced skull fracture seen on CT imaging (bone window view) in a 4-year-old who fell and hit her head on a curb.

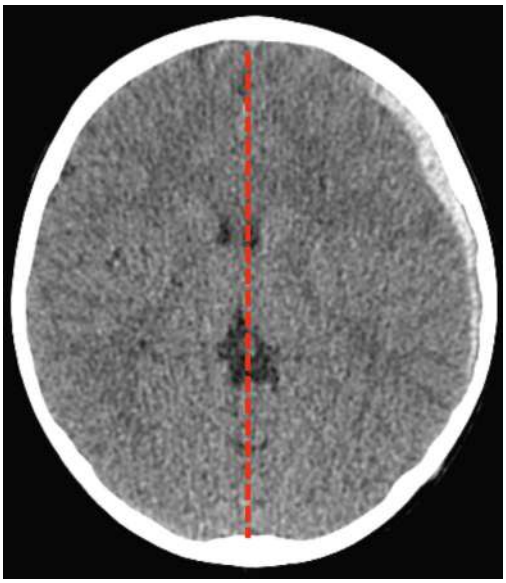

Fig. 82.6 Subdural hematoma. Left subdural hematoma observed on CT imaging in a 10-year-old child after a motor vehicle accident. Note effacement of the left lateral ventricle and midline shift (see *dashed line* for midline reference).

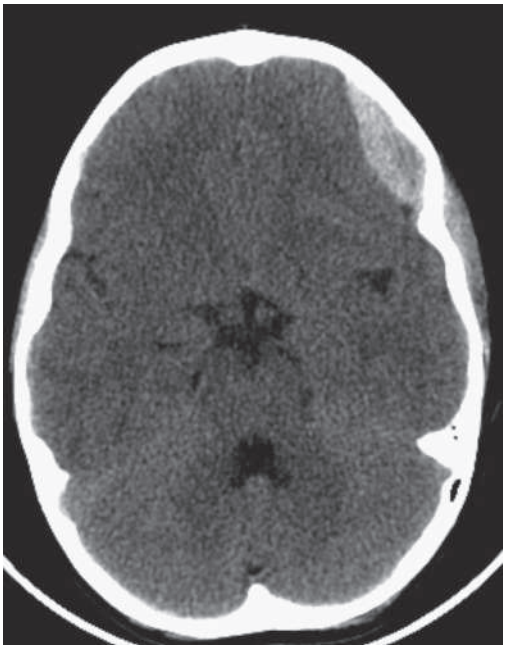

Fig. 82.5 Epidural hematoma. Left frontal epidural hematoma observed on CT imaging in a 12-year-old child who fell off his bike onto a concrete surface.

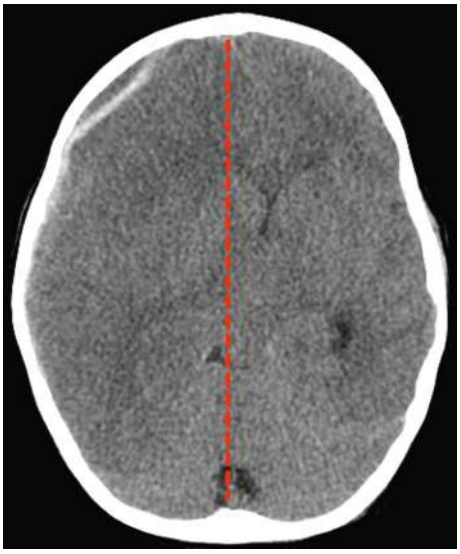

Fig. 82.7 Subdural hematoma. Hyperacute right frontal subdural hematoma observed on CT imaging in a 5-year-old after a motor vehicle accident. Note that the hyperacute aspect of the subdural hematoma is dark on CT imaging in the early stage after injury. Also, note that there is marked midline shift of intracranial contents, as both lateral ventricles are displaced into the left side of the skull.

preventing secondary insults and managing raised ICP. Initial stabilization of infants and children with severe TBI includes rapid sequence tracheal intubation with spine precautions along with maintenance of normal extracerebral hemodynamics, including blood gas values (Pao_2 and $Paco_2$), MAP, and temperature. Intravenous fluid boluses may be required to treat hypotension. Euvolemia is the target, and hypotonic fluids must be rigorously avoided; *normal saline is the fluid of choice*. Pressors may be needed as guided by monitoring of central venous pressure, with avoidance of both fluid overload and exacerbation of brain edema. A trauma survey should be performed. Once stabilized, the patient should be taken for CT scanning to rule out the need for emergency neurosurgical intervention. If surgery is not required, an ICP monitor should be inserted to guide the treatment of intracranial hypertension. Repeat CT scan may help determine whether a new lesion requiring surgical intervention has developed; this should be obtained if there is a change in examination or for refractory intracranial hypertension.

During stabilization or at any time during the treatment course, patients can present with signs and symptoms of *cerebral herniation* (pupillary dilation, systemic hypertension, bradycardia, extensor posturing). Because herniation and its devastating consequences can sometimes be reversed if promptly addressed, it should be treated as a medical emergency, with use of hyperventilation with a fraction of inspired oxygen of 1.0 titrated to reversal of pupillary dilation and

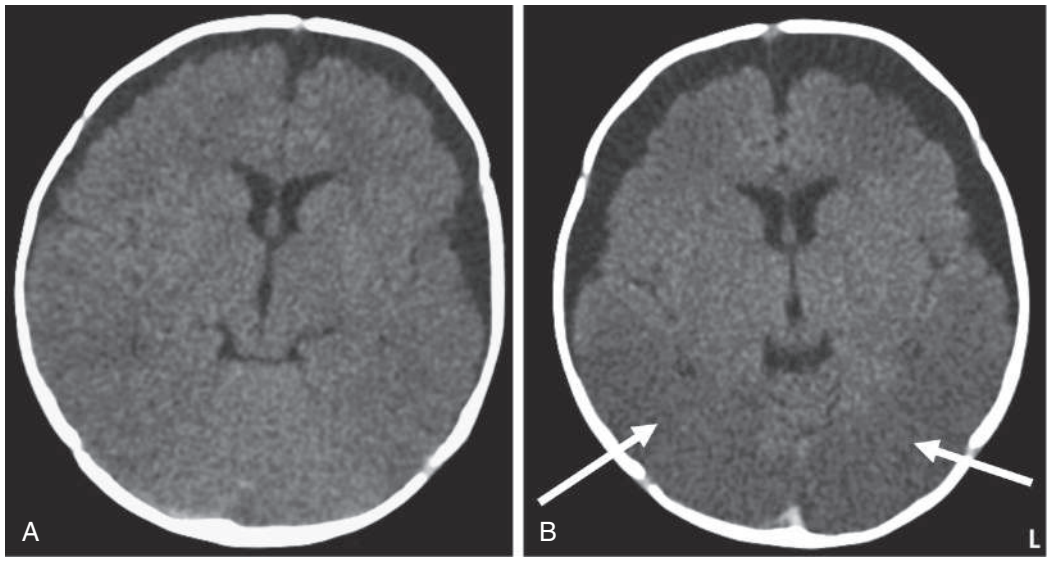

Fig. 82.8 Subdural hematoma. In a 3-month-old child who suffered from abusive head trauma, initial CT imaging (A) demonstrates chronic subdural hematoma bilaterally. Three days after hospitalization (B), the subdural hematomas are slightly larger but infarctions are noted in the posterior areas of brain parenchyma (*arrows*).

Fig. 82.9 Hemorrhage and edema. In a 16-year-old who fell from his dirt bike, CT imaging demonstrates intraparenchymal hemorrhage and significant surrounding edema *(arrow).*

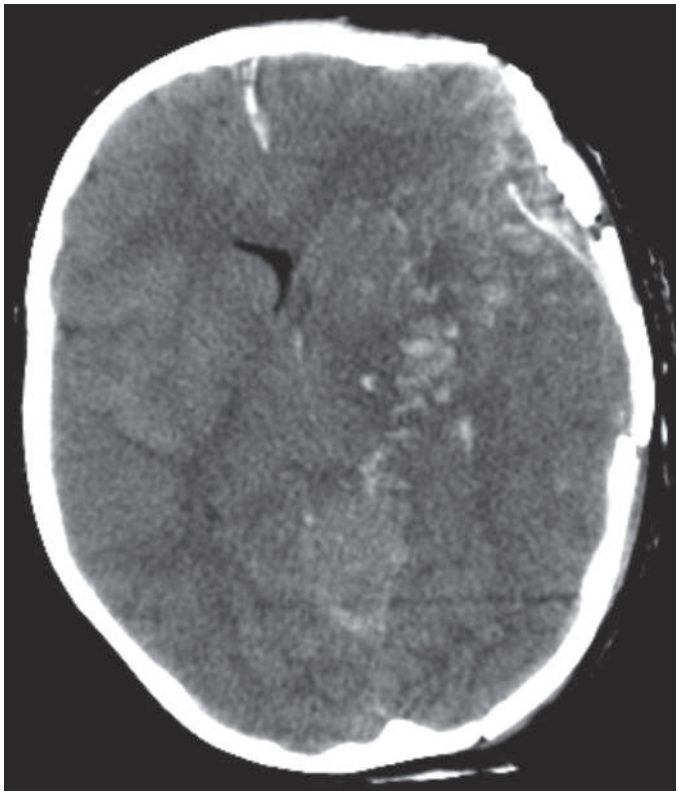

Fig. 82.10 Skull fractures and hemorrhage. An 11-year-old child was hit in the head by a horse, and CT imaging demonstrates multiple comminuted skull fractures with fragments of bone within the brain parenchyma, multifocal areas of intraparenchymal hemorrhage, and obliteration of the left lateral ventricle.

administration of either hypertonic saline (3% solution, 5-10 mL/kg IV) or mannitol (0.25-1.0 g/kg IV). If an external ventricular drain is in place, it should be opened to continuous drainage. Pentobarbital administration can also be considered if a prompt clinical response has not been observed.

ICP should be maintained at <20 mm Hg; age-dependent CPP targets are approximately 50 mm Hg for children 2-6 years of age, 55 mm Hg for those 7-10 years of age, and 65 mm Hg for those 11-16 years of age. **First-tier** therapy includes elevation of the head of the bed, ensuring midline positioning of the head, controlled mechanical ventilation, and analgesia and sedation (i.e., narcotics and benzodiazepines). If neuromuscular blockade is needed, it may be desirable to monitor EEG continuously because *status epilepticus* can occur; this complication will not be recognized in a paralyzed patient and is associated with raised ICP and unfavorable outcome. If a ventricular rather than parenchymal catheter is used to monitor ICP, therapeutic CSF drainage is available and can be provided either continuously (often targeting an ICP >5 mm Hg) or intermittently in response to ICP spikes, generally >20

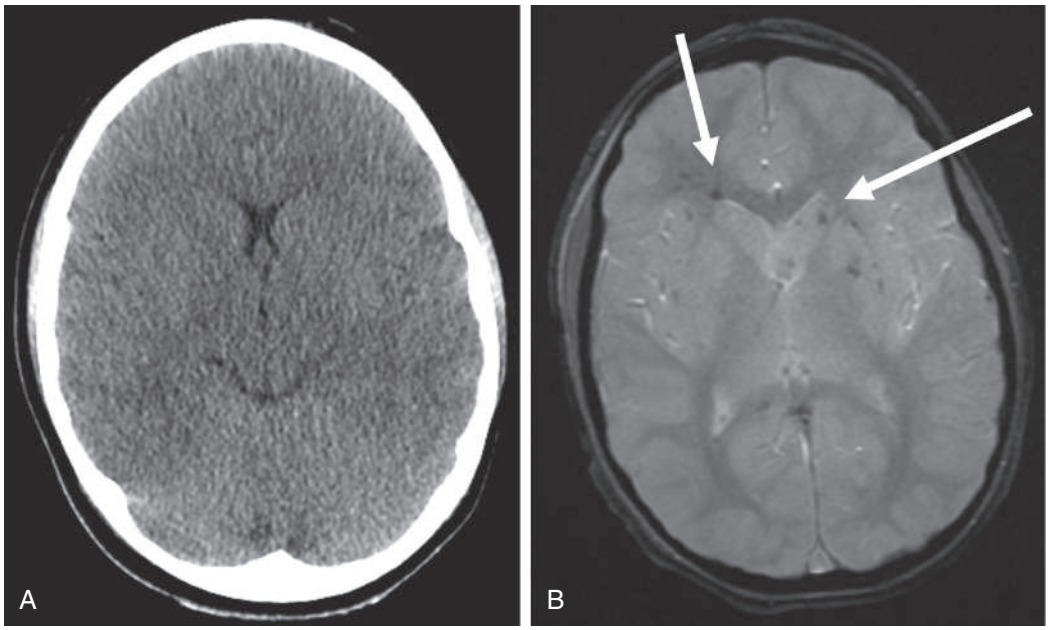

Fig. 82.11 Hemorrhages and axonal injury. In a 6-year-old child who was hit by a car while riding his bike, initial CT imaging demonstrates no obvious abnormality (**A**). However, immediate MRI demonstrates multiple areas of punctate hemorrhages (lucencies) consistent with diffuse axonal injury (**B**, *arrows*).

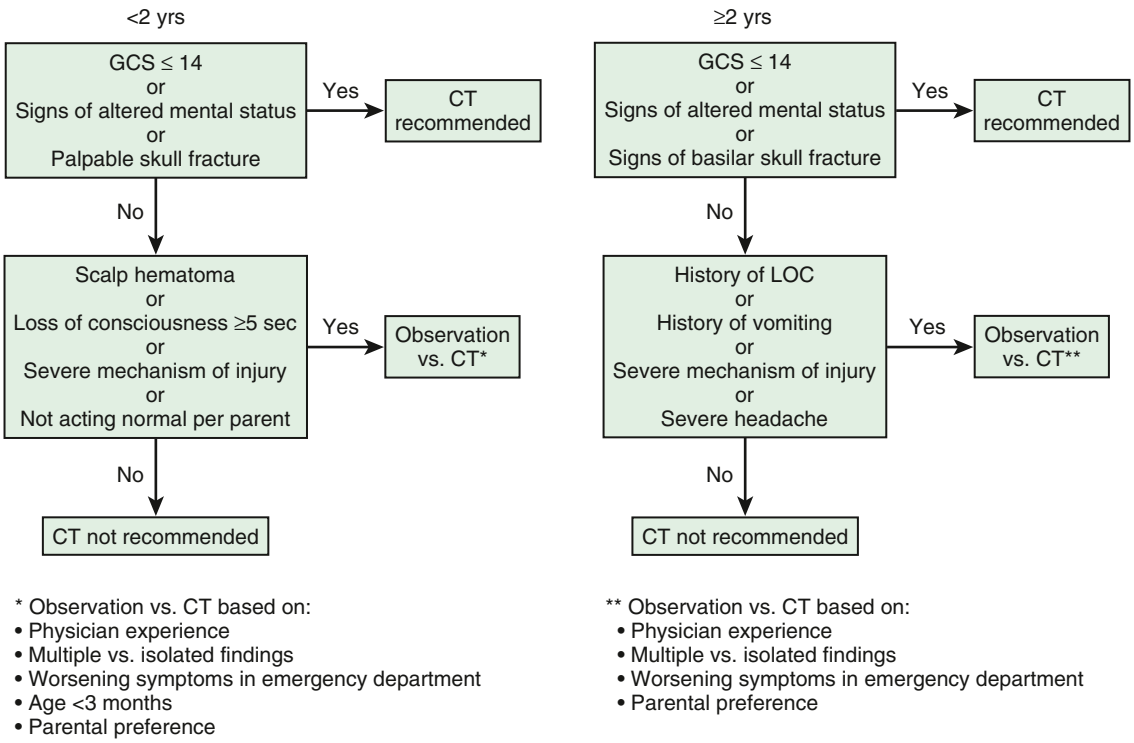

Fig. 82.12 Algorithm for head computed tomography (CT) scan using predictive rules. GCS, Glasgow Coma Scale; LOC, level of consciousness. *(Modified from Kupperman N, Holmes JF, Dayan PS, et al. Identification of children at very low risk of clinically important brain injuries after head trauma: A prospective cohort study.* Lancet. *2009;374:1160-1170.)*

mm Hg. Other first-tier therapies include the osmolar agents hypertonic saline or mannitol. Bolus administration of 3% **hypertonic saline** (between 2 and 5 mL/kg over 10-20 minutes) has guideline-based level II evidence supporting its use to treat ICP spikes >20 mm Hg or using a fixed (q4-q6h) dosing interval. It can also be given as a continuous infusion of 3% saline at 0.1-1.0 mL/kg/hr. **Mannitol** (0.25-1.0 g/kg IV over 20 minutes) represents an alternative. These agents can be used concurrently. It is recommended to avoid serum osmolality >320 mOsm/L. A Foley urinary catheter should be placed to monitor urine output.

If increased ICP remains refractory to treatment, careful reassessment of the patient is needed to rule out unrecognized hypercarbia, hypoxemia, fever, hypotension, hypoglycemia, pain, and seizures. Repeat imaging should be considered to rule out a surgical lesion. Guideline-based **second-tier** therapies for refractory raised ICP are available, but evidence favoring a given second-tier therapy is limited.

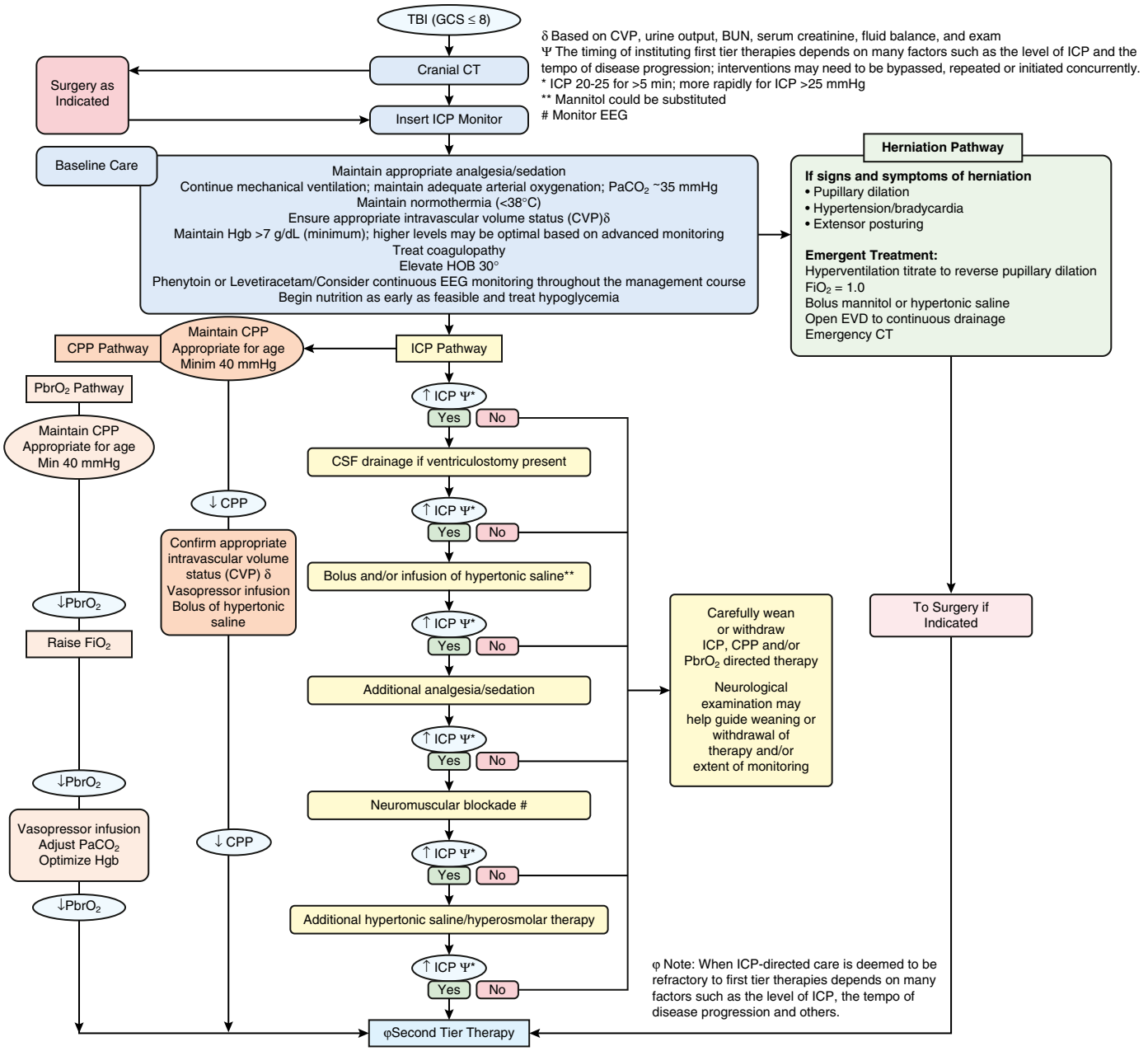

Fig. 82.13 Algorithm for use at the bedside to guide first-tier therapies to treat severe pediatric traumatic brain injury (TBI). This evidence- and consensus-based document that accompanied the third edition of the guidelines includes baseline care *(gray)*, an intracranial pressure (ICP) pathway *(yellow)*, a herniation pathway *(green)*, a cerebral perfusion pressure (CPP) pathway *(orange)*, a brain tissue partial pressure of oxygen ($PbrO_2$) pathway (purple), and surgical intervention (red). The caregiver should integrate all the available information and implement the evidence in the guidelines in the context of each patient's unique response to therapies to craft the most optimal treatment regimen. Although a linear approach in each pathway is provided, variations in tempo and timing during which therapies are implemented will vary from case to case. In some cases, a single intervention for raised ICP may suffice, whereas in others, multiple simultaneous interventions may be required. The *blue box* indicates the need for second-tier therapy (see Fig. 82.14). BUN, Blood urea nitrogen; CSF, cerebrospinal fluid; CT, computed tomography; CVP, central venous pressure; EEG, electroencephalogram; EVD, external ventricular drain; FiO_2, fraction of inspired oxygen concentration; GCS, Glasgow Coma Scale; Hgb, hemoglobin; HOB, head of bed; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen. *(From Kochanek PM, Bell MJ, Simon DW, et al. Traumatic brain injury. In: Zimmerman JJ, Totta AT, eds. Fuhrman & Zimmerman's Pediatric Critical Care, 6th ed. Philadelphia: Elsevier; 2022: Fig. 118.11, p. 1391.)*

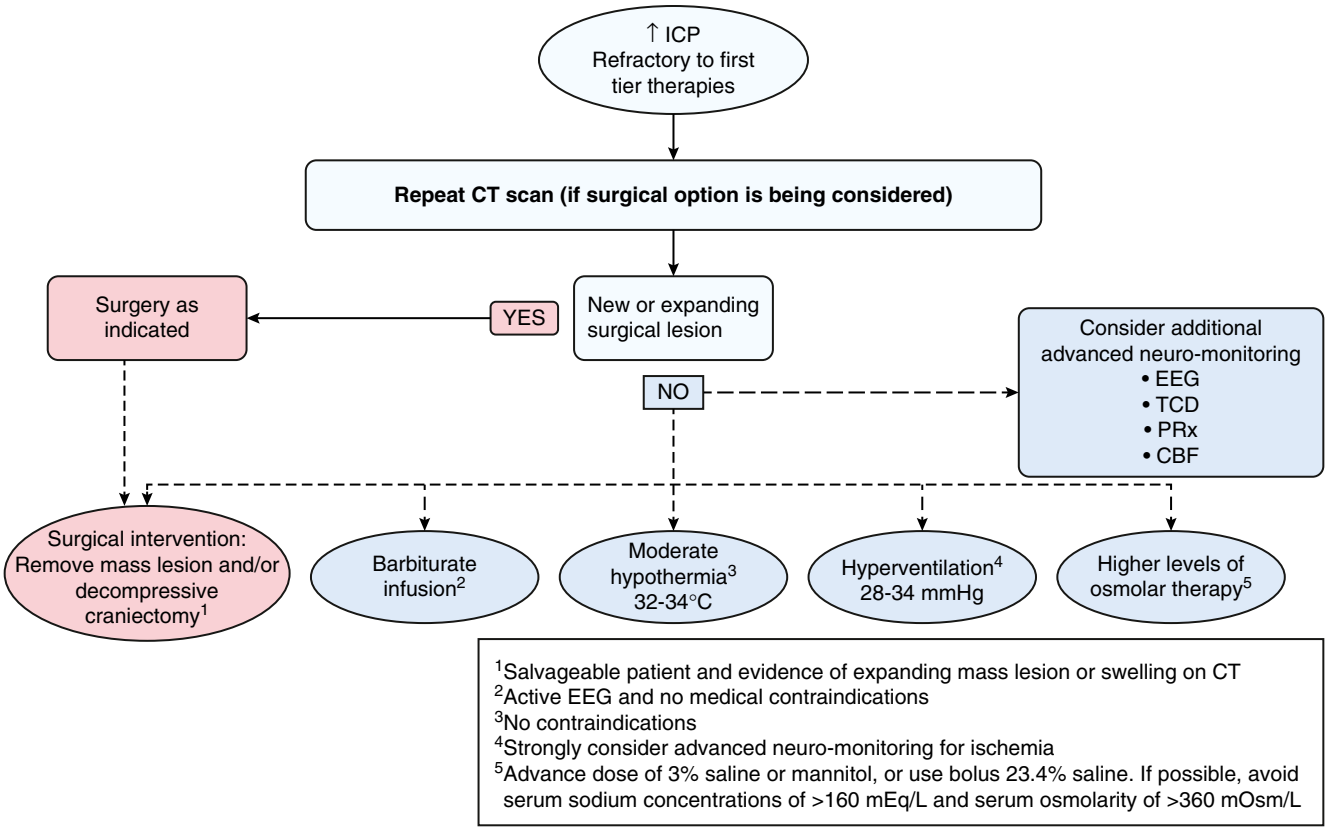

Fig. 82.14 Bedside algorithm to guide second-tier therapies to treat refractory intracranial hypertension in severe pediatric traumatic brain injury (TBI). This evidence- and consensus-based document that accompanied the third edition of the guidelines represents the treatment options when tier 1 approaches are inadequate. These therapies may be applied singly, serially, or in combination. In addition, as shown, management of refractory intracranial hypertension in the second-tier phase may be aided by advanced monitoring. CBF, Cerebral blood flow; CT, computed tomography; EEG, electroencephalogram; ICP, intracranial pressure; PRx, pressure reactivity index; TCD, transcranial Doppler ultrasonography. (*From Kochanek PM, Bell MJ, Simon DW, et al. Traumatic brain injury. In: Zimmerman JJ, Totta AT, eds.* Fuhrman & Zimmerman's Pediatric Critical Care, *6th ed. Philadelphia: Elsevier; 2022: Fig. 118.12, p. 1394.*)

In some centers, decompressive **craniectomy** is used. Others use a **pentobarbital infusion**, with a loading dose of 5-10 mg/kg over 30 minutes followed by 5 mg/kg every hour for 3 doses and then maintenance with an infusion of 1 mg/kg/hr. Careful blood pressure monitoring is required because of the possibility of drug-induced hypotension and the frequent need for support with fluids and/or pressors. Mild hypothermia (32–34°C [89.6–93.2°F]) to control refractory ICP is controversial but can be induced and maintained by means of surface cooling. Sedation and neuromuscular blockade are used to prevent shivering, and rewarming should be slow. Hypotension should be prevented during rewarming. Refractory raised ICP can also be treated with hyperventilation ($Paco_2$ = 25-30 mm Hg). Combinations of these second-tier therapies are often required.

Supportive Care

Euvolemia should be maintained, and isotonic fluids are recommended throughout the ICU stay. Either SIADH or CSW can develop and are important to differentiate, because management of SIADH is fluid restriction and that of CSW is sodium replacement. Severe hyperglycemia (blood glucose level >200 mg/dL) should be avoided and treated. The blood glucose level should be monitored frequently. Early nutrition with enteral feedings is advocated. Corticosteroids should generally not be used unless adrenal insufficiency is documented. Tracheal suctioning can exacerbate raised ICP. Timing of the use of analgesics or sedatives around suctioning events and/or use of tracheal or IV lidocaine can be helpful. Seizures are common after severe acute TBI. Early posttraumatic seizures (within 1 week) will complicate management of TBI and are often difficult to treat. Anticonvulsant prophylaxis with fosphenytoin or levetiracetam is recommended. Late posttraumatic seizures (≥7 days after TBI) and, if recurrent, late posttraumatic epilepsy are not prevented by prophylactic anticonvulsants, whereas early posttraumatic seizures are prevented by initiating anticonvulsants soon after TBI. Antifibrinolytic agents (tranexamic acid) reduce hemorrhage size, as well as the development of new focal ischemic cerebral lesions and improve survival in adults with severe TBI.

Prognosis

Mortality rates for children with severe TBI who reach the pediatric ICU range between 10% and 30%. Ability to control ICP is related to patient survival, and the extent of cranial and systemic injuries correlates with quality of life. Motor and cognitive sequelae resulting from severe TBI generally benefit from rehabilitation to minimize long-term disabilities. Recovery from TBI may take months or years to achieve. Physical therapy, and in some centers methylphenidate or amantadine, helps with motor and behavioral recovery. Pituitary insufficiency may be an uncommon but significant complication of severe TBI.

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Chapter 83

Brain Death: Death by Neurologic Criteria

Matthew P. Kirschen and Wynne Morrison

Brain death, also known as **death by neurologic criteria**, is legally and culturally accepted as death in most of the world. In the United States, the **Uniform Determination of Death Act (UDDA)** defines brain death as the irreversible (some use "permanent") cessation of all functions of the entire brain, including the brainstem. The UDDA or a similar statute has been adopted in all states. Guidelines for the declaration of brain death in infants and children were published jointly by the Society of Critical Care Medicine (SCCM), American Academy of Pediatrics (AAP), and Child Neurology Society (CNS) in 2011. In 2020, the World Brain Death Project published a consensus statement with recommendations for the minimum clinical standards for determination of brain death in adults and children.

EPIDEMIOLOGY

Brain death by definition must occur as a result of catastrophic permanent global brain injury. Approximately 20% of children who die in pediatric intensive care units (PICUs) are declared brain dead. The most common etiologies of brain injury leading to brain death are hypoxic-ischemic injury from cardiac arrest, shock and/or respiratory failure without cardiac arrest, traumatic brain injury, intracranial infections, toxic ingestions, and causes of malignant cerebral edema. Mimics of brain death include botulism, Guillain-Barré syndrome, and high cervical cord injuries.

CLINICAL EVALUATION AND DIAGNOSIS

Brain death is determined by a careful, thorough clinical evaluation. The fundamental components of brain death are **coma**, **absence of brainstem reflexes**, and **apnea**. The first step in the brain death evaluation is to confirm that the catastrophic brain injury occurred because of an etiology known to lead to brain death. The next step is to ensure that there are no confounding conditions that could mimic or falsely suggest brain death. This is done by meticulously ensuring the patient is not hypotensive or hypothermic; does not have severe metabolic abnormalities like hypoglycemia, hyponatremia, or acidosis; and that sufficient time has passed to allow for clearance of all sedating medication or other toxins that could confound the examination. This involves review of the medical history, neuroimaging, electroencephalography (EEG), and laboratory data to rule out reversible causes of coma. Additionally, the patient should be observed for a sufficient amount of time (typically at least 24 hours after CPR or from their severe acute brain injury) to ensure there is no recovery of neurologic function. Checklists are very helpful in ensuring no prerequisites are missed (Fig. 83.1). Confounding factors must be corrected, if feasible, before initiation of the brain death evaluation. If all confounders are unable to be adequately corrected, ancillary testing is required to diagnose brain death. Brain death evaluation should not be performed in infants <37 weeks corrected gestational age.

Brain Death Neurologic Examination

The clinical examination evaluates for coma; absence of motor responses of the head, neck, and extremities; and brainstem areflexia including apnea in a setting of an adequate respiratory stimulus. The patient must be unresponsive to tactile, auditory, and visual stimulation other than spinally mediated reflexes. If it is unclear if motor movements are spinally mediated, ancillary testing may be necessary before brain death can be diagnosed. Brainstem reflexes must be absent. Table 83.1 lists the components of the neurologic examination, including brainstem reflexes to be tested, the brainstem location of each reflex, and the exam finding that is consistent with brain death. Several injuries and conditions can preclude completion or interpretation of the clinical examination. These include spinal cord injury, orbital/facial trauma, and severe neuromuscular disorders. In these situations, an ancillary test must be performed before declaring brain death. It is still necessary to perform all examination components that can be completed, and every component assessed must be consistent with brain death to allow declaration.

Apnea Test

Apnea is the absence of respiratory effort. The purpose of the required apnea test is to evaluate whether the chemoreceptors in the brainstem's medulla, which stimulate respiration when exposed to hypercarbia and acidosis, are functional. The patient should be euvolemic, normotensive, and euthermic before beginning the apnea test. The apnea test can result in cardiopulmonary decompensation and should only be performed in a PICU by clinicians with skills to stabilize or resuscitate the patient if needed. Before the apnea test, the patient is preoxygenated with 100% oxygen for approximately 10 minutes, and ventilation is adjusted to achieve a $Paco_2$ of approximately 40 mm Hg. A baseline arterial blood gas (ABG) documents the starting $Paco_2$ value. The patient is then removed from intermittent mechanical ventilation and provided apneic oxygenation by delivering 100% oxygen via continuous positive airway pressure (CPAP) on the ventilator or via flow-inflating resuscitation bag with a functioning peak end-expiratory pressure (PEEP) valve. The patient's hemodynamics and pulse oximetry oxygen-hemoglobin saturation (Spo_2) are monitored continuously while the physician observes for respiratory effort. An ABG sample is obtained approximately 5-10 minutes into the test and every 2 minutes thereafter until the target $Paco_2$ is surpassed; ventilatory support is resumed at that time. Absence of respiratory effort with a $Paco_2$ ≥60 mm Hg *and* >20 mm Hg above baseline is consistent with brain death. If at any point during the test the patient becomes hypoxic (Spo_2 <85%) or hypotensive, the test is aborted and ventilatory support resumed.

OBSERVATION PERIODS

To determine brain death in the United States, current guidelines recommend the neurologic examination and apnea test be performed by different attending physicians separated by an observation period. The examination determines that the child has met criteria for brain death. An observation period before the examination is based on the patient's age: For infants (≥37 weeks corrected gestational age) and children <24 months, observe for at least 48 hours. For patients >2 years, observe for at least 24 hours. Before testing, core body temperature should be maintained ≥36° C. In addition in adults, systolic blood pressure (SBP) should be ≥100 mm Hg and mean arterial blood pressure (MAP) should be ≥75 mm Hg; in children SBP and MAP should be ≥5th percentile for age.

Similar MAPs are recommended for patients on venoarterial ECMO. Furthermore, before treating metabolic disorders, intoxication and effects of therapeutic medications that depress the CNS and peripheral nervous system (paralytics) must be excluded. In children, two different clinicians must perform independent neurological and apnea examinations separated by a minimal interval of 12 hours.

ANCILLARY STUDIES

Ancillary studies are not required for the diagnosis of brain death and should only be used to assist the clinician in declaring brain death (1) when components of the neurologic examination or apnea test cannot be completed safely because of the underlying medical condition of the patient; (2) if there is uncertainty about the results of the neurologic examination; (3) if a medication effect may be present; or (4) to reduce the observation period between examinations. If an ancillary test is used to shorten the observation period, the physician is still required to complete two clinical examinations and apnea tests, along with the ancillary study.

The most common ancillary tests are EEG and radionuclide perfusion scintigraphy (or cerebral blood flow) studies. Other tests are available (Table 83.2); however, these have not been incorporated into clinical practice in the United States, although they are used outside of the United States in some practice settings. A valid **electroencephalogram** to support a diagnosis of brain death must be performed according to the American EEG Society standards and technical requirements. Confounders should be excluded, and the EEG must demonstrate

Checklist for Documentation of Brain Death

Brain Death Examination for Infants and Children[a]

Age of Patient	Timing of First Examination	Interexamination Interval
Term newborn 37 weeks gestational age and up to 30 days old	☐ First examination may be performed 24 hours after birth OR following cardiopulmonary resuscitation or other severe brain injury	☐ At least 24 hours ☐ Interval shortened because ancillary study (Section 4) is consistent with brain death
31 days to 18 years old	☐ First examination may be performed 24 hours following cardiopulmonary resuscitation or other severe brain injury	☐ At least 12 hours OR ☐ Interval shortened because ancillary study (Section 4) is consistent with brain death

Section 1. Prerequisites for Brain Death Examination and Apnea Test

A. Irreversible and Identifiable Cause of Coma (please check)

☐ Traumatic brain injury ☐ Anoxic brain injury ☐ Known metabolic disorder ☐ Other (specify) _____

B. Correction of Contributing Factors That Can Interfere with the Neurologic Examination

	Examination 1		Examination 2	
a. Core body temperature is >95°F (35°C)	☐ Yes	☐ No	☐ Yes	☐ No
b. Systolic blood pressure or MAP in acceptable range (Systolic BP not less than 2 standard deviations below age-appropriate norm) based on age	☐ Yes	☐ No	☐ Yes	☐ No
c. Sedative/analgesic drug effect excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No
d. Metabolic intoxication excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No
e. Neuromuscular blockade excluded as a contributing factor	☐ Yes	☐ No	☐ Yes	☐ No

☐ If ALL prerequisites are marked YES, then proceed to section 2, OR

☐ _____ confounding variable was present. Ancillary study was therefore performed to document brain death (Section 4).

Section 2. Physical Examination (please check); Note: Spinal Cord Reflexes Are Acceptable

	Examination 1, Date/Time: _____		Examination 2, Date/Time: _____	
a. Flaccid tone, patient unresponsive to deep painful stimuli	☐ Yes	☐ No	☐ Yes	☐ No
b. Pupils are midposition or fully dilated and light reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
c. Corneal, cough, gag reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
d. Sucking and rooting reflexes are absent (in neonates and infants)	☐ Yes	☐ No	☐ Yes	☐ No
e. Oculovestibular reflexes are absent	☐ Yes	☐ No	☐ Yes	☐ No
f. Spontaneous respiratory effort while on mechanical ventilation is absent	☐ Yes	☐ No	☐ Yes	☐ No

☐ The _____ (specify) element of the examination could not be performed because _____.
Ancillary study (EEG or radionuclide CBF) was therefore performed to document brain death (Section 4).

Section 3. Apnea Test

	Examination 1, Date/Time: _____	Examination 2, Date/Time: _____
No spontaneous respiratory efforts were observed despite final $PaCO_2$ ≥60mmHg and a ≥20mmHg increase above baseline (Examination 1). No spontaneous respiratory efforts were observed despite final $PaCO_2$ ≥60mmHg and a ≥20mmHg increase above baseline (Examination 2).	Pretest $PaCO_2$: _____ Apnea duration: _____ min Post-test $PaCO_2$: _____	Pretest $PaCO_2$: _____ Apnea duration: _____ min Post-test $PaCO_2$: _____

Apnea test is contraindicated or could not be performed to completion because _____.
Ancillary study (EEG or radionuclide CBF) was therefore performed to document brain death (Section 4).

Section 4. Ancillary Testing

Ancillary testing is required (1) when any components of the examination or apnea testing cannot be completed; (2) if there is uncertainty about the results of the neurologic examination; or (3) if a medication effect may be present. Ancillary testing can be performed to reduce the interexamination period; however, a second neurologic examination is required. Components of the neurologic examination that can be performed safely should be completed in close proximity to the ancillary test.

Date/Time:_____

☐ EEG report documents electrocerebral silence OR ☐ Yes ☐ No

☐ CBF study report documents no cerebral perfusion ☐ Yes ☐ No

Section 5. Signatures

Examiner 1
I certify that my examination is consistent with cessation of function of the brain and brainstem. Confirmatory examination to follow.
Printed name _____
Signature _____
Specialty _____
Pager #/license # _____
Date mm/dd/yyyy _____
Time _____

Examiner 2
I certify that my examination ☐ and/or ancillary test report ☐ confirms unchanged and irreversible cessation of function of the brain and brainstem. The patient is declared brain dead at this time.
Date/time of death _____
Printed name _____
Signature _____
Specialty _____
Pager #/license # _____
Date mm/dd/yyyy _____
Time _____

[a]Two physicians must perform independent examinations separated by specified intervals.
BP = blood pressure; CBF = cerebral blood flow; EEG = electroencephalography; MAP = mean arterial pressure.

Fig. 83.1 Checklist for documentation of brain death. *(From Nakagawa TA, Ashwal S, Mathur M, et al. Guidelines for the determination of brain death in infants and children: An update of the 1987 Task Force recommendations—executive summary.* Ann Neurol. *2012;71:573-585, Table 2.)*

Table 83.1 Neurologic Examination to Evaluate a Patient for Brain Death

EXAM COMPONENT	HOW TO PERFORM	RESPONSE CONSISTENT WITH BRAIN DEATH
Coma	Visual response: blink to visual threat Auditory response: clapping and yelling the child's name loudly Tactile response: apply deep pressure to the condyles at the level of the temporomandibular joints, the supraorbital notch bilaterally, the sternum, and all four extremities proximally and distally	No response to visual or auditory stimuli; noxious stimuli do not produce grimacing, facial or body muscle movement, or any motor response other than spinally mediated reflexes
Pupillary light reflex (CNs II and III)	Shine a bright light into each eye while closely observing pupillary size and reactivity	Absence of ipsilateral and contralateral pupillary response, with pupils fixed in a midsize or dilated position (4-6 mm) in both eyes
Corneal reflex (CNs III, V, VII)	Touch the cornea of each eye with a cotton swab at the external border of the iris, applying light pressure and observing for any eyelid movement	Absence of eyelid movement
Oculocephalic reflex (CNs III, VI, and VIII)	Confirm integrity of the cervical spine. Secure the endotracheal tube to prevent dislodgement; briskly rotate the head horizontally to both sides and observe for movement of the eyes	Absence of movement of the eyes relative to head movement; eyes follow the head movement, staying in mid-position
Oculovestibular reflex (CNs III, IV, VI, and VIII)	Irrigate the ear canal with 50-60 mL of ice water for at least 60 sec while observing for eye movement; test each side separately and with a 5-min interval in between	Absence of eye movement
Gag and cough reflex (CNs IX and X)	Touch the posterior pharynx with a tongue depressor or a rigid suction catheter to stimulate a gag; touch the tracheobronchial wall at the level of the carina with placement of a suction catheter through the endotracheal tube to stimulate a cough	Absence of both cough and gag
Sucking and rooting reflexes	Place a gloved finger inside the baby's mouth to stimulate sucking; stroke the external surface of both cheeks and corners of the mouth to stimulate rooting	Absence of sucking and rooting

CN, Cranial nerve.

Table 83.2 Ancillary Tests for Determining Brain Death

TEST	CONFOUNDER/LIMITATION*	SENSITIVITY/ SPECIFICITY
BRAIN BLOOD FLOW		
Computed tomography angiography	Requires transport to the scanner Image variability based on injection technique Potential to miss a slow flow state Risk of nephrotoxicity Not recommended by AAN 2023 Guidelines[#]	52–97% / 100%
Digital subtraction angiography[†]	Requires transport to angiography suite Risk of nephrotoxicity Image variability based on injection technique	100% / 100%
Magnetic resonance angiography	Requires transport to the scanner Image variability based on injection technique	93–100% / 100%
Radionuclide angiography[†]	Limited evaluation of brainstem	99% / 56%
Radionuclide scintigraphy[†]	Requires transport to the scanner Planar imaging may have limited evaluation of brainstem	Planar: 78% / 100% SPECT: 88% / 100%
Transcranial Doppler ultrasonography[†]	Potential for technical difficulties in performance Potential for lack of windows	90% / 98%
ELECTROPHYSIOLOGIC FUNCTION		
Electroencephalography	Risk of environmental artifact Confounded by sedation, hypothermia and toxic-metabolic derangements Predominantly provides information about cortical function	53–80% / 97%
Evoked potentials-auditory	Can be absent in comatose patients with other intact brainstem reflexes Confounded by sedation, hypothermia, isolated eighth nerve and brainstem lesions Only evaluates auditory pathways Performance/interpretation may be limited by experience	NA / NA
Evoked potentials-somatosensory	Can be absent in comatose patients with ongoing brain function Confounded by cervical spine injury, isolated brainstem lesions, sedation, and hypothermia Only evaluates somatosensory pathways Performance/interpretation may be limited by experience	100% / 78%
Evoked potentials-visual	Can be absent in comatose patients with ongoing brain function Confounded by sedation, retinal or optic nerve lesions Only evaluates visual pathways Performance/interpretation may be limited by experience	NA / NA

*Performance/interpretation of all ancillary tests may be limited by experience
[†]Accepted by the World Brain Death Project (WBDP).
[#]Report of the AAN Guidelines Subcommittee, AAP, CNS, SCCM. Pediatric and adult brain death/death by neurologic criteria consensus guideline. *Neurology* 2023;101:1-21.
NA, Not available.
From Lewis A, Kirschen MP, Badenes R. Quality improvement in the determination of death by neurologic criteria around the world. *Crit Care.* 2023;27(1):96.

electrocerebral silence. A **radionuclide cerebral blood flow study** consists of intravenous injection of a radiopharmaceutical agent followed by imaging of the brain by planar or single-photon emission computed tomography (SPECT) imaging. A study that demonstrates absence of intracranial blood flow and cerebral perfusion is supportive of brain death. CT and MR angiography are not recommended.

Interpretation of both EEG and cerebral blood flow studies should only be performed by trained and qualified individuals. If the study shows any evidence of electrical activity or cerebral blood flow, brain death cannot be declared. A 24-hour waiting period is recommended before repeating the brain death evaluation.

DOCUMENTATION

Documentation is an important aspect of the brain death evaluation and determination and should follow a checklist, including the following points:

1. Etiology of brain injury
2. Absence of confounding factors, including hypothermia, hypotension, metabolic abnormalities, and recent doses of sedative or neuromuscular blocking agents
3. Absence of motor response to tactile, auditory, and visual stimuli
4. Absence of brainstem reflexes, including pupillary light reflex, oculocephalic/oculovestibular reflex, corneal reflex, cough reflex, and gag reflex
5. ABG values during the apnea test and statement about respiratory effort
6. Results of ancillary testing (if indicated)

AFTER DECLARATION OF BRAIN DEATH

After brain death has been declared, the child is legally dead. The time of death is the time the final required component of the evaluation is completed: either ABG results or ancillary test. Families may be approached by representatives of organ procurement organizations to discuss options for organ donation after brain death. For families that choose not to donate organs, the next appropriate step in the care of the child is removal of technologic supports, including mechanical ventilation, after which the child's heart will become asystolic. It is important for care providers to be supportive of the family dealing with this difficult situation. Child life and palliative care specialists can be helpful in guiding families during this time. Technologic support is typically stopped within a few hours of declaring brain death, although in some situations it can be delayed at the discretion of the physician and in accordance with hospital protocols.

OBJECTIONS TO THE CONCEPT OF BRAIN DEATH

The concept of brain death may not be accepted by families for personal, religious, or cultural reasons. Some families have difficulty comprehending the fact that their child meets criteria for legal death despite having a heartbeat, blood pressure, and being warm to the touch. Other families maintain hope for recovery, and some have religious views that death can only be declared after cessation of cardiorespiratory function. Some individuals have challenged the brain death guidelines claiming that they do not sufficiently evaluate "all functions of the entire brain, including the brainstem," as mandated by the UDDA, particularly as some patients who meet brain death criteria continue to show evidence of *integrative functioning,* such as control over free water homeostasis (absence of diabetes insipidus), control of temperature regulation, and capacity for growth and wound healing. Others argue that the intent of the UDDA is met by the current clinical evaluation. Objections to performing the brain death evaluation or declaration of death should be handled by a multidisciplinary team with experience in these situations. These teams often include physicians, social workers, ethicists, chaplains, hospital administrators, and lawyers as appropriate.

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Chapter 84

Syncope

Aarti S. Dalal and George F. Van Hare

Syncope is defined as a sudden transient loss of consciousness with inability to maintain postural tone. The most common cause of syncope in the normal pediatric population is **neurocardiogenic syncope** (vasovagal syncope, fainting). **Vasovagal syncope** is classically associated with a prodrome that includes diaphoresis, warmth, pallor, or feeling lightheaded and is often triggered by acute position changes or by a specific situation or event such as pain, medical procedures, or emotional distress (Table 84.1). This type of syncope is characterized by hypotension and bradycardia. Approximately 30–50% of children will have had a **fainting** episode before 18 years of age. The symptoms of vasovagal syncope can overlap with those of postural orthostatic tachycardia syndrome (POTS), a constellation of symptoms characterized by symptoms of rapid heart rate and supported by a positional increase in heart rate by 40 beats per minute with normal blood pressure (see Chapter 84.1).

Most patients with a vasovagal syncope episode will have prodromal features followed by loss of motor tone. Once in a horizontal position, consciousness returns rapidly, usually in 1-2 minutes; some patients may have a brief period of stiffening or jerking, which should not be confused with a **seizure** (Table 84.2). Syncope must also be distinguished from **vertigo** and **ataxia** (Table 84.3).

Although this type of syncope is very common in adolescence and has an excellent prognosis, other causes for loss of consciousness are more dangerous; thus syncope may be the first sign of more serious conditions (Table 84.4). Indeed, the occurrence of syncope may well be the pediatrician's best opportunity to diagnose a life-threatening condition before the patient subsequently succumbs. The task of the clinician therefore is not only to counsel the family and the patient concerning the common form but also to rule out a number of important life-threatening cardiac problems.

MECHANISMS

Syncope by whatever mechanism is caused by a lack of adequate cerebral blood flow with loss of consciousness and inability to remain upright.

Primary **cardiac causes** of syncope (see Table 84.4) include conditions that predispose a patient to arrhythmias or conditions such as congenital or acquired structural heart disease. Arrhythmic causes of syncope include Wolff-Parkinson-White syndrome (particularly with atrial fibrillation), ventricular tachycardia (VT), and occasionally supraventricular tachycardia (see Chapter 484). VT may be associated with hypertrophic cardiomyopathy (HCM), arrhythmogenic cardiomyopathy, repaired congenital heart disease, or an inherited arrhythmia syndrome such as catecholaminergic polymorphous ventricular tachycardia (CPVT) or long QT syndrome (LQTS) (Table 84.5). Other arrhythmias that may lead to syncope are bradyarrhythmias such as sinus node dysfunction and high-grade second- or third-degree atrioventricular (AV) block. Syncope may also be caused by cardiac obstructive lesions, such as critical aortic stenosis, or coronary artery anomalies, such as an aberrant left coronary artery arising from the right sinus of Valsalva. Patients with primary pulmonary hypertension or Eisenmenger syndrome may also experience syncope. In all the obstructive forms of syncope, exercise increases the likelihood of an episode because the obstruction interferes with the ability of the heart to increase cardiac output in response to exercise.

Noncardiac causes of loss of consciousness include epilepsy, basilar artery migraine, hysterical syncope, and psychogenic nonepileptic seizures (see Table 84.1). Occasionally, patients with narcolepsy may present with syncope. Hypoglycemia and hyperventilation may also present as syncope.

Table 84.1 Noncardiac Causes of Syncope

REFLEX VASODEPRESSOR SYNCOPE
Neurocardiogenic (vasovagal)
Emotion (seeing blood)
Pain (needle phobia)
Reflex asystolic syncope (pallid breath-holding)

MISCELLANEOUS SITUATIONAL REFLEX
Tussive
Sneeze
Exercise, after exercise
Swallowing
Stretching
Defecation
Micturition
Hair grooming
Valsalva (increased intrathoracic pressure)
Trumpet playing
Weightlifting
Breath-holding spells (cyanotic)

SYSTEMIC ILLNESS
Hypoglycemia
Anemia
Infection
Hypovolemia, dehydration
Adrenal insufficiency
Narcolepsy, cataplexy
Pulmonary embolism
Pheochromocytoma
Mastocytosis
Ruptured ectopic pregnancy

CENTRAL NERVOUS SYSTEM
Seizure (atonic, absence, myoclonic-astatic)
Hyperekplexia
Stroke, transient ischemic attack
Friedreich ataxia
Subarachnoid hemorrhage

OTHER NEUROLOGIC
Dysautonomia
Myotonic dystrophy
Kearns-Sayre syndrome
Congenital myasthenia gravis
Basilar artery migraine
Arnold Chiari malformation

DRUG EFFECTS
β-Blocking agents
Vasodilating agents
Opiates
Sedatives
Diuretics
Anticonvulsant agents
Antihistamines
Antidepressant agents
Anxiolytic agents
Drugs of abuse
Insulin, oral hypoglycemic agents
Carbon monoxide

OTHER ETIOLOGIES
Carotid sinus sensitivity
Subclavian steal
Panic attack, anxiety
Conversion disorder

Table 84.2 Comparison of Clinical Features of Syncope and Seizures

FEATURES	SYNCOPE	SEIZURES
Relation to posture	Common	No
Time of day	Diurnal	Diurnal or nocturnal
Precipitating factors	Emotion, injury, pain, crowds, heat, exercise, fear, dehydration, coughing, micturition, venipuncture, prolonged standing	Sleep loss, drug/alcohol withdrawal, illness, medication nonadherence
Skin color	Pallor	Cyanosis or normal
Diaphoresis	Common	Rare
Aura or premonitory symptoms	Often minutes or longer, but can be very brief	Brief
Convulsion	Rare	Common
Other abnormal movements	Minor irregular twitching	Rhythmic jerks
Injury	Rare	Common (with convulsive seizures)
Urinary incontinence	Rare	Common
Tongue biting	No	Common with convulsive seizures
Postictal confusion	Rare	Common
Postictal headache	No	Common
Focal neurologic signs	No	Occasional
Cardiovascular signs	Common to have low blood pressure and heart rate during event; cardiovascular exam may be completely normal after event unless there is an underlying cardiac disorder	Rare
Abnormal findings on EEG	Rare (generalized slowing may occur during the event)	Common

From Winkel D, Cassimatis D. Episodic impairment of consciousness. In: Jankovic JM, Mazziotta JC, Pomeroy SL, Newman NJ, eds. *Bradley and Daroff's Neurology in Clinical Practice*, 8th ed. Philadelphia: Elsevier; 2021.

Table 84.3 Syncope and Dizziness

	VERTIGO	PRESYNCOPE	DISEQUILIBRIUM	LIGHTHEADEDNESS
Patient complaint	"My head is spinning." "The room is whirling."	"I feel I might pass out." "I feel faint." "I feel like blacking out."	"I feel unsteady." "My balance is off."	"I feel dizzy." "I feel disconnected, drugged."
Associated features	Motion, swaying, spinning, nystagmus	Syncope: loss of postural tone, brief loss of consciousness Situational	Poor balance No vertigo or ataxia	Anxiety, hyperventilation, paresthesias, respiratory alkalosis, panic attacks
Usual cause	Vestibular disorders	Impaired cerebral perfusion	Sensory and/or central neurologic dysfunction	Decreased venous return
Key differential diagnoses	Peripheral (labyrinthine-cochlear) vs central neurologic disorder	Neurocardiogenic (vagal) vs cardiac syncope vs neuropsychiatric syncope	Sensory deficit vs central neurologic disease	Anxiety/depression vs hyperventilation vs medication effects

Adapted from Cohen G. Syncope and dizziness. In: Kliegman RM, Lye PS, Bordini BJ, et al., eds. *Nelson Pediatric Symptom-Based Diagnosis*; 2018: Table 6.1, p. 84.

Table 84.4 Causes of Cardiovascular Syncope: Potentially Fatal If Unrecognized

ARRHYTHMIAS

Bradyarrhythmias

1. Sinus node dysfunction (especially in patients with congenital heart defects)
2. Atrioventricular block (congenital or acquired; Lyme, Fabry, Chagas diseases)
3. Kearns-Sayre syndrome
4. Pacemaker malfunction

Tachyarrhythmias

1. Supraventricular
   a. Wolff-Parkinson-White syndrome
   b. Supraventricular tachycardia/atrial arrhythmias (especially in patients with congenital heart defects)
2. Ventricular: ventricular tachycardia/torsades/ventricular fibrillation
   a. Channelopathies
      - Long QT syndromes
      - Catecholaminergic polymorphic ventricular tachycardia
      - Brugada syndrome
      - Short QT syndrome
   b. Drug induced
   c. Idiopathic
      - Ventricular fibrillation
      - Ventricular tachycardia from outflow tract

STRUCTURAL/FUNCTIONAL HEART DISEASE

Cardiomyopathy

1. Hypertrophic cardiomyopathy
2. Dilated cardiomyopathy
3. Arrhythmogenic right ventricular dysplasia
4. Left ventricular noncompaction

Coronary Anomalies

1. Anomalous origin
2. Kawasaki disease
3. Multisystemic inflammatory syndrome in children (MIS-C) secondary to SARS-CoV-2

Valvar Aortic Mitral or Pulmonary Stenosis

Takotsubo Disease

Acute Myocarditis

Congenital Heart Disease (Repaired and Unrepaired)

Pulmonary Hypertension, Pulmonary Embolus

Aortic Dissection (Marfan Syndrome)

Cardiac Masses (Myxoma, Rhabdomyoma, Thrombus)

Eisenmenger Syndrome

From MacNeill E, Vashist S. Approach to syncope and altered mental status. *Pediatr Clin N Am.* 2013;60:1083-1106.

EVALUATION

The most important goal in the evaluation of the new patient with syncope is to diagnose life-threatening causes of syncope so that these causes can be managed and more severe outcomes avoided. Many patients presenting with sudden cardiac arrest caused by conditions such as LQTS will have previously experienced an episode of syncope, so the presentation with syncope is an opportunity to prevent sudden death.

The most important tool in evaluation of syncope is a careful **personal** and **family history**. The characteristics of cardiac syncope differ significantly from benign causes of syncope such as neurocardiogenic syncope (Table 84.6). Several red flags can be identified that should lead the clinician to suspect that the mechanism is a life-threatening cardiac cause rather than simple fainting (Table 84.7). The occurrence *during* exercise suggests an arrhythmia or an outflow tract or coronary artery obstruction. Noncardiac (postexercise) syncope is seen in athletes *after* a strenuous workout or competition and has no associated cardiac features. The occurrence of syncope resulting in injury also suggests an arrhythmia, as it indicates a sudden onset with a lack of adequate prodromal symptoms. The occurrence of syncope while recumbent would be quite unusual in a patient with neurocardiogenic syncope and therefore suggests a cardiac or neurologic cause. Occasionally, a patient with syncope caused by a tachyarrhythmia will report the sensation of a racing heart before the event, but this is often not present.

A careful family history is essential in evaluation of syncope. Specifically, if there are first-degree relatives with inherited syndromes, such as LQTS, CPVT, or HCM, this should lead to more specific evaluation of the patient. If relatives died suddenly at a young age without a clear and convincing cause, inherited cardiac arrhythmias or cardiomyopathies should also be suspected. Other questions that may increase suspicion for an inherited arrhythmia include family history of congenital deafness, unexplained recurrent syncope, poorly controlled seizures, single-vehicle car accidents, or drowning events.

Patients with a history of heart disease requiring surgical repair may have causes of syncope that are specific to their repair. Sinus node dysfunction is common after the Senning or Mustard procedure for transposition of the great vessels or after the Fontan procedure for single-ventricle palliation. VT may be seen after repair of tetralogy of Fallot. A patient with a history of repair of a ventricular septal defect or an AV canal defect should be evaluated for the late occurrence of AV block. Patients with an implanted pacemaker should be evaluated for pacemaker lead failure.

The **physical examination** may also offer clues (see Table 84.7) that point toward cardiac syncope. Patients with HCM or aortic stenosis may have a prominent cardiac impulse and/or an ejection murmur. A patient with primary pulmonary hypertension will have a displaced apical impulse, with a loud and single second

Table 84.5 Primary Electrical Abnormalities: Features, ECG, and Treatment

PRIMARY ELECTRICAL ABNORMALITIES	FEATURES	ECG	TREATMENT
LQTS: Romano-Ward, Jervell–Lange-Nielsen, acquired	• Familial genetic or acquired disorders • Ion channel pathologic gene variant (~17 genes)* • Presents in torsades de pointes • Romano-Ward is most common inherited • LQTS Jervell–Lange-Nielsen has congenital deafness	• Prolonged QT measured from the onset of the Q wave to the end of the T wave in lead II • Varies with HR but >0.44 in men, >0.46 in children and women for HR 50-90 beats/min is prolonged • Torsades de pointes can occur • Can deteriorate from polymorphic ventricular tachycardia to ventricular fibrillation	• β-Blocker therapy • Recommendations on exercise intensity by a cardiologist • ICD if β blockers fail
Brugada syndrome	• Inherited autosomal dominant arrhythmogenic syndrome characterized by life-threatening ventricular arrhythmias • Pathologic gene variant in *SCN5A* and 13 other genes	• ECG abnormalities are from repolarization and depolarization abnormalities • Coved-type ST-segment elevations in the right precordial leads • J wave amplitude ≥2 mm followed by a negative T wave	• Placement of ICD
Wolff-Parkinson-White	• Owing to one or more reentrant pathways inducing SVT or atrial fibrillation • Up to 14% associated with malignant tachycardias • Malignant arrhythmias from short reentrant pathway repolarization or multiple pathways	• Short PR interval • Delta waves present	• Undergo EPS and ablation
Dilated cardiomyopathy: ventricular tachycardia/ fibrillation	• Cardiac dilation and systolic dysfunction • Inherited or acquired • Lamin AC pathologic gene variant a common cause of DCM and SCD	• Marked LVH • Poor R-wave progression • Left atrial enlargement • Right axis deviation	• Permanent pacemaker and ICD placement
Catecholamine-exercise: ventricular tachycardia	• Ventricular ectopy induced by exercise or emotional stress • Variant in gene that encodes Ca-mediated sarcoplasmic fibers • Lethal in 30–50% if left untreated	• Preexercise ECG is usually normal, stress testing recommended • ECG with exercise • Nonsustained wide ventricular tachycardia	• β-Blocker therapy • Recommendations on exercise intensity by a cardiologist • ICD if β blockers fail

DCM, Dilated cardiomyopathy; EPS, electrophysiology study; HR, heart rate; ICD, implantable cardioverter defibrillator; LQTS, long QT syndrome; LVH, left ventricular hypertrophy; SCD, sudden cardiac death; SVT, supraventricular tachycardia.
*Major genes: *KCNQ1, KCNH2, SCN5A* in ~75% cases.
Modified from Ellison S. Sudden cardiac death in adolescents. *Prim Care Clin Office Pract.* 2015;42:57-76.

Table 84.6 Differentiating Features for Causes of Syncope

NEUROCARDIOGENIC
Symptoms after prolonged motionless standing, sudden unexpected pain, fear, or unpleasant sight, sound, or smell; pallor
Syncope in a well-trained athlete *after* exertion (without heart disease)
Situational syncope during or immediately after micturition, cough, swallowing, or defecation
Syncope with throat or facial pain (glossopharyngeal or trigeminal neuralgia)
ORGANIC HEART DISEASE (PRIMARY ARRHYTHMIA, OBSTRUCTIVE HYPERTROPHIC CARDIOMYOPATHY, PULMONARY HYPERTENSION)
Brief sudden loss of consciousness, no prodrome, history of heart disease
Syncope while sitting or supine
Syncope with exertion
History of palpitations
Family history of sudden death
NEUROLOGIC
Seizures: preceding aura, postevent symptoms lasting >5 min (includes postictal state of decreased level of consciousness, confusion, headache, or paralysis)
Migraine: syncope associated with antecedent headaches with or without aura
OTHER VASCULAR
Carotid sinus: syncope with head rotation or pressure on the carotid sinus (as in tumors, shaving, tight collars)
Orthostatic hypotension: syncope immediately on standing, especially after prolonged bed rest
DRUG INDUCED
Patient is taking a medication that may lead to long QT syndrome, orthostasis, or bradycardia
PSYCHIATRIC ILLNESS
Frequent syncope, somatic complaints, no heart disease

From Cohen G. Syncope and dizziness. In: Kliegman RM, Lye PS, Bordini BJ, et al., eds. *Nelson Pediatric Symptom-Based Diagnosis.* Philadelphia: Elsevier; 2018: Table 6.4.

Table 84.7 Red Flags in Evaluation of Patients with Syncope

Syncope with activity or exercise or supine
Syncope not associated with prolonged standing
Syncope precipitated by loud noise or extreme emotion
Absence of presyncope or lightheadedness
Family history of syncope, drowning, sudden death, familial ventricular arrhythmia syndromes,* cardiomyopathy
Syncope requiring CPR
Injury with syncope
Anemia
Other cardiac symptoms
Chest pain
Dyspnea
Palpitations
History of cardiac surgery
History of Kawasaki disease
Implanted pacemaker
Abnormal physical examination
Murmur
Gallop rhythm
Loud and single second heart sound
Systolic click
Increased apical impulse (tachycardia)
Irregular rhythm
Hypotension or hypertension
Digital clubbing
Cyanosis

*Long QT syndrome, Brugada syndrome, catecholamine polymorphic ventricular tachycardia, arrhythmogenic cardiomyopathy.

heart sound, with an ejection click or murmur of pulmonary insufficiency. Patients with repaired congenital heart disease will have obvious scars on their chest and abdomen from prior cardiac surgery or device implantation.

All patients presenting with syncope *should* have an **electrocardiogram**, looking primarily for QT interval prolongation, preexcitation, ventricular hypertrophy, T-wave abnormalities, and conduction abnormalities. Additional tests that may be needed include echocardiography, exercise testing, cardiac MRI, or 24-hour Holter monitoring. In patients for whom there is a strong suspicion of a paroxysmal arrhythmia, an insertable cardiac monitor (loop recorder) may offer the most effective means of diagnosis. Additional tests may be useful to look for anemia, hypoglycemia, drugs of abuse, and other etiologies noted in Table 84.1 as determined by the history and physical examination.

TREATMENT

Therapy for vasovagal syncope includes avoiding triggering events (if possible), fluid and salt supplementation, and if needed, specific therapies targeting the orthostatic hypotension (i.e., midodrine) (Table 84.8). Immediately after the event, the patient should remain supine until symptoms abate to avoid recurrence.

Treatment for cardiac causes of syncope will be determined by the diagnosis. If supraventricular tachycardia (SVT) is found, then a catheter ablation may be indicated. If bradycardia from sinus node dysfunction or AV block is the cause of the syncope, a pacemaker may be warranted. Patients with syncope from medically refractory malignant arrhythmias, as may be seen in HCM, LQTS, arrhythmogenic cardiomyopathy, or CPVT, require an implantable cardioverter-defibrillator. Patients with structural heart disease (valvular disease or coronary artery anomalies) should be referred for surgery.

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Table 84.8 Treatment of Neurocardiogenic Syncope/Vasovagal Syncope (V-VS)

Patient education on the diagnosis and prognosis of V-VS is recommended. In all patents with the common faint or V-VS, an explanation of the diagnosis, education targeting awareness of and possible avoidance of triggers (prolonged standing, warm environments, coping with dental and medical settings), and reassurance about the benign nature of the condition should be provided.
Physical counterpressure maneuvers can be useful in patients with V-VS who have a sufficiently long prodromal period. Patients with a syncope prodrome should be instructed to assume a supine position to prevent a faint and minimize possible injury. In patients with a sufficiently long prodrome, physical counter-maneuvers (leg crossing, limb and/or abdominal contraction, squatting, isometric handgrip, arm tensing) are a core management strategy.
Midodrine is reasonable in patients with recurrent V-VS with no history of hypertension, heart failure, or urinary retention. Midodrine is a prodrug that is metabolized to desglymidodrine, which is a peripherally active α-agonist used to ameliorate the reduction in peripheral sympathetic neural outflow responsible for venous pooling and vasodepression in V-VS.
The usefulness of orthostatic training is uncertain in patients with frequent V-VS. There are 2 main methods of orthostatic training. Patients undergo repetitive tilt-table tests in a monitored setting until a negative tilt-table test occurs and then are encouraged to stand quietly against a wall for 30-60 min daily, or patients simply stand quietly against a wall at home for a prolonged period daily.
Fludrocortisone might be reasonable for patients with recurrent V-VS and inadequate response to salt and fluid intake, unless contraindicated. Fludrocortisone has mineralocorticoid activity resulting in sodium and water retention and potassium excretion, which results in increased blood volume. Serum potassium level should be monitored because of potential drug-induced hypokalemia. POST II (Prevention of Syncope Trial II) reported a marginally insignificant 31% risk of reduction in adults with moderately frequent V-VS, which was significant in patients after a 2-wk dose stabilization period.
Encouraging increases in salt and fluid intake may be reasonable in selected patients with V-VS, unless contraindicated. Evidence for the effectiveness of salt and fluid intake for patients with V-VS is limited. Nonetheless, in patients with recurrent V-VS and no clear contraindication, such as a history of hypertension, renal disease, heart failure, or cardiac dysfunction, it may be reasonable to encourage ingestion of 2-3 L of fluid per day and a total of 6-9 g (100-150 mmol) of salt per day, or about 1-2 heaping teaspoonfuls. The long-term balance of risks and benefits of a strategy of increasing salt and water intake is unknown.
In selected patients with V-VS, it may be reasonable to reduce or withdraw medications that cause hypotension when appropriate. A careful examination of the patient's history for medications that may lower blood pressure (hypotensive agents) should be performed. Care should be taken to withdraw or reduce medications only when safe to do so and in conjunction with the prescribing healthcare provider.
In patients with recurrent V-VS, a selective serotonin reuptake inhibitor might be considered. Serotonin has central neurophysiologic effects on blood pressure and heart rate and acutely induces syncope during tilt-table testing.

Modified from Shen WK, Sheldon RS, Benditt DG, et al. 2017 ACC/AHA/HRS guideline for the evaluation and management of patients with syncope: A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society [published correction appears in *Circulation*. 2017 Oct 17;136(16):e271-e272]. *Circulation*. 2017;136(5):e60-e122.

84.1 Postural Tachycardia Syndrome

Gisela G. Chelimsky and Thomas Chelimsky

Several complex and interrelated mechanisms allow humans to stand despite the pull of gravity on the cerebral circulation. In the supine posture, most blood sits in the thoracic cavity, with 25–30% of total volume in the splanchnic vasculature. When an adult stands up, about 500 mL of blood shifts to the lower extremities and to the splanchnic vasculature. The decrease in hydrostatic pressure in the carotid sinuses produces vasoconstriction in the peripheral vessels mediated by sympathetic outflow and in the splanchnic vasculature. This action is mediated by norepinephrine, adenosine triphosphate (ATP), and neuropeptide Y. The muscles in the legs and gluteal area work as a pump when the individual is upright and during exercise to help return the blood to the heart.

Understanding postural tachycardia syndrome, or postural orthostatic tachycardia syndrome **(POTS)**, requires an understanding of other orthostatic conditions. Many adolescents have lightheadedness or tunnel vision in the first few seconds of assuming the upright posture. This phenomenon, termed **initial orthostatic hypotension (IOH)**, can lead to *syncope,* but usually is very short, perhaps 30-60 seconds, and occurs primarily with active standing. Blood pressure (BP) may drop 30% of baseline at 10-20 seconds of standing and may be associated with tachycardia. BP returns to baseline in 30-60 seconds, whereas heart rate (HR) typically returns to a new, higher value above the baseline when supine. Because of its transient rapidity, IOH escapes detection with standard BP machines and requires beat-to-beat monitoring of BP and HR. The clinical diagnosis requires a careful history. The symptoms usually happen after prolonged recumbence and when the individual stands. The person complains of lightheadedness and "blacking out" or tunnel vision 5-10 seconds after standing.

In contrast to IOH, **orthostatic hypotension (OH)** is defined as a *sustained* decrease in the systolic BP of >20 mm Hg or diastolic BP >10 mm Hg in the first 3 minutes of upright tilt. OH rarely occurs in children. The patient often has no orthostatic symptoms while upright despite very low pressures (Fig. 84.1). This distinguishes OH from POTS, which *requires* symptoms while upright. A third orthostatic disorder, **reflex syncope** (i.e., vasovagal or neurally mediated), is defined as relatively sudden change in autonomic nervous system activity that leads to a sudden decrease in BP, HR, and cerebral perfusion (Fig. 84.2).

In children, POTS is defined as a syndrome characterized by HR increase of >40 beats/min during the first 10 minutes of upright tilt test without associated hypotension, (>30 beats/min if >19 years old) while replicating orthostatic symptoms that occur when upright (Fig. 84.3). Improvement of symptoms in the supine position is expected. The diagnosis of POTS also requires *daily* orthostatic symptoms. In patients with POTS, the larger decline in cardiac stroke volume appears to be the primary trigger for the tachycardia, which may result from various pathophysiologic mechanisms, such as the following:

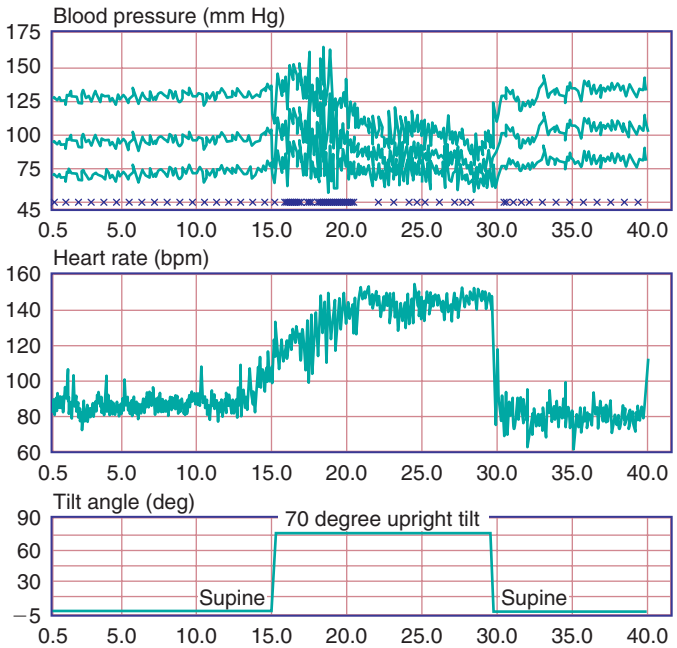

Fig. 84.1 Example of orthostatic hypotension.

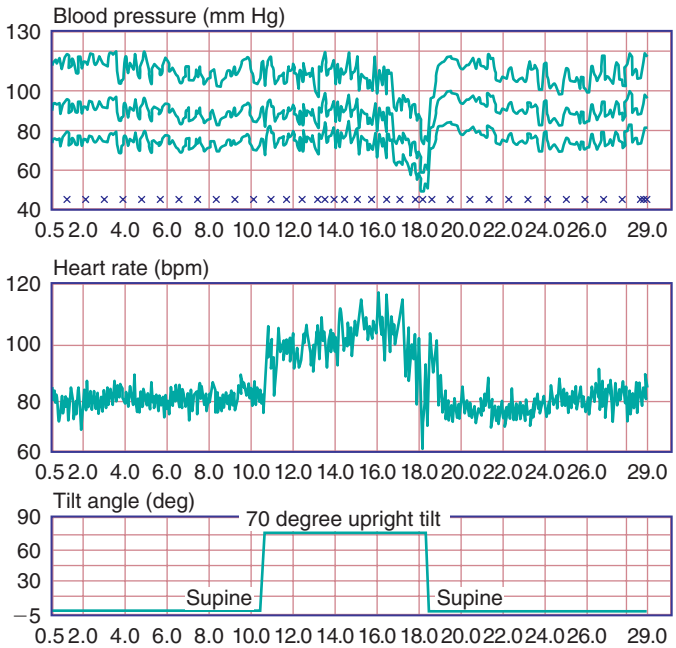

Fig. 84.2 Example of neurally mediated syncope.

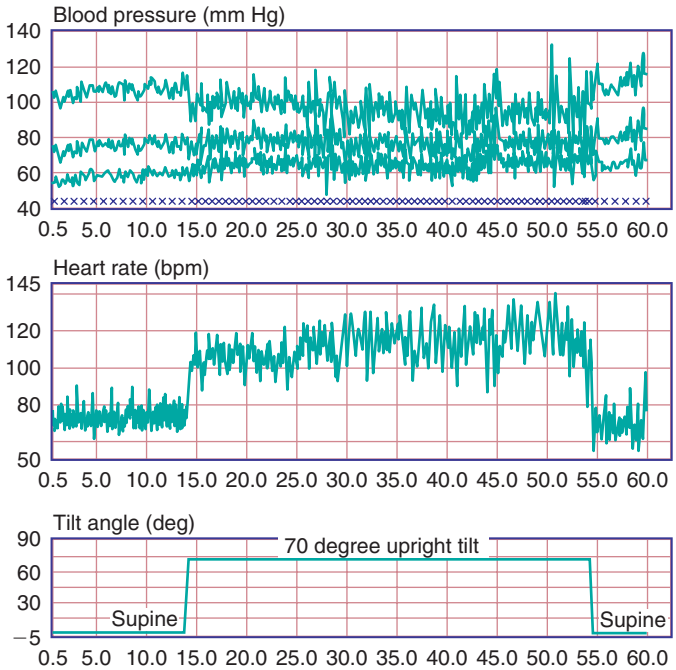

Fig. 84.3 Example of postural tachycardia syndrome.

- **Neuropathic** POTS, an autonomic neuropathy impairing sympathetic venoconstriction in the lower extremities or splanchnic circulation, decreasing stroke volume and consequently resulting in tachycardia.
- **Hypovolemic** POTS, a common contributor, often related to decreased aldosterone with reduced renin activity, resulting in tachycardia caused by decreased blood volume.
- **Hyperadrenergic** POTS, with norepinephrine levels rising threefold to fourfold in the standing position (norepinephrine normally doubles on standing), which may occur in norepinephrine transporter deficiency or strong stimulation of central baroreflex responses.
- **Autoimmune** POTS, typically assumed based on a postviral chronology, but seldom proven; such a form may or may not exist. The antiganglionic antibody is almost never elevated in these patients. Nonetheless, a group of patients report that intravenous immunoglobulin (IVIG) is helpful to them. Whether they benefit from the increase in intravascular volume or an actual immune effect is unknown.

Some patients have orthostatic symptoms while upright but do not meet criteria for syncope, OH, or POTS. This group has **orthostatic intolerance not otherwise specified (OI-NOS)**.

CLINICAL PRESENTATION

The symptoms that intrinsically relate to POTS are those that are replicated during upright tilt testing or standing. Many other symptoms also occur in patients with POTS, fitting the description of comorbid conditions, but not reproduced while upright. A patient may have nausea while upright associated with lightheadedness and have a diagnosis of POTS. Another patient may complain of nausea on awakening and have POTS, but have no nausea while upright. In the former patient the nausea is a symptom of POTS itself, whereas in the latter nausea is an associated condition. The symptoms that often directly relate to POTS include lightheadedness, orthostatic nausea, orthostatic headaches, fatigue, tunnel vision, and brain fog. About 20–30% of pediatric patients with POTS will also have syncope (Fig. 84.4). Other comorbid conditions frequently occur in these patients but are not caused by POTS (i.e., not an orthostatic phenomenon). These comorbidities include (1) sleep issues, usually delayed onset of sleep, frequent awakening, and not feeling refreshed in the morning; (2) joint hypermobility and aches in different parts of the body; (3) abdominal pain; (4) headaches and migraines; (5) nausea and vomiting; (6) depression and anxiety; and (7) Raynaud-like symptoms and other, less frequent problems (e.g., urinary symptoms).

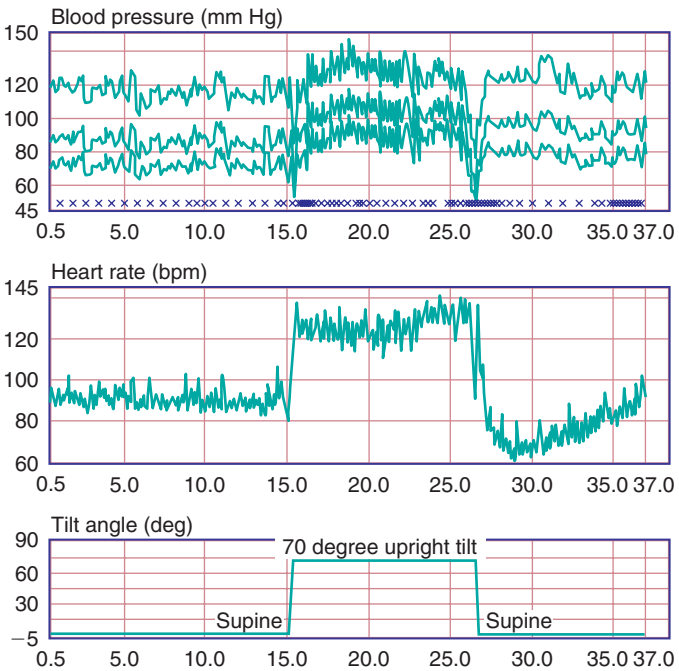

Fig. 84.4 Example of postural tachycardia syndrome (POTS) followed by a neurally mediated syncope.

The association between upper gastrointestinal (GI) symptoms and POTS is well described. Nausea, early satiety, and bloating are described in association with POTS. Such GI symptoms relate mechanistically to POTS only when they occur in the upright position. Many patients with POTS have comorbid GI symptoms that are not a consequence of the orthostatic challenge. Therefore only the GI symptoms replicated during tilt testing will improve with treatment aimed at orthostasis. Patients with POTS have changes in the electrical activity of the stomach while upright, which may explain the upright GI symptoms; they usually do not have delayed gastric emptying. The emptying is either normal or accelerated, implying that the cause of nausea is not gastroparesis.

Patients with **hypermobility Ehlers-Danlos syndrome** (h-EDS) may have POTS. Typically, such individuals have more migraines and syncope. Joint hypermobility itself in *adults* is associated with more autonomic complaints such as syncope, presyncope, palpitations, chest discomfort, fatigue, and heat intolerance. Those with hypermobility have more frequent positive tilt tests than healthy controls. Interestingly, in children, joint hypermobility does not influence the number of comorbidities or autonomic disorders. Similarly, those with pediatric chronic overlapping pain conditions with or without POTS have the same comorbidities, suggesting that neither POTS nor hypermobility are drivers of the comorbidities or the chronic overlapping pain condition, but rather another associated disorder (see Chapter 212).

DIAGNOSIS

Orthostatic intolerance is clinically diagnosed by detailed history attending specifically to symptoms as they relate to body position. Dizziness that begins in the supine position cannot be a manifestation of orthostatic intolerance. Furthermore, those symptoms that do develop while upright should improve or resolve when supine. Importantly, the history should include a detailed description of current physical exercise habits, with frequency, type, and endurance. One should also assess sleep, diet (mainly evaluating intake of salt), fluid intake, and other comorbidities. The physical examination is also important and should include a cardiac and neurologic evaluation with supine and standing BP and HR. Examination of the extremities may provide information about venous pooling, such as mild edema or reddish-purple discoloration when sitting or standing. Cold, clammy hands can signify excess sympathetic activity.

To diagnose POTS the patient needs to undergo a *head-up tilt test for at least 10 minutes*. It is important to have the patient supine for at least 20 minutes before the tilt test. POTS can also be assessed by a standing test, measuring BP and HR at 1, 3, 5, and 10 minutes standing, but to have a reliable test similar to the tilt test, the patient needs to be supine for 1 hour before standing. The HR increase with active standing is typically less than with tilt, because the lower-extremity muscle pump is less active in tilt. The diagnosis of POTS requires replication of the day-to-day symptoms while upright, not just the increased HR while upright. A small but significant proportion of healthy teenagers in school will have an increased HR that may be diagnosed as POTS but will not have associated symptoms.

Other tests may include electrocardiogram, echocardiogram, and Holter monitor when there is concern of a primary cardiac cause of tachycardia or if there is a need to determine if symptoms correlate with tachycardia (see Chapter 84). Supine and standing plasma catecholamines help confirm the diagnosis of POTS, as one expects to see either the normal doubling of norepinephrine levels from supine to standing or a tripling with hyperadrenergic POTS. Beyond tilt table testing, autonomic testing will also include cardiac response to deep breathing (checking cardiac parasympathetic function), Valsalva maneuver (checking cardiac sympathetic and parasympathetic functions and vasomotor sympathetic function), and quantitative axon reflex sudomotor test (to assess for an autonomic neuropathy and vasomotor sympathetic dysfunction).

Table 84.9 First-Line Medications in Treatment of Postural Tachycardia Syndrome (POTS)

DRUG	MECHANISM OF ACTION	SIDE EFFECTS	TREATMENT GUIDELINES
Fludrocortisone	Low dose: sensitizes α-receptors Higher doses: mineralocorticoid effect	Peripheral edema, headache, irritability, hypokalemia, hypomagnesemia, acne	Monitor basic metabolic panel and magnesium
Midodrine	α_1-Agonist; produces vasoconstriction	Scalp tingling, urinary retention, goosebumps, headache, supine hypertension	Monitor supine blood pressure 30-60 min after dose
Metoprolol succinate/ tartrate	β Blocker	Worsening of asthma, dizziness, fatigue	Use with caution in asthma If fatigue is severe, use at bedtime
Propranolol	Nonselective β blocker	Bradycardia, gastrointestinal symptoms, lightheadedness, sleepiness, hypotension, syncope	Use with caution in diabetes and asthma
Pyridostigmine	Peripheral acetylcholinesterase inhibitor that increases synaptic acetylcholine in autonomic ganglia and at peripheral muscarinic receptors	Symptoms of excessive cholinergic activity (diarrhea, urinary incontinence, salivation)	Very useful if patient has POTS and constipation Use with caution in asthma Contraindicated in urinary or bowel obstruction

Additional studies depend on the clinical symptoms and include morning cortisol (to rule out Addison disease) and thyroid studies if the patient has unusually severe fatigue or is not responsive to usual treatment. Serum tryptase and urine methylhistamine are tested if mast cell activation disorder is suspected, based on a history of flushing during the spells. If an autoimmune cause for the POTS is a concern, antibodies such as voltage-gated potassium channel and acetylcholine receptor antibodies could be checked, but this etiology for POTS is being questioned. Patients rarely (<5 in 1,000) benefit from IVIG; if this mechanism is really causing POTS, such patients should experience peak benefit at about 10 days after the infusion rather than immediately (which may simply reflect increasing intravascular volume). If the patient has hypertension, plasma and urine metanephrines should be measured to test for a pheochromocytoma. In addition, if symptoms are associated with perimenstrual timing, an assessment of sex hormone axis is helpful, with occult polycystic ovarian syndrome or low testosterone levels sometimes present.

MANAGEMENT

The core of POTS management is **nonpharmacologic**. Medications will be of little benefit without these measures being undertaken first. The best measure for treating POTS is a regular **aerobic exercise** program. Given the combination of orthostatic symptoms and severe deconditioning found in most patients, the exercise program must be introduced in a slow, progressive manner. Patients with POTS typically have moderate to severe exercise intolerance, and compared with sedentary healthy controls, have decreased peak oxygen uptake. After 3 months of exercise, POTS patients have an increase in cardiac mass and size, blood volume, and peak oxygen uptake, as reflected in a better exercise performance. The tachycardia in POTS is caused by a decrease in stroke volume and not an intrinsic circulatory problem. An exercise program should start with water exercises combined with recumbent aerobic activities (recumbent bike or rowing machine), slowly increasing the exercise time to 45 minutes at least 5 times per week. When tolerance increases, patients can advance to more upright aerobic activities. These aerobic activities need to be combined with light core- and limb-strengthening exercises.

Exercise usually cannot be performed without simultaneous expansion of the intravascular volume. To this end, encourage teenagers to drink >80 oz of fluids daily and to add 2 g of salt to their usual diet in both the morning and the early afternoon. **Salt supplementation** increases plasma and blood volume, improves orthostatic tolerance, and decreases baroreflex sensitivity. Salt also reduces nitric oxide production, resulting in less vasodilation. Trial and error of different salt formulations can help to identify the best method for each individual patient. Salt tablets are simple and inexpensive but may make some people nauseous. An alternative is simply to obtain empty capsules on the internet and fill them with table salt. A "0" size capsule contains about 400 mg of salt.

The content of sodium in the body determines the extracellular fluid volume that in turn dictates orthostatic tolerance. Patients with POTS who have lower urinary sodium excretion have more symptoms than those with higher urinary sodium (>123 mmol/24 hours), and they often respond less well to salt supplementation. Those with severe orthostatic symptoms either in the morning or before sports should drink 16 oz of plain water, which is known to increase sympathetic response mainly in individuals with baroreflex dysregulation. The effect starts soon after drinking the water and lasts for about 1 hour. Compression garments may also be useful. These can be thigh or waist high; the waist-high compression garments may not be tolerated.

Medications can be added when the nonpharmacologic interventions are not sufficient. Different centers use different strategies, and there is no single correct evidence-based approach. Table 84.9 addresses first-line medications that primary care physicians could use; only the most common side effects are included.

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Chapter 85

Shock

Scott L. Weiss, Pierre Tissières, and Mark J. Peters

Shock is an acute, life-threatening process of cardiovascular insufficiency characterized by inadequate delivery of oxygen and nutrients (e.g., glucose) by the circulatory system to meet the metabolic demands of vital organs that results in cellular dysfunction and injury. The initial imbalance between oxygen/nutrient delivery through the circulation and oxygen/nutrient consumption within organ systems can be compensated for by increasing tissue oxygen extraction. However, with further limitations in delivery of oxygen and nutrients as the shock state progresses, energy production gradually shifts from aerobic metabolism to less efficient anaerobic metabolic pathways, and a cellular bioenergetic crisis can ensue. If this process is not corrected, numerous adverse vascular, inflammatory, metabolic, cellular, and endocrine responses contribute to a state of **multiple organ dysfunction syndrome (MODS)**, cardiovascular collapse, and death.

It is important to recognize that the shock state can be present *before* the onset of hypotension, especially in children, and that inadequate cellular metabolism of oxygen and nutrients (not just impaired delivery) contributes to the clinical manifestations and outcomes observed in patients with shock. Therefore it is necessary to recognize early symptoms and signs of impaired circulation, including tachycardia, altered mental status (e.g., irritability, confusion, lethargy), tachypnea (often secondary to acidemia), abnormal capillary refill time, diminished peripheral pulses, and oliguria, in combination with metabolic markers such as acidemia, hyperlactatemia, and low central venous oxygen saturation. Hypotension, when present, is also important to recognize, but children—especially infants and preschool-age children—with *compensated* shock may be able to maintain a normal blood pressure (BP) for age until the later phases of shock. When hypotension is present, the child has reached a state of *uncompensated shock* and is at risk of irreversible organ damage and death without immediate treatment.

EPIDEMIOLOGY

Shock occurs in approximately 2% of all hospitalized infants, children, and adults in developed countries, and the mortality rate varies substantially depending on the etiology and clinical circumstances. Of patients who do not survive, many do not die in the initial acute phase of shock, but rather because of associated complications and MODS. MODS is defined as dysfunction in two or more organ systems; the presence of MODS in patients with shock substantially increases the probability of death. In 2017, there were an estimated 20.3 million cases of sepsis, with 2.9 million deaths, worldwide among children younger than 5 years and 4.9 million cases of sepsis, with 454,000 deaths, among older children and adolescents. In the United States, over 70,000 children are hospitalized with sepsis each year at an annual healthcare cost of $7.31 billion. In pediatrics, educational efforts and the use of standardized management guidelines that emphasize early recognition and intervention, along with the rapid transfer of critically ill patients to a pediatric intensive care unit (PICU), have decreased mortality from shock.

TYPES OF SHOCK

Shock classification systems generally define five major types of shock: hypovolemic, cardiogenic, obstructive, distributive, and dissociative (Table 85.1 and Fig. 85.1). **Hypovolemic shock**, the most common cause of shock in children worldwide, is most frequently caused by acute fluid losses resulting from diarrhea, vomiting, or hemorrhage. A special cause of hypovolemic shock is hemorrhagic shock, which may be caused by traumatic injury or gastrointestinal (GI), peritoneal, vaginal, soft tissue, or other sources of severe bleeding. **Cardiogenic shock** is seen in patients with congenital heart disease (before or after surgery, including heart transplantation) or those with congenital or acquired cardiomyopathies, including acute myocarditis and multisystem inflammatory syndrome in children (MIS-C). **Obstructive shock** stems from any lesion that creates a mechanical impediment to ventricular blood outflow, which includes pericardial tamponade, tension pneumothorax, pulmonary embolism, and ductal-dependent left-sided heart lesions (hypertrophic left heart syndrome, aortic coarctation, interrupted aortic arch, and critical aortic valve stenosis). **Distributive shock** is caused by inappropriate vasodilation, pooling of blood in the peripheral vasculature, leakage of blood plasma into the interstitium through a compromised endothelial barrier, and microvascular shunting. Common causes of distributive shock in children include sepsis, anaphylaxis, and accidental or intentional drug overdose (e.g., calcium channel blockers, atypical antipsychotics). Neurogenic shock is a type of distributive shock caused by a sudden disruption of sympathetic nerve stimulation to the vascular smooth muscle leading to a profound decrease in vasomotor tone, typically with severe traumatic brain or cervical spine injury. Unlike other types of shock, the unopposed vagal activity classically results in bradycardia, or at least absence of the usual tachycardic response to hypotension. **Dissociative shock** is a special category of shock in which cellular oxygen delivery or utilization is severely impaired despite sustained or supranormal tissue perfusion and is typically caused by exposure to a toxic metabolite or drug, such as severe anemia, methemoglobinemia, carbon monoxide poisoning, or thiamine deficiency (beriberi).

Septic shock is life-threatening cardiovascular dysfunction in patients with suspected or confirmed infection and confers a high risk for mortality in children compared to those with uncomplicated infections or sepsis without shock. Sepsis in children is operationalized as a Phoenix Sepsis Score of at least 2 points from a composite four-organ system model that includes criteria for respiratory, neurologic, coagulation, and cardiovascular dysfunction, with septic shock requiring at least 1 point in the cardiovascular subscore (Table 85.2). Many children with septic shock also have MODS, including respiratory, kidney, hematologic (disseminated intravascular coagulation [DIC]), hepatobiliary, and neurologic dysfunction. Septic shock classically presents as a type of distributive shock with high cardiac output and low systemic vascular resistance (SVR). However, most children with sepsis also have features of hypovolemic shock from poor oral intake, GI fluid losses, and vascular leak as well as cardiogenic shock due to decreased myocardial contractility. In younger children, septic shock often presents with low cardiac output and high SVR in which features of cardiogenic and hypovolemic shock predominate.

PATHOPHYSIOLOGY

An initial insult triggers shock, leading to a decrease in effective cardiac output with inadequate oxygen delivery to organs and tissues. Compensatory mechanisms attempt to maintain BP by increasing cardiac output and SVR. The body also attempts to optimize oxygen delivery to the tissues by increasing oxygen extraction and redistributing blood flow to the brain, heart, and kidneys at the expense of the skin, skeletal muscles, and GI tract. These responses lead to an initial state of **compensated shock** in which BP is often maintained near normal levels for age. If resuscitative treatment is not initiated or is inadequate during this period, **uncompensated shock** develops, with hypotension and tissue damage that may lead to irreversible organ damage, MODS, and, ultimately, death.

In the early phases of shock, multiple compensatory physiologic mechanisms act to maintain BP and preserve tissue perfusion and oxygen delivery. Cardiovascular effects include increases in heart rate (HR), stroke volume, and vascular smooth muscle tone, which are regulated through sympathetic nervous system activation and neurohormonal responses. Respiratory compensation involves greater carbon dioxide (CO_2) elimination in response to the metabolic acidosis and increased CO_2 production from poor tissue perfusion. Renal excretion of hydrogen ions (H^+) and retention of bicarbonate (HCO_3^-) also increase in an effort to maintain normal body pH (see Chapter 73.7). Maintenance of intravascular volume is facilitated via renal sodium retention mediated by activation of the renin-angiotensin-aldosterone and atrial natriuretic factor axes, cortisol and catecholamine synthesis

Table 85.1 Types of Shock

TYPES OF SHOCK	PATHOPHYSIOLOGY	APPEARANCE	EXAMPLES	TREATMENTS
Hypovolemic*	Decreased cardiac output due to volume depletion → decreased preload	Tachycardia and vasoconstriction maintain adequate circulation up to 30% of circulating volume Narrowed pulse pressure, delayed capillary refill, orthostatic changes, late hypotension, AMS, and decreased UOP	Nonhemorrhagic (vomiting and diarrhea) Hemorrhagic (trauma)	IV fluid bolus Vasopressors Blood replacement
Cardiogenic	Decreased cardiac output due to myocardial dysfunction, increased afterload, and/or lack of ventricular filling	Tachycardia, vasoconstriction, cool extremities, narrow pulse pressure, delayed capillary refill, respiratory distress, rales or gallop rhythm, enlarged liver, JVD, cardiomegaly on chest radiograph Significant gradient between upper and lower extremity blood pressures	Cardiomyopathies, infectious myocarditis, and systemic inflammatory process, autoimmune disease, impaired coronary perfusion, cardiopulmonary bypass, acidosis, HIE, and dysrhythmias Infants: ductal-dependent lesions, tachydysrhythmias	Judicious IV fluid resuscitation, ionotropic agents to improve contractility, vasodilators to reduce afterload, and management of tachyarrhythmias PGE for infants <2 mo
Distributive	Decreased cardiac output and systemic vascular resistance due to peripheral vasodilation → decreased afterload and preload, redistribution of blood flow away from vital organs, and loss of sympathetic outflow	Tachycardic, vasodilated, flushed, warm extremities, wide pulse pressure, bounding pulses, flash capillary refill Anaphylaxis: rash; facial swelling; lip, tongue, or airway swelling; bronchospasm; hypotension Spinal shock: unable to raise HR, hypotension Neurogenic: Control ↑ ICP	Septic shock Toxic ingestions Anaphylaxis Spinal cord injuries	IV fluids, vasopressors, antibiotics Specific antidotes Remove triggers, IV fluids, IM epinephrine, antihistamines, vasopressors IV fluids, vasoconstrictors
Obstructive	Decreased cardiac output due to increased afterload of the right ventricle from an obstructive process	Tachycardia, delayed capillary refill, cool extremities, narrow pulse pressure, distended neck veins, distant heart tones, asymmetric breath sounds	Tension pneumothorax Pulmonary embolism Cardiac tamponade	Anticoagulants Drain pericardial effusion Evacuate pneumothorax
Dissociative	High cardiac output failure due to inadequate oxygen-releasing capacity	Tachycardia ± delayed capillary refill, cool extremities, weakened pulse, pallor or flushed cheeks	Anemia Carbon monoxide Methemoglobinemia Cyanide	Gradual fluid replacement and blood replacement 5 mL/dL Oxygen, hyperbaric chamber Methylene blue Hydroxocobalamin and cyanide antidote kit (sodium thiosulfate, sodium nitrate, amyl nitrite) plus oxygen

*Most common.
AMS, Altered mental status; HIE, hypoxic ischemic encephalopathies; HR, heart rate; IM, intramuscular; ICP, intracranial pressure; IV, intravenous; JVD, jugular venous distention; PGE, prostaglandin; UOP, urine output.
Modified from Baumer-Mouradian SH, Drendel AL. Shock. In: Kliegman RM, Toth H, Bordini BJ, Basel D, eds. *Nelson Pediatric Symptom-Based Diagnosis,* 2nd ed. Philadelphia: Elsevier;2023: Table 10.4.

and release, and antidiuretic hormone secretion. Despite these compensatory mechanisms, the underlying shock and host response lead to vascular endothelial cell injury and loss of endothelial adhesion proteins that allow significant leakage of intravascular fluid into the interstitial extracellular space.

Another important aspect of the initial pathophysiology of shock is the impact on cardiac output. All forms of shock affect cardiac output through several mechanisms, with changes in HR, preload, afterload, and myocardial contractility occurring separately or in combination (see Fig. 85.1). **Hypovolemic shock** is characterized primarily by fluid loss and decreased preload. Tachycardia and an increase in SVR are the initial compensatory responses that seek to maintain cardiac output, systemic BP, and tissue perfusion. Without adequate volume replacement, hypotension inevitably develops, followed by tissue ischemia and further clinical deterioration. When there is preexisting low plasma oncotic pressure (caused by nephrotic syndrome, malnutrition, hepatic dysfunction, acute severe burns, etc.), further volume loss and exacerbation of shock may result from worsening vascular leak.

In contrast, the underlying pathophysiologic mechanism leading to **distributive shock** is a state of abnormal vasodilation and decreased SVR. In sepsis, loss of normal regulation of vasomotor tone is due to a combination of factors, including excessive nitric oxide (NO) produced from an increase in inducible NO synthase, altered sympathetic and parasympathetic tone, and diminished circulating levels and/or reduced responsiveness to vasopressin, endogenous catecholamines, and cortisol. In anaphylaxis, vasodilation is caused by an acute release of histamine and other mediators from mast cells. Irrespective of the inciting event, the sudden fall in SVR is accompanied initially by a maldistribution of blood flow away from vital organs and a compensatory increase in cardiac output caused by an increase in HR and, potentially, left ventricular stroke volume. This process leads to significant decreases in both preload and afterload. Therapies for distributive shock must address both these problems simultaneously.

Cardiogenic shock may be seen in patients with myocarditis, cardiomyopathy, arrhythmias, and congenital heart disease (generally after cardiac surgery) (see Chapter 483). In these patients, myocardial contractility is directly impaired, leading to systolic and/or diastolic dysfunction. The later phases of all forms of shock frequently have a negative impact on the myocardium, leading to development of a cardiogenic component to the initial shock state.

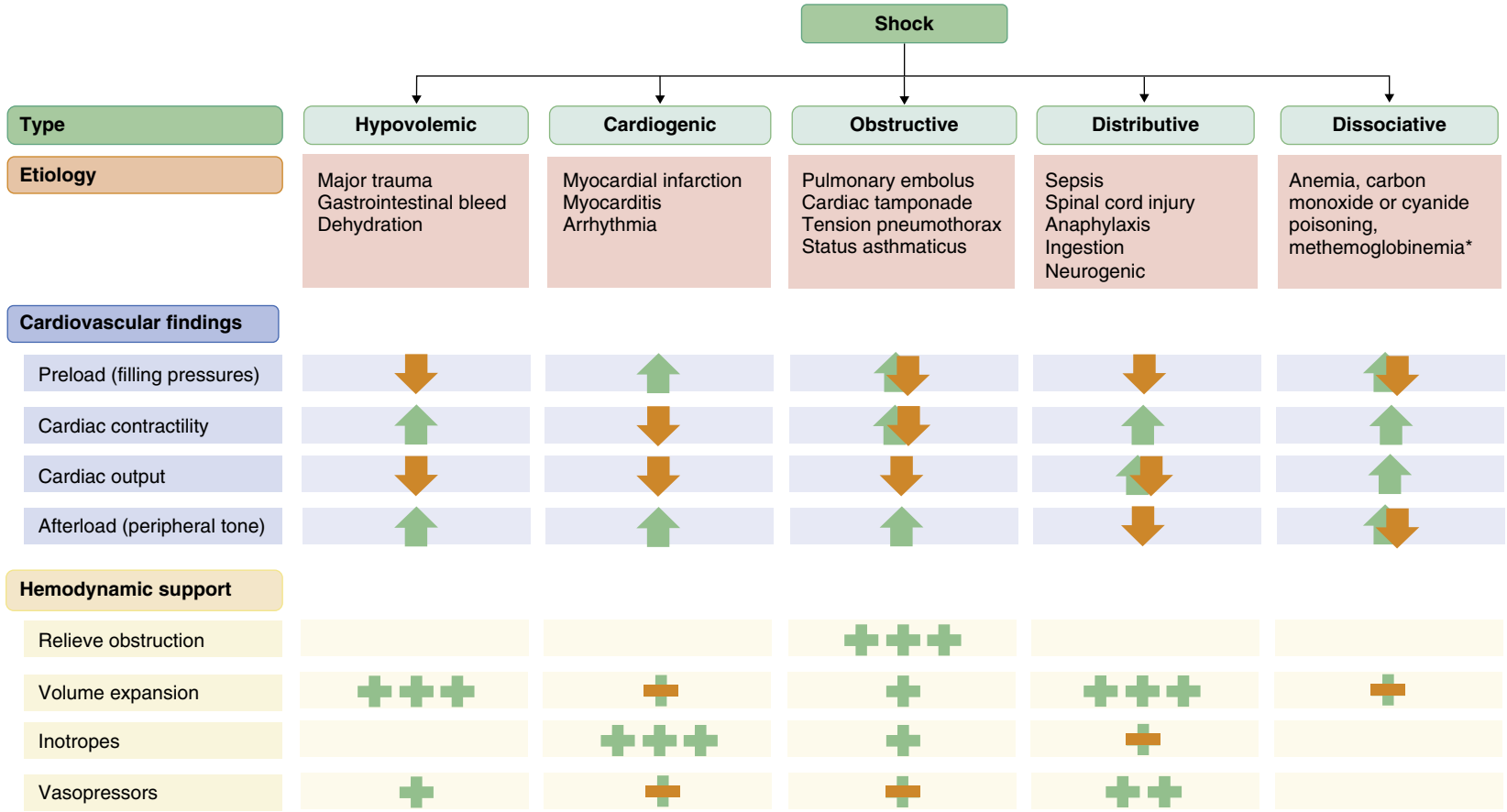

Fig. 85.1 The causes, cardiovascular findings, and hemodynamic support for different types of shock. Under cardiovascular findings, *bidirectional arrows* indicate variation in findings among patients with the particular type. Under hemodynamic support, the number of *+ signs* indicates the importance of therapy. A combined *+ and −* indicates that the intervention could help some patients but must be used with caution. *Treat specific etiology transfusion or specific antidotes. *(Modified from Angus DC. Approach to the patient with shock. In: Goldman L, Schafer AI, eds.* Goldman-Cecil Medicine, *26th ed. Philadelphia: Elsevier; 2020:642, Fig. 98-1.)*

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Table 85.2 The Phoenix Sepsis Score[a]

VARIABLES	0 POINTS	1 POINT	2 POINTS	3 POINTS
RESPIRATORY, 0–3 POINTS				
	PaO_2:FIO_2 ≥400 or SpO_2:FIO_2 ≥292[b]	PaO_2:FIO_2 <400 on any respiratory support or SpO_2:FIO_2 <292 on any respiratory support[b,c]	PaO_2:FIO_2 100–200 and IMV or SpO_2:FIO_2 148–220 and IMV[b]	PaO_2:FIO_2<100 and IMV or SpO_2:FIO_2 <148 and IMV[b]
CARDIOVASCULAR, 0–6 POINTS		1 point each (up to 3)	2 points each (up to 6)	
	No vasoactive medications[d]	1 Vasoactive medication[d]	≥2 Vasoactive medications[d]	
	Lactate <5 mmol/L[e]	Lactate 5–10.9 mmol/L[e]	Lactate ≥11 mmol/L[e]	
AGE BASED[f]	Mean Arterial Pressure, mm Hg[g]			
<1 mo	>30	17–30	<17	
1 to 11 mo	>38	25–38	<25	
1 to <2 yr	>43	31–43	<31	
2 to <5 yr	>44	32–44	<32	
5 to <12 yr	>48	36–48	<36	
12 to 17 yr	>51	38–51	<38	
COAGULATION, 0–2 POINTS[H]		1 point each (maximum 2 points)		
	Platelets ≥100 × 10^3/μL	Platelets <100 × 10^3/μL		
	International normalized ratio ≤1.3	International normalized ratio >1.3		
	D-dimer ≤2 mg/L FEU	D-dimer >2 mg/L FEU		
	Fibrinogen ≥100 mg/dL	Fibrinogen <100 mg/dL		
NEUROLOGIC, 0–2 POINTS[i]				
	Glasgow Coma Scale score >10; pupils reactive[j]	Glasgow Coma Scale score ≤10[j]	Fixed pupils bilaterally	
PHOENIX SEPSIS CRITERIA				
Sepsis	Suspected infection and Phoenix Sepsis Score ≥2 points			
Septic shock	Sepsis with ≥1 cardiovascular point(s)			

[a]The score may be calculated in the absence of some variables (eg, even if lactate level is not measured and vasoactive medications are not used, a cardiovascular score can still be ascertained using blood pressure). It is expected that laboratory tests and other measurements will be obtained at the discretion of the medical team based on clinical judgment. Unmeasured variables contribute no points to the score. Ages are not adjusted for prematurity, and the criteria do not apply to birth hospitalizations, neonates whose postconceptional age is younger than 37 weeks, or those 18 years of age or older.

[b]SpO_2:FIO_2 ratio is only calculated if SpO_2 is 97% or less.

[c]The respiratory dysfunction of 1 point can be assessed in any patient receiving oxygen, high-flow, noninvasive positive pressure, or IMV respiratory support, and includes a PaO_2:FIO_2 ratio of less than 200 and a SpO_2:FIO_2 ratio of less than 220 in children who are not receiving IMV. For children receiving IMV with a PaO_2:FIO_2 less than 200 and SpO_2:FIO_2 less than 220, see criteria for 2 and 3 points.

[d]Vasoactive medications include any dose of epinephrine, norepinephrine, dopamine, dobutamine, milrinone, and/or vasopressin (for shock).

[e]Lactate reference range is 0.5 to 2.2 mmol/L. Lactate can be arterial or venous.

[f]Age is not adjusted for prematurity, and the criteria do not apply to birth hospitalizations, children whose postconceptional age is younger than 37 weeks, or those 18 years or older.

[g]Use measured MAP preferentially (invasive arterial if available or noninvasive oscillometric), and if measured MAP is not available, a calculated MAP (1/3 × systolic + 2/3 × diastolic) may be used as an alternative.

[h]Coagulation variable reference ranges: platelets, 150 to 450 × 103/μL; D-dimer, <0.5mg/L FEU; fibrinogen, 180 to 410mg/dL. The INR reference range is based on the local reference prothrombin time.

[i]The neurological dysfunction subscore was pragmatically validated in both sedated and nonsedated patients, and those receiving or not receiving IMV support.

[j]The Glasgow Coma Scale score measures level of consciousness based on verbal, eye, and motor response (range, 3–15, with a higher score indicating better neurological function).

FEU, fibrinogen equivalent units; IMV, invasive mechanical ventilation; INR, international normalized ratio of prothrombin time; MAP, mean arterial pressure; PaO_2:FIO_2, arterial partial pressure of oxygen to fraction of inspired oxygen ratio; SpO_2, oxygen saturation measured by pulse oximetry (only SpO_2 of ≤97%).

SI conversion factor: To convert lactate from mmol/L tomg/dL, divide by 0.111.

From Schlapbach LJ, Watson RS, Sorce LR, et al. International Consensus Criteria for Pediatric Sepsis and Septic Shock. *JAMA*. Published online January 21, 2024. https://doi.org/10.1001/jama.2024.0179.

Obstructive shock manifests as an acute increase in SVR typically in response to a sudden decrease in cardiac output that resembles a state of functional hypovolemia. A compensatory increase in HR and afterload provides temporary support, but compensation will soon fail without relief of the mechanical obstruction.

Dissociative shock is caused by the inability to deliver oxygen due to severe anemia or a congenital or acquired hemoglobinopathy, such as carbon monoxide intoxication. Alternatively, oxygen delivery may be preserved, but consumption can be impaired by a metabolic disorder or acquired state of mitochondrial dysfunction, such as cyanide

Table 85.3 Differential Diagnosis of Systemic Inflammatory Response Syndrome (SIRS)

INFECTION
Bacteremia or meningitis (*Streptococcus pneumoniae, Haemophilus influenzae* type b, *Neisseria meningitidis*, group A *Streptococcus*, *Staphylococcus aureus*)
Viral illness (influenza, enteroviruses, hemorrhagic fever group, herpes simplex virus, respiratory syncytial virus, cytomegalovirus, Epstein-Barr virus, COVID-19)
Encephalitis (arboviruses, enteroviruses, herpes simplex virus)
Rickettsiae (Rocky Mountain spotted fever, Ehrlichia, Q fever)
Syphilis
Vaccine reaction (pertussis, influenza, measles)
Toxin-mediated reaction (toxic shock, staphylococcal scalded skin syndrome)

CARDIOPULMONARY
Pneumonia (bacteria, virus, mycobacteria, fungi, allergic reaction)
Pulmonary emboli
Heart failure
Arrhythmia
Pericarditis
Myocarditis

METABOLIC-ENDOCRINE
Adrenal insufficiency (adrenogenital syndrome, Addison disease, corticosteroid withdrawal)
Electrolyte disturbances (hyponatremia or hypernatremia, hypocalcemia or hypercalcemia)
Diabetes insipidus
Diabetes mellitus
Inborn errors of metabolism (organic acidosis, urea cycle, carnitine deficiency, mitochondrial disorders)
Hypoglycemia

GASTROINTESTINAL
Gastroenteritis with dehydration
Volvulus
Intussusception
Appendicitis
Peritonitis (spontaneous, associated with perforation or peritoneal dialysis)
Necrotizing enterocolitis
Hepatitis
Hemorrhage
Pancreatitis

HEMATOLOGIC/IMMUNE
Anemia (sickle cell disease, blood loss, nutritional)
Methemoglobinemia
Splenic sequestration crisis
Leukemia or lymphoma
Hemophagocytic syndromes
Cytokine release syndrome s/p CAR-T therapy
Immune reconstitution syndrome
Graft-versus-host disease

NEUROLOGIC
Intoxication (drugs, carbon monoxide, intentional or unintentional overdose)
Intracranial hemorrhage
Infant botulism
Trauma (child abuse, accidental)
Guillain-Barre syndrome
Myasthenia gravis

OTHER
Anaphylaxis (food, drug, insect sting, idiopathic)
Hemolytic-uremic syndrome
Kawasaki disease
Erythema multiforme, toxic epidermal necrolysis
MIS-C
Poisoning, iron, cyanide
Toxic envenomation
Systemic JIA
Macrophage activation syndrome
Idiopathic systemic capillary leak (Clarkson) syndrome

CAR-T, Chimeric antigen receptor T-cell; JIA, juvenile idiopathic arthritis; MIS-C, multisystem inflammatory syndrome in children; S/P, status post.
From Baumer-Mouradian SH, Drendel AL. Shock. In: Kliegman RM, Bordini BJ, Toth H, Basel D, eds. *Nelson Pediatric Symptom-Based Diagnosis*, 2nd ed. Elsevier: Philadelphia; 2022: Table 10.6.

toxicity. Notably, varying degrees of dissociative shock may also be present in other shock types, especially sepsis, in which acquired pyruvate dehydrogenase deficiency or mitochondrial dysfunction have been increasingly recognized.

Septic shock is generally a unique combination of distributive, hypovolemic, and cardiogenic shock, as well as dissociative shock. Hypovolemia from insufficient fluid intake, GI losses, and/or vascular leak is common. Cardiogenic shock results from the myocardial-depressant effects of sepsis, and distributive shock is the result of decreased SVR. The degree to which a patient exhibits each of these responses varies, but there are frequently alterations in preload, afterload, and myocardial contractility.

In septic shock, it is important to distinguish between the inciting infection and the host inflammatory response. Normally, host immunity prevents the development of sepsis through activation of the reticular endothelial system along with the cellular and humoral immune systems. This host immune response produces an *inflammatory cascade* mediated by hormones, cytokines, and chemokines. If this inflammatory cascade is uncontrolled, derangement of the microcirculatory system leads to subsequent organ and cellular dysfunction.

Systemic inflammatory response syndrome (SIRS) is an inflammatory cascade that is initiated by the host response to an infectious or noninfectious trigger (Table 85.3). This inflammatory cascade is triggered when the host defense system does not adequately recognize and/or eliminate the triggering event. The inflammatory cascade initiated by shock can lead to hypovolemia, cardiac and vascular failure, acute respiratory distress syndrome (ARDS), insulin resistance, decreased cytochrome P450 activity (decreased steroid synthesis), coagulopathy, and unresolved or secondary infection. Tumor necrosis factor (TNF) and other inflammatory mediators increase vascular permeability, causing diffuse vascular leak, decreased vascular tone, and an imbalance between perfusion and metabolic demands of the tissues. Early increases in TNF, interleukin (IL)-1, and IL-6 stimulate the release of both proinflammatory and antiinflammatory mediators, causing fever, vasodilation, and myocardial dysfunction. Simultaneous upregulation of antiinflammatory mediators (such as circulating levels of IL-4, IL-10, and transforming growth factor-β), downregulation of hematopoietic growth factors (such as IL-7), and increased expression of immune cell surface checkpoint proteins (such as programmed death [PD]-1 and its PD ligand [PD-L1/2]), as well as production of immature immune cells through emergency myelopoiesis contribute to a state of immune dysregulation that can impair pathogen clearance and allow for secondary infections.

The inflammatory cascade is initiated by toxins or superantigens through macrophage binding or lymphocyte activation. The vascular endothelium is both a target of tissue injury and a source of mediators that may cause further injury. Biochemical responses include the production of arachidonic acid metabolites, release of myocardial-depressant factors and endogenous opiates, activation of the complement system, and production and release of other mediators, which

Table 85.4 Signs of Decreased Perfusion

ORGAN SYSTEM	↓ PERFUSION	↓↓ PERFUSION	↓↓↓ PERFUSION
Central nervous system	—	Restless, apathetic, anxious	Agitated/confused, stuporous, coma
Respiratory	—	↑ Ventilation	↑↑ Ventilation
Metabolic	—	Compensated metabolic acidemia	Uncompensated metabolic acidemia
Gastrointestinal	—	↓ Motility	Ileus
Kidney	↓ Urine volume ↑ Urinary specific gravity	Oliguria (<0.5 mL/kg/hr)	Oliguria/anuria
Skin	Delayed capillary refill	Cool extremities	Mottled, cyanotic, cold extremities
Cardiovascular system	↑ Heart rate	↑↑ Heart rate ↓ Peripheral pulses	↑↑ Heart rate ↓ Blood pressure, central pulses only

may be proinflammatory or antiinflammatory. The balance among these mediator groups for an individual patient contributes to the progression (and resolution) of disease and affects the prognosis.

CLINICAL MANIFESTATIONS

Table 85.1 and Figure 85.1 show a classification system for shock. Categorization is important, but there may be significant overlap among these groups, especially in septic shock. The clinical presentation of shock depends in part on the underlying etiology, but if unrecognized and untreated, all forms of shock follow a common progression of clinical signs and pathophysiologic changes that may ultimately lead to irreversible organ injury and death. Among the first physiologic responses is sympathetic adrenergic system activation and its related signs and symptoms.

Shock may initially manifest as only tachycardia, with or without tachypnea. Progression leads to decreased urine output, poor peripheral perfusion, respiratory distress or failure, alteration of mental status, and low BP (Table 85.4). A significant misconception is that shock occurs only with low BP. Hypotension is often a late finding, especially in infants and young children, and is not a criterion for the diagnosis of shock because of a complex set of compensatory mechanisms that attempt to preserve BP and peripheral perfusion. Hypotension reflects an advanced state of uncompensated shock and is associated with increased morbidity and mortality.

Hypovolemic shock often manifests initially as tachycardia and orthostatic hypotension and is associated with dry mucous membranes, dry axillae, poor skin turgor, and decreased urine output. Depending on the degree of dehydration, the patient with hypovolemic shock may present with either normal or slightly cool distal extremities, and peripheral pulses may be normal, decreased, or absent depending on disease severity.

The presenting signs of **cardiogenic shock** are often tachypnea, cool extremities, delayed capillary filling time, poor peripheral and/or central pulses, reduced pulse pressure, declining mental status, and decreased urine output caused by the combination of decreased cardiac output and compensatory peripheral vasoconstriction (see Chapter 491.1).

Obstructive shock often also manifests as inadequate cardiac output because of a physical restriction of forward blood flow with tachycardia, delayed capillary refill, cool extremities, diminished peripheral pulses, and decreased pulse pressure (difference between systolic and diastolic BP) or presence of pulsus paradoxus. The acute presentation may quickly progress to cardiac arrest. Obstructive shock due to tension pneumothorax typically includes signs of respiratory distress, hypoxia, and diminished breath sounds. Pericardial tamponade includes Beck's triad of hypotension, jugular vein distention, and muffled heart sounds. A saddle pulmonary embolism often presents with a sudden cardiac arrest. Left-heart obstructive lesions may present in newborns with discrepant perfusion of the upper and lower extremities.

Distributive shock includes signs of vasodilation, including tachycardia, flash capillary refill, warm extremities, bounding peripheral pulses, and increased pulse pressure, often with diastolic hypotension. In neurogenic shock, tachycardia may be absent or frank bradycardia may be present. Similar to distributive shock, signs of vasodilation may be present, although in the immediate phase, the patient can feel cool peripherally with delayed capillary refill.

Septic shock can be difficult to diagnose because of the wide spectrum of presenting signs and symptoms. A key historical clue is the presence of fever (or hypothermia) along with evidence for either a *systemic* (e.g., bacteremia, rickettsial disease, fungemia, viremia) or *localized* (e.g., meningitis, pneumonia, pyelonephritis, peritonitis, necrotizing fasciitis) infection. Infants and young children most commonly present with "cold shock," with features of hypovolemic and cardiogenic shock predominating, including tachycardia, delayed capillary refill, cool extremities, diminished peripheral pulses, and decreased pulse pressure. Older children and adolescents, especially those with sepsis from indwelling central venous catheters, more commonly present with "warm shock" that resembles distributive shock, including tachycardia, flash capillary refill, warm extremities, bounding peripheral pulses, and increased pulse pressure. However, the pathobiology of sepsis can evolve over time and with treatment in children, such that "warm shock" may shift to "cold shock" or vice versa.

In addition to the traditional description of septic shock, a subgroup immunophenotype presents with **hyperferritinemia**. Ferritin levels >3,000 mg/mL often predict a poor prognosis and the need for intensive care unit (ICU) admission. Hyperferritinemic septic shock may be due to familial primary genetic hemophagocytic lymphohistiocytosis (HLH) (usually age <2 years; see Chapter 556.2) or, more often, secondary HLH initiated by an infectious agent or macrophage activation syndrome (MAS) (see Chapter 207) associated with autoimmune diseases (Table 85.6).

Regardless of etiology, uncompensated shock, with hypotension, high SVR, decreased cardiac output, respiratory failure, obtundation, and oliguria, occurs late in the progression of disease. Table 85.1 lists the hemodynamic findings in various shock states. Additional clinical findings in shock include cutaneous lesions such as petechiae, diffuse erythema, ecchymoses, ecthyma gangrenosum, and peripheral gangrene. Jaundice can be present either as a sign of infection or as a result of MODS.

DIAGNOSIS

Shock is a clinical diagnosis that should be primarily based on a thorough history and physical examination (see Tables 85.1, 85.4, and 85.6). Important clues to consider in the history are recent trauma or bleeding, exposure to new medications or substances, preceding or concurrent symptoms of infection or fluid losses, the patient's comorbid conditions, and a brief review of systems. The physical examination should include rapid assessment of vital signs (including pulse oximetry), mental status/level of consciousness, extremity temperature, peripheral and central pulses, capillary refill, and presence of rashes or skin changes.

Increasingly, point-of-care ultrasound (POCUS) is being incorporated into the initial assessment of children with shock to assess intravascular volume status, likelihood of a positive hemodynamic response to fluid

Table 85.5 Considerations in Management of Hyperferritinemic Sepsis Beyond Usual Diagnostic and Therapeutic Measures Used in Sepsis Patients Without Hyperferritinemia

WHAT OCCULT INFECTION IS PRIMING AND WHAT CO-INFECTION IS PRESENT FOR THE HYPERFERRITINEMIC PROCESS?
Perform diagnostic workup for **viruses** (e.g., herpes simplex virus 1, HHV-6, HHV-8, Epstein-Barr virus, adenovirus, cytomegalovirus, parvovirus, Ebola, COVID-19, Dengue, hepatitis A, HIV, severe fever with thrombocytopenia syndrome virus, influenza, hemorrhagic fevers), **parasites** (e.g., toxoplasmosis, leishmaniasis, malaria, scrub typhus, babesiosis), **intracellular bacteria** (e.g., tuberculosis, atypical mycobacteria, mycoplasma, fusobacteria, babesiosis, ehrlichiosis), rickettsia, and **fungi** (e.g., histoplasmosis).
Begin empiric therapy and specific therapies according to context.
Give IVIG if no specific therapy is available to neutralize infection.
IS HEMOLYSIS AND FREE HEMOGLOBIN DRIVING THE HYPERFERRITINEMIC PROCESS?
Measure free hemoglobin and ferritin sequentially.
Minimize blood transfusions.
If unable to reverse hemolysis or hyperferritinemia, consider 5 days of plasma exchange to remove free hemoglobin and ferritin and to resolve inflammation.
IS AN ANTIINFLAMMATORY STRATEGY NEEDED TO SAFELY CONTROL INFLAMMASOME ACTIVATION?
If ferritin is >3,000 ng/mL in the high-resource PICU setting, or >500 ng/mL in the resource-poor PICU setting, then mortality risk is increased.
Methylprednisone, IVIG, and interleukin 1 receptor antagonist (anakinra) can be safely given to reduce mortality risk in these children.

HHV, human herpes virus; PICU; pediatric intensive care unit; IVIG, IV immunoglobulin. Modified from Carcillo JA, Kernan KK, Horvat CM, et al. Why and how is hyperferritinemic sepsis different from sepsis without hyperferritinemia? *Pediatr Crit Care Med.* 21(5):509-512, Table 1, p. 511.

therapy, and myocardial function. Cardiac and lung POCUS may also provide important diagnostic information about the etiology of shock, such as the presence of pericardial fluid to support tamponade, pneumothorax, or dilated right ventricle to support pulmonary embolus. The focused assessment with sonography for trauma (FAST) is commonly performed to screen for pericardial effusion and hemoperitoneum.

LABORATORY FINDINGS

Although the initial diagnosis of shock can and should be based on clinical data from the history and physical examination, the overall evaluation of shock should also include early laboratory testing to screen for hyperlactatemia (as a sign of increased anaerobic metabolism), acidemia, and electrolyte disturbances, including hypoglycemia and hypocalcemia. In children with septic shock, elevations in both venous and arterial blood lactate levels in the emergency department (ED) are associated with risk of organ dysfunction when measured in the ED and are associated with higher risk of death if elevated at the time of PICU admission. Although the optimal cutoff remains to be defined, arterial lactate ≥2 mmol/L is worrisome and associated with worse outcome. Laboratory evidence of concurrent MODS should also be sought, including a complete blood count, renal function tests, liver function tests, and coagulation profile (including fibrinogen and D-dimer or fibrin split products). Elevated neutrophil counts with increased immature forms (i.e., bands, myelocytes, promyelocytes) and elevated CRP and procalcitonin levels may be seen with infection. A blood gas analysis may be helpful to assess the degree of respiratory dysfunction, and an elevated venous to arterial P_{CO_2} gap ≥5 mm Hg (≥0.67 KPa) may signify an early shock state. For septic shock, at least one blood culture should be collected along with other cultures as supported by the history and physical. Ferritin levels should be determined in all patients with septic shock. In the presence of hyperferritinemia, laboratory studies for HLH and MAS should be obtained, including fibrinogen, triglycerides, CBC, soluble IL-2 receptor, natural killer (NK) cells, and specific genetic testing.

The hallmark of *uncompensated* shock is an imbalance between oxygen delivery (Do_2) and oxygen consumption (Vo_2). Oxygen delivery normally exceeds oxygen consumption by threefold. The oxygen extraction ratio is approximately 25%, thus producing a normal central venous oxygen saturation (Svo_2) of approximately 75%, most commonly measured from a catheter at the junction of the superior vena cava and right atrium. Svo_2 values <70% reflect an increased oxygen extraction ratio and document a decrease in oxygen delivery relative to consumption. This increase in tissue oxygen extraction is an attempt to maintain adequate oxygen delivery at the cellular level. This state is manifested clinically by increased lactic acid production (e.g., high anion gap, metabolic acidemia) caused by anaerobic metabolism and a compensatory increase in tissue oxygen extraction. Notably, in dissociative shock, hyperlactatemia is often accompanied by an elevated Svo_2 >80–85%, which reflects a state of impaired oxygen use despite adequate tissue perfusion. *Elevated blood lactate levels reflect poor tissue oxygen delivery noted in all forms of shock.*

TREATMENT

Almost all healthcare professionals that care for ill children will be faced with managing the clinical syndrome of shock, given that many childhood illnesses, such as gastroenteritis, infection, trauma, and toxic ingestions, can precipitate shock. Without timely medical intervention, the child in shock will inevitably follow a common pathway to MODS and death. Early recognition and resuscitation are therefore critical to limit morbidity and mortality associated with shock.

General Principles of Shock Management

Initial management begins with early recognition of the compensated or uncompensated shock state based on the history, physical examination, and laboratory assessments outlined earlier. Once recognized, immediate efforts to restore oxygen (and other nutrient) delivery by supporting the circulation and identifying and reversing the underlying etiology of shock are necessary (Fig. 85.2). Restoration of oxygen delivery includes ensuring airway patency and adequacy of breathing, providing supplemental oxygen if hypoxemia (Spo_2 <92–94%) is present, establishing vascular access, expanding the circulating blood volume, supporting the cardiac and vascular system with appropriate vasoactive agents when necessary, and frequently reassessing the patient's response to initial therapy. The management strategies discussed in the following sections apply to all shock types, with additional discussion at the end of the section for type-specific management recommendations.

Vascular access should be established within the first few minutes of shock recognition, ideally with at least two large-bore peripheral intravenous (IV) catheters. If peripheral IV access is not successful within 5 minutes, intraosseous (IO) access should be established until more definitive access is secured. Central venous access should be considered for patients with unstable peripheral IV access, persistence of shock despite 40-60 mL/kg fluid bolus therapy *(fluid-refractory shock),* or need for vasoactive medications or concentrated dextrose/electrolyte administration. In addition to optimizing safe administration of certain medications, central venous access will also enable measurement of Svo_2. Placement of an arterial catheter should be considered for patients with fluid-refractory shock who require active titration of vasoactive medications and/or those who may need serial laboratory tests, including frequent reassessment of blood lactate or electrolyte derangements. Notably, placement of a central venous or arterial catheter requires specialized skills that may not be immediately available, in which case continued resuscitation through peripheral IV or IO access, including initiation of vasoactive medications, is safe and appropriate.

Volume resuscitation with fluid bolus therapy in aliquots of 10-20 mL/kg pushed over 5-10 minutes is currently recommended for most types of shock and in most settings in children (see special considerations in septic shock later and Fig. 85.3). Several observational studies have demonstrated improved outcomes in children with shock with initial volume resuscitation titrated to improvements in hemodynamic targets, including decrease in HR; increase in BP; normalization of capillary refill, peripheral pulse strength, and extremity temperature;

Table 85.6 Physical Examination and Selected Laboratory Signs in Shock

Central nervous system	Acute delirium, restlessness, disorientation, confusion, and coma, which may be secondary to decreased cerebral perfusion pressure (mean arterial pressure minus intracranial pressure). Patients with chronic hypertension or increased intracranial pressure may be symptomatic at normal blood pressures. Cheyne-Stokes respirations may be seen with severe decompensated heart failure. Blindness can be a presenting complaint or complication.
Temperature	Hyperthermia results in excess tissue respiration and greater systemic oxygen delivery requirements. Hypothermia can occur when decreased systemic oxygen delivery or impaired cellular respiration decreases heat generation.
Skin	Cool distal extremities (combined low serum bicarbonate and high arterial lactate levels) aid in identifying patients with hypoperfusion. Pallor, cyanosis, sweating, and decreased capillary refill and pale, dusky, clammy, or mottled extremities indicate systemic hypoperfusion. Dry mucous membranes and decreased skin turgor indicate low vascular volume. Low toe temperature correlates with the severity of shock.
General cardiovascular	Neck vein distention (e.g., heart failure, pulmonary embolus, pericardial tamponade) or flattening (e.g., hypovolemia), tachycardia, and arrhythmias. Decreased coronary perfusion pressures can lead to ischemia, decreased ventricular compliance, and increased left ventricular diastolic pressure. A "mill wheel" heart murmur may be heard with an air embolus.
Heart rate	Usually elevated. However, paradoxical bradycardia can be seen in patients with preexisting cardiac disease and severe hemorrhage. Heart rate variability is associated with poor outcomes.
Systolic blood pressure	May actually increase slightly when cardiac contractility increases in early shock and then fall as shock advances.
Diastolic blood pressure	Correlates with arteriolar vasoconstriction and may rise early in shock and then fall when cardiovascular compensation fails.
Pulse pressure	Defined as systolic minus diastolic pressure and related to stroke volume and the rigidity of the aorta. Increases early in shock and decreases before systolic pressure decreases.
Pulsus paradoxus	An exaggerated change in systolic blood pressure with respiration (systolic blood pressure declines >10 mm Hg with inspiration) seen in asthma, cardiac tamponade, and air embolus.
Mean arterial blood pressure	Diastolic blood pressure + [pulse pressure/3]
Shock index	Heart rate/systolic blood pressure. Normal = 0.5-0.7. A persistent elevation of the shock index (>1.0) indicates impaired left ventricular function (as a result of blood loss or cardiac depression) and is associated with increased mortality.
Respiratory	Tachypnea, increased minute ventilation, increased dead space, bronchospasm, hypocapnia with progression to respiratory failure, acute lung injury, and adult respiratory distress syndrome.
Abdomen	Low-flow states may result in abdominal pain, ileus, gastrointestinal bleeding, pancreatitis, acalculous cholecystitis, mesenteric ischemia, and shock liver.
Renal	Because the kidney receives 20% of cardiac output, low cardiac output reduces the glomerular filtration rate and redistributes renal blood flow from the renal cortex toward the renal medulla, thereby leading to oliguria. Paradoxical polyuria in early sepsis may be confused with adequate hydration.
Metabolic	Respiratory alkalosis is the first acid-base abnormality, but metabolic acidosis rapidly occurs as shock progresses. Hyperglycemia, hypoglycemia, and hyperkalemia may develop. Hyperferritinemia suggests a poor prognosis.

From Angus DC. Approach to the patient with shock. In Goldman L, Schafer AI, eds. *Goldman-Cecil Medicine,* 26th ed. Philadelphia: Elsevier; 2020:643, Table 98-1.

improved urine output; and fall in blood lactate by ≥10–20%. Fluid boluses totaling up to 60 mL/kg may be needed in the first hour of resuscitation, with volumes exceeding 200 mL/kg over several hours. Fluid should be administered via IV push or a rapid infuser system. IV push delivery may be facilitated by attaching a large syringe with a three-way stopcock to the IV tubing from the fluid bag, creating a "push-pull system" that allows the user to rapidly draw up fluid into the syringe and then administer to the patient without repeatedly disconnecting and reconnecting the syringe to the patient's IV. In patients >50 kg, a pressure bag or rapid infuser may be used to rapidly administer fluid through a large-gauge peripheral IV. Notably, in neonates, additional caution should be paid to fluid resuscitation, as tolerance may be limited by reduced myocardial ventricular compliance at baseline.

Importantly, not all children with shock will continue to improve with repeated volume resuscitation, particularly those with cardiogenic and dissociative shock, severe anemia, or malnutrition. Before repeating a fluid bolus, the clinician should determine if the patient responded in a hemodynamically desirable way after the prior fluid bolus and ensure that signs of fluid overload, such as rales, gallop rhythm, or hepatomegaly, have not developed. POCUS may also be helpful to identify ongoing hypovolemia and predict response to ongoing volume resuscitation. For children with evidence of fluid overload, adequate intravascular volume, or lack of hemodynamic improvement with prior fluid boluses, resuscitation should shift from volume resuscitation to vasoactive medications. Trials of earlier initiation of vasoactive support are ongoing to further clarify the optimal role of volume resuscitation in pediatric shock.

The optimal fluid type for initial shock resuscitation remains a matter of debate. Most studies have not demonstrated a clear benefit for use of colloids, such as 4–5% albumin, over crystalloids, though there may be a small clinical benefit for resuscitation with colloids in septic shock. There is also evidence supporting a risk of kidney injury and coagulopathy with the use of synthetic colloids, such as hydroxyethyl starch and gelatin, and their use is currently not recommended. Because crystalloids are inexpensive, easy to administer, and readily available, current guidelines generally recommend initial resuscitation begin with these fluids. Exceptions include children with hemorrhagic shock and dissociative shock resulting from severe anemia for whom early blood product transfusion is preferred.

Crystalloid volume resuscitation may include 0.9% normal saline or balanced/buffered fluids, such as lactated Ringer solution, Hartmann solution, and Plasma-Lyte. Saline consists of only sodium and chloride in a 1:1 ratio with a supraphysiologic chloride concentration, whereas balanced fluids have an anion buffer and electrolyte composition closer to human blood plasma, though formulations vary. As a result, high-volume resuscitation with 0.9% saline often induces a hyperchloremic metabolic acidemia. Although 0.9% remains the most commonly used crystalloid

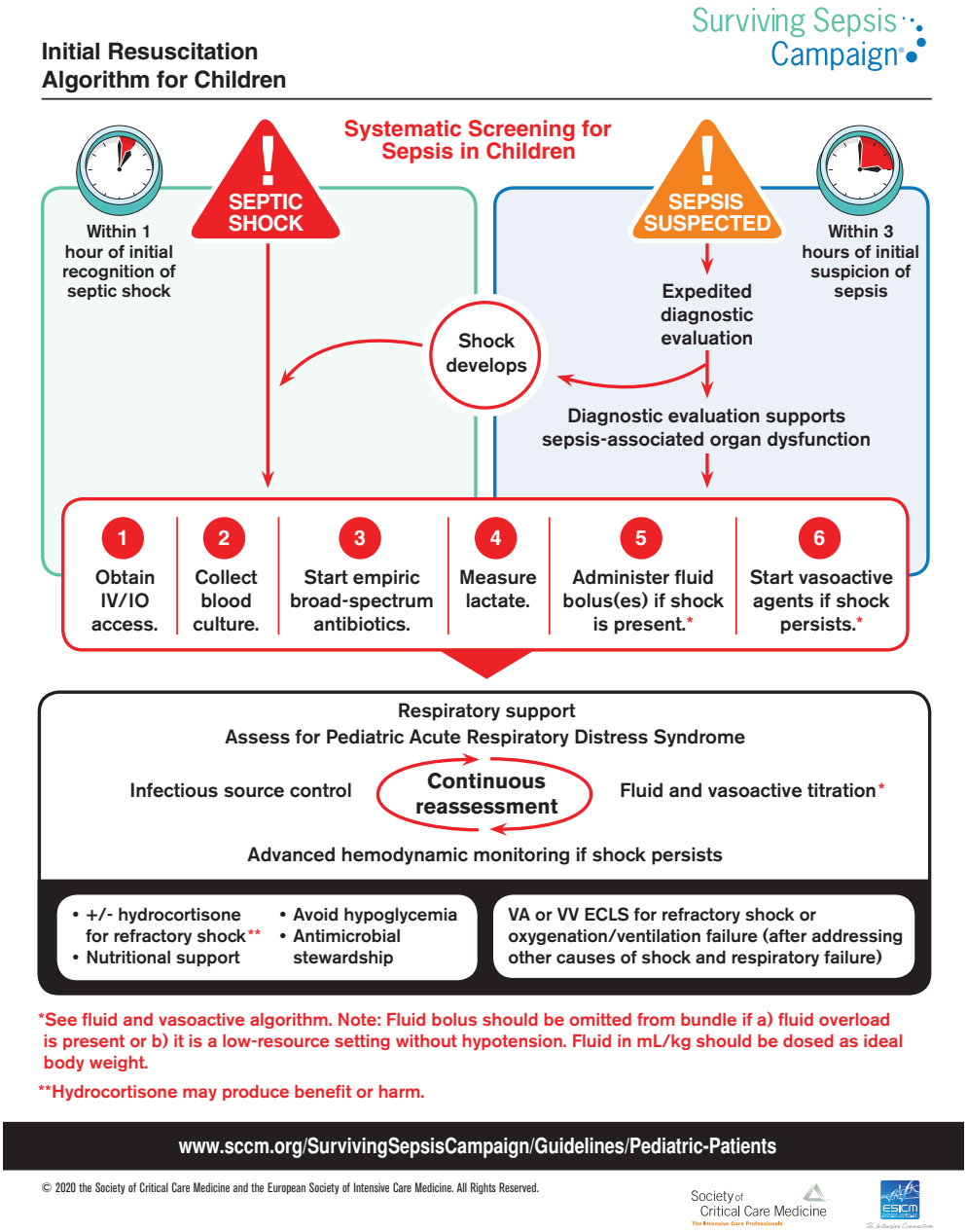

Fig. 85.2 Surviving Sepsis Campaign 2020 Initial Resuscitation Algorithm for Children. For children with clinical signs of shock, the following six key management steps should be completed within 1 hour of initial recognition of shock: (1) obtain intravenous/intraosseous access, (2) collect blood culture, (3) start empiric broad-spectrum antibiotics, (4) measure blood lactate, (5) administer crystalloid fluid therapy with volume and rate reflecting healthcare setting and titrated to patient response, and (6) initiate vasoactive medications if shock persists despite fluid and other therapy. VA, venoarterial; VV, venovenous; ECLS, extracorporeal life support. *(© 2020 the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. All Rights Reserved. https://www.sccm.org/getattachment/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients/Initial-Resuscitation-Algorithm-for-Children.pdf.aspx?lang=en-US.)*

for pediatric volume resuscitation, increasing data suggest that balanced/buffered fluids are associated with less acute kidney injury, inflammation, coagulopathy, endotheliopathy, and death. However, pediatric studies comparing balanced/buffered fluids with 0.9% saline have reported conflicting results, and adult interventional trials have not shown a consistent benefit for either crystalloid fluid type. Consequently, pending further data from ongoing studies, either 0.9% saline or balanced/buffered crystalloids are appropriate for initial volume resuscitation.

Resuscitation with blood products should be prioritized for children with hemorrhagic shock. The *Advanced Trauma Life Support* guidelines recommend resuscitation with red blood cells, plasma, and platelets in a ratio of 1:1:1 to limit coagulopathy and other risks associated with large-scale transfusion. For children with other forms of shock, the criteria to transfuse red blood cells are not clear, though it is reasonable to target hemoglobin levels >9 g/dL for children who remain hemodynamically unstable with low Svo_2 and/or high blood lactate despite other interventions. Notably, transfusion of plasma or platelets should be reserved to treat active bleeding or reduce risk of bleeding before an invasive procedure rather than used solely to correct laboratory abnormalities or as volume expanders.

Vasoactive medications should be initiated for children with fluid-refractory shock, with early consideration for inotropes, such as epinephrine, when myocardial dysfunction is present and vasopressors, such as norepinephrine, when vasoplegia is present (Table 85.7). For children with septic shock, two randomized trials have demonstrated that epinephrine as first-line vasoactive therapy is more effective at reducing mortality than dopamine. As such, epinephrine is the preferred first-line vasoactive therapy for fluid-refractory septic shock.

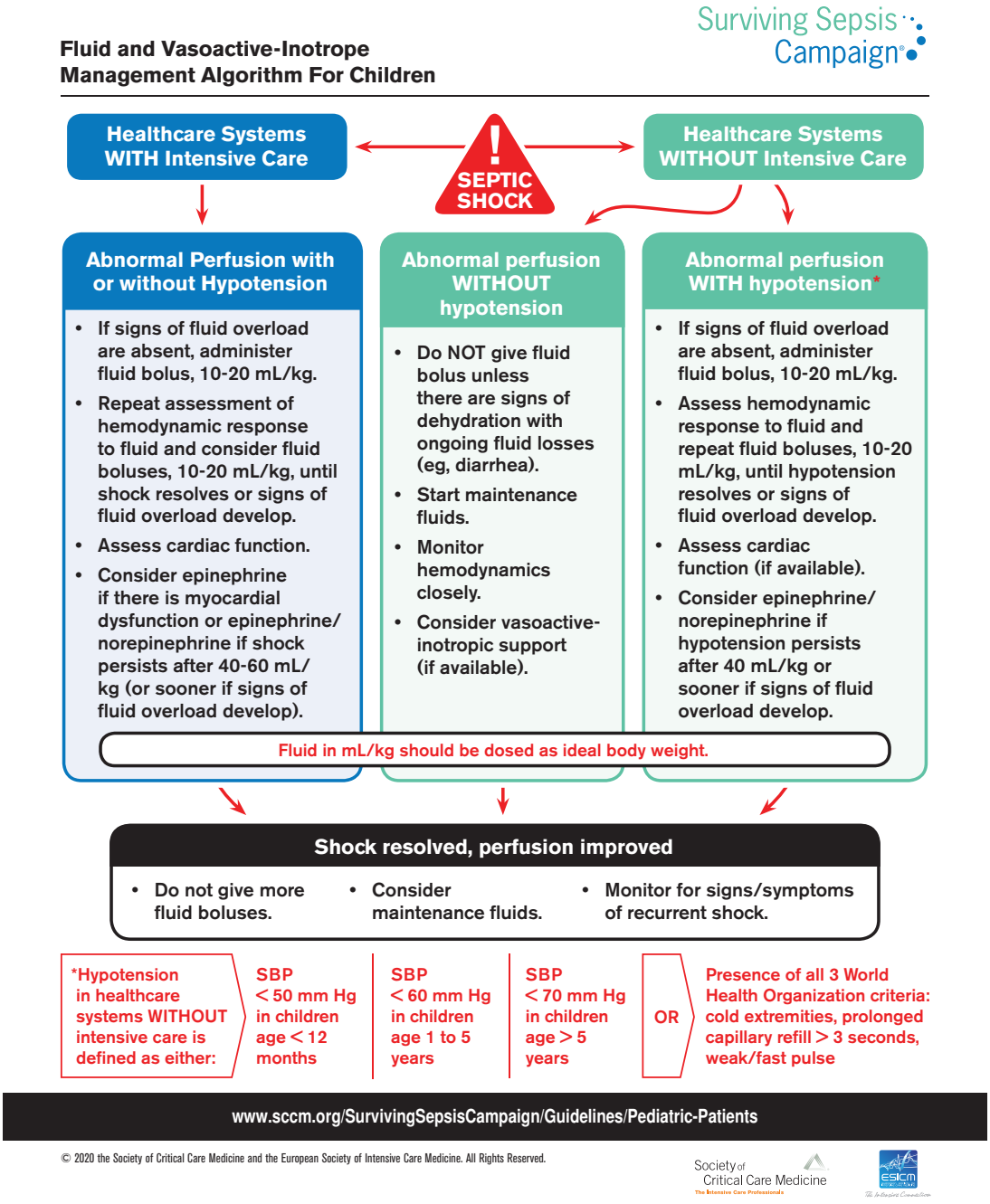

Fig. 85.3 Surviving Sepsis Campaign 2020 Fluid and Vasoactive-Inotrope Management Algorithm for Children. For children with septic shock treated in healthcare systems in which intensive care is accessible (either locally or via transport), fluid bolus therapy up to 40-60 mL/kg is recommended in the first hour of therapy until shock resolves or signs of fluid overload develop. For children with septic shock treated in healthcare systems in which intensive care is not available locally or via transport, fluid bolus therapy is not recommended unless hypotension is present. For all children, early assessment of cardiac function is recommended with consideration for initiation of epinephrine (or alternative inotrope) if myocardial dysfunction is evident. SBP, systolic blood pressure. (*© 2020 the Society of Critical Care Medicine and the European Society of Intensive Care Medicine. All Rights Reserved.* https://www.sccm.org/getattachment/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients/Initial-Resuscitation-Algorithm-for-Children.pdf.aspx?lang=en-US.)

Epinephrine is also a potent inotrope and is the recommended initial vasoactive agent in children with cardiogenic shock. However, in children with a low-SVR state, as may be seen with distributive, septic, or neurogenic shock, norepinephrine should be preferentially prescribed as the first-line vasoactive therapy. Although vasoactive agents are ideally administered through a central venous line, these medications can be safely initiated through a peripheral IV or an IO in dilute concentrations while central venous access is obtained.

Electrolyte abnormalities, such as hypoglycemia and hypocalcemia, may precipitate or worsen shock. Blood glucose and ionized calcium can both be measured rapidly via bedside point-of-care testing, and if present, hypoglycemia and hypocalcemia should be corrected during the initial resuscitation. Other patterns of electrolyte abnormalities may indicate the presence of an underlying inborn error of metabolism, particularly in a neonate with shock. Any provider treating a patient with known or suspected inborn error of metabolism should consult immediately with a specialty center while resuscitating with volume and dextrose.

Airway management is an essential component of the initial management of shock. Early intervention to maintain an unobstructed

Table 85.7 Vasoactive Medications to Treat Shock

DRUG	EFFECT(S)	DOSING RANGE	COMMENT(S)
Epinephrine	↑ Heart rate and ↑ cardiac contractility Vasodilator at low doses, but potent vasoconstrictor at doses >0.1 mcg/kg/min	0.05-2.0 µg/kg/min	May ↓ renal perfusion at high doses ↑ Myocardial O_2 consumption Risk of arrhythmia at high doses
Norepinephrine	Potent vasoconstriction ↑ Cardiac contractility (but may be blunted by increased afterload)	0.05-2.0 µg/kg/min	↑ Blood pressure secondary to ↑ systemic vascular resistance ↑ Left ventricular afterload
Dopamine	↑ Cardiac contractility Significant peripheral vasoconstriction at >10 µg/kg/min	3-20 µg/kg/min	↑ Risk of arrhythmias at high doses
Dobutamine	↑ Cardiac contractility Peripheral vasodilator	3-10 µg/kg/min	—
Phenylephrine	Potent vasoconstriction No effect on cardiac contractility	0.25-2.0 µg/kg/min	Can cause sudden hypertension
Vasopressin	Potent vasoconstriction	0.5-20 milliunits/kg/min	Can cause sudden hypertension
Angiotensin II	Potent vasoconstrictor	Stepwise increase 5-10-25-40-80 ng/kg/min over 3 hr with titration down to 1.25-40 ng/kg/min after 3 hr	Can cause sudden hypertension, arterial ischemia
Methylene blue	Reduce responsiveness to cGMP-dependent (e.g., ischemia-reperfusion, NO mediated) vasodilators	Bolus 1-2 mg/kg, then consider continuous infusion 0.5-.01 mg/kg/hr	Causes blue/green discoloration of skin and urine
Milrinone	Increased cardiac contractility Improves cardiac diastolic function Peripheral vasodilation	0.25-1.0 µg/kg/min	Phosphodiesterase inhibitor—slows cyclic adenosine monophosphate breakdown
Prostaglandin E_1	Vasodilator Maintains an open ductus arteriosus in the newborn with ductal-dependent congenital heart disease	0.01-0.2 µg/kg/min	Can lead to hypotension Risk of apnea

airway may be needed in patients who are obtunded or have suffered a traumatic neck or chest injury. Supplemental oxygen should be provided to correct hypoxemia if Spo_2 is <92–94%. Although universal supplemental oxygen administration can, in theory, augment tissue oxygen delivery by increasing oxygen content of the blood, this approach is of little benefit if the oxyhemoglobin saturation is >92–94%, and some studies suggest harm from hyperoxia. However, universal administration of high fraction of inspired oxygen is likely to be beneficial for patients with severe anemia or dissociative shock. When oxygen is required, use of a 100% non-rebreather mask provides the highest amount of noninvasive supplemental oxygen delivery.

Indications for intubation and mechanical ventilation include acute hypoxemic or hypercarbic respiratory failure or persistence of circulatory failure, in which case a reduction in metabolic demand facilitated by sedation and ventilatory support can be helpful. Sedation and endotracheal intubation reduce the work of breathing, which can divert cardiac output away from the muscles of respiration and improve perfusion to other organs. However, extra caution needs to be taken during intubation and the transition from negative pressure to positive pressure ventilation. Positive pressure ventilation will decrease venous return in a patient who is already hypovolemic, which could precipitate cardiovascular collapse. It is therefore prudent to have fluid boluses readily available and vasoactive agents started or immediately ready to administer during this transition. Of the sedative agents available for intubation, ketamine is generally preferred because of its favorable hemodynamic effects that typically augment cardiac output and BP. As several studies have reported adverse outcomes after intubation with etomidate, pediatric septic shock guidelines recommend against using etomidate in these patients.

Specific Management Considerations by Shock Type

For children with **cardiogenic shock** due to congenital heart disease, cardiomyopathies, myocarditis, MIS-C, or other causes, decreased myocardial contractility must be reversed by early treatment with inotropes, such as epinephrine, dopamine, dobutamine, or milrinone. Gentle volume resuscitation to optimize preload may also be helpful, but excessive fluid administration can worsen volume overload and further compromise heart function. Despite adequate cardiac output with the support of inotropic agents, a high SVR with poor peripheral perfusion and acidosis may persist in cardiogenic shock. Therefore, if not already started, inodilators such as milrinone may improve systolic function and decrease SVR without causing a significant increase in HR. Furthermore, this agent has the added benefit of enhancing diastolic relaxation. Dobutamine or other vasodilating agents, such as nitroprusside, may also be considered in this setting (see Table 85.7).

In **obstructive shock**, action is often needed to relieve the point of mechanical obstruction. Examples include thoracentesis for tension pneumothorax, pericardiocentesis for cardiac tamponade, and administration of systemic fibrinolytic medications for pulmonary embolism. For neonates or young infants (typically <2-3 weeks of age) with shock caused by ductal-dependent congenital heart disease, a prostaglandin infusion should be started to maintain systemic cardiac output while preparing to transfer to a pediatric specialty center.

The management of **septic shock** should follow the recommendations of the 2020 Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children (see Fig. 85.2 and Fig. 85.3). These guidelines recommend six initial management steps in the first hour after shock

recognition, including obtaining IV/IO access, collecting a blood culture, administering empiric broad-spectrum antibiotics, measuring lactate, providing volume resuscitation, and initiating vasoactive medication if shock persists despite fluid therapy. Early administration of antibiotics targeted to the most likely pathogens for each patient has been associated with reduced mortality and more rapid resolution of organ dysfunction.

Notably, the Surviving Sepsis Campaign suggests volume resuscitation with up to 40-60 mL/kg in bolus fluid (10-20 mL/kg per bolus) over the first hour, titrated to clinical markers of cardiac output and discontinued if signs of fluid overload develop, for children with septic shock treated in geographic regions that have access to intensive care (either locally or via transport) or in any setting when hypotension is present. However, in healthcare systems with no availability to access intensive care, fluid bolus therapy was associated with increased risk of mortality in the FEAST clinical trial when hypotension was not present, and thus fluid management should focus on starting maintenance fluids only in these settings (see Fig. 85.3).

Fluid-Refractory and Catecholamine-Resistant Shock

If shock persists despite volume resuscitation and vasoactive support with an initial catecholaminergic agent, such as epinephrine, the child has **fluid-refractory and catecholamine-resistant shock**. Such children have an increased risk for MODS and death, especially if requirement for vasoactive support is high, blood lactate exceeds 8 mmol/L (or is rising after 6 hours of resuscitation), and/or myocardial dysfunction is present. Several additional management considerations must be taken into account in this scenario, including evaluation for atypical and/or reversible etiologies, second-line vasoactive medications, stress-dose corticosteroids, and extracorporeal membrane oxygenation (ECMO).

Atypical and reversible etiologies that may contribute to refractory shock include hypothyroidism and intraabdominal hypertension/abdominal compartment syndrome. In addition, one must consider the presence of obstructive shock (tamponade, pneumothorax), an unrecognized closing ductus arteriosus, uncontrolled hemorrhage (which often requires surgical intervention), anaphylaxis, and need for removal of an infectious source (e.g., infected catheter, empyema, abdominal abscess).

Stress-dose corticosteroids are indicated for patients with septic shock who have absolute adrenal insufficiency, such as that caused by congenital adrenal hyperplasia, septic shock with purpura, prior steroid therapy for chronic illness, or hypopituitarism. Some children with septic shock may also develop *critical illness–related corticosteroid insufficiency* with an inadequate adrenal response to a severe stress. Stress doses of hydrocortisone (50-100 mg per m^2 per day) are recommended for those with risk factors for absolute adrenal insufficiency (e.g., septic shock with purpura, prior steroid therapy for chronic illness, known pituitary or adrenal abnormalities) and can be considered for children with fluid-refractory, catecholamine-resistant shock without a reversible etiology pending further data from ongoing clinical trials.

Second-line vasoactive therapy should be considered for patients in whom shock persists despite titration of the initial vasoactive agent. For patients with "warm" shock or evidence of low SVR initially treated with norepinephrine, the addition of vasopressin or epinephrine may be considered. Case reports, case series, and one trial indicate that administration of vasopressin is associated with an increase in mean arterial BP and urine output in children with fluid-refractory, catecholamine-resistant septic shock. However, in a multicenter trial of 65 children with vasodilatory shock, low-dose vasopressin did not decrease the time to hemodynamic stability off of vasoactive agents versus placebo (49.7 vs 47.1 hours), and there was a concerning trend toward increased mortality in the vasopressin group (30% vs 16%, $p = 0.24$). For patients with "cold" shock or evidence of myocardial dysfunction, priority should be given to improving cardiac contractility with inotropes. First-line therapy with epinephrine is recommended, with addition of dopamine, dobutamine, or norepinephrine as second-line agents, but these agents should be carefully titrated, as they may contribute to arrhythmias and increase myocardial oxygen demand. Initiation of inodilators, such as milrinone, can help to augment contractility, improve lusitropy (diastolic relaxation), and lower SVR but are generally longer-acting and should be carefully titrated to avoid worsening hypotension. Notably, it may be difficult to accurately differentiate between "warm" (low SVR) from "cold" (high SVR) shock using only clinical signs, such as extremity temperature, strength of peripheral pulses, and capillary refill time. Frequent reassessment and response to therapy are therefore paramount to ensure optimal titration of vasoactive therapies.

ECMO is a rescue option for patients suffering refractory septic shock, with reported survival rates of ~70% for newborns and ~50% for older children. One study suggests that central cannulation via sternotomy may achieve survival rates of 74% for refractory septic shock. In cardiogenic shock due to myocarditis treated with ECMO, survival rates of 70% have been reported. Although counterintuitive because of the need for systemic anticoagulation, ECMO has also been used successfully in hemorrhagic shock in a small series. In most cases of refractory shock, venoarterial ECMO is preferred over the venovenous route due to the presence of hemodynamic instability. A ventricular assist device may be considered as an alternative to ECMO in some children with cardiogenic shock.

Targets for Shock Reversal

Clinical signs of successful resuscitation include a decrease in HR and respiratory rate, increase in BP, improved urine output to >0.5 mL/kg/hr, normalization of mental status, decreased capillary refill time, warmth of distal extremities, and improved peripheral pulses. Serial laboratory measurements should aim for a rise in Svo_2 to >70% and a decreasing trend in blood lactate levels as evidence for increased tissue oxygen extraction and adequate oxygen delivery to meet cellular metabolic demand. In one observational study of septic shock in children, normalization of blood lactate to <2 mmol/L within 4 hours was associated with reduced organ dysfunction. Blood pH and base deficit may also be used as laboratory surrogates for improved tissue perfusion, but these may be affected by the degree of hyperchloremia after fluid resuscitation or by changes in ventilation.

Other parameters to monitor for improvement in shock include serial POCUS to assess volume status, cardiac output, and tissue perfusion; cutaneous near-infrared spectroscopy (NIRS) to measure regional tissue perfusion; and other devices that can estimate cardiac output based on the relationship among BP, stroke volume, arterial compliance, and SVR (e.g., pulse contour waveform analysis). If cardiac output is measured, aiming for a cardiac index between 3.3 and 6.0 L/min/m^2 is appropriate.

Though children can have isolated cardiovascular dysfunction with shock, many have additional associated organ dysfunctions or MODS. Ongoing support of noncardiovascular organ dysfunction is often required even after improvement or resolution of shock.

PROGNOSIS

In septic shock, mortality rates are as low as 3% in previously healthy children and 6–9% in children with chronic illness (compared with 25–30% in adults). With early recognition and therapy, the mortality rate for pediatric shock continues to improve, but shock and MODS remain one of the leading causes of nonaccidental death in infants and children. The risk of death involves a complex interaction of factors, including the underlying etiology, presence of chronic illness, host immune response, and timing of recognition and therapy.

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Chapter 86

Acute Care of Respiratory Distress and Failure

Alexandre T. Rotta, Martin C.J. Kneyber, and Ashok P. Sarnaik

The term *respiratory distress* is used to denote signs and symptoms of an abnormal respiratory pattern. A child with nasal flaring, tachypnea, chest wall retractions, stridor, grunting, dyspnea, or wheezing has respiratory distress. Taken together, the magnitude of these findings is used to judge clinical severity. Nasal flaring is nonspecific, but the other signs are useful in localizing the site of pathology (see Chapter 421). *Respiratory failure* is defined as the inability of the lungs to provide sufficient oxygen (hypoxic respiratory failure) or remove carbon dioxide (ventilatory failure) to meet metabolic demands. Therefore, whereas respiratory distress is determined by a clinical impression, respiratory failure is diagnosed when inadequate oxygenation or ventilation (or both) are present. Respiratory distress can occur in patients without respiratory disease, and respiratory failure can occur in patients without respiratory distress.

RESPIRATORY DISTRESS

A careful physical examination must be performed when evaluating a child in respiratory distress. **Nasal flaring**, although nonspecific, is an extremely important sign of distress in infants. It may indicate discomfort, pain, fatigue, acidosis, or breathing difficulty. The state of **responsiveness** is another crucial sign. Lethargy, disinterest in surroundings, and weak cry are suggestive of exhaustion, hypercarbia, and impending respiratory failure. Abnormalities of the rate and depth of **breathing** can occur with both pulmonary and nonpulmonary causes of respiratory distress. In diseases of decreased lung compliance, such as pneumonia and pulmonary edema, breathing is characteristically rapid and shallow (decreased tidal volume). In obstructive airway diseases, such as asthma and laryngotracheitis, breathing generally is deep with increased tidal volume, but less rapid. Rapid and deep breathing (tachypnea and hyperpnea) without other respiratory signs should raise suspicion of possible nonpulmonary or nonthoracic causes of respiratory distress, such as response to metabolic acidosis (e.g., diabetic ketoacidosis, renal tubular acidosis) or stimulation of the respiratory center (e.g., encephalitis, ingestion of central nervous system stimulants). Suprasternal, intercostal, and subcostal **retractions** are manifestations of increased inspiratory effort, weak chest wall, or both. Inspiratory **stridor** indicates airway obstruction above the thoracic inlet, whereas expiratory **wheezing** results from airway obstruction below the thoracic inlet. **Grunting** is most commonly heard in diseases with decreased functional residual capacity (e.g., pneumonia, pulmonary edema) or peripheral airway obstruction (e.g., bronchiolitis).

Respiratory Disease Manifesting as Respiratory Distress

Clinical examination is paramount in localizing the site of pathology and creating a differential diagnosis. Extrathoracic airway obstruction occurs anywhere above the thoracic inlet and is marked by inspiratory stridor, retractions, and prolongation of inspiration. In contrast, features of intrathoracic airway obstruction are prolongation of expiration and expiratory wheezing. Typical manifestations of alveolar interstitial pathology are rapid, shallow respirations, chest wall retractions, and grunting (Tables 86.1 and 86.2).

Respiratory Distress Without Respiratory Disease

Although respiratory distress most frequently results from diseases of lungs, airways, and chest wall, pathology in other organ systems can manifest as respiratory distress and lead to misdiagnosis and inappropriate management (Table 86.3). Respiratory distress resulting from heart failure or diabetic ketoacidosis may be misdiagnosed as asthma and improperly treated with albuterol, resulting in worsened hemodynamic state or ketoacidosis. Careful history and physical examination provide essential clues in avoiding misdiagnosis.

Cardiovascular Disease Manifesting as Respiratory Distress

A child with cardiovascular pathology may present with respiratory distress caused by either *decreased lung compliance* or *cardiogenic shock* (Table 86.4). Diseases that result in increased pulmonary arterial blood flow (e.g., left-to-right shunts) or increased pulmonary venous pressure (e.g., left ventricular dysfunction from hypertension or myocarditis, obstructed total anomalous pulmonary venous return) cause an increase in pulmonary capillary pressure and transudation of fluid into the pulmonary interstitium and alveoli. The increased pulmonary blood and water content lead to decreased lung compliance and result in rapid shallow breathing.

It is important to recognize that interstitial lung edema may not only manifest as alveolar fluid but as small airway obstruction as well. **Wheezing** as a sign of congestive cardiac disease is common in infants and young children and should be recognized. Patients with cardiac lesions that result in low cardiac output often present in shock. For example, obstructive lesions of the left side of the heart (e.g., critical coarctation of the aorta) and acquired or congenital cardiomyopathy result in decreased perfusion and metabolic acidosis, as well as respiratory distress because of chemoreceptor and baroreceptor stimulation. The likelihood of a particular cardiovascular illness manifesting as respiratory distress depends on age at presentation (Table 86.5).

Neurologic Disease Manifesting as Respiratory Distress

Central nervous system (CNS) dysfunction can lead to alterations in respiratory patterns and manifest as respiratory distress. Increased intracranial pressure (ICP) may manifest as respiratory distress. Early rise in ICP results in stimulation of respiratory centers, leading to increases in the rate **(tachypnea)** and depth **(hyperpnea)** of respiration. The resultant decrease in arterial blood partial pressure of carbon dioxide ($Paco_2$) and elevation of cerebrospinal fluid (CSF) pH leads to cerebral vasoconstriction and temporary amelioration of intracranial hypertension. Stereotypical respiratory patterns are associated

Table 86.1 Typical Localizing Signs for Pulmonary Pathology

SITE OF PATHOLOGY	RESPIRATORY RATE	RETRACTIONS	AUDIBLE MANIFESTATION
Extrathoracic airway	↑	↑↑↑↑	Stridor
Intrathoracic extrapulmonary	↑	↑↑	Wheezing
Intrathoracic intrapulmonary	↑↑	↑↑	Wheezing
Alveolar or interstitial	↑↑↑	↑↑↑	Grunting, crackles

Table 86.2 Examples of Anatomic Sites of Lesions Causing Respiratory Failure

LUNG	RESPIRATORY PUMP
CENTRAL AIRWAY OBSTRUCTION	**THORACIC CAGE**
Choanal atresia Tonsilloadenoidal hypertrophy Retropharyngeal/peritonsillar abscess Laryngomalacia Epiglottitis Vocal cord paralysis Laryngotracheitis Subglottic stenosis Vascular ring/pulmonary sling Mediastinal mass Foreign body	Kyphoscoliosis Diaphragmatic hernia Flail chest Eventration of diaphragm Asphyxiating thoracic dystrophy Prune-belly syndrome Dermatomyositis Abdominal distention
PERIPHERAL AIRWAY OBSTRUCTION	**BRAINSTEM**
Asthma Bronchiolitis Foreign body Aspiration of gastric contents Cystic fibrosis α_1-Antitrypsin deficiency	Arnold-Chiari malformation Central hypoventilation syndrome CNS depressants, including drug overdose Trauma Increased intracranial pressure CNS infections
ALVEOLAR OR INTERSTITIAL DISEASE	**SPINAL CORD**
Lobar pneumonia* ARDS Surfactant deficiency Interstitial pneumonia Hydrocarbon pneumonitis Pulmonary hemorrhage/hemosiderosis Vaping lung injury Smoke inhalation Drowning	Trauma Transverse myelitis Spinal muscular atrophy Poliomyelitis Compression (tumor, abscess, bleed) Acute flaccid myelitis
	NEUROMUSCULAR
	Phrenic nerve injury Birth trauma Infant botulism Guillain-Barré syndrome Muscular dystrophy Myasthenia gravis Organophosphate poisoning

*Including bacteria and viral; fungal or parasitic less common.
ARDS, Acute respiratory distress syndrome; CNS, central nervous system.

Table 86.3 Nonpulmonary Causes of Respiratory Distress

DOMAIN	EXAMPLE(S)	MECHANISM(S)
Cardiovascular	Left-to-right shunt Congestive heart failure Cardiogenic shock	↑ Pulmonary blood/water content Metabolic acidosis Baroreceptor stimulation
CNS	Increased intracranial pressure Encephalitis Neurogenic pulmonary edema Toxic encephalopathy	Stimulation of brainstem respiratory centers
Metabolic	Diabetic ketoacidosis Organic acidemia Hyperammonemia	Stimulation of central and peripheral chemoreceptors
Renal	Renal tubular acidosis Hypertension	Stimulation of central and peripheral chemoreceptors Left ventricular dysfunction → increased pulmonary blood/water content
Infection	Toxic shock syndrome Septic shock Meningococcemia	Cytokine stimulation of respiratory centers Baroreceptor stimulation from shock Metabolic acidosis

CNS, Central nervous system.
Courtesy Dr. Ashok Sarnaik.

with dysfunction at various levels of the brain. Cerebral hemisphere and midbrain lesions result in hyperpnea and tachypnea. In such situations, arterial blood gas (ABG) measurements typically show respiratory alkalosis without hypoxemia. Pathology affecting the pons and medulla manifests as irregular breathing patterns such as **apneustic breathing** (prolonged inspiration with brief expiratory periods), **Cheyne-Stokes breathing** (alternate periods of rapid and slow breathing), and irregular, ineffective breathing or apnea (Table 86.6). Along with respiratory changes, other manifestations of CNS dysfunction and increased ICP generally are present, such as focal neurologic signs, pupillary abnormalities, hypertension, and bradycardia (see Chapter 82). Occasionally, severe CNS dysfunction can result in **neurogenic pulmonary edema** and respiratory distress, which may follow excessive sympathetic discharge resulting in increased pulmonary venous hydrostatic pressure and increased pulmonary capillary permeability. **Central neurogenic hyperventilation** is characteristically observed in illnesses such as urea cycle defects and encephalitis. **Bradycardia** and **apnea** may be caused by CNS-depressant medications, poisoning, prolonged hypoxia, trauma, or infection (see Table 86.2).

Toxic Metabolic States Manifesting as Respiratory Distress

Direct stimulation of respiratory centers resulting in respiratory alkalosis is encountered in intoxication involving agents such as salicylates and theophylline. Similarly, intoxication with general CNS stimulants, such as cocaine and amphetamines, may result in increased respiration. Presence of endogenous (e.g., organic acids) or exogenous (e.g., methanol, ethylene glycol, salicylates) toxins causes metabolic acidosis and compensatory hyperventilation, which can manifest as respiratory distress. ABG measurements show decreased pH and compensatory hypocarbia with normal oxygenation. Conversely, metabolic disorders with hyperammonemia cause respiratory alkalosis (decreased $Paco_2$ with increased pH) as ammonia directly stimulates the respiratory centers. Cyanide poisoning and methemoglobinemia may also produce respiratory distress.

Other Nonpulmonary Entities Manifesting as Respiratory Distress

Sepsis and **septic shock** may cause respiratory distress from hypovolemic stimulation of baroreceptors, cytokine stimulation of respiratory centers, and lactic acidosis; they can also lead to **acute respiratory distress syndrome** (ARDS). Other indirect causes of ARDS include systemic inflammatory conditions, trauma, transfusion-related acute lung injury, and pancreatitis. Similarly, renal disease may manifest as respiratory distress by causing metabolic acidosis (e.g., renal tubular acidosis or renal failure) or hypertensive left ventricular failure and fluid overload.

RESPIRATORY FAILURE

Respiratory failure occurs when oxygenation and ventilation are insufficient to meet the metabolic demands of the body. Respiratory failure may result from an abnormality in (1) lung and airways, (2) chest wall and muscles of breathing, or (3) central and peripheral chemoreceptors. Clinical manifestations depend largely on the site of pathology. Although respiratory failure is traditionally defined as respiratory

Table 86.4 Cardiovascular Pathology Manifesting as Respiratory Distress

I. DECREASED LUNG COMPLIANCE

A. Left-to-right shunts

1. Ventricular septal defect, atrial septal defect, patent ductus arteriosus, atrioventricular canal, truncus arteriosus
2. Cerebral or hepatic arteriovenous fistula

B. Ventricular failure

1. Left heart obstructive lesions
   a. Aortic stenosis
   b. Coarctation of the aorta
   c. Interrupted aortic arch
   d. Mitral stenosis
   e. Hypoplastic left heart syndrome
2. Myocardial infarction
   a. Anomalous left coronary artery from the pulmonary artery (ALCAPA)
   b. Ventriculocoronary arterial connections (coronary sinusoids)
3. Hypertension
   a. Acute glomerulonephritis
4. Inflammatory/infectious
   a. Myocarditis
   b. Pericardial effusion
5. Idiopathic/genetic
   a. Dilated cardiomyopathy
   b. Hypertrophic obstructive cardiomyopathy
   c. Takotsubo syndrome

C. Pulmonary venous obstruction

1. Total anomalous pulmonary venous connection with obstruction
2. Cor triatriatum

II. SHOCK RESULTING IN METABOLIC ACIDOSIS

A. Left heart obstructive lesions

B. Acute ventricular failure

1. Myocarditis, myocardial infarction

Table 86.5 Typical Chronology of Heart Disease Presentation in Children

AGE	MECHANISM	DISEASE
Newborn (1-10 days)	↑ Arteriovenous pressure difference	Arteriovenous malformation (brain, liver)
	Ductal closure	Single ventricle lesions or severe ventricular outflow obstruction
	Independent pulmonary and systemic blood flow	Transposition of the great arteries
	Pulmonary venous obstruction	Total anomalous pulmonary venous return (TAPVR)
Young infant (1-6 mo)	↓ Pulmonary vascular resistance	Left-to-right shunt lesions
	↓ Pulmonary artery pressure	Anomalous left coronary artery from the pulmonary artery (ALCAPA)
Any age	Heart rate disturbance	Tachyarrhythmias or bradyarrhythmias
	Infection	Myocarditis, endocarditis, pericarditis
	Abnormal cardiac myocytes	Cardiomyopathy
	Excess afterload	Hypertension

dysfunction resulting in arterial partial pressure of oxygen (Pa_{O_2}) <60 mm Hg when breathing ambient air and Pa_{CO_2} >50 mm Hg resulting in acidemia, the patient's general state, respiratory effort, and potential for impending exhaustion are more important indicators than ABG values.

Pathophysiology

Respiratory failure can be classified into *hypoxic* respiratory failure (failure of oxygenation) and *hypercarbic* respiratory failure (failure of ventilation). Systemic venous (pulmonary arterial) blood is arterialized through equilibration with alveolar gas in the pulmonary capillaries and is carried back to the heart by pulmonary veins. Arterial blood oxygen and carbon dioxide content are influenced by the composition of the inspired gas, effectiveness of alveolar ventilation, pulmonary capillary perfusion, and diffusion capacity of the alveolar capillary membrane. An abnormality in any of these steps can result in respiratory failure. **Hypoxic respiratory failure** results from intrapulmonary shunting and venous admixture or insufficient diffusion of oxygen from alveoli into pulmonary capillaries. This physiology can be caused by small airways obstruction, increased barriers to diffusion (e.g., interstitial edema, fibrosis), and conditions in which alveoli are collapsed or filled with fluid (e.g., pneumonia, atelectasis, pulmonary edema). In most cases, hypoxic respiratory failure is associated with decreased functional residual capacity and can be managed by lung volume recruitment with positive pressure ventilation. **Hypercarbic respiratory failure** is caused by decreased minute ventilation (i.e., tidal volume multiplied by respiratory rate). This can result from centrally mediated disorders of respiratory drive, increased dead space ventilation, or obstructive airway disease. *Hypoxic and hypercarbic respiratory failure may coexist as a combined failure of oxygenation and ventilation.*

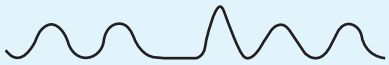
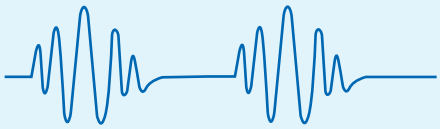
Ventilation-Perfusion Mismatch

For exchange of O_2 and CO_2 to occur, alveolar gas must be exposed to blood transiting in close proximity through the pulmonary capillaries. Both ventilation and perfusion are lower in nondependent areas (upper lobes in upright position) of the lung and higher in dependent areas (lower lobes in upright position). The difference in perfusion ($\dot{Q}$) is greater than the difference in ventilation ($\dot{V}$). Perfusion in excess of ventilation results in incomplete arterialization of systemic venous (pulmonary arterial) blood and is referred to as **venous admixture**. Perfusion of unventilated areas is referred to as **intrapulmonary shunting**. Conversely, ventilation that is in excess of perfusion is wasted; that is, it does not contribute to gas exchange and is referred to as **dead space ventilation**. Dead space ventilation results in return of greater amounts of atmospheric gas (which has not participated in gas exchange and has negligible CO_2) back to the atmosphere during exhalation. The respiratory dead space is divided into the **anatomic dead space** and the **alveolar dead space**. The *anatomic dead space* includes the conducting airways from the nasopharynx to the terminal bronchioles, ends at the alveoli, and has no contact with the pulmonary capillary bed. The *alveolar dead space* refers to areas of the lung where alveoli are ventilated but not perfused. Under normal conditions, this usually occurs in West zone I, where alveolar pressure is greater than pulmonary capillary pressure, thus restricting blood flow. Under clinical conditions, this alveolar dead space may result from dynamic hyperinflation, high levels of positive end-expiratory pressure (PEEP), or large tidal volume in mechanically ventilated patients. Additionally, conditions that cause decreased pulmonary artery perfusion (e.g., pulmonary embolism, decreased cardiac output, hypovolemia) can result in alveolar dead space. The result is a decrease in mixed expired CO_2 (P_{ECO_2}) and an increase in the $Pa_{CO_2} - P_{ECO_2}$ gradient. Dead space as a fraction of tidal volume (V_D/V_T) is calculated as:

$$(Pa_{CO_2} - P_{ECO_2}) \div Pa_{CO_2}$$

Normal V_D/V_T is approximately 0.33. Venous admixture and intrapulmonary shunting predominantly affect oxygenation, resulting in an alveolar partial pressure of oxygen (P_{AO_2}) to Pa_{O_2} ($A\text{-}a_{O_2}$) gradient without elevation in Pa_{CO_2}. This occurs due to greater ventilation of perfused areas, which is sufficient to normalize Pa_{CO_2} but not Pa_{O_2} because of their respective dissociation curves. The relative straight-line

Table 86.6 Respiratory Patterns in Neurologic Disease

INJURY SITE	PATTERN*	COMMENTS
Normal		Variable V_T with normal respiratory pauses and sighs
Cortex		Hyperpnea and tachypnea
Midbrain		*Cheyne-Stokes breathing:* Gradually increasing and decreasing V_T
Pons		*Apneustic breathing:* Prolonged inspiration followed by prolonged expiration
Medulla and pons		*Biot breathing:* Rapid and irregular respirations with pauses

*Pattern tracings represent lung volume over time.
V_T, Tidal volume.

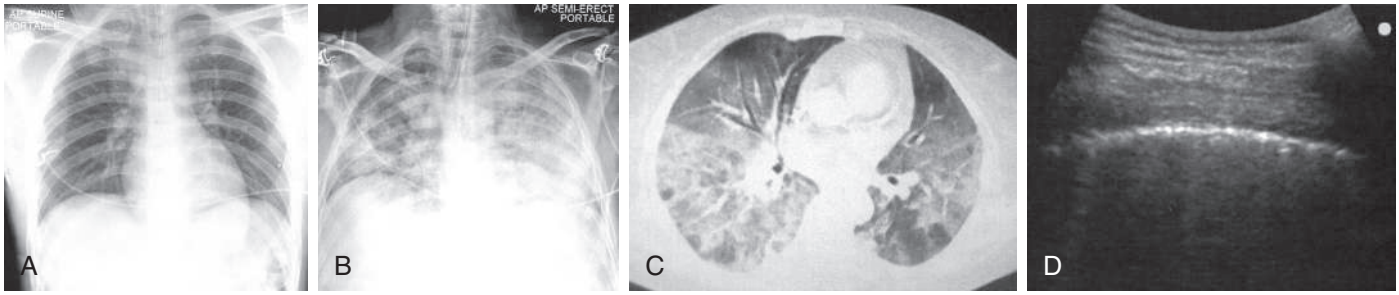


Fig. 86.1 Acute respiratory distress syndrome (ARDS). **A,** Normal chest radiograph. **B,** Chest radiograph demonstrating bilateral alveolar infiltrates consistent with ARDS. **C,** Chest CT showing bilateral pneumonitis and consolidation with air bronchograms consistent with ARDS. **D,** Lung ultrasonogram illustrating smooth pleural line, absence of horizontal A lines, and presence of vertical B lines suggestive of ARDS. *(Modified from MacSweeney R, McAuley DF. Acute respiratory distress syndrome.* Lancet. *2016;388:2416-2430, Fig. 3.)*

relationship of the hemoglobin-CO_2 dissociation allows for averaging of capillary P_{CO_2} (P_{cCO_2}) from hyperventilated and hypoventilated areas. Because the association between oxygen tension and hemoglobin saturation plateaus with increasing Pa_{O_2} (i.e., "S-shaped" curve), the decreased hemoglobin-O_2 saturation in poorly ventilated areas cannot be compensated for by well-ventilated areas where hemoglobin-O_2 saturation has already reached near-maximum. This results in decreased arterial oxyhemoglobin saturation (Sa_{O_2}) and Pa_{O_2}. Elevation of Pa_{CO_2} in such situations is indicative of coincident alveolar hypoventilation. Examples of diseases leading to venous admixture include asthma and aspiration pneumonia and pulmonary embolism, and those of intrapulmonary shunt include lobar pneumonia and ARDS.

Diffusion

Even if ventilation and perfusion are matched, gas exchange requires diffusion across the interstitial space between the alveoli and pulmonary capillaries. Under normal conditions, there is sufficient time for the pulmonary capillary blood to equilibrate with alveolar gas across the interstitial space. When the interstitial space is thickened by extravasated fluid or inflammatory cells, diffusion is impaired. Because the diffusion capacity of CO_2 is 20 times greater than that of O_2, diffusion defects manifest as hypoxemia rather than hypercarbia. Even with the administration of 100% oxygen, P_{AO_2} increases to approximately 660 mm Hg from 100 mm Hg at sea level, and the concentration gradient for diffusion of O_2 is increased by only 6.6 times. Therefore, with diffusion defects, lethal hypoxemia will set in before clinically significant CO_2 retention results. In fact, in such situations, Pa_{CO_2} is often decreased because of the hyperventilation that accompanies hypoxemia. The presence of hypercarbia in diseases that impair diffusion is indicative of alveolar hypoventilation from coexisting airway obstruction, CNS depression, or exhaustion. Examples of disease that impair diffusion are interstitial pneumonia, scleroderma, pulmonary lymphangiectasia, and ARDS.

Acute Respiratory Distress Syndrome

Some patients with respiratory failure meet criteria for ARDS, a pulmonary condition of myriad etiologies characterized by hypoxemia of acute onset and chest radiograph findings consistent with acute pulmonary parenchymal disease (Fig. 86.1). ARDS affects both children and adults and can be the result of pulmonary (direct) or extrapulmonary (indirect) insults. Causes of direct ARDS include pneumonia, aspiration of gastric contents or toxic chemicals, lung contusion, and smoke inhalation. Causes of indirect ARDS include sepsis, transfusion-related lung injury, and pancreatitis, to name a few. The diagnostic criteria for pediatric acute respiratory distress syndrome (PARDS) are outlined in Table 86.7.

Table 86.7 Pediatric Acute Respiratory Distress Syndrome (PARDS 2.0) Definition

Age	Excludes patients with perinatal-related lung disease		
Timing	Within 7 days of a known clinical insult		
Origin of edema	Not fully explained by cardiac failure or fluid overload		
Chest imaging	New opacities (unilateral or bilateral) consistent with acute pulmonary parenchymal disease and which are not due primarily to atelectasis or pleural effusion[a]		
Oxygenation[b]	IMV: OI ≥ 4 or OSI ≥ 5 NIV[c]: Pa_{O_2}/ F_{IO_2} ≤ 300 or SP_{O_2}/ F_{IO_2} ≤ 250		
	Stratification of PARDS severity: Apply ≥ 4 after initial diagnosis of PARDS		
	IMV PARDS	Mild/moderate: OI <16 or OSI <12	Severe: OI ≥16 or OSI ≥12
	NIV PARDS[c]	Mild/moderate: Pa_{O_2}/ F_{IO_2}>100 or SP_{O_2}/ F_{IO_2} >150	Severe: Pa_{O_2}/ F_{IO_2} ≤ 100 or SP_{O_2}/ F_{IO_2} ≤ 150
Special Populations[d]			
Cyanotic heart disease	Above criteria, with acute deterioration in oxygenation not explained by cardiac disease		
Chronic lung disease	Above criteria, with acute deterioration in oxygenation from baseline		

[a]Children in resource-limited settings where imaging is not available who otherwise meet PARDS criteria are considered to have possible PARDS.
[b]Oxygenation should be measured at steady state and not during transient desaturation episodes. When S_{PO_2} is used, ensure that S_{PO_2} is ≤ 97%.
[c]Diagnosis of PARDS on NIV (NIV PARDS) requires full facemask interface with continuous airway positive pressure/positive end-expiratory pressure ≥ 5cm H_2O.
[d]Stratification of PARDS severity does not apply to these populations.
IMV, invasive mechanical ventilation; NIV noninvasive ventilation; OI, oxygenation index; OSI, oxygen saturation index; PARDS, pediatric acute respiratory distress syndrome; S_{PO_2}, pulse oximeter oxygen saturation; Pa_{O_2}, partial pressure of arterial oxygen; F_{IO_2}, fraction of inspired oxygen.
OI = mean airway pressure (MAP) (cm H2O) × F_{IO_2} /Pa_{O_2} (mm Hg).
OSI = MAP (cm H2O) × F_{IO_2} /S_{PO_2}.
Adapted from Executive Summary of the Second International Guidelines for the Diagnosis and Management of Pediatric Acute Respiratory Distress Syndrome (PALICC-2): *Pediatr Crit Care Med* 2023;24:143–168.

MONITORING A CHILD IN RESPIRATORY DISTRESS AND RESPIRATORY FAILURE

Clinical Examination

Clinical observation is the most important component of monitoring. The presence and magnitude of abnormal clinical findings, their progression with time, and their temporal relation to therapeutic interventions serve as guides to diagnosis and management (see Chapter 421). As much as possible, the child with respiratory distress or failure should be observed in the position of greatest comfort and in the least threatening environment.

Pulse oximetry is the most commonly used technique to monitor oxygenation. Noninvasive and safe, it is the standard of care in bedside monitoring of children during transport, procedural sedation, surgery, and critical illness. It indirectly measures arterial hemoglobin-O_2 saturation by differentiating oxyhemoglobin from deoxygenated hemoglobin through their respective light absorption at wavelengths of 660 nm (red) and 940 nm (infrared). A pulsatile circulation is required to enable detection of arterialized blood entering the capillary bed. Percentage of arterial oxyhemoglobin is reported as Sa_{O_2}; however, the correct description is *oxyhemoglobin saturation as measured by pulse oximetry* (Sp_{O_2}). Such precision is needed because Sp_{O_2} may not always reflect Sa_{O_2}. It is important to be familiar with the hemoglobin-O_2 dissociation curve (see Chapter 421) to estimate Pa_{O_2} at a given oxyhemoglobin saturation. Because of the shape of the hemoglobin-O_2 dissociation curve, changes in Pa_{O_2} above 70 mm Hg are not readily identified by pulse oximetry. Also, at the same Pa_{O_2}, there may be significant change in Sp_{O_2} at a different blood pH value. In most situations, Sp_{O_2} >95% is a reasonable goal, especially in emergency care. In patients receiving supplemental oxygen, a target saturation range of 94–96% should be considered in order to decrease unnecessary exposure that could result in oxygen toxicity. There are exceptions, such as in patients with large left-to-right shunts (e.g., ventricular septal defect, patent ductus arteriosus) or with single-ventricle cardiac lesions in whom the pulmonary and systemic circulations are receiving blood flow from the same ventricle (e.g., after stage I palliation for hypoplastic left heart syndrome). In the latter, a lower Sp_{O_2} (75–85%) is desired to avoid excessive blood flow to the lungs and reduced blood flow to the systemic circulation that can lead to morbidity and death. Because most commercially available pulse oximeters recognize all types of hemoglobin as either oxyhemoglobin or deoxygenated hemoglobin, they provide inaccurate information in the presence of carboxyhemoglobin and methemoglobin. In carbon monoxide poisoning, **carboxyhemoglobin** absorbs light in the same (red) wavelength as oxyhemoglobin, leading to overestimation of oxygen saturation. **Methemoglobin** absorbs light in both the oxygenated and deoxygenated wavelengths, which can cause either an overestimation or underestimation of oxygen saturation. Data suggest that increasing methemoglobin concentrations tend to drive Sp_{O_2} toward 85%, no matter the actual percent of oxyhemoglobin. At lower methemoglobin levels, the pulse oximetry reading is falsely low, whereas high levels lead to a falsely high pulse oximetry reading. Newer specialized pulse oximeters can distinguish dyshemoglobinemias and prevent false readings, but their use is not widespread. It should be recognized that dangerous levels of hypercarbia may exist in patients with ventilatory failure, who have satisfactory Sp_{O_2} if they are receiving supplemental oxygen. Pulse oximetry should not be the only monitoring method in patients with primary ventilatory failure, such as neuromuscular weakness and CNS depression. It is also unreliable in patients with poor perfusion and poor pulsatile flow to the extremities. Pulse oximetry may underestimate the degree of hypoxia in Black patients. Despite these limitations, pulse oximetry is a noninvasive, easily applicable, and effective means of assessing oxygenation in most patients.

Volumetric capnography (end-tidal CO_2 [$Petco_2$] measurement) is helpful to noninvasively assess the effectiveness of ventilation and pulmonary circulation. The $Petco_2$ can be used to determine the alveolar dead space fraction (V_D/V_T) and is calculated as follows:

$$V_D/V_T = (Paco_2 - Petco_2) \div Paco_2$$

Changes in the alveolar dead space fraction usually correlate well with changes in the gradient of $Paco_2$ and $Petco_2$ ($Paco_2 - Petco_2$). Thus a change in $Paco_2 - Petco_2$ can be used as an index of changes in alveolar dead space. Diseases resulting in increased alveolar dead space (e.g., asthma with dynamic hyperinflation) or decreased pulmonary blood flow (e.g., pulmonary embolism, low cardiac output) lead to decreases in $Petco_2$ and an increase in $Paco_2 - Petco_2$. $Petco_2$ alone may overestimate adequacy of ventilation.

Blood Gas Abnormalities

Arterial blood gas analysis offers valuable assistance in diagnosis, monitoring, and management of a child in respiratory distress and failure. Because arterial blood sampling in children can be impractical without an indwelling catheter, a *capillary blood gas* (CBG) sample often is obtained, especially in emergency situations. A properly arterialized CBG sample obtained by warming the digit or heel that yields free-flowing blood is an acceptable surrogate. The blood sample needs to be processed without delay. CBG provides a good estimate of $Paco_2$ and arterial pH, but less so for Pao_2. In patients who mainly require monitoring of ventilation (especially those whose oxygenation is being monitored with pulse oximetry), a *venous blood gas* sample provides a reasonable estimate of arterial pH and $Paco_2$ values, provided tissue perfusion is adequate. Venous Pco_2 ($Pvco_2$) is approximately 6 mm Hg higher and pH approximately 0.03 lower than the arterial values. Pvo_2 has a poor correlation with Pao_2. Mixed venous O_2 saturation obtained from a central venous catheter in the right atrium is a useful marker of the balance between oxygen delivery and oxygen consumption. In patients with a constant arterial O_2 content and O_2 consumption, mixed venous O_2 saturation offers valuable information about cardiac output.

Blood gas analysis is important not only for determining the adequacy of oxygenation and ventilation but also for determining the site of respiratory pathology and planning treatment (see Chapter 421). Briefly, in the presence of pure alveolar hypoventilation (e.g., airway obstruction above carina, decreased CO_2 responsiveness, neuromuscular weakness), the blood gas will show respiratory acidosis with an elevated $Paco_2$ but a relative sparing of oxygenation. $\dot{V}/\dot{Q}$ mismatch (peripheral airway obstruction, bronchopneumonia) will be reflected in increasing hypoxemia and variable levels of $Paco_2$ (low, normal, high) depending on severity of disease. Intrapulmonary right-to-left shunting and diffusion defects (alveolar-interstitial diseases such as pulmonary edema, ARDS) will be associated with a large A-ao_2 gradient and hypoxemia with relative sparing of CO_2 elimination, unless there is coincident fatigue or CNS depression.

Acid-Base Abnormalities

It is crucial to analyze the magnitude and appropriateness of changes in pH, $Paco_2$, and bicarbonate concentration ($[HCO_3^-]$) because they provide useful clues to the underlying pathophysiology and presence of more than one disorder. To do so, it is useful to assume baseline values of pH 7.40, $Paco_2$ 40 mm Hg, and $[HCO_3^-]$ 24 mEq/L. Newborns have a lower renal threshold for bicarbonate and therefore have slightly different baseline values of pH 7.38, $Paco_2$ 35 mm Hg, and $[HCO_3^-]$ 20 mEq/L.

Metabolic Acidosis with Respiratory Compensation

Patients with metabolic acidosis have decreased pH resulting from decreased serum $[HCO_3^-]$. Chemoreceptor stimulation results in hyperventilation and respiratory compensation that may clinically manifest as respiratory distress. Normal compensation does not completely correct the pH, but rather minimizes a change in pH that would otherwise occur without compensation. The adequacy of respiratory compensation is judged by the extent of the decline in $Paco_2$ in response to the decline in $[HCO_3^-]$ or pH. A normal compensation for metabolic acidosis results in a fall in $Paco_2$ by 1.2 mm Hg for every 1 mEq/L fall in $[HCO_3^-]$. The most commonly used method to analyze the adequacy of respiratory compensation is Winter's formula:

$$Paco_2 \text{ mm Hg} = (HCO_3^- \times 1.5) + 8 \pm 2$$

A quick method is to look at the last two digits of pH (provided it is not <7.10), which should be within 2 mm Hg of $Paco_2$. For example, pH 7.27, $Paco_2$ 26 mm Hg, and $[HCO_3^-]$ 12 mEq/L represent metabolic acidosis with a normal respiratory compensation response. On the other hand, pH 7.15, $Paco_2$ 30 mm Hg, and $[HCO_3^-]$ 10 mEq/L constitutes metabolic acidosis with inadequate respiratory compensation. The reasons for inadequate compensation include decreased CO_2 responsiveness (e.g., narcotic poisoning, cerebral edema), abnormalities of lungs and airways, or neuromuscular weakness. A decrease in $Paco_2$ that is greater than what could be expected as a normal compensatory response to metabolic acidosis is indicative of a mixed disorder. A pH 7.20, $Paco_2$ 15 mm Hg, and $[HCO_3^-]$ 7.5 mEq/L represent metabolic acidosis with a concomitant respiratory alkalosis because the decline in $Paco_2$ is greater than what can be expected as normal compensation. A combination of metabolic acidosis and respiratory alkalosis is often encountered in serious conditions such as cardiogenic shock (e.g., stimulation of baroreceptors), sepsis, or toxic-metabolic states (e.g., salicylates, organic acidemia).

Respiratory Acidosis with Metabolic Compensation

Patients with respiratory acidosis have decreased pH as a result of elevated $Paco_2$. An acute increase in $Paco_2$ of 10 mm Hg results in a decrease in pH by 0.08. Thus a child with severe critical asthma and a $Paco_2$ of 60 mm Hg will have a blood pH of approximately 7.24. Chronically elevated (>3-5 days) $Paco_2$ is accompanied by renal compensation and increase in serum $[HCO_3^-]$, limiting the fall in pH to 0.03 for every 10 mm Hg rise in $Paco_2$. Thus an infant with bronchopulmonary dysplasia who has a basal $Paco_2$ of 60 mm Hg will have a blood pH of approximately 7.34. These findings are helpful in distinguishing acute from chronic changes in $Paco_2$. Also, for a given level of CO_2 accumulation, a decrease in pH that is greater than expected is indicative of concomitant metabolic acidosis, and a decline in pH that is less than expected is caused by accompanying metabolic alkalosis.

Assessment of Oxygenation and Ventilation Deficits

For standardizing management, following clinical progress, and determining prognosis for patients with defects in oxygenation or ventilation, the following indicators have been proposed, each with its strengths and limitations:

- **A-ao_2 gradient** is calculated by the subtraction, $Pao_2 - Pao_2$. For the comparison to be valid, both values must be taken at the same time and with the same fraction of oxygen in the inspired gas (Fio_2).
- **Pao_2/Fio_2 ratio** (P/F ratio) is calculated by dividing Pao_2 by Fio_2. The P/F ratio is the measure of oxygenation adequacy employed in the Berlin definition of ARDS in adults (Table 86.8). According to the Berlin definition, a P/F ≤300 mm Hg is consistent with mild ARDS, a P/F ratio between 100 and 200 mm Hg is consistent with moderate ARDS, and a P/F ratio ≤100 mm Hg is consistent with severe ARDS. Although the intent is to gauge the degree of $\dot{V}/\dot{Q}$ mismatch, intrapulmonary shunt, and diffusion defect, the status of alveolar hypoventilation could have a significant impact on P/F ratio.
- **Spo_2/Fio_2 ratio** may be used as a surrogate measure of oxygenation adequacy when Pao_2 is not available. It is calculated by dividing the pulse oximeter saturation by the Fio_2. P/F ratios of 200 mm

Table 86.8 The Berlin Definition of ARDS

- Acute onset (within 7 days of new or worsening respiratory symptoms)
- Bilateral radiographic opacities that are not fully explained by effusion, atelectasis, or masses
- Arterial hypoxemia defined by thresholds:
  - *Mild:* 200 <Pao_2/Fio_2 ratio ≤300 mm Hg, on CPAP* or PEEP† ≥5 cm H_2O (observed mortality 27%)
  - *Moderate:* 100 <Pao_2/Fio_2 ratio ≤200 mm Hg, on PEEP ≥5 cm H_2O (observed mortality 32%)
  - *Severe:* Pao_2/Fio_2 ratio ≤100 mm Hg, on PEEP ≥5 cm H_2O (observed mortality 45%)
- Identified risk factor for ARDS (if no clear risk factor, exclude heart failure as a cause)
- Not exclusively the result of cardiac causes

ARDS, acute respiratory distress syndrome; CPAP, continuous positive airway pressure; Fio_2, fraction of inspired oxygen; Pao_2, partial pressure of oxygen; PEEP, positive end-expiratory pressure.

*Delivered by noninvasive or invasive ventilation.

†Delivered by invasive mechanical ventilation.

From Meyer NJ, Gattinoni L, Calfee CS. Acute respiratory distress syndrome. *Lancet.* 2021;398:622-637, Panel 1, p. 622.

Hg and 300 mm Hg correlate approximately with S/F ratios of 235 and 315, respectively. This relationship is most valid for Spo_2 values between 80% and 97%.

Pao_2/PAo_2 ratio is determined by dividing Pao_2 by PAo_2. The level of alveolar ventilation is accounted for in the calculation of Pao_2. Therefore Pao_2/PAo_2 is more indicative of $\dot{V}/\dot{Q}$ mismatch and alveolar capillary integrity.

Oxygenation index (OI) is aimed at standardizing oxygenation to the level of concomitant therapeutic interventions (e.g., mean airway pressure [MAP] and FIo_2) that influence oxygenation. None of the indicators of oxygenation mentioned earlier take into account the degree of positive pressure respiratory support. The OI is calculated as follows:

$$OI = (MAP \times FIo_2 \times 100) / Pao_2$$

Oxygenation saturation index (OSI) is analogous to OI and useful when Pao_2 measurements are not available. It substitutes Spo_2 for Pao_2 in the formula as follows:

$$OSI = (MAP \times FIo_2 \times 100) / Spo_2$$

Both the OI and OSI are used in the Pediatric Acute Lung Injury Consensus Conference (PALICC) definition of PARDS. The main limitation of OI and OSI is that level of ventilation is not accounted for in the assessment.

MANAGEMENT

The goal of management for respiratory distress and respiratory failure is to ensure a patent airway and provide necessary support for adequate oxygenation of the blood and removal of CO_2. Compared with hypercapnia, **hypoxemia** is a life-threatening condition; therefore initial therapy for respiratory failure should be aimed at ensuring adequate oxygenation.

Oxygen Administration

Supplemental oxygen administration is the least invasive and most easily tolerated therapy for hypoxemic respiratory failure. **Nasal cannula** oxygen provides low levels of oxygen supplementation and is easy to administer. Oxygen is humidified in a bubble humidifier and delivered via nasal prongs inserted into the nares. In children, a flow rate <5 L/min is most often used because of increasing nasal irritation with higher flow rates. A common formula for an estimation of the FIo_2 during use of a nasal cannula in older children and adults follows:

$$FIo_2 \text{ (as a percentage)} = 21\% + (\text{Nasal cannula flow [L/min]} \times 3)$$

The typical FIo_2 value (expressed as a percentage rather than a fraction of 1) using this method is between 23% and 40%, although the FIo_2 varies according to the size of the child, the respiratory rate, and the volume of air moved with each breath. In a young child, because typical nasal cannula flow rates are a greater percentage of total minute ventilation, significantly higher FIo_2 may be provided. Alternatively, a **simple mask** may be used, which consists of a mask with open side ports and a valveless oxygen source. Variable amounts of room air are entrained through the ports and around the side of the mask, depending on the fit, size, and minute volume of the child. Oxygen flow rates administered through a simple mask generally vary from 5 to 10 L/min, yielding typical FIo_2 values (expressed as a percentage rather than a fraction of 1) between 30% and 65%. If more precise delivery of oxygen is desired, other mask devices should be used.

A **Venturi mask** provides preset FIo_2 through a mask and reservoir system by entraining precise flow rates of room air into the reservoir along with high-flow oxygen. The adapter at the end of each mask reservoir determines the flow rate of entrained room air and the subsequent Fio_2 adapters provide Fio_2 of 0.30-0.50. Oxygen flow rates of 5-10 L/min are recommended to achieve the desired FIo_2 and to prevent rebreathing. Partial rebreather and non-rebreather masks use a reservoir bag attached to a mask to provide higher FIo_2. **Partial rebreather masks** have two open exhalation ports and contain a valveless oxygen reservoir bag. Some exhaled gas can mix with reservoir gas, although most exhaled gas exits the mask via the exhalation ports. Through these same ports, room air is entrained, and the partial rebreather mask can provide FIo_2 up to 0.60 for as long as oxygen flow is adequate to keep the bag from collapsing (typically 10-15 L/min). As with nasal cannulas, smaller children with smaller tidal volumes entrain less room air, and their delivered FIo_2 will be higher. **Non-rebreather masks** include two one-way valves, one between the oxygen reservoir bag and the mask and the other on one of the two exhalation ports. This arrangement minimizes mixing of exhaled and fresh gas and entrainment of room air during inspiration. The second exhalation port has no valve, a safeguard to allow some room air to enter the mask in the event of disconnection from the oxygen source. A non-rebreather mask can provide FIo_2 up to 0.95. The use of a non-rebreather mask in conjunction with an oxygen blender allows delivery of FIo_2 between 0.50 and 0.95 (Table 86.9). When supplemental oxygen alone is inadequate to improve oxygenation, or when ventilation impairments coexist, additional therapies may be necessary.

Airway Adjuncts

Maintenance of a patent airway is a critical step in establishing adequate oxygenation and ventilation. Artificial pharyngeal airways may be useful in patients with oropharyngeal or nasopharyngeal airway obstruction and in those with neuromuscular weakness in whom inherent extrathoracic airway resistance contributes to respiratory compromise. An **oropharyngeal airway** is a stiff plastic spacer with grooves along each side that is placed in the mouth to run from the teeth along the tongue to its base just above the vallecula. The spacer prevents the tongue from opposing the posterior pharynx and occluding the airway. Because the tip sits at the base of the tongue, it is usually not tolerated by patients who are awake or whose gag reflex is strong. The **nasopharyngeal airway**, or *nasal trumpet,* is a flexible tube that can be inserted into the nose to run from the nostril along the top of the hard and soft palate with the tip ending in the hypopharynx. It is useful in bypassing obstruction from enlarged adenoids or from contact of the soft palate with the posterior pharynx. Because it is inserted past the adenoids, a nasopharyngeal airway should be used with caution in patients with bleeding tendencies.

Inhaled Gases

Helium-oxygen mixture (heliox) is useful in overcoming airway obstruction and improving ventilation. Helium is much less dense and slightly more viscous than nitrogen. When substituted for nitrogen in the inspired gas, helium helps maintain laminar flow across an obstructed airway, decreases airway resistance, and improves ventilation. It is especially helpful in diseases of large airways obstruction in which turbulent airflow is more common, such as acute laryngotracheobronchitis, subglottic stenosis, and vascular ring. To be effective, helium should be administered in concentrations of at least 60%, so associated hypoxemia may limit its use in patients requiring >40% oxygen.

Table 86.9 Approximate Oxygen Delivery According to Device and Flow Rates in Infants and Older Children*

DEVICE	FLOW (L/min)	FIo_2 DELIVERED
Nasal cannula	0.1-6	0.21-0.4
Simple face mask	5-10	0.4-0.6
Partial rebreather	6-15	0.55-0.7
Non-rebreather	6-15	0.7-0.95
Venturi mask	5-10	0.25-0.5
Hood/tent	7-12	0.21-1.0
High-flow systems	1-60	0.21-1.0

*Individual delivery varies and depends on the patient's size, respiratory rate, and gas volume moved with every breath.

Inhaled nitric oxide (iNO) is a powerful pulmonary vasodilator. Its use may improve pulmonary blood flow and $\dot{V}/\dot{Q}$ matching in patients with diseases that elevate pulmonary vascular resistance, such as persistent pulmonary hypertension of the newborn, primary pulmonary hypertension, and secondary pulmonary hypertension from chronic excess pulmonary blood flow (e.g., ventriculoseptal defect) or collagen vascular diseases. iNO is administered in doses ranging generally from 5 to 20 parts per million of inspired gas. Although administration of iNO to unintubated patients is possible, it is most commonly used in patients undergoing mechanical ventilation via an endotracheal tube.

Positive Pressure Respiratory Support

Noninvasive positive pressure respiratory support is useful in treating both hypoxemic and hypoventilatory respiratory failure. Positive airway pressure helps with aeration of partially atelectatic or fluid-filled alveoli, prevention of alveolar collapse at end exhalation, and increase in functional residual capacity (FRC). These actions improve pulmonary compliance and hypoxemia, and decrease intrapulmonary shunt. In addition, positive pressure ventilation is useful in preventing collapse of extrathoracic airways by maintaining positive airway pressure during inspiration. Improving compliance and overcoming airway resistance also improves tidal volume and, therefore, ventilation.

A **high-flow nasal cannula (HFNC)** delivers conditioned (heated and humidified) gas at flows generally ranging from 0.5 to 2 L/kg/min up to a maximum of 60 L/min. The F_{IO_2} can be adjusted by provision of gas flow through an oxygen blender, or directly, when a dedicated commercial high-flow system is employed. A properly sized cannula for HFNC support should have prongs that occupy no more than 50% of the cross-sectional area of the nostrils, thus allowing for ample leakage of gas (open system). Therefore although elevated pressures may be generated in areas of the nasopharynx, very low levels of positive expiratory pressure (<1 cm H_2O) thought to be clinically insignificant are transmitted to the intrathoracic airway. The principal mechanisms of action of HFNC are washout of CO_2 from the pharyngeal anatomic dead space and facilitation of gas movement across the nasopharyngeal airway resistor. This is in contrast to **continuous positive airway pressure (CPAP)**, a clinically equivalent support modality predicated on the use of a tight-fitting interface (closed system) in the form of nasal prongs, masks, or helmet. CPAP creates a stable level of operator-selected airway pressure that is transmitted to the intrathoracic airway. CPAP levels of 6-7 cm H_2O have been shown to unload the diaphragm and decrease work of breathing in infants with bronchiolitis. CPAP is most useful in diseases of mildly decreased lung compliance and low FRC, such as bronchiolitis with atelectasis and pneumonia. Patients with diseases of extrathoracic airway obstruction, in which extrathoracic negative airway pressures during inspiration result in airway narrowing (e.g., laryngotracheitis, laryngomalacia, obstructive sleep apnea, postextubation airway edema), may also benefit from CPAP. Potential risks include nasal irritation, pressure injury, hyperinflation from excessive CPAP in smaller patients, and abdominal distention from swallowed air.

Noninvasive positive airway pressure ventilation (NIPPV) provides positive airway pressure during exhalation and a higher pressure that supports inspiration, also termed *bilevel noninvasive ventilation* (see Chapter 86.1).

Endotracheal Intubation and Mechanical Ventilation

When hypoxemia or significant hypoventilation persists despite the interventions already described, endotracheal intubation and mechanical ventilation are indicated. Additional indications for intubation include maintaining airway patency in patients who have the potential for airway compromise, such as those with actual or potential neurologic deterioration, and in patients with hemodynamic instability.

Proper monitoring is essential to ensuring a safe and successful endotracheal intubation. Pulse oximetry, heart rate, and blood pressure monitoring are mandatory and should be forgone only in situations calling for emergency intubation. All necessary equipment, including bag-mask ventilation device, laryngoscope, endotracheal tube (ETT) with stylet, and suction equipment, must be available and working properly before intubation. The proper internal diameter (ID) for the ETT can be estimated using the following formula:

$$ID = (\text{Age [yr]}/4)+4$$

Table 86.10 provides average values for age, size, and depth of insertion for tracheal tubes. Preoxygenation of the patient with high F_{IO_2} is essential and will allow maximum procedure time before the onset of hypoxemia. Although intubation can be accomplished without sedation and pharmacologic paralysis in selected patients, the physiologic benefits of these measures to the patient and to the facilitation of the intubation usually far outweigh the risks. Administration of a sedative and analgesic followed by a neuromuscular-blocking agent is a common pharmacologic regimen for facilitating intubation. In fact, sedation and paralysis with neuromuscular blocking agents should be considered standard unless contraindicated. The particular type and dose of each agent often depends on the underlying disease and clinician preference. Table 86.11 lists commonly used agents. *Dexmedetomidine* has been a standard sedating agent for maintenance during mechanical ventilation. An alternative to this pharmacologic approach is **rapid sequence intubation**, used when endotracheal intubation is urgent or the patient is suspected of having a full stomach and at increased risk of aspiration (see Chapter 79).

Once adequate sedation and/or paralysis has been achieved, ventilation should be assisted with a **bag-mask device**. After optimal preoxygenation, intubation can be performed. The clinician uses the dominant hand to open the patient's mouth and insert the laryngoscope blade gently along the tongue to its base. The airway opening can be visualized by lifting up and away from the clinician, along the axis of the laryngoscope handle. When a *straight* (Miller) laryngoscope blade is used to visualize the glottis, the tip of the blade lifts the epiglottis anteriorly. When a *curved* (Macintosh) blade is used to visualize the glottis, the tip of the blade should be advanced into the vallecula and then lifted. Secretions often obscure visualization at this step and should be suctioned clear. Once clear visualization of the vocal cords is accomplished, the ETT can be placed through the vocal cords. Rapid confirmation of ETT placement is essential and should be assessed by as many of the following steps as possible: (1) presence of exhaled CO_2 determined by a colorimetric device, capnometry, or, preferably, capnography, attached in-line with the ETT; (2) auscultation of both lung fields for equal breath sounds and the epigastrium; (3) bilateral chest wall expansion; and (4) condensation (misting) inside the ETT. An increasing heart rate, if heart rate had decreased before or during

Table 86.10 Average Size and Depth Dimensions for Tracheal Tubes

PATIENT AGE	INTERNAL DIAMETER (mm)	OROTRACHEAL DEPTH (cm)	NASOTRACHEAL DEPTH (cm)
Premature	2.0-3.0	8-9	9-10
Full-term neonate	3.0-3.5	10	11
6 mo	4.0	11	13
12-24 mo	4.5	13-14	16-17
4 yr	5.0	15	17-18
6 yr	5.5	17	19-20
8 yr	6.0	19	21-22
10 yr	6.5	20	22-23
12 yr	7.0	21	23-24
14 yr	7.5	22	24-25
Adult	8.0-9.0	23-25	25-28

Courtesy Dr. Ashok Sarnaik.

Table 86.11 Medications Commonly Used for Intubation

DRUG	DOSE	ONSET (min)	DURATION (min)	COMMENTS
SEDATIVES/ANESTHETICS				
Midazolam	0.1 mg/kg IV	3-5	60-120	Amnesia Respiratory depression
Lorazepam	0.1 mg/kg IV	3-5	120-240	Amnesia Respiratory depression
Ketamine	1-2 mg/kg IV 4-6 mg/kg IM	2-3	10-15	↑ HR, BP, and ICP Bronchodilation, sialorrhea
Propofol	1-3 mg/kg IV	0.5-2	10-15	↓ BP Apnea
Thiopental	4-7 mg/kg IV	0.5-1	5-10	↓ BP Apnea
ANALGESICS				
Fentanyl	2-5 µg/kg IV	3-5	30-90	Respiratory depression Chest wall rigidity
Morphine	0.1 mg/kg IV	5-15	120-240	↓ BP Respiratory depression
NEUROMUSCULAR BLOCKING AGENTS				
Vecuronium	0.1 mg/kg IV	1.5-2	30-75	↑ HR Renal elimination
Rocuronium	0.6-1.2 mg/kg IV 1 mg/kg IM	1-1.5	15-60	↑ HR Renal elimination
Cisatracurium	0.1 mg/kg IV	3-5	25-30	Histamine release Nonrenal elimination

BP, Blood pressure; HR, heart rate; ICP, intracranial pressure; IM, intramuscularly; IV, intravenously.

the attempt, and a rising or normal Spo_2 reading are suggestive of successful tube placement. Preoxygenation may significantly delay any drop in Spo_2 with improper tube placement, leading to a delay in its recognition. A properly placed ETT should be well secured to avoid displacement or dislodgement. As soon as feasible, a chest radiograph should also be obtained to confirm proper position of the ETT, which should lie with the tip about halfway between the thoracic inlet and the carina (see Chapter 79).

Transient Manual Ventilation in Immediate Preintubation and Postintubation Periods

Establishment of supportive ventilation via bag-mask or bag-ETT is required before transport of the patient to a setting of continued critical care. The technique of manual ventilation should take into account the underlying pathology. Mechanical ventilation of patients with diseases characterized by low FRC (e.g., pneumonia, pulmonary edema, ARDS) should include the application of PEEP to prevent alveolar derecruitment. Lung volume recruitment can be accomplished with a PEEP valve on a self-inflating ventilation bag or by careful manipulation of exhaust gas using an anesthesia bag. Such diseases are also characterized by a short time constant for lung deflation and therefore are best managed with relatively small tidal volumes and high ventilation rates.

In contrast, diseases characterized by airway obstruction, such as critical asthma, have prolonged deflation time constants and are therefore best managed with relatively slow rates and high tidal volumes.

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86.1 Mechanical Ventilation

Martin C.J. Kneyber, Ashok P. Sarnaik, and Alexandre T. Rotta

The decision to institute mechanical ventilation is based mainly on the need to assist native pulmonary function in patients with acute respiratory failure; supporting performance of the left ventricle (LV), decreasing metabolic demand, and modulating of cerebral blood flow in intracranial hypertension are additional indications. Respiratory distress leading to fatigue and impending exhaustion are also indications for respiratory support, even in the presence of adequate gas exchange. Although there are no absolute criteria for derangement of gas exchange, Pao_2 <60 mm Hg while breathing >60% oxygen, $Paco_2$ >60 mm Hg, and pH <7.25 are often used in the decision-making to institute respiratory support. Positive pressure ventilation is a powerful means of decreasing LV afterload, and it is used for this purpose in patients with cardiogenic shock resulting from LV dysfunction. Mechanical ventilation is also used in patients whose breathing is unreliable (e.g., unconscious patients, those with neuromuscular dysfunction) and when deliberate hyperventilation is desired, such as in patients with intracranial hypertension.

Mechanical ventilation is not intended to normalize gas exchange. The goals are to maintain sufficient oxygenation and ventilation to ensure tissue viability until the disease process that has compromised the patient's lung function has resolved, while minimizing excessive work of breathing and complications. When precisely employed, mechanical ventilation is a lifesaving intervention, yet care must be taken to avoid ventilator-induced lung injury (VILI). Several factors have been identified as contributors to VILI. These include lung strain from the delivery of excessive tidal volume **(volutrauma)**, injury from the repetitive opening and closing of alveoli **(atelectrauma)**, injury from excessive pressure delivery **(barotrauma)**, local and systemic cytokine release **(biotrauma)**, and damage caused by oxygen toxicity (Figs. 86.2 and 86.3).

BASIC CONCEPTS OF VENTILATOR MANAGEMENT

Equation of Motion

A pressure gradient is required for air to move from one place to another. During natural spontaneous ventilation, inspiration results from generation of negative intrapleural pressure from contraction of the diaphragm and intercostal muscles, drawing air from the atmosphere across the airways into the alveoli. During mechanical ventilation, inspiration results from positive pressure created by compressed gases through the ventilator, which pushes air across the airways into alveoli. In both spontaneous and mechanical ventilation, exhalation results from alveolar pressure generated by the elastic recoil of the lung

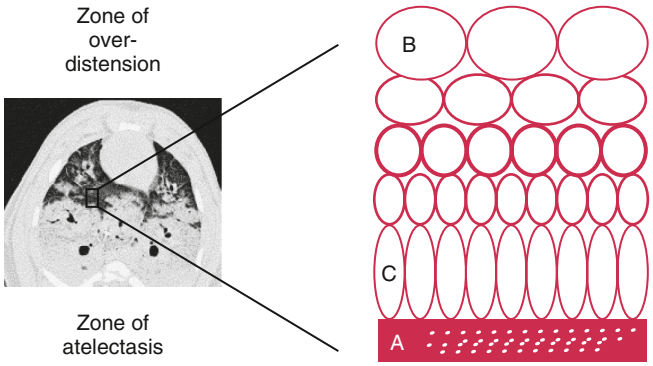
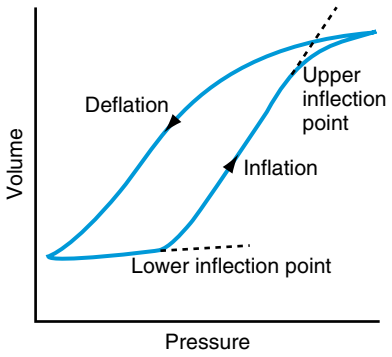


Fig. 86.2 Atelectrauma. The interface between collapsed and consolidated lung *(A)* and overdistended lung units *(B)* is heterogeneous and unstable. Depending on ambient conditions, this region is prone to cyclic recruitment and derecruitment and localized asymmetric stretch of lung units *(C)* immediately apposed to regions of collapsed lung. *(From Pinhu L, Whitehead T, Evans T, et al. Ventilator-associated lung injury.* Lancet. *2003;361:332-340.)*



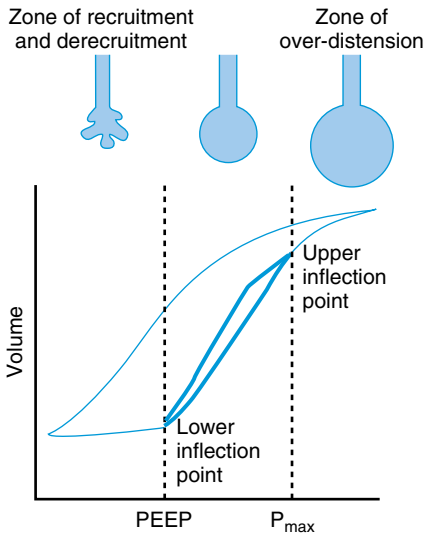


Fig. 86.3 Pulmonary pressure-volume relation in a patient with acute lung injury. *Top,* The lower inflection point is typically 12-18 cm H_2O and the upper inflection point 26-32 cm H_2O. *Bottom,* Specific protective ventilation strategies require that positive end-expiratory pressure (PEEP) is set just above the lower inflection point and the pressure limit (P_{max}) just below the upper inflection point. Thus the lung is ventilated in the safe zone between the zone of recruitment and derecruitment and the zone of overdistention, and both high-volume and low-volume injuries are avoided. This zone is located on the deflation limb of the pressure-volume curve, making use of the pulmonary hysteresis. *(From Pinhu L, Whitehead T, Evans T, et al. Ventilator-associated lung injury.* Lancet. *2003;361:332-340.)*

1. Pressure gradient is required to move air from one place to another
2. Movement of air is opposed by flow-resistive and elastic properties of the system

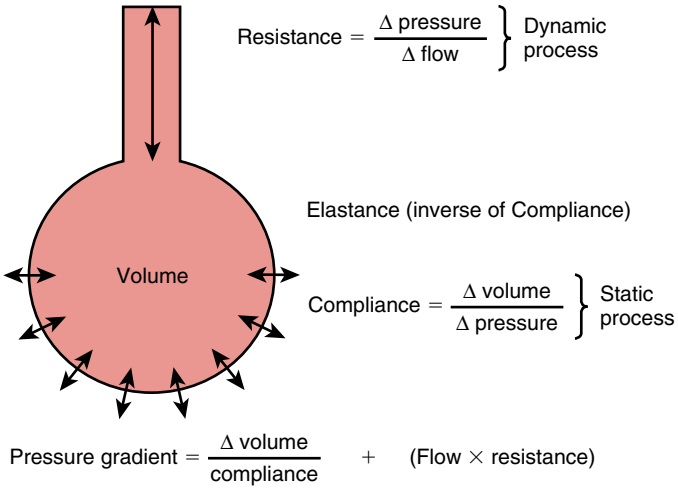


Fig. 86.4 Equation of motion. A pressure gradient is required to move air from one place to another. In the lungs, the required pressure gradient must overcome the lung and chest wall elastance (static component) and the flow-resistive properties (dynamic component). The static component is increased in alveolar interstitial diseases and stiff chest wall, whereas the dynamic component is increased with airway obstruction.

and the chest wall. Pressure necessary to move a given amount of air into the lung is determined by two factors: lung and chest wall elastance and airway resistance. Figure 86.4 describes the relationship in pressure gradient, compliance, and resistance. *Elastance*—defined as the change in pressure (ΔP) divided by the change in volume (ΔV)—refers to the property of a substance to oppose deformation. It is opposite of *compliance* (ΔV ÷ ΔP), the property of a substance to allow distention or lengthening when subjected to pressure. Compliance (C) is therefore expressed as 1/elastance.

The pressure needed to overcome tissue elastance is measured in conditions in which there is no flow (at end inspiration and end expiration) and is therefore a reflection of static conditions in the lung. It is influenced by tidal volume (Vᴛ) and compliance (P = ΔV ÷ C). It is increased with high Vᴛ and low compliance. This pressure gradient is used to calculate the static compliance of the respiratory system (C_{STAT}).

Resistance (R) refers to the opposition to generation of flow. It is measured as the amount of pressure needed to generate a unit of flow (ΔP ÷ ΔFlow). Pressure needed to overcome airway resistance is calculated as flow multiplied by resistance. Because this pressure is needed only when the flow is occurring through the airways, it is referred to as the *dynamic component*. Pressure to overcome flow-resistive properties is measured when there is maximum flow and is therefore under dynamic conditions. It is increased in conditions with greater airway resistance and flow rate. Flow rate depends on the time allowed for inspiration and expiration. At higher respiratory rates, there is less time available for each inspiration and expiration, necessitating higher flows; therefore higher pressure is required to overcome flow-resistive properties. The pressure gradient necessary to move air from one place to another is the sum of pressure needed to overcome the elastic and flow-resistive properties of the lung. This pressure gradient is taken into account to calculate the dynamic compliance of the respiratory system (C_{DYN}). The difference in change in pressure between static conditions and dynamic conditions is attributable to airway resistance.

Functional Residual Capacity

During inspiration, oxygen-enriched gas enters alveoli. During exhalation, oxygen continues to be removed by the pulmonary capillary

circulation. Functional residual capacity (FRC) is the volume of gas left in the alveoli at end expiration; in mechanically ventilated patients, it is generally referred to as *end-expiratory lung volume* (EELV). It is the only source of gas available for gas exchange during exhalation. In diseases with decreased FRC (e.g., pediatric acute respiratory distress syndrome [PARDS], pulmonary edema), P_{AO_2} declines sharply throughout expiration, resulting in hypoxemia. Two ventilator strategies used to improve oxygenation in such situations are the application of PEEP and increasing the *inspiratory time* (TI) (Fig. 86.5). Positive end-expiratory pressure (PEEP) increases EELV by stabilizing recruited alveoli, whereas a longer TI allows longer exposure of pulmonary capillary blood to a higher concentration of O_2 during inspiration (see also Chapter 421).

Time Constant

At the beginning of inspiration, the atmospheric pressure is higher than the pressure in the alveoli, resulting in movement of air into the alveoli. During mechanical ventilation, the ventilator circuit serves as the patient's atmosphere. As alveoli expand with air, the alveolar pressure rises throughout inspiration until it equilibrates with the ventilator pressure, at which time airflow ceases. Expiration starts when the ventilator pressure falls below the alveolar pressure. Alveolar pressure decreases throughout expiration until it reaches the ventilator pressure, at which time no further egress of air from the alveoli occurs. If inspiration or expiration is terminated before pressure equilibration between alveoli and the ventilator is allowed to occur, alveolar expansion during inspiration or alveolar emptying during expiration is incomplete. Incomplete inspiration results in delivery of decreased VT, whereas incomplete expiration is associated with air trapping and the presence of residual PEEP in the alveoli that is greater than the PEEP set at the ventilator, referred to as **auto-PEEP**. Some time is required for pressure equilibration to occur between alveoli and the atmosphere, which is reflected in the *time constant* (TC). It takes 3 TCs for 95% (and 5 TCs for 99%) of pressure equilibration to occur. The TC depends on compliance (C) and resistance (R), and their relationship is depicted in Figure 86.6. TC is calculated as compliance multiplied by resistance (C × R) and is measured in seconds.

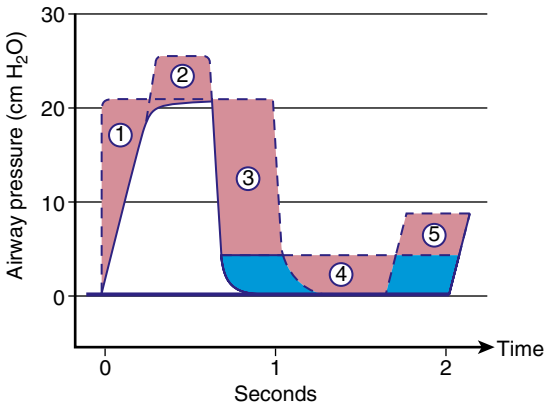


Fig. 86.5 Five different ways to increase mean airway pressure. *(1)* Increase the respiratory flow rate, producing a square wave inspiratory pattern; *(2)* increase the peak inspiratory pressure; *(3)* reverse the inspiratory-expiratory ratio or prolong the inspiratory time without changing the rate; *(4)* increase positive end-expiratory pressure; and *(5)* increase the ventilatory rate by reducing the expiratory time without changing the inspiratory time. *(From Harris TR, Wood BR. Physiologic principles. In Goldsmith JP, Karotkin EH, eds.* Assisted Ventilation of the Neonate, *3rd ed. Philadelphia: Saunders;1996.)*

Diseases with decreased compliance (increased elastance) are characterized by high elastic recoil pressure, which results in more rapid equilibration of alveolar and ventilator pressures, thereby decreasing TC. Diseases with increased airway resistance are associated with slower flow rates, require longer time for movement of air from one place to another, and therefore have increased TC. Airways expand during inspiration and narrow during expiration. Therefore expiratory time constant (TCE) is longer than inspiratory time constant (TCI). In intrathoracic airway obstruction (e.g., asthma, bronchiolitis, aspirated foreign body), airway narrowing is much more pronounced during expiration. Therefore although both TCE and TCI are prolonged in such diseases, TCE is much more prolonged than TCI. Patients with such diseases therefore are best ventilated with slower rates, larger VT, and longer expiratory time than inspiratory time. In diseases characterized by decreased compliance, both TCE and TCI are short; however, the TCE is closer to TCI than in normal lungs because the stiffer alveoli recoil with greater force. Patients with these diseases are best ventilated with smaller VT to prevent VILI, increased respiratory rate, and a relatively longer inspiratory time in each breath to improve oxygenation.

Critical Opening Pressure

Collapsed or atelectatic alveoli require a considerable amount of pressure to open. Once open, the alveoli require relatively less pressure for continued expansion. The process of opening atelectatic alveoli is called **recruitment**. In a normal lung, alveoli remain open at end expiration, and therefore the lung requires relatively less pressure to receive its VT. In a disease process in which alveoli collapse at end expiration (e.g., PARDS), a substantial amount of pressure is required to open the alveoli during inspiration. This pressure causes VILI by two mechanisms: *barotrauma* at the terminal airway-alveolar junction and *volutrauma* as a result of overdistention of alveoli that are already open (see Figs. 86.2 and 86.3). Although pulmonary parenchymal disease is rarely uniform and each of the millions of alveoli may have its own mechanical characteristics, a composite volume-pressure relationship could be conceptualized for the whole lung (Fig. 86.7).

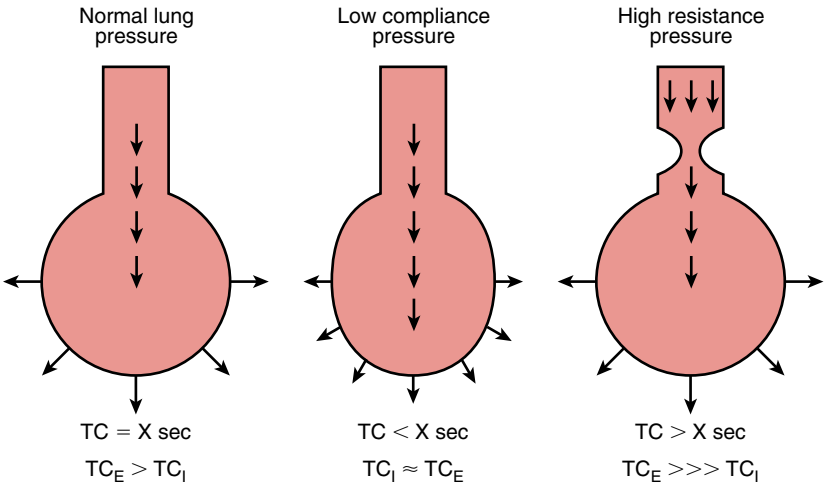


Fig. 86.6 Time constant (TC). A certain amount of time is necessary for pressure equilibration (and therefore completion of delivery of gas) to occur between the proximal airway and alveoli. TC, a reflection of time required for pressure equilibration, is a product of compliance and resistance. In diseases of decreased lung compliance, less time is needed for pressure equilibration to occur, whereas in diseases of increased airway resistance, more time is required. Expiratory TC (TC_E) is increased much more than inspiratory TC (TC_I) in obstructive airway diseases because airway narrowing is exaggerated during expiration.

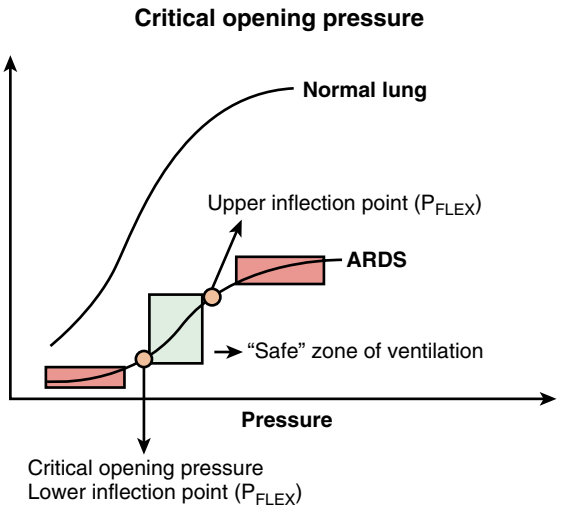


Fig. 86.7 Volume-pressure relationship in normal lung and in acute respiratory distress syndrome (ARDS). In ARDS, atelectatic alveoli require a considerable amount of pressure to open. Critical opening pressure, also referred to as lower P_{FLEX}, is the airway pressure above which further alveolar expansion occurs with relatively less pressure. Upper P_{FLEX} is the airway pressure above which further increase in pressure results in less alveolar expansion; this is the area of alveolar overdistention. Keeping tidal volume between upper and lower P_{FLEX} values is considered less injurious to the lung.

In these situations, the lower and upper portions of the curve are relatively horizontal and the middle portion is more vertical. At the beginning of inspiration, atelectatic alveoli are being recruited, requiring high pressure for a relatively small increase in volume. Once they are recruited, further increase in volume requires relatively less pressure. The pressure at which most alveoli are open is called *critical opening pressure;* this point is also referred to as the *lower inflection point* (lower P_{FLEX}). After the lower P_{FLEX}, greater volume can be delivered for relatively less pressure until the upper P_{FLEX} is reached, at which point the volume-pressure curve again becomes relatively horizontal. The goal of mechanical ventilation in alveolar interstitial pathology is to deliver a V_T between the lower and upper inflection points, the so-called *safe zone of ventilation.* If V_T is delivered with a change in inflation pressure that includes the lower P_{FLEX}, alveoli are likely to open *and* close during every breath, a process termed **tidal recruitment** that is injurious to the lung (atelectrauma), especially at the terminal airway-alveolar junction. If V_T is delivered with a change of pressure that includes the upper P_{FLEX}, overdistention of alveoli is likely to occur, resulting in volutrauma and barotrauma. Keeping tidal ventilation between the upper and lower P_{FLEX} values is accomplished by maintaining a level of PEEP to produce baseline alveolar recruitment and delivering a relatively small V_T. This lung-protective ventilation is also known as "open lung" strategy and is the preferred approach in diffuse alveolar interstitial diseases such as PARDS.

Mechanical ventilation may be delivered either noninvasively with a patient-machine interface other than an ETT or invasively after endotracheal intubation.

NONINVASIVE MECHANICAL VENTILATION

Delivering positive pressure mechanical respiratory support without the use of endotracheal intubation is called noninvasive positive pressure ventilation **(NIPPV)**. This type of respiratory support has been increasingly used in the pediatric intensive care setting.

The most common techniques applied are continuous positive airway pressure **(CPAP)** or biphasic (inspiratory and expiratory) positive airway pressure **(BiPAP)**. Of note, CPAP is only the delivery of a continuous airway pressure; therefore by definition, it is not a true form of noninvasive ventilation because a minute volume is generated exclusively by the patient, not by the device. A variety of devices with increasing sophistication has been developed in recent years, and different interfaces are available, such as nasal prongs, nasal and full-face masks, and helmets. Especially in the pediatric population, an age-appropriate, properly sized, and comfortable interface that minimizes air leak is critical for the successful application of NIPPV. NIPPV has been successfully used in acute and chronic hypoxic and/or hypercarbic respiratory failure. Indications range from acute lower airway obstruction, such as asthma, or acute upper airway obstruction, including postextubation airway swelling, to parenchymal lung diseases such as pneumonia and mild to moderate PARDS. Acute and chronic respiratory failure from neuromuscular weakness or chest wall deformities have been the classic indication for its use. NIPPV can also be used to help prevent reintubation after prolonged mechanical ventilation.

BiPAP provides positive airway pressure during exhalation and additional positive pressure during inspiration. These pressures can be adjusted independently to suit individual needs and comfort, and a respiratory rate can be delivered. The additional positive pressure during inspiration helps improve alveolar ventilation in low compliance and obstructive lung disease. During exhalation, expiratory positive airway pressure can decrease the effects of airway closure by raising intraluminal pressure and ameliorating intrathoracic airway collapse. During inspiration, inspiratory positive airway pressure unloads inspiratory muscle work.

These mechanics may explain many of the physiologic benefits of NIPPV, including an increase in lung compliance and FRC, a decrease of dynamic airway narrowing, augmentation of V_T and alveolar ventilation, and decreased work of breathing. Physiologic benefits of NIPPV in obstructive (e.g., asthma) and restrictive (e.g., PARDS) lung disease are schematically presented in Figures 86.8 and 86.9. Additional benefits result from improving cardiopulmonary interactions, especially LV afterload reduction, thereby improving cardiac output in patients with acute or chronic LV dysfunction.

NIPPV is often well tolerated and may be associated with fewer complications compared to invasive mechanical ventilation; airway trauma from endotracheal intubation can be avoided, and less sedation is required. Breaks can be given for the administration of oral medications and clearance of respiratory secretions, and selected stable patients can be fed by mouth. The rate of nosocomial infections, ventilator-associated pneumonia, and VILI is expected to decrease as well. In addition, aerosol therapy delivered by NIPPV appears to be more effective.

Complications of NIPPV include pressure injury, upper airway mucosal irritation, abdominal distention, aspiration, feeding intolerance, and pulmonary hyperinflation with resulting interstitial emphysema, pneumomediastinum, and pneumothorax. Patients initiated on NIPPV need close cardiorespiratory monitoring because the respiratory failure may progress, leading to the need for endotracheal intubation. Patients with more severe respiratory distress and those who do not show improvement of respiratory indices (i.e., respiratory rate, SpO_2/FIO_2 ratio, reduction in FIO_2) within 2 hours of initiation are more likely to require invasive ventilation. Patients with underlying severe systemic diseases such as sepsis, multiorgan dysfunction, and malignancies are less likely to respond favorably to NIPPV. Absolute contraindications include loss of airway reflexes, acute severe neurologic insults, cardiorespiratory arrest, and severe hemodynamic instability. Patients with midface abnormalities or facial trauma and burns should not be considered candidates for NIPPV. Other contraindications include the immediate postoperative period after facial and upper airway surgery, recent gastrointestinal surgery, or patients with bowel obstruction and vomiting. Patients who are severely agitated and confused should not be initiated on NIPPV. NIPPV has been shown to decrease intubation rates and reintubation rates after liberation from invasive mechanical ventilation, and has been increasingly used to treat acute or chronic respiratory failure in pediatric patients.

INVASIVE MECHANICAL VENTILATION

Mechanical ventilation involves considering the four phases of the respiratory cycle: (1) initiation of respiration and a variable that is controlled, often referred to as *mode;* (2) inspiratory phase characteristics, which determine the duration of inspiration and how the pressure or

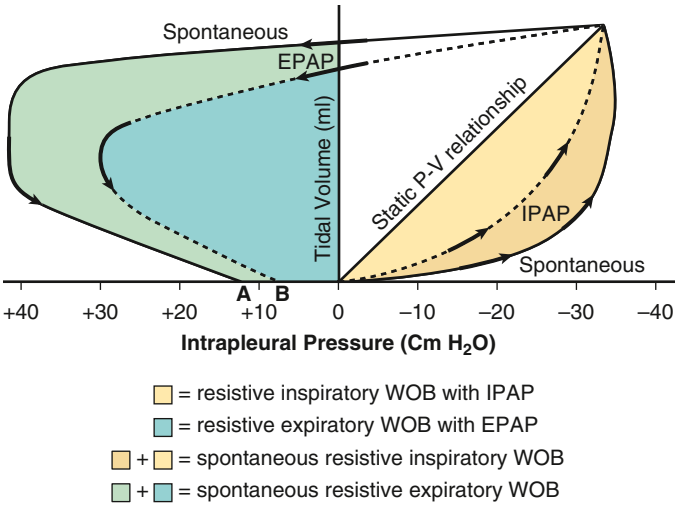


Fig. 86.8 Work of breathing (WOB) in status asthmaticus with and without noninvasive positive pressure ventilation. In the expiratory limb of the respiratory cycle, the equal pressure point is displaced distally, causing airways to begin to close at a higher lung volume (increased closing capacity), leading to dynamic hyperinflation, and auto–positive end-expiratory pressure (auto-PEEP). *(A),* Application of expiratory positive airway pressure (EPAP) stents the airways, reducing intrathoracic airway collapse, dynamic hyperinflation, auto-PEEP *(B),* and WOB. In the inspiratory limb, the patient needs to generate less negative pressure to initiate inspiration because of lower auto-PEEP. Inspiratory muscles are further unloaded by inspiratory positive airway pressure (IPAP) throughout inspiration for the given tidal volume. Both expiratory and inspiratory WOB are thus reduced by application of noninvasive positive pressure ventilation. P-V, Pressure-volume. *(From Sarnaik AA, Sarnaik AP. Noninvasive ventilation in pediatric status asthmaticus: Sound physiologic rationale but is it really safe, effective, and cost-efficient?* Pediatr Crit Care Med. *2012;13:484-485.)*

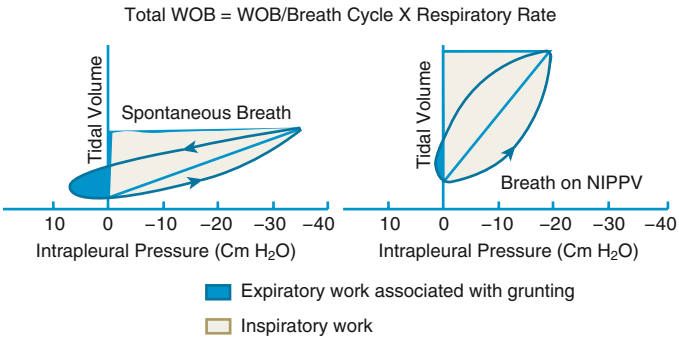


Fig. 86.9 Beneficial physiologic pulmonary effects of noninvasive positive pressure ventilation (NIPPV) in restrictive lung disease (e.g., ARDS). *Left,* Without NIPPV, the slope of pressure-volume relationship is flatter, resulting in lower tidal volume for a given inflation pressure and necessitating an increased respiratory rate to maintain required minute alveolar ventilation. Start of inspiration is at a lower lung volume, indicating decreased functional residual capacity (FRC). Expiration is active toward the end as a result of grunting aimed at increasing FRC. *Right,* On institution of NIPPV, the slope of the pressure-volume relationship is increased, resulting in greater tidal volume for a given inflation pressure, with a subsequent decrease in respiratory rate and inspiratory work of breathing (WOB). FRC is increased because of expiratory positive airway pressure (EPAP), resulting in improved oxygenation and decreased expiratory work associated with grunting.

volume is delivered; (3) termination of inspiration, often referred to as *cycle;* and (4) expiratory phase characteristics. Ventilation should not completely take over the work of breathing unless indicated in specific clinical conditions, such as in severe traumatic brain injury or pulmonary hypertensive crisis, but rather should assist the patient's own respiratory effort, if present.

Initiation of Inspiration and the Control Variable (Mode)

The initiation of inspiration may be set to occur at a predetermined rate and interval regardless of patient effort, or it could be timed in response to patient effort. Once inspiration is initiated, the ventilator breath either is controlled entirely by the ventilator *(control mode)* or supports the patient's inspiratory effort to a predetermined inspiratory volume or pressure target *(support mode).* Advances in technology allow for greater patient-ventilator synchrony to occur. The ventilator may be set to be *triggered* by the signal it receives as a result of patient effort. This feature may be in the form of lowering of either pressure *(pressure trigger)* or airflow *(flow trigger)* in the ventilator circuit generated by the patient's inspiratory effort. If no such signal is received because of lack of patient effort, the ventilator delivers a breath at an interval selected by the operator. Most ventilators make use of flow triggering.

Control Modes

Intermittent Mandatory Ventilation Mode. In intermittent mandatory ventilation **(IMV)**, inspiration is initiated at a set frequency with a timing mechanism independent of patient effort. In between machine-delivered breaths, the patient can breathe spontaneously from a fresh source of gas. IMV allows for adjustment of ventilator support according to the patient's needs, making it useful in the weaning process. Lack of synchrony between machine-delivered breaths and patient efforts may result in ineffective ventilation and patient discomfort, especially when IMV is delivered at a high rate. In such cases the patient may require sedation and pharmacologic neuromuscular blockade for efficient delivery of VT. To obviate this problem, **synchronized IMV (SIMV)** is preferred, whereby the machine-delivered breaths are triggered by the patient's inspiratory efforts (Fig. 86.10). In between the machine-delivered breaths, a fresh source of gas is available for spontaneous patient breaths. In the absence of patient effort, the patient receives a predetermined backup rate. Even with SIMV, ventilator-patient asynchrony can occur because VT, inflation pressure, and inspiratory time are determined by the ventilator alone.

Assist-Control Mode. In assist-control (AC) mode, every patient breath is triggered by pressure or flow generated by patient inspiratory effort and "assisted" with either preselected inspiratory pressure or volume. The rate of delivered breaths is therefore determined by the patient's inherent respiratory rate. A backup total (patient and ventilator) obligatory rate is set to deliver a minimum number of breaths. For illustration, on AC mode with a backup rate of 20 breaths/min and a patient's inherent rate of 15 breaths/min, the ventilator will assist all the patient's breaths and the patient will receive 5 additional breaths/min. On the other hand, a patient with an inherent rate of 25 breaths/min will receive all 25 breaths assisted. Although useful in some patients, the AC mode cannot be used in the weaning process, which involves gradual decrease in ventilator support.

Control Variable

Once initiated, either the VT or the pressure delivered by the machine can be controlled. The machine-delivered breath is thus referred to as either volume controlled or pressure controlled (Table 86.12). With **volume-controlled ventilation (VCV)**, machine-delivered volume is the primary control, and the inflation pressure generated depends on the respiratory system's compliance and resistance. Changes in respiratory system compliance and resistance are therefore easily detected from changes observed in inflation pressure. In **pressure-controlled ventilation (PCV)**, the pressure change above the baseline is the primary control, and the VT delivered to the lungs depends on the respiratory system's C and R. Changes in respiratory system C and R do not affect inflation pressure and may therefore go undetected unless the exhaled VT is closely monitored. VCV and PCV have their own advantages and disadvantages (see Table 86.12). Favoring one mode over the other is largely driven by institutional preference and personal beliefs. VCV is characterized by a constant inspiratory flow with

a constant, preset VT, whereas PCV makes use of a decelerative flow pattern, with a variable delivered VT. A potential benefit of PCV is that the inspiratory pressures are limited, making it a more attractive mode in disease conditions where there is airway obstruction, preventing the normally compliant alveolus from being exposed to large VT. Generally speaking, PCV is more efficient than VCV in terms of amount of VT delivered for a given inflation pressure during ventilation of a lung that has nonuniform TC, as in asthma. In VCV, relatively less-obstructed airways are likely to receive more of the machine-delivered volume throughout inspiration than relatively more obstructed airways with longer TC (Fig. 86.11A). This situation would result in uneven ventilation, higher peak inspiratory pressure (PIP), and a decrease in C_{DYN}. In PCV, because of a constant inflation pressure that is held throughout inspiration, relatively less obstructed lung units with shorter TC would achieve pressure equilibration earlier during inspiration than the relatively more obstructed areas. Thus units with shorter TCs would attain their final volume earlier in inspiration, and those with longer TCs would continue to receive additional volume later in inspiration (see Fig. 86.11B). This situation would result in more uniform distribution of inspired gas, delivery of more VT for the same inflation pressure, and improved C_{DYN} compared with VCV.

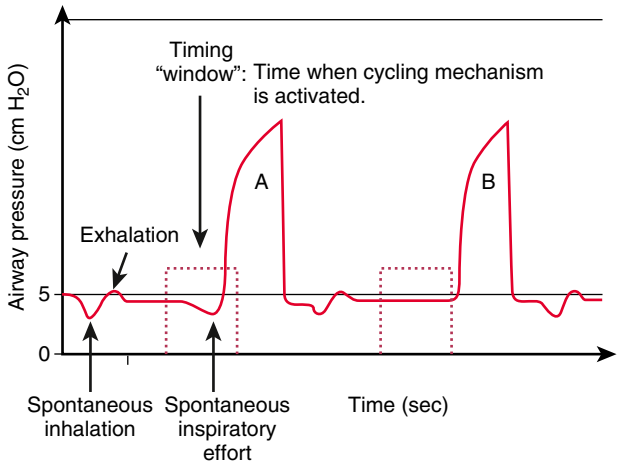


Fig. 86.10 Synchronized intermittent mandatory ventilation. At set intervals, the ventilator's timing circuit becomes activated and a timing "window" appears *(dashed line area)*. If the patient initiates a breath in the timing window, the ventilator delivers a mandatory breath *(A)*. If no spontaneous effort occurs, the ventilator delivers a mandatory breath at a fixed time after the timing window *(B)*. *(From Banner MJ, Gallagher TJ. Respiratory failure in the adult: Ventilatory support. In: Kirby RR, Smith RA, Desautels DA, eds.* Mechanical Ventilation. *New York: Churchill Livingstone;1985.)*

Pressure-regulated volume control (PRVC) combines the characteristics of VCV and PCV. In this mode, VT and TI are controlled as primary variables, but the ventilator determines the lowest amount of pressure needed to deliver the desired VT. Inflation pressure is thus continuously adjusted to deliver the prescribed VT over the TI, depending on the patient's respiratory C and R.

Support Modes

Pressure-support ventilation (PSV) and **volume-support ventilation (VSV)** are designed to support the patient's spontaneous respirations. With PSV, initiation of inspiration is triggered by the patient's spontaneous breath, which is then "supported" by a rapid rise in ventilator pressure to a preselected level. The inspiration is continued until the inspiratory flow rate falls to a set level (generally 25% of peak flow rate) as the patient's lungs inflate. Each inspiration is initiated and terminated by the patient, thus TI is controlled by the patient's own efforts. PSV has no backup rate, so a ventilator breath will not be delivered to the apneic patient. PSV can be combined with SIMV so that any breath above the SIMV rate is supported by PSV. Allowing the patient to control as much of the rate, VT, and inspiratory time as possible is considered to be a more comfortable form of mechanical ventilation than those in which the VT (or inflation pressure) and TI are preset. PSV as the sole source of mechanical ventilator support is often inadequate for patients with severe lung disease and those with a depressed respiratory drive, but may be especially useful in patients being weaned and in those who require mechanical ventilation for relatively minor lung disease or for neuromuscular weakness.

VSV is similar to PSV, in that all the spontaneous breaths are supported. In VSV, inspiratory pressure to support spontaneous breaths is adjusted to guarantee a preset VT goal. If there is a change in respiratory mechanics or patient effort, the inspiratory pressure to support the breath initiated by patient effort is automatically adjusted to achieve the set VT.

Inspiratory Phase Characteristics

Inspiratory flow waveform, TI, and pressure rise time can be adjusted in the inspiratory phase to suit the patient's respiratory mechanics.

In PCV the duration of TI is directly set in seconds. In VCV the TI can be adjusted by adjusting the inspiratory flow (volume/time) and/or setting an inspiratory pause before exhalation starts. Irrespective of ventilator mode, the choice of TI value depends on the respiratory rate, which determines the total duration of each breath, and on the estimation of inspiratory and expiratory TCs. Decreasing the flow rate delivery increases TI, and vice versa. With an increase in TI, the pulmonary capillary blood is exposed to a higher level of P_{AO_2} for a longer time. This feature is beneficial in diseases with decreased EELV, such as PARDS and pulmonary edema. An increase

Table 86.12 Characteristics of Pressure-Controlled and Volume-Controlled Methods of Ventilation

	PRESSURE-CONTROLLED VENTILATION	VOLUME-CONTROLLED VENTILATION
Control setting(s)	Inflation pressure Inspiratory time Rise time	Tidal volume Flow rate Inspiratory flow pattern (constant vs decelerating)
Machine-delivered volume	Depends on respiratory system compliance and resistance	Constant
Inflation pressure	Constant	Depends on respiratory system compliance and resistance
Endotracheal tube leak	Somewhat compensated	Leaked volume part of tidal volume
Distribution of ventilation	More uniform in lungs with varying time constant units	Less uniform in lungs with varying time constant units
Patient comfort	Possibly compromised	Possibly enhanced
Weaning	Inflation pressure adjustment required to deliver desired tidal volume	Tidal volume remains constant; inflation pressure automatically weaned

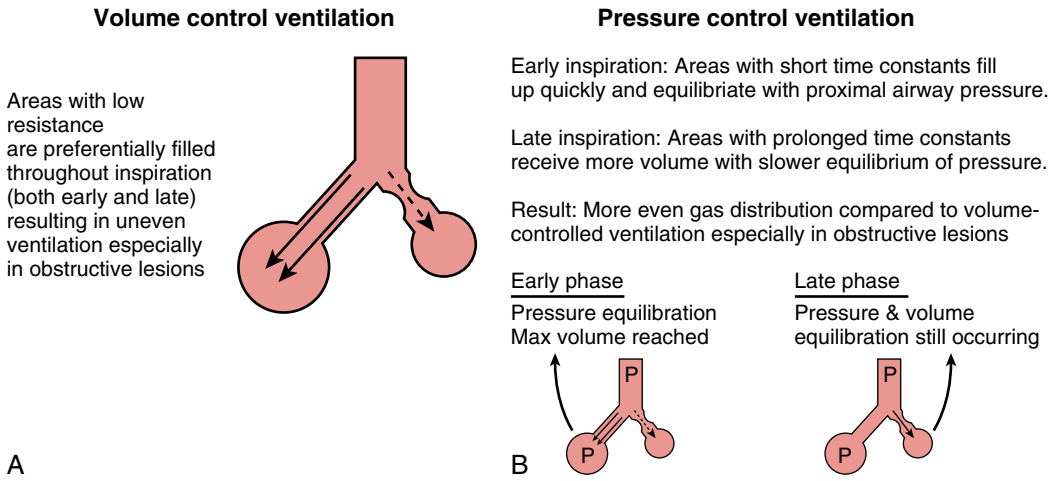


Fig. 86.11 A, In volume-controlled ventilation (VCV), tidal volume (V_T) is delivered to the less obstructed areas throughout inspiration. Obstructed areas of the lung therefore receive a lower proportion of V_T, resulting in uneven ventilation. B, In pressure-controlled ventilation (PCV), less obstructed areas equilibrate with inflation pressure and therefore receive most of their V_T early during inspiration. More obstructed areas, with prolonged time constants, require longer time for pressure equilibration and therefore continue to receive a portion of their V_T later during inspiration. The entire V_T is more evenly distributed than with volume-cycled ventilation.

in T_I also increases V_T without increasing inflation pressure in PCV if inspiratory flow is still occurring at end expiration. It must be recognized that at a given ventilator rate, an increase in T_I decreases expiratory time (T_E). Therefore any strategy that employs an increase in the inspiratory component of the respiratory cycle should ensure that the decreased T_E is still sufficient for complete exhalation.

Inspiratory flow waveform can be adjusted in VCV mode as either a constant flow (square waveform) or a decelerating flow (descending ramp waveform). With a square waveform, flow is held constant throughout inspiration. In a descending ramp waveform, flow is maximal at the start of inspiration and declines throughout its duration. It is debatable which flow pattern is better for a given disease.

In PCV and PSV, the prescribed PIP is reached through delivery of airflow. *Pressure rise time* reflects the time required for the ventilator to reach PIP and can be adjusted by control of flow at the beginning of the inspiratory phase. The inspiratory flow rise time may be adjusted to prevent too rapid a rise in inspiratory pressure, which can be uncomfortable for a patient who is awake and lead to dyssynchrony.

Termination of Inspiration (Cycle)

The two most commonly used inspiratory terminating mechanisms in control modes are time-cycled and volume-cycled. With a **time-cycled** mechanical breath, inspiration is terminated after a preselected T_I has elapsed, whereas with **volume-cycled** breath, the inspiration ends after a preselected volume has been delivered by the machine into the ventilator circuit. A time-cycled breath is almost always pressure-limited, with the PIP held constant for the duration of inspiration. A volume-cycled breath can be pressure-limited as a safety mechanism to avoid barotrauma. The inspiration-terminating mechanism is set somewhat differently in support modes. In PSV the inspiration is set to end after the inspiratory flow decreases below a certain percentage (usually 25%) of peak inspiratory flow. This happens when the patient no longer desires to receive additional V_T. Such a breath is termed **flow-cycled**. In VSV the inspiration is terminated when the patient has received the selected V_T.

Expiratory Phase Maneuvers

The most useful expiratory phase maneuver is the application of PEEP, which is applied to both the control breath and the assisted breath. The most important clinical benefits of PEEP are to stabilize recruited alveoli to increase EELV in patients with alveolar-interstitial diseases and thereby improve oxygenation. Any situation where there is zero end-expiratory pressure (ZEEP), as is the case when the patient is disconnected from the ventilator circuit (even if briefly), will result in alveolar **derecruitment** and decline in oxygenation. In patients with obstructive lesions in which insufficient exhalation results in air trapping and auto-PEEP, extrinsic PEEP (applied through a mechanical device) can prevent airway closure during expiration and improve ventilation. Other salutary effects of PEEP include redistribution of extravascular lung water away from gas-exchanging areas, improved $\dot{V}/\dot{Q}$ relationship, stabilization of the chest wall, and reduction in work of breathing in patients with intrinsic PEEP. The effect of PEEP on lung C is variable, depending on the level of PEEP provided and the patient's pulmonary mechanics. By shifting tidal ventilation to a more favorable part of the pressure-volume curve, PEEP may maintain more recruited alveoli, delay airway closure, and improve lung C. Excessive PEEP, on the other hand, may lead to overdistention of alveoli and reduced C. The effect of PEEP in individual patients can be ascertained by measuring exhaled V_T and calculating C_{DYN}. Other potentially deleterious effects of PEEP include decreased venous return, increased pulmonary vascular resistance, and decreased cardiac output.

ADDITIONAL VENTILATORY MODALITIES

Airway Pressure Release Ventilation

Airway pressure release ventilation (**APRV**) aims to improve oxygenation in patients with preserved respiratory drive suffering from severe hypoxemic respiratory failure due to alveolar-interstitial disease. This modality applies a CPAP, designated $CPAP_{HIGH}$, to recruit and maintain EELV with brief intermittent release phases of $CPAP_{LOW}$ to allow alveolar gas to escape. $CPAP_{HIGH}$ is analogous to PIP, and $CPAP_{LOW}$ is similar to setting PEEP. In contrast to the patient receiving conventional mechanical ventilation, a patient receiving APRV spends the majority of time in the $CPAP_{HIGH}$ phase, which may last as long as 3-5 seconds with a brief (0.3-0.5 seconds) time in the $CPAP_{LOW}$ phase. These atypically long T_Is are tolerated because of a floating expiratory valve in the ventilator circuit that permits spontaneous breathing during $CPAP_{HIGH}$ phase. Therefore even if the $CPAP_{HIGH}$ phase can be considered "inspiratory" and the $CPAP_{LOW}$ phase "expiratory" in regard to the ventilator, the patient is able to breathe spontaneously during both these phases. The longer ventilator T_I recruits lung units, and the ability to breathe spontaneously during this phase allows distribution of gas flow to atelectatic lung regions. The outcome benefit of APRV in pediatric hypoxemic respiratory failure has not been proven.

High-Frequency Ventilation

Mechanical ventilation at supraphysiologic rates and low V_T, known as high-frequency ventilation (**HFV**), improves gas exchange in a select group of patients who show no response to more traditional ventilatory modalities. The mechanism of alveolar ventilation in HFV is very different from that in conventional ventilation, in that HFV is less dependent

on VT and more dependent on asymmetric velocities and convective dispersion of inspired gas. Patients with severe persistent hypoxic failure are most likely to benefit from HFV. HFV is also helpful in patients with bronchopleural fistula and persistent air leaks. The main tenet of HFV is to recruit lung volume with a high mean airway pressure (MAP) and produce smaller fluctuations in alveolar pressure during inspiration and expiration, thus maintaining a satisfactory EELV and reducing alveolar stretch. The two most investigated techniques of HFV are HFOV and HFJV.

The most commonly used HFV modality is **high-frequency oscillatory ventilation (HFOV)**, which employs a mechanism to generate to-and-fro air movement. Additional air is drawn in (entrained) through a parallel circuit via a Venturi effect. Air is pushed in during inspiration and actively pulled out during expiration. The main determinants of oxygenation are F_{IO_2} and MAP, whereas ventilation is determined by changes in pressure (amplitude) around the MAP and frequency. The optimal frequency varies for the individual patient and disease process and depends on the so-called *corner frequency,* where the pressure cost of ventilation is the lowest. In PARDS this usually means frequency >8 Hz, irrespective of age.

In **high-frequency jet ventilation (HFJV)**, a high-frequency interrupter is interposed between a high-pressure gas source and a small cannula that is incorporated in the ETT. The cannula propels tiny amounts of gas (jets) at high velocity and high frequency through the ETT. An additional amount of gas is entrained from a parallel circuit. Unlike in HFOV, expiration occurs passively in HFJV as a result of elastic recoil of the lung and the chest wall. PEEP is set through the parallel circuit by a conventional ventilator in-line. Respiratory rate is generally set at 420 breaths/min. Major determinants of oxygenation are F_{IO_2} and PEEP, and the major determinant of ventilation is PIP.

CONVENTIONAL VENTILATOR SETTINGS

Fraction of Inspired Oxygen

The shape of the hemoglobin-O_2 dissociation curve dictates that oxygen content in the blood is not linearly related to P_{AO_2}. A P_{AO_2} value that results in an oxyhemoglobin saturation of ≤97% is reasonable in most situations, because a higher P_{AO_2} would cause minimal increase in arterial oxygen content, and a modest (10 mm Hg) drop in P_{AO_2} would result in minimal decrease in oxyhemoglobin saturation. In most cases, a P_{AO_2} value of >60 mm Hg is a reasonable goal. F_{IO_2} values that are higher than those necessary to attain oxyhemoglobin saturations of approximately 95% expose the patient to unnecessary oxygen toxicity. Whenever possible, F_{IO_2} values should be decreased to a level ≤0.40 as long as oxyhemoglobin saturation remains ≥92%. In patients with severe lung disease, oxyhemoglobin saturation of 88–92% may be acceptable.

Mode

The choice of mode of ventilation depends on the disease entity that is being treated and how much ventilator-patient interaction is desired. SIMV or AC is chosen as the control mode; PCV, VCV, or PRVC as the variable that is to be controlled; and pressure support and volume support are the choices for support modes. SIMV pressure-controlled modes are most commonly used in children.

Tidal Volume and Rate

As previously discussed, alveolar ventilation, the chief determinant of P_{ACO_2}, is calculated using VT, respiratory rate, and VD. A change in VT results in a corresponding change in alveolar ventilation without affecting VD-ventilation. A change in respiratory rate will affect alveolar ventilation and the VD-ventilation. Choice of VT and rate depends on the TC. In a patient with relatively normal lung compliance, an age-appropriate ventilator rate and a VT of 5-8 mL/kg would be appropriate initial settings. Diseases associated with decreased TC (decreased static compliance; e.g., PARDS, pneumonia, pulmonary edema) are best treated with small (4-6 mL/kg) VT and relatively rapid rates (e.g., 25-40 breaths/min). Diseases associated with prolonged TCs (increased airway resistance; e.g., asthma, bronchiolitis) are best treated with relatively slow rates and higher (10-12 mL/kg) VT. In PCV the delivered VT depends on the C and R of the patient's respiratory system and needs to be monitored to ensure the appropriate amount for a given situation. The operator titrates the inflation pressure, depending on the volume of exhaled VT. It should be emphasized that achieving a *normal* P_{ACO_2} value is not a goal of mechanical ventilation. Some degree of hypercapnia (permissive hypercapnia) should be accepted, especially when one is attempting to limit injurious inflation pressures or VT.

Inspiratory Time and Expiratory Time

TI and TE are adjusted by setting inspiratory flow rate and/or inspiratory pause in VCV and by setting the precise TI in PCV. Increasing the TI results in increased MAP, improved oxygenation in diseases with decreased EELV, and potentially a better distribution of VT in obstructive lung disease. Sufficient expiratory time must be provided to ensure adequate emptying of the alveoli.

Positive End-Expiratory Pressure

The best level of PEEP depends on the disease entity that is being treated, and it may change in the same patient from time to time. Decisions are often based on the P_{AO_2}/F_{IO_2} ratio and the measurement of C_{DYN}. For patients with PARDS, the adult-based $PEEP/F_{IO_2}$ grid may be useful.

PATIENT-VENTILATOR ASYNCHRONY

Patient-ventilator asynchrony occurs when the patient's respiratory pattern does not match that of the ventilator. This can occur during all phases of respiration. Adverse effects of patient-ventilator asynchrony include wasted effort, ineffective delivery of desired VT, excessive generation of intrathoracic pressure resulting in injury and adverse effects on cardiac output, increased work of breathing, and patient discomfort. Although several mechanisms exist to facilitate patient-ventilator synchrony, a certain amount of asynchrony is inevitable unless the patient is pharmacologically sedated and paralyzed.

Triggering the Ventilator

The patient must be able to trigger the ventilator without excessive effort. Ventilators can be pressure-triggered or flow-triggered. With **pressure triggering**, the inspiratory valve opens and flow is delivered when a set negative pressure is generated within the patient-ventilator circuit during inspiration. The amount of pressure required to trigger an inspiration depends on the pressure trigger sensitivity. In **flow triggering**, the ventilator provides a base flow of gas through the ventilator-patient circuit. When a flow sensor on the expiratory limb of the patient-ventilator circuit detects a decrease in flow as a result of the patient's inspiratory effort, the inspiratory valve opens and a ventilator breath is delivered. The degree of change in flow required to trigger an inspiration depends on the flow trigger sensitivity. Flow triggering is considered to be more comfortable, primarily because the patient receives some flow before triggering the ventilator, in contrast to pressure triggering, in which no flow is provided until the ventilator breath is triggered through generation of negative pressure. Increasing the trigger sensitivity by decreasing the change in either pressure or flow needed to trigger an inspiration decreases the work of breathing and may improve comfort. However, reducing the required pressure or flow excessively could result in accidental triggering and unwanted breaths by turbulence, caused by condensation in the ventilator circuit, endotracheal tube (ETT) air leaks, or cardiac oscillations.

Selection of Appropriate Inspiratory Time

The duration of TI should match the patient's own inspiratory phase. If TI is too long, the patient's drive to exhale may begin before the ventilator breath has cycled off. When this occurs, exhalation occurs against inspiratory flow and a closed exhalation valve, resulting in increased work of breathing, excessive rise in intrathoracic pressure, and discomfort. If TI is too short, the patient may be still inhaling without respirator support. In general terms, TI is usually initiated at 0.5-0.7 second for neonates, 0.8-1 second in older children, and 1-1.2 second for adolescents and adults, but should really be driven by the inspiratory TC. Adjustments need to be made through individual patient observations and according to the type of lung disease present. In patients with severe lung disease (both obstructive and restrictive), unnatural TI and TE values may have to be selected, as discussed earlier. In such situations, adequate analgesia, sedation, and, in extreme cases, neuromuscular blockade may be needed.

Selection of Inspiratory Flow Pattern

In VCV, inappropriate flow may be another source of patient-ventilator dyssynchrony. After initiation of inspiration, if the set amount of flow is

inadequate to meet patient demand, a state of **flow starvation** occurs, resulting in excessive work of breathing and discomfort. Such patients may require a decelerating inspiratory flow pattern, in which a higher flow is provided in the beginning of inspiration and less toward the end as the lungs fill up. On the other hand, such a pattern may be uncomfortable for a patient who desires more gradual alveolar filling. The selection of inspiratory flow pattern should be based on the individual patient's respiratory mechanics. In PCV and PSV, the inspiratory rise time determines the manner in which the airway pressure is raised and VT delivered. Considerations for choosing the appropriate rise time in PCV and PSV are similar to those for choosing the inspiratory flow pattern in VCV.

Use of Support Modes

A conscious patient should be allowed to have spontaneous breaths that are supported by either PSV or VSV. This approach minimizes the mandatory breaths generated by the ventilator that are beyond the patient's control to modulate. Therefore continued assessments should be made to determine whether the patient is able to maintain ventilatory requirements more in support modes and less in control modes.

Use of Sedation and Neuromuscular Blockade

Having a conscious yet comfortable patient is a desirable goal during mechanical ventilation. Spontaneous breaths with good muscle tone and presence of cough are important for adequate clearance of tracheobronchial secretions. The patient's ability to indicate distress is also important in identifying and preventing potential injurious factors. In certain situations, management of patient-ventilator asynchrony assumes much greater importance when the asynchrony is causing unacceptable derangement of gas exchange and VILI. Both alveolar interstitial lung pathology and obstructive airway diseases may necessitate unnatural and uncomfortable settings for respiratory rate, TI, and inflation pressures. In such patients, deep sedation is often necessary; dexmedetomidine, benzodiazepines, and opiates are the agents most commonly used for this purpose. In extreme situations, pharmacologic neuromuscular blockade is required to abolish any patient effort and respiratory muscle tone. When such pharmacologic paralysis is used, deep sedation must be ensured so that the patient does not sense pain and discomfort. Pharmacologic sedation and paralysis can ensure total control of the patient's ventilation by mechanical means and may result in lifesaving improvement in gas exchange with reduction in inflation pressures. However, long-term use of such agents may be associated with undesirable consequences and higher morbidity. The risk of inadequate clearance of tracheobronchial secretions and atelectasis is potentially greater. Long-term use of pharmacologic sedation may be associated with chemical dependency and withdrawal manifestations, and prolonged neuromuscular blockade is associated with neuromyopathy in critically ill patients. The benefits of sedation and pharmacologic paralysis therefore should be carefully balanced with the risks, and periodic assessments should be made to determine the need for their continuation.

Cardiopulmonary Interactions

Mechanical ventilation can have salutary and adverse effects on cardiac performance. By decreasing oxygen consumption necessary for work of breathing, oxygen supply to vital organs is improved. Positive pressure breathing decreases LV afterload, thus enhancing stroke volume and cardiac output in patients with a failing myocardium (e.g., myocarditis). On the other hand, the decreased systemic venous return may further compromise stroke volume in hypovolemic (preload-dependent) patients. Such patients will require intravascular fluid loading when subjected to positive pressure ventilation. Also, an increase in pulmonary vascular resistance (PVR) caused by positive intrathoracic pressure may result in further decompensation of a poorly performing right ventricle. PVR is at its lowest value at an optimum FRC. When FRC is too low or too high, PVR (and therefore the right ventricular afterload) is increased. Both desirable and undesirable effects of cardiopulmonary interactions may coexist and require ongoing assessment and necessary interventions (Table 86.13).

Table 86.13 Suggested Mechanical Ventilation Strategies in Various Clinical Situations

SITUATION	DISEASE	STRATEGY
Low compliance, normal resistance	ARDS	PCV, APRV, HFOV
Normal compliance, high resistance	Asthma	PCV, PRVC
Normal compliance, normal resistance, for weaning	Head trauma, drug overdose, subglottic stenosis	VCV

APRV, Airway pressure release ventilation; ARDS, acute respiratory distress syndrome; HFOV, high-frequency oscillatory ventilation; PCV, pressure-controlled ventilation; PRVC, pressure-regulated volume control; VCV, volume-controlled ventilation.

MONITORING RESPIRATORY MECHANICS

Exhaled Tidal Volume

Exhaled tidal volume (VTE) is measured by a pneumotachometer in the ventilator circuit during exhalation; in small children, it is preferably measured near the connection of the ETT. Measurement of VTE more accurately describes the VT that is contributing to the patient's alveolar ventilation. In PCV the VTE depends on the patient's respiratory system compliance and resistance and therefore offers valuable diagnostic clues. A decrease in VTE during PCV is indicative of either decrease in compliance or increase in resistance and is helpful in directing the clinician to appropriate investigation and management. An increase in VTE is indicative of improvement and may require weaning of inflation pressures to adjust the VTE.

Peak Inspiratory Pressure

In VCV and PRVC, the PIP is the secondary variable determined by the patient's respiratory system compliance and resistance. An increase in PIP in these modes is indicative of decreased C (e.g., atelectasis, pulmonary edema, pneumothorax) or increased R (e.g., bronchospasm, obstructed ETT). During VCV and PRVC, decreasing the respiratory rate or prolonging the TI will result in a lower PIP in patients with prolonged TCs because more time will be available for alveoli to fill. In such patients, a decrease in PIP (or plateau pressure when an inspiratory pause is set during VCV) suggests increased C or decreased R of the respiratory system.

Respiratory System Dynamic Compliance and Static Compliance

The changes in PIP (or plateau pressure) during VCV and PRVC, and in VTE during PCV, are determined by C_{DYN} of the respiratory system (lung and chest wall). C_{DYN} is calculated as follows

$$C_{DYN} = V_{TE} \div (PIP - PEEP)$$

C_{DYN} takes into account both the flow-resistive and the elastic properties of the respiratory system. Changes in C_{DYN} can be used to assess effects of different levels of PEEP as tidal ventilation is shifted along the slope of the volume-pressure curve (see Fig. 86.7). An increase in PEEP in alveolar-interstitial diseases (increased elastance), resulting in an increase in C_{DYN}, suggests alveolar recruitment, whereas a decrease in C_{DYN} may indicate overdistention. Similarly, in obstructive diseases (increased R), adjustment in PEEP levels to ameliorate airway collapse during exhalation can be guided by monitoring C_{DYN}. To assess only the elastic recoil of the lung, measurement of C_{STAT} when there is no airflow is required. This measurement is performed by using an inspiratory hold maneuver with the patient under neuromuscular blockade and observing pressure-time and flow-time waveforms (Fig. 86.12). During this maneuver, inspiratory flow ceases while the expiratory valve continues to remain closed, thus allowing pressure to equilibrate throughout the ventilator circuit and the patient's lungs. This pressure, referred to as the *plateau pressure* (P_{plat}), reflects alveolar pressure. C_{STAT} is calculated as follows:

$$C_{STAT} = V_{TE} \div (P_{plat} - PEEP)$$

The difference between C_{DYN} and C_{STAT} is attributable to airway resistance. This difference is minimal in alveolar-interstitial diseases but substantial in airway obstruction.

Assessment of Auto-PEEP

Auto-PEEP is assessed with the use of an expiratory pause maneuver in which inspiration is delayed and alveolar pressure is allowed to

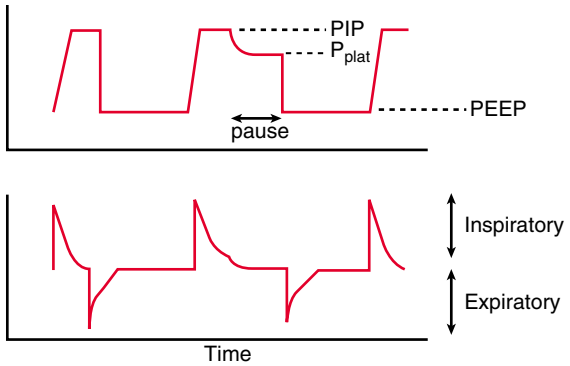


Fig. 86.12 Alveolar pressure is best determined by measurement of plateau pressure (P_{plat}). Inspiration is paused for an extended period, and alveolar gas pressure is allowed to equilibrate with the ventilator circuit pressure. Airway pressure at the end of the inspiratory pause is P_{plat}. The difference between peak inspiratory pressure (PIP) and P_{plat} is meant to overcome flow-resistive properties of the lung, whereas P_{plat} reflects the pressure needed to overcome elastic properties of the lung and chest wall. PEEP, Positive end-expiratory pressure.

equilibrate with the airway. In diseases with airway obstruction, insufficient alveolar emptying may occur if exhalation time is not adequate. The alveolar pressure in excess of the set PEEP at the completion of the expiratory pause is measured as auto-PEEP or intrinsic PEEP. Auto-PEEP can have adverse effects on ventilation and hemodynamic status. It can be managed by decreasing the respiratory rate or TI and thus allowing longer time for exhalation. Auto-PEEP may also be managed by increasing the set PEEP (*extrinsic* PEEP), thereby delaying airway closure during exhalation and improving alveolar emptying.

Assessment of Dead Space Ventilation

Positive pressure ventilation and application of PEEP may result in a decrease in venous return, cardiac output, and therefore pulmonary perfusion. Ventilation of poorly perfused alveoli results in dead space ventilation, which does not contribute to gas exchange. The VD/VT fraction can be calculated (see Chapter 86). Normal VD/VT is 0.33. Increased VD/VT is indicative of poorly perfused alveoli. Patients with increased VD/VT may require intravascular volume infusion or other means of augmenting the cardiac output to improve pulmonary perfusion. The VD/VT fraction is calculated and displayed by commercially available capnographs, which measure endotracheal $PetCO_2$ continuously.

VENTILATOR-INDUCED LUNG INJURY (VILI)

As with most medical therapies, mechanical ventilation can be harmful. Pathophysiology of VILI can be multifactorial. Large tidal volumes and high inspiratory pressures delivered with increased frequency cause cyclic strain, which may lead to disruption of the tight junctions between the alveolar epithelial and capillary endothelial cells, with intracapillary blebs resulting in alveolar and interstitial edema. This may cause the release of proinflammatory mediators (**biotrauma**) that further injure the lung and travel in the blood outside the lung, contributing to the development of multiorgan failure. Evidence shows that in patients with ARDS, avoidance of VT ≥10 mL/kg and P_{plat} ≥30 cm H_2O limits diffuse alveolar damage.

Atelectrauma is shear stress on the alveolar walls caused by cyclic opening and closing of the alveoli. PEEP can be used to prevent collapse and keep alveoli open. It is important that alveolar units are neither overdistended nor collapsed. Careful adjustments of PEEP may also permit the clinician to wean a patient from a high FIO_2, another potential source of lung injury, through exposure to reactive oxygen species (**oxytrauma**). Although most patients receive an FIO_2 of 1.0 at the time of endotracheal intubation and at the beginning of mechanical ventilation, increasing PEEP to recruit alveoli without overdistention should be quickly instituted to improve oxygenation and permit weaning of the FIO_2. Although the FIO_2 value below which there is no risk of oxygen toxicity is unknown, most clinicians aim for a value <0.6. Regional mechanics may play a role in lung injury.

Ventilator-Associated Pneumonia

The pathophysiology of ventilator-associated pneumonia (VAP) is multifactorial. Aspiration of oral and/or gastric secretions, colonization of the ETT, and suppression of cough reflexes from sedation all play a role. New-onset fever and leukocytosis accompanied by demonstration of an infiltrative process on chest radiography are consistent with a diagnosis of VAP. This complication can lead to worsened gas exchange, increased duration of ventilation, and even death. Elevation of the head of the bed to 30 degrees after initiation of mechanical ventilation and use of a protocol for oral decontamination during mechanical ventilation are common means of reducing the risk for VAP. The most effective strategy to minimize any of the aforementioned complications is regular assessment of extubation readiness and liberation from mechanical ventilation as soon as clinically possible.

Weaning

Weaning from mechanical ventilation should be considered as a patient's respiratory insufficiency begins to improve. Most pediatricians favor gradual weaning from ventilator support. With SIMV, the ventilator rate is slowly reduced, allowing the patient's spontaneous breaths (typically assisted with pressure or volume support) to assume a larger proportion of the minute ventilation. When the ventilator rate is low (<5 breaths/min) such that its contribution to minute ventilation is minimal, assessment of extubation readiness is performed. An alternative method of gradual weaning is transition to PSV. In this mode, no ventilator rate is set, allowing all triggered breaths to be assisted with pressure support. The clinician reduces the pressure support slowly to a low value (<5-10 cm H_2O), at which point assessment of extubation readiness is performed. During either technique, weaning should be halted if tachypnea, increased work of breathing, hypoxemia, hypercapnia, acidosis, diaphoresis, tachycardia, or hypotension occurs.

The most objective means of assessing extubation readiness is a **spontaneous breathing trial (SBT)**. Before performance of an SBT, a patient should be awake with intact airway reflexes, capable of handling oropharyngeal secretions, and with stable hemodynamic status. In addition, gas exchange should be adequate, defined as PaO_2 >60 mm Hg while receiving FIO_2 <0.4 and PEEP ≤5 cm H_2O. If these criteria are present, a patient should be started on CPAP with minimal (≤5 cm H_2O) or no pressure support. If this SBT is tolerated with no episodes of respiratory or cardiovascular decompensation, successful extubation is likely.

Some neonates and small children cannot be calmed or consoled long enough to complete the SBT. In this situation, extubation readiness must be assessed on a low level of ventilator support. Data suggest a low risk of extubation failure if the patient is comfortable and has stable hemodynamic status, with adequate gas exchange and spontaneous VT >6.5 mL/kg while receiving <20% of total minute ventilation from the ventilator. Certain patient populations are at increased risk for extubation failure, such as young infants, children mechanically ventilated for longer than 7 days, and patients with chronic respiratory or neurologic conditions. These children often benefit from transition to a noninvasive form of respiratory support (e.g., high-flow nasal cannula, CPAP, or BiPAP) upon liberation from mechanical ventilation to increase the odds of successful extubation.

The likelihood of **postextubation upper airway obstruction**, the most common cause of extubation failure in children, cannot be predicted by the results of an SBT or bedside measurements of physiologic variables. Traumatic endotracheal intubation and subglottic swelling from ETT irritation, especially in patients who exhibit agitation while receiving mechanical ventilation, are common causes of airway narrowing after extubation. Administration of intravenous corticosteroids (dexamethasone 0.5 mg/kg every 6 hr for four doses before extubation) has been shown to decrease the incidence of postextubation airway obstruction. In patients in whom postextubation airway obstruction develops, the need for reintubation may be obviated by administration of nebulized racemic epinephrine and helium-oxygen mixtures.

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blood cells, which begin to appear in the circulation in 4 or 5 days. Hypoxemia also increases 2,3-DPG, resulting in a rightward shift of the oxyhemoglobin dissociation curve and favoring release of oxygen from the blood to the tissues. This is counteracted by the leftward shift of the oxyhemoglobin dissociation curve caused by the respiratory alkalosis from hyperventilation. The result is a net null change in the oxyhemoglobin curve and an increase in oxygen-hemoglobin binding in the lung, raising Sao_2. Climbers at extreme altitude respond with marked hyperventilation, alkalosis, and leftward shift. This leftward shift favors oxygen loading in a hypoxic environment and increases Sao_2.

ACUTE MOUNTAIN SICKNESS

Epidemiology and Risk Factors

The incidence of high-altitude illness depends on several variables, including the rate of ascent, previous altitude exposure, and individual genetic susceptibility. Sleeping altitude, final altitude reached, and duration of stay at altitude are also risk factors for AMS development. Individual susceptibility for the development of AMS plays a significant role in risk assessment. Most individuals with previous histories of AMS after acute ascent are likely to experience similar symptoms with repeated visits to altitude. Gender and age do not affect the incidence of AMS.

AMS is very common with **rapid ascent**. Climbers around the world who ascend quickly (1 or 2 days) from sea level to altitudes of 4,000-6,000 m (~13,000-20,000 ft) have a very high incidence of AMS (27–83%). The rapid ascent profile associated with air travel to high altitude locations also results in high AMS rates. Trekkers who fly into the Khumbu region to explore the Mt. Everest area have a higher incidence of AMS (47%) compared with those who walk (23%). Skiers who visit resorts in the western United States from sea level generally fly or drive to the region but sleep at relatively moderate altitudes: 2,000-3,000 m (~6,500-9,800 ft). Among this population, AMS occurs in approximately 25%.

Pathophysiology

The symptoms of AMS develop several hours after arrival at high altitude, whereas the development of HAPE and HACE generally require several days of altitude exposure. Because hypoxemia occurs within minutes of arrival, it cannot be the direct cause of high-altitude illness, but rather the initiating factor for a cascade of events that lead to the development of the altitude clinical syndromes.

The clinical manifestations of AMS/HACE are primarily the result of central nervous system (CNS) dysfunction caused by hemodynamic mechanical factors and biochemical mediators of permeability. The CNS vasodilatory response to hypoxemia causes an increase in cerebral blood flow and volume. Significant elevation of brain volume is observed in moderate to severe AMS and HACE but has not been demonstrated in mild AMS. Hypoxic alteration of CNS vascular autoregulation and hypertension from exercise may increase pressure transmission to the brain's capillary beds, resulting in transcapillary leakage and vasogenic edema. Inflammatory mediators also contribute to vascular permeability and edema formation. HIF-mediated vascular endothelial growth factor, the inducible form of nitric oxide synthase, reactive cytokines, and free radical formation can increase permeability. Both mechanical and biochemical activation of the trigeminovascular system have been proposed as the cause of *high-altitude headache*, the primary symptom of AMS. Although vasogenic edema has been implicated in severe AMS and HACE, MRI reveals signal changes in subjects with and without clinical AMS.

Many of these responses to hypoxia and altitude exposure occur both in individuals who develop symptoms and those who remain free of AMS. To address the discrepancy in symptomatic illness, the "tight fit" hypothesis was proposed. This theory suggests that the development of AMS/HACE is due to a lack of intracranial space to accommodate increasing volume from brain swelling and edema that develop at altitude. The adequacy of the intracranial and intraspinal space to buffer changes in brain and cerebrospinal fluid (CSF) volume is the central concept. Buffering occurs as the intracranial CSF is displaced via the foramen magnum into the space available in the spinal canal, followed by increased CSF absorption and decreased CSF production. Individuals with less CSF buffering capacity have less compliance and are hypothesized to become more symptomatic (develop AMS).

Diagnosis

The diagnosis of AMS in older children and adults requires the history of a recent gain in altitude, presence at the new altitude for at least several hours, and the report of a headache plus one or more of the following symptoms: gastrointestinal (GI) upset (anorexia, nausea, or vomiting), general weakness or fatigue, dizziness, or lightheadedness. The **2018 Lake Louise Acute Mountain Sickness Score** is based on self-report of symptoms and aids clinicians in making the diagnosis and quantifying AMS severity in older children and adolescents (Table 87.1). Symptoms develop within a few hours after ascent and generally reach maximum severity between 24 and 48 hours, followed by gradual resolution. Sleep disturbance caused by periodic breathing is common in all visitors to high altitudes and is not part of the adult diagnostic criteria; sleep disturbance is likely the result of hypoxia rather than AMS. There are no diagnostic physical signs in cases of mild AMS. Any evidence of CNS dysfunction, such as mild ataxia or altered mentation, is early evidence of HACE. Similarly, whereas shortness of breath on exertion is common at high altitudes, dyspnea at rest is an early indicator of HAPE.

Table 87.1 2018 Lake Louise Acute Mountain Sickness Score

HEADACHE
0 – None at all
1 – Mild headache
2 – Moderate headache
3 – Severe headache, incapacitating
GASTROINTESTINAL SYMPTOMS
0 – Good appetite
1 – Poor appetite or nausea
2 – Moderate nausea or vomiting
3 – Severe nausea and vomiting, incapacitating
FATIGUE AND/OR WEAKNESS
0 – Not tired or weak
1 – Mild fatigue/weakness
2 – Moderate fatigue/weakness
3 – Severe fatigue/weakness, incapacitating
DIZZINESS/LIGHTHEADEDNESS
0 – No dizziness/lightheadedness
1 – Mild dizziness/lightheadedness
2 – Moderate dizziness/lightheadedness
3 – Severe dizziness/lightheadedness, incapacitating
AMS CLINICAL FUNCTIONAL SCORE
Overall, if you had AMS symptoms, how did they affect your activities?
0 – Not at all
1 – Symptoms present, but did not force any change in activity or itinerary
2 – My symptoms forced me to stop the ascent or to go down on my own power
3 – Had to be evacuated to a lower altitude
To obtain the AMS score, add number from each category earlier. Although no official severity rankings exist, many consider mild AMS to be 3-5 points, moderate AMS 6-9 points, and severe AMS 10-12 points.

From Roach RC, Hackett PH, Oelz O, et al. The 2018 Lake Louise Acute Mountain Sickness Score. *High Alt Med Biol.* 2018;19(1):4–6, Table 1.

The diagnosis of AMS in children with early language skills (age 4-11 years) may be made with cautious use of the 2018 Lake Louise criteria (see Table 87.1). The language used in this adult questionnaire may be too complex and may underestimate AMS if not understood by the child. This is particularly true for questions regarding headache (the key symptom of AMS) and GI symptoms.

In preverbal young children and infants, recognition of AMS relies on observable signs and exclusion of other causes. In this age range, AMS is manifested by increased fussiness, decreased playfulness, decreased appetite, and sleep disturbance. In most cases of AMS in very young children, all these symptoms are present. Fussiness is defined as a state of irritability that is not easily explained by another cause, such as tiredness, wet diaper, hunger, teething, or pain from an injury. Fussy behavior may include crying, restlessness, or muscular tension. Decreased playfulness may be profound. Alterations of appetite may progress to frank vomiting. Sleep disturbance can manifest with either increased or decreased sleep when compared with normal patterns. Most often, decreased sleep and the inability to nap are noted.

The Children's Lake Louise Score (CLLS) has been successfully tested in preverbal children <4 years old by parents briefed on the use of the scoring system. The CLLS combines a score for the amount and intensity of unexplained fussiness with a symptom score of how well the child has eaten, played, and slept in the past 24 hours. Evaluating for the presence of headache can be accomplished by asking if the "head hurts" or by using a visual "faces" pain scale. GI symptoms are evaluated by asking children if they are "hungry" rather than trying to evaluate their appetite. A combined score of ≥7 is indicative of AMS (Fig. 87.1). Many of the symptoms manifested by AMS in children may also result from the disruption of the normal routine with travel. A change in environment, sleeping accommodation, or eating options can result in a fussy child. The threshold scores for AMS diagnostic criteria are modified to account for these baseline variations. Educating parents to recognize the symptoms of AMS in themselves is also important, as an ill parent can indirectly compromise a child's safety.

Other acute illnesses can mimic AMS in young children. *It must be emphasized that altered mental status, neurologic abnormalities, breathing difficulty, and cyanosis are not part of uncomplicated AMS.* **Any of these signs warrant immediate medical attention.** If serious bacterial illness, a surgical condition, or another problem meriting specific intervention is suspected in a child, descent to lower altitude is recommended to eliminate the confounding variable of altitude illness.

Periodic Breathing

Periodic breathing at altitude is common at all ages during sleep, resulting in brief repeated episodes of oxyhemoglobin desaturation. Prepubertal children (9-12 years old) have similar nighttime oxygen desaturations as their parents; however, they have somewhat more stable breathing patterns with less periodicity. Although periodic breathing is not a sign of AMS, the exacerbation of hypoxia during sleep plays a role in AMS development. Newborn infants normally have periodicity in their respiratory pattern, and this periodicity is increased by high-altitude exposure and sleep. Oxygen saturations of awake neonates born at 3,100 m (~10,100 ft) in Colorado range from 88% to 91%. During sleep with increased periodic breathing, oxygen saturation may drop to 81% during the first week of life. The amount and magnitude of respiratory periodicity decrease as the child matures, and saturation during sleep increases to 86% after 2 months. A stable mature pattern is usually reached by 6 months of age. Preterm babies may demonstrate marked periodicity with prolonged desaturation because of their immaturity. Acute ascent with a child born preterm is best delayed until maturity, when normal pulmonary function and respiratory drive can be demonstrated. Parents of normal young babies may become distressed as they note marked periodic breathing patterns in their child after ascent to moderate altitude. Clinicians can reassure parents that this is generally not a precursor of true apnea; desaturation can occur with periodic breathing in sleep, especially at higher altitudes.

Management

The management of AMS must include strict adherence to the principle that further ascent to a higher sleeping altitude is contraindicated after the symptoms of altitude illness occur. Halting ascent or activity to allow further acclimatization may reverse the symptoms; however, continuing the ascent exacerbates the underlying pathologic processes and may lead to disastrous results. Stopping further ascent and waiting for acclimatization treats most AMS in 1-4 days. Mild cases of AMS may be treated without descent if monitoring by a reliable caregiver is available. Conservative treatment may be provided, including rest, analgesics for headache, and antiemetics for nausea. When conservative measures are inadequate, acetazolamide and/or oxygen titrated to maintain Sao_2 >94% are generally effective. Although no studies have formally assessed its use in pediatric patients, anecdotal reports have demonstrated efficacy of acetazolamide in treating mild AMS in this population. AMS that becomes worse or does not respond to maintenance of altitude, rest, and pharmacologic intervention mandates descent. Descent (500-1,000 m, ~1,600-3,300 ft) is effective treatment for all forms of altitude illness and should be tailored to the individual response. The presence of neurologic abnormalities (e.g., ataxia or altered mentation) mandates descent because these signs indicate a progression of AMS to severe altitude illness (HACE).

Supplemental oxygen administration relieves AMS symptoms, including small amounts (1-2 L/min) given during sleep. In the wilderness, oxygen tanks are impractically heavy and are usually unavailable in adequate amounts; therefore oxygen therapy is usually reserved for the more serious manifestations of high-altitude illness. Hyperbaric therapy that simulates descent is also effective.

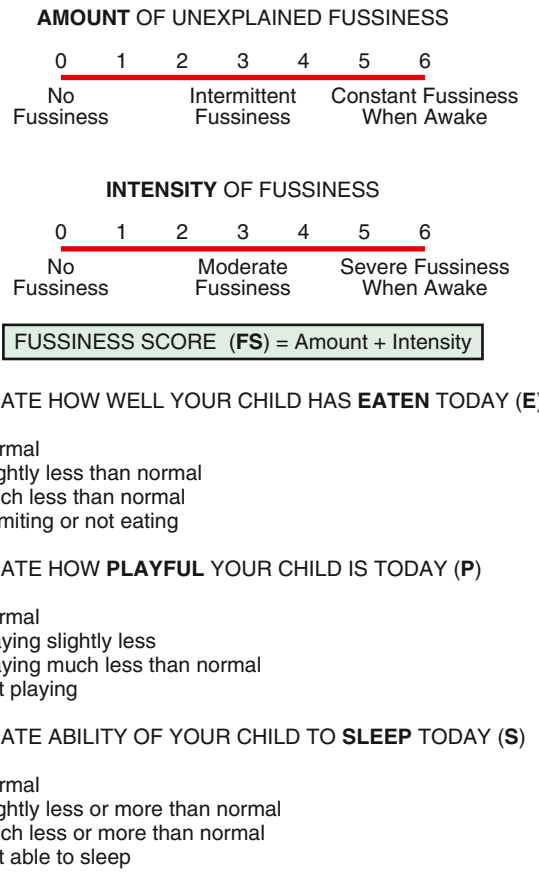

Fig. 87.1 Children's Lake Louise Score (CLLS). Fussiness is defined as a state of irritability that is not easily explained by a cause, such as tiredness, hunger, teething, or pain from an injury. Fussy behavior may include crying, restlessness, or muscular tension. Please rate your child's typical fussy behavior *during the last 24 hours* without the benefit of your intervention.

Treatment of headache and nausea can be beneficial for mild AMS, and in many cases this may be all that is necessary. Evidence supports the use of ibuprofen and acetaminophen for the treatment of high-altitude headache in children; aspirin and combination products containing aspirin should be avoided in children because of possible association with Reye syndrome. For nausea and vomiting, ondansetron may be used.

Acetazolamide is a carbonic anhydrase inhibitor that induces a renal bicarbonate diuresis, causing a metabolic acidosis that increases ventilation and arterial oxygenation. This respiratory stimulation improves sleep when the hypoxemia caused by periodic breathing is eradicated by acetazolamide. Acetazolamide accelerates acclimatization and, if given early in the development of AMS, rapidly resolves symptoms. Anecdotal experience supports the use of acetazolamide in children, particularly when conservative measures have been insufficient (Table 87.2). Treatment for 48 hours is usually adequate for resolution of symptoms. Acetazolamide may be prepared as a solution by a compounding pharmacy.

Adverse reactions to acetazolamide in adults include paresthesias, polyuria, and taste alterations for carbonated beverages. Less common reactions include nausea, drowsiness, tinnitus, transient myopia, and rarely, rash. Acetazolamide is a nonantibiotic sulfa compound that carries a low risk of cross-reactivity for individuals with an allergy to sulfa antibiotics. A history of anaphylaxis or severe skin reactions to any sulfa-containing medication contraindicates the use of acetazolamide. Acetazolamide should be avoided in breastfeeding mothers and pregnant women.

Dexamethasone is an effective alternative treatment for AMS in adults. Although dexamethasone can resolve the symptoms of AMS, it does not play a role in acclimatization, and symptoms may recur when the treatment is withdrawn. Adverse reactions to dexamethasone of concern in the pediatric population are pancreatitis, pseudotumor cerebri, and interference with normal growth. Although these reactions are generally seen with prolonged use, dexamethasone should be used for treatment in children only in extreme situations where alternatives such as descent or oxygen therapy are unavailable.

Prevention

Individuals who have a known susceptibility to the development of AMS and those for whom slow ascent is impractical may consider prophylactic medication. *Acetazolamide remains the compound of choice for AMS prophylaxis.* Numerous studies have demonstrated its effectiveness in adults starting 24 hours before ascent and continuing for the first 2 days at high altitude. Controlled studies for prophylaxis with acetazolamide in children are unavailable; however, anecdotal evidence supports its use (see Table 87.2). Ibuprofen, when compared with acetazolamide, has been found to be equally efficacious in preventing headache in adults. Dexamethasone also prevents AMS; however, the potential adverse effects in children preclude its use for prophylaxis in this age group. Recommendations for hyperhydration are frequently given in the lay literature, yet no evidence supports this advice. Drinking excessive amounts of free water may lead to hyponatremia and possibly complicate altitude illness.

HIGH-ALTITUDE CEREBRAL EDEMA

Epidemiology and Risk Factors

HACE is rare and may occur in children. Prompt recognition and treatment are necessary, because if unrecognized, it is rapidly fatal. HACE is generally seen in adults with prolonged stays above 4,000 m (~13,000 ft), but in rare cases has been reported as low as 2,100 m (~6,900 ft). HACE is usually associated with concurrent AMS or HAPE, but can occur on its own.

Pathophysiology

HACE is regarded as the extreme expression of the same pathophysiology underlying AMS. The edema and increased intracranial pressure are believed to be primarily caused by a vasogenic process where fluid moves from the vascular to the interstitial space due to a combination of increased hydrostatic pressure and increased vascular permeability. In the later stages of HACE, a cytotoxic component may contribute to the edema. These proposed mechanisms are supported by MRI studies revealing white matter changes consistent with vasogenic and cytotoxic edema.

Diagnosis

HACE is differentiated from severe AMS by the presence of **neurologic signs**. Most common are ataxia and altered mental status, including confusion, progressive decrease in responsiveness, and eventually coma. Less common are focal cranial nerve palsies, motor and sensory deficits, and seizures. CT imaging is consistent with edema and increased intracranial pressure. MRI shows a high T2 signal in the white matter, specifically in the splenium of the corpus callosum, with diffusion-weighted technique.

Management

Descent remains the most effective treatment for HACE. Supplemental oxygen, if available, is useful, especially if descent is not possible or

Table 87.2 Medications for Treatment of Altitude-Associated Illness in Children*

MEDICATION	CLASSIFICATION	INDICATION	DOSE AND ROUTE	ADVERSE EFFECTS
Acetazolamide	Carbonic anhydrase inhibitor	AMS treatment	2.5 mg/kg PO every 12 hours; maximum 250 mg/dose	Collateral effects include paresthesias, altered taste and visual acuity, electrolyte disturbance
		AMS or re-entry HAPE prevention[1]	1.25 mg/kg PO every 12 hours; maximum dose 125 mg/dose	Collateral effects reduced at lower doses
Dexamethasone	Steroid	AMS or HACE treatment[2,3]	0.15 mg/kg PO/IM/IV every 6 hours; maximum 4 mg/dose	Hypertension, GI hemorrhage, pancreatitis, growth inhibition
Nifedipine	Calcium-channel blocker	HAPE treatment or prevention[4]	If > 50 kg use adult dosing of 30 mg extended-release PO every 12 hours	Flushing, gastrointestinal distress, hypotension
Amlodipine	Calcium-channel blocker	HAPE treatment or prevention[4,5]	*1-5 years:* 0.1-0.6 mg/kg/dose PO daily; maximum 5 mg/day *6-17 years:* 2.5-5.0 mg PO daily (tablet or liquid suspension)	Flushing, abdominal pain, dizziness, hypotension

*No studies in children for high-altitude indications.

[1]AMS prophylaxis is not routinely recommended in children but indicated when rapid ascent profile is unavoidable or previous altitude illness occurred in a child about to undergo similar ascent profile. AMS and re-entry HAPE prophylaxis should be started 24 hours before ascent and continued for 2 days at altitude.

[2]Oxygen and descent are the treatment of choice for severe AMS. If acetazolamide is not tolerated, dexamethasone may be used. Oxygen, descent and dexamethasone should be used in HACE.

[3]Prophylactic use of dexamethasone for AMS is not warranted because of potential adverse effects. Use slow graded ascent or acetazolamide.

[4]In emergency settings where oxygen and descent are not an option, amlodipine or nifedipine may be used for treatment. Extended-release (ER) nifedipine formulations cannot be broken to obtain smaller doses. If ≥ 50 kg, 30 mg extended-release nifedipine is preferred.

[5]Amlodipine offers advantages over nifedipine for small children because of once daily dosing and availability as liquid or appropriately sized tablet.

Adapted from Luks AM, Beidleman BA, Freer L et al. Wilderness Medical Society Clinical Practice Guidelines for the Prevention, Diagnosis and Treatment of Acute Altitude Illness: 2024 Update. *Wilderness Environ Med.* 2023;Oct 11:S1080-6032(23)00167-9.

delayed. Portable hyperbaric treatment is beneficial, but its use should not delay descent. Dexamethasone should be administered at a dose of 0.15 mg/kg per dose given orally every 6 hours to a maximum of 4 mg per dose (see Table 87.2). The few mild cases of HACE reported in children have recovered with dexamethasone *and* descent.

HIGH-ALTITUDE PULMONARY EDEMA

Epidemiology and Risk Factors

HAPE is a noncardiogenic pulmonary edema caused by intense pulmonary vasoconstriction and subsequent high capillary pressure, secondary to hypoxia, resulting in altered permeability of the alveolocapillary membrane and the extravasation of intravascular fluid into the extravascular space of the lung. The development of HAPE depends on factors affecting pulmonary vasoreactivity, rate of ascent, altitude achieved, and time spent at that altitude. HAPE generally occurs in the setting of recent ascent, most often at altitudes above 3,000 m (~9,800 ft), but in some cases at altitudes as low as 1,740 m (~5,700 ft). Among children HAPE occurs in 2 distinct settings. Most commonly, HAPE occurs in a child who resides at low altitude who travels to high altitude. Reentry HAPE affects children who reside at high altitude but become ill on their return home after descent to lower altitudes (see Special Considerations). HAPE may also occur with or without ascent in children who develop acute respiratory illnesses that exacerbate hypoxia at high altitude. Fatal outcomes of HAPE in children have been reported. Most mild and moderate cases resolve without difficulty; however, if unrecognized and untreated, rapid progression to death can occur, especially when infection or cardiac conditions complicate the illness.

HAPE affects male and female children more equally than adults, among whom the observed male predominance appears due to strenuous sport activities and military assignments. The occurrence, and even the pathophysiology, of HAPE may vary by population and genetic background. Several conditions may predispose a child to HAPE (Table 87.3). Preexisting viral respiratory infections have been linked to HAPE, especially in children. Cardiorespiratory conditions associated with pulmonary hypertension, such as atrial and ventricular septal defects, pulmonary vein stenosis, congenital absence of a pulmonary artery, and obstructive sleep apnea, also predispose to HAPE. Down syndrome is a risk factor for HAPE development, as are previously repaired congenital heart defects and the presence of hypoplastic lungs. Undiagnosed structural cardiopulmonary abnormalities may result in severe hypoxia and/or altitude illness once ascent occurs; for this reason, a new diagnosis of HAPE in a child warrants active investigation of underlying causes.

Table 87.3 Conditions Associated with Increased Risk of HAPE

ENVIRONMENTAL
Ascent above 2,500 m (~8,200 ft)
Rapid rate of ascent (generally >1,000 m [~3,300 ft] per day)
Cold exposure
CARDIAC
Anomalies causing increased pulmonary blood flow or increased pulmonary arterial pressure
• Ventricular septal defect, atrial septal defect, patent foramen ovale, patent ductus arteriosus
• Anomalous pulmonary venous return or pulmonary vein stenosis
• Unilateral absent pulmonary artery or isolated pulmonary artery of ductal origin
Coarctation of the aorta
Congestive heart failure
PULMONARY
Chronic lung disease
Bronchopulmonary dysplasia
Cystic fibrosis (FEV-1 <30% predicted)
Pulmonary hypoplasia
Supplemental oxygen requirement at sea level
Pulmonary hypertension
Perinatal respiratory distress
Persistent pulmonary hypertension of the newborn
Perinatal asphyxia or depression
Sleep apnea
INFECTIOUS
Upper respiratory tract infection
Bronchitis/bronchiolitis
Pneumonitis
Otitis media
PHARMACOLOGIC
Any medication causing central nervous system and respiratory depression
Alcohol
Sympathomimetics
SYSTEMIC
Down syndrome (trisomy 21)
History of premature birth or low birthweight

Physiology

Alveolar hypoxia results in vasoconstriction of the pulmonary arterioles just proximal to the alveolar capillary bed. Hypoxic pulmonary vasoconstriction is a normal physiologic response to optimize ventilation/perfusion ($\dot{V}/\dot{Q}$) matching by redistributing regional pulmonary blood flow to areas of highest ventilation, thereby optimizing arterial oxygenation. However, under conditions that result in widespread alveolar hypoxia, extensive pulmonary vasoconstriction will lead to significant elevations in pulmonary arterial pressure, and uneven pulmonary vasoconstriction can result in localized overperfusion, increased capillary pressures, distention, and leakage in the remaining vessels. This explains the patchy and heterogeneous edema that is classically observed in HAPE. The combination of pulmonary hypertension and uneven pulmonary vasoconstriction appears to be necessary in the pathogenesis of HAPE. Children and adolescents acutely exposed to high-altitude hypoxia demonstrate pulmonary hypertension, with increases in pulmonary artery pressure inversely related to age. Once the vascular leak occurs and alveolar fluid accumulates, a defect in transepithelial sodium transport impairs the clearance of alveolar fluid and contributes to HAPE.

The conditions that predispose to HAPE are often directly referable to elements in the cascade of pathophysiology. Viral infections result in inflammation that may predispose the pulmonary endothelium to mechanical injury and increase susceptibility to alveolar fluid accumulation and HAPE during ascent. Exercise and cold stress at altitude may increase hypoxemia and exacerbate pulmonary hypertension. Overperfusion of a restricted vascular bed is illustrated by cases of congenital unilateral absence of a pulmonary artery in which the entire cardiac output is delivered to one lung, predisposing to pulmonary hypertension and overperfusion injury. Although data from mechanistic studies of children are lacking, adult HAPE-susceptible subjects have been characterized as having significantly elevated pulmonary artery pressure during altitude exposure and illness, altered vascular permeability, augmented hypoxic pulmonary vasoreactivity during hypoxia and normoxic exercise, blunted hypoxic ventilatory responsiveness, smaller lung volumes, and impaired alveolar fluid clearance.

Diagnosis

The diagnosis of HAPE is based on clinical findings and their evolution in the context of recent ascent from lower elevation. There is no single diagnostic test or constellation of laboratory findings. Symptoms commonly develop within 24-96 hours, and onset of symptoms often occurs during the first or second night at altitude, when hypoxia may be exacerbated during sleep. HAPE is rarely observed beyond 5 days after ascent to altitude (unless additional ascent occurs) because pulmonary vascular remodeling and acclimatization have taken place. The diagnosis of HAPE is made by observing the combination of symptoms, including dyspnea at rest, cough, weakness, or decreased exercise performance, and signs including crackles or wheezing in at least one lung field, central cyanosis, tachypnea, or tachycardia. Determining the onset and timing of the illness relative to ascent and radiographic evidence of alveolar infiltrates may help confirm the diagnosis.

The symptoms of AMS and HAPE show considerable overlap, and AMS may precede the development of HAPE in approximately half of patients. Frequently patients with HAPE first exhibit general malaise, which may progress to more specific signs of cardiopulmonary distress. Young children may show agitation and general debility. Older children may complain of headache, and children of all ages frequently experience nausea and vomiting. Cough is a common pulmonary sign. Dyspnea at rest, orthopnea, cyanosis, tachycardia, and chest pain herald worsening compromise, which may advance within hours to production of pink-tinged sputum.

Findings on physical exam frequently are less severe than a patient's chest radiograph and the hypoxemia on pulse oximetry would predict. Children often appear pale, with or without visible cyanosis. Low-grade fever (<38.5°C) is common, and respiratory rate is generally increased. Auscultation typically reveals rales, usually greater in the right lung than the left, on presentation. The radiographic pattern of pulmonary edema can be highly variable, from patchy and peripheral to more homogeneous in severe cases. Often, the right lung shows more radiographic changes of edema than the left (Fig. 87.2). Cardiomegaly is an uncommon finding, but peribronchial and perivascular cuffing are frequent, as is enlargement of the pulmonary artery silhouette and dilation of more peripheral pulmonary arteries. Portable ultrasound has been shown useful to diagnose HAPE through the finding of "comet tails," artifacts created by microreflections of the ultrasound beam within interlobular septae thickened by interstitial and/or alveolar edema. Significant arterial oxygen desaturation, as measured by pulse oximetry, is a consistent finding, with saturations frequently below 75%. A complete blood count often reveals a leukocytosis with a left shift of the granulocyte series.

The differential diagnosis of HAPE includes viral and bacterial pneumonia, bronchitis/bronchiolitis, asthma, vaping-associated lung disease, and other forms of cardiogenic and noncardiogenic pulmonary edema as well as pulmonary embolism. HAPE is most frequently misdiagnosed as pneumonia or a viral respiratory illness, especially when suspicion of altitude-associated pathology is not appropriately high. The presenting signs of cough, dyspnea, and orthopnea, followed by sputum production, can easily be misinterpreted as pneumonia, an impression that is reinforced by the frequent accompaniment of low-grade fever. Respiratory viral infections increase the risk of developing HAPE, which may lead to further confusion in diagnosis.

Complications of HAPE in children often relate to underlying, sometimes undiagnosed, cardiopulmonary pathology or coexisting viral infections, which potentiate the severity of pulmonary edema and pulmonary hypertension. Acute altitude exposure in such circumstances may lead to severe presentations that progress rapidly to extreme hypoxemia or cardiac failure and death. Children with Down syndrome, with or without structural cardiac anomalies, show increased susceptibility to HAPE and rapid symptom progression. Neonatal respiratory distress with pulmonary hypertension has been linked to exaggerated hypoxic pulmonary vasoreactivity in early adulthood and thereby a theoretical predisposition to HAPE. Other conditions related to pulmonary overcirculation (atrial and ventricular septal defects, patent foramen ovale, patent ductus arteriosus), small cross-sectional area of the pulmonary vascular bed (unilateral absent pulmonary artery, pulmonary hypoplasia), obstruction to pulmonary venous return (total anomalous pulmonary venous return, pulmonary vein stenosis), or left-sided obstruction (coarctation of the aorta) potentiate HAPE. Recent inflammatory processes, such as viral infection, predispose to HAPE and may worsen hypoxemia. Infection with respiratory syncytial virus in particular may trigger severe pulmonary hypertension.

Management

Descent with supplemental oxygen is the treatment of choice for HAPE in children. When feasible, or in the absence of medical care, rapid descent of at least 500-1,000 m (~1,500-3,300 ft) usually results in rapid recovery. As with all altitude illness, the magnitude of the descent is tailored to the resolution of symptoms. Oxygen and bed rest without descent can be safe and effective treatment for mild HAPE in children where careful medical observation is available.

Supplemental oxygen at altitude is administered at 2-6 L/min by nasal cannula for 48-72 hours to maintain an arterial oxygen saturation of at least 90%. Increasing oxygen saturation above 90% does not result in further reduction in pulmonary artery pressure and does not accelerate edema resolution in adults. Oxygen flow can be weaned with improvement in symptoms and saturations; at flow rates below 2-4 L/min, children may be sufficiently stable and comfortable to continue treatment at home under the monitoring of family. Instructions to avoid physical exertion and exposure to cold should be given to reduce exposure to factors known to elevate pulmonary artery pressure. Most children experience complete resolution of mild HAPE within 24-72 hours of oxygen therapy when treated at the altitude of symptom onset.

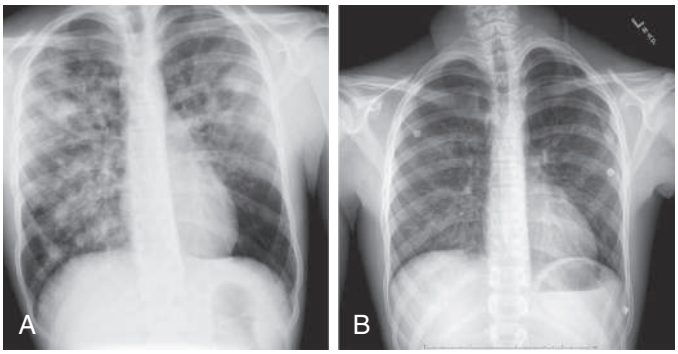

Fig. 87.2 High-altitude pulmonary edema (HAPE). A healthy teenager who resides at low altitude flew to Denver, Colorado, with a school group and immediately drove to a ski resort at 9,300 feet. The following day he felt dizzy and complained of headache. Symptoms progressed over the next 2 days to include emesis, dyspnea, cough, and fatigue. He was taken to an emergency department, where pulse oximetry showed an arterial saturation of 51%. Chest x-ray was obtained. **A,** This diagnostic image of HAPE was obtained at the altitude of presentation. The chest x-ray shows patchy, nodular infiltrates generalized through the right lung and the left upper lobe. The patient was started on supplemental oxygen and transported to Denver. Saturations improved with descent and were 94% on room air at time of arrival. **B,** Repeat radiograph obtained at lower altitude 2 days after presentation with HAPE. This diagnostic image shows substantial resolution of patchy pulmonary edema. *(Courtesy Children's Hospital Colorado, Department of Radiology.)*

Pharmacotherapy for pediatric HAPE is rarely needed because oxygen and descent are so effective. In emergency situations without the options of supplemental oxygen or descent, pharmacotherapy aimed at reducing pulmonary hypertension is indicated (see Table 87.2). Although not systematically studied in children, nifedipine is indicated for the treatment of adult HAPE. Amlodipine offers advantages over nifedipine in children because of daily dosing and availability of a liquid suspension. Patients should be monitored for hypotension during calcium channel blocker administration.

SPECIAL CONSIDERATIONS

Reentry HAPE and HAPE in High-Altitude Residents Without Travel

Children residing at high altitude may experience reentry HAPE upon reascent to the altitude of residence after a sojourn to low altitude. Although stays at low altitude as short as 24 hours may be sufficient to trigger reentry HAPE, most cases occur after several days at lower altitude. Several case series have demonstrated that children between 4 and 18 years of age are much more likely to develop reentry HAPE than adults. Observations from Colorado and Peru suggest that reentry HAPE may occur in 6–17% of children 2-19 years of age compared with <1–3% of adult residents. Various explanations have been proposed for the greater incidence and severity of reentry HAPE among children, including general lack of moderated behavior on ascent, increased likelihood of preexisting inflammatory processes, developmental differences in endothelial cell tight junctions, occult chronic pulmonary artery hypertension, and retained pulmonary arteriolar muscularity with potential for elevated pulmonary arterial pressure and potentially uneven pulmonary arterial vasoconstriction.

Reentry HAPE has a significant probability of recurrence and may justify pharmacologic prophylaxis to prevent the accumulated burden

of morbidity. There are no controlled trials of prophylaxis for reentry HAPE in children; however, acetazolamide has been used empirically (see Table 87.2), based on its blunting of hypoxic pulmonary vasoconstriction in adults and the potential risk of hypotension and reflex tachycardia with calcium channel blockers.

HAPE can also occur in children residing at high altitude without travel, and it should be considered in the differential diagnosis of children who present with hypoxemia at high altitude. The chest radiograph may be consistent with HAPE or viral pneumonia. When rapid improvement with oxygen and little to no response to bronchodilators suggest HAPE, the use of antibiotics and other treatments can be minimized.

Symptomatic High-Altitude Pulmonary Hypertension

Infants and young children residing at high altitude may experience symptomatic high-altitude pulmonary hypertension (SHAPH). All infants, regardless of altitude of gestation and birth, have thickened and muscularized interlobular and intralobular pulmonary arteries and pulmonary artery pressures that are initially near systemic. Although muscular regression and fall in pulmonary artery pressure occur rapidly at sea level, infants permanently residing at high altitude demonstrate slowed regression of these characteristics through infancy and even childhood. Similar changes may occur in infants who experience pulmonary complications at birth (respiratory distress syndrome of prematurity, persistent pulmonary hypertension of the newborn). Infants with SHAPH become symptomatic with exaggerated hypoxemia and signs of subacute pulmonary hypertension; these signs correlate with pathologic findings of right ventricular hypertrophy and dilation, increased muscularization of the pulmonary arterial bed, and eventual right-sided congestive heart failure. Although supplemental oxygen and medications may be used, definitive treatment is relocation to a lower altitude.

Cognitive Dysfunction

It is known that adults may have reversible changes in cognitive function with acute exposure to high altitude. A small study evaluating cognitive function in healthy 10- to 17-year-old children found impairment in verbal short-term memory, episodic memory, and executive functions 24 hours after ascent to 3,450 m (~11,400 ft). These findings were no longer present upon reassessment 3 months after returning to sea level. Similar results were found in children with permanent residence at high altitude; however, additional study is needed to assess the long-term implications of these findings.

Travel with Young Infants

Newborn infants retain some of the circulatory characteristics of recent fetal life, and these can pose a unique risk for altitude exposure. The fetal circulation has high pulmonary resistance, low pulmonary blood flow, and both intracardiac and extracardiac shunts that optimize oxygenation via the placenta instead of the fetal lungs. After birth, a transition begins that closes fetal shunts and establishes normal pulmonary circulation and oxygen transport. Exposure to marked hypoxia can result in reversion to fetal shunting patterns despite the absence of a placenta. Normal infants at sea level complete these changes in 4-6 weeks, though for infants born at moderate or high altitude, changes may last 3 months or longer. Travel to high altitude with young infants is generally safe after 4-6 weeks, when circulatory changes have occurred, breastfeeding is established, and congenital abnormalities may have been detected.

Air travel with young infants frequently raises questions about the effects of exposure to hypobaric hypoxia, as the pressurization of aircraft cabins may vary up to an altitude equivalent of 8,500 ft (~2,600 m). Even transoceanic flights are generally not long enough to trigger AMS or HAPE. However, infants may experience transient desaturation with feedings during flight and likely experience discomfort due to dry air and stress resulting from noise and vibration, much as adults do. Former preterm infants without chronic lung disease who have attained 3 months corrected gestational age do not appear to experience greater hypoxia during air travel than term infants; infants with more significant lung disease merit hypoxic challenge or provision of supplemental oxygen in flight.

Sickle Cell Disease/Trait

Children with sickle cell disease or sickle cell trait should avoid travel to altitude, as hypoxemia may trigger intravascular sickling, leading to acute vasoocclusive pain crises or splenic infarction or sequestration. Up to 20% of pediatric patients with sickle cell disease and sickle-thalassemia disease may experience a vasoocclusive crisis at moderate altitude or in pressurized aircraft. Oxygen is advised for air travelers with known sickle cell disease. Although many children with sickle cell trait remain asymptomatic, children can experience splenic ischemia or infarction with severe left upper quadrant pain.

Recommendations for High-Altitude Travel with Children

A comprehensive approach to travel to high altitude with children should focus on 3 phases: planning the ascent and assessment of risk, recognition and management of altitude-associated illness, and follow-up of any illness relative to future travel or diagnostic testing necessary. Planning for travel to high altitude with children should consider rate of ascent, formulation of an emergency plan for communication and evacuation, and availability of medical care at the high-altitude destination. Slow ascent with time for acclimatization is the best prevention for all forms of altitude illness. Ideally, the first night should not be spent at an altitude higher than 2,800 m (9,000 ft), and then 2-3 nights should be spent at 2,500-3,000 m (~8,200-9,800 ft), with a subsequent increase (to a new sleeping altitude) of not more than 500 m (1,600 ft) each night. One extra night of acclimatization (at the same sleeping altitude) should be taken for every 1,000 m (~3,300 ft) gained. Rapid ascent by air may be avoidable through alternative routes or means of transportation. Difficult descent situations (where further ascent may be necessary before descent is possible) should be avoided with children. Widespread coverage by cellular and satellite phone service may give a false sense of security in remote regions where both terrain and weather can limit the arrival of definitive help.

Prompt recognition of altitude-associated illness requires awareness of the context in which illness occurs and familiarity with the signs and symptoms. Parents are generally adept at recognizing deviation from baseline behavior of their children. Scales such as the Lake Louise Acute Mountain Sickness Score and CLLS may aid parents in modifying activity and/or seeking treatment. Clinicians should emphasize to parents that breathing difficulty, cyanosis, cough productive of pink-tinged sputum, altered mental status, and neurologic abnormalities are *not* part of uncomplicated AMS, but instead are serious signs of potential HAPE or HACE that deserve immediate medical attention.

Descent is the mainstay of therapy for all forms of altitude-associated illness in children. When descent is not feasible or illness is mild, other therapeutic options may be considered. Severe altitude illness or death can be avoided in children by adherence to three general principles:

1. Recognition of the early signs of altitude illness and willingness by adult caregivers to acknowledge them
2. No further ascent, especially to sleep at a higher altitude, when experiencing even minor symptoms/signs of altitude illness
3. Immediate descent if signs/symptoms worsen while resting/receiving treatment at the altitude of onset

Altitude-associated illness in children merits follow-up with the primary care physician. Uncomplicated AMS with full resolution of symptoms upon descent or treatment does not require diagnostic workup, but may prompt discussion of slower ascent, specific plans for treatment, or even prophylaxis for future travel. Signs of HAPE or severe hypoxemia in a child out of proportion to the altitude reached should prompt further diagnostic evaluation, including consideration of echocardiography. Underlying cardiac conditions may not be apparent on physical examination at low altitude; therefore cardiac catheterization or echocardiography under conditions of controlled hypoxia or hypoxic exercise may be necessary. Families of HAPE-susceptible children should be advised to avoid travel during or shortly after viral infections.

ACKNOWLEDGMENTS

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Chapter 88

Drowning and Submersion Injury

William Benjamin Prince

Drowning is the second most frequent cause of unintentional injury death among children in the United States after traffic accidents. Prevention is the most important step to reducing the impact of drowning injury, followed by early initiation of cardiopulmonary resuscitation (CPR) at the scene.

ETIOLOGY

Children are at risk of drowning when they are exposed to a water hazard in their environment. The World Congress on Drowning and the World Health Organization (WHO) definition of drowning is "the process of experiencing respiratory impairment from submersion/immersion in liquid." Drowning outcomes are classified as death, no morbidity, or morbidity further divided into moderately or severely disabled, vegetative state/coma, and brain death. Use of confusing descriptive terms such as "near," "wet," "dry," "secondary," "silent," "passive," and "active" should not be used.

EPIDEMIOLOGY

From 2010 to 2020, an average of 4012 people per year were victims of **fatal drowning**, and an estimated 8061 persons per year were treated in U.S. hospital emergency departments (EDs) for **nonfatal drowning**. Compared with other types of injuries, drowning has one of the highest case fatality rates and is in the top 10 causes of death related to unintentional injuries for all pediatric age-groups. In 2019, the highest drowning death rates were seen in children age 1-4 years (crude rate of 2.4 per 100,000); in children age 1-4 years, drowning was the number-one cause of death from *unintentional injury* in the United States in 2019 (Fig. 88.1). Rates of fatal drowning hospitalization declined by ~25% during the same period (Fig. 88.2).

The risk of drowning and the circumstances leading to it vary by age. Drowning risk also relates to other host factors, including male sex, alcohol or drug use, a history of seizures, autism, or cardiac arrhythmia, and swimming lessons. Environmental risk factors include exposure to water and varying supervision. These factors are embedded in the context of geography, climate, socioeconomic status, and culture.

Children <1 Year Old

Most (75%) drowning deaths in children younger than 1 year occur in the **bathtub**, when an infant is left alone or with an older sibling. Infant tub seats or rings may exacerbate the risk by giving caregivers a false sense of security that the child is safe in the tub. The next major risk to children <1 year is the large (5-gallon) household bucket. These buckets are approximately 30 cm (1 ft) tall and designed not to tip over when half-full. The average 9-month-old child tends to be top-heavy and thus can easily fall headfirst into a half-full bucket, become stuck, and quickly drown.

Children 1-4 Years Old

Drowning rates are consistently highest in 1- to 4-year-old children, likely because of their curious but unaware nature, coupled with the rapid progression of their physical capabilities. A common factor in many of these deaths is a lapse in adult supervision, often reportedly <5 minutes. Most U.S. drownings occur in residential **swimming pools**. Usually, the child is in their own home, and the caregiver does not expect the child to be near the pool.

In rural areas, children 1-4 years old often drown in irrigation ditches or nearby ponds and rivers. The circumstances are like those noted previously, in a body of water that is near the house. Drowning is one of the leading causes of *farm injury–related deaths* in children.

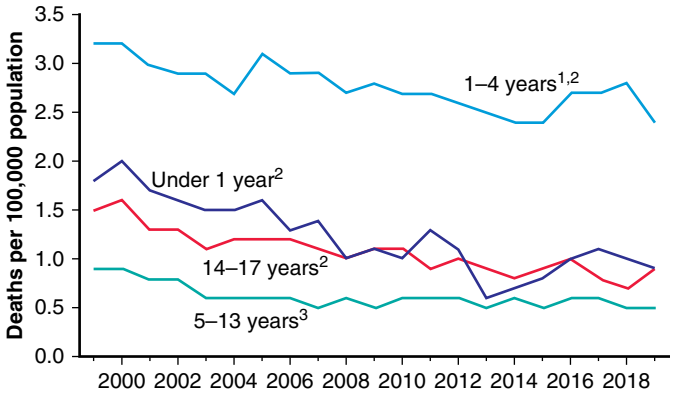

Fig. 88.1 Unintentional drowning death rates among children age 0-17 years, by age group: United States, 1999–2019. [1]Rates significantly higher than those for other age groups over the study period, $p < 0.05$. [2]Significant decreasing trend from 1999 through 2019, $p < 0.05$. [3]Significant decreasing trend from 1999 through 2005 $p < 0.05$; stable trend from 2005 through 2019.Notes: Unintentional drowning deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes W65–W74 Accidental drowning and submersion. Rates shown are crude rates (deaths per 100,000). Source: National Center for Health Statistics, National Vital Statistics System, Mortality. *(From Spencer MR, Hedegaard H, Warner M. Unintentional drowning deaths among children aged 0-17 years: United States, 1999-2019. NCHS Data Brief. 2021;413. Fig. 2.)*

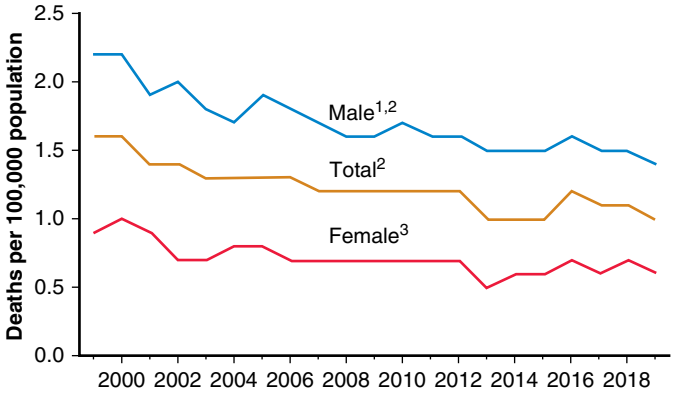

Fig 88.2 Unintentional drowning death rates among children age 0-17 years, by sex: United States, 1999–2019. [1]Rates significantly higher than those for females over the study period, $p < 0.05$. [2]Significant decreasing trend from 1999 through 2019, with different rates of change over time, $p < 0.05$. [3]Significant decreasing trend from 1999 through 2014; stable trend from 2014 through 2019, $p < 0.05$. Notes: Unintentional drowning deaths are identified using *International Classification of Diseases, 10th Revision* underlying cause-of-death codes W65–W74 Accidental drowning and submersion. Drowning deaths totaled 756 in 2019 among children age 0-17 years. Rates shown are crude rates (deaths per 100,000). Source: National Center for Health Statistics, National Vital Statistics System, Mortality. *(From Spencer MR, Hedegaard H, Warner M. Unintentional drowning deaths among children aged 0-17 years: United States, 1999-2019. NCHS Data Brief. 2021;413, Fig. 1.)*

School-Age Children

School-age children are at increased risk of drowning in natural bodies of water such as lakes, ponds, rivers, and canals. Hazards such as unknown depths, undefined areas, and presence of currents and waves increase this risk. Although swimming pools account for most nonfatal drownings across all ages, **natural waterways** account for a higher death rate in children 10-19 years old. Unlike for preschool children,

swimming or boating activities are important factors in drowning injuries in school-age children.

Adolescents

The second peak incidence in drowning death rates occurs in older adolescents, age 15-19 years. Almost 90% drown in open water. In this age-group particularly, striking disparities in drowning deaths exist in gender and ethnicity. Drowning death is roughly twice as common for males when compared with females, but among adolescents, the rate is almost 10 times higher among males. The gender disparity may likely be related to males' greater exposure to aquatic environments, overestimation of swimming ability, underestimation of dangerous situations, increased risk-taking behavior, and greater alcohol use.

Dangerous underwater breath-holding behaviors (DUBBs) are often performed by experienced healthy swimmers or fitness enthusiasts (hypoxic training) or when teenagers hold breath-holding contests during horseplay. DUBBs have been primarily reported in regulated swimming facilities. Behaviors include intentional hyperventilation before submersion, static apnea, and extended periods of underwater distance swimming or breath-hold intervals.

Ethnic Disparities

There is significant ethnic disparity seen across drowning rates and causes. Among children age 0-19 years, the drowning rates from 2014 to 2018 are highest among Black (1.79 per 100,000) and Indigenous Nations people and Alaska Native (1.49 per 100,000) individuals. Rates are lower among White (1.06 per 100,000), Asian American and Pacific Islander (0.85 per 100,000), and Hispanic (0.82 per 100,000) individuals. Age dramatically influences drowning disparities. Black children drown at significantly higher rates than those for White and Hispanic children at every age from 5 to 18 years. Black children are more likely to drown in unguarded public pools, apartment pools, or hotel pools; White children are more likely to drown in private residential pools. Reasons for disparities in drowning rates may include cultural attitudes toward swimming, prohibitive cost and location of swimming lessons, fears about swimming, and lack of lifeguards at pools in many communities.

Underlying Conditions

Several underlying medical conditions are associated with drowning at all ages. **Epilepsy** is a known risk factor in drowning, with a relative risk for fatal and nonfatal drowning 7.5- to 10-fold higher than children without seizures. Drowning is the most common cause of death from unintentional injury for people with epilepsy. **Cardiac etiologies**, including arrhythmias, myocarditis, and prolonged QT or catecholaminergic polymorphic ventricular tachycardia syndromes, have been found in some children who die suddenly in the water, particularly in those with a family history of syncope, cardiac arrest, prior drowning, or QT prolongation. Exertion and fright while swimming can trigger arrhythmia among individuals with long QT and should be considered a possible cause for unexplained submersion injuries, particularly among proficient swimmers in low-risk settings (see Chapter 484.5).

Children with autism spectrum disorder (ASD) are at a significantly higher risk of drowning when compared with the general population; wandering was the most reported behavior leading to drowning in children with ASD. Children with muscle disease or peripheral neuropathies have an increased risk for drowning because of the degree of fatigability.

Drowning may also be an **intentional injury**. A history of the event that changes or is inconsistent with the child's developmental stage is the key to recognition of intentional drowning. Physical examination and other physical injuries rarely provide clues. **Child abuse** is more often recognized in bathtub-related drownings. **Suicide** usually occurs in lone swimmers in open water.

Alcohol Use

The use of alcohol and drugs greatly increases the risk of drowning. A meta-analysis found that 30–70% of swimming and boating fatal drowning victims have a measurable blood alcohol concentration. Alcohol can impair judgment, leading to riskier behavior, decreased balance and coordination, hypothermia, and blunted ability to self-rescue. Alcohol use while boating is also associated with low life jacket use. Furthermore, an intoxicated adult may provide less effective supervision of children around water.

Sports and Recreation

Most U.S. drowning deaths occur during recreational activities. Drowning is the leading cause of *noncardiac sports-related deaths*. Surveys confirm that not using a personal flotation device (PFD) is common during boating activities. In 2021 the U.S. Coast Guard reported that 83% of those who drowned in boating accidents were not wearing a PFD.

Global Impact of Drowning

Drowning injury is the third leading cause of unintentional death worldwide, with the majority (90%) of fatalities occurring in low- and middle-income countries. More than half of the global drowning occurs in the WHO Western Pacific and Southeast Asia regions. Global drowning rates are vastly underestimated, because many drowning deaths in this region go unreported, and many immediate fatalities are unrecognized. In addition, these data exclude any cases of drowning as the result of intentional harm or assault, accidents of watercraft or water transport, and drowning related to forces of nature or cataclysmic storms, which usually claim large numbers of lives per incident; thus true numbers of fatal drowning are likely much higher.

Some patterns of pediatric drowning are similar in all countries. By most accounts, the highest rates are seen in males and in children 1-4 years old. The predominant locations are near or around the home, involving bodies of water used for activities of daily living. These include water-collecting systems, ponds, ditches, creeks, and watering holes. In tropical areas, death rates increase during monsoon season, when ditches and holes rapidly fill with rain, and are highest during daylight hours, when caregivers are busy with daily chores.

Drowning during natural disasters such as **storms** and **floods** is important in all areas of the world. The largest numbers of reported flood-related deaths occur in developing nations; most are drownings that occur during the storm surge. In the United States and much of Europe, advances in weather monitoring and warning systems have reduced such deaths. U.S. flooding incidents, including hurricanes Katrina and Sandy, showed that drowning caused the most deaths, particularly when people became trapped in their vehicles, were unable or refused to evacuate homes, or attempted to rescue others.

PATHOPHYSIOLOGY

Drowning victims drown quickly and quietly and do not signal distress or call for help. Vocalization is precluded by efforts to achieve maximal lung volume to keep the head above the water or by aspiration leading to laryngospasm (Fig. 88.3). Young children can struggle for only 10-20 seconds and adolescents for 30-60 seconds before final submersion. The *instinctive drowning response* is a phenomenon where actual or perceived suffocation in water triggers autonomic nervous system responses resulting in unlearned, instinctive drowning movements. A swimmer in distress is vertical in the water, with arms extended to the side to lift the body up and bring the mouth above water to breathe. This splashing or efforts to breathe are often misconstrued by nearby persons as merely playing in the water, until the victim sinks.

Anoxic-Ischemic Injury

During drowning there is a period of voluntary breath-holding, typically less than 1 minute, before small amounts of water enter the hypopharynx, triggering laryngospasm as a protective reflex. There is a progressive decrease in arterial blood oxyhemoglobin saturation (Sao_2), and the person soon loses consciousness from hypoxia. Profound hypoxia and medullary depression lead to terminal apnea. Laryngospasm resolves, allowing additional fluid (water, stomach contents) into the lungs. At the same time, the cardiovascular response progresses to decreasing cardiac output and oxygen delivery to other organs. By 3-4 minutes, myocardial hypoxia leads to peripheral vasoconstriction, decreased cardiac output, and abrupt circulatory

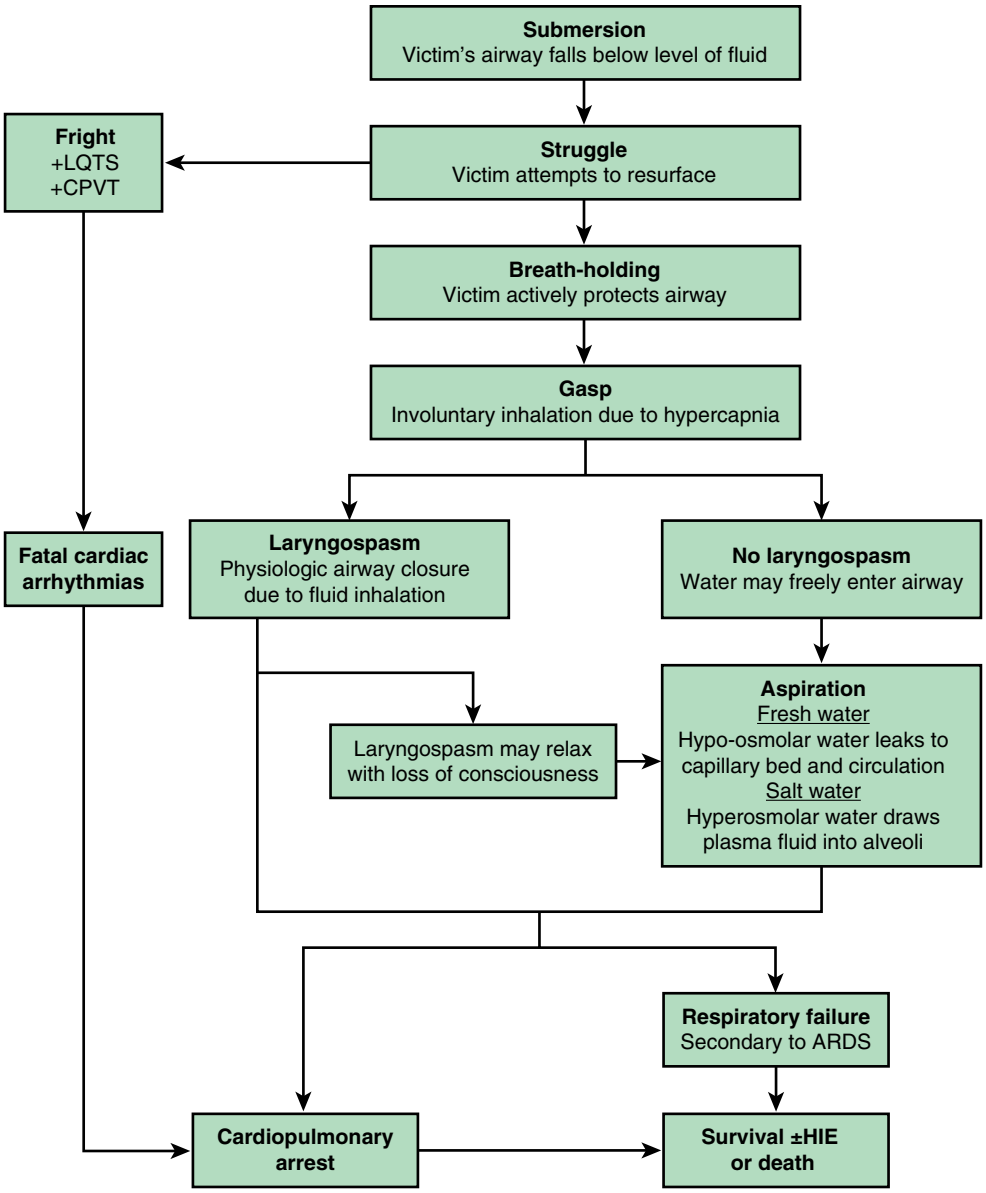

Fig. 88.3 Pathophysiologic events of the drowning process. LQTS, Long QT syndrome; CPVT, catecholaminergic polymorphic ventricular tachycardia; HIE, hypoxic-ischemic encephalopathy; ARDS, acute respiratory distress syndrome. *(Courtesy Andrew Schmidt, DO, MPH.)*

failure. Cardiac arrhythmias progress from tachycardia, to bradycardia, followed by ineffective cardiac contractions with electrical activity (**pulseless electrical activity**). With early initiation of CPR, spontaneous circulation may initially be successfully restored. The extent of the global **hypoxic-ischemic injury** determines the outcome and becomes more evident over subsequent hours.

With modern intensive care, the cardiorespiratory effects of resuscitated drowning victims are usually manageable and are less often the cause of death than irreversible hypoxic-ischemic central nervous system (CNS) injury (see Chapter 82). CNS injury is the most common cause of mortality and long-term morbidity. Although the duration of anoxia before irreversible CNS injury begins is uncertain, it is probably on the order of 3-5 minutes. Submersion <5 minutes is associated with a favorable prognosis, whereas those >25 minutes are generally fatal.

Several hours after cardiopulmonary arrest, **cerebral edema** may occur, although the mechanism is not entirely clear. Severe cerebral edema can elevate intracranial pressure (ICP), contributing to further ischemia; intracranial hypertension is an ominous sign of profound CNS damage.

All other organs and tissues may exhibit signs of hypoxic-ischemic injury. In the lung, damage to the pulmonary vascular endothelium can lead to **acute respiratory distress syndrome** (ARDS; see Chapter 86). Aspiration may also compound pulmonary injury. Myocardial dysfunction, arterial hypotension, decreased cardiac output, arrhythmias, and cardiac infarction may also occur. Acute kidney injury, cortical necrosis, and renal failure are common complications of major hypoxic-ischemic events (see Chapter 572.1). Vascular endothelial injury may initiate disseminated intravascular coagulation, hemolysis, and thrombocytopenia. Many factors contribute to gastrointestinal damage; bloody diarrhea with mucosal sloughing may be seen and often portends a fatal injury. Serum levels of hepatic transaminases and pancreatic enzymes are often acutely increased. Violation of normal mucosal protective barriers predisposes the victim to bacteremia and sepsis.

Pulmonary Injury

Pulmonary aspiration occurs in many drowning victims, but the amount of aspirated fluid is usually small (see Chapter 446). Aspirated water does not obstruct airways and is readily moved into the

pulmonary circulation with positive pressure ventilation. More importantly, it can wash out surfactant and cause alveolar instability, ventilation-perfusion mismatch, and intrapulmonary shunting. The disruption of the alveolar capillary membrane leads to alveolar edema resulting in local ARDS-like syndrome.

In humans, aspiration of small amounts (1-3 mL/kg) can lead to marked hypoxemia and a 10–40% reduction in lung compliance. The composition of aspirated material can also affect the patient's clinical course: gastric contents, oropharyngeal flora, pathogenic organisms, toxic chemicals, and other foreign matter can injure the lung or cause airway obstruction. Aspiration is typically considered the source of pneumonia in cases of drowning, and antibiotics should be initiated based on radiographic evidence and clinical suspicion; no mortality benefit has been shown in those patients who received empiric or prophylactic antimicrobial therapy. Clinical management is not significantly different in saltwater and freshwater aspirations, because most victims do not aspirate enough fluid volume to make a clinical difference.

Cold Water Injury

Drowning should be differentiated from cold water **immersion** injuries, in which the victim remains afloat, keeping the head above water without respiratory impairment in cold waters. The definition of cold water varies from <15–20°C (<59–68°F).

Heat loss through conduction and convection is more efficient in water than in air. Children are at increased risk for **hypothermia** because of their relatively high ratio of body surface area (BSA) to mass, decreased subcutaneous fat, and limited thermogenic capacity. Body temperature may also continue to fall after removal from the water because of cold air, wet clothes, hypoxia, and hospital transport time. Hypothermia in pediatric drowning victims may be observed even after drowning in relatively warm water and in warm climates (see Chapter 90).

Immersion in cold water has immediate respiratory and cardiovascular effects. Victims experience **cold water shock**, a dynamic series of cardiorespiratory physiologic responses that can cause drowning. In adults, immersion in icy water results in intense involuntary reflex hyperventilation and a decrease in breath-holding ability to <10 seconds, which leads to fluid aspiration. Severe bradycardia, the *diving reflex*, occurs in adults but is transient and rapidly followed by supraventricular and ectopic tachycardia and hypertension. There is *no evidence* that the diving reflex has any protective effect.

Even after surviving the chaotic minutes of cold-water shock, after an additional 5-10 minutes of cold-water immersion, the victim can become incapacitated. Cooling of large and small muscles disables the victim's ability to grab hold, swim, or perform other self-rescue maneuvers. Severe hypothermia with body temperatures below 28°C (82.4°F) can lead to cardiac arrhythmia and asystole.

Depending on water and air temperature, insulation, BSA, thermogenic capacity, physical condition, swimming efforts, or high-water flow rates, heat loss with continued immersion can significantly decrease core temperature to hypothermic levels within 30-60 minutes.

The symptoms and severity of hypothermia are categorized based on body temperature. The victim with mild hypothermia has a core body temperature of 32–35°C (90–95°F) with intact thermogenic mechanisms (shivering and nonshivering thermogenesis, vasoconstriction) and active movements. Compensatory mechanisms usually attempt to restore normothermia at body temperatures >32°C (89.6°F). Lower core temperatures lead to impaired cognition, coordination, and muscle strength and, with it, less ability to self-rescue. Thermoregulation may fail, and spontaneous rewarming will not occur. With moderate hypothermia (28 to <32°C [82 to <90°F]), loss of consciousness leads to water aspiration. Progressive bradycardia, impaired myocardial contractility, and loss of vasomotor tone contribute to inadequate perfusion, hypotension, and possible shock. At body temperatures <28°C (82.4°F), extreme bradycardia is usually present with decreases in cardiac output, and the propensity for spontaneous ventricular fibrillation or asystole is high. Central respiratory center depression with moderate to severe hypothermia results in hypoventilation and eventual apnea. A deep coma, with fixed and dilated pupils and absence of reflexes at very low body temperatures (<25–29°C [77–84.2°F]), may give the false appearance of death.

If the cooling process is quick—and cardiac output lasts long enough for sufficient heat loss to occur before the onset of severe hypoxia—the brain can cool to a level that may be considered in the *neuroprotective* range, approximately 33°C (91.4°F) in controlled, experimental conditions. However, if submersion leading to drowning occurs before development of a neuroprotective level of hypothermia, severe anoxia devastates tissue organs. The theoretical benefits, implications, and consequences of hypothermia in drowning victims are areas of controversy. Known adverse effects are associated with hypothermia, and these must be balanced against the potential benefits observed in experimental data. One should clearly differentiate among **controlled hypothermia**, such as that used in the operating room before the onset of hypoxia or ischemia; **accidental hypothermia**, such as occurs in drowning, which is uncontrolled and variable, with onset during or shortly after hypoxia-ischemia; and **therapeutic hypothermia**, involving the purposeful and controlled lowering and maintenance of body (or brain) temperature after a hypoxic-ischemic event.

In drowning victims with uncontrolled accidental hypothermia associated with icy water submersion, there are isolated and rare reports of good neurologic recovery after prolonged (10-150 minutes) cardiopulmonary arrest. Almost all these rare survivors have been in freezing water (<5°C [41°F]) and had core body temperatures <30°C (86°F), often much lower. Presumably, very rapid and sufficiently deep hypothermia developed in these fortunate survivors before irreversible hypoxic-ischemic injury occurred. Intact neurologic functioning after sustaining a severe hypothermic submersion is likely associated with a combination of variables, including submersion times (most important), water temperature, immediate resuscitation, quality and duration of resuscitation, idioventricular bradycardia, and rewarming speed.

Most often, hypothermia is a poor prognostic sign, and a neuroprotective effect has not universally been demonstrated. A 2014 study from Washington State found that submersion duration <6 minutes is most strongly related to good outcome, not water temperature. In another study of comatose drowning patients admitted to the pediatric intensive care unit (PICU), 65% of hypothermic patients (body temperature <35°C [95°F]) died, compared with a 27% observed mortality rate in nonhypothermic victims. Thus a beneficial effect of drowning-associated hypothermia has not been seen in most pediatric submersion victims.

MANAGEMENT

Duration of submersion, speed of the rescue, effectiveness of resuscitative efforts, and clinical course determine the outcome in submersion victims (Fig. 88.4). Two groups may be identified based on responsiveness at the scene. The first group consists of children who require minimal resuscitation at the scene and quickly regain spontaneous respiration and consciousness. They have good outcomes and minimal complications. In awake, alert victims with hypoxemia, the first line of therapy is supplemental oxygen. These victims should be transported from the scene to the ED for further evaluation and observation. The second group comprises children in cardiac arrest who require aggressive or prolonged resuscitation and have a high risk of multiple organ system complications, major neurologic morbidity, or death. Compared with cardiac arrest from other causes, cardiac arrest from drowning has a higher survival rate.

Initial management of drowning victims requires coordinated and experienced prehospital care following the ABCs (airway, breathing, circulation) of emergency resuscitation. CPR of drowning victims must include providing adequate ventilation as the initial phase of respiratory arrest, as these children may still have intact circulation. However, this phase will progress to cardiac arrest if hypoxia persists. Children with severe hypoxic injury and symptoms often remain comatose and lack brainstem reflexes despite the restoration of oxygenation and circulation. Subsequent ED and PICU care often involve advanced life support (ALS) strategies and management of multiorgan dysfunction with discussions about end-of-life care.

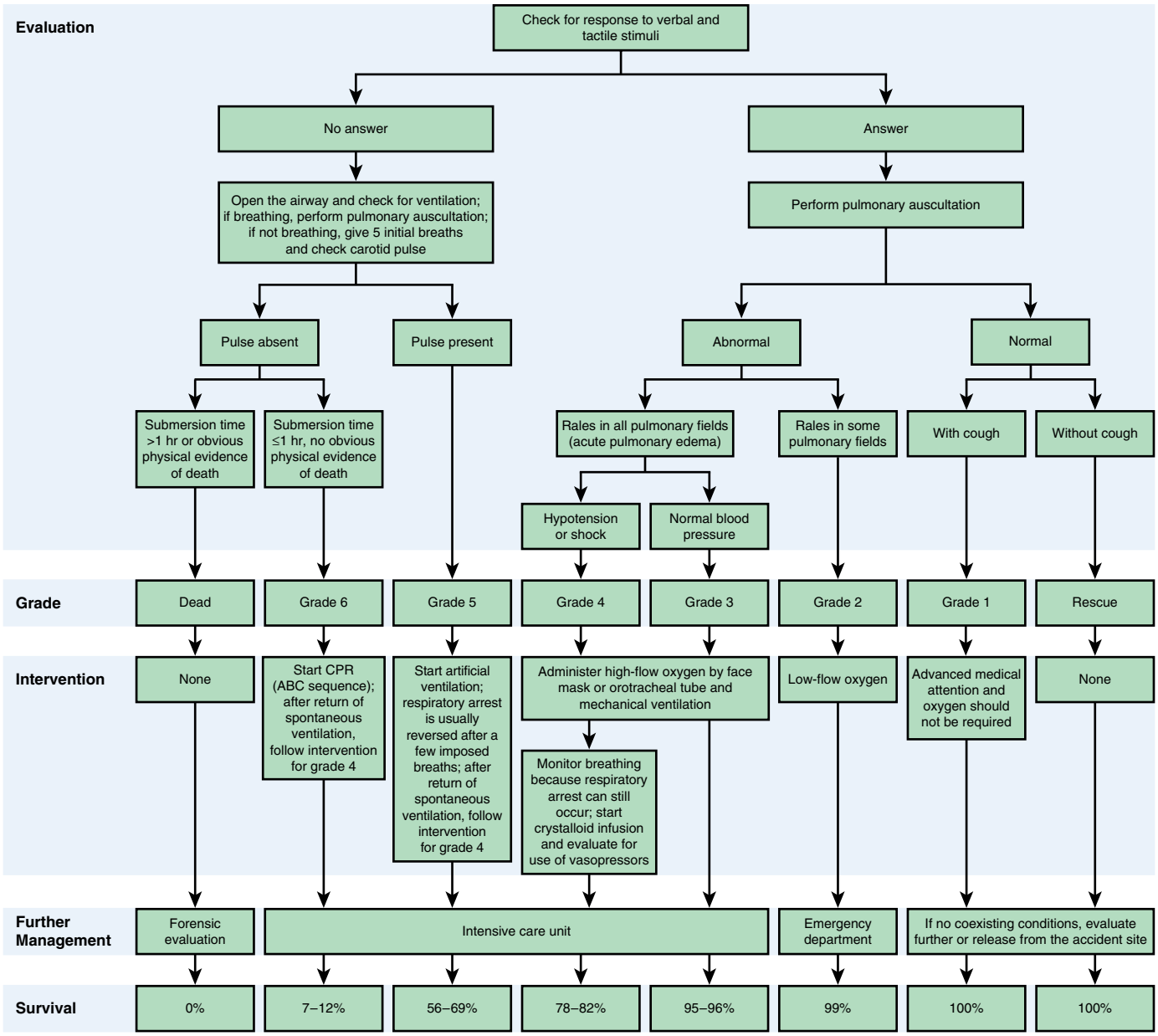

Fig. 88.4 Treatment of persons who have drowned, with classification system. *(From Szpilman D, Bierens J, Handley A, Orloweski J. Drowning. N Engl J Med 2012;366:2102–2110. Fig. 1.)*

Initial Evaluation and Resuscitation

See Chapter 79.

Immediate resuscitation at the submersion site, even before arrival of emergency medical services (EMS) personnel, is the most effective method to improve outcomes after drowning. Neurologic prognosis is significantly improved by prompt bystander CPR and activation of prehospital ALS. The goal is to reverse the anoxia from submersion and limit secondary hypoxic injury after submersion. Every minute that passes without the reestablishment of adequate breathing and circulation dramatically decreases the possibility of a good outcome. When safe for the victim and the rescuer, institution of in-water resuscitation for nonbreathing victims by trained personnel may improve the likelihood of survival. In-water resuscitation protocols recommend performing up to 1 minute of ventilation before attempting to bring the unconscious and apneic patient to shore. For patients in deep water, in-water resuscitation requires rescue flotation equipment or at least 2 rescuers. Practically, victims usually need to be extricated from the water as quickly as possible so that effective CPR can be provided.

Initial resuscitation must focus on rapidly restoring oxygenation, ventilation, and adequate circulation. The airway should be clear of vomitus and foreign material, which may cause obstruction or aspiration. Abdominal thrusts *should not* be used for fluid removal, because many victims have a distended abdomen from swallowed water; abdominal thrusts may increase the risk of regurgitation and aspiration. In cases of suspected airway foreign body, chest compressions or back blows are preferable maneuvers.

The cervical spine (C-spine) should be protected in anyone with potential traumatic neck injury (see Chapters 80 and 81). Cervical spine injury is a rare concomitant injury in drowning; approximately 0.5% of submersion victims have C-spine injuries, and history of the event and victim's age should guide suspicion of C-spine injury. Drowning victims with C-spine injury are usually preteens or teenagers whose drowning event involved diving, a motor vehicle crash, a fall from a height, a water sport accident, child abuse, or other clinical signs of serious traumatic injury. In such cases, the neck should be maintained in a neutral position and protected with a well-fitting cervical collar. Patients

rescued from unknown circumstances may also warrant C-spine precautions. In low-impact submersions, spinal injuries are exceedingly rare, and routine spinal immobilization is not warranted.

If the victim has ineffective respirations or apnea, ventilatory support must be initiated immediately. Mouth-to-mouth or mouth-to-nose breathing by trained bystanders often restores spontaneous ventilation. As soon as it is available, supplemental oxygen should be administered to all victims. Positive pressure bag-mask ventilation with 100% inspired oxygen should be instituted in patients with respiratory insufficiency. If apnea, cyanosis, hypoventilation, or labored respiration persists, trained personnel should perform endotracheal intubation as soon as possible. Intubation is also indicated to protect the airway in patients with depressed mental status or hemodynamic instability. Hypoxia must be corrected rapidly to optimize the chance of recovery.

Concurrent with securing of airway control, oxygenation, and ventilation, the child's cardiovascular status must be evaluated and treated according to the usual resuscitation guidelines and protocols. Heart rate and rhythm, blood pressure, temperature, and end-organ perfusion require urgent assessment. CPR should be instituted immediately in pulseless, bradycardic, or severely hypotensive victims, as studies have shown receiving bystander CPR is associated with neurologically favorable survival in all age groups. Continuous monitoring of the electrocardiogram (ECG) allows appropriate diagnosis and treatment of arrhythmias. Slow capillary refill, cool extremities, and altered mental status are potential indicators of shock (see Chapter 85).

Recognition and treatment of hypothermia are unique aspects of cardiac resuscitation in the drowning victim. Core temperature must be evaluated, especially in children, because moderate to severe hypothermia can depress myocardial function and cause arrhythmias. Wet clothing should be removed to prevent ongoing heat losses, although in the hemodynamically stable patient, rewarming should be initiated in the controlled environment of the receiving ED or PICU. Unstable patients (i.e., arrhythmias) should be warmed to 34°C (93.2°F), taking care not to overheat (see Chapter 90, Fig. 90.2).

Often, intravenous (IV) fluids and vasoactive medications are required to improve circulation and perfusion. Vascular access should be established as quickly as possible for the administration of fluids or pressors. Intraosseous catheter placement is a potentially lifesaving vascular access technique that avoids the delay usually associated with multiple attempts to establish IV access in critically ill children. Epinephrine is the initial drug of choice in victims with brady-asystolic cardiopulmonary arrest (IV dose is 0.01 mg/kg using the 1:10,000 [0.1 mg/mL] solution given every 3-5 minutes, as needed). Epinephrine can be given intratracheally (endotracheal tube dose is 0.1-0.2 mg/kg of 1:1,000 [1 mg/mL] solution) if no IV access is available. An intravascular bolus of lactated Ringer solution or 0.9% normal saline (10-20 mL/kg) is often used to augment preload; repeated doses may be necessary.

Hospital-Based Evaluation and Treatment

Most pediatric drowning victims should be observed for at least 4-6 hours, even if they are asymptomatic on presentation to the ED. Serial monitoring of vital signs and oxygenation by pulse oximetry, repeated pulmonary examination, and neurologic assessment should be performed in all drowning victims. Additional studies may also be warranted, depending on the specific circumstances (possible abuse or neglect, traumatic injuries, or suspected intoxication). Almost half of asymptomatic or minimally symptomatic alert children (who did not require ALS in the prehospital setting or who have an initial ED Glasgow Coma Scale [GCS] score of ≥13) experience some level of respiratory distress or hypoxemia progressing to pulmonary edema during the initial 4-6 hours after submersion. Most alert children with early respiratory symptoms respond to oxygen and, despite abnormal initial radiographs, become asymptomatic with a return of normal room-air pulse oximetry oxyhemoglobin saturation (Spo_2) and pulmonary examination by 4-6 hours. Subsequent delayed respiratory deterioration is extremely unlikely in such children. Low-risk patients who present with normal mental status and normal respiratory function may be considered for discharge after 4-6 hours of observation if there is no deterioration of respiratory symptoms and appropriate follow-up can be ensured.

Initial ED management of symptomatic patients with respiratory distress or lethargy may require further testing depending on clinical severity. Initial studies may include blood gas monitoring, a complete metabolic panel, a complete blood count, and chest radiography. Toxicology tests, including drug and alcohol levels, should be considered when appropriate.

There has been much misinformation about **dry drowning** and **secondary drowning**. These are misnomers and not accepted medical terms. Dry drowning has been described historically as cases in which no water was found in the lungs at autopsy. Secondary drowning has been used interchangeably to describe patients who clinically worsen due to pulmonary edema after aspiration of water. These terms cause harm by misdiagnosing cases of sudden death as drowning when there is an alternative diagnosis. They also cause confusion when describing and monitoring drowning events. Drowning victims with no or minimal clinical signs of distress will either improve or worsen within 4–6 hours, and patients will not unexpectedly die of drowning days or weeks later without preceding signs.

Cardiorespiratory Management

For children who are not in cardiac arrest, the level of respiratory support should be appropriate to the patient's condition and is a continuation of prehospital management. Frequent assessments are required to ensure that adequate oxygenation, ventilation, and airway control are maintained (see Chapter 86). Hypercapnia should generally be avoided in potentially brain-injured children. Patients with altered mental status, actual or potential hypoventilation, or markedly elevated work of breathing should receive mechanical ventilation to avoid hypercapnia and decrease the energy expenditures of labored respiration. Noninvasive ventilation (NIV) strategies such as bilevel positive airway pressure (BiPAP) and high-flow nasal canula (HFNC) have been associated with rapid improvement in the early phase of oxygenation in patients without altered mental status to reduce mortality.

Measures to stabilize cardiovascular status should also continue. Conditions contributing to myocardial insufficiency include hypoxic-ischemic injury, hypoxia, hypothermia, acidosis, high airway pressures during mechanical ventilation, alterations of intravascular volume, and electrolyte disorders. Heart failure, shock, arrhythmias, or cardiac arrest may occur. Continuous ECG monitoring is mandatory for recognition and treatment of arrhythmias (see Chapter 484).

The provision of adequate oxygenation and ventilation is a prerequisite to improving myocardial function. Patients should be given 100% inspired oxygen until oxygen saturation can be reasonably measured. Fluid resuscitation and inotropic agents are often necessary to improve heart function and restore tissue perfusion (see Chapter 79). Increasing preload with IV fluids may be beneficial through improvements in stroke volume and cardiac output. Overzealous fluid administration, however, especially in the presence of poor myocardial function, can worsen pulmonary edema.

For patients with persistent cardiopulmonary arrest on arrival in the ED after *non–icy water* drowning, the decision to withhold or stop resuscitative efforts can be addressed by review of the history and the response to treatment. Because there are reports of good outcome after ongoing CPR in the ED, most drowning victims should be treated aggressively on presentation. However, for children who do not show ready response to aggressive resuscitative efforts, the need for prolonged ongoing CPR after non–icy water submersion almost invariably predicts death or persistent vegetative state. Consequently, in most cases, discontinuation of CPR in the ED is probably warranted for victims of non–icy water submersion who do not respond to resuscitation within 25-30 minutes. Final decisions regarding whether and when to discontinue resuscitative efforts must be individualized, with the understanding that the possibility of good outcome is generally very low with protracted resuscitation efforts. In circumstances of severe ARDS or cardiac insufficiency, extracorporeal life support has been successfully employed.

Neurologic Management

Drowning victims who present to the hospital awake and alert usually have normal neurologic outcomes. In comatose victims, irreversible

CNS injury is highly likely. The most critical and effective neurologic intensive care measures after drowning are rapid restoration and maintenance of adequate oxygenation, ventilation, and perfusion. Core body temperature and glucose management are important modulators of neurologic injury after hypoxia-ischemia.

Comatose drowning patients are at risk for intracranial hypertension. There is little evidence that ICP monitoring and therapy to reduce intracranial hypertension improve outcomes for drowning victims. Patients with elevated ICP usually have poor outcomes—either death or persistent vegetative state. Children with normal ICP can also have poor outcomes, although less frequently. Conventional neurologic intensive care therapies, such as fluid restriction; hyperventilation; and administration of muscle relaxants, osmotic agents, diuretics, barbiturates, and corticosteroids, have not been shown to benefit the drowning victim, either individually or in combination. There is some evidence that these therapies may reduce overall mortality but increase the number of survivors with severe neurologic morbidity.

Seizures after hypoxic brain injury are common, although detection is often difficult in the ICU because these patients are frequently sedated. Continuous electroencephalographic (EEG) monitoring in critically ill patients revealed a 13% incidence of seizures, 92% of which were exclusively nonconvulsive. However, EEG monitoring has only limited value in the management of drowning victims, except to detect seizures or as an adjunct in the clinical evaluation of brain death (see Chapter 83). Seizures should be treated, if possible, to stabilize cerebral oxygen use, although benefits are inconclusive. Fosphenytoin or phenytoin (loading dose of 10-20 mg of phenytoin equivalents/kg, followed by maintenance dosing with 5-8 mg of phenytoin equivalents/kg/day in two or three divided doses; levels should be monitored) may be considered as an anticonvulsant; it may have some neuroprotective effects and may mitigate neurogenic pulmonary edema. Benzodiazepines, barbiturates, and other anticonvulsants may also have some role in seizure therapy, although no conclusive studies have shown improved neurologic outcome.

With optimal management, many initially comatose children can have impressive neurologic improvement, but usually do so within the first 24-72 hours. Unfortunately, half of deeply comatose drowning victims admitted to the PICU die of their hypoxic brain injury or survive with severe neurologic damage. Deeply comatose drowning victims who do not show substantial improvement on neurologic examination after 24-72 hours and whose coma cannot be otherwise explained should be seriously considered for limitation or withdrawal of support.

Additional Management Issues

Many drowning victims may have traumatic injury (see Chapter 80), especially if their drowning event involved participation in high-energy water sports such as personal watercraft, boating, diving, or surfing. A high index of suspicion for such injury is required. *Spinal precautions should be maintained in victims with altered mental status and suspected traumatic injury.*

Hypoxic-ischemic injury can have multiple systemic effects, although protracted organ dysfunction is uncommon in the absence of severe CNS injury. Hyperglycemia is associated with a poor outcome in critically ill pediatric drowning victims. Glucose control in patients after drowning should be focused on avoiding hypoglycemia, hyperglycemia, and wide or rapid fluctuations in serum glucose to prevent further harm.

Manifestations of acute kidney injury may be seen after hypoxic-ischemic injury (see Chapter 572). Diuretics, fluid restriction, and dialysis are occasionally needed to treat fluid overload or electrolyte disturbances; renal function usually normalizes in survivors. Rhabdomyolysis after drowning has been reported.

Profuse bloody diarrhea and mucosal sloughing usually portend a grim prognosis; conservative management includes bowel rest, nasogastric suction, and gastric pH neutralization. Nutritional support for most drowning victims is usually not difficult, because most children either die or recover quickly and resume a normal diet within a few days. Enteral tube feeding or parenteral nutrition is occasionally indicated in children who do not recover quickly.

Hyperthermia after drowning or other types of brain injury may increase the risk of mortality and exacerbate hypoxic-ischemic CNS damage. Almost half of drowning victims have a fever during the first 48 hours after submersion. Hyperthermia is usually not caused by infection and resolves without antibiotics in approximately 80% of patients. Generally, prophylactic antibiotics are not recommended. However, there is general consensus that fever or hyperthermia (core body temperature >37.5°C [99.5°F]) in comatose drowning victims resuscitated from cardiac arrest should be prevented at all times in the acute recovery period (at least the first 24-48 hours).

Psychiatric and psychosocial sequelae in the family of a pediatric drowning victim are common. Grief, guilt, and anger are typical among family members, including siblings. Divorce rates increase within a few years of the injury, and parents often report difficulties with employment or substance abuse. Friends and family may blame the parents for the event. Professional counseling, pastoral care, or social work referral should be initiated for drowning victims and their families.

Hypothermia Management

Attention to core body temperature starts in the field and continues during transport and in the hospital. The goal is to prevent or treat moderate or severe hypothermia. Damp clothing should be removed from all drowning victims. Rewarming measures are generally categorized as passive, active external, or active internal (see Chapter 90). **Passive rewarming measures** can be applied in the prehospital or hospital setting and include the provision of dry blankets, a warm environment, and protection from further heat loss. These should be instituted as soon as possible for hypothermic drowning victims who have not had a cardiac arrest.

Full CPR with chest compressions is indicated for hypothermic victims if no pulse can be found or if narrow complex QRS activity is absent on ECG (see Chapters 79 and 90). When core body temperature is <30°C (86°F), resuscitative efforts should proceed according to the American Heart Association guidelines for CPR, but IV medications may be given at a lower frequency in moderate hypothermia because of decreased drug clearance. When ventricular fibrillation is present in severely hypothermic victims (core temperature <30°C [86°F]), defibrillation should be initiated, but may not be effective until the core temperature is ≥30°C (86°F), at which time successful defibrillation may be more likely.

Significant controversy surrounds the discontinuation of prolonged resuscitative efforts in hypothermic drowning victims. Body temperature should be considered before resuscitative efforts are terminated. Other considerations include whether the victim may have been immersed before submerged, whether water was icy, or the cooling was very rapid with fast-flowing cold water. Victims with profound hypothermia may appear clinically dead, but full neurologic recovery is possible, although rare. Attempts at lifesaving resuscitation should not be withheld based on initial clinical presentation unless the victim is obviously dead (dependent lividity or rigor mortis). Rewarming efforts should usually be continued until the temperature is 32–34°C (89.6–93.2°F); if the victim continues to have no effective cardiac rhythm and remains unresponsive to aggressive CPR, resuscitative efforts can be discontinued.

Complete rewarming is not indicated for all arrest victims before resuscitative efforts are abandoned. Discontinuing resuscitation in victims of non–icy water submersion who remain asystolic despite 30 minutes of CPR is probably warranted. Physicians must use their individual clinical judgment about deciding to stop resuscitative efforts, taking into account the unique circumstances of each incident.

Once a drowning victim has undergone successful CPR after a cardiac arrest, temperature management should be carefully considered and body temperature continuously monitored. In victims in whom resuscitation duration was brief and who are awake soon after resuscitation, attempts to restore and maintain normothermia are warranted. Careful monitoring is necessary to prevent unrecognized worsening hypothermia, which can have untoward consequences.

For drowning victims who remain comatose after successful CPR, more contentious issues include rewarming of hypothermic patients and controlled application of therapeutic hypothermia. Although there is no evidence basis or opinion consensus, many investigators

cautiously recommend that hypothermic drowning victims who remain unresponsive because of hypoxic-ischemic encephalopathy after restoration of adequate spontaneous circulation should not be actively rewarmed to normal body temperatures. Active rewarming should be limited to victims with core body temperatures <32°C (89.6°F), but temperatures 32–37.5°C (89.6–99.5°F) should be allowed without further rewarming efforts.

More controversial is the **induction of therapeutic hypothermia** in drowning victims who remain comatose because of hypoxic-ischemic encephalopathy after CPR for cardiac arrest. *A specific recommendation for therapeutic hypothermia, especially in children, is not yet generally accepted.* The Advanced Life Support Task Force of the International Liaison Committee on Resuscitation (2002) did not recommend therapeutic hypothermia in drowned children resuscitated after cardiopulmonary arrest, citing insufficient evidence and older studies demonstrating a potential deleterious effect in pediatric drowning victims. Several subsequent studies evaluating extracorporeal membrane circulation, rewarming, and therapeutic hypothermia in pediatric and adult drowning patients have shown no significant improvement in neurologic outcome or mortality.

The Therapeutic Hypothermia After Out-of-Hospital Pediatric Cardiac Arrest (THAPCA) randomized controlled trial (RCT) investigators analyzed post hoc the findings of *targeted temperature management* (TTM) in pediatric comatose survivors of out-of-hospital cardiac arrest caused by drowning. Drowning comprised 28% of the landmark pediatric TTM (33°C vs 36.8°C) RCT, and the authors' principal observation is that targeting hypothermia, compared with targeting normothermia, did not result in better survival.

PROGNOSIS

The outcomes for drowning victims are remarkably bimodal: The great majority of victims either have a good outcome (intact or mild neurologic sequelae) or a poor outcome (severe neurologic sequelae, persistent vegetative state, or death), with very few exhibiting intermediate neurologic injury at hospital discharge. Subsequent evaluation of good-outcome survivors may identify significant persistent cognitive deficits. Of hospitalized pediatric drowning victims, 15% die and as many as 20% survive with severe permanent neurologic damage.

Strong predictors of outcome are based on the incident and response to treatment at the scene. Intact survival or mild neurologic impairment has been seen in 91% of children with submersion duration <5 minutes and in 87% with resuscitation duration <10 minutes. Children with normal sinus rhythm, reactive pupils, or neurologic responsiveness at the scene virtually always had good outcomes (99%). Poor outcome is highly likely in patients with deep coma, apnea, absence of pupil responses (fixed dilated pupils), and hyperglycemia in the ED; with submersion durations >10 minutes; and with failure of response to CPR given for 25 minutes. In one comprehensive case series, all children with resuscitation durations >25 minutes either died or had severe neurologic morbidity, and all victims with submersion durations >25 minutes died. Long-term health-related quality of life and school performance in those who had received either bystander- or emergency medical service personnel–initiated CPR were high if their submersion duration was <5 minutes. Higher morbidity, higher mortality, and lower quality of life were reported in patients with >10 minutes submersion duration. In several studies of pediatric drowning, submersion duration was the best predictor of outcome and water temperature was not. However, there are rare case reports of intact recovery after non–icy water drowning with longer submersion or resuscitation duration.

The GCS score has some limited utility in predicting recovery. Children with a score ≥6 on hospital admission generally have a good outcome, whereas those with a score ≤5 have a much higher probability of poor neurologic outcome. Improvement in the GCS score during the first several hours of hospitalization may indicate a better prognosis. Overall, early GCS assessments fail to adequately distinguish children who will survive intact from those with major neurologic injury.

Neurologic examination and progression during the first 24-72 hours are the best prognosticators of long-term CNS outcome. Children who regain consciousness within 48-72 hours, even after prolonged resuscitation, are unlikely to have serious neurologic sequelae. Laboratory and technologic methods to improve prognostication have not yet proved superior to neurologic examination. Serial neurologic evaluations after CPR should be performed over the ensuing 48-72 hours, with consideration given to limitation or withdrawal of support in patients who do not have significant neurologic recovery, even though this may occur before absolute prognostic certainty is achieved. Patients with minimal improvement during this initial period rarely show significant subsequent neurologic recovery despite aggressive resuscitation efforts and remain in a persistent vegetative state or die. Survivors with severe neurologic limitations necessitate neurorehabilitation to restore function and facilitate psychomotor development and prevent long-term damage caused by contractures, deformities, or scoliosis.

PREVENTION

The most effective way to decrease the injury burden of drowning is prevention. Drowning is a multifaceted problem, but several evidence-based preventive strategies are effective. The pediatrician has a prime opportunity to identify and inform families at risk of these strategies through anticipatory guidance. Advocacy should focus on anticipatory guidance regarding the appropriate supervision of children, access to swim lessons, presence of lifeguards, barriers to swimming pools, and use of PFDs. A family-centered approach to anticipatory guidance for water safety helps explore and identify the water hazards that each family is exposed to in their environment. The practitioner can then discuss the best tools and strategies for prevention that are relevant for the family. It is important to identify the risk both in and around the home and in other locations they may frequent, often when vacationing, such as vacation or relatives' homes. If the family recreates near or on open water, they also need to learn about safety around boats and open water. In a rural environment, water collection systems and natural bodies of water may pose great risk.

Parents must build layers of water protection around their children. Table 88.1 provides an approach to the hazards and preventive strategies relevant to the most common sources of water involved in childhood drowning. A common preventive strategy for exposure to all water types and all ages is ensuring **appropriate supervision**. Pediatricians should define for parents what constitutes appropriate supervision at the various developmental levels of childhood. Many parents either underestimate the importance of adequate supervision or are simply unaware of the risks associated with water. Even parents who say that constant supervision is necessary will often admit to brief lapses while their child is alone near water. Parents also overestimate the supervisory abilities of older siblings; many bathtub drownings occur when an infant or toddler is left with a child <5 years old.

Drowning most often occurs quickly and quietly during periods of inadequate supervision. Supervisory behavior is composed of three components: proximity, attention, and continuity. The caregiver must be alert, must not be consuming alcohol or other drugs or socializing, and must be attentive and focused entirely on watching the child. If the child cannot swim independently, *touch supervision* is required, meaning that the caregiver should always be within arm's reach. Adolescents require active adult supervision and avoidance of alcohol or drug use during water activities.

Learning to swim offers another layer of protection. Children may start swim lessons at an early age that are developmentally appropriate and aimed at the individual child's readiness and skill level. Swim lessons are beneficial and provide some level of protection to young children. A study from Bangladesh, where drowning accounts for 20% of all deaths in children age 1-4 years, showed that swim lessons and water safety curricula are cost-effective and led to a decrease in mortality from drowning. As with any other water safety intervention, parents need to know that swimming lessons and acquisition of swim skills cannot be solely relied on to prevent drowning. *No child can be drown-proof.* A supervising caretaker should be aware of where and how to get help and know how to safely rescue a child in trouble. Because only those trained in water rescue can safely attempt it, families should be encouraged to swim in designated areas only when and where a lifeguard is on duty.

Table 88.1 Approach to Prevention Strategies for Drowning

	HOME	RECREATION	NEIGHBORHOOD
Water hazards	• Swimming pools • Ponds • Bathtubs • Large buckets • Drain entrapment	• Playing in water (swimming, wading) • Playing near water • Being on water (boating)	• Irrigation ditches • Watering holes • Water drainage

Common risks	• Lapse in supervision
	• Unexpected toddler exposure
	• Delayed discovery of child
	• Reliance on water wings or pool toys
	• Reliance on sibling or bath seat for bathing supervision
	• Epilepsy
	• Autism
	• ADHD
	• LQTS
		• Lapse in supervision
		• Change in weather
		• Unfamiliarity with or change(s) in water conditions:
		  • Steep drop-off
		  • Current/tide
		  • Low temperature
		• Alcohol and other drug use
		• Peer pressure
			• Lapse in supervision, particularly when caregiver is socializing
			• Risky behavior when with peers

Prevention strategies	• Recognize hazards and risks • Provide constant adult supervision around water • Install 4-sided, isolation locked fencing of pools • Install rescue equipment and phone at poolside • Learn swimming and water survival skills • Avoid unsupervised baths in older child/teen with seizure disorder; instead, shower • Learn first aid and CPR	• Provide constant adult supervision • Swim in lifeguarded areas • Know when and how to wear US Coast Guard–approved PFDs • Avoid alcohol and other drugs • Learn swimming and water survival skills • Teach children about water safety • Be aware of current weather and water conditions • Buddy system • Learn first aid and CPR	• Identify hazardous bodies of water • Prevent access to water with barriers • Provide fenced-in "safe area" for water recreation • Provide lifeguarded swim sites • Provide access to low-cost swim/water survival lessons

ADHD, attention deficit hyperactivity disorder; CPR, cardiopulmonary resuscitation; LQTS, long QT syndrome; PFDs, personal floatation devices.

Children and adolescents should never swim alone regardless of their swimming abilities. Even as they become more independent and participate in recreational activities without their parents, they should be encouraged to seek areas that are watched by **lifeguards**. The United States Lifesaving Association (USLA) reports that more than 75% of drownings at USLA sites occurred at times when the beaches were unguarded. It is important to emphasize that even if the child is considered a strong swimmer, the ability to swim in a pool does not translate to being safe in open water, where water temperature, currents, and underwater obstacles can present additional and unfamiliar challenges. For swimmers, supervision by lifeguards reduces drowning risk, because lifeguards monitor risk behaviors and are trained in the difficult and potentially dangerous task of rescuing drowning victims.

Two of the preventive strategies listed in Table 88.1 deserve special mention. The most vigorously evaluated and effective drowning intervention applies to swimming pools. Compared with no fencing, installation of four-sided **isolation fencing** surrounding in-ground and aboveground pools with a secure, self-locking gate decreases the number of pool immersion injuries among young children by more than 50%. Guidelines for appropriate fencing, provided by the U.S. Consumer Product Safety Commission (CPSC), are very specific; they were developed through testing of active toddlers in a gymnastics program on their ability to climb barriers of different materials and heights, and recent studies show them to be effective in preventing drowning in young children. In families who have a pool on their property, caregivers often erroneously believe that if a child falls into the water, there will be a loud noise or splash to alert them. Unfortunately, these events are usually silent, delaying timely rescue. This finding highlights the need for a fence that separates the pool from the house, not just surrounds the entire property. The CPSC recommends power safety covers be installed on pools, as well as door alarms if the pool is not completely separated from the house and the yard by a fence. Entrapment and hair entanglement in open drains or pipes are other risks commonly associated with drowning in the pediatric population; special drain covers, safety vacuum release systems, and filter pumps with multiple drains can help prevent this.

The use of U.S. Coast Guard–approved **lifejackets or PFDs** should be advised with all families spending time around open water, not just those who consider themselves boaters. A PFD should be chosen with respect to the weight of the child and the proposed activity. Young children should wear PFDs that will float their head up. Parents should be urged to wear PFDs as well, because their use of PFDs is associated with greater use by their children. Toys such as water wings and "floaties" should not be relied on as drowning prevention measures. The use of life jackets decreases boat-related drowning morbidity and mortality by 50%; unfortunately, their use remains low.

Effective preventive efforts must also consider **cultural practices**. Different ethnic groups may have certain attitudes, beliefs, dress, or other customs that may affect their water safety. The higher drowning risk of minority children needs to be addressed by community-based prevention programs.

In addition to anticipatory guidance, pediatricians can play an active role in drowning prevention by participating in advocacy efforts to improve legislation for pool fencing, PFD use, and alcohol consumption in various water activities. Several counties in the United States, Australia, and New Zealand have laws requiring isolation fencing for pools. Their effectiveness has been limited by a lack of enforcement. Similarly, all states have boating-under-the-influence laws but, similarly, rarely enforce them. Furthermore, efforts at the community level may be needed to ensure the availability of swimming lessons for underserved populations and lifeguarded swim areas.

The Drowning Chain of Survival refers to a series of steps that, when followed, attempt to reduce mortality associated with drowning. The steps of the chain include prevent drowning, recognize distress, provide flotation, remove from water, and provide care as needed. These interventions may be used by the drowning victim for self-rescue or via bystanders who recognize child distress, initiate rescue, and provide resuscitation. The timeline shows that rescue and resuscitation must occur within minutes to save lives, and care should be taken by rescuers to not become victims themselves.

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Chapter 89

Burn Injuries

Tina L. Palmieri

Burns are among the top five leading causes of *unintentional injury* in children, after motor vehicle crashes, suffocation, drowning, and poisoning. There has been a decline in the incidence of burn injury requiring medical care that has coincided with a stronger focus on burn treatment and prevention, increased fire and burn prevention education, greater availability of regional treatment centers, widespread use of smoke detectors, greater regulation of consumer products and occupational safety, and societal changes such as reductions in smoking and alcohol abuse.

EPIDEMIOLOGY

Approximately 1.1 million people in the United States require medical care for burn injuries each year, with over 100,000 children admitted to a hospital or treated in the emergency department (ED). **Fires** remain a major cause of mortality in children, but children <14 years old have a lower relative risk of dying in a fire than the general population.

Thermal burns are caused when an external heat source comes in contact with the skin and tissues causing injury; thermal burns may occur from contact with hot surfaces, hot liquids, steam, or flame. **Scald burns** are most prevalent in children ≤4 years old and account for 65% of burn-related admissions in this age-group. Although the incidence of hot water scalding has been reduced by legislation requiring water heaters to be preset at 48.9°C (120°F), scald injury remains the leading cause of hospitalization for burns in this age-group. **Steam** inhalation used as a home remedy to treat respiratory infections is a rare potential cause of burns. **Flame burns** are the most common cause of burn injury in all age-groups ≥5 years old. Electrical and chemical burns are also more common in older children and adults than in young children. **Clothing ignition** events have declined since passage of the Federal Flammable Fabric Act requiring sleepwear to be flame-retardant. Polyester is the fabric most resistant to ignition by a small flame source. Polyester burns deeply as it melts, but it self-extinguishes when the flame source is removed. Cotton, on the other hand, continues to burn after the flame source has been removed, resulting in large, deep burns. Polyester melts downward, sparing the face and respiratory tract; cotton burns upward toward the face. Pellet stoves, glass front stoves, and flat top stoves are frequent sources of hand burns in children, as is contact with hot hair appliances, such as curling irons and hair straighteners. Approximately 18% of burns are the result of **child abuse** (usually scalds), making it important to assess the pattern and site of injury and their consistency with the patient's history (see Chapter 17). **Friction burns** from treadmills are also a problem. Hands are the most commonly injured sites, with burns ranging from deep second-degree to fourth-degree with tendon disruption and fractures from the friction injury. *Anoxia,* not the actual burn, is a major cause of morbidity and mortality in house fires.

Review of the history usually shows a common pattern: a v-shaped distribution of the scald burns to the chest and abdomen if liquid is pulled from a table or stove, burns in the pant leg area if clothing ignites, burns in a splash pattern from a hot liquid spill, and burns on the palm of the hand from contact with a hot stove or curling iron. However, **glove or stocking burns** of the hands and feet; single-area deep burns on the trunk, buttocks, or back; and small, full-thickness burns (e.g., cigarette burns) in young children should raise the suspicion of child abuse.

Burn care involves a range of activities: prevention, acute care and resuscitation, wound management, pain relief, reconstruction, rehabilitation, and psychosocial adjustment. Children with massive burns require early and appropriate psychologic and social support as well as resuscitation. Surgical debridement, wound closure, and rehabilitative efforts should be instituted concurrently to promote optimal outcomes. To maximize survival, the clinical approach includes aggressive surgical removal of devitalized tissue with timely skin closure via grafting, infection control, and judicious use of antibiotics; life support with endotracheal intubation and mechanical ventilation; and use of early enteral nutrition. Children who have sustained burn injuries differ in appearance from their peers, necessitating supportive efforts for reentry to school and social and sporting activities.

PREVENTION

The aim of burn prevention is a continuing reduction in the number of serious burn injuries (Table 89.1). Effective first aid and triage can decrease both the extent (area) and the severity (depth) of injuries. The use of flame-retardant clothing and smoke detectors, control of hot water temperature (thermostat settings) to 48.9°C (120°F) within buildings, and prohibition of cigarette smoking have been partially successful in reducing the incidence of burn injuries. Treatment of children with significant burn injuries in dedicated burn centers facilitates medically effective care, improves survival, and leads to greater cost efficiency. Survival of at least 80% of patients with burns of 90% of the total body surface area (TBSA) is possible for children and young adults. Death is more likely in children with irreversible anoxic brain injury sustained at the time of the burn. Some burns occur on a seasonal basis, including:

Winter:
- Glass-front fireplaces/pellet stoves and radiators increase hand burns
- Treadmill injuries as more people exercise inside—child imitates adults or young child touches belt
- Soup scald burns from spilling liquid while removing bowl from microwave

Summer:
- Fireworks, sparklers—temperatures reach 537.8°C (1,000°F)
- Burn contact with hot grill; hand/feet burn from hot embers
- Burns from children walking or falling into a campfire
- Lawnmowers

Spring/Fall:
- Burning leaves
- Gasoline burns
- Tap water scalds
- House fires from propane heater explosion

Pediatricians can play a major role in preventing the most common burns by educating parents and healthcare providers. Simple, effective, efficient, and cost-effective preventive measures include the use of appropriate clothing and smoke detectors and the planning of routes for emergency exit from the home. The National Fire Protection Association (NFPA) recommends replacing smoke detector batteries

Table 89.1 Burn Prophylaxis

PREVENT FIRES
Install and use smoke detectors.
Control the hot water thermostat; maximum water temperature should be 48.9°C (120°F).
Keep fire, matches, and lighters out of the reach of children.
Avoid cigarette smoking, especially in bed.
Do not leave lit candles unattended.
Keep hair appliances such as curling irons and straighteners out of the reach of children.
Use caution when cooking, especially with oil.
Keep cloth items off heaters.
PREVENT INJURY
Stop, drop, and roll (do not run) if clothing catches fire; wrap in a blanket.
Practice escape procedures.
Crawl beneath smoke if a fire occurs indoors.
Use educational materials.*

*National Fire Protection Association pamphlets and videos.

Table 89.2 Indications for Referral to a Burn Center

Partial-thickness burns affecting >10% TBSA
Full-thickness burn affecting >5% TBSA
Third-degree burns
Electrical burns caused by high-tension wires or lightning
Chemical burns
Inhalation injury, regardless of the amount of TBSA burned
Inadequate home or social environment
Suspected child abuse or neglect
Burns to the face, hands, feet, perineum, genitals, or major joints
Burns in patients with preexisting medical conditions that may complicate the acute recovery phase
Associated injuries (fractures)

TBSA, Total body surface area.
Adapted from American Burn Association/American College of Surgeons. Guidelines for the operation of burn centers. *J Burn Care Res.* 2007;28(1):134–141 and Bettencourt AP, Romanowski KS, Joe V, et al. Updating the Burn Center Referral Criteria: Results from the 2018 eDelphi Consensus Study. *J Burn Care Res.* 2020;41(5):1052–1062.

Table 89.3 Acute Treatment of Burns

First aid, including washing of wounds and removal of devitalized tissue
Fluid resuscitation
Provision of energy requirements
Control of pain
Prevention of infection
Early excision and grafting
Prevention of excessive metabolic expenditures
Control of bacterial wound flora
Early mobility, range of motion, and strength exercises

annually and the smoke detector alarm every 10 years (or earlier, if indicated on the device).

ACUTE CARE, RESUSCITATION, AND ASSESSMENT

Indications for Admission

Burns covering >10% TBSA, burns associated with smoke inhalation, burns resulting from high-tension (voltage) electrical injuries, and burns associated with suspected child abuse or neglect should be treated emergently and referred to a burn center for definitive care (Table 89.2). Small first- and second-degree burns of the hands, feet, face, perineum, and joint surfaces may require admission if close follow-up care is difficult to provide. Children who have been in enclosed-space fires and those who have significant face and neck burns should be evaluated carefully for airway or neurologic compromise, including monitoring for 24 hours in the hospital for potential central nervous system (CNS) effects of anoxia from carbon monoxide (CO) poisoning or pulmonary effects from smoke inhalation.

First Aid Measures

Acute care should include the following measures:

1. Extinguish flames by rolling the child on the ground; cover the child with a blanket, coat, or carpet.
2. Remove smoldering clothing or clothing saturated with hot liquid. Jewelry, particularly rings and bracelets, should be removed or cut away to prevent constriction and vascular compromise during the edema phase in the first 24-72 hours after burn injury.
3. In cases of **chemical injury**, brush off any remaining chemical, if powdered or solid; then use copious irrigation or wash the affected area with water. Call the local poison control center for the neutralizing agent to treat a chemical ingestion.
4. Wash the burned area with soap and cool running water. For burns on less than 10% of the body, irrigate with cool tap water for 10-20 minutes. Significant large-burn injury (>15% TBSA) decreases body temperature control so the use of cold water is contraindicated.
5. Cover the burned area with clean, dry sheeting or dressing. Avoid using tape.
6. If the burn is caused by *hot tar,* cool the burn and then use mineral oil to remove the tar.
7. Administer analgesic medications.

Emergency Care

Supportive measures are as follows (Table 89.3 and Table 89.4):

1. Rapidly review the cardiovascular and pulmonary status and document preexisting or physiologic lesions (asthma, congenital heart disease, renal or hepatic disease).
2. Ensure and maintain an adequate airway (Fig. 89.1). For any child with a facial burn or suspected inhalation of smoke, the following actions are indicated:
   a. Start 100% oxygen and measure carboxyhemoglobin (CO) levels as well as a blood gas, because cutaneous oxygen saturations are not accurate in CO poisoning (see Chapters 79 and 86).
   b. Assess for laryngeal edema (examine mouth; assess for stridor, retractions) and intubate for evidence of significant airway compromise.
   c. Assess oxygenation to evaluate for lung damage from smoke inhalation. Bronchoscopy may be helpful in the intubated child to further delineate the extent of smoke inhalation injury. Use a humidified ventilator circuit to prevent dry secretions that can obstruct an airway.
3. Children with burns >15% TBSA require intravenous (IV) fluid resuscitation to maintain adequate perfusion. IV access is preferably obtained in a nonburned area, but if none is readily available, placing the initial line through a burn may be necessary. Monitor peripheral IV sites closely for infiltration, as extremities will become edematous after burn injury. In an emergency situation in which IV access is unattainable, an intraosseous (IO) line may be placed. The IO line should be replaced in a timely fashion with a central line, as IO needles may be unable to sustain the large fluid volume needed for major burn resuscitation. Patients with inhalation injury, regardless of the extent of TBSA burn, require large volumes of fluid for resuscitation due to insensible losses from the injured airway epithelium. Significant high-tension and electrical injuries require venous access to ensure sufficient fluid resuscitation volumes, as forced alkaline diuresis may be needed in fluid-refractory myoglobinuria to avoid renal damage. Lactated Ringer solution, 10-20 mL/kg/hr (normal saline may be used if lactated Ringer solution is not available), is initially infused until proper fluid replacement can be calculated. Consultation with a specialized burn unit should be made to coordinate fluid therapy, including the type of fluid, the preferred formula for calculation, and preferences for the use of colloid agents, particularly if transfer to a burn center is anticipated.
4. For patients with circumferential burns of the extremities, elevate the extremities and monitor perfusion (capillary refill, pulses), as compartment syndrome (see Chapter 80) may develop and require escharotomy.
5. Evaluate the child for associated injuries. Children with burns may have associated accidental traumatic injuries (fall) or nonaccidental injuries (child abuse). In cases of high-voltage electrical burn (>1,000 volts), especially if there has also been a fall from a height, injuries to the spine, bones, and thoracic or intraabdominal organs may occur (see Chapter 80). Cervical spine precautions should be observed until this injury is ruled out. If ventricular fibrillation occurs at the scene of an electrocution, cardiopulmonary resuscitation (CPR) should be instituted promptly, and cardiac monitoring started on the patient's arrival at the ED (see Chapter 79).
6. Children with burns of >15% TBSA should not initially receive oral fluids because gastric distention may develop. These children may require insertion of a nasogastric tube in the ED to prevent aspiration.
7. A Foley catheter should be inserted into the bladder to monitor urine output in children who require IV fluid resuscitation.

Table 89.4 Phases of Burn Care

PHASE AND TIMING	PHYSIOLOGIC CHANGES	OBJECTIVES
1: Resuscitation, 0-72 hours	Massive capillary leak, edema, and burn shock	Airway, breathing, and circulation optimization via accurate fluid resuscitation and thorough evaluation
2: Acute treatment phase, day 3 through discharge	Hyperdynamic and catabolic state, immunosuppression, risk of infection	Enteral nutrition to optimize wound healing; excision and biologic wound closure of full-thickness wounds with excision and grafting within 7 days of injury
3: Rehabilitation, day 1 through discharge	Gradual waning of initial catabolic state, wounds heal, scars form, and strength recovers	Maintain and restore range of motion; reduce edema; strengthen muscles; facilitate return to home, work, and school

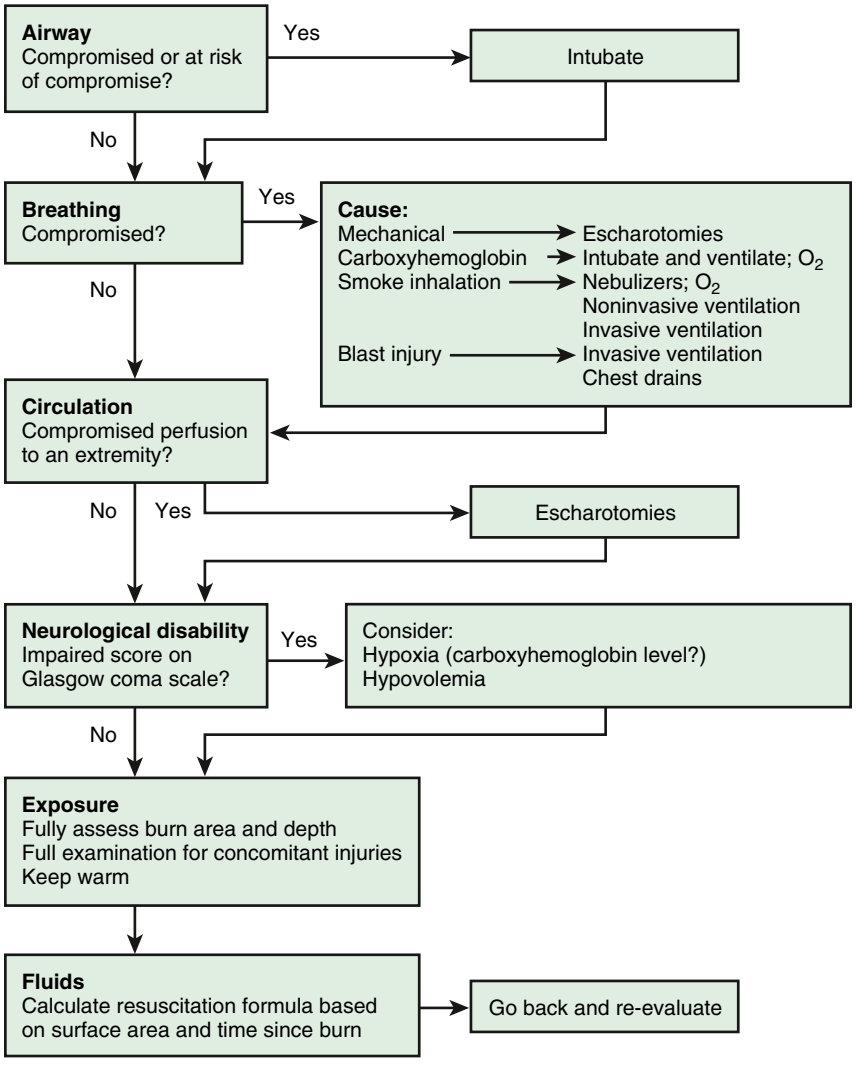

Fig. 89.1 Algorithm for primary survey of a major burn injury. (*From Hettiaratchy S, Papini R. Initial management of a major burn. I. Overview. BMJ. 2004;328:1555–1557.*)

8. In general, wounds should be wrapped with a clean sheet or dressing until it is decided whether to treat the patient on an outpatient basis or refer to an appropriate facility.
9. For children trapped in a fire, a CO measurement (carboxyhemoglobin [HbCO]) should be obtained and 100% oxygen administered until the result is known. Pulse oximetry is unreliable in CO poisoning.
10. Review child immunizations, including tetanus immunization. Use diphtheria, tetanus toxoids, and acellular pertussis (DTaP) for tetanus prophylaxis for children <7 years old, and use tetanus, diphtheria, and pertussis (TdaP) for children ≥7 years old (see Chapter 257).

Classification of Burns

Proper triage and treatment of burn injury require assessment of the extent and depth of the injury (Table 89.5 and Fig. 89.2). **First-degree burns** involve only the epidermis and are characterized by swelling, erythema, and pain (similar to mild sunburn). Tissue damage is usually minimal, and there is no blistering. Pain resolves in 48-72 hours; in a small percentage of patients, the damaged epithelium peels off, leaving no residual scars.

A **second-degree burn** involves injury to the entire epidermis and a variable portion of the dermal layer (vesicle and blister formation are characteristic). A *superficial* second-degree burn is extremely painful because many remaining viable nerve endings are exposed. Superficial

Table 89.5 Categories of Burn Depth

	FIRST-DEGREE BURN	SECOND-DEGREE BURN (PARTIAL THICKNESS)	THIRD-DEGREE BURN (FULL-THICKNESS)
Surface appearance	Dry, no blisters Minimal or no edema Erythematous Blanches, bleeds	Moist blebs, blisters Underlying tissue is mottled pink and white, with fair capillary refill Bleeds	Dry, leathery eschar Mixed white, waxy, khaki, mahogany, soot-stained No blanching or bleeding
Pain	Very painful	Very painful	Insensate centrally, edges (usually less deep) may still have sensation
Histologic depth	Epidermal layers only	Epidermis, papillary, and reticular layers of dermis May include domes of subcutaneous layers	Through all layers of the skin to subcutaneous tissue (loss of muscle, bone is fourth-degree burn)
Healing time	2-5 days with no scarring	Superficial: 5-21 days with no grafting Deep partial: 21-35 days with no infection, but scar is expected; if infected, converts to full-thickness burn	Large areas require grafting, but small areas may heal from the edges after weeks

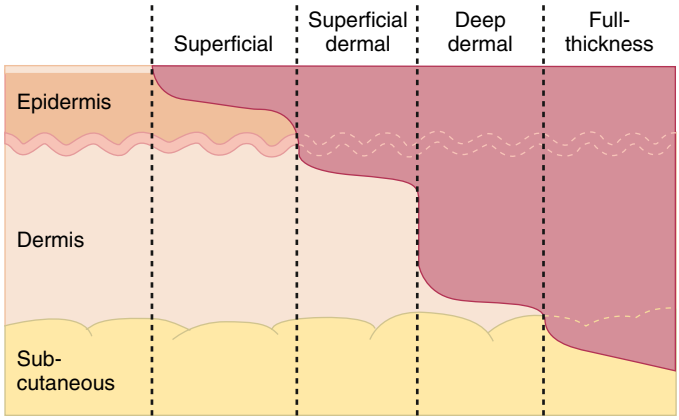

Fig. 89.2 Diagram of different burn depths. (*From Hettiaratchy S, Papini R. Initial management of a major burn. II. Assessment and resuscitation. BMJ. 2004;329:101–103.*)

second-degree burns heal in 7-14 days as the epithelium regenerates in the absence of infection. *Mid-level to deep* second-degree burns will generally heal in 14-21 days, but often result in significant scarring. Deep second-degree burns tend to be dry, pale, and white (flame) or red (scald); they are often grafted to mitigate scarring (Fig. 89.3). Pain may be less with these burns than in more superficial burns because fewer nerve endings remain viable; however, the edge of the burn, which will be less deep, will still cause pain. Fluid losses and metabolic effects of deep dermal (second-degree) burns are essentially the same as those of third-degree burns. If a blister is intact in a burned area, the burn is at least second-degree but may be deeper. Definitive diagnosis of burn depth is not possible because the blister blocks visualization of the burned tissue under the blister.

Full-thickness, or **third-degree burns**, involve destruction of the entire epidermis and dermis, leaving no residual epidermal cells to repopulate the damaged area. The wound heals by wound contraction or skin grafting. Wounds are either white or leathery (flame burn) or mottled, nonblanching, and cherry red (scald) (Fig. 89.4). The absence of painful sensation and capillary filling demonstrates the loss of nerve and capillary elements. Pain exists at the edges of the burn. Hence, using pain to determine burn depth is not accurate.

Technologies can help accurately determine the depth of burns. Laser *Doppler imaging* can be used from 25 days after the burn. It produces a color map of the affected tissue; *yellow* indicates second-degree burns, reflecting the presence of capillaries, arterioles, and venules, and *blue* reflects very low or absence of blood flow, which indicates third-degree burns. Although early reports are promising, the clinical utility of laser Doppler imaging for burn depth determination is not clearly established.

Estimation of Total Body Surface Area for a Burn

Appropriate burn charts for different childhood age-groups should be used to accurately estimate the extent of TBSA burned. The extent and depth of the burn are the largest determinants of fluid resuscitation requirements. Mortality and morbidity also depend on the extent and depth of the burn. Children have a larger surface area to mass ratio than adults, and the variable growth rate of the child's head and extremities makes it necessary to use body surface area (BSA) charts, such as that modified by Lund and Brower, to accurately calculate burn size (Fig. 89.5). Another method of estimating burn size is to employ the palm rule. The palm of the child's hand (from base of palm to fingertip) is 1% of the child's TBSA. A quick method of estimating burn size is to hold your hand up to the child's hand to gauge the area and use that to determine burn size. The **rule of nines** used in adults should only be used in children >14 years old or >20 kg as a rough estimate to institute therapy before transfer to a burn center. The rule of nines divides body regions by 9% BSA: head and neck, chest and upper back, each arm, abdomen, lower back, upper leg, and lower leg; hand or genitals (1%).

TREATMENT

Outpatient Management of Minor Burns

A patient with first- and second-degree burns <10% TBSA may be treated on an outpatient basis unless pain is uncontrolled on oral agents, the family cannot successfully complete wound care, or there are issues of child neglect or abuse. These outpatients do not require prophylactic antibiotics. Blisters should be left intact and dressed with a nonstick dressing such as Telfa or Xeroform. Topical creams do not penetrate the blister and are not indicated unless the blister ruptures. Dressings should be changed once daily, after the wound is washed with lukewarm water. Very small wounds, especially those on the face, may be treated with bacitracin ointment and left open. **Debridement** (i.e., removal) of the devitalized skin is indicated when the blisters rupture. A variety of wound dressings are available for application to second-degree burns; the affected area should be subsequently wrapped with a dry, clean dressing. Silver dressings are popular because they provide pain relief, prevent wound desiccation, reduce wound colonization, and can be left in place for 5-7 days (Table 89.6). Although silver dressings are antimicrobial, wound infections can occur beneath these dressings. Patients should be instructed to seek immediate medical care for signs and symptoms of infection (elevated temperature, malaise, pain) and should be reevaluated at least weekly by the medical team. The great majority of superficial burns heal in 7-10 days, with deep second-degree burns taking longer to heal. Burns that have not healed within 2 weeks (or clearly will not be healed in 2 weeks) have a >97% chance of developing a significant scar and should be referred to a burn center.

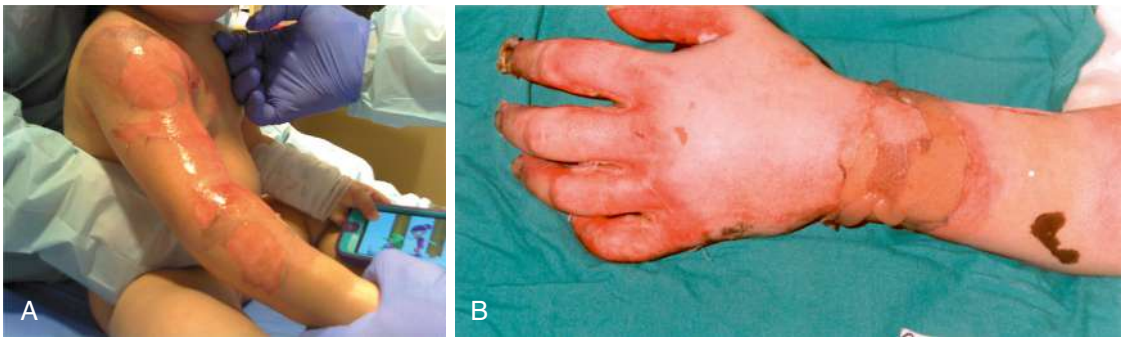

Fig. 89.3 Second-degree burns. **A**, Superficial partial-thickness (second-degree) burn, which is pink and glistening. **B**, Deep partial-thickness (second-degree) burn. The white-appearing area over the dorsum of the hand is a deep partial-thickness burn. (*From Singer AJ, Lee CC. Thermal burns. In: Walls RM, Hockberger RS, Gausche-Hill M, et al., eds. Rosen's Emergency Medicine, 9th ed. Philadelphia: Elsevier; 2018: Figs. 56.1 and 56.2, p. 717.*)

Fig. 89.4 Full-thickness (third-degree) burn over both feet. The central area is depressed and has a yellowish color indicating it is full thickness. (*Modified from Singer AJ, Lee CC. Thermal burns. In: Walls RM, Hockberger RS, Gausche-Hill M, et al., eds. Rosen's Emergency Medicine, 9th ed. Philadelphia: Elsevier; 2018: Fig. 56.3, p. 717.*)

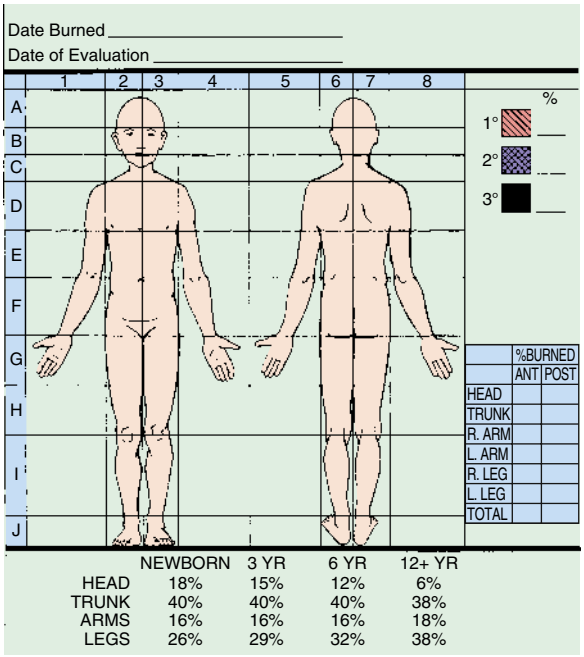

Fig. 89.5 Chart to determine developmentally related percentage of body surface area affected by burn injury. ANT, Anterior; POST, posterior; R., right; L., left. (*Courtesy Shriners Hospital, Burn Institute, Boston Unit.*)

Table 89.6 Select Silver Antimicrobial Dressings for Burns

DRESSING	CHARACTERISTIC(S)
Mepitel Ag	Silicone mesh dressing
Mepilex Ag	Foam dressing
ACTICOAT	Polyethylene nonadherent net dressing
AQUACEL Ag	Absorptive Hydrofiber
Silverlon	Knitted nylon nonadherent dressing

The palm of the hand is one of the most frequently burned areas in children, particularly toddlers. Because the skin on the palm of the hand is thicker than other parts of the body, burns to the palm often heal. Generally, blisters of the palm can be left intact unless they are already open, or they are so large that they will likely rupture (usually about 1-2 cm in height), or purulence is draining from the blister. If leaving a blister intact, inform the family to either return to the office if the blister ruptures or instruct them on how to remove the blister and apply bacitracin to the wound. If a palm burn has not healed in 2 weeks (or it is clear that it will not be healed), referral to a burn center is needed.

The depth of scald injuries is difficult to assess early, as the wounds are often reddish in color. Nonoperative treatment is appropriate initially. Generally, third-degree scald burns will become increasingly pale and white by 4-5 days post injury, whereas those that heal will be a lighter pink color. A wound that has not healed in 2 weeks will likely need grafting (Fig. 89.6). This conservative approach obviates the risk of anesthesia and unnecessary grafting.

Fluid Resuscitation

Fluid resuscitation, if required, should begin as soon as possible (at the scene, in the ED, or before transfer) after the injury has occurred because delays of as little as 30 minutes affect outcomes. Numerous formulas exist to help guide practitioners in calculating fluid resuscitation needs in patients with burns. For most children, the *Parkland formula* is an appropriate *guideline* to determine starting IV fluid resuscitation rate; however, fluids should be adjusted hourly based on the patient's response. The steps in calculating the starting rate are as follows:

1. Calculate the 24-hour fluid requirement: 4 mL lactated Ringer solution per (times) weight in kg per (times) % TBSA burned. The TBSA burned is a whole number, NOT a percentage.
2. Determine the volume of fluid to be given in the first 8 hours: for the Parkland formula, that is half of the 24-hour requirement.
3. Calculate the starting hourly infusion rate: divide the volume to be given in the first 8 hours by 8 to determine the starting rate. The

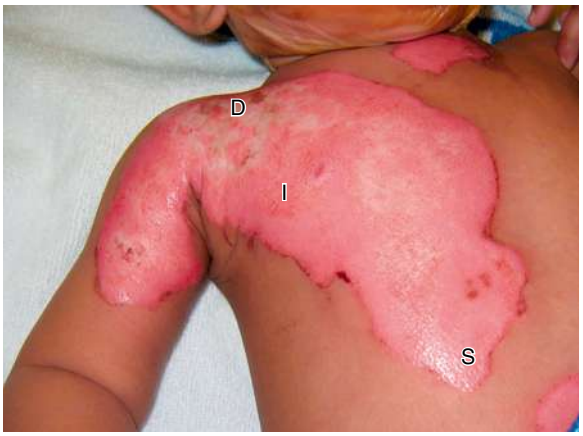

Fig. 89.6 Tea scald over the chest and shoulder of a child showing heterogeneity of burn depth. D, Deep; I, intermediate; S, superficial. (*From Enoch S, Roshan A, Shah M. Emergency and early management of burns and scalds. BMJ. 2009;338:937–941.*)

infusion rate is adjusted hourly based on urine output goals of 0.8-1 mL/hour in children <20 kg or <12 years of age and 0.4-0.5 mL/kg/hr (maximum of 30 mL/hr) in children >12 years or >20 kg.

Providers should increase the fluid rate by 10% if urine output is below the hourly target and decrease the fluids by 10% if over the target. Because major burns have a hypermetabolic response, tachycardia is NOT an accurate measure of resuscitation in a child with a major burn. Acid-base balance, mental status, serum lactate, and noninvasive monitoring are useful adjuncts to evaluate the adequacy of resuscitation. Because of interstitial edema and sequestration of fluid in muscle cells, patients may gain up to 20% over baseline (preburn) body weight. Patients with burns of >20% TBSA often require a large venous access (central venous line) to deliver the fluid required over the critical first 24 hours; these patients are best cared for in a specialized pediatric burn unit. In addition to fluid resuscitation, children <20 kg should receive standard maintenance fluids (see Chapter 74).

During the second 24 hours after the burn, patients begin to reabsorb edema fluid and to experience diuresis. IV fluid requirements after resuscitation will consist of isotonic crystalloid infusion for insensible losses (see Chapter 73) plus the fluid losses from the burn wound. Controversy surrounds whether *colloid* should be provided in the early period of burn resuscitation. One preference is to administer albumin if a patient is not responding to crystalloid resuscitation. In children <12 months old, sodium tolerance is limited; the volume and sodium concentration of the resuscitation solution should be decreased if the urinary sodium level is rising. The adequacy of resuscitation should be constantly reassessed by integrating vital signs with urine output, blood gas, serum lactate, base deficit, hematocrit, and serum protein measurements. Some patients require arterial and central venous lines, particularly those undergoing multiple excision and grafting procedures, for monitoring and fluid replacement purposes. Central venous pressure monitoring may be indicated to assess circulation in patients with hemodynamic or cardiopulmonary instability. Femoral vein cannulation is a safe access for fluid resuscitation, especially in infants and children. Burn patients who require frequent blood gas monitoring benefit from radial or femoral arterial catheterization.

Oral supplementation may start as soon as enteral access is obtained. Early nutrition helps to minimize effects of the hypermetabolic response. Milk formula, artificial feedings, homogenized milk, or soy-based products can be given by bolus or constant infusion through a nasogastric or small bowel feeding tube. These feedings are not part of the initial 24-hour fluid resuscitation, as absorption may be variable. When oral fluids are tolerated after several days, IV fluids are decreased proportionately to keep the total fluid intake constant, particularly if pulmonary dysfunction is present.

Colloids such as albumin are lost through the burn wound. To maintain oncotic pressure and protein binding, a **5% or 25% albumin infusion** may be used to maintain the serum albumin levels at a desired 2 g/dL. Infusion of **packed red blood cells** is recommended if the hematocrit falls to <20% (hemoglobin = 7 g/dL). Most patients are hemoconcentrated during resuscitation; thus transfusion in the first 24-48 hours is rare unless there is accompanying trauma. **Fresh-frozen plasma** (FFP) is indicated if clinical and laboratory assessment shows a deficiency of clotting factors, a prothrombin level >1.5 times control, or a partial thromboplastin time >1.2 times control in children who are bleeding or are scheduled for an invasive procedure or a grafting procedure that could result in an estimated blood loss of more than half of blood volume. Although FFP use for volume resuscitation during the first 24 hours of injury is advocated by some, this strategy has not yet undergone rigorous evaluation through randomized prospective trials.

Sodium supplementation may be required for children with burns of >20% TBSA, particularly if 0.5% silver nitrate solution is used as the topical antibacterial burn dressing. Sodium losses with silver nitrate therapy are regularly as high as 350 mEq/m^2 burn surface area. The aim is to maintain serum sodium levels >130 mEq/L and urinary sodium concentration >30 mEq/L. Young children <5 years are especially susceptible to hyponatremia and cerebral edema. IV **potassium supplementation** is supplied to maintain a serum potassium level >3 mEq/dL. Potassium losses may be significantly increased when 0.5% silver nitrate solution is used as the topical antibacterial agent or when aminoglycoside, diuretic, or amphotericin therapy is required. Magnesium and ionized calcium can also become rapidly depleted and should be assessed at least daily for the first week and weekly thereafter in major burns.

Prevention of Infection and Surgical Management of the Burn Wound

In general, prophylactic antibiotic administration is not indicated for burn injuries because it predisposes patients to development of resistant pathogens. Topical antimicrobial creams or silver agents reduce wound colonization; systemic antibiotics do not reach the nonviable tissue in the burn wound. There is conflicting evidence as to whether relocation of the IV catheter every 48-72 hours decreases or increases the incidence of catheter-related sepsis in burn injury. Central venous catheters should be monitored closely for infection. Many burn units replace or relocate central lines every 5-7 days, even if the site is not inflamed and there is no suspicion of catheter-related sepsis, particularly if the line is near a burn wound. The incidence of central line–associated bloodstream infection is directly related to the distance between the catheter and the burn wound. The fragile tissue and frequency of patient turning and movement, combined with the moisture of the burn wound, make it imperative to securely attach central venous catheters with sutures placed securely in at least three locations to prevent catheter movement, kinking, or accidental removal.

Mortality related to burn injury is associated not with the toxic effect of thermally injured skin, but with the metabolic and bacterial consequences of a large open wound, reduction of the patient's immune response, and malnutrition. These abnormalities set the stage for life-threatening bacterial infection originating from the burn wound. Thorough early wound cleaning, application of topical antimicrobial creams, and early wound excision and grafting promote wound healing and improve aesthetic and functional outcomes. Topical antimicrobial agents for burn wound treatment include bacitracin (second-degree burns or burns that will heal in a week), silver sulfadiazine cream (third-degree burns), mafenide acetate (Sulfamylon) cream (third-degree burns on ears, cartilage), or 0.5% silver nitrate solution (third-degree burns with sulfa allergy) (Table 89.7). Regardless of the choice of topical antimicrobial agent, it is essential that all third-degree burn tissue be fully excised and grafted before bacterial colonization progresses to systemic infection. Children with a burn of >20% TBSA should be housed in reverse isolation with all personnel required to wear gown, gloves, mask, and hat to prevent cross-contamination and to provide a temperature- and humidity-controlled environment that minimizes hypermetabolism.

Deep third-degree burns of >10% TBSA benefit from early excision and grafting. To improve outcome, sequential excision and grafting of

Table 89.7 Topical Agents Used for Burns

AGENT	EFFECTIVENESS	SIDE EFFECTS	EASE OF USE
Bacitracin	Gram-positive organisms; good for wounds that will heal in 7-10 days	May cause yeast overgrowth rash or pustules if on intact skin; resolves with discontinuation	Clear ointment, 1-2 times daily, easy to clean off
Silver sulfadiazine cream (Silvadene)	Broad spectrum including gram-positive and -negative organisms, some fungus; may cause leukopenia	Leukopenia, self-limited; may be painful Leaves adherent residue	Changed twice daily Residue *must* be washed off with each dressing change
Mafenide acetate cream* (Sulfamylon)	Targets resistant gram-negative organisms, particularly *Pseudomonas*, some gram-positive coverage Rapid and deep wound penetration; used on cartilage (ears) and deep wound infection	Carbonic anhydrase inhibitor, may cause metabolic acidosis	Changed twice daily; application may be painful Residue *must* be washed off with each dressing change
0.5% Silver nitrate solution	Bacteriostatic Broad spectrum, including some fungi Superficial penetration	Permanent staining of surfaces from silver oxidation; electrolyte disturbances from hypotonic solution, potential methemoglobinemia	Closed bulky dressing soaked every 2 hr and changed 1-2 times daily

*Mafenide acetate solution at concentrations of 2.5% or 5% for use on heavily colonized, multidrug-resistant organisms to be used for 5 days only.

third-degree and deep second-degree burns may be required in children with large burns. Prompt excision with immediate wound closure is achieved with **autografts**, skin obtained from another part of the patient's body, which may be meshed to increase the efficiency of coverings. Alternatives for wound closure, such as allografts, dermal substitutes, and other biologic dressings, may be important for wound coverage in patients with extensive injury to limit fluid, electrolyte, and protein losses and to reduce pain and minimize temperature loss. Cultured epidermal cells (autologous keratinocytes), grown from a skin biopsy from the patient, are a costly alternative and are not always successful. Another approach employs an autologous cell spray (theoretically containing stem cells) as an adjunct to meshed skin for wound closure. An experienced burn team can safely perform early stage or total excision while burn fluid resuscitation continues. Important keys to success are (1) accurate preoperative and intraoperative determination of burn depth, (2) the choice of excision area and appropriate timing, (3) control of intraoperative blood loss, (4) specific instrumentation, and (5) the type of wound coverage chosen.

Nutritional Support

Supporting the increased energy requirements of a patient with a burn is a high priority. The burn injury produces a hypermetabolic response characterized by both protein and fat catabolism. Depending on the time lapse since the burn, children with a burn of 40% TBSA require basal energy expenditure (oxygen consumption) approximately 50–100% higher than predicted for their age. Early excision and grafting can decrease the energy requirement. Pain, anxiety, and immobilization increase the physiologic demands. Additional energy expenditure is caused by cold stress if environmental humidity and temperature are not controlled; this is especially true in young infants, in whom the large BSA:mass ratio allows proportionately greater heat loss than in adolescents and adults. Providing environmental temperatures of 28–33°C (82.4–91.4°F), adequate covering during transport, and liberal use of analgesics and anxiolytics can decrease caloric demands. Appropriate sleep intervals are necessary and should be part of the regimen. Early enteral nutrition, initially with high-carbohydrate, high-protein caloric content (1,800 kcal/m^2/24-hr maintenance plus 2,200 kcal/m^2 of burn/24 hr) reduces metabolic stress.

The objective of nutrition supplementation programs is to maintain body weight and minimize weight loss by meeting metabolic demands. This reduces the loss of lean body mass. Calories are provided at approximately 1.5 times the basal metabolic rate, with 3-4 g/kg of protein/day. The focus of nutritional therapy is to support and compensate for the metabolic needs. Multivitamins, particularly the B vitamin group, vitamin C, vitamin A, vitamin D, vitamin E, copper, selenium, and zinc, are also necessary.

Alimentation should be started as soon as is practical, preferably enterally, to meet all caloric needs and maintain gastrointestinal (GI) tract function throughout treatment. Patients with burns of >40% of TBSA need a flexible nasogastric or small bowel feeding tube to facilitate continuous delivery of calories without the risk of aspiration at the time of admission. To decrease the risk of infectious complications, parenteral nutrition should be avoided or discontinued as soon as is practical after delivery of sufficient enteral calories is established. Continuous GI feeding is essential, even if feeding is interrupted for frequent visits to the operating room, until full grafting takes place. In third-degree burns >20% the use of anabolic agents such as *oxandrolone* to improve wound healing and promote protein synthesis or anticatabolic agents (propranolol) to reduce metabolic stress is common practice. It is vital to continue enteral feeding while using these agents to obtain maximal response. Liver function studies should be monitored weekly when giving oxandrolone, and oxandrolone should be discontinued if liver function deteriorates.

Topical Therapy

Topical therapy is widely used to decrease wound colonization from a wide variety of wound pathogens (see Table 89.7). Preferences vary among burn units. Each topical agent has advantages and disadvantages in application, comfort, and bacteriostatic spectrum. However, all agents impair wound healing. The type of organism on a wound varies with the age of the wound. In the first week, gram-positive organisms predominate. During weeks 2-4, gram-negative organisms are frequently found in burn wounds. Prolonged open burn wounds eventually tend to develop resistant gram-negative organisms, fungus, or mold. The choice of topical antimicrobial depends on wound age and depth. *Bacitracin* is a clear ointment effective against gram-positive organisms and is often used in wounds that will heal within a week. If placed on nonburned skin, it may cause a yeast rash or pimples that resolve with discontinuation. *Silver sulfadiazine* is a white cream containing silver with a broad spectrum of coverage, including

gram-positive and gram-negative organisms and some fungi. It is used commonly in deep third-degree burns that require grafting and may cause transient self-limiting leukopenia if applied over large areas. *Mafenide acetate* is a white cream with the ability to diffuse through the burn eschar; it is the treatment of choice for injury to cartilaginous surfaces, such as the ear. Mafenide acetate solution at a concentration of 5% is useful for the treatment of burn wounds that are heavily colonized with multidrug-resistant gram-negative bacteria and is often used postoperatively to keep grafts moist. The carbonic anhydrase inhibition activity of mafenide acetate may cause metabolic acidosis if large surface areas are treated in a small child. No sulfa-containing agent should be used if the child has a history of sulfa allergies. Silver nitrate solution may be used in children with sulfa allergy because of its broad spectrum of coverage. However, it causes gray staining of the environment and wound from silver oxidation as well as electrolyte disturbances because of the hypotonic nature of the solution.

Inhalation Injury

Inhalation injury is serious in the infant and child, particularly if preexisting pulmonary conditions are present (see Chapter 86). Inhalation injury should be suspected based on history of sustained exposure to smoke in association with the burn injury, such as being confined in a closed space or from an indoor explosion, with decreased level of consciousness or with evidence of carbon deposits in the oropharynx or nose, singed facial hair, or carbonaceous sputum. Mortality estimates vary, depending on the type of inhalation injury and the extent of exposure. Each of the three types of inhalation injury (toxic gases, upper airway edema, and lower airway injury) has a different treatment.

Toxic Gases

Carbon monoxide poisoning from the burning of organic materials is caused by displacement of oxygen from the hemoglobin molecule by CO, leading to tissue hypoxia (see Chapter 94). CO poisoning should be treated with 100% oxygen until carboxyhemoglobin levels drop below 10%. Toxic fumes, including cyanides from combustible plastics as well as sulfur and nitrogen oxides and alkalis formed during the combustion of synthetic fabrics, produce corrosive chemicals that may erode the mucosa and cause significant tissue sloughing. Exposure to smoke may cause degradation of surfactant and decrease its production, resulting in atelectasis. Inhalation injury and burn injury are synergistic, and the combined effect can increase morbidity and mortality.

Injury from gases generally manifests early in the course of treatment. Acute asphyxia is the leading cause of death at the fire scene and can cause anoxic brain injury, particularly in children. Signs of CNS injury from hypoxemia caused by asphyxia or CO poisoning vary from irritability to depression. CO poisoning may be *mild,* with slight dyspnea, headache, nausea, and decreased visual acuity and higher cerebral functions; *moderate,* with irritability, agitation, nausea, dimness of vision, impaired judgment, and rapid fatigue; or *severe,* producing confusion, hallucination, ataxia, cardiovascular collapse, acidosis, and coma. Measurement of HbCO is important for diagnosis and treatment. Pulse oximetry is NOT a reliable marker of oxygenation in CO poisoning. If significant CO exposure is suspected, a blood gas with co-oximetry and a HbCO level should be obtained to determine Pao_2 and CO toxicity extent. CO poisoning and hypoxia are assumed to be present until the tests are performed, and patients should receive 100% oxygen until the HbCO level is <10% and adequate oxygenation is confirmed. Significant CO poisoning (level >25%) may require hyperbaric oxygen therapy; the risk of transporting a burn patient to the hyperbaric chamber needs to be carefully considered. **Cyanide poisoning** should be suspected if a metabolic acidosis persists despite adequate fluid resuscitation and in environments containing synthetic polymers (see Chapter 94). Unless specifically suspected, most burn centers do not routinely screen for cyanide poisoning.

Upper Airway Edema

The treatment priority for edema of the upper airway caused by inhalation injury focuses on establishing and maintaining a patent airway. If airway obstruction is apparent, prompt and early nasotracheal or orotracheal intubation is indicated to maintain airway patency and assure adequate ventilation and oxygenation. The most experienced provider should perform the intubation, as edema may allow only one attempt. The endotracheal tube size should be chosen carefully, as replacement during the first 1-3 days is often not possible. Endotracheal tubes should *not be secured* with tape if a facial burn is present, as the tape will not adhere to the moist surface. The endotracheal tube can be secured to a tooth, to the maxilla, or tied in two planes. Monitoring the security of the endotracheal tube and assuring it remains in the same location at the level of the teeth is essential, as edema may alter tube position.

Parenchymal Injury

Intubation and mechanical ventilation may be required in patients who have significant hypoxia, hypercarbia, or mental status changes caused by smoke inhalation. Wheezing and bronchospasm are common, and use of inhaled bronchodilators is often helpful. Smoke inhalation injury is gauged via clinical progression and bronchoscopy. Aggressive pulmonary toilet and chest physiotherapy are necessary, as casts and airway obstruction from debris are common. Extubation should be delayed until the patient has adequate oxygenation and ventilation, is able to sustain the increased minute ventilation and work of breathing that accompanies burn injury, and edema has resolved. A spontaneous breathing trial and a cuff leak test are often used to gauge readiness for extubation. Children with an anticipated need for mechanical ventilation >2 weeks may benefit from tracheostomy, as it provides a secure, comfortable airway with decreased sedation requirements. Tracheostomy should only be performed under general anesthesia by experienced surgeons using optimal positioning, proper tracheostomy tube size, and hemostatic conditions. In children with deep burns of the face, tracheostomy provides a secure airway that facilitates excision and grafting yet allows for oral movement, including a pacifier.

Patients with severe inhalation injury or with other causes of respiratory deterioration that lead to pediatric acute respiratory distress syndrome who do not improve with conventional pressure-controlled ventilation (progressive oxygenation failure, as manifested by oxygen saturation <90% while receiving Fio_2 of 0.9-1.0 and positive end-expiratory pressure of at least 12 cm H_2O) may benefit from high-frequency ventilation or nitric oxide inhalation treatment. Nitric oxide usually is administered through the ventilator at 5 parts per million (ppm) and increased to 30 ppm. This method of therapy reduces the need for extracorporeal membrane oxygenation (ECMO; see Chapter 86). ECMO may be indicated for failure of these conventional techniques.

Pain Relief and Psychologic Adjustment

See Chapter 93.

It is important to provide adequate analgesia, anxiolysis, sedation, and psychologic support to reduce early metabolic stress, decrease the potential for posttraumatic stress disorder (PTSD), and allow future stabilization as well as physical and psychologic rehabilitation. Patients and family members require team support to work through the grieving process and accept long-term changes in appearance.

Children with burn injury have frequent and wide fluctuations in pain intensity. Appreciation of pain depends on the depth of the burn; the stage of healing; the patient's age, stage of emotional development, and cognition; the experience and efficiency of the treating team; the use of analgesics and other drugs; the patient's pain threshold; and interpersonal and cultural factors. From the onset of treatment, **preemptive pain control** during dressing changes is crucial. The use of a variety of nonpharmacologic interventions and pharmacologic agents must be reviewed throughout the treatment period. Opioid analgesia, prescribed in an adequate dose and timed to cover dressing changes, is essential to comfort management. A supportive person who is consistently present and knows the patient profile can integrate and encourage patient participation in burn care. The problem of *undermedication* is most prevalent in adolescents, in whom fear of drug dependence may inappropriately influence treatment. A related problem is that the child's specific pain experience may be misinterpreted;

for anxious patients, those who are confused and alone, or those with preexisting emotional disorders, even small wounds may illicit intense pain. Anxiolytic medication added to the analgesic is usually helpful and has more than a synergistic effect. Equal attention is necessary to decrease stress in the intubated patient. Other modalities of pain and anxiety relief **(relaxation techniques)** can decrease the physiologic stress response.

A multimodal pain strategy is recommended for burns, as burn pain is a combination of background, acute, procedural, neuropathic, and inflammatory pain. The specific agents used will vary by institution and provider training. *Background pain,* which exists primarily in burns >20%, should be addressed with long-acting oral agents administered twice daily, such as methadone or long-acting morphine. This helps to maintain a steady state of pain relief. *Acute pain* from the injury (all burn sizes) is generally treated initially with oral acetaminophen, escalating to a short-acting opioid such as morphine, hydromorphone, oxycodone, or similar agents orally. If oral administration is not sufficient (a common scenario in major burn injury), intermittent IV opioids are used. The use of *codeine* is not recommended because of the possibility of ultrarapid metabolism of codeine. *Procedural pain,* such as for dressing changes, is short-lived but severe. Potent IV opioids such as fentanyl, morphine, or hydromorphone are effective but require appropriate monitoring. Naloxone is rarely needed but should be immediately available to reverse the effect of IV narcotics. Ketamine 1-4 mg/kg IV can be employed for children with high opioid requirements; however, continuous cardiovascular monitoring is mandatory, and ketamine should be administered by a provider trained in advanced airway techniques. *Neuropathic pain* (pins and needles sensation) should be addressed with scheduled oral gabapentin given 4 times daily. *Inflammatory pain* can be effectively treated with nonsteroidal antiinflammatory agents unless the patient has upcoming surgery, as this may increase surgical complications. *Midazolam* is very useful for conscious sedation at a dose of 0.01-0.02 mg/kg for nonintubated patients and 0.05-0.1 mg/kg for intubated patients as an IV bolus and may be repeated in 10 minutes; if used with an opioid, continuous cardiovascular monitoring is warranted. Oral midazolam for premedication before a dressing change at 0.5 mg/kg can be highly effective in reducing anxiety surrounding dressings. Dexmedetomidine infusion may be required for children with high levels of anxiety or who are refractory to benzodiazepine therapy, but this requires monitoring in an intensive care unit (ICU) setting. Postoperative pain after burn surgery, which is severe because of the combination of donor sites and the wound itself, is often treated with a multimodal continuous infusion of an opioid (hydromorphone or morphine) and sedative (dexmedetomidine and/or ketamine). This combination decreases opioid requirements and improves pain but requires monitoring in an ICU. Regional blocks by a trained anesthesiologist can mitigate donor site pain.

During the process of weaning from IV analgesics, the dose of opiates is reduced by 25% over 1-3 days, sometimes with the addition of oral opioids and then acetaminophen as opioids are tapered. When weaning off antianxiety medications, the approach involves reducing the dose of benzodiazepines, at 25–50% per dose, daily over 1-3 days.

Regular evaluation of burned children during hospitalization by a trained psychologist or psychiatrist is necessary, as PTSD, anxiety, depression, acute stress disorder, and other psychiatric issues are common after burn injury. Early recognition and treatment of the patient and family improve psychosocial outcomes. As a result, there is a growing use of *psychotropic medication* in the care of children with burns, including prescription of selective serotonin reuptake inhibitors as antidepressants, the use of neuroleptic agents in the critical care setting, and the treatment of PTSD with prazosin.

Reconstruction and Rehabilitation

To ensure maximum cosmetic and functional outcome, occupational and physical therapy must begin on the day of admission, continue throughout hospitalization, and for many patients, continue after discharge. Physical rehabilitation involves body and limb positioning, splinting, exercises (active and passive movement), assistance with activities of daily living, and gradual ambulation. These measures maintain adequate joint and muscle activity with as normal a range of movement as possible after healing or reconstruction. **Pressure therapy** is necessary to reduce hypertrophic scar formation; a variety of prefabricated and custom-made garments are available for use in different body areas. These custom-made garments deliver consistent pressure on scarred areas; shorten the time of scar maturation; and decrease scar thickness, redness, and associated itching. Continued adjustments to scarred areas (scar release, grafting, rearrangement) and multiple minor cosmetic surgical procedures are necessary to optimize long-term function and improve appearance. Replacement of areas of alopecia and scarring has been achieved with the use of tissue-expander techniques. The use of ultrapulse laser for reduction of scarring is an adjunct in scar management. Pruritis can be a severe issue in the rehabilitative phase. Commonly used oral agents include antihistamines such as loratadine, hydroxyzine, and diphenhydramine, as well as gabapentin or H2 blockers. Topical agents include moisturizers, topical steroid creams, or colloidal oatmeal baths. Refractory itching may be treated with desensitization therapy or laser treatment, although literature supporting these therapies is scarce.

School Reentry and Long-Term Outcome

Optimally the child will return to school immediately after discharge. Occasionally, a child may need to attend on an altered schedule because of rehabilitation needs. It is important for the child to return to the normal routine of attending school and being with peers to begin the resocialization process. Planning for a return to home and school often requires a **school reentry program** that is individualized to each child's needs. For a school-age child, planning for the return to school occurs simultaneously with planning for discharge. The hospital schoolteacher contacts the local school and plans the program with the school faculty, nurses, social workers, recreational/child-life therapists, and rehabilitation therapists. This team should work with students and staff to ease anxiety, answer questions, and provide information. Burns and scars evoke fears in those who are not familiar with this type of injury and can result in a tendency to withdraw from or reject the burned child. A school reentry program designed based on the child's developmental and educational needs can alleviate these fears and facilitate the child's reintegration into the school environment.

Major medical advances have made it possible to save the lives of children with massive burns. Although some children have lingering physical difficulties, most have a satisfactory quality of life. The comprehensive burn care that includes experienced multidisciplinary aftercare plays an important role in recovery. Table 89.8 lists the long-term disabilities and complications of burns.

ELECTRICAL BURNS

Three types of burns are caused by electricity: electrical burns, caused by electricity passing through the body; arc burns, caused by the heat released from high-amperage currents discharging through the air; and thermal contact burns, from touching a hot electrical device. Electrical burns are divided into high voltage (>1,000 volts) and low voltage (<1,000 volts). Electricity is delivered via alternating current (AC), which is generally used in households, or direct current (DC), often used in industry or car batteries. The majority of pediatric electrical burns involve 110 volts AC electricity and occur in the household. **Minor electrical burns** in children usually occur as a result of biting on an extension cord or inserting an object in an electrical outlet. These injuries produce localized burns to the mouth or finger. Children who chew electrical cords usually sustain burns to portions of the upper and lower lips that come in contact with the extension cord, particularly the corners of the mouth. Because these are *nonconductive* injuries (do not extend beyond the site of injury), hospital admission is not necessary. Care is focused on the area of the injury visible in the mouth, ensuring it is low voltage and does not cause entry or exit wounds or cardiac issues. Treatment with topical antibiotic creams is sufficient until the patient is seen in a burn unit outpatient department or by a plastic surgeon for potential reconstruction or excision of the burn site.

A more serious category of electrical burn is the **high-voltage electrical burn**, for which children must be admitted for observation,

Table 89.8 Common Long-Term Complications and Disabilities in Patients with Burn Injuries

COMPLICATIONS AFFECTING THE SKIN AND SOFT TISSUE	**PSYCHIATRIC AND NEUROLOGIC DISABILITIES**
Hypertrophic scars	Sleep disorders
Susceptibility to minor trauma	Adjustment disorders
Dry skin	Posttraumatic stress disorder
Contractures	Depression
Itching and neuropathic pain	Body image issues
Alopecia	Neuropathy and neuropathic pain
Chronic open wounds	Long-term neurologic effects of carbon monoxide poisoning
Skin cancers	Anoxic brain injury
Epidermal inclusion cysts	**LONG-TERM COMPLICATIONS OF CRITICAL CARE**
Cutaneous abscesses	Deep vein thrombosis, venous insufficiency, or varicose veins
ORTHOPEDIC DISABILITIES	Tracheal stenosis, vocal cord disorders, or swallowing disorders
Amputations	Renal or adrenal dysfunction
Contractures	Hepatobiliary or pancreatic disease
Heterotopic ossification	Cardiovascular disease
Temporary reduction in bone density	Reactive airway disease or bronchial polyposis
Decreased endurance and weakness	**PREEXISTING DISABILITIES THAT CONTRIBUTED TO THE INJURIES**
METABOLIC DISABILITIES	Risk-taking behavior
Heat sensitivity	Untreated or poorly treated psychiatric disorder
Obesity	
Glucose intolerance	
Hypertension	

Modified from Sheridan RL, Schultz JT, Ryan CM, et al. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 6-2004: A 35-year-old woman with extensive, deep burns from a nightclub fire. *N Engl J Med.* 2004;350:810–821.

regardless of the extent of the surface area burn. Deep muscle injury is typical and cannot be readily assessed initially. These injuries occur in high-voltage installations, such as electric power stations or railroads; children climb an electric pole and touch an electric box out of curiosity or accidentally touch a high-tension electrical wire. Such injuries have a mortality rate of 3–15% for children who arrive at the hospital for treatment. Survivors have a high rate of morbidity, including major limb amputations. Points of entry of current through the skin and the exit site show characteristic features consistent with current density and heat. The majority of entrance wounds involve the upper extremity, with small exit wounds in the lower extremity. The current is conducted throughout the body, regardless of entry and exit points. Virtually any structure in the body is at risk (Table 89.9). Damage to the abdominal viscera, thoracic structures, and nervous system (confusion, coma, paralysis) in areas remote from obvious extremity injury occurs and must be sought, particularly in injuries with multiple current pathways or those in which the victim falls from a high pole. *Cardiac abnormalities,* manifested as ventricular fibrillation or cardiac arrest, are common; patients with high-tension electrical injury need an initial electrocardiogram (ECG) and cardiac monitoring until they are stable and have been fully assessed. Higher-risk patients have abnormal ECG findings and a history of loss of consciousness. Renal damage from *deep muscle necrosis* and subsequent myoglobinuria is another complication; such patients need forced alkaline diuresis to minimize renal damage. Soft tissue (muscle) injury of an extremity may produce a **compartment syndrome** (see Chapter 80). Aggressive removal of all dead and devitalized tissue, even with the risk of functional loss, remains the key to effective management of the electrically damaged extremity. Early debridement facilitates early closure of the wound. Damaged major vessels must be isolated and buried in a viable muscle to prevent exposure. Survival depends on immediate intensive care; functional result depends on long-term care and delayed reconstructive surgery. The incidence of cataract formation is also increased in patients who have sustained electrical injuries; patients should be referred to an ophthalmologist for regular examinations.

Arc burns generally are caused by clothing *ignition* from the superheated arc that can be emitted from high-amperage current discharge. The hallmark of this injury is a large cutaneous burn following clothing lines and covered in thick soot. Discreet entrance and exit points are not generally seen. Muscle injury is rare, as current does not actually traverse the skin. Treatment should follow the principles for major flame burn injury treatment.

Contact burns, in which tissue destruction is localized to a small area of contact with an electrical box with no evidence of electricity conducted through the body, are generally treated as any other burn injury. Careful history and physical examination should be performed to assure that there was no transmission of electricity.

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89.1 Lightning Burns

Tina L. Palmieri

Worldwide, lightning occurs approximately 50 times per second, primarily via ground strikes involving 30,000-100,000 amperes at 30,000 Kelvin temperature. Fortunately, the incidence of lightning burns is low, with 400 injuries and 40 deaths per year attributed to lightning. Lightning injury occurs via (1) direct strike (electrical current), (2) thermal burns from conversion of electrical energy to heat, or (3) mechanical trauma from the acoustic shock wave, flying debris, fall, or muscle contraction. The most common form of lightning burn, accounting for approximately half of lightning injuries, is **ground current**, in which lightning strikes the ground or an object near an individual and travels through the ground to the individual. **Side splash** injuries constitute ~30% of lightning injuries and occurs when current jumps from a nearby object, then follows the path of least resistance to an individual. Direct strikes account for 5% of lightning injuries. Sudden death after a direct strike is due to simultaneous cardiac and respiratory arrest from depolarization of cardiac muscle cells and paralysis of the medullary respiratory center.

Lightning cutaneous burns depend on the current path, the type of clothing worn, the presence of metal, and cutaneous moisture. Entry, exit, and path lesions are possible; the prognosis is poorest for lesions of the head or legs. Internal organ injury along the path is common

Table 89.9 Electrical Injury: Clinical Considerations

SYSTEM	CLINICAL MANIFESTATIONS	MANAGEMENT
General	—	• Extricate the patient • Perform ABCs of resuscitation; immobilize the spine • Obtain history: voltage, type of current • Obtain complete blood count with platelets, electrolytes, BUN, creatinine, and glucose
Cardiac	Dysrhythmias: asystole, ventricular fibrillation, sinus tachycardia, sinus bradycardia, premature atrial contractions, premature ventricular contractions, conduction defects, atrial fibrillation, ST- and T-wave changes	• Treat dysrhythmias • Provide cardiac monitor, electrocardiogram, and radiographs with suspected thoracic injury • Perform creatinine phosphokinase with isoenzyme measurements if indicated
Pulmonary	Respiratory arrest, acute respiratory distress, aspiration syndrome	• Protect and maintain the airway • Provide mechanical ventilation if indicated, chest radiograph, and arterial blood gas levels
Renal	Acute kidney injury, myoglobinuria	• Provide aggressive fluid management unless central nervous system injury is present • Maintain adequate urine output, >1 mL/kg/hr if myoglobinuria; addition of HCO_3^-, mannitol may be needed to alkalinize urine and stimulate diuresis, respectively • Consider central venous or pulmonary artery pressure monitoring • Measure urine myoglobin; perform urinalysis; measure BUN, creatinine
Neurologic	Immediate: loss of consciousness, motor paralysis, visual disturbances, amnesia, agitation; intracranial hematoma	• Treat seizures • Provide fluid restriction if indicated
	Secondary: pain, paraplegia, brachial plexus injury, syndrome of inappropriate antidiuretic hormone secretion, autonomic disturbances, cerebral edema	• Consider spine radiographs and MRI, especially cervical
	Delayed: paralysis, seizures, headache, peripheral neuropathy	• Perform CT or MRI scan of the brain if indicated
Cutaneous/oral	Oral commissure burns, tongue and dental injuries; skin burns resulting from ignition of clothes, entrance and exit burns, and arc burns	• Document entrance and exit wounds • Treat cutaneous burns; determine patient's tetanus status • Obtain consultation for plastic surgery of ear, nose, and throat, if indicated
	Electrical burns to mouth could include oral commissures and lips; low-voltage electrical burns secondary to high conductivity of saliva	• Ensure no entry or exit wounds and no cardiac involvement • Confirm all injuries are localized • Management is observation until eschar sloughs off and granulation tissue fills in • If bleeding at corner of mouth from labial artery, pinch lower lip to stop bleeding and consult surgeon • High risk for scarring; refer to burn center for long-term management
Abdominal	Viscus perforation and solid-organ damage; ileus; abdominal injury rare without visible abdominal burns	• Place nasogastric tube if patient has airway compromise or ileus • Obtain serum ALT, AST, amylase, BUN, and creatinine measurements and CT scans as indicated
Musculoskeletal	Compartment syndrome from subcutaneous necrosis limb edema and deep burns	• Monitor patient for possible compartment syndrome
	Long-bone fractures, spine injuries	• Obtain radiographs and orthopedic/general surgery consultations as indicated
Ocular	Visual changes, optic neuritis, cataracts, extraocular muscle paresis	• Obtain an ophthalmology consultation to document and follow for cataract formation

AST, Aspartate transaminase; ALT, alanine transaminase; BUN, blood urea nitrogen.
Adapted from Hall ML, Sills RM. Electrical and lightning injuries. In: Barkin RM, ed. *Pediatric Emergency Medicine*. St Louis: Mosby; 1997: p. 484.

and *does not* relate to the severity of the cutaneous burn. Linear burns, usually first- or second-degree, are in the locations where sweat is present. **Feathering**, also called *Lichtenberg figures,* is an arborescent pattern appearing on the skin and is pathognomonic for lightning injury (Fig. 89.7). The feathering skin appearance, thought to be caused by changes in cutaneous blood flow, is transient and disappears within several hours. Lightning may ignite clothing or produce serious cutaneous burns from heated metal in the clothing. Internal complications of lightning burns include cardiac arrest caused by asystole, transient hypertension, premature ventricular contractions, ventricular fibrillation, and myocardial ischemia. Most severe cardiac complications resolve if the patient is supported with CPR (see Chapter 79). CNS complications include cerebral edema, hemorrhage, seizures, mood changes, depression, and paralysis of the lower extremities. Rhabdomyolysis and myoglobinuria (with possible renal failure) also occur but are rare. Ocular manifestations include vitreous hemorrhage, iridocyclitis, retinal tearing, or retinal detachment. Rupture of the tympanic membrane occurs in 50–80% of those sustaining a direct strike.

Treatment of lightning injury generally follows traditional trauma management with one exception: In the event of multiple lighting injuries (mass casualty), a "reverse triage" system is employed, in which initial treatment is focused on those who appear to be in cardiac arrest,

Fig. 89.7 Lightning burn: Lichtenberg feathering. (*Courtesy Dr. Mary Ann Cooper.*)

which is often reversible. Early attention to ventilation after restoration of cardiac rhythm in lightning-injured patients is crucial to prevent recurrent cardiovascular collapse and hypoxic brain injury. This triage algorithm is employed because those who have cardiorespiratory function immediately after the strike rarely succumb to their injury before hospital arrival. Ultimate outcomes depend on injury severity, mental status, organ involvement, cardiac arrest presence, and arrhythmias. Lightning survivors who have a normal ECG and normal vital signs and no obvious injury can be discharged home if they *do not* have history of a direct strike, loss of consciousness, focal neurologic complaint, major trauma, significant burns, or chest pain or dyspnea. However, they should be referred for ophthalmologic evaluation and audio-vestibular evaluation should there be ocular or otic injury. Neurologic effects of lightning injury may be significant. CNS dysfunction can be immediate or delayed and includes spinal cord injury, ischemic stroke, or *keraunoparalysis* (temporary condition that mimics spinal cord injury) as well as trauma-related injuries such as skull fractures or spinal cord injury. Personality alterations and sleep disorders may develop over time post injury.

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Chapter 90

Cold Injuries

Jennifer Dow

Children and youth are exposed to cold environments through outdoor recreation, occupational activities, or housing crises. Although cold injuries are commonly attributed to subfreezing temperatures, it is a misnomer that it must be below 0°C (32°F) for systemic injury or local tissue damage to occur. Injury from cold occurs when the body's ability to generate heat is overwhelmed by environmental loss.

MECHANISMS OF HEAT TRANSFER

Environmental heat or cold injury occurs when the metabolic capacity for thermoregulation cannot maintain core body temperature in the setting of extreme environmental temperatures. The hypothalamus controls the production and conservation of heat, responding to central and peripheral receptors. Local skin temperature is partially responsible for the regulation of peripheral blood flow. Heat production is a product of cellular metabolism and by both voluntary (exercise) and involuntary (shivering) muscle use, while vasoconstriction and behavioral action influence conservation. Heat is transferred to the environment by five mechanisms: radiation, conduction, convection, respiration, and evaporation.

Radiation is the transfer of heat from one object to another without physical contact. This type of heat loss is moderated by vasoconstriction, diminishing warm blood flow to the periphery, and behavioral adaptation of wearing insulating layers. Medications or conditions that prohibit the vasoconstrictive response contribute to heat loss by radiation. Children may not have the knowledge or experience to recognize when additional clothing is necessary; adults are obliged to ensure that appropriate clothing is available. In a dry environment, radiation is the predominant method of heat transfer. **Conduction** is the direct transfer of heat to another object and is the primary mechanism of heat loss when a body is immersed, as water has up to 30 times more thermal conductivity than air. Heat is also conducted when an individual touches a cold object (e.g., a cold rock, snow, metal chair). Behavioral adaptations include avoidance and placement of insulation between the individual and the surface. **Convective** loss of body heat to cooler circulating air or water can be mitigated by clothing and vasoconstriction. Convection is a method of rewarming, using hot air as a delivery method. **Evaporative** heat loss results from the conversion of water (sweat) to vapor; like *respiratory* loss, it is a small but obligate contribution to thermal balance.

HYPOTHERMIA

Accidental hypothermia is the unintentional drop in core temperature below 35°C (95°F), occurring when the combination of physiologic and behavioral mechanisms to maintain core temperature are overwhelmed by environmental losses. Although cold and wet environments pose the most significant risk, accidental hypothermia can occur in any season and in most climates. The predominant clinical manifestations are reflective of disruptions of the cardiopulmonary and central nervous systems (Table 90.1). Cerebral function begins to diminish at a core temperature of 33–34°C (91.4–93.2°F), with early manifestations being irritability, confusion, and poor decision-making, progressing to lethargy, somnolence, and coma. Cerebral oxygen requirements are decreased by cooling, affording transient protection in cardiac standstill or cold-water drowning events. The initial cardiopulmonary response to cold is an increase in cardiac output and ventilation to support the metabolic demand of shivering. Further cardiac cooling manifests as bradycardia and abnormalities of cardiac conduction (atrial and ventricular dysrhythmias, including fibrillation) (Fig. 90.1). The crucial factors for reducing morbidity and mortality due to hypothermia are prevention, prompt recognition, and rapid treatment.

Risk Factors and Prevention of Hypothermia

The risk factors associated with hypothermia are extensive. Illnesses, medications, and substance use can disrupt the normal physiologic responses to cold. Vasoconstriction is disrupted by ethanol, vasodilatory medications, and infections. Central nervous system (CNS) trauma, stroke, medications (antidepressants, mood stabilizers, anxiolytics), and endocrine disorders (hypothyroid, adrenal insufficiency, diabetes, hypoglycemia, hypopituitarism) disrupt the hypothalamic response to cold. Mental illness, intoxication (opiates, organophosphates, barbiturates, carbon monoxide), and lack of awareness, as seen in the extremes of age, may impair the ability to recognize cold. General conditions of malnutrition and inability to move make it such that the patient does not have the caloric reserves to shiver or cannot move safely out of the cold. Autonomic dysfunction may produce hypothermia. Knowledge of these conditions ideally results in a heightened attentiveness to the potential for hypothermia. Active prevention includes awareness of the weather conditions and the utilization of appropriate clothing. Insulation

Table 90.1 Physiologic Characteristics of the Four Zones of Hypothermia

STATE	CORE TEMPERATURE °C (°F)	CHARACTERISTICS
Mild	35 (95)	Urine temperature, 34.8°C (94.6°F); increased shivering thermogenesis; increase in metabolic rate
	34 (93.2)	Amnesia and dysarthria develop; normal blood pressure; maximum respiratory stimulation
	33 (91.4)	Ataxia, apathy develop
Moderate	32 (89.6)	Stupor; 25% decrease in oxygen consumption
	31 (87.8)	Decreased shivering thermogenesis
	30 (86)	Atrial fibrillation and other dysrhythmias; poikilothermia; pulse and cardiac output two-thirds normal; insulin ineffective
	29 (85.2)	Progressive decrease in level of consciousness, pulse, and respiration; pupils dilated
Severe	28 (82.4)	Ventricular fibrillation susceptibility; 50% decrease in oxygen consumption and pulse
	27 (80.6)	Losing reflexes and voluntary motion
	26 (78.8)	Major acid-base disturbances; no reflexes or response to pain
	25 (77)	Cerebral blood flow one-third normal; cardiac output 45% normal; pulmonary edema may develop
	24 (75.2)	Significant hypotension
	23 (73.4)	No corneal or oculocephalic reflexes
	22 (71.6)	Maximum risk of ventricular fibrillation; 75% decrease in oxygen consumption
Profound	20 (68)	Lowest resumption of cardiac electromechanical activity; pulse 20% of normal
	19 (66.2)	Flat electroencephalogram
	18 (64.4)	Asystole develops
	14.2 (57.6)	Lowest accidental hypothermia survival in an infant
	13.7 (56.7)	Lowest accidental hypothermia survival in an adult
	9 (48.2)	Lowest therapeutic hypothermia survival

From Zafren K, Danzl DF. Accidental hypothermia. In: Walls RM, Hockberger RS, Gausche-Hill M, et al., eds. *Rosen's Emergency Medicine*, 9th ed. Philadelphia: Elsevier; 2018, Table 132.1, p. 1744.

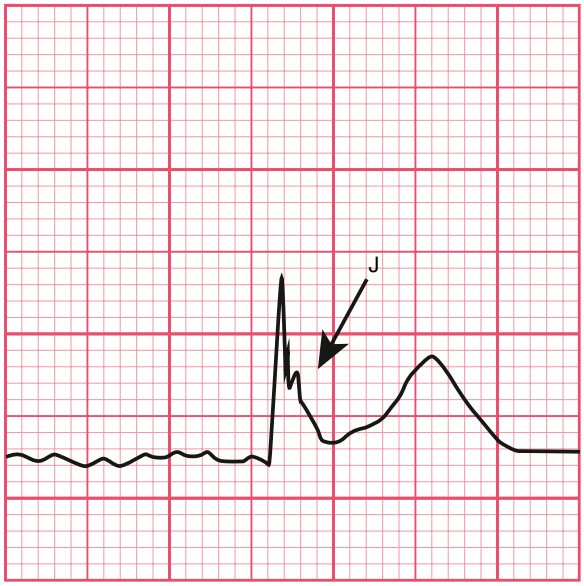

Fig. 90.1 Characteristic J or Osborne wave of hypothermia (temp <32°C) closely follows QRS. It may be mistaken for a T wave with narrow QT interval if the true T wave is not appreciated. The slightly rounded peak distinguishes it from R′ of bundle branch block. (*From Gunnarsson B, Heard CMB. Accidental hypothermia. In: Zimmerman JJ, Clark RSB, Fuhrman BP, et al., eds. Fuhrman & Zimmerman's Pediatric Critical Care, 6th ed. Elsevier: Philadelphia; 2022: Fig. 114.1, p. 1333.*)

and ease of layering are factors to be considered when choosing clothing. Removing a layer while engaging in aerobic activity helps prevent sweating and subsequent evaporative heat loss; replacing it when activity slows prevents loss by radiation through the inadequate insulation. Socks and gloves should fit properly, without circulatory impingement, and be constructed of materials other than cotton. Covering the head and face prevents losses through these exposed areas. Infants and young children will lose more heat by radiation through the head than adults because of its relatively increased surface area. The utilization of wind-blocking materials mitigates loss due to convection, and waterproofing keeps clothing dry and minimizes losses resulting from convection and radiation. Additional preventative measures are ensuring adequate nutrition for the activity, recognizing an increased metabolic demand in the cold, and having access to shelter for warmth.

Clinical Presentation of Hypothermia

Hypothermia is a cold injury syndrome with progressive signs and symptoms (see Table 90.1 and Fig. 90.2). The differential diagnosis is broad, and the clinician must be aware of the environment from which the patient presents. It is also essential that the clinician recognize that each patient is unique and presents with subtle differences. A patient may continue to shiver below the 30°C (86°F) "cut-off" but manifest all other signs of moderate to severe hypothermia. Standard classification is based on measured core temperature, whereas field classification is based on signs and symptoms (see Fig. 90.2). Treatment of all stages includes preventing further heat loss and initiating rewarming (Fig. 90.3).

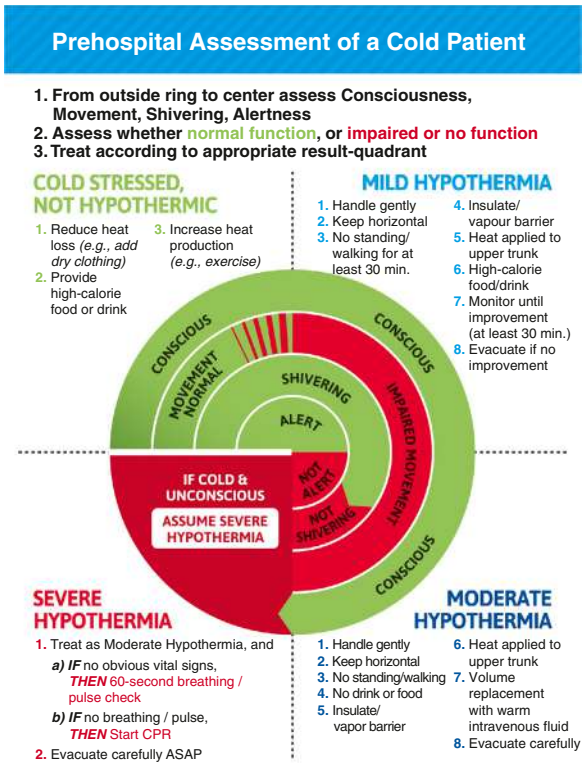

Fig. 90.2 Algorithm for field assessment and treatment of a cold patient. (*Sources: BICOrescue.com; Zafren K, Giesbrecht GG, Danzl DF, et al. Wilderness Medical Society practice guidelines for the out-of-hospital evaluation and treatment of accidental hypothermia: 2014 update. Wilderness Environ Med. 2014;25(4 Suppl):S66-S85.*)

Cold Stress

Cold stress is marked by shivering and a core temperature >35°C (95°F). Measures to prevent further heat loss and increase heat production are all that are necessary for reversal. This may entail increasing physical activity to generate warmth, relocating to a warm environment, or adding clothing layers.

Mild Hypothermia

Patients with mild hypothermia are conscious and alert with measured core temperatures of 32–35°C (89.6–95°F). Most will shiver, even violently, if there are enough energy reserves. As the core temperature drops, the patient may begin to demonstrate discoordination or loss of fine motor control. Hemodynamic parameters are generally stable, with tachycardia and tachypnea observed due, in part, to the increased catecholamine response and support of the metabolic demands of shivering. Protection from further heat loss, removal and replacement of wet clothing, and calorie replacement should be initiated simultaneously. Application of insulation (e.g., sleeping bag) and a vapor barrier will optimize passive rewarming. Active external rewarming can be initiated using hot water bottles or rewarming heat packs applied to the neck, chest, upper torso, axilla, and groin. Try to avoid burns to exposed skin. Patients with mild hypothermia retain consciousness but may demonstrate diminished alertness. Transport for further evaluation and observation is recommended if they do not return to full alertness and function in the field.

Moderate Hypothermia

Moderate hypothermia, with core temperatures of 28–32°C (82.4–89.6°F), is the slowing phase of symptom progression. Patients present with bradycardia, respiratory depression, and altered mental status, manifesting as depressed level of consciousness, often stuporous, and hyporeflexia. Shivering generally stops at 30°C (86°F), but there is variation among patients. Active external rewarming should be initiated with heat applied to the upper torso, chest, axilla, and back. Fluid replacement is initiated with intravenous fluids, ideally containing glucose, warmed to 40–42°C (104–107.6°F). Cardiac monitoring is indicated, as a cold heart and hypothermia-associated acidosis increases the risk of unstable arrhythmias. Hemodynamically stable patients may be transported to any hospital; however, if unstable, a hospital with extracorporeal membrane oxygenation (ECMO) is recommended.

Severe/Profound Hypothermia

Core temperatures <28°C (82.4°F) are characterized by stupor, leading to coma with loss of cerebrovascular autoregulation. Further cardiovascular instability manifests as bradycardia, hypotension, and a significant risk for unstable tachycardias, often beginning as atrial fibrillation with progression to ventricular dysrhythmias. There is no coordinated musculoskeletal activity. Patients with severe hypothermia may appear dead. Cardiopulmonary resuscitation (CPR) should be initiated if there is no cardiac activity, as determined by a pulse check of at least 1 minute duration or the absence of organized electrical activity on a monitor. Bedside echocardiography may also be used to identify cardiac activity. Vasoactive medications should be held until the core temperature is >30°C (86°F) and then administered at twice the dosing interval until 35°C (95°F). Defibrillation or cardioversion, if indicated, is attempted once, at maximum power, then held until the core temperature is above 30°C (86°F).

In hypothermic cardiac arrest, rescuers should initiate CPR regardless of the patient's temperature. Contraindications to initiation of CPR include if there is obvious fatal injury, ice or snow is visualized in the airway, chest wall compression is impossible, or rescuers are at risk. The usual signs of death—rigor, pupillary dilation, and lividity—are unreliable in the hypothermic patient.

Complications of hypothermia include compartment syndrome, rhabdomyolysis, hyperkalemia or hypokalemia, hemoconcentration, hypercoagulability, disseminated intravascular coagulation (DIC), confusion (paradoxical undressing), Takotsubo cardiomyopathy, and mydriasis. Core temperature **afterdrop** is a decrease in core temperature after removal from the cold and/or when external rewarming begins; external rewarming extremities with frostbite is another risk factor.

Hypothermia is fatal if not treated. Prevention and risk mitigation through awareness of weather conditions, appropriate clothing and layering systems, and breaks for rewarming during outdoor activities will limit its incidence. Adults supervising children and adolescents participating in outdoor activities must be aware that behavior changes and apparent clumsiness might signal the onset of hypothermia.

SOFT TISSUE COLD INJURY

Soft tissue injuries caused by cold are divided into freezing and nonfreezing injuries. Frostbite is a freezing injury, whereas frostnip, chilblains (pernio), cold immersion, and cold-induced fat necrosis are nonfreezing injuries.

FROSTBITE

Frostbite is an injury occurring at or below freezing temperatures. It can have devastating effects with tissue loss leading to functional debility. It is preventable. Frostbite, like hypothermia, is a condition occurring when tissue heat loss is greater than the warmth delivered by peripheral perfusion. Minimizing exposure to cold, either by avoidance, use of appropriate clothing, and responding to changing conditions appropriately, are keys to frostbite prevention. Clothing, especially hand and footwear, should insulate well and not be constricting. Vasoconstriction inhibits peripheral cutaneous warming. Inhibitors of peripheral perfusion, such as vasoconstricting medications, circulatory disorders (e.g., Raynaud syndrome), and chronic skin conditions (e.g., psoriasis), increase frostbite risk. Emollients applied to the skin do not protect from the cold. Any complaints of numbness are to be taken seriously, and the child should be assessed for signs of cold injury in a protected environment. Frostnip, although not a freezing injury, does indicate that the temperature and exposure conditions may promote frostbite.

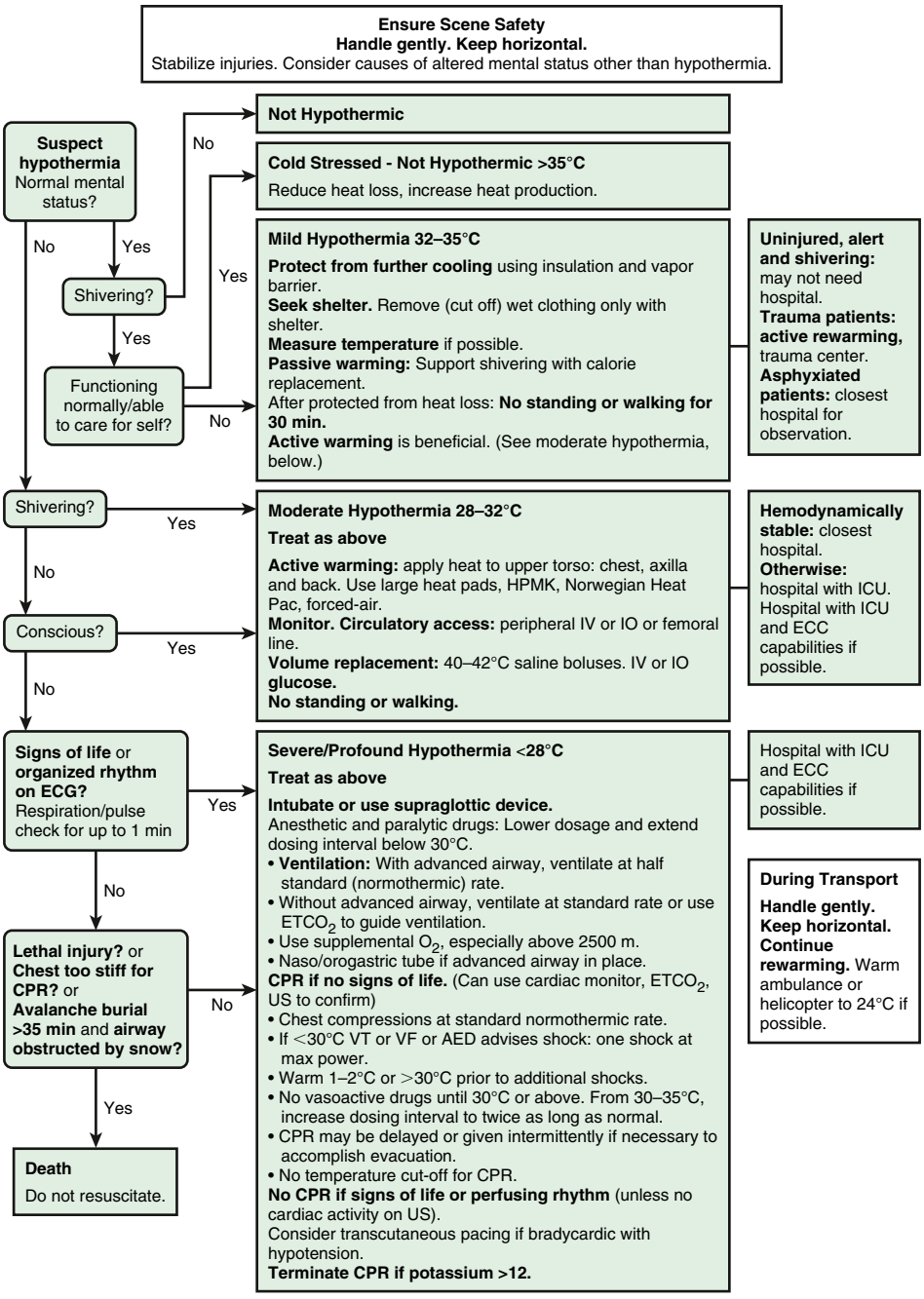

Fig. 90.3 Recommendations for out-of-hospital evaluation and treatment of accidental hypothermia. AED, Automatic external defibrillator; CPR, cardiopulmonary resuscitation; ECC, extracorporeal circulation; ECG, electrocardiogram; $ETCO_2$, end-tidal carbon dioxide; HPMK, Hypothermia Prevention Management Kit; ICU, intensive care unit; IO, intraosseous; IV, intravenous; US, ultrasound; VF, ventricular fibrillation; VT, ventricular tachycardia. (*From Zafren K, Giesbrecht GG, Danzl DF, et al. Wilderness Medical Society practice guidelines for the out-of-hospital evaluation and treatment of accidental hypothermia: 2014 update. Wilderness Environ Med. 2014;25:S66–S85, Fig. 2.*)

Table 90.2 Different Degrees of Frostbite and Their Physiologic Characteristics

GRADE I INJURY	GRADE II INJURY	GRADE III INJURY	GRADE IV INJURY
• Superficial • Edema and redness without tissue necrosis in the affected area • Numbness, firm white-yellow plaque • No blisters or necrosis • Occasional skin desquamation (5-10 days later)	• Blister formation • Erythema, substantial edema • Vesicles with clear or milky fluid • Blisters • Desquamation and black eschar formed	• Tissue necrosis • Hemorrhagic deeper blisters • Skin necrosis • Blue-gray discoloration	• Development of gangrene, requiring amputation • Full-thickness skin, subcutaneous tissue, muscle, tendon, and bone freezing • Little edema • Initially mottled, deep red or eventually dry, black, and mummified

Modified from Joshi K, Goyary D, Mazumder B, et al. Frostbite: Current status and advancements in therapeutics. *J Therm Biol*. 2020;93:102716, Table 1.

Pathophysiology of Frostbite

Frostbite is a freezing injury with four phases: prefreeze, freeze-thaw, vascular stasis, and late ischemic. The degree of cold, duration of exposure, and physiologic compromise caused by medications and underlying illness determine how severe the injury will be. The tissue cooling of **prefreeze** is marked by local vasoconstriction and ischemia without the formation of ice crystals. Intracellular and extracellular ice crystal development causes cellular damage during the **freeze-thaw phase**. Reperfusion leads to ischemic-reperfusion injury and initiation of the inflammatory cascade. **Vascular stasis** is characterized by both blood leaking from vessels and the formation of thrombi. Progressive tissue ischemia from micro-emboli, local thrombosis, and persistent

Fig. 90.4 Frostbite with clear vesiculations. (*Courtesy Dr. Bill Mills.*)

Fig. 90.5 Early appearance of severe frostbite of the hand after thawing. A purple color and absence of blisters are very unfavorable prognostic signs. (*Courtesy Dr. Ken Zafren.*)

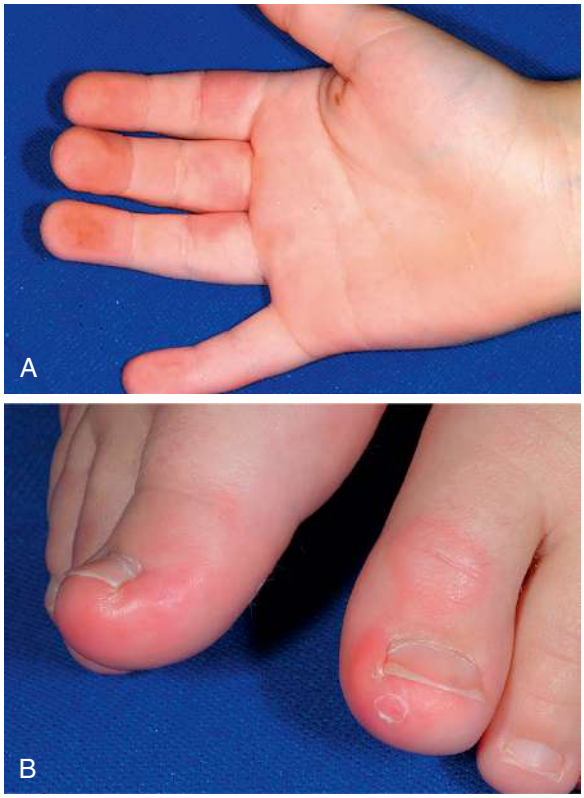

Fig. 90.7 A, Perniosis (chilblains). Edematous, red, painful nodules appeared on the fingers after exposure to cold. B, Perniosis (chilblains). Note the inflamed nodules on the toes of this adolescent girl. Although nodules resolved, painful nodules continued to develop on an annual basis beginning in January and lasting until April. She was otherwise healthy. (*From Paller AS, Mancini AJ. Hurwitz Clinical Pediatric Dermatology, 6th ed. Elsevier: Philadelphia; 2022, Figs. 20.48 and 20.49, p. 566.*)

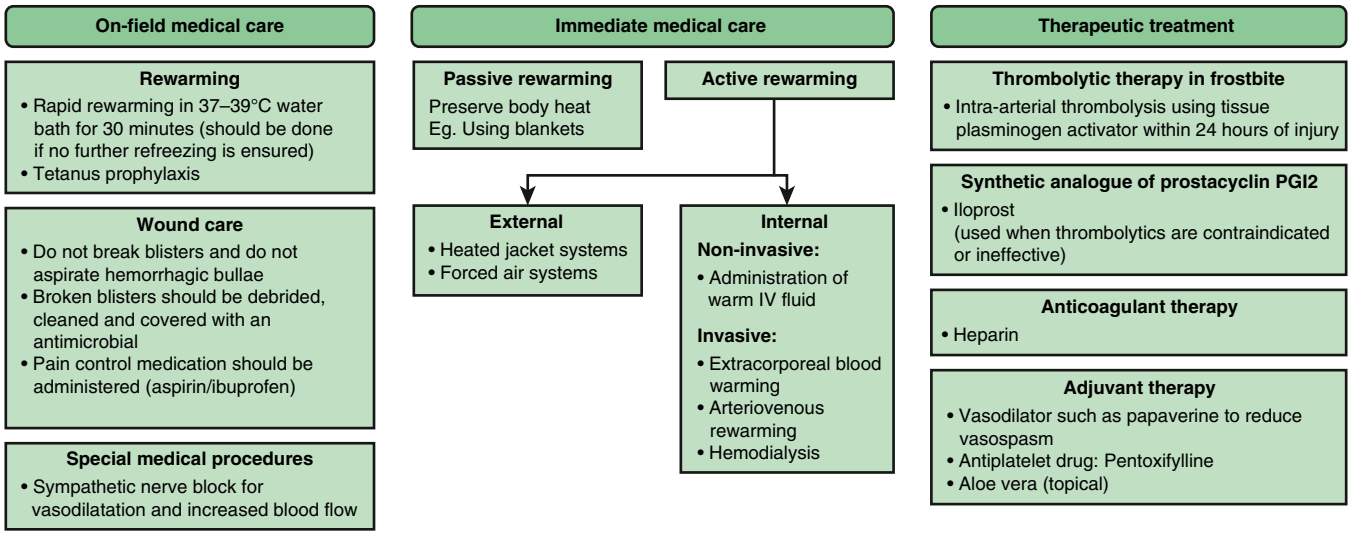

Fig. 90.6 Treatment protocol for the management of frostbite. (*Modified from Joshi K, Goyary D, Mazumder B, et al. Frostbite: Current status and advancements in therapeutics. J Therm Biol. 2020;93:102716, Fig. 2.*)

reperfusion injury marks the **late-ischemic phase**. Compromise of microcirculation and cellular destruction from crystal formation are the main factors contributing to cellular death.

Clinical Presentation of Frostbite

The depth of injury is the basis for the classification of frostbite injury. In the field, frostbite is classified as superficial or deep. Upon arrival to a healthcare facility, a degree or grade of injury is assigned after the tissue has thawed and any advanced imaging is performed (Table 90.2).

First-degree frostbite is marked by numbness and local erythema with a pale raised plaque in the area of injury. Only mild tissue sloughing occurs, and there is no infarction. **Second-degree** injury presents with clear, fluid-filled blisters and surrounding erythema (Fig. 90.4). Local edema may be present. First- and second-degree frostbite injury results in minimal tissue loss and is considered superficial in the field. **Third-degree** frostbite extends into the dermis and dermal vascular plexus. The resulting blisters are hemorrhagic. **Fourth-degree** injury involves the dermis and underlying tissues, extending into muscle and bone (Fig. 90.5). Third- and fourth-degree frostbite has anticipated tissue loss and is field classified as deep.

Treatment of Frostbite

Prevention is preferred for any environmental injury, but rapid recognition and treatment will mitigate the long-term impact. Once frostbite is suspected, the patient should be assessed for concomitant hypothermia. The injury must be protected from the cold and prevented from refreezing if spontaneous thawing has begun. Any constricting items, such as jewelry, are removed. Thawing should be initiated with a circulating water bath at 37–39°C (98.6–102.2°F). Pain medication should be administered. There are numerous combined therapies for frostbite, including anticoagulants, thrombolytics, and vasodilators (Fig. 90.6). The indications for each therapy depend on the extent of injury, length of time since tissue thaw, local availability, and individual national regulatory decisions. It is recommended that the clinician be aware of their local resources and protocols. Regardless, treatment with these agents must be initiated within 12-72 hours of tissue thaw.

NONFREEZING COLD INJURY

Nonfreezing cold injuries include but are not limited to frostnip, chilblains (pernio), cold-immersion foot, and cold-induced fat necrosis.

Frostnip is associated with vasoconstriction of skin exposed to the cold with ice crystals, or frost, forming on the skin surface. The tissue may be numb, and local pallor is present. There is no cellular damage, and the condition resolves rapidly upon warming. Frostnip does indicate that conditions are appropriate for frostbite, and preventative measures should be taken.

Chilblains, also called **pernio**, is an idiopathic condition suspected to be a vasculopathy. Typically occurring in cold, damp conditions, vasculitic-appearing lesions develop on the fingers and toes, ears, and exposed areas of the legs after environmental exposure (Fig. 90.7). It is suspected that vasoconstriction and inflammatory reaction are responsible for the lesions. Recognition and prevention of further cold exposure is key to treatment. The lesions are self-limiting, and symptoms may be addressed with nonsteroidal antiinflammatory drugs (NSAIDs) and topical soothing creams. Continued exposure to cold can cause persistent lesions. Lesions similar to chilblains have been noted in children with COVID-19 infection. **Familial chilblain lupus**, an autosomal dominant variant of lupus, is caused by variants in the *TREX1* and *SAMHD1* genes (see Chapter 90.1). Patients develop cold-induced erythematous peripheral skin lesions and manifest systemic disease typical of lupus. In addition, fever and arthralgias may be present.

Immersion foot or **trench foot** occurs with continuous immersion in warm or cold water. The injury occurs more rapidly in cold water. Continuous exposure to the wet environment, whether through actual immersion in water or saturated footwear, causes hyperemia, edema, and ultimately blister formation with skin sloughing. The condition can progress to ischemia and gangrene. Awareness of wet footwear and subsequent changing, or drying, of shoes and socks is the method of prevention. Vapor barrier socks or boots do not prevent sweat from accumulating and creating a wet environment. Like other cold injuries, treatment consists of thoroughly drying and warming the tissue. Antibiotics are not necessary unless signs of infection are present.

Cold-induced fat necrosis is secondary to local cold injury to the superficial adipose tissue. It presents with raised, erythematous nodules or plaques, evolving over 12-72 hours after exposure to cold. Distribution in children is predominantly on the face, specifically the cheeks and forehead. Obese children and adolescents may have lesions on areas poorly protected from the cold, including the buttocks, thighs, abdominal pannus, and under the chin. Lesions are self-limiting and typically resolve in 10-20 days. Treatment consists of rewarming, avoidance of the cold, and NSAIDs as necessary for discomfort.

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90.1 Cold-Induced Autoinflammatory and Other Genetic Disorders

James J. Nocton and James W. Verbsky

A number of **autoinflammatory** and other genetic disorders have been identified that are characterized by an *exacerbation of symptoms upon exposure to cold temperatures*. These disorders differ from **cold injury**, **cold urticaria**, and problems related primarily to vasoconstriction because they typically manifest very early in life and are associated with a wider spectrum of signs and symptoms, reflecting either underlying systemic inflammation or the protean effects of specific genetic variants. A relatively lower ambient temperature or rapid cooling and evaporation from the skin are often sufficient to produce the signs and symptoms of these disorders; therefore the relationship to cold temperature is not always obvious. The genetic variants associated with most of these disorders impact cellular signaling pathways that lead to the expression of proinflammatory cytokines in the absence of an extrinsic trigger; therefore most of these diseases are classified as autoinflammatory.

These conditions should be suspected primarily in infants or very young children who develop persistent, recurrent, or periodic fevers associated with rashes or arthralgias that cannot be explained by an infectious disease or another chronic inflammatory or rheumatic disease. Signs and symptoms associated with these diseases may begin as early as the first week of life. The very early onset distinguishes these genetic diseases from acquired conditions such as Raynaud phenomenon, pernio, cryoglobulinemia, cold urticaria, and other cold-induced problems potentially related to acquired autoimmunity. The rashes are most often evanescent and appear similar to urticaria; however, they are usually not pruritic and are histologically different from urticaria. Laboratory evidence of chronic inflammation is often present, including elevations of the erythrocyte sedimentation rate and C-reactive protein. The association with cold exposure may be subtle and not initially apparent.

The diagnostic algorithm for these disorders should begin with a thorough history and a careful examination, paying particular attention to potential additional signs of conjunctivitis, a frequent accompanying feature, decreased limb movement that might indicate arthralgia or arthritis, the morphology of any cutaneous lesions, and the association of symptoms and signs with cooling or colder temperatures. Unlike cold urticaria, the hivelike lesions often associated with these disorders cannot be precipitated by a cold stimulation test using the application of an ice cube to the skin. Measurement of serum inflammatory markers may help distinguish autoinflammatory disease from more benign conditions; infectious diseases may need to be excluded with appropriate testing. A skin biopsy may provide information that will help narrow the differential diagnosis by identifying either a neutrophilic dermatosis, granulomatous inflammation, or vasculitis characteristic of one of these diseases. Ultimately, focused genetic sequencing can

be performed, searching for specific genetic variants that will confirm a diagnosis.

Familial cold autoinflammatory syndrome (FCAS), along with neonatal-onset multisystem inflammatory disorder (NOMID) and Muckle-Wells syndrome (MWS), constitute the **cryopyrin-associated periodic syndromes (CAPS)** (see Chapter 204). These diseases are all the result of pathogenic variants in *NLRP3* which encodes the protein **cryopyrin**, a component of the inflammasome complex, which is critical in the production of the proinflammatory cytokines interleukin (IL)-1β and IL-18. Although each of these diseases may be exacerbated by cold exposure or cooling, the association with cold is most consistent in those with **FCAS**. **FCAS** should be considered in infants who develop episodes of a hivelike rash, often beginning in the neonatal period, accompanied by fever, conjunctivitis, joint pain, neutrophilia, thrombocytosis, and elevated inflammatory markers, and triggered by exposure to cold or low ambient temperatures. The rash is typically not pruritic and histologically consists of a neutrophilic perivascular and perieccrine inflammatory infiltrate. Episodes are short and generally last less than 24 hours. **MWS** is more severe than FCAS, causing more frequent hivelike rashes and fevers, along with arthralgias, conjunctivitis, and aseptic meningitis, and with potential eventual progression to hearing loss. Like FCAS, the onset of symptoms is most often in infancy, and the histology of skin lesions in these two disorders is similar. **NOMID** is the most severe form of CAPS and is associated with a nonpruritic urticarial rash often present at birth and more profound neurologic and bone disease. CAPS are inherited in an autosomal dominant manner, and the diagnosis is made based on clinical features and the identification of a variant in the NLRP3 gene. Variants in *NLRP12* and in *NLRC4* have also been associated with similar clinical syndromes sometimes referred to as **FCAS2** and **FCAS4**, respectively. Treatment with the IL-1 inhibitors anakinra and canakinumab has been effective in most individuals with CAPS.

PLCG2-associated antibody deficiency and immune dysregulation (PLAID) (sometimes referred to as **FCAS3**) is an autosomal dominant disease resulting from a pathogenic variant of *PLCG2*, which encodes a transmembrane enzyme expressed primarily in myeloid and lymphoid cells that regulates inflammasome activity and proinflammatory cytokine production. PLAID causes pruritic urticaria from birth induced by ambient cold temperatures or cooling and lasting for minutes to hours. In some individuals, acral blistering lesions resembling a burn may also be present during infancy on the ears, nose, and fingers. Histology of urticarial lesions reveals increased mast cells. Because PLCG2 is expressed in mast cells and affects mast cell degranulation, these subjects can have more classic hives as compared with other FCAS syndromes. Other lesions reveal noncaseating granulomas. Older individuals may develop syncope induced by cold exposure and a burning sensation in the throat when eating cold foods. Hypogammaglobulinemia may lead to frequent sinopulmonary and other infections. The diagnosis is made based on clinical features and the identification of variants in the PLCG2 gene. Treatment of PLAID includes avoiding evaporative cooling and minimizing cold exposure, antihistamines, and for those with evidence of immunodeficiency, intravenous immunoglobulin infusions to prevent frequent infections.

STING-associated vasculopathy with onset in infancy (SAVI) is an autosomal dominant disease resulting from a pathogenic variant in *TMEM173*, which encodes **stimulator of interferon genes (STING)**, an activator of interferon gene transcription (see Chapter 205). Signs and symptoms usually appear in infancy but may also appear later and include fever and a variety of cutaneous lesions. Violaceous nodules and plaques on the cheeks, ears, and nose and telangiectasias, pustules, or blisters, often most noticeable on the extremities, may occur. The skin lesions are exacerbated by cold temperatures, and some develop ulcerative or gangrenous lesions. In time, interstitial lung disease progressing to fibrosis has been described. Histology reveals vasculitis of medium and small vessels. The diagnosis is made based on clinical features and the identification of the variant in the TMEM173 gene. Responses to treatment with corticosteroids and immunomodulators, including cyclophosphamide and mycophenolate mofetil, have been variable and inconsistent. Janus kinase inhibitors, which inhibit interferon receptor signaling, have shown promise in treatment of these disorders.

Familial chilblain lupus is a rare condition triggered by cold exposure that presents with painful, bluish-red, papular or nodular lesions of the skin in acral locations. Ulceration can occur, but deep ulceration and necrosis are infrequent, and the lesions tend to heal without scarring. This is an autosomal dominant disorder caused by heterozygous variants in *TREX1* or *SAMHD1*, the same genes containing variants associated with Aicardi-Goutières syndrome (AGS). AGS is a syndrome characterized by developmental delay, abnormal neurologic signs, microcephaly with brain calcifications, and CNS pleocytosis, as well as skin lesions resembling chilblains. Both *TREX1* and *SAMHD1* are involved in DNA degradation, and their deficiencies result in intracellular nucleic acid that stimulates interferon production. AGS and familial chilblain lupus can be considered a spectrum of severity of the same genetic defect.

Factor XII–associated cold autoinflammatory syndrome is an autosomal dominant disease resulting from a pathogenic variant in *F12* encoding the coagulation factor XII. The variant leads to spontaneous activation of factor XII, which in turn increases bradykinin and IL-1 levels. Individuals with this mutation develop an urticarial-like rash that begins in the first few weeks of life precipitated by cold. The rash is nonpruritic and evanescent, and as individuals age it is accompanied by more severe systemic symptoms of chills, headaches, arthralgias, and fatigue. Serum inflammatory markers are elevated, and skin histology reveals perivascular macrophage and neutrophilic infiltrates. The diagnosis is made by identifying a variant in *F12*. Treatment with the IL-1 receptor antagonist anakinra or the bradykinin B2 receptor antagonist icatibant has shown promise in a small number of individuals.

Crisponi syndrome/cold-induced sweating syndrome (CS/CISS) is an autosomal recessive disease resulting from variants in *CRLF1* or *CLCF1*. These genes encode proteins involved in neurologic development, including facial motor neurons and the sympathetic nervous system; therefore this syndrome is not classified as an autoinflammatory syndrome. Symptoms and signs are typically apparent in the neonatal period and include fever, camptodactyly, and involuntary episodic contractions of facial and pharyngeal muscles resulting in breathing and feeding difficulties. There is high neonatal mortality, and those that survive develop cold-induced profuse sweating in childhood. Scoliosis and other dysmorphic features (depressed nasal bridge, high arched palate) are also common. The diagnosis is made by identifying a variant most commonly in *CRLF1*. Treatment of the neonatal symptoms is supportive. The cold-induced sweating is managed with clonidine, amitriptyline, or moxonidine.

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Chapter 91

Anesthesia and Perioperative Care

John P. Scott

The continuum of anesthesia includes varying degrees of sedation (i.e., mild, moderate, or deep) and general anesthesia. All forms of **sedation** are characterized by some preservation of purposeful movement (see Chapter 92), whereas **general anesthesia** is defined by the complete loss of consciousness. Potent pharmacologic agents are required to suppress the perception and physiologic response to noxious stimuli. Perioperatively, the anesthesiologist is responsible for providing hypnosis and analgesia while preserving physiologic homeostasis (Table 91.1). This begins with the performance of a comprehensive preanesthesia history (Table 91.2). Although anesthetic risk has greatly decreased with advancements in pharmacology and monitoring technology, the persistent risk of perioperative morbidity and mortality demands vigilance. The risk is elevated in certain disease states (Table 91.3).

PREANESTHETIC EVALUATION

All children presenting for surgery should undergo a preanesthetic history and multiorgan system assessment with assignment of **American Society of Anesthesiologists Physical Status (ASA-PS)** (Table 91.4). Children of ASA-PS I-II generally require a brief focused history and physical examination with no additional testing. Patients with a complex medical history of ASA-PS ≥III require a more comprehensive preanesthetic assessment, often with ancillary preoperative testing. Every patient should be screened for anesthetic risks, including drug allergies, previous reactions to anesthetics, and family history of problems with anesthesia (e.g., sudden perioperative death, hyperthermia after surgery), which may indicate risk of malignant hyperthermia.

Respiratory System

Recent respiratory tract infections should be noted. *Clear rhinorrhea without fever or evidence of lower respiratory disease is not associated with increased anesthetic risk.* Respiratory illnesses associated with fever, mucopurulent nasal discharge, productive cough, or lower respiratory symptoms (wheezing, rales) are associated with increased airway reactivity and anesthetic complications (laryngospasm, bronchospasm, reduced mucociliary clearance, atelectasis, and hypoxemia) for up to 6 weeks thereafter. Thus elective procedures requiring general anesthesia should be postponed 4-6 weeks in this setting.

Children with reactive airway disease require a thorough preanesthetic assessment. Acute, potentially fatal bronchospasm can occur during induction of anesthesia and endotracheal intubation for routine, minor surgery in children with asthma. Risk factors for anesthetic complications include previous asthma exacerbations requiring (1) hospital admission within the previous year, (2) emergency department (ED) care within the last 6 months, (3) previous intensive care unit (ICU) admission, or (4) previous parenteral systemic corticosteroids. Ideally, children should be free of wheezing for least several days before surgery, even if this necessitates increased controller medication administration (β-adrenergic agonist and corticosteroids). Active wheezing may be an indication to delay elective surgery. Chronic respiratory conditions such as bronchopulmonary dysplasia and cystic fibrosis are also associated with significant intraoperative risks. Every effort should be made to ensure that children with such disorders achieve optimal respiratory status before surgery.

Table 91.1 Goals of Anesthesia

Analgesia
Amnesia
Hypnosis
Akinesia
Maintenance of physiologic homeostasis
Vigilance

Airway Evaluation

Induction of general anesthesia is associated with reduced spontaneous ventilation and airway reflexes. Prediction of difficult bag-mask ventilation and/or intubation before anesthesia is critical. Congenital anomalies associated with airway compromise include micrognathia, macroglossia, and thoracic anomalies (Table 91.5). Conditions that impair mouth opening (e.g., temporomandibular joint disease) should be noted. A history of wheezing or stridor may indicate postoperative airway complications and difficult intraoperative airway management. It is imperative to ask about a history of sleep-disordered breathing, including obstructive and central sleep apnea, as this may lead to increased risk of perianesthetic respiratory complications in children. Polysomnography is the gold standard for diagnosis and grading of sleep disordered breathing. The **STBUR** (snoring, trouble breathing, unrefreshed) questionnaire is used to identify patients with sleep-disordered breathing who may be at risk for perioperative respiratory complications. Postoperative admission for monitoring may be indicated for patients with moderate and severe forms of sleep-disordered breathing.

Cardiovascular System

Most anesthetic agents possess myocardial depressant properties. All patients should be screened for the presence of heart disease. Important cardiovascular considerations include history of congenital heart disease (CHD), cyanosis, arrhythmias, or cardiomyopathy. Room-air pulse oximetry should be performed as part of the preanesthetic evaluation. Accurate diagnosis of cardiac murmurs in neonates is essential. A history of cardiac dysrhythmias should be investigated because inhalational anesthetics may be arrhythmogenic. A pediatric cardiologist should evaluate children with known CHD undergoing surgery. Preoperative ancillary studies may include chest x-ray, electrocardiogram (ECG), echocardiogram, or cardiac catheterization. Lesions associated with increased anesthetic risk include single-ventricle heart disease, fixed obstructive outflow tract lesions (aortic valve and pulmonary valve stenosis), and cardiomyopathy. Children with these conditions should be cared for by a **cardiac anesthesia service**. Antibiotic prophylaxis for the prevention of bacterial endocarditis should be administered when appropriate in accordance with the American Heart Association (AHA) guidelines.

Hematologic System

Evidence of coagulopathy should be sought. Easy bruising, familial bleeding disorders, and anticoagulant (e.g., aspirin, heparin, direct oral anticoagulant [DOAC], warfarin) use should be discussed. Preoperative adequacy of hemostatic function (e.g., platelet count, fibrinogen, prothrombin time, partial thromboplastin time) and correction of coagulopathic disorders may be indicated for complex procedures associated with significant risk of perioperative hemorrhage. In neonates, assurance of vitamin K prophylaxis and adequate coagulation status is critical before any major surgery. Although anemia may be well tolerated in healthy children, anesthesia and surgery increase oxygen consumption. Preoperative anemia should be corrected when oxygen delivery is limited or blood loss is expected. In the patient with life-threatening hemorrhage (trauma), massive transfusion protocols of 1:1:1 replacement of packed red blood cells:fresh-frozen plasma:platelets should be used. Initiation of early antifibrinolytic therapy in the setting of life-threatening hemorrhage has been linked to reduced early morality.

Neurologic System

A history of neurologic and neuromuscular disorders should be sought. Preoperative developmental assessments may be helpful in interpreting age-dependent variation in the response to pain. Maintenance of appropriate perioperative anticonvulsant therapy is essential

Table 91.2 The Preanesthetic History

Child's Previous Anesthetic and Surgical Procedures
- Review previous anesthetic records:
  - Ease of mask ventilation
  - Grade of laryngoscopy; type and size of laryngoscope; endotracheal tube size
  - Issues during emergence (awakening) from anesthesia (postoperative vomiting, emergence delirium)
  - History of hyperthermia or acidosis in the child or family members

Perinatal Problems (Especially for Infants)
- Prematurity
- Need for supplemental oxygen or intubation and ventilation
- History of apnea and bradycardia
- History of cardiovascular compromise
- Other major illnesses and hospitalizations
- Family history of anesthetic complications, malignant hyperthermia, or pseudocholinesterase deficiency

Respiratory Problems
- Long-term exposure to environmental tobacco smoke
- Obstructive breathing score
- STBUR (snoring, trouble breathing, unrefreshed)
- Cyanosis (especially in infants <6 mo of age)
- Recurrent respiratory infections
- Recent lower respiratory tract infection
- Previous laryngotracheitis (croup) or laryngomalacia
- Reactive airway disease
- Airway abnormalities, facial anomalies, mucopolysaccharidosis

Cardiac Problems
- Murmur or history of congenital heart disease
- Dysrhythmia
- Exercise intolerance
- Syncope
- Cyanosis

Gastrointestinal Problems
- Reflux and vomiting
- Feeding difficulties
- Failure to thrive
- Liver disease
- Exposure to infectious pathogens

Neuromuscular Problems
- Neuromuscular diseases
- Developmental delay
- Myopathy
- Seizure disorder

Hematologic Problems
- Anemia
- Bleeding diathesis
- Tumor
- Immunocompromise
- Prior blood transfusions and reactions

Renal Problems
- Renal insufficiency, oliguria, anuria
- Fluid and electrolyte abnormalities

Psychosocial Considerations
- Drug abuse, use of cigarettes or alcohol
- Physical or sexual abuse
- Family dysfunction
- Previous traumatic medical or surgical experience
- Psychosis, anxiety, depression

Gynecologic Considerations
- Sexual history (sexually transmitted infections)
- Possibility of pregnancy

Current Medications
- Prior administration of corticosteroids

Allergies
- Drugs
- Iodine
- Latex products
- Surgical tape
- Food (especially soy and egg albumin)

Other
- Dental condition (loose or cracked teeth)
- When and what the child last ate (especially in emergency procedures)

in children with seizure disorders because the seizure threshold may be lowered perioperatively. Children with obstructive hydrocephalus typically require ventriculoperitoneal (VP) shunt insertion to divert cerebrospinal fluid (CSF) and to prevent intracranial hypertension (ICH). Repeated shunt malfunction is common, and these children may present for shunt revision with signs of ICH (vomiting, altered mentation, sundowning). Similarly, shunt patency and function should be ensured preoperatively in children with VP shunts presenting for non-neurosurgical procedures.

Psychologic Assessment

Surgery and painful medical procedures are psychologically traumatic events for children and families. Children who require anesthesia may experience fear and anxiety. They may also sense stressful signals from parents and caregivers. Children undergoing surgery may exhibit negative behavioral changes postoperatively. These maladaptive behavioral responses may include enuresis, separation anxiety, temper tantrums, and nighttime crying, as well as fear of strangers, medical providers, and hospitals. Sleep quality may be altered postoperatively, resulting in further behavioral compromise. Preoperative psychologic preparation programs have been developed to reduce the incidence of perioperative behavioral changes. **Parental presence during induction (PPI)** has not been shown to improve postoperative behavior. Oral preoperative midazolam (0.5 mg/kg) produces rapid-onset anxiolysis and amnesia and may decrease negative behavioral changes.

Genetic Evaluation

Children with genetic conditions may have syndrome-specific anesthetic considerations. For example, children with trisomy 21 may have cardiac anomalies, macroglossia, upper airway obstruction, and hypothyroidism (see Chapter 99.2). Atlantoaxial instability, common in trisomy 21, has been linked to cervical dislocation and spinal cord trauma with neck extension during intubation. Some anesthesiologists recommend extension and flexion lateral neck films to detect instability before surgery. For children with other known genetic disorders, it is essential to review specific anesthetic considerations.

PREOPERATIVE PREPARATION

Preoperative Fasting

Preoperative fasting guidelines have been developed to reduce the incidence of aspiration of gastric contents during anesthesia. Aspiration may lead to laryngospasm, bronchospasm, and postoperative pneumonitis. Aspiration of gastric contents may be a potentially lethal complication in children with chronic lung disease or critical illness. Table 91.6 lists preoperative fasting guidelines (e.g., nothing by mouth, or nil per os [NPO] status). Clear, sweet liquids (e.g., Pedialyte, 5% dextrose

Table 91.3 Specific Pediatric Diseases and Their Anesthetic Implications

DISEASE	IMPLICATIONS
RESPIRATORY SYSTEM	
Asthma	Intraoperative bronchospasm that may be life threatening
	Pneumothorax or atelectasis
	Optimal preoperative medical management is essential
Difficult airway	Special equipment and personnel may be required
	Should be anticipated with dysmorphic features or storage diseases
	Patients with trisomy 21 may require atlantooccipital joint evaluation
	Increased risk with acute airway obstruction, epiglottitis, laryngotracheobronchitis, or airway foreign body
Bronchopulmonary dysplasia	Barotrauma with positive pressure ventilation
	Oxygen toxicity, pneumothorax a risk
Cystic fibrosis	Airway reactivity, bronchorrhea, increased intraoperative pulmonary shunt and hypoxia
	Risk of pneumothorax, pulmonary hemorrhage
	Atelectasis, risk of prolonged postoperative ventilation
	Patient should be assessed for cor pulmonale
Sleep apnea	Pulmonary hypertension and cor pulmonale must be excluded
	Careful postoperative observation for obstruction required
CARDIAC	
	Bacterial endocarditis prophylaxis as indicated
	Use of air filters; careful purging of air from the intravenous equipment
	Physician must understand the effects of various anesthetics on the hemodynamics of specific lesions
	Possible need for preoperative evaluation of myocardial function and pulmonary vascular resistance
	Provide information about pacemaker function and ventricular device function
HEMATOLOGIC	
Sickle cell disease	Possible need for simple or exchange transfusion based on preoperative hemoglobin concentration and percentage of hemoglobin S
	Avoid hypoxemia, hypothermia, dehydration, and hyperviscosity states
Oncology	Pulmonary evaluation of patients who have received bleomycin, *bis*-chloroethyl-nitrosourea, chloroethyl-cyclohexyl-nitrosourea, methotrexate, or radiation to the chest
	Avoidance of high oxygen concentration
	Cardiac evaluation of patients who have received anthracyclines; risk of severe myocardial depression with volatile agents
	Potential for coagulopathy
RHEUMATOLOGIC	
	Limited mobility of the temporomandibular joint, cervical spine, arytenoid cartilages
	Careful preoperative evaluation required
	Possible difficult airway
GASTROINTESTINAL	
Esophageal, gastric	Potential for reflux and aspiration
Liver	Altered metabolism of many anesthetic drugs
	Potential for coagulopathy and uncontrollable intraoperative bleeding
RENAL	
	Altered electrolyte and acid-base status
	Altered clearance of many anesthetic drugs
	Need for preoperative dialysis in selected cases
	Succinylcholine to be used with extreme caution and only when the serum potassium level has recently been shown to be normal
NEUROLOGIC	
Seizure disorder	Avoidance of anesthetics that may lower the seizure threshold
	Optimal control ascertained preoperatively
	Preoperative serum anticonvulsant measurements
Increased intracranial pressure	Avoidance of agents that increase cerebral blood flow
	Maintain cerebral perfusion pressure.
Neuromuscular disease	Avoidance of depolarizing relaxants; at risk for hyperkalemia
	Patient may be at risk for malignant hyperthermia; avoid volatile anesthetics in myopathies
Developmental delay	Patient may be uncooperative during induction and emergence
Psychiatric	Monoamine oxidase inhibitor (or cocaine) may interact with meperidine, resulting in hyperthermia and seizures
	Selective serotonin reuptake inhibitors may induce or inhibit various hepatic enzymes that may alter anesthetic drug clearance
	Illicit drugs may have adverse effects on cardiorespiratory homeostasis and may potentiate the action of anesthetics
ENDOCRINE	
Diabetes	Greatest risk is unrecognized intraoperative hypoglycemia; intraoperative blood glucose level monitoring needed especially when insulin is administered
SKIN	
Burns	Difficult airway
	Fluid shifts
	Bleeding
	Risk of rhabdomyolysis and hyperkalemia from succinylcholine after burns for many months
IMMUNOLOGIC	
	Retroviral drugs may inhibit benzodiazepine clearance
	Immunodeficiency requires careful infection control practices
	Cytomegalovirus-negative blood products, irradiation, or leukofiltration may be required
METABOLIC	
	Careful assessment of glucose homeostasis in infants

in water [D5W]) facilitate gastric emptying, prevent hypoglycemia, and may be given up to 2 hours before anesthesia. Breast milk may be given to infants up to 4 hours before surgery. Solids should be avoided for 6-8 hours before surgery. Conditions associated with delayed gastric emptying may require prolonged periods of fasting. The optimal duration of preoperative fasting in otherwise well patients without risk factors for delayed gastric emptying remains a source of controversy. Many efforts have sought to shorten NPO duration for clear liquids from 2 hours to 1 hour in order to preserve fluid and glycemic balance in children presenting for surgery.

Table 91.4 American Society of Anesthesiology Physical Status Classification

Class 1: Healthy patient, no systemic disease
Class 2: Mild systemic disease with no functional limitations (mild chronic renal failure, iron-deficiency anemia, mild asthma)
Class 3: Severe systemic disease with functional limitations (hypertension, poorly controlled asthma or diabetes, congenital heart disease, cystic fibrosis)
Class 4: Severe systemic disease that is a constant threat to life (critically and/or acutely ill patients with major systemic disease)
Class 5: Moribund patients not expected to survive 24 hr, with or without surgery
Additional classification: "E"—emergency surgery

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Table 91.5 Common Difficult Airway Syndromes

Achondroplasia
Airway tumors, hemangiomas
Apert syndrome
Beckwith-Wiedemann syndrome
Choanal atresia
Cornelia de Lange syndrome
Cystic hygroma/teratoma
DiGeorge syndrome
Fractured mandible
Goldenhar syndrome
Juvenile rheumatoid arthritis
Mucopolysaccharidosis
Pierre Robin syndrome
Smith-Lemli-Opitz syndrome
Treacher-Collins syndrome
Trisomy 21
Turner syndrome

The Full Stomach

Gastric emptying may be delayed for up to 96 hours after an acute episode of trauma or surgical illness. To mitigate risk of aspiration, it is desirable to secure the airway as rapidly as possible during induction of anesthesia in patients at risk for having a full stomach. Under these circumstances, rapid sequence induction of anesthesia is indicated (**rapid sequence induction**; see Chapter 86).

Parental Presence During Induction of Anesthesia

Parents or guardians may expect to be with their child during the induction of anesthesia. Removing a fearful child from a parent is stressful for the child and caregivers. Premedication with an oral benzodiazepine (e.g., midazolam) frequently provides calm, smooth parental separation conditions. When parental separation cannot be achieved comfortably with premedication and behavioral modification (patient education and desensitization to the operative environment), PPI may be indicated. Although PPI in the hands of a confident, competent anesthesia practitioner may replace the need for preoperative medication, it does not reliably predict smooth induction. PPI has not been shown to decrease emergence delirium or postoperative behavioral changes, and it does not appear to be superior to premedication with oral midazolam.

GENERAL ANESTHESIA

Analgesia

Pediatric anesthesiologists are responsible for providing analgesia to children for procedures within operating room (OR) and non-OR settings (Table 91.7). Multimodal techniques exist to provide pain relief during operative procedures for children of all ages, including critically ill infants. Effective analgesia is essential to blunt physiologic responses to painful stimuli (surgery) and modulate the deleterious physiologic and metabolic consequences. The response to painful and stressful stimuli may provoke **systemic inflammatory response syndrome (SIRS)**, which has been linked to increased catabolism, physiologic instability, and mortality (see Chapter 85).

Table 91.6 Guidelines for Preoperative Fasting ("2-4-6-8 Rule")*

TIME BEFORE SURGERY (hr)	ORAL INTAKE
2	Clear, sweet liquids
4	Breast milk
6	Infant formula, fruit juices, gelatin
8	Solid food

*These are general guidelines and may differ among hospitals.

Hypnosis and Amnesia

The attenuation of both consciousness **(hypnosis)** and conscious recall **(amnesia)** is critical during pediatric anesthesia care. Awareness during procedures may be as physically and psychologically deleterious as the experience of pain. A primary goal of anesthetic management is to minimize fear and anxiety during both painful and nonpainful procedures. Many drugs provide anxiolysis and amnesia for such events (Table 91.8). However, it is important to remember that sedative-hypnotic agents may alter consciousness without producing analgesia; *analgesia* and *hypnosis* are not synonymous. It is also possible to provide analgesia (local, spinal, or epidural) without altering consciousness.

Sedation describes a medically induced state in the continuum between wakefulness and general anesthesia in which patients maintain the ability to respond purposefully to varying degrees of stimulation (see Table 91.7). *Light (minimal) sedation* is defined as anxiolysis with minimally reduced reflexes or airway patency with normal response to verbal commands. In *moderate sedation,* the patient continues to respond purposefully to verbal commands, either alone or with light touch. *Deep sedation* is defined by preservation of purposeful movement with repeated or painful stimulation. **General anesthesia** is characterized by unconsciousness, amnesia, and reduced physiologic reflexes, including cardiorespiratory reflexes (**airway-protective** and **vasomotor reflexes**). It is common to transition between states of sedation and general anesthesia with loss of consciousness, airway patency, and airway-protective reflexes; in this scenario, loss of cardiovascular stability may occur. Individuals providing sedation and anesthesia for children must be able to identify the anesthetic state of the patient and support cardiorespiratory insufficiency.

Akinesia (Immobility or Muscular Relaxation)

Akinesia, the absence of movement, is commonly indicated to ensure safe and adequate operative conditions. Neuromuscular blocking agents (NMBAs) may be used to produce akinesia (see Table 91.8). However, the absence of movement is not indicative of hypnosis, amnesia, or analgesia. Whenever NMBAs are used, *sedation and analgesia must be provided.*

Monitoring

Administration of anesthesia increases the need to monitor and support physiologic integrity and homeostasis because of potentially life-threatening physiologic consequences (see Tables 91.7 and 91.8). Consequently, the ASA mandates routine monitoring of oxygenation, ventilation, and circulation during the provision of anesthesia. This includes assessment of continuous pulse oximetry, capnography, electrocardiography, intermittent blood pressure measurements (every 5 minutes), and temperature when temperature instability is anticipated. The use of advanced invasive (arterial and central venous pressure) or noninvasive (near-infrared spectroscopy) monitoring varies based on procedural complexity and ASA-PS.

Table 91.7 Definitions of Anesthesia Care

MONITORED ANESTHESIA CARE

A designated anesthesia service in which an anesthesiologist has been requested to participate in the care of a patient undergoing a diagnostic or therapeutic procedure.

Monitored anesthesia care includes all aspects of anesthesia care: a preprocedure assessment, intraprocedure care, and postprocedure anesthesia management.

During monitored anesthesia care, the anesthesiologist or a member of the anesthesia care team provides a number of specific services, which may include but are not limited to the following:

- Discussing anesthesia care with the family and child, obtaining consent for anesthesia, allaying anxiety and answering questions—family-centered anesthesia care.
- Monitoring of vital signs, maintenance of the patient's airway, and continual evaluation of vital functions.
- Diagnosing and treating clinical problems that occur during the procedure.
- Administering sedatives, analgesics, hypnotics, anesthetic agents, or other medications as necessary to ensure patient safety and comfort.
- Providing other medical services as needed to accomplish the safe completion of the procedure.

Anesthesia care often includes the administration of medications for which the loss of normal protective reflexes or loss of consciousness is likely.

Monitored anesthesia care refers to those clinical situations in which the patient remains able to protect the airway for the majority of the procedure.

If the patient is rendered unconscious and/or loses normal protective reflexes for an extended period, this is considered a general anesthetic.

LIGHT SEDATION

Administration of anxiolysis or analgesia that obtunds consciousness but does not obtund normal protective reflexes (cough, gag, swallow, hemodynamic) or spontaneous ventilation; patient responds normally to verbal commands.

MODERATE SEDATION

No interventions are required to maintain a patent airway or spontaneous ventilation; patient responds purposefully to verbal commands either on their own or with light touch.

DEEP SEDATION

Sedation that obtunds consciousness and normal protective reflexes or possesses a significant risk of blunting normal protective reflexes (cough, gag, swallow, hemodynamic); hemodynamic and respiratory insufficiency may occur.

GENERAL ANESTHESIA

Administration of hypnosis, sedation, and analgesia that results in the loss of normal protective reflexes.

REGIONAL ANESTHESIA

Induction of neural blockade (either central, neuraxial, epidural, or spinal; or peripheral nerve block, e.g., digital nerve block, brachial plexus block), which provides analgesia and is associated with regional motor blockade.

Consciousness is not obtunded.

Special expertise is required.

Frequently, in children, anxiolysis and sedation are also necessary for this technique to be successful.

Regional anesthesia (e.g., caudal epidural blockade) is used to supplement general anesthesia and provide postoperative analgesia.

LOCAL ANESTHESIA

Provision of analgesia by local infiltration of an appropriate anesthetic agent.

Does not require the presence or involvement of an anesthesiologist, although an anesthesiologist may provide local anesthesia services.

Specific Medications

Inhalational Anesthetics

Inhalational anesthetics are frequently used for the induction and maintenance of general anesthesia in children. Pediatric inhalational anesthetics include sevoflurane, isoflurane, and desflurane. Although halothane is the prototypical pediatric inhalational anesthetic and may be used in other parts of the world, it has been replaced by sevoflurane and is no longer used in the United States and Europe.

The **minimum alveolar concentration (MAC)** of an inhalational anesthetic is the alveolar concentration (expressed as percent at 1 atmosphere) that provides sufficient depth of anesthesia for surgery in 50% of patients. For potent inhalational agents, the alveolar concentration of an anesthetic reflects the arterial concentration of anesthetic in the blood perfusing the brain. MAC is a measure of anesthetic potency analogous to the $\mathbf{ED_{50}}$ (effective dose in 50% of recipients) of a drug. MAC is age dependent; it is lower in premature than in full-term infants and decreases from term through infancy to preadolescence. In adolescence, MAC again increases, falling thereafter.

Respiratory Effects. The advantages of inhalational anesthesia are rapid onset and offset with the convenient route of delivery and respiratory excretion. These agents provide profound analgesia and amnesia. Inhalational volatile anesthetic agents are poorly soluble in blood but rapidly equilibrate between alveolar gas and blood. They may irritate the airway and provoke laryngospasm. All inhalational anesthetics depress ventilation in a dose-dependent manner. Thus expired carbon dioxide (CO_2) and $Paco_2$ (arterial partial pressure of CO_2) will increase in spontaneously breathing children. Volatile anesthetics shift the CO_2 response curve to the right, thus decreasing the normal increase in minute ventilation with increasing $Paco_2$. Inhalational anesthesia decreases end-expiratory lung volume (functional residual capacity). Small lung volumes are associated with reduced lung compliance, increased pulmonary vascular resistance, and restrictive lung defects. Volatile agents depress normal hypoxic pulmonary vasoconstriction, increasing intrapulmonary arteriovenous shunting and hypoxemia.

Cardiovascular Effects. All volatile anesthetics reduce cardiac output and peripheral vascular resistance; hypotension is common. This is accentuated in hypovolemic patients and more pronounced in neonates. Inhalational anesthetics also depress baroreceptor and heart rate responses. The administration of inhalational anesthesia may result in decreased tissue oxygen delivery. Perioperatively, cellular metabolism increases, creating a potential imbalance between oxygen demand and oxygen delivery. Development of intraoperative dysoxia is a sign of this imbalance. All volatile inhalational anesthetic agents cause **cerebrovasodilation** and uncouple cerebral blow flow with cerebral metabolic rate. Although inhalational anesthetics decrease cerebral oxygen consumption, they may disproportionately increase cerebral oxygen blood flow. Thus inhalational anesthetics should be used with caution in children who have elevated intracranial pressure (ICP) or impaired cerebral perfusion (i.e., traumatic brain injury).

Sevoflurane

Sevoflurane is the most commonly used inhalational agent for induction and maintenance of general anesthesia in children. Sevoflurane possesses minimal airway irritant properties and is a useful induction agent when co-administered with nitrous oxide. Emergence from sevoflurane anesthesia is rapid; however, there is a significant incidence of **emergence delirium**, especially with inadequate pain control. This effect may be attenuated with adequate analgesia and supplemental hypnotic agents (e.g., midazolam, dexmedetomidine, propofol). Metabolism of sevoflurane by cytochrome P450 (CYP) yields free fluoride, which may be nephrotoxic. Sevoflurane degradation by desiccated CO_2 absorbents at low fresh gas flows (<2 L/min) may produce

Table 91.8 Selected Drugs Used in Anesthesia

DRUG	USES AND IMPLICATIONS
MUSCLE RELAXANTS	
Succinylcholine	A depolarizing neuromuscular blocking agent with rapid onset and offset properties Used to facilitate endotracheal intubation and maintain muscle relaxation in emergency situations; rarely used Associated with the development of malignant hyperthermia in susceptible patients Degraded by plasma cholinesterase, which may be deficient in some individuals; such a deficiency may result in prolonged effect Fasciculations may be associated with immediate increases in intracranial and intraocular pressures and postoperative muscle pain
Vecuronium, rocuronium, cisatracurium, all aminosteroids	Nondepolarizing neuromuscular blockers Have less rapid onset than succinylcholine but are longer acting Prolonged ICU use may lead to profound muscle weakness Vecuronium and rocuronium are metabolized by the liver and excreted in bile; they are the most commonly used neuromuscular blocking agents Cisatracurium is metabolized by plasma cholinesterase and therefore may be of benefit in patients with hepatic or renal disease
HYPNOTICS	
Propofol	Rapid-acting hypnotic amnestic agent No analgesic properties Respiratory depressant Increases seizure threshold Antiemetic Propofol infusion syndrome may occur with prolonged intravenous infusion (>24 hr)
Etomidate	Cardiovascular stability on induction Inhibits corticosteroid synthesis Increases ICU mortality after use Associated with myoclonus and pain on injection
Ketamine	Hypnotic analgesic Causes sialorrhea and may be co-administered with an antisialagogue, such as atropine or glycopyrrolate Induces endogenous catecholamine release and tachycardia Bronchodilator Increases intracranial and intraocular pressures Decreases the seizure threshold
SEDATIVE-ANXIOLYTICS	
Benzodiazepines	Produce sedation, anxiolysis, amnesia, and hypnosis All agents raise the seizure threshold, are metabolized by the liver, and depress respiration, especially when administered with opioids Effective as premedication Diazepam may be painful on injection and has active metabolites Midazolam can be administered by various routes Lorazepam has no active metabolites Reversed with flumazenil
Dexmedetomidine	Produces anxiolysis, sedation, and sympatholysis by α_2-receptor stimulation centrally; has mild analgesic properties Side effects include hypertension, hypotension, and bradycardia Commonly used for procedural sedation; IV, IN, and IM dosing available Continuous infusion useful for ICU sedation
ANALGESIC-SEDATIVES	
Opioids	Gold standard for providing analgesia All cause respiratory depression Morphine and, to a lesser extent, hydromorphone may cause histamine release The synthetic opioids fentanyl, sufentanil, and short-acting alfentanil may have a greater propensity to cause chest wall rigidity when administered rapidly or in high doses and are also associated with the rapid development of tolerance; these drugs have particular utility in cardiac surgery because of the hemodynamic stability associated with their use Remifentanil is an ultrashort-acting synthetic opioid that is metabolized by plasma cholinesterase; it may have particular utility when deep sedation and analgesia are required along with the ability to assess neurologic status intermittently
INHALATIONAL AGENTS	
Nitrous oxide	Produces amnesia and analgesia at low concentrations Danger of hypoxic gas mixture if the oxygen concentration is not monitored and preventive safety mechanisms are not in place
Potent vapors, sevoflurane, desflurane, isoflurane	"Complete anesthetics"—induce hypnosis, analgesia, and amnesia All are myocardial depressants, and some are vasodilators May trigger malignant hyperthermia in susceptible individuals Sevoflurane is used for induction of anesthesia in children All bronchodilate at equipotent concentrations Isoflurane and desflurane are associated with laryngospasm and should not be used for anesthesia induction

IV, Intravenous; IN, intranasal; IM, intramuscular.

the nephrotoxin Compound A. Large-scale studies of sevoflurane-associated renal injury in humans are lacking. However, the U.S. Food and Drug Administration (FDA) has recommended maintenance of fresh gas flow rates >2 L/min for surgical cases lasting more than 2 hours of monitored anesthesia care.

Isoflurane

Isoflurane is a pungent volatile anesthetic and airway irritant and is not suitable for induction because of the high incidence of complications, such as laryngospasm. However, maintenance of anesthesia with isoflurane is common after induction with sevoflurane or an intravenous (IV) hypnotic. Emergence from anesthesia with isoflurane is slower than for sevoflurane. Isoflurane administration in the setting of desiccated CO_2 absorbents may yield the production of carbon monoxide.

Desflurane

Desflurane is a potent airway irritant associated with coughing, breath holding, and laryngospasm and is *not* useful for induction. Desflurane has the lowest solubility and potency of all commonly used volatile agents. It is frequently administered for maintenance of anesthesia. Emergence from desflurane anesthesia is rapid because of its low tissue solubility.

Nitrous Oxide

Nitrous oxide (N_2O) is a tasteless, colorless, odorless gas with potent analgesic properties. It produces a state of euphoria (thus its nickname, "laughing gas"). The MAC of N_2O is >100; consequently, it may not be used as a sole agent to maintain anesthesia. N_2O produces little hemodynamic or respiratory depression. It is typically used in combination with volatile and IV anesthetic agents during maintenance of general anesthesia. The deleterious effects of N_2O include postoperative nausea and vomiting (PONV) and, with long-term use (i.e., days), bone marrow suppression. N_2O diffuses out of blood rapidly and is contraindicated in patients with closed gas-filled body cavities (pneumothorax, lung cysts, bowel injury).

Intravenous Anesthetic Agents

IV anesthetics may be administered for induction and maintenance of anesthesia in bolus form or as continuous infusions. Common IV agents include propofol, opioids, benzodiazepines, ketamine, dexmedetomidine, and barbiturates. For children with vascular access, IV induction should be routine. All IV agents affect cardiorespiratory function.

Propofol

Propofol is the most commonly administered IV induction agent. Administered in doses of 2-5 mg/kg, propofol rapidly produces unconsciousness. Propofol may burn and itch on injection. After induction of anesthesia, propofol is a useful agent for maintaining hypnosis and amnesia and may be used as a sole anesthetic agent for nonpainful procedures (e.g., radiation therapy) and imaging studies. When combined with opioids, propofol provides excellent anesthesia for brief painful procedures, such as lumbar puncture and bone marrow aspiration. Although hemodynamic stability, and even spontaneous respirations, may be maintained during propofol administration, it remains a potent anesthetic that can obtund airway reflexes, respiration, and hemodynamic function. As such, some hospitals have limited its use to anesthesia professionals. Propofol may produce both respiratory depression and hypotension. Extrapyramidal symptoms are a rarer complication. Prolonged use may cause hemodynamic collapse, bradycardia, metabolic acidosis, cardiac failure, rhabdomyolysis, hyperlipidemia, profound shock, and death (**propofol infusion syndrome**). Prolonged propofol administration (>24-48 hours) in the ICU in children is not recommended. Propofol is formulated in 10% soy emulsion with egg emulsifiers and was once thought to be contraindicated in patients with soy or egg allergy. According to the American Academy of Allergy, Asthma, and Immunology, patients with soy and egg allergies may safely receive propofol for anesthesia.

Etomidate

Etomidate is an imidazole derivative used for the induction of anesthesia, frequently in emergent situations. Its onset of action is slower than propofol. Etomidate lacks significant cardiovascular depressant effects, making it a popular induction agent in patients with hemodynamic compromise and cardiac disease. However, etomidate inhibits 11β-hydroxylase, thereby suppressing mineralocorticoid and glucocorticoid synthesis for up to 72 hours after a single induction dose. Etomidate is associated with increased mortality when used as a sedative in the ICU (for which it is contraindicated); the effect of a single induction dose on mortality remains controversial. Any decision to use etomidate must weigh the short-term benefits of hemodynamic stability with the serious risks of adrenal suppression.

Ketamine

Ketamine (1-3 mg/kg IV) produces rapid induction of general anesthesia that lasts for 15-30 minutes. Ketamine is effective when given intramuscularly (IM), subcutaneously (SC), intranasally (IN), or orally (PO). However, the dose must be increased for alternative routes. Ketamine dissociates connections between the cerebral cortex and limbic system *(dissociative anesthesia)* through inhibition of *N*-methyl-D-aspartate receptors. Ketamine is also an analgesic and may be used as a sole IV agent to provide general anesthesia. It has few side effects and generally preserves blood pressure and cardiac output. However, ketamine increases myocardial oxygen demand and should be used cautiously in patients with impaired myocardial oxygen delivery or ventricular outflow tract obstruction. With low-dose (1-2 mg/kg) ketamine, airway reflexes and spontaneous ventilation may be maintained; at higher doses (3-5 mg/kg), loss of airway reflexes, apnea, and respiratory depression occur. Aspiration of gastric contents remains a risk during deep sedation with ketamine. IV ketamine is a useful general anesthetic agent for short procedures.

Ketamine has been linked to disturbing postanesthetic dreams and hallucinations after emergence from anesthesia. In adults the incidence of this effect is 30–50%; in prepubertal children it may be 5–10%. Benzodiazepines (e.g., midazolam) reduce these sequelae and may be given to children receiving ketamine. Ketamine is also a potent secretagogue, enhancing oral and bronchial secretions. An antisialagogue, such as atropine or glycopyrrolate, should also be considered before the administration of ketamine. Ketamine is a bronchodilator and is a useful agent for sedating patients with asthma in the ICU. Ketamine has been reported to increase ICP and therefore is contraindicated in patients with elevated ICP.

Opioids

Opioids are superb analgesics for painful procedures and postprocedural pain (see Chapters 92 and 93). Opioids are respiratory depressants that suppress CO_2 responsiveness and can produce apnea. Importantly, in equianalgesic doses, all opioids are equally potent respiratory depressants. Other inhalational or IV anesthetics generally potentiate opioid-induced respiratory depression.

Morphine is a long-acting opioid analgesic with important age-dependent pharmacokinetics. Equivalent doses of morphine per kilogram are associated with higher blood levels in neonates than in older children, with plasma concentrations approximating three times those of adults. Morphine exhibits a longer elimination half-life (14 hours) in young children than in adults (2 hours). The immature blood-brain barrier of neonates is more permeable to morphine. Morphine is often associated with hypotension and bronchospasm from histamine release and should be used with caution in children with asthma. Morphine has renally excreted active metabolites and is relatively contraindicated in renal failure. Because of morphine's prolonged duration of action and cardiorespiratory side effects, the fentanyl class of synthetic opioids has increased in popularity for perioperative analgesia.

Fentanyl is a potent synthetic opioid with a shorter duration of action and a more stable hemodynamic profile than morphine. Fentanyl attenuates the hemodynamic response to surgery and provides stable operating conditions. Effective analgesia and anesthesia may be provided with IV fentanyl administered as a 2-3 μg/kg bolus followed

by a 1-3 μg/kg/hr continuous infusion. Nitrous-narcotic anesthetic techniques that incorporate fentanyl are effective for maintenance of stable hemodynamics while still providing adequate hypnosis and analgesia. Fentanyl is the most commonly used *synthetic* opioid, but other formulations of varying potency are available (alfentanil < fentanyl < sufentanil). *Sufentanil* is ten times more potent than fentanyl and is frequently used during pediatric cardiac anesthesia. *Alfentanil* is approximately 25% as potent as fentanyl. *Remifentanil* has very rapid onset and offset of action. In doses of 0.25 μg/kg/min, surgical anesthesia can be maintained with this agent. Remifentanil is metabolized through nonspecific ester hydrolysis and has a short elimination half-life (<10 minutes), advantageous for rapid emergence from anesthesia. Unfortunately, this short duration of action has been linked to inadequate postprocedural analgesia and increased need for postprocedural opioid analgesic supplementation, limiting remifentanil's use.

Benzodiazepines

Benzodiazepines induce hypnosis, anxiolysis, sedation, and amnesia and have anticonvulsant properties. In high doses, benzodiazepines cause respiratory depression and are synergistic with opioids and barbiturates in their respiratory depressant effects. Benzodiazepines are γ-aminobutyric acid (GABA) agonists.

Midazolam is the most commonly used benzodiazepine in pediatric anesthesia. Short acting and water soluble, it can be injected without pain. It is a potent hypnotic-anxiolytic-anticonvulsant and is approximately four times more potent than diazepam. Midazolam may be administered orally, nasally, rectally, intravenously, or intramuscularly. Midazolam (0.10-0.15 mg/kg IV) has minimal effect on respiratory rate, heart rate, or blood pressure and provides excellent preoperative anxiolysis and amnesia. Premedication with oral midazolam (0.5-1.0 mg/kg) mixed in sweet-flavored syrup induces anxiolysis in approximately 90% of children without hemodynamic or respiratory depressant effects. However, children may experience loss of coordination (head control), blurred vision, and rarely, dysphoria. A child sedated with midazolam should not be left unattended. Most children readily accept an inhalational anesthetic by face mask after oral midazolam premedication. The widespread use of preoperative oral midazolam has decreased the practice of PPI.

Dexmedetomidine

Dexmedetomidine is a central α_2 adrenergic receptor agonist similar to clonidine. Dexmedetomidine lacks respiratory depressant effects and produces anxiolysis, sedation, mild analgesia, and sympatholysis. Rapid administration may produce hypertension and bradycardia, whereas continuous infusions may produce hypotension and bradycardia. Dexmedetomidine is frequently used for sedation in ICU patients and for procedures. Dexmedetomidine has become a popular adjuvant for general anesthesia during pediatric cardiac surgery.

Barbiturates

Sodium thiopental is the classic barbiturate IV induction agent, although it is now rarely used. Side effects of thiopental include respiratory depression, apnea, and hypotension. Induction with 3-5 mg/kg of thiopental produces unconsciousness within seconds, lasting 5-10 minutes. Thiopental is not useful for maintenance of anesthesia, which requires other IV or inhalational anesthetics. Pentobarbital is a barbiturate traditionally administered IV for sedation in children during imaging procedures of intermediate duration (e.g., diagnostic studies) that require akinesia. **Pentobarbital** is a potent respiratory depressant, particularly when combined with opioids and benzodiazepines. Pentobarbital has a prolonged duration of action. Pentobarbital sedation for nonpainful procedures generally results in delayed emergence. **Sodium methohexital** (Brevital) is another IV induction agent, similar to sodium thiopental in respiratory depressant effects. Barbiturates lack analgesic properties, and painful procedures require supplemental analgesia.

Neuromuscular Blocking Agents

Neuromuscular blockade is performed to facilitate endotracheal intubation and akinesia during surgery. NMBAs may be *depolarizing* (e.g., succinylcholine) or *nondepolarizing* (e.g., vecuronium, rocuronium, cisatracurium). **Succinylcholine** has a high-risk profile in children. Its use is associated with postoperative pain from muscle spasms; hyperkalemia; elevated intracranial, intraocular, and intragastric pressures; malignant hyperthermia; myoglobinuria; and renal damage. Consequently, succinylcholine is rarely used, except to provide rapid relief of laryngospasm. Endotracheal intubation is most often facilitated with nondepolarizing NMBAs. **Rocuronium** is most commonly used for intubation because of its rapid onset of action. For procedures that last >40 minutes, **vecuronium** and **cisatracurium** are also suitable to induce muscle relaxation for intubation. After intubation, repeat administration of NMBAs may be indicated to maintain muscle relaxation to facilitate surgery. Prolonged use of nondepolarizing NMBAs in critical illness may contribute to myopathy, especially when combined with high-dose corticosteroids.

INDUCTION OF GENERAL ANESTHESIA

The goal of induction of general anesthesia is the safe transition to a state of unconsciousness. Induction in children is typically achieved with inhalational anesthetics, although IV agents are indicated when patients have IV access. Many children will not tolerate the establishment of vascular access before induction of anesthesia, and it is routine to induce anesthesia by face mask with inhaled anesthetics. Before the induction of anesthesia, monitors applied may include pulse oximetry, ECG, and noninvasive blood pressure cuff. The child is then cautiously introduced to the face mask, which contains a high gas flow (5-7 L/min O_2), frequently mixed with N_2O. Inhalation of N_2O and O_2 for 60-90 seconds induces a state of euphoria. Nitrous oxide blunts the airway responses to potent volatile inhalational agents, and sevoflurane may then be safely introduced into the inhaled gas mixture. This leads to unconsciousness within 30-60 seconds while the child continues to breathe spontaneously.

After induction, IV access is obtained and standard intraoperative monitoring initiated. Thereafter, definitive airway management is performed. Airway management for short procedures (i.e., myringotomy tubes) frequently includes a mask airway and spontaneous ventilation; this is safe when the airway is secure and patent and aspiration risk is low. Longer procedures (>30-60 minutes) are not usually performed with mask airways. Definitive artificial airways include laryngeal mask airways and endotracheal tubes (ETTs). The **laryngeal mask** is a supraglottic airway generally reserved for procedures in spontaneously ventilating patients and does not effectively prevent the aspiration of gastric contents.

For complex surgical procedures, **endotracheal intubation** is generally required (e.g., intraabdominal, intrathoracic, airway procedures). Although endotracheal intubation may be performed under deep inhalational anesthesia, the depth of anesthesia required to attenuate airway reflexes may produce hemodynamic instability. Therefore NMBAs are frequently administered to facilitate intubation. The depolarizing NMBA succinylcholine is rarely used, and nondepolarizing NMBAs such as rocuronium and vecuronium are most frequently used (see earlier). After muscle relaxation, direct laryngoscopy and endotracheal intubation can be performed. Correct ETT placement is confirmed by direct laryngoscopy, end-tidal CO_2 measurement, and assessment of bilaterally equal breath sounds. Additional confirmatory tests include chest radiograph and fiberoptic bronchoscopy. After endotracheal intubation, controlled mechanical ventilation is required in the setting of neuromuscular blockade (see Chapter 86).

Children with full stomach precautions may require **rapid sequence induction**. Before performing a rapid sequence induction, preoxygenation with 100% oxygen for 2-5 minutes increases alveolar oxygen content and delays hypoxemia if intubation is difficult. Rapid sequence induction involves concurrent administration of hypnotic agents and NMBAs. Assisted ventilation before or after drug administration is avoided because of the risk of gastric distention, regurgitation, and aspiration. Traditionally, after administering a sedative and NMBA, the Sellick maneuver (cricoid pressure) was performed by applying firm pressure in a posterior direction against the cricoid cartilage. This displaces the cricoid cartilage into the esophagus and was thought to form an artificial sphincter to prevent reflux of the gastroesophageal contents. However, evidence suggests that cricoid pressure may be counterproductive, as it does not appear to prevent pulmonary aspiration

and may increase time to intubation. Because of this controversy, the clinician must consider the risks and benefits of cricoid pressure in each case.

The major risk of rapid sequence induction is intubation failure. In this situation the child is paralyzed without a protected airway, and ventilation may be hazardous or impossible. Only experienced airway specialists should undertake rapid sequence induction. It should be avoided in patients with a history of failed endotracheal intubation or features (micrognathia) associated with difficult intubation. Under these circumstances, bronchoscopic awake intubation may be indicated.

Complications During Induction

During induction of anesthesia, the transition between full wakefulness to unconsciousness is fraught with potential complications, including laryngospasm, bronchospasm, vomiting, and aspiration. Concerns for vomiting and aspiration dictate adherence to preanesthetic fasting guidelines and may be an indication for rapid sequence anesthetic induction.

During induction of anesthesia, especially with inhalational anesthetics, a period of excitement may occur. This period is associated with heightened airway reflexes, which can lead to coughing, gagging, laryngospasm, and bronchospasm. **Laryngospasm** is the reflex closure of the larynx, which prevents spontaneous or assisted ventilation. The child may make violent inspiratory efforts against a closed glottis, generating significantly negative intrathoracic pressure and resulting in postobstructive pulmonary edema. Laryngospasm can be prolonged, and hypoxia may ensue. Laryngospasm occurs in up to 2% of all anesthetic inductions in children <9 years old and is much less common in older patients. Laryngospasm occurs twice as frequently in children with active or recent upper respiratory tract infection. A history of tobacco exposure increases the likelihood of laryngospasm significantly.

Laryngospasm can be relieved by increasing the depth of anesthesia, either intravenously or through inhalation (although with the glottis closed, further administration of inhalational anesthesia is not possible). Neuromuscular blockade relieves laryngospasm, and an acute situation may be an indication for succinylcholine administration. Continuous positive airway pressure administration may be beneficial in alleviating laryngospasm. Laryngospasm may also occur during emergence from anesthesia because airway tone is increased during the transition to wakefulness.

Bronchospasm may result from increased airway reactivity during the hyperexcitable stage of induction or secondary to histamine release induced by anesthetic agents. Endotracheal intubation may provoke bronchospasm, especially in patients with asthma, which may be associated with life-threatening hypoxemia and inability to ventilate. Alternative airway management strategies such as laryngeal mask should be considered when appropriate in children with severe reactive airway disease. The use of histamine-releasing anesthetic agents has been associated with severe bronchospasm and, in rare instances, cardiorespiratory failure. Environmental tobacco smoke is another risk factor.

Hypoxemia during induction may be secondary to reduced functional residual capacity, atelectasis, and ventilation-perfusion ($\dot{V}/\dot{Q}$) mismatch. Volatile anesthetics blunt hypoxic pulmonary vasoconstriction, further contributing to $\dot{V}/\dot{Q}$ abnormalities. **Hypersecretion** may result in airway obstruction and should managed with antisialagogues, such as glycopyrrolate and atropine. The newer inhalation agents are less potent secretagogues, and the routine use of atropine premedication is much less common but often indicated when ketamine is used.

Hemodynamic complications may also develop during induction of anesthesia. **Hypotension** is common and may be exaggerated in the setting of hypervolemia, decreased myocardial function, or congenital heart disease. Inhalational anesthetics sensitize the myocardium to circulating catecholamines, and induction and excitement are associated with a hypercatecholaminergic state.

MAINTENANCE OF ANESTHESIA

Maintenance of anesthesia is the period between induction and emergence. The child should be unaware of pain, unresponsive to painful stimuli, and physiologically supported. Anesthesia is typically maintained with a volatile anesthetic (e.g., isoflurane, sevoflurane) supplemented with opioid-based analgesia. IV hypnotic agents (e.g., dexmedetomidine, benzodiazepines) may be administered to augment hypnosis and amnesia. Choice of ventilatory strategy (spontaneous, assisted, or controlled) varies according to procedure type and patient condition (see Chapter 86). Surgical trauma may result in hypothermia and hypovolemia caused by blood loss and significant fluid shifts (third spacing). Management of these physiologic disturbances is the responsibility of the anesthesiologist during maintenance.

Temperature Management

Thermoregulation is critical during anesthesia. The absence of movement and inhibition of shivering reduce thermogenesis. Although temperature sensing may remain normal, the autonomic response to hypothermia is reduced. Anesthetic agents cause vasoparesis, which further impairs thermoregulation and increases heat loss. In newborns, inhalational anesthetics inhibit nonshivering thermogenesis from brown fat, increasing the risk for hypothermia. Mechanisms of heat loss during anesthesia include radiation, convection, evaporation, and conduction. Radiant and convective heat loss are most common and may be minimized by preheating the operating room and by use of radiant heat lamps and forced-air warming blankets. Humidification and warming of inspired gases may also be useful.

Fluid Management

Most anesthetics produce vasodilation and increase venous capacitance, effectively reducing myocardial preload. Surgical bleeding and insensible/third space fluid losses further contribute to intravascular volume depletion. Volume expansion with isotonic salt-containing solutions (normal saline, lactated Ringer, Plasma-Lyte) may be required to maintain cardiac output and organ perfusion. Increased renin-angiotensin-aldosterone axis activation and antidiuretic hormone (ADH) secretion further complicate fluid regulation.

Intraoperative fluid management must account for (1) deficits acquired during preoperative fasting, (2) maintenance fluid requirements, (3) surgical blood loss, and (4) insensible fluid loss. Infants should receive glucose-containing isotonic fluid to prevent perioperative hypoglycemia. Table 91.9 is a guideline for determining fluid deficits and maintenance requirements in the OR. For longer procedures, fluid deficits should be replaced with isotonic fluid over the first 3 hours of intraoperative management. Deficits are generally calculated as the number of hours of fasting status multiplied by the hourly maintenance rate for the child. Half the deficit is replaced during the first hour and half during the subsequent 2 hours. If hypotension or tachycardia persists in the early stages of anesthesia, more rapid replacement of the fluid deficit may be indicated.

Third space interstitial fluid losses should be replaced with isotonic salt solutions. For smaller operations, such as herniorrhaphy, pyloromyotomy, and minor procedures, fluid replacement at 3-5 mL/kg/hr is indicated for insensible losses. Complex abdominal or thoracic procedures with large insensible losses may require an additional 8-10 mL/kg/hr of IV fluid replacement. Crystalloid solution is indicated for blood loss as a 3:1 ratio. Allogenic blood products should be replaced as a 1:1 ratio. Colloid (albumin) administration also may decrease the amount of crystalloid replacement needed for blood loss. During large-volume transfusions, active fluid warming should be performed to prevent hypothermia. With major surgery and resultant SIRS, capillary

Table 91.9 Intraoperative Pediatric Fluid Replacement

INFUSION RATE	PATIENT WEIGHT
4 mL/kg/hr	1-10 kg
2 mL/kg/hr	10-20 kg
1 mL/kg/hr	per kg >20 kg
Example: 22 kg child requires (4 × 10) + (2 × 10) + (1 × 2) = 62 mL/hr	

integrity is lost, and third space losses are common. Failure to replace fluid loss and restore intravascular volume may lead to shock.

Perioperative **hypoglycemia** may result from preoperative fasting, most often in neonates or in children with metabolic disorders. In neonates, perioperative glucose monitoring is indicated, and glucose replacement is frequently required. In older children with normal nutritional status, isotonic salt solutions without glucose are adequate. In patients receiving total parenteral alimentation containing high glucose concentrations (>10%), continuous glucose administration should be ensured to avoid rebound hypoglycemia.

Postprocedural care includes supervision of emergence and recovery from anesthesia and surgery. **Emergence** describes the transition period between the anesthetized state and consciousness. During emergence, patients experience decreased anesthetic effect and increased physiologic and psychologic responses to painful stimuli (e.g., reactive autonomic tone, excitement, anxiety). Inhalational anesthetic agents are rapidly excreted during ventilation, and muscle relaxants can be reversed; however, the effects of opioids, benzodiazepines, and IV hypnotics may be prolonged. Normal physiologic functions such as spontaneous ventilation resume, and hemodynamic function improves. Before leaving the OR after routine elective procedures, the child should be conscious with intact airway reflexes and a patent airway. The effects of muscle relaxants should be reversed. Ideally, emergence should be as brief as possible, with maintenance of analgesia and anxiolysis and restoration of cardiorespiratory function. However, critically ill patients scheduled for ICU admission may require postoperative endotracheal intubation and mechanical ventilation. In these patients, deeper levels of sedation and analgesia should be maintained after the procedure.

During emergence, it is essential to assess whether **residual neuromuscular blockade** (NMB) exists. If weakness or respiratory depression is observed in the postoperative phase, prolonged NMB should be considered. *Reversal of residual NMB is standard anesthetic practice.* With the virtual abandonment of succinylcholine, only nondepolarizing NMBAs are routinely used for intubation. The termination of NMB depends on metabolism and elution away from the neuromuscular junction. Classically, nondepolarizing muscle relaxants are reversed by increasing the acetylcholine concentration at the neuromuscular junction with acetylcholine esterase inhibitors (neostigmine, edrophonium), which work through competitive antagonism. Vagolytic agents (e.g., atropine, glycopyrrolate) must be co-administered to prevent bradycardia. This process, even for the shortest-acting muscle relaxant, rocuronium, can take several minutes. An intubating dose of rocuronium to rapidly induce paralysis in emergency situations may not spontaneously reverse for 20 minutes or longer (compared with about 3 minutes for succinylcholine). The effects of long-acting, nondepolarizing NMBAs (vecuronium, pancuronium) are invariably reversed. Acetylcholine esterase inhibitor efficacy is dependent on the degree of NMB at the time of administration, and residual NMB is common despite reversal with these agents. **Sugammadex** is an alternative reversal agent that has a very low rate of residual NMB induced by the aminosteroids rocuronium and vecuronium. Its mechanism of action involves noncompetitive antagonism through encapsulation of neuromuscular agents.

POSTANESTHESIA CARE UNIT

In the postanesthesia care unit (PACU), the child is observed until there is adequate recovery from anesthesia. Achievement of spontaneous breathing, adequate pulse oximetry saturation (>95%), and hemodynamic stability are key recovery end-points. The child should be arousable, responsive, and oriented before discharge from the PACU. The amount of time spent in the PACU varies based on disposition (transfer to acute care or ICU, transfer to day surgery postrecovery unit, or discharge to home). Parents should be permitted to comfort their children in the PACU. Discharge from the PACU depends on the child's overall functional status, which includes physiologic endpoints, adequate analgesia, and control of PONV. Various scoring systems have been used for determining readiness for discharge from the PACU (Table 91.10).

Postanesthetic Complications

Respiratory insufficiency after general anesthesia is common. Prolonged emergence from anesthesia and respiratory depression may be caused by the residual effects of opioids, hypnotic agents, or NMBAs. Pain may also cause significant hypoventilation, especially after thoracic or abdominal surgery. Delayed emergence from anesthesia may result from retention of inhaled anesthetics worsened by hypoventilation. Hypothermia, especially in neonates, delays metabolism and excretion of anesthetics and prolongs neuromuscular blockade. Hypoventilation after surgery is associated with the development of **atelectasis**. Microatelectasis may lead to postoperative infections. When airway obstruction is present, maintenance of airway patency may necessitate oropharyngeal or nasopharyngeal airway placement. In the setting of profound respiratory depression, endotracheal intubation and mechanical ventilation may be indicated.

Opioid reversal with naloxone may be indicated in rare instances when excessive **opioid effect** is suspected. However, naloxone reverses both the respiratory depressant and the analgesic properties. After naloxone administration, a somnolent child with respiratory depression may experience increased pain. Opioid reversal requires bedside attention by the physician to monitor the child's behavioral, hemodynamic, and respiratory status. Importantly, naloxone is shorter acting than most opioid analgesics, which may result in renarcotization.

Postoperative stridor occurs in up to 2% of all pediatric patients. The use of appropriately sized ETTs and assurance of an air leak <30 cm H_2O

Table 91.10 Postanesthesia Recovery Scores

ALDRETE RECOVERY SCORE	≥9 REQUIRED FOR DISCHARGE
ACTIVITY—VOLUNTARILY OR ON COMMAND	
Moves four extremities	2
Moves two extremities	1
No motion	0
BREATHING	
Deep breath, cough, cry	2
Dyspnea or shallow breathing	1
Apnea	0
BLOOD PRESSURE	
Within 20% of preanesthetic value	2
Within 20–50% of preanesthetic value	1
>50% outside preanesthetic value	0
COLOR	
Pink	2
Pale, blotchy, dusky	1
Cyanotic	0
CONSCIOUSNESS	
Fully aware, responds	2
Arouses to stimulus	1
Unresponsive	0
STEWARD RECOVERY SCORE	**6 REQUIRED FOR DISCHARGE**
ACTIVITY	
Moves limbs purposefully	2
Nonpurposeful movement	1
Still	0
CONSCIOUSNESS	
Awake	2
Responsive	1
Unresponsive	0
AIRWAY	
Coughing on command or crying	2
Maintaining patent airway	1
Requires airway maintenance	0

pressure decreases the risk of airway trauma or edema. A history of stridor increases the likelihood of postoperative complications. Stridor may be severe enough after extubation to require reintubation. Racemic epinephrine aerosols and dexamethasone are commonly employed therapies; their use requires prolonged observation because of the potential for rebound stridor. Stridor in infants may be an indication for overnight observation.

Cardiovascular complications are less frequently encountered in the PACU. Fluid administration may be required to augment cardiac output, perfusion, and urine output. Large-volume fluid resuscitation (>30 mL/kg) in the postoperative period may be an indication of evolving shock physiology, and sources of hypovolemia (e.g., occult bleeding) or myocardial dysfunction (e.g., tamponade, pneumothorax) should be considered.

Emergence delirium immediately after anesthesia is noted in 5–10% of children and is more common in those 3-9 years old. Manifestations include restlessness, combativeness, disorientation, and inconsolability. Almost all anesthetic agents have been linked to the development of delirium, especially newer volatile anesthetic agents (e.g., sevoflurane, desflurane). Potential postoperative complications, such as hypoglycemia and hypoxemia, should also be ruled out. Occasionally, it is necessary to provide additional sedation (e.g., propofol, dexmedetomidine, benzodiazepines), although these agents prolong postanesthesia recovery time and may not effectively reduce delirium.

Awareness During Anesthesia

A fundamental aim of anesthesia is to prevent recall by inducing hypnosis and amnesia. In adults, certain anesthetic techniques and surgical procedures have been associated with increased incidence of recall. The long-term sequelae of recall in children are unknown. Continuous cerebral bispectral index (BIS) electroencephalographic monitoring has been used to assess consciousness and aid in the prevention of intraoperative awareness. Unfortunately, pediatric studies have not confirmed the usefulness of BIS monitoring as a means of determining anesthetic depth. Existing data do not support the routine use of BIS monitoring during pediatric anesthesia. Volatile anesthetic agents reliably produce dose-dependent hypnotic and amnestic effects and remain a mainstay of general anesthesia.

Postoperative Nausea and Vomiting

After general anesthesia, 40–50% of children may experience PONV that generally lasts for several hours. This complication prolongs recovery room times and requires significant nursing attention. The etiology is not completely understood but is likely multifactorial and related to the emetic effects of anesthetics, pain, and surgical stress. Opioid analgesics may also provoke nausea and vomiting. Other risk factors for PONV include surgery lasting greater than 30 minutes, age ≥3 years, strabismus surgery, and a history of PONV in the patient or their relatives. Importantly, preoperative fasting does not decrease the incidence of PONV. Indeed, hydration and glucose supplementation appear to be important factors in decreasing PONV. Multimodal analgesia with nonopioid agents (e.g., acetaminophen, ibuprofen, ketorolac) and regional or local anesthesia may be associated with reduced PONV. The serotonin antagonist ondansetron is an effective treatment of PONV. Ondansetron prophylaxis is recommended for patients at increased risk of PONV. Serotonin antagonists are contraindicated in children taking serotonin reuptake inhibitors for migraine headaches. Dexamethasone may also be used for the treatment of PONV.

Thermoregulation and Malignant Hyperthermia

After anesthesia, thermoregulation remains abnormal for several hours. **Hypothermia**, especially in neonates, may be associated with cardiorespiratory depression and prolongation of the effect of opioids and NMBAs. Although hypothermia has deleterious effects, active rewarming should be performed cautiously to avoid hyperthermia and cutaneous burns. Postoperative shivering is common and may occur in the absence of hypothermia. **Hyperthermia**, with temperatures in excess of 39°C (102.2°F), is of concern in the postoperative period. When high fevers occur within hours of the use of an inhalational anesthetic, especially if succinylcholine was used, malignant hyperthermia (MH) must be ruled out.

Malignant hyperthermia is a hypermetabolic syndrome triggered by volatile anesthetic agents and succinylcholine. The onset of MH may be acute, fulminant, and lethal without appropriate interventions. The disease is genetically heterogeneous, with >10 genes contributing to susceptibility, but typically displays an autosomal dominant inheritance pattern. A family history of death or febrile reactions during anesthesia should alert the anesthesiologist to its potential. Pathogenic variants within the gene encoding for the ryanodine receptor (the calcium channel of the sarcoplasmic reticulum) predispose to MH susceptibility and have been identified in 20–40% of humans with MH. Certain **myopathies** are associated with the risk of MH, including Duchenne muscular dystrophy, central core disease, and King Denborough syndrome.

The pathophysiology of MH involves uncontrolled intracellular calcium release from skeletal muscle sarcolemma, resulting in prolonged muscle contraction, adenosine triphosphate (ATP) depletion, and muscle cell death. Rhabdomyolysis results in the release of myoglobin, creatine phosphokinase (CPK), and potassium into the blood. The clinical course of MH is characterized by rapid onset of high fever (>38.5°C [101.3°F]), muscle rigidity, acidosis (metabolic and respiratory), high end-tidal CO_2, and multiorgan dysfunction. Death may ensue secondary to hemodynamic collapse from shock and cardiac dysrhythmias. Signs of MH generally occur within the first 2 hours of anesthesia but (rarely) can occur up to 24 hours later.

When MH is suspected, treatment involves discontinuation of all inhalational anesthetics, correction of the metabolic acidosis, and administration of the muscle relaxant dantrolene. The initial dose of dantrolene is 2.5 mg/kg, and repeat doses, up to a maximum of 10 mg/kg, are indicated for persistent fever, muscle rigidity, acidosis, and tachycardia. Once symptoms are controlled, the patient should be observed for at least 24 hours, because recrudescence may occur. The MH mortality rate was once >70% and is now <5% with standardized treatment algorithms. An MH cart with sufficient supplies of dantrolene should be present at every site where pediatric anesthesia is provided.

Certain phenomena suggest an increased risk of MH. Masseter spasm during induction, with rigid clenching of the masseter muscles and an inability to open the mouth, may signal MH susceptibility. Acute myoglobinuria associated with an MH-triggering agent is another clue. The child may not be hypermetabolic or febrile but may have dark urine, high CPK levels, and risk of myoglobin-induced renal tubular damage. The finding of dark urine after administration of an anesthetic requires further investigation, including measurement of electrolytes and CPK. Prevention of MH in susceptible patients requires the avoidance of triggering agents, which include inhalational anesthetics and succinylcholine. IV anesthesia and nitrous-opioid techniques are safe. MH-safe anesthesia machines devoid of trace concentrations of volatile anesthetic vapors should be used. Dantrolene prophylaxis is not recommended because MH is rapidly treatable, and the drug causes respiratory depression and muscle weakness. For a child in whom MH is suspected, the MH hotline, 1-800-MHHYPER (1-800-644-9737), should be used to notify the Malignant Hyperthermia Association of the United States (MHAUS). MHAUS registers susceptible patients and provides diagnostic and therapeutic information. Preanesthesia susceptibility testing includes genetic analysis of the ryanodine receptor gene, muscle biopsies, in vitro contraction studies, and possibly measurement of muscle CO_2 production in response to intramuscular caffeine.

Mediastinal Masses

Children with anterior mediastinal masses such as lymphomas, teratomas, and other primary mediastinal tumors are at serious risk for cardiorespiratory failure during anesthesia secondary to airway compromise, difficult ventilation, cardiac tamponade, vascular obstruction, and circulatory collapse. These patients generally require surgical tissue diagnosis before treatment is initiated. Significant compression of vital structures can occur with seemingly mild symptoms. Tachypnea, orthopnea, wheezing, and avoidance of prone or supine positions are significant indications of serious risk. Echocardiographic or CT evidence of pericardial tamponade, right ventricular compression, or compression of the pulmonary artery suggests severe risk. Biopsy with light sedation under local anesthesia may be indicated. When anesthesia is required, preservation of spontaneous ventilation is critical during

induction of anesthesia. Rigid bronchoscopy may be used to assist with ventilation in the setting of external airway compression. Provisions to provide mechanical circulatory support (cardiopulmonary bypass) should also be available. In high-risk children, consideration should be given to initiating treatment with corticosteroids, radiation therapy, and chemotherapy before obtaining a tissue diagnosis.

Postoperative Apnea

Neonates and infants are at increased risk for the development of postoperative apnea after exposure to potent hypnotic and analgesic medications. Both central and obstructive apnea may occur. Postanesthetic apnea is most common within the first 12 hours, although apnea has been reported in premature infants up to 48 hours later. Risk factors for postoperative apnea include history of apnea, caffeine treatment, chronic hypoventilation, and anemia. The risk of apnea is inversely proportional to postconceptual age (PCA) at surgery and is highest in premature neonates less than 36 weeks estimated gestational age. This risk is minimal by the time premature infants have reached 60 weeks PCA. When surgery is required in early infancy, overnight observation and monitoring may be indicated. In term infants >44 weeks PCA without risk factors, management should include observation and monitoring for 6 hours with at least one sleep-wake-feed cycle without hypoxia, bradycardia, or supplemental oxygen. Premature infants with risk factors <52 weeks PCA require admission for observation for 12 hours after anesthesia.

POSTOPERATIVE PAIN MANAGEMENT

Postprocedural pain management should ensure adequate analgesia and anxiolysis (see Chapter 93). Preoperative education focusing on pain management through development of skills designed to decrease anticipatory anxiety and participation in treatment planning can be helpful for children and families. Pediatric pain management relies on multimodal therapy, including opioid and nonopioid analgesics. Nonsteroidal antiinflammatory drugs, cyclooxygenase-2 inhibitors, acetaminophen, opioids, and regional analgesia all have roles in postoperative pain management. Repeated evaluation is critical to effective pain management. Adjunctive therapy, such as pet therapy, may also decrease the need for potent analgesics postoperatively.

Patient-controlled analgesia (PCA) and **parent/nurse-controlled analgesia (PNCA)** are widely accepted postoperative pain regimens. PCA/PNCA may be used to administer a low-dose continuous (basal) infusion of opioid with intermittent (bolus) supplements as needed. The practitioner must determine the basal rate, bolus dose, lockout interval, and acceptable number of bolus doses per hour. PCA/PNCA safety requires appropriate medication dosing and assumes that patients are unlikely to overdose because somnolence will limit repeated self-administration. In young children, proper PCA/PNCA use may be more difficult to ensure, although children as young as 5 years have been able to use PNCA successfully. In older children and adolescents, PCA is a standard modality of postoperative pain management.

Regional Anesthesia

Regional anesthesia is the use of anesthetics to block the conduction of afferent neural impulses to the central nervous system. Forms of regional anesthesia include local anesthesia, peripheral nerve blocks, nerve plexus blocks, and neuraxial (epidural and subarachnoid/spinal) blocks. Anesthetics may be administered as a single injection or as a continuous infusion. Regional anesthesia may be used for both intraoperative and postoperative analgesia and has been linked to shortened recovery times and hospital stays in children. A major benefit of regional anesthesia is lesser central cardiorespiratory depressant effects. Injection of local anesthetics (e.g., lidocaine, bupivacaine) into the affected area may provide procedural analgesia lasting for hours to days. Wound infiltration with local anesthetics at the conclusion of surgery may also decrease early postoperative pain.

Neuraxial (epidural, spinal) analgesia is common in pediatric practice. The epidural space lies between the dura and the pia and arachnoid membranes, an area through which all nerve roots pass. Caudal epidural analgesia is placed through the sacral hiatus, inferior to the distal end of the spinal cord. This site is often used for pelvic and lower-limb anesthesia during urologic and orthopedic surgery in infants and toddlers. A single dose of caudal epidural anesthesia may provide hours of pain relief, and a continuous infusion may provide effective pain relief for hours to days. The epidural injection of opioids can provide analgesia for 12-24 hours and is a potential supplement to postoperative analgesia. Longer-acting local anesthetics (e.g., bupivacaine, ropivacaine) combined with an opioid (e.g., fentanyl, preservative-free morphine) are typically used in single-injection and continuous epidural therapy. It is also possible to provide epidural PCA with a continuous infusion pump and the patient's ability to self-administer analgesia as needed. Epidural analgesia can also provide pain relief in patients with chronic pain or pain caused by advanced malignant conditions.

Complications of neuraxial anesthesia include cephalad spread of blockade with respiratory depression, paralysis of respiratory muscles, and brainstem depression. Common complications of neuraxial analgesia are paresthesias and, if opioids are used, pruritus, nausea, and vomiting. Neuraxial opioid use necessitates antipruritic and antiemetic therapy. Infection and epidural hematoma are extremely rare. Neuraxial opioids, especially when administered intrathecally, may cause respiratory depression and require postoperative monitoring.

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91.1 Anesthetic Neurotoxicity

John P. Scott

Laboratory animal studies have suggested a link between anesthetic exposure at an early age and neurotoxicity in developing brains. Existing nonclinical data implicate *N*-methyl-D-aspartate and γ-aminobutyric acid (GABA) pathways in apoptosis and neuronal cell death. Histopathologic changes and adverse neurodevelopmental outcomes have been associated with exposure to both inhalational and IV anesthetics, including isoflurane, sevoflurane, ketamine, benzodiazepines, and propofol. Animal studies were initially performed in nonprimates (rodents), and controversy remains concerning experimental design (dose, duration of treatment, species differences). However, work in nonhuman primates has also shown an increased incidence of adverse neurodevelopmental outcomes after prolonged and/or multiple exposures to volatile anesthetics.

Human studies of anesthesia-induced neurotoxicity have yielded conflicting results. Further complicating the situation are other potential triggers for adverse neurodevelopmental outcomes, including comorbidities, surgical trauma, and perioperative cardiorespiratory status. Multiple population-based epidemiologic studies have suggested a potential association between anesthetic exposure and adverse neurodevelopmental outcomes after multiple or prolonged anesthetic exposures. Large-scale European and Canadian cohort studies using national registries have revealed subtle differences in standardized psychometric testing of early school-age children after exposure to general anesthesia. Interestingly, other studies in children have failed to yield similar results. The Pediatric Anesthesia and Neurodevelopmental Assessment (PANDA), a multicenter matched-sibling control study, revealed no association between brief anesthetic exposure for inguinal hernia repair and aptitude on psychometric testing. Similarly, the General Anaesthesia and Awake-Regional Anaesthesia in Infancy (GAS) study, a prospective multicenter randomized controlled trial comparing general and neuraxial spinal anesthesia in infants for hernia repair, *did not* demonstrate any significant differences in neurodevelopment at 2 years of age between groups. A follow-up study at 5 years of age similarly showed no difference in neurodevelopment between groups receiving general and spinal anesthesia. Importantly, studies have not shown an association between adverse neurodevelopmental outcomes and anesthetic exposure <3 hours.

Alternatives to general anesthesia for many procedures in young children do not exist. Regional anesthetic techniques and narcotic-based anesthetics may gain popularity. Dexmedetomidine may also have some neuroprotective properties. Currently, there are insufficient data to make conclusions regarding the safety of one anesthetic approach over another. Ultimately, the potential for neurotoxicity must be balanced against the necessity of providing adequate anesthesia for children presenting for surgery.

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Chapter 92

Procedural Sedation

John P. Scott

See also Chapters 91 and 93.

Sedation describes the continuum between wakefulness and general anesthesia (see Table 91.7). Many of the same medications used to induce general anesthesia may be used to provide sedation (see Table 91.8). Analogous to the provision of anesthesia, performance of procedural sedation requires a comprehensive presedation evaluation, intraprocedural monitoring, and postsedation recovery care. The term **conscious sedation** refers to a condition in which a patient is sleepy, comfortable, and cooperative but maintains airway-protective and ventilatory reflexes. Depending on the choice of pharmacotherapy, sedation may not provide analgesia. Sedation that is sufficient to obtund painful responses describes deep sedation. **Deep sedation** is a state of unarousability to voice and may be accompanied by suppression of reflex responses, with preservation of ability to respond purposefully to repeated or painful stimulation.

Pediatric procedural sedation requires vigilance and knowledge to ensure safety and is governed by the same guidelines as anesthesia care (Table 92.1). Adherence to guidelines for appropriate monitoring and management of sedation in children is imperative. Sedative doses that cause minimal sedation in one patient may produce complete unconsciousness and apnea in another. Anxiolysis or light sedation with chloral hydrate, benzodiazepines, and dexmedetomidine is often sufficient for nonpainful procedures. The use of dexmedetomidine for procedural sedation is safe, but recovery time can be prolonged and success variable. For painful procedures (e.g., bone marrow aspiration), the combination of hypnosis and analgesia is required. The addition of opioids to sedation regimens increases the risk of respiratory insufficiency. Short-acting anesthetics (e.g., propofol, methohexital, remifentanil) provide effective procedural sedation, but their use carries a higher likelihood of inadvertent induction of general anesthesia. Use of these medications requires the presence of an anesthesiologist and/or specially trained, experienced, credentialed, and qualified physicians.

Many pediatric subspecialists provide sedation and anesthesia care for children. The use of anesthetic agents is not limited to anesthesiologists, but anesthesiology departments are obligated to help develop, manage, and oversee sedation services. Together, hospitals and providers, including anesthesiologists, share responsibility for the oversight and credentialing of individuals administering sedation and anesthesia.

The elements of a safe pediatric procedural sedation system include the following:

- Clearly defined knowledge and skill sets
- Adequate prerequisite training
- Credentialing of providers
- Maintenance of certification
- Ensuring that sedation sites meet recognized standards
- Continuous quality improvement

Table 92.2 provides an approach to proper language to help the child cope with procedural pain.

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Table 92.1 Systematic Approach to Sedation in Children

Comprehensive medical history and organ system assessment, anticipating underlying medical problems that predispose the patient to anesthetic complications
Careful physical examination focused on the cardiorespiratory system and airway
Appropriate fasting
Informed consent
Pediatric drug dosing (mg/kg)
Appropriately sized equipment
Documentation of vital signs and condition on a time-based record
Rapid response ("code") team to respond to emergencies with "crash cart"
Fully equipped and staffed recovery area
Discharge criteria documenting recovery from sedation

Table 92.2 Suggested Language for Parents and Healthcare Providers

LANGUAGE TO AVOID	LANGUAGE TO USE
You will be fine; there is nothing to worry about. (reassurance)	What did you do in school today? (distraction)
This is going to hurt/this will not hurt. (vague; negative focus)	It might feel like a pinch. (sensory information)
The nurse is going to take some blood. (vague information)	First, the nurse will clean your arm, you will feel the cold alcohol pad, and next . . . (sensory and procedural information)
You are acting like a baby. (criticism)	Let's get your mind off of it; tell me about that film . . . (distraction)
It will feel like a bee sting. (negative focus)	Tell me how it feels. (information)
The procedure will last as long as . . . (negative focus)	The procedure will be shorter than . . . (television program or other familiar time for child) (procedural information; positive focus)
The medicine will burn. (negative focus)	Some children say they feel a warm feeling. (sensory information; positive focus)
Tell me when you are ready. (too much control)	When I count to 3, blow the feeling away from your body. (coaching to cope; distraction-limited control)
I am sorry. (apologizing)	You are being very brave. (praise; encouragement)
Do not cry. (negative focus)	That was hard; I am proud of you. (praise)
It is over. (negative focus)	You did a great job doing the deep breathing, holding still . . . (labeled praise)

Adapted from Krauss BS, Calligaris L, Green SM, Barbi E. Current concepts in management of pain in children in the emergency department. *Lancet.* 2016;387:83–92.

Chapter 93

Pediatric Pain Management

Stacy J.B. Peterson and Steven J. Weisman

Pain is both a sensory and an emotional experience. Infants, children, and adolescents experience a wide range of acute and chronic pain etiologies. When unrecognized and undertreated, pain extracts a significant physiologic, biochemical, and psychologic toll on both the child and the family. Many disease processes and most interventional diagnostic or treatment procedures in pediatrics are associated with pain. Similarly, traumatic, developmental, cognitive, psychologic, and social experiences can also trigger and maintain chronic pain.

DEFINITION AND CATEGORIES OF PAIN

The International Association for the Study of Pain (IASP) defines **pain** as "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage." Furthermore, the IASP expanded the definition to include the following six key notes:

1. Pain is always a personal experience that is influenced to varying degrees by biologic, psychologic, and social factors.
2. Pain and nociception are different phenomena. Pain cannot be inferred solely from activity in sensory neurons.
3. Through their life experiences, individuals learn the concept of pain.
4. A person's report of an experience as pain should be respected.
5. Although pain usually serves an adaptive role, it may have adverse effects on function and social and psychologic well-being.
6. Verbal description is only one of several behaviors to express pain; inability to communicate does not negate the possibility that a human experiences pain.

Important elements to emphasize in this definition are (1) pain encompasses both peripheral physiologic and central neural components and (2) pain may or may not be associated with ongoing tissue damage. The experience of pain lies primarily in the strength and patterning of central neural connectivity (Fig. 93.1). Although immediate upstream neural activation can originate from inflammatory, structural, or biochemical events, processes not only in the periphery but also in the spinal cord and the brain influence the intensity and duration of pain. Similarly, central neural processes in the brain are associated with the location, intensity, and distress associated with pain. Chronic pain can develop when the upstream neural signaling continues to activate central neural circuits, such as with continued peripheral inflammatory or structural pain-associated processes. Sometimes, this signaling does not regress and the individual experiences ongoing chronic pain after the resolution of the original process.

Often, however, pediatricians face the most difficult problems when either acute pain becomes chronic or chronic pain develops and is maintained without a definable infectious, inflammatory, metabolic, or structural cause. When no "cause" can be found, patients are often referred to mental health specialists, or the cause for the pain is labeled as "stress." Children read this message as, "The doctor thinks I am faking pain, or I am crazy." Parents see their child suffering and often seek care from additional providers, with the child undergoing numerous tests, procedures, medication trials, and visits and many physicians looking for the cause of the pain so it can be "fixed" or to "get an answer." Meanwhile, the child is often missing school, social, and physical activities. In addition, they often develop poor sleep habits, nonrestorative sleep, and exhibit increasing fatigue.

It is recognized that chronic pain, in the absence of a specific identified structural, biochemical, or inflammatory cause, develops through the initiation, maintenance, and strength of central neural connectivity patterns (see Chapter 212). *Centrally mediated pain* derives from neural connectivity patterns in the brain that include centers involved in autonomic nervous system control, memory, and other cognitive centers, as well as emotional centers of the brain. In pediatrics, birth history and child development overlay these central patterns that contribute to the development of chronic pain. Parents may understand the concept of a "sticky nervous system" as the perpetuator of the continued pain in such a child. This model of brain connectivity patterns, or "top-down" mediators of chronic pain, is important, because it explains how psychologic and other nonpharmacologic interventions work to reduce chronic pain and suffering.

Table 93.1 specifies important pain categories typically treated (somatic, visceral, and neuropathic) and defines the elements and characteristics of **nociception**, the peripheral physiologic aspect of pain perception. Nociception refers to how specialized fibers (largely, but not exclusively, the small, unmyelinated A-delta and C fibers) in the peripheral nervous system transmit nerve impulses (usually transmitting signals originating from peripheral mechanoreceptors and chemoreceptors) through synapses in the spinal cord's dorsal horn through (but not exclusively through) the spinothalamic tracts to the brain's higher centers, where the development of neural connectivity patterns creates the experience of pain.

ASSESSMENT AND MEASUREMENT OF PAIN IN CHILDREN

Assessing pain entails much more than merely quantifying it. Whenever feasible, the physician should ask the patient about the character, location, quality, duration, frequency, and intensity of the pain. Depending on their age, children may be able to answer some or all the questions independently or with assistance from their parents. Severity can also be assessed via utilization of various scales, which will be discussed later. Some children may not report pain because of fears of talking to strangers, disappointing, or bothering others, receiving an injection if they report pain, returning to the hospital if they admit to pain, and other negative reactions. For infants and nonverbal children, their parents, pediatricians, nurses, and other caregivers are constantly challenged to interpret whether the child's distressed behaviors represent pain, fear, hunger, or a range of other perceptions or emotions. Similarly, lack of normal interest in play without behavioral distress signals can be manifestations of pain. Therapeutic trials of comfort measures (cuddling, feeding) and analgesic medication may be helpful in clarifying the triggers of the behaviors.

Behavior and physiologic signs are useful but can be misleading. A toddler may scream and grimace during an ear examination because of fear rather than pain. Conversely, children with inadequately relieved persistent pain from cancer, sickle cell disease, trauma, or surgery may withdraw from their surroundings and appear very quiet, leading observers to conclude falsely that these children are comfortable or sedated. In adolescents, increased reports of pain may be misinterpreted as "drug seeking" behaviors. In these situations, it is important to assess pain appropriately and determine how to best improve pain and function. Although this may be best accomplished by adjustment to analgesic medications, it may also involve the optimization of other nonpharmacologic techniques. This approach, although increasing the number or amount of interventions, may make the child become more, not less, interactive and alert as pain control improves. Similarly, neonates and young infants may close their eyes, furrow their brows, and clench their fists in response to pain. Adequate analgesia is often associated with eye opening and increased involvement in surroundings. A child who is experiencing significant chronic pain may play normally to distract attention away from pain. These coping behaviors are sometimes misinterpreted as evidence of the child's "faking" or exaggerating pain.

Age-Specific and Developmentally Specific Measures

Because infants, young children, and nonverbal children cannot express the quantity of pain they experience, several pain scales have been devised attempting to quantify pain in these populations (Fig. 93.2 and Table 93.2).

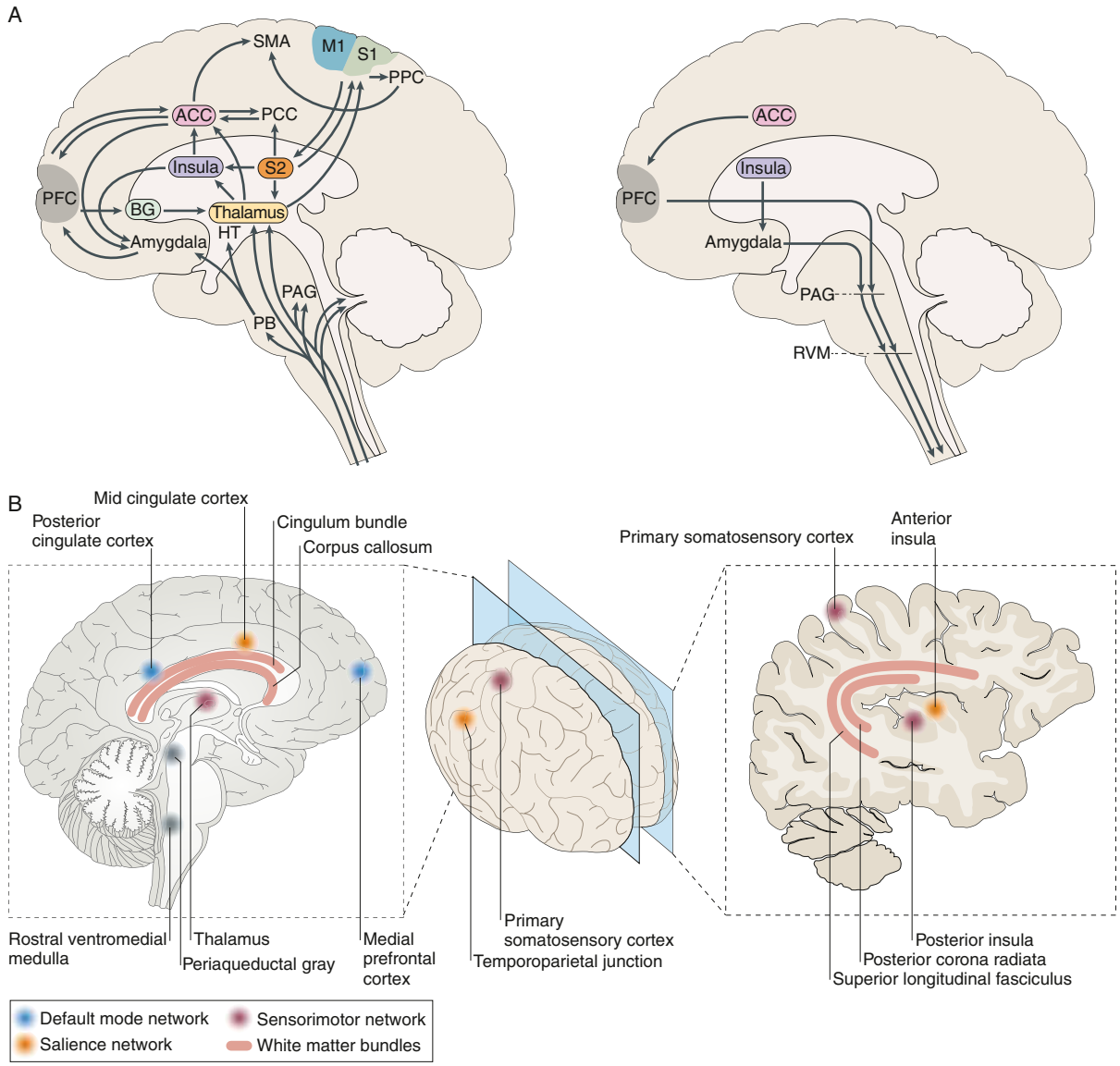


Fig. 93.1 Brain pathways, regions, and networks involved in acute and chronic pain. ACC, Anterior cingulate cortex; PCC, posterior cingulate cortex; BG, basal ganglia; HT, hypothalamus; PAG, periaqueductal gray; PB, parabrachial nuclei; PFC, prefrontal cortex; PPC, posterior parietal cortex; SMA, supplementary motor area; RVM, rostral ventromedial medulla. (**A**, *left panel from Apkarian AV, Bushnell MC, Treede RD, Zubieta JK. Human brain mechanisms of pain perception and regulation in health and disease. Eur J Pain. 2005;9:463–484;* **A**, *right panel from Schweinhardt P, Bushnell MC. Pain imaging in health and disease—how far have we come? J Clin Invest. 2010;120:3788–3797;* **B** *from Davis KD, Flor H, Greely HT, et al. Brain imaging tests for chronic pain: Medical, legal and ethical issues and recommendations. Nat Rev Neurol. 2017;13:624–638.)*

Table 93.1 Pain Categories and Characteristics

PAIN CATEGORY	DEFINITION	EXAMPLES	CHARACTERISTICS
Somatic	Pain resulting from injury to or inflammation of tissues (e.g., skin, muscle, tendons, bone, joints, fascia, vasculature)	Burns, lacerations, fractures, infections, inflammatory conditions	*In skin and superficial structures:* sharp, pulsatile, well localized *In deep somatic structures:* dull, aching, pulsatile, not well localized
Visceral	Pain resulting from injury to or inflammation of viscera	Angina, hepatic distention, bowel distention or hypermobility, pancreatitis	Aching and cramping; nonpulsatile; poorly localized (e.g., appendiceal pain perceived around umbilicus) or referred to distant locations (e.g., angina perceived in shoulder)
Neuropathic	Pain resulting from injury to, inflammation of, or dysfunction of the peripheral or central nervous system	Complex regional pain syndrome (CRPS), phantom limb pain, Guillain-Barré syndrome, sciatica	Spontaneous; burning; lancinating or shooting; dysesthesias (pins and needles, electrical sensations); **hyperalgesia** (amplification of noxious stimuli); **hyperpathia** (widespread pain in response to a discrete noxious stimulus); **allodynia** (pain in response to nonpainful stimulation); pain may be perceived distal or proximal to site of injury, often corresponding to innervation pathways (e.g., sciatica)

Behavioral Indicators

Facial grimacing: The Neonatal Facial Coding System uses several facial actions that may be indicators of pain. Pain is characterized by a bulging brow with tight creases in between; tightly closed eyelids; a deeply furrowed nasolabial groove; a horizontal, wide opened mouth; and a taut tongue that may be quivering along with the chin.

Crying: May be an indicator of pain.

Activity: Withdrawal or immobilization of a limb may be an indicator of pain.

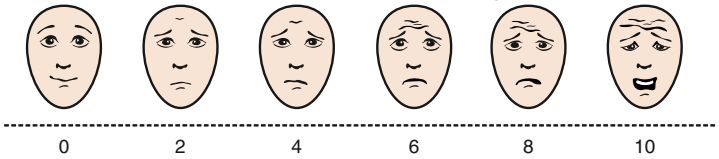
Response to comfort measures: Feeding, swaddling, holding, and ensuring that the infant is neither wet nor cold may help to discriminate between pain and other conditions.

Physiologic indicators: Alterations in heart rate, blood pressure, SpO_2, respiratory rate, or alterations in pattern of respiration may be nonspecific indicators of pain.

Self-Report of Pain

Categorical description: Toddlers or young children are asked to say if they are having "a little bit," a "middle amount," or "a lot" of pain.

Faces Scales: Children who do not have an appreciation of ordinal numbering are asked to rate their pain based upon cartoons depicting facial indicators of distress.



Numerical Rating Scale (NRS): Older children and teenagers are asked to rate their pain on a scale of "0" (no pain) to "10" (worst pain).

Visual Analog Scale (VAS): Children or teenagers are asked to move an indicator along a mechanical slide to depict the level of pain; the clinician reads a number along a 10-cm indicator on the back to determine the numeric score.

Fig. 93.2 Clinically useful pain assessment tools. *(Adapted from Burg FD, Ingelfinger JR, Polin RA, et al., eds. Current Pediatric Therapy, 18th ed. Philadelphia: Saunders; 2006:16; and Hicks CL, von Baeyer CL, Spafford P, et al. The Faces Pain Scale—revised: Toward a common metric in pediatric pain measurement. Pain. 2001;93:173–183.)*

Table 93.2 Pain Measurement Tools

NAME	FEATURES	AGE RANGE	ADVANTAGES	VALIDATION AND USES	LIMITATIONS
Visual Analog Scale (VAS)	Horizontal 10-cm line; subject marks a spot on the line between anchors of "no pain" and "most pain imaginable"	6-8 yr and older	Good psychometric properties; validated for research purposes	Acute pain Surgical pain Chronic pain	Cannot be used in younger children or in those with cognitive limitations Requires language skills and numerical processing; upper anchor of "most pain" requires an experiential reference point that is lacking in many children
Numerical Rating Scale (NRS)	Integers from 0 to 10, inclusive, corresponding to a range from no pain to most pain	6-8 yr and older	Good psychometric properties; validated for research purposes	Acute pain Surgical pain Chronic pain	Same as for VAS
Faces Scales (e.g., FACES-R, Wong-Baker, Oucher, Bieri, McGrath scales)	Subjects rate their pain by identifying with line drawings of faces or photos of children	3 yr and older	Can be used at younger ages than VAS and NRS	Acute pain Surgical pain	Choice of "no pain" face affects responses (neutral vs smiling); not culturally universal
Behavioral or combined behavioral-physiologic scales (e.g., FLACC, N-PASS, CHEOPS, OPS, FACS, NIPS)	Scoring of observed behaviors (e.g., facial expression, limb movement) ± heart rate and blood pressure	Some work for any ages; some work for specific age-groups, including preterm infants	May be used in both infants and nonverbal children	FLACC, N-PASS: Acute pain Surgical pain	Nonspecific; overrates pain in toddlers and preschool children; underrates persistent pain; some measures are convenient, but others require videotaping and complex processing; vital sign changes unrelated to pain can occur and may affect total score
Autonomic measures (e.g., heart rate, blood pressure, heart rate spectral analyses)	Scores changes in heart rate, blood pressure, or measures of heart rate variability (e.g., "vagal tone")	All ages	Can be used at all ages; useful for patients receiving mechanical ventilation		Nonspecific; vital sign changes unrelated to pain may occur and may artifactually increase or decrease score
Hormonal-metabolic measures	Plasma or salivary sampling of "stress" hormones (e.g., cortisol, epinephrine)	All ages	Can be used at all ages		Nonspecific; changes unrelated to pain can occur; inconvenient; cannot provide "real-time" information; standard normal values not available for every age bracket

VAS, visual analog scale; NRS, numerical rating scale; FLACC, face, legs activity, cry, and consolability pain scale for preverbal/nonverbal patients; N-PASS, neonatal pain agitation and sedation scale.

The Newborn and Infant

There are several behavioral distress scales for the infant and young child, mostly emphasizing the patient's facial expressions, crying, and body movement. Facial expression measures appear most useful and specific in neonates. Autonomic and vital signs can indicate pain, but because they are nonspecific, they may reflect other processes, including fever, hypoxemia, and cardiac or renal dysfunction (Tables 93.3 and 93.4).

Table 93.3 Signs and Symptoms of Pain in Infants and Young Children

PHYSIOLOGIC CHANGES	BEHAVIORAL CHANGES
• Increase in heart rate, respiratory rate, blood pressure, muscle tone • Oxygen desaturation • Sweating • Flushing • Pallor	• Change in facial expression (grimacing, furrowing of the brow, nasal flaring, deep nasolabial groove, curving of the tongue, quivering of the chin) • Finger clenching • Thrashing of limbs • Writhing • Back arching • Head banging • Poor feeding • Sleep disturbance • Pseudoparalysis

From Krauss BS, Calligaris L, Green SM, Barbi E. Current concepts in management of pain in children in the emergency department. *Lancet.* 2016;387:83–92.

Table 93.4 CRIES Neonatal Pain Assessment Scale

	0	1	2
Crying	No	High pitched but consolable	Inconsolable
Requires oxygen for saturation >95%	No	FiO_2 <30%	FiO_2 >30%
Increased vital signs	No	HR or BP <20%	HR or BP >20%
Expression	No	Grimace	Grimace and grunt
Sleepless	No	Wakes often	Constantly awake

Score <4 initiate nonpharmacologic measures
Score >4 initiate pharmacologic and nonpharmacologic measures
BP, Blood pressure; HR, heart rate.
From Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*, 10th ed. Philadelphia: Elsevier; 2022, Table 23.2, p. 487.

The Older Child

Children age 3-7 years old become increasingly articulate in describing the intensity, location, and quality of pain. Pain is occasionally referred to adjacent areas; referral of hip pain to the thigh or area above the knee is common in this age range. Self-report measures for children this age include using drawings, pictures of faces, or graded color intensities. Children ≥8 years old can usually use verbal numerical rating scales (NRS) or visual analog pain scales (VAS) accurately (see Fig. 93.2). Verbal numerical ratings are preferred and considered the gold standard: valid and reliable ratings can be obtained from children ≥8 years of age. The NRS consists of numbers from 0 to 10, in which 0 represents no pain and 10 represents very severe pain. There is debate about the label for the highest pain rating, but the current agreement is *not* to use the phrase "worst pain possible," because children can always imagine a greater pain. In the United States, regularly documented pain assessments are required for hospitalized children and children attending outpatient hospital clinics and emergency departments. Pain scores do not always correlate with changes in heart rate or blood pressure.

The Cognitively Impaired Child

Measuring pain in cognitively impaired children remains a challenge. Understanding pain expression and experience in this population is important because behaviors may be misinterpreted as indicating that cognitively impaired children are more insensitive to pain than neurotypical children. Children with trisomy 21 may express pain less precisely and more slowly than the general population. Pain in children with autism spectrum disorder (ASD) may be difficult to assess because these children may be both *hyposensitive* and *hypersensitive* to many different types of sensory stimuli, and they may have limited communication abilities. Although self-reports of pain can be elicited from some children who are cognitively impaired, observational measures have better validation among these children. The **Noncommunicating Child's Pain Checklist—Postoperative Version** is recommended for children up to 18 years old. In addition, the FLACC pain scale has been validated in nonverbal and cognitively impaired children (Table 93.5). Maladaptive behaviors and reduction in function may also indicate pain. Children with severe cognitive impairments experience pain frequently, and children with the fewest abilities experience the most pain. For this reason, providers must be able to recognize subtle signs and symptoms of pain (see Table 93.3)

Table 93.5 Revised FLACC for Pain Assessment in the Cognitively Impaired*

	0	1	2
Face	No particular expression or smile	Occasional grimace/frown; withdrawn or disinterested (appears sad or worried)	Consistent grimace or frown; frequent/constant quivering chin, clenched jaw (distressed-looking face; expression of fright or panic)
Legs	Normal position or relaxed	Uneasy, restless, tense (occasional tremors)	Kicking or legs drawn up (marked increase in spasticity, constant tremors, or jerking)
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense (mildly agitated [e.g., head back and forth, aggression]; shallow, splinting respirations, intermittent sighs)	Arched, rigid, or jerking (severe agitation, head banging; shivering [not rigors]; breath-holding, gasping or sharp intake of breath; severe splinting)
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint (occasional verbal outburst or grunt)	Crying steadily, screams or sobs, frequent complaints (repeated outbursts, constant grunting)
Consolability	Content, relaxed	Reassured by occasional touching, hugging, or talking; distractible	Difficult to console or comfort (pushing away caregiver, resisting care or comfort measures)

*Revised descriptors for children with disabilities shown in brackets.
0= Relaxed/comfortable
1–3 = Mild discomfort
4–6 = Moderate pain
7–10 = Severe pain
FLACC Scoring System: May be used in preverbal, mechanically ventilated, or cognitively impaired patients; it is an acronym that includes 5 indicators, each scored as a 0, 1, or 2, that form a 10-point composite scale with a range from 0 (no pain) to 10 (worst pain). FLACC: Score each category between 0 and 2. The total score may be any number from 0 to 10.
From Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*, 10th ed. Philadelphia: Elsevier; 2022, Table 23.3, p. 488.

CONCEPTUAL FRAMEWORK FOR TREATMENT OF PEDIATRIC PAIN

Many models of pain focus on factors that explain the interindividual variability in pain perception and the chronicity and impairment experienced with pain. Central to these models are interrelationships among biologic, cognitive, affective, and social factors that influence children's pain and disability, commonly referred to as *biopsychosocial models* of pain. **Biologic** factors include the child's physical health, central nervous system (CNS) factors (pain processing), gender, pubertal status, and genetic factors. Individual child **cognitive and affective** factors related to perception of pain include anxiety, fear, negative affect, pain behaviors, and functional disability, whereas **social** factors include such areas as culture, socioeconomic status, school environment, social and peer interactions, adverse childhood events, and parental and family factors. For children, **developmental** factors need to be considered, such as cognitive and motor development, birth history, and epigenetic factors (the interaction in development between genetic and environmental factors).

A framework that considers the interplay of biologic, psychologic, and social factors is useful for understanding pediatric pain and to guide pain assessment and the delivery of pain prevention and management. Many simple interventions designed to promote relaxation and patient control can work either alone or synergistically with pain medications for relief of pain and related distress. Moreover, psychologic interventions are often coupled with physical therapy interventions to assist in the management of disabling chronic pain.

Pharmacologic Treatment of Pain

The pharmacokinetics and pharmacodynamics of analgesics vary with age. This results in drug responses in infants and young children that differ from those in older children and adults. The elimination half-life of most analgesics is prolonged in neonates and young infants because of their immature hepatic enzyme systems and reduced glomerular filtration. Clearance of analgesics may also be variable in young infants and children. Renal blood flow, glomerular filtration, and tubular secretion increase dramatically in the first few weeks after birth, approaching adult values by 3-5 months of age. Renal clearance of analgesics is often greater in toddlers and preschool-age children than in adults, whereas in premature infants, clearance is reduced. Age-related differences in body composition and protein binding also exist. Total body water as a fraction of body weight is greater in neonates than in children or adults. Tissues with high perfusion, such as the brain and heart, account for a larger proportion of body mass in neonates than do other tissues, such as muscle and fat. Because of decreased serum concentrations of albumin and α_1-acid glycoprotein, neonates have reduced protein binding of some drugs, resulting in higher amounts of free, unbound, pharmacologically active drugs.

Acetaminophen, Aspirin, and Nonsteroidal Antiinflammatory Drugs

Acetaminophen and nonsteroidal antiinflammatory drugs (NSAIDs) have replaced aspirin as the most used antipyretics and oral, nonopioid analgesics (Table 93.6). This is because of the association of Reye syndrome with the use of aspirin in children with a viral infection, such as influenza or chickenpox.

Acetaminophen, a generally safe, nonopioid analgesic and antipyretic, has the advantage of intravenous (IV), rectal, and oral routes of administration. Acetaminophen is not associated with the gastrointestinal (GI) or antiplatelet effects of aspirin and NSAIDs, making it a particularly useful drug in patients with cancer. Unlike aspirin and NSAIDs, acetaminophen has only mild antiinflammatory action. Although acetaminophen alone may not adequately treat various types of pain, in conjunction with other agents, it can lead to improved pain control and decreased opioid use. One effective management strategy can be to schedule acetaminophen and/or NSAIDs to decrease the need for opioids, while still maintaining good pain control.

Acetaminophen toxicity can result from a large single dose or cumulative excessive dosing over days or weeks (see Chapter 94). Toxicity manifests as fulminant hepatic necrosis and liver failure in infants, children, and adults. Drug biotransformation processes are immature in neonates, very active in young children, and somewhat less active in adults. Young children are more resistant to acetaminophen-induced hepatotoxicity than are adults as a result of metabolic differences. Sulfation predominates over glucuronidation in young children, leading to a reduction in NAPQI production.

Aspirin is indicated for certain rheumatologic conditions and for inhibition of platelet adhesiveness, as in the treatment of Kawasaki disease. Concerns about Reye syndrome have resulted in a substantial decline in pediatric aspirin use. In general, aspirin should not be used for routine pain control in children. It is important to be aware of

Table 93.6 Commonly Used Nonopioid Medications (Antiinflammatory Medications)

MEDICATION	DOSAGE	COMMENT(S)
Acetaminophen	10-15 mg/kg PO q4h 10 mg/kg IV q4h 15 mg/kg IV q6h 10 mg/kg IV q6h (<2 yr) 20-30 mg/kg/PR q4h 40 mg/kg/PR q6-8h *Maximum daily dosing:* 75 mg/kg/24 hr (children) 60 mg/kg/24 hr (<2 yr) 30-45 mg/kg/24 hr (neonates)	Minimal antiinflammatory action; no antiplatelet or adverse gastric effects; overdosing can produce fulminant hepatic failure.
Ibuprofen	8-10 mg/kg PO q6h 10 mg/kg IV q4-6h to maximum of 400 mg *Maximum daily dose:* 2,400 mg	Antiinflammatory; transient antiplatelet effects; may cause gastritis; extensive pediatric safety experience.
Naproxen	5-7 mg/kg PO q8-12h *Maximum daily dose:* 1,000 mg	Antiinflammatory; transient antiplatelet effects; may cause gastritis; more prolonged duration than that of ibuprofen.
Ketorolac	Loading dose 0.3 mg/kg, then 0.25-0.3 mg/kg IV q6h to a maximum of 5 days; maximum single dose 15 mg for those < 50 kg and 30 mg for those ≥ 50 kg	Antiinflammatory; reversible antiplatelet effects; may cause gastritis; useful for short-term situations in which oral dosing is not feasible.
Diclofenac sodium	2-3 mg/kg/day divided in 2 or 3 doses *Maximum daily dose:* 150 mg	Antiinflammatory; reversible antiplatelet effects; lower risk of gastritis and ulceration compared with other NSAIDs.
Celecoxib	Only approved for children ≥2 yr; ≥10 kg to ≤25 kg: 50 mg PO bid >25 kg: 100 mg PO bid	Antiinflammatory; no or minimal antiplatelet or gastric effects; cross-reactivity with sulfa allergies.

aspirin-containing medications that may be available over the counter when treating patients.

NSAIDs are used widely to treat pain and fever in children. Most currently available NSAIDs are nonselective cyclooxygenase (COX) inhibitors, that is, drugs that nonselectively block the activity of both COX-1 (found in gastric mucosa and platelets) and COX-2 (active in inflammatory pathways and cortical renal blood flow regulation) enzymes that synthesize prostaglandins. In children with juvenile idiopathic arthritis, ibuprofen and aspirin are equally effective, but ibuprofen is associated with fewer side effects and better drug adherence. NSAIDs, used adjunctively in surgical patients, reduce opioid requirements (and therefore opioid side effects) by as much as 35–40%. Although NSAIDs can be useful postoperatively, they should be used as an adjunct to, not as a substitute for, opioids in patients with acute moderate to severe pain.

Ketorolac is useful in treating moderate to severe acute pain in patients who are unable or unwilling to take oral NSAIDs. Intravenous diclofenac is also available in other countries. U.S. Food and Drug Administration (FDA) recommendations limit ketorolac to five consecutive days of administration. IV ibuprofen (Caldolor) is FDA approved for the management of pain and fever in infants and children >6 months of age, but is not widely available.

Adverse effects of NSAIDs are uncommon but may be serious when they occur, including gastritis with pain and bleeding; decreased renal blood flow that may reduce glomerular filtration and enhance sodium reabsorption, in some cases leading to tubular necrosis; hepatic dysfunction and liver failure; inhibition of platelet function; and an increased incidence of cardiovascular events in patients predisposed to stroke and myocardial infarction. Although the overall incidence of bleeding is very low, gastric bleeding is the most common cause of serious morbidity related to this class of analgesics. NSAIDs should not be used in the child with a bleeding diathesis or at risk for bleeding and should be used with caution postsurgically. Use after surgeries such as tonsillectomy has been debated, but current postoperative guidelines do include the use of NSAIDs. Renal injury from short-term use of ibuprofen in euvolemic children is quite rare; the risk is increased by hypovolemia or cardiac dysfunction. The safety of both ibuprofen and acetaminophen for short-term use is well established (see Table 93.6).

The only **COX-2 specific NSAID** currently available in the United States is oral celecoxib, whereas in other countries parenteral parecoxib and oral rofecoxib are also available. The coxib drugs are selective COX-2 enzyme inhibitors. Therefore they are effective antiinflammatory and analgesic molecules that generally do not result in platelet inhibition with enhanced bleeding or in gastric inflammation or ulceration, findings that may be seen with the nonselective COX inhibitors in the NSAID class. COX-2 selective NSAIDs do inhibit regulation of cortical renal blood flow and therefore carry the same risk of renal toxicity and acute tubular necrosis, particularly in the setting of low cardiac output states or dehydration. Celecoxib is therefore an appropriate primary or adjunctive analgesic to use in children after surgery, in children with gastric mucosal pathology, or in oncology patients in whom concern for hemostasis contraindicates conventional NSAIDs.

Use of NSAIDs for pain management in children less than 6 months is not generally recommended due to immature glomerular filtration. However, limited use between 3 and 6 months may be appropriate.

Opioids

Opioids are analgesic substances either derived from the opium poppy **(opiates)** or synthesized to have a similar chemical structure and mechanism of action **(opioids)**. The term "narcotics" (narcotic analgesics) should be avoided for these agents, as it connotes criminality and lacks pharmacologic descriptive specificity. Opioids are administered for moderate and severe pain, such as acute postoperative pain, pain from trauma, sickle cell crisis pain, and cancer pain. Opioids can be administered by the oral, rectal, oral transmucosal, transdermal, intranasal, epidural, intrathecal, IV, subcutaneous (SC), or intramuscular (IM) route. Regardless of route of administration, the site of action is at mu (μ) opioid receptors in the peripheral nervous system, spinal cord, brainstem, and higher CNS centers. Infants and young children are sometimes underdosed with opioids because of concern about significant respiratory side effects. Opioids' respiratory depressant effects result from infants' lower metabolic clearance of opioids and higher blood levels with frequent dosing. With proper understanding of the pharmacokinetic and pharmacodynamics of opioids, children can receive effective relief of pain and suffering with a good margin of safety, regardless of pharmacokinetic maturity, age, or size (Tables 93.7-93.9).

Opioids act by mimicking the actions of endogenous opioid peptides, binding to receptors in the brain, brainstem, spinal cord, and to a lesser extent in the peripheral nervous system, thus leading to inhibition of nociception. Opioids also bind to μ receptors in the pleasure centers of the midbrain, particularly in genetically susceptible individuals, a factor responsible for the euphoric effect in some individuals and the predilection to psychologic dependence and addictive behavior. Opioids also have dose-dependent respiratory depressant effects when interacting with the μ-opioid receptors in the respiratory centers of the brainstem, depressing ventilatory drive and blunting ventilatory responses to both hypoxia and hypercarbia. These respiratory depressant effects are increased with co-administration of other sedating drugs, particularly benzodiazepines or barbiturates.

Optimal use of opioids requires proactive and anticipatory management of side effects (see Table 93.8) as well as dose adjustments for renal or hepatic disease (Table 93.10). Common side effects include sedation, constipation, nausea, vomiting, urinary retention, and pruritus. Tolerance usually develops to the side effect of **nausea**, which typically subsides with long-term dosing, but nausea may require treatment with antiemetics, such as a phenothiazine, butyrophenones, antihistamines, or a serotonin receptor antagonist such as ondansetron or granisetron. Pruritus and other complications during patient-controlled analgesia with opioids may be effectively managed by low-dose IV naloxone.

The most common troubling, but treatable, side effect is **constipation**. Patients who take opioids for chronic pain for long periods predictably develop tolerance to the sedative and analgesic effects of opioids over time, but tolerance to constipation does not occur, and constipation remains a troublesome and distressing problem in almost all patients with long-term opioid administration. Stool softeners and stimulant laxatives should be administered to most patients receiving opioids for more than a few days. Osmotic and bulk laxatives are less effective, usually producing more distention and discomfort. A peripherally acting opiate μ-receptor antagonist, **methylnaltrexone**, promptly and effectively reverses opioid-induced constipation in patients with chronic pain who are receiving opioids daily. Methylnaltrexone is approved for use as either an injectable or oral formulation, but only the SC injection is commercially available, which most children will object to receiving. Naldemedine and naloxegol are other agents with actions similar to methylnaltrexone. **Lubiprostone** is a colonic chloride channel inhibitor that impairs water reabsorption in the colon and is very effective for opioid-induced constipation.

Media and government attention to the "opioid epidemic" has reasonably led to scrutiny of the prescription of opioids to children, and FDA approval of opioid formulations for children has raised alarm and criticism by some vocal critics of the use of opioids for medical purposes. Thus one of the potent barriers to effective management of pain with opioids is the fear of addiction held by many prescribing pediatricians and parents alike. Pediatricians should understand the phenomena of tolerance, dependence, withdrawal, and addiction (Table 93.11). **Opioid addiction** is the result of the complex interplay of genetic predisposition, psychiatric pathology, and social forces, including poverty, joblessness, hopelessness, and despair. The dramatic increase in the amount of opioid abuse and overdoses and opioid-related deaths, although highest in the adult non-Hispanic American Indian or Alaska Native population age 35–44 years old, has also significantly risen in children and adolescents. Among persons 14–18 years, overdose deaths increased 114% from 2019 to 2021 with 2,037 (91.3%) of adolescent overdose deaths in 2021 involving at least one opioid. Despite this rise in abuse of opioids, a longitudinal study of children and adolescents treated for medical reasons with opioids found that there was no increased risk of the development of substance abuse, at least until their

Table 93.7 Pediatric Dosage Guidelines for Opioid Analgesics

DRUG	EQUI-ANALGESIC DOSES		PARENTERAL DOSING		IV:PO DOSE RATIO	ORAL DOSING		COMMENTS
	IV	ORAL	<50 kg	≥50 kg		<50 kg	≥50 kg	
Fentanyl	10 µg	100 µg	0.5-1 µg/kg q1-2h 0.5-1.5 µg/kg/hr	0.5-1 µg/kg q1-2h 0.5-1.5 µg/kg/hr	Oral transmucosal: 1:10 Transdermal: 1:1	Oral transmucosal: 10 µg/kg Transdermal: 12.5-50 µg/hr	Transdermal patches available; patch reaches steady state at 24 hr and should be changed q72h	70-100 times as potent as morphine with rapid onset and shorter duration. With high doses and rapid administration, can cause chest wall rigidity. Useful for short procedures; transdermal form should be used only in opioid-tolerant patients with chronic pain.
Hydrocodone	N/A	1.5 mg	N/A	N/A	N/A	0.15 mg/kg	10 mg	Weak opioid; only available in form with acetaminophen.
Hydromorphone	0.2 mg	0.6 mg	0.01 mg q2-4h 0.002 mg/kg/hr	0.01 mg q2-4h 0.002 mg/kg/hr	1:3	0.04-0.08 mg/kg q3-4h	2-4 mg q3-4h	Five times the potency of morphine; no histamine release and fewer adverse events than morphine.
Methadone	1 mg	2 mg	0.1 mg/kg q8-24h	0.1 mg/kg q8-24h	1:2	0.2 mg/kg q8-12h PO; available as liquid or tablet	2.5 mg TID	Duration 12-24 hr; useful in certain types of chronic pain; requires additional vigilance because it will accumulate over 72 hr and produce delayed sedation. When patients tolerant of opioids are switched to methadone, they show incomplete cross-tolerance and improved efficacy. Because methadone is associated with prolonged QTc, monitoring is needed for children receiving high and extended dosing.
Morphine	1 mg	3 mg	0.05 mg/kg q2-4h 0.01-0.03 mg/kg/hr	0.1 mg/kg q2-4h 0.01-0.03 mg/kg/hr	1:3	Immediate release: 0.3 mg/kg q3-4h Sustained release: 20-35 kg: 10-15 mg q8-12h 35-50 kg: 15-30 mg q8-12h	Immediate release: 15-20 mg q3-4h Sustained release: 30-90 mg q8-12h	Potent opioid for moderate/severe pain; may cause histamine release. Sustained-release form must be swallowed whole; if crushed, becomes immediate acting, leading to acute overdose.
Oxycodone	N/A	3 mg	N/A	N/A	N/A	0.1-0.2 mg q3-4h; available in liquid (1 mg/mL)	Immediate release: 5-10 mg q4h Sustained release: 10-120 mg q8-12h	Strong opioid only available as an oral agent in North America; more potent than and preferable to hydrocodone. Sustained-release form must be swallowed whole; if crushed, becomes immediate acting, leading to acute overdose.

N/A, not available.

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Table 93.8 Management of Opioid-Induced Adverse Effects

Respiratory depression	*Naloxone:* 0.01-0.02 mg/kg up to a full reversal dose of 0.1 mg/kg. May be given IV, IM, IN, SC, or via ETT. The full reversal dose should initially be used for apnea in opioid-naive patients. In opioid-tolerant patients, a reduced dose should be given and titrated up slowly to treat symptoms but prevent acute withdrawal. Ventilation may need to be supported during this process. Dose may be repeated every 2 min to a total of 10 mg. Adult maximum dose is 2 mg/dose. Give with caution to patients who are receiving long-term opioid therapy, as it may precipitate acute withdrawal. Duration of effect is 1-4 hr; therefore close observation for recurrent symptoms is essential.
Excessive sedation without evidence of respiratory depression	Change opioid or decrease the dose. In palliative patients or other special circumstances, can consider treating with stimulants. *Methylphenidate**:* 0.3 mg/kg per dose PO (typically 10-20 mg/dose to a teenager) before breakfast and lunch. Do not administer to patients receiving clonidine, because dysrhythmias may develop. *Dextroamphetamine*: 2.5-10 mg on awakening and at noon. Not for use in young children or in patients with cardiovascular disease or hypertension. *Modafinil:* Pediatric dose not established. May be useful in selected patients. Typical adult dose: 50-200 mg/day.
Nausea and vomiting	*Metoclopramide*†*:* 0.15 mg/kg IV up to 10 mg/dose q6-12h for 24 hr. *Trimethobenzamide:* if weight <15 kg, 100 mg PO or PR q6h; if >15 kg, 200 mg PO or PR q6h. (*Note:* Suppository contains benzocaine 2%.) Not for use in newborn infants or premature infants. 5-HT_3 receptor blockers: *Ondansetron:* 0.15 mg/kg up to 8 mg IV q6-8h not to exceed 32 mg/day (also available as a sublingual tablet). *Granisetron:* 10 to 20 µg/kg IV q12-24h. *Prochlorperazine**‡ (Compazine): >2 yr or >20 kg, 0.1 mg/kg per dose q8h IM or PO up to 10 mg/dose. Change opioid.
Pruritus	*Hydroxyzine*: 0.5 mg/kg PO q6h. *Nalbuphine:* 0.1 mg/kg IV q6h for pruritus caused by intraaxial opioids, especially fentanyl. Administer slowly over 15-20 min. May cause acute reversal of systemic µ-receptor effects and leave κ-agonism intact. *Naloxone:* 0.5-2 mcg/kg/hr IV infusion (titrate up to decrease pruritus and reduce infusion if pain increases). *Ondansetron:* 0.05-0.1 mg/kg IV or PO q8h. *Cyproheptadine*†*:* 0.1-0.2 mg/kg PO q8-12h. Maximum dose 12 mg. Change opioid.
Constipation	Encourage water consumption, high-fiber diet, and vegetable fiber. *Bulk laxatives:* Metamucil, Maltsupex. *Lubricants:* Mineral oil 15-30 mL PO daily as needed (not for use in infants because of aspiration risk). *Surfactants:* Sodium docusate (Colace): <3 yr: 10 mg PO q8h 3-6 yr: 15 mg PO q8h 6-12 yr: 50 mg PO q8h >12 yr: 100 mg PO q8h *Stimulants:* Bisacodyl suppository (Dulcolax): <2 yr: 5 mg PR qhs >2 yr: 10 mg PR qhs *Senna syrup* (218 mg/5 mL): >3 yr: 5 mL qhs *Enema:* Fleet hypertonic phosphate enema (older children; risk of hyperphosphatemia). *Electrolytic/osmotic:* Milk of magnesia; for severe impaction: polyethylene glycol (GoLYTELY, MiraLAX). Methylnaltrexone is an opioid antagonist that works in the colon and does not cross the blood-brain barrier to reverse analgesia; given as subcutaneous injection every day or every other day (0.15 mg/kg) and is effective in producing stool in 30-60 min in most patients.
Urinary retention	Straight catheterization, indwelling catheter. Decrease opioids, use naloxone drip.

*Avoid in patients taking monoamine oxidase inhibitors.
†May be associated with extrapyramidal side effects, which may be more often seen in children than in adults.
‡Consider pretreatment with diphenydramine to decrease risk of anti-dopaminergic adverse events (e.g., dystonia).
ETT, Endotracheal tube; IV, intravenously; IM, intramuscularly; IN, intranasally; PO, orally; PR, rectally; SC, subcutaneously.
Modified from Burg FD, Ingelfinger JR, Polin RA, et al., eds. *Current Pediatric Therapy,* 18th ed. Philadelphia: Saunders; 2006, p 16.

mid-20s. Thus the rational short- or even long-term use of opioids in children does not lead to a predilection for or risk of addiction in a child not otherwise at risk because of genetic background, economic factors, or social milieu.

It is equally important for pediatricians to realize that even patients with recognized substance abuse diagnoses are entitled to effective analgesic management, which often includes the use of opioids. If legitimate concerns exist about addiction in a patient, safe, effective opioid pain management is often best provided by specialists in pain management and addiction medicine. Table 93.12 outlines the U.S. Centers for Disease Control and Prevention (CDC) opioid recommendations for **chronic pain** (primarily in adults).

There is no longer a reason to administer opioids by IM injection. Continuous IV infusion of opioids is an effective option that permits more constant plasma concentrations and clinical effects than intermittent IV bolus dosing without the pain associated with IM injection. The most common approach in pediatric centers is to administer a low-dose basal opioid infusion while permitting patients to use a **patient-controlled analgesia (PCA)** device to titrate the dosage above the infusion (Fig. 93.3) (see Chapter 91). Compared with children given intermittent IM morphine, children using PCA reported better pain scores. PCA has several other advantages: (1) dosing can be adjusted to account for individual pharmacokinetic and pharmacodynamic variation and for changing pain intensity during the day; (2) psychologically the patient is more in control, actively coping with the pain; (3) overall opioid consumption tends to be lower; (4) fewer opioid side effects occur; and (5) patient satisfaction is generally much higher. Children as young as 5-6 years old can effectively use PCA. The device can also

be activated by parents or nurses, known as **PCA-by-proxy (PCA-P) or parent-nurse controlled analgesia (PNCA)**, which produces analgesia in a safe, effective manner for children who cannot activate the PCA demand button themselves because they are too young or intellectually or physically impaired. PCA overdoses have occurred when well-meaning, inadequately instructed parents pushed the PCA button in medically complicated situations, with or without the use of PCA-P, highlighting the need for patient and family education, use of protocols, physiologic monitoring, and adequate nursing supervision.

Because of the high risk of adverse side effects (respiratory depression), the FDA has issued **contraindications** for the pediatric use of codeine and tramadol (Table 93.13).

Table 93.9 Equianalgesic Doses and Half-Life ($T_{1/2\beta}$) of Some Commonly Used Opioids

OPIOID	IM/IV DOSE (mg)	ORAL DOSE (mg)	$T_{1/2\beta}$ (hr)
Morphine	10	30	2-3
Oxycodone	15	20-30	2-3
Fentanyl	0.15-0.2	—	3-5
Alfentanil	0.75-1.5	—	1-2
Sufentanil	0.02	—	2-3
Methadone	10	10-15	15-40
Hydromorphone	1.5	7.5	3-4
Tramadol†	100	100	5-7
Buprenorphine	0.4	0.8 (sublingual)	3-5
Pentazocine	60	150	3-5
Nalbuphine	10-20	—	2-4
Butorphanol	2	—	2-3

†Only part of its analgesic action results from action on μ-opioid receptors.
NOTES:
- Published reports vary in the suggested doses considered to be equianalgesic to morphine. Therefore titration to clinical response in each patient is necessary.
- Suggested doses are the results of single-dose studies only. Therefore use of the data to calculate total daily dose requirements and repeated or continuous doses may not be appropriate.
- There may be incomplete cross-tolerance between these drugs. In patients who have been receiving one opioid for a prolonged period, it is usually necessary to use a dose lower than the expected equianalgesic dose when changing to another opioid and to titrate to effect.

Modified from Macintyre PE, Ready LB. *Acute Pain Management: A Practical Guide*, 2nd ed. Philadelphia: Saunders; 2001, p 19.

Local Anesthetics

Local anesthetics are widely used in children for topical application, cutaneous infiltration, peripheral nerve block, neuraxial blocks (intrathecal or epidural infusions), and IV infusions (see Chapter 91). Local anesthetics can be used with excellent safety and effectiveness. Local anesthetics interfere with neural transmission by blocking neuronal sodium channels. Excessive systemic dosing can cause seizures, CNS depression, and (by cardiac and arteriolar sodium channel blockade) hypotension, arrhythmias, cardiac depression, and cardiovascular collapse. Local anesthetics therefore require a strict maximum dosing schedule. Pediatricians should be aware of the need to calculate these doses and adhere to guidelines.

Topical local anesthetic preparations do not generally result in measurable systemic blood levels and can reduce pain in diverse circumstances: suturing of lacerations, placement of peripheral IV catheters, lumbar punctures, and accessing indwelling central venous ports (Table 93.14). The application of tetracaine, epinephrine (adrenaline), and cocaine (TAC) results in good anesthesia for suturing wounds but should not be used on mucous membranes or the hypervascular faces of young children. An alternative combination of lidocaine, epinephrine, and tetracaine (LET) is preferred to avoid the psychomimetic properties of cocaine. EMLA, a topical eutectic mixture of lidocaine and prilocaine used to anesthetize intact skin, is frequently applied for venipuncture, lumbar puncture, and other needle procedures. A 5% liposomal lidocaine cream (LMX4) is also effective as a topical anesthetic. Another unique device is the needle-free J-tip, which uses a CO_2 cartridge to deliver lidocaine into the subcutaneous tissue via a micro-atomizing tip. This can be used to

Table 93.10 Opioid Use Guidelines in Hepatic and Renal Dysfunction

DRUG	PKA	PROTEIN BINDING (%)	PHASE 1 METABOLISM	PHASE 2 METABOLISM	ACTIVE METABOLITE	BILIARY EXCRETION[1] (%)	RENAL EXCRETION[2]	USE IN RENAL FAILURE
Morphine	8.0	30	None	Glucuronidation	M6G	10	Metabolites	Use with caution[a,c]
Fentanyl	8.4	80	CYP3A4	None	None		Norfentanyl	Preferred[b,e]
Hydromorphone	8.2	20	None	Glucuronidation	H6G		H3G & H6G	Use with caution[a,d]
Methadone	8.3	90	CYP2B6 CYP3A4, CYP2D6	None	None	20-40	Metabolites	Use with caution[b,e]
Codeine	8.2	25	CYP2D6	None	Morphine, Hydrocodone M6G		M6G	No[b,d]
Oxycodone	8.5	45	CYP3A4, CYP2D6	None	Oxymorphone		Noroxycodone	Use with caution[f]
Oxymorphone	8.2	10	CYP3A4	Glucuronidation	None		Noroxymorphone	Use with caution[a,c]
Remifentanil	7.1	70	Esterase	None	None		Metabolite	

[1]In the setting of hepatic dysfunction, all opioids should be used cautiously ("go low, go slow"). Meperidine (inactive metabolite associated with seizures) and codeine (cannot be metabolized into active metabolite, morphine) should not be used. Fentanyl may be the best opioid to use (in severe liver dysfunction, plasma cholinesterase may not be available to metabolize remifentanil).
[2]In the setting of renal failure, metabolites of morphine, codeine, hydromorphone, hydrocodone, and meperidine can accumulate, producing increased therapeutic and adverse effects.
[a]Parent drug removed by dialysis; [b]Parent drug not/poorly dialyzed; [c]Metabolites removed by dialysis; [d]Metabolites not/poorly dialyzed; [e]Metabolites inactive;
From Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*, 10th ed. Philadelphia: Elsevier; 2022, Table 23.6, p. 496.

Table 93.11 Practical Aspects of Prescribing Opioids

- Morphine, hydromorphone, or fentanyl is regarded as first choice for severe pain.
- Dosing should be titrated and individualized. There is no "right" dose for everyone.
- The right dose is the dose that relieves pain with a good margin of safety.
- Dosing should be more cautious in infants, in patients with coexisting diseases that increase risk or impair drug clearance, and with concomitant administration of sedatives.
- Hydromorphone is metabolized by CYP2D6 and fentanyl by CYP3A4 and to some extent 2D6; drugs that compete for 2D6 enzyme will raise blood levels and increase risk of respiratory depression.
- Morphine is metabolized by glucuronidation to an active metabolite, morphine-6-glucuronide, which accumulates and causes CNS toxicity in renal impairment.
- Anticipate and treat peripheral side effects, including constipation, nausea, and itching.
- Give doses at sufficient frequency to prevent the return of severe pain before the next dose.
- Use a drug delivery method, such as patient-controlled anesthesia or continuous infusions, that avoids the need for "prn" decision-making.
- With opioid dosing for >1 wk, taper gradually to avoid abstinence syndrome.
- When converting between parenteral and oral opioid doses, use appropriate potency ratios (see Table 93.9).
- *Tolerance* refers to decreasing drug effect with continued administration of a drug. Over time a patient will need higher dosing to achieve the same clinical effect; however, tolerance to sedation and respiratory depression develop more rapidly than tolerance to analgesia. Thus with higher doses, patients do not experience oversedation or respiratory depression.
- *Dependence* refers to the need for continued drug dosing to prevent abstinence syndrome when a drug is abruptly discontinued or its dose reduced. Abstinence syndrome is characterized by irritability, agitation, autonomic arousal, nasal congestion, piloerection, diarrhea, jitteriness, and yawning; it is produced by administration of potent opioids for >5-7 days.
- *Addiction*, a psychiatric pathology, refers to psychologic craving, compulsive drug-seeking behavior, and drug use despite medical harm. Addiction has strong genetic and environmental determinants. Opioid therapy will not lead to addiction in nonsusceptible individuals, and opioid underdosing does not prevent addiction; it may in fact increase drug-seeking behavior for relief of pain (e.g., watching the clock), referred to as "pseudoaddiction."

start IVs or provide superficial analgesia before a procedure (e.g., lumbar puncture).

Lidocaine is the most commonly used local anesthetic for cutaneous infiltration. Maximum safe doses of lidocaine are 5 mg/kg without epinephrine and 7 mg/kg with epinephrine. Although concentrated solutions (2%) are commonly available from hospital pharmacies, more dilute solutions (0.25% and 0.5%) are equally as effective as 1–2% solutions. The diluted solutions cause less burning discomfort on injection and permit use of larger volumes without achieving toxic doses. In the surgical setting, cutaneous infiltration is more often performed with bupivacaine 0.25% or ropivacaine 0.2% because of the much longer duration of effect; maximum dosage of these long-acting amide anesthetics is 2-3 mg/kg and 3-4 mg/kg, respectively. Liposomal bupivacaine injectable suspension (Exparel) is approved for children age 6 years old and above. It is an excellent choice for surgical wound infiltration. The maximum dose for children is 4 mg/kg.

Neuropathic pain may respond well to the local application of a 5% lidocaine topical patch (Lidoderm) for 12 hours/day (see Table 93.14), although access to lidocaine topical patches may be limited by insurance coverage. Over-the-counter 4% lidocaine patches are available without prescription. Peripheral and central neuropathic pain also may respond to IV lidocaine infusions, which may be used in hospital settings for refractory pain, complex regional pain syndromes, and pain associated with malignancies or the therapy of malignancies, such as oral mucositis after bone marrow transplantation. In these patients, 1-2 mg/kg/hr should be administered and the infusion titrated to achieve a blood lidocaine level in the 2-5 μg/mL range, with use of twice-daily therapeutic blood monitoring.

UNCONVENTIONAL MEDICATIONS IN PEDIATRIC PAIN

Unconventional analgesic medication refers to a wide number of drugs developed for other indications but found to have analgesic properties. These drugs have been used for acute and chronic pain and include antidepressants, antiepileptic drugs, and neurotropic drugs (Tables 93.15 and 93.16).

The unconventional analgesics are generally used to manage neuropathic pain conditions, migraine disorders, fibromyalgia syndrome, and some forms of functional chronic abdominal pain syndromes. These agents also are used as components of multimodal analgesia in the management of surgical, somatic, and musculoskeletal pain. Figure 93.4 presents a decision-making tree to help the physician select the appropriate analgesic category for various types of pain.

Although several unconventional pain medications are FDA approved for analgesic use, most are not approved for use in youth with acute or chronic pain. Thus these drugs should be used with caution, with a focus on mitigating pain to allow a child to participate effectively in therapies and return to normal activity as soon as possible. The use of psychotropic medications should be guided by the principles applied to pharmacologic treatment of any symptom or disease. Target symptoms should be identified and medication side effects monitored. To determine dosing regimens, the physician should consider the child's weight and the effects that the medical condition and other medications, such as psychotropic drugs, may have on the child's metabolism. Therapeutic blood level monitoring can be considered. Side effects should be addressed in detail with both parent and child and specific instructions given for responding to possible adverse events. Directly addressing concerns about addiction, dependence, and tolerance may be necessary to decrease treatment-related anxiety and improve medication adherence.

Antidepressant Medications

Antidepressants are useful in adults with chronic pain, including neuropathic pain, headaches, and rheumatoid arthritis, independent of their effects on depressive disorders. Antidepressants' analgesic mechanism of action is inhibition of norepinephrine reuptake in the CNS. In children, because clinical trials have been limited, the practitioner should use antidepressants cautiously to treat chronic pain or associated depressive or anxiety symptoms. The FDA has issued a "black box warning" to inform the public of a small but significant increase in suicidal thoughts and attempts in children and adolescents receiving antidepressants. A meta-analysis of studies involving children and adolescents receiving antidepressants for pain indicated that no suicides had been completed. The pediatrician should address this issue with parents of patients being treated with antidepressants and should develop monitoring plans consistent with current FDA recommendations (see Table 93.16).

Tricyclic antidepressants (TCAs) have been studied in children with chronic pain and found to be effective in pain relief for symptoms that include neuropathic pain, functional abdominal pain, and migraine. TCA efficacy may be based on inhibition of the neurochemical pathways involved in norepinephrine and serotonin reuptake and interference with other neurochemicals involved in the perception or neural conduction of pain. Because sedation is a common side effect, TCAs may also be effective in treating the sleep disorders that frequently accompany pediatric pain. Biotransformation of TCAs is extensive in healthy children. Typically, TCAs are administered only at bedtime, especially the more sedating tricyclic medications such as amitriptyline. Alternatively, the patient can be started on a bedtime dose of a TCA, which may be able to then be titrated to a daily divided dose, with the larger dose given at bedtime. It should be noted that pain symptoms usually remit at lower doses than those recommended

Table 93.12 CDC Practice Guideline for Prescribing Opioids for Pain (2022) Excluding Sickle Cell Anemia, Cancer, Palliative Care and End of Life Care

DETERMINING WHETHER OR NOT TO INITIATE OPIOIDS FOR PAIN

All patients with pain should receive treatment that provides the greatest benefits relative to risks. (See *Recommendation 1* for determining whether or not to initiate opioids for acute pain [i.e., pain lasting <1 month] and *Recommendation 2* for determining whether or not to initiate opioids for subacute pain [i.e., pain lasting 1–3 months] or chronic pain [i.e., pain lasting >3 months].)

Recommendation 1

Nonopioid therapies are at least as effective as opioids for many common types of acute pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider opioid therapy for acute pain if benefits are anticipated to outweigh risks to the patient. Before prescribing opioid therapy for acute pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy.

Recommendation 2

Nonopioid therapies are preferred for subacute and chronic pain. Clinicians should maximize use of nonpharmacologic and nonopioid pharmacologic therapies as appropriate for the specific condition and patient and only consider initiating opioid therapy if expected benefits for pain and function are anticipated to outweigh risks to the patient. Before starting opioid therapy for subacute or chronic pain, clinicians should discuss with patients the realistic benefits and known risks of opioid therapy, should work with patients to establish treatment goals for pain and function, and should consider how opioid therapy will be discontinued if benefits do not outweigh risks.

SELECTING OPIOIDS AND DETERMINING OPIOIDS DOSAGES

Recommendation 3

When starting opioid therapy for acute, subacute, or chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release and long-acting (ER/LA) opioids.

Recommendation 4

When opioids are initiated for opioid-naïve patients with acute, subacute, or chronic pain, clinicians should prescribe the lowest effective dosage. If opioids are continued for subacute or chronic pain, clinicians should use caution when prescribing opioids at any dosage, should carefully evaluate individual benefits and risks when considering increasing dosage, and should avoid increasing dosage above levels likely to yield diminishing returns in benefits relative to risks to patients.

Recommendation 5

For patients already receiving opioid therapy, clinicians should carefully weigh benefits and risks and exercise care when changing opioid dosage. If benefits outweigh the risks of continued opioid therapy, clinicians should work closely with patients to optimize nonopioid therapies while continuing opioid therapy. If benefits do not outweigh risks of continued opioid therapy, clinicians should optimize other therapies and work closely with patients to gradually taper to lower dosages or, if warranted based on the individual circumstances of the patient, appropriately taper and discontinue opioids. Unless there are indications of a life-threatening issue such as warning signs of impending overdose (e.g., confusion, sedation, or slurred speech), opioid therapy should not be discontinued abruptly, and clinicians should not rapidly reduce opioid dosages from higher dosages.

DECIDING DURATION OF INITIAL OPIOID PRESCRIPTION AND CONDUCTING FOLLOW-UP

Recommendation 6

When opioids are needed for acute pain, clinicians should prescribe no greater quantity than needed for the expected duration of pain severe enough to require opioids.

Recommendation 7

Clinicians should evaluate benefits and risks with patients within 1–4 weeks of starting opioid therapy for subacute or chronic pain or of dosage escalation. Clinicians should regularly reevaluate benefits and risks of continued opioid therapy with patients.

ASSESSING RISK AND ADDRESSING POTENTIAL HARMS OF OPIOID USE

Recommendation 8

Before starting and periodically during continuation of opioid therapy, clinicians should evaluate risk for opioid-related harms and discuss risk with patients. Clinicians should work with patients to incorporate into the management plan strategies to mitigate risk, including offering naloxone.

Recommendation 9

When prescribing initial opioid therapy for acute, subacute, or chronic pain, and periodically during opioid therapy for chronic pain, clinicians should review the patient's history of controlled substance prescriptions using state prescription drug monitoring program (PDMP) data to determine whether the patient is receiving opioid dosages or combinations that put the patient at high risk for overdose.

Recommendation 10

When prescribing opioids for subacute or chronic pain, clinicians should consider the benefits and risks of toxicology testing to assess for prescribed medications as well as other prescribed and nonprescribed controlled substances.

Recommendation 11

Clinicians should use particular caution when prescribing opioid pain medication and benzodiazepines concurrently and consider whether benefits outweigh risks of concurrent prescribing of opioids and other central nervous system depressants.

Recommendation 12

Clinicians should offer or arrange treatment with evidence-based medications to treat patients with opioid use disorder. Detoxification on its own, without medications for opioid use disorder, is not recommended for opioid use disorder because of increased risks for resuming drug use, overdose, and overdose death.

From Dowell D, Ragan KR, Jones CM, et al: CDC clinical practice guidelines for prescribing opioids for pain – United States, 2022. *MMWR* 2022;71(3):1-95.

or required for the treatment of mood disorders. Most children and adolescents do not require more than 0.25-1 mg/kg of amitriptyline or nortriptyline once daily at bedtime.

Attention should also be paid to hepatic microsomal enzyme metabolism, because CYP2D6 inhibitors, such as cimetidine and quinidine, can increase levels of TCAs. Anticholinergic side effects, which are less common in children than in adults, may remit over time. Constipation, orthostatic hypotension, and dental caries from dry mouth should be addressed by emphasizing the importance of hydration, good oral hygiene, and regular dental visits. Other side effects include weight gain, mild bone marrow suppression, and liver dysfunction. Some practitioners recommend monitoring CBC and liver function values at baseline and periodically during therapy. TCA blood levels can be obtained as well, but the need for therapeutic blood monitoring should be assessed on an individual basis. Reasons for blood level monitoring include concerns for altered metabolism, adherence, overdose, or sudden change in mental status.

All TCAs inhibit cardiac conduction pathways and prolong the QT interval. Sudden cardiac death has been reported in children taking TCAs, principally desipramine, probably related to QTc prolongation. There is no general agreement for monitoring the electrophysiologic effects of these drugs, but it is prudent to obtain a careful personal and family history focusing on cardiac arrhythmias, heart disease, and syncope before the initiation of treatment. A baseline electrocardiogram (ECG) should be obtained, with care taken to ensure that

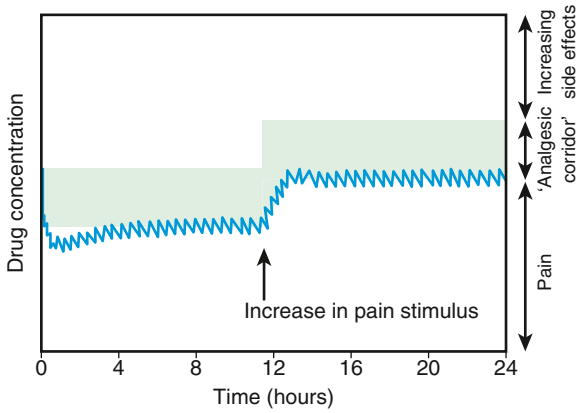

Fig. 93.3 Patient-controlled analgesia is more likely to keep blood concentrations of opioid within the "analgesic corridor" and allows rapid titration if there is an increase in pain stimulus requiring higher blood levels of opioid to maintain the analgesia. *(From Burg FD, Ingelfinger JR, Polin RA, et al., eds. Current Pediatric Therapy,18th ed. Philadelphia: Saunders; 2006:16.)*

Table 93.13 Summary of FDA Recommendations

- Use of codeine to treat pain or cough in children <12 yr old is contraindicated.
- Use of tramadol to treat pain in children <12 yr old is contraindicated.
- Use of tramadol for treatment of pain after tonsillectomy or adenoidectomy in patients <18 yr old is contraindicated. (Codeine was already contraindicated in such patients.)
- Use of codeine or tramadol in children 12-18 yr old who are obese or who have an increased risk of serious breathing problems, such as those with obstructive sleep apnea or severe lung disease, is not recommended.
- Use of codeine or tramadol in breastfeeding women should be avoided.

From FDA warns against use of codeine and tramadol in children and breastfeeding women. *Med Lett.* 2017;59(1521):86–88.

the QTc is <450 msec. If the dose of amitriptyline or nortriptyline is increased beyond 0.5 mg/kg/day, an ECG should be performed for each dosing increase. With TCAs, as with other antidepressants, physical dependence and a known discontinuation syndrome can occur. The **discontinuation syndrome** includes agitation, sleep disturbances, appetite changes, and GI symptoms. These medications should be tapered slowly to assist in distinguishing among symptoms that indicate rebound, withdrawal, or the need for continuing the medication.

Selective serotonin reuptake inhibitors (SSRIs) have minimal efficacy in the treatment of a variety of pain syndromes in adults. SSRIs are very useful when symptoms of depression or anxiety are present and cannot be addressed adequately by nonpharmacologic means. Escitalopram (Lexapro), fluoxetine (Prozac), and sertraline (Zoloft) have been approved by the FDA for use in children and adolescents. SSRIs have a significantly milder side effect profile than TCAs (most side effects are transient), and they have no anticholinergic side effects. Chief side effects include GI symptoms, headaches, agitation, insomnia, sexual dysfunction, and anxiety. Rarely, hyponatremia, or the syndrome of inappropriate antidiuretic hormone secretion (SIADH), may occur. Interactions with other medications that have serotonergic effects may also occur. When multiple medications with serotonergic activity are used in combination, there may be increased likelihood that a life-threatening **serotonin syndrome** may occur, with associated symptoms of myoclonus, hyperreflexia, autonomic instability, muscle rigidity, and delirium (see Chapter 94). It is important to note that although triptans have serotonergic effects, it is unlikely that the combination will lead to serotonin syndrome. This is because it is hypothesized that serotonin receptors 2A and 1A are the receptors involved in serotonin syndrome, whereas triptans are selective for serotonin antagonists 1B and 1D. There is also a **discontinuation syndrome** associated with shorter-acting SSRIs (e.g., paroxetine), which includes dizziness, lethargy, paresthesias, irritability, and vivid dreams. To avoid this, dosages of medications should be tapered slowly over several weeks.

The **selective serotonin-norepinephrine reuptake inhibitors (SNRIs)** duloxetine and venlafaxine have demonstrated significant efficacy with chronic neuropathic and other pain syndromes because they inhibit both serotonin and norepinephrine reuptake, and they may directly block associated pain receptors as well. Venlafaxine has no pain indication labeling. Duloxetine is FDA approved for managing neuropathic pain (specifically, diabetic neuropathy) and fibromyalgia

Table 93.14 Topical Pharmacologic Management of Acute Pain in Children

DRUG	DOSE	NOTES
INTACT SKIN		
Lidocaine 2.5% and prilocaine 2.5% (EMLA cream)	<3 mo old or <5 kg: 1 g 3-12 mo and >5 kg: 2 g 1-6 yr and >10 kg: 10 g 7-12 yr and >20 kg: 20 g	60 min is needed to achieve maximum effect; cover cream with an occlusive dressing (Tegaderm)
Lidocaine, liposomal 5% (LMX4)	1-20 g as noted earlier	30-60 min needed to achieve maximum effect; cover with an occlusive dressing (Tegaderm)
Lidocaine 70 mg and tetracaine 70 mg (Synera patch)	Age ≥3 yr: apply patch	20-30 min needed to achieve maximum effect
Tetracaine 4% (Ametop)	>1 mo and <5 yr: apply 1 tube of gel (1 g) >5 yr: apply up to 5 tubes of gel (5 g)	30 min before venipuncture 45 min before intravenous cannulation
WOUNDS		
Lidocaine, epinephrine, tetracaine (LET) solution or gel*	Age ≥1 yr: apply to wound	20 min needed for maximum effect

*Also referred to as ALA on the basis of alternative names for the constituents: adrenaline, lignocaine, amethocaine. These mixtures are locally made by hospital formularies, with a common formula being lidocaine 4% plus epinephrine 0.1% plus tetracaine 0.5%. The cocaine-based formulation was historically avoided on wounds of digits, ears, penis, nose, mucous membranes, close to the eye, or deep wounds involving bone, cartilage, tendon, or vessels. The lidocaine-based formulation can be used in such settings.

Adapted from Krauss BS, Calligaris L, Green SM, Barbi E. Current concepts in management of pain in children in the emergency department. *Lancet.* 20166;387:83–92.

Table 93.15 Commonly Used Adjunctive Analgesics

DRUG NAME (TRADE NAME)	SUGGESTED STARTING DOSE AND DOSING INTERVAL MAXIMUM DOSE PER DAY	ADVANTAGES (INDICATION FOR USE)	DISADVANTAGES (SIDE EFFECTS)
Gabapentin (Neurontin)	10-15 mg/kg per day divided bid or tid Max dose: 50 mg/kg per day (3 g/day)	Adjunct for the management of pediatric neuropathic pain, epilepsy	Drug reaction with eosinophilia and systemic symptoms (DRESS), anaphylaxis, somnolence, dizziness, peripheral edema, emotional lability, respiratory depression when combined with opioids
Pregabalin (Lyrica)	2.5 mg/kg per day divided bid or tid Max dose: 600 mg per day	Adjunct for the management of neuropathic pain associated with spinal cord injury, fibromyalgia, and epilepsy	Ataxia, blurred vision, visual field loss, constipation, drowsiness, headaches, peripheral edema, weight gain, tremor
Clonidine (Catapres)	5-25 mcg/kg per day divided every 4-8 hours if PO dosing Max dose: 2.4 mg/day	Used to treat hypertension and mitigate drug withdrawal symptoms; also used as a pain or peripheral nerve block additive	Drowsiness, dizziness, fatigue, headache, dry mouth, hypotension
Dexmedetomidine (Precedex)	Loading dose: 0.5-1 mcg/kg Infusion rate: 0.2-0.7 mcg/kg per hour titrated to effect Suggested max dose: 2.5 mcg/kg per hour	Sedative and analgesic properties; intraoperative bolus dose of 1 mcg/kg decreases postoperative morphine consumption and 2 mg/kg decreases emergence delirium	Bradycardia, hypotension
Tizanidine (Zanaflex)	Patients >18 yr: starting dose 2 mg q6-8h Max single dose: 16 mg Max daily dose: 36 mg	Antispasmodic agent	Dizziness, drowsiness, bradycardia, hypotension, fatigue, hallucinations, xerostomia
Diazepam (Valium)	PO: 0.1-0.8 mg/kg/day IV: 0.05-0.3 mg/kg/dose every 4-8 hr Max dose: 10 mg Use lowest needed dose; use lower dose when combined with opioids or other sedating medications	Antispasmodic, anxiolytic, sedative, seizure prophylaxis, promotes sleep	Somnolence, unsteady gait
Cyclobenzaprine (Flexeril)	Patients >15 yr: 5 mg PO bid-tid Max dose: 10 mg PO tid	Antispasmodic	Blurry vision, dizziness, drowsiness, lightheadedness, xerostomia
Ketamine	Loading dose: 0.25-0.5 mg/kg IV before incision Infusion rate: 0.1-1 mg/kg per hr intraoperatively 0.05-0.1 mg/kg per hr postoperatively Max parenteral dose 3,600 mg/day	Sedation, analgesic adjunct, especially beneficial for opioid-tolerant or chronic pain patients	Hallucinations, double/blurry vision, jerky muscle movements, drowsiness, loss of appetite, nausea
Lidocaine	Loading dose: 1-1.5 mg/kg IV Infusion rate: 1-2 mg/kg per hr intraoperatively Max dose: 4.5 mg/kg (not to exceed 300 mg in 2 hr)	Used during intraabdominal procedures to prevent severe postoperative pain	Cardiac arrhythmia, epilepsy/seizures, renal failure

Modified from Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children,* 10th ed. Philadelphia: Elsevier; 2022, Table 23.12, p. 510.

syndrome. It is approved for the treatment of pediatric fibromyalgia in adolescents 13-17 years of age and for the treatment of generalized anxiety disorder in children 7-17. A significant advantage of SNRIs over TCAs when used for headache prophylaxis or neuropathic pain is that they have therapeutic effects on mood and anxiety at dosages effective for pain control.

Because both SSRIs and SNRIs have fewer anticholinergic side effects than TCAs, adherence to them is better than in psychiatric populations taking TCAs. Side effects of both types of drugs include GI symptoms, hyperhidrosis, dizziness, and agitation, but these effects generally wane over time. Hypertension and orthostatic hypotension may occur; in addition, the patient's blood pressure should be closely followed, and appropriate hydration should be stressed. Note that whereas appetite stimulation and weight gain are associated with all TCAs, duloxetine is often associated with weight loss, frequently a desirable side effect, especially in overweight adolescents.

All antidepressants, including the TCAs, SSRIs, and SNRIs, are thought to have the potential to increase the risk of suicidal ideation and the risk of suicide in patients, as noted earlier. The FDA states, "All pediatric patients being treated with antidepressants for any indication should be observed closely for clinical worsening, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases." However, the FDA also notes, "Although there has been a long-standing concern that antidepressants may have a role in inducing worsening of depression and the emergence of suicidality in certain patients, a causal role for antidepressants in inducing such behaviors has not been established. Nevertheless, patients being treated with antidepressants should be observed closely for clinical worsening and suicidality, especially at the beginning of a course of drug therapy, or at the time of dose changes, either increases or decreases."

Table 93.16 Medications for Pediatric Chronic Pain

MEDICATION	DOSING	COMMENTS
TRICYCLIC ANTIDEPRESSANTS		
Amitriptyline, nortriptyline	For patients ≥50 kg: Initial dose 5-10 mg PO qhs; titrate over 2-3 weeks to 25-50 mg PO qhs For patients 25-50 kg: Initial dose 0.1 mg/kg PO qhs. Titrate over 2-3 weeks to max dose of 0.5 mg/kg	Obtain 12-lead ECG for prolonged QT interval Side effects are related to anticholinergic effects, including tachycardia, dry mouth, urinary retention, and sedation Use with caution with other antidepressants because of risk of serotonin syndrome Concomitant use with CYP2D6 inhibitors may lead to increased serum concentration
SELECTIVE SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITORS		
Duloxetine (Cymbalta)	For patients > 13 yr: Dose 30-60 mg PO daily; max 600 mg/day	Review risk of suicidality
ANTICONVULSANTS		
Gabapentin (Neurontin)	For patients ≥50 kg: Initial dose 100-300 mg PO 1-2 times daily; titrate slowly to max dose of 1,800 mg/day divided tid; higher dosing possible in select patients For patients <50 kg: Initial dose 2-5 mg/kg PO daily; titrate slowly to max dose of 35 mg/day divided tid; higher dosing possible in select patients	Side effects include drowsiness, concentration and memory impairments, and peripheral edema (rare) Dose adjustment necessary with renal impairment
Pregabalin (Lyrica)	Patients >12 yr of age: Initial dose 25-75 mg PO 1-2 times daily; titrate up to max of 300 mg/day divided bid or tid	Side effects include drowsiness, headaches, peripheral edema (rare), and thrombocytopenia (rare)
Titrate all medications according to clinical benefit and side effects; use lowest effective dose. Antidepressants and anticonvulsants may increase the risk of suicidal thinking and behavior in children, adolescents, and young adults. Monitor closely for changes in mood or behavior.		

Modified from Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children,* 10th ed. Philadelphia: Elsevier; 2022, Table 25.2, p. 580.

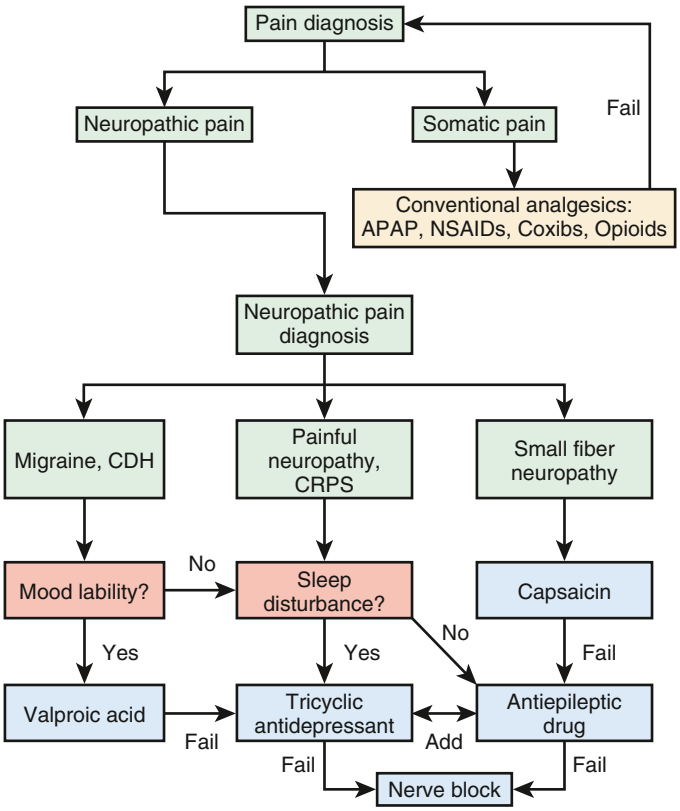

Fig. 93.4 Algorithm for selection of conventional and nonconventional analgesics. APAP, Acetaminophen; CDH, chronic daily headaches; CRPS, complex regional pain syndrome; NSAIDs, nonsteroidal antiinflammatory drugs.

Antiepileptic Drugs

Antiepileptic drugs (AEDs), such as gabapentin, pregabalin, carbamazepine, and valproic acid, are believed to relieve chronic pain by blocking sodium (valproate and the gabapentinoids) or calcium (carbamazepine and oxcarbazepine) channels at the cellular neuronal level, thereby suppressing spontaneous electrical activity and restoring the normal threshold to depolarization of hypersensitive nociceptive neurons, without affecting normal nerve conduction. These medications are particularly useful in patients with mood disorders who have neuropathic pain. In adults, the FDA has approved carbamazepine for trigeminal neuralgia; valproate for migraine prophylaxis; and pregabalin for neuropathic pain complicating diabetes, herpes zoster, and for management of fibromyalgia. AEDs generally have GI side effects in addition to sedation, anemia, ataxia, rash, and hepatotoxicity. The majority are also associated with weight gain. Carbamazepine and oxcarbazepine are also associated with Stevens-Johnson syndrome.

Liver function and CBC should be monitored at the start of therapy and periodically with AEDs. Carbamazepine and valproic acid have narrow therapeutic windows and variability in therapeutic blood medication levels, in addition to many drug-drug interactions, and may cause liver disease and renal impairment. Drug levels should be measured with each dose increase and periodically thereafter. Carbamazepine, in particular, causes autoinduction of hepatic microsomal enzymes, which can further complicate obtaining a therapeutic medication level. Female patients should have pregnancy testing before taking valproate, and those who are sexually active must be cautioned to use effective contraception, because neural tube defects are associated with carbamazepine.

Less toxic AEDs (gabapentin and pregabalin) have supplanted the use of valproate and carbamazepine in patients with pain. These agents have their own side effect profiles, but they are much less toxic than their predecessors and do not require monitoring of liver or bone marrow function or blood levels. Furthermore, they are also far less lethal in accidental or deliberate overdose.

Gabapentin is approved for treatment of postherpetic neuralgia and is also widely prescribed for other pain disorders. It has demonstrated some efficacy in treating children with chronic pain, particularly neuropathic pain, and is used in treatment of chronic headache disorders, complex regional pain syndromes, chemotherapy-induced neuropathy, and diabetic neuropathy in both children and adults. Gabapentin has a relatively benign side effect profile and no drug interactions. Side effects include somnolence, dizziness, and ataxia; children occasionally demonstrate side effects not reported in adults, such as impulsive

or oppositional behavior, agitation, and occasionally depression. These side effects do not seem to be dose related.

Pregabalin works by similar mechanisms as gabapentin and may have a lower side effect profile. It is most often dosed twice a day rather than three times a day, which may lead to increased adherence. Both gabapentin and pregabalin undergo virtually no hepatic metabolism, with no significant drug-drug interactions, a common concern in patients with chronic pain, who frequently take multiple medications—for both the pain and the underlying medical condition associated with the pain. However, because both AEDs depend on renal function for clearance, doses must be adjusted in the presence of renal dysfunction.

Topiramate also demonstrates greater success than traditional AEDs in treating trigeminal neuralgia in adults and in migraine prophylaxis. Topiramate is approved for migraine prophylaxis in children and adolescents from the age of 12-17. Topiramate therapy results more frequently in cognitive dysfunction and short-term memory loss than gabapentin or pregabalin, and although these neurocognitive effects are often well tolerated, they should be monitored. The pediatrician should also be aware that topiramate is associated with weight loss, whereas other AEDs are typically associated with significant weight gain. This side effect is particularly valuable in weight-conscious adolescents, whereas in the anorexic cancer patient, a TCA would be preferable to induce appetite and weight gain. In at-risk populations, routine weight checks are recommended.

Benzodiazepines

Children and adolescents with chronic pain may have comorbid psychologic conditions, such as depressed mood, sleep disturbances, and anxiety disorders, including generalized anxiety disorder, separation anxiety, posttraumatic stress disorder (PTSD), and panic attacks. Psychologic factors affect a youth's perception of pain and mechanisms of coping with a pain disorder. A *conditioned response* to pain may be to feel out of control and increase anxiety and pain, and conversely, *anticipatory anxiety* related to pain will inhibit activities and recovery. Feelings of helplessness sensitize the child to increasing amounts of pain, leading the child to perseverate on pain, think catastrophically, and feel hopeless. Changes in children's normal routines, with a negative impact on participation in valued activities, may further promote hopelessness, resulting in increased pain experiences and development of a depressive disorder.

Benzodiazepines are anxiolytic medications that also have muscle relaxant effects. They have a role in the treatment of acute pain in the hospital, where they are useful adjuncts because they inhibit painful muscle spasms in postsurgical patients. They also can suppress the anxiety that often occurs in hospitalized children, anxiety that interferes with restorative sleep and amplifies the child's perception of pain. Benzodiazepines are useful to calm children with anxiety and anticipatory anxiety about planned painful procedures. They are frequently used as a part of procedural sedation or preoperatively before surgical procedures.

Because dependence, tolerance, and withdrawal may occur with prolonged use, benzodiazepines are generally not recommended for the routine management of *chronic pain* or anxiety in children. Further, the risk of respiratory depression when benzodiazepines are combined with opioid therapy has contributed to the increasing number of opioid-related deaths in the United States. In concert with psychotherapy, benzodiazepines may help control anxiety symptoms that amplify the perception of pain, but we recommend the appropriate use of benzodiazepines in the chronic setting occur under the direction of a psychiatrist. In addition, other alternatives such as hydroxyzine may provide similar benefit without the negative aspects encountered with chronic benzodiazepine use.

Infrequently, benzodiazepines may cause behavioral disinhibition, psychosis-like behaviors, or, in large doses, respiratory depression. When dosing these medications, the pediatrician should consider that many benzodiazepines are metabolized by the cytochrome P450 microsomal enzyme system. This issue may be less significant with lorazepam and oxazepam, which undergo first-pass hepatic conjugation. Side effects common to benzodiazepines include sedation, ataxia, anemia, increased bronchial secretions, and depressed mood. If a benzodiazepine is administered for more than 5 consecutive days, the dosage should be slowly tapered. Abrupt discontinuation of therapy can lead to autonomic instability, delirium, agitation, seizures, and profound insomnia. The routine use of benzodiazepines to treat anxiety during hospitalization is not recommended and should only be used under expert guidance.

Antipsychotics and Major Sedatives

Low doses of antipsychotic medications are often used to address the more severe anxiety, agitation, and behavioral decompensation sometimes associated with severe pain. The use of these medications is controversial because associated adverse events may be severe and irreversible. Typical antipsychotics used in the past, including thioridazine (Mellaril), haloperidol (Haldol), and chlorpromazine (Thorazine), are associated with a decreased seizure threshold, dystonia, agranulocytosis, weight gain, cardiac conduction disturbances, tardive dyskinesia, orthostatic hypotension, hepatic dysfunction, and life-threatening laryngeal dystonia and have little role in the routine treatment of pain in children. Chlorpromazine is approved in adults for intractable hiccups, and its use may be appropriate in select settings such as the palliative setting, although this is not considered a first-line medication. Side effects are generally less severe with atypical antipsychotics. Because these effects may still occur, however, the pediatrician should obtain a baseline ECG, liver function values, and CBC and, if possible, obtain a child psychiatry consultation. If the pediatrician is using typical antipsychotics, an inventory of movement disturbances, such as the Abnormal Involuntary Movement Scale (AIMS) test, should be performed at baseline and at every follow-up visit, because movement disorders can worsen with abrupt withdrawal of medications or can become irreversible.

Atypical antipsychotics are generally associated with less severe side effect profiles, particularly dyskinesias and dystonias. Use of olanzapine (Zyprexa), which is particularly helpful with insomnia and severe anxiety, requires assessing and monitoring blood levels of glucose, cholesterol, and triglyceride; olanzapine's side effects may include diabetes, hypercholesterolemia, or significant weight gain. The anticholinergic side effects associated with quetiapine (Seroquel) warrant frequent monitoring of blood pressure. Risperidone at doses >6 mg may cause side effects similar to those of typical antipsychotics. Aripiprazole (Abilify) has been used for severe anxiety and/or for treatment-resistant depression. All antipsychotics are associated with the rare but potentially lethal **neuroleptic malignant syndrome**, which includes severe autonomic instability, muscular rigidity, hyperthermia, catatonia, and altered mental status (see Chapter 33).

Other Pain Control Medications

Alpha-adrenergic receptor agonists such as clonidine are typically used as antihypertensive agents. However, they are often helpful as both anxiolytics and sleep-onset agents in the anxious hospitalized child. The α-agonists also have central effects on pain reduction. **Clonidine** can be given orally or transdermally if the child's blood pressure permits. In certain settings, IV **dexmedetomidine**, an α-agonist sedating agent, can be used preoperatively for anxiety, in the intensive care unit (ICU) for sedation, and may be used for pain in certain circumstances. Weaning off dexmedetomidine can often be accomplished with a transition to clonidine. **Propranolol** and metoprolol are both β-blocking agents typically used for the child with autonomic instability and for thalamic storm. They may also be used in migraine prophylaxis. There are reports that β blockers can enhance depression in a child who already has a major depressive disorder, and discussion with a child psychiatrist may be helpful in decisions about using propranolol if needed. Both clonidine and propranolol have been found useful for the agitated child with ASD. Another α-agonist, **guanfacine**, is more likely to be used during the day for the child with ASD because it is less sedating than clonidine. Despite research on the impact of clonidine on chronic pain, no data are available to determine if guanfacine is as effective in reducing pain. **Ketamine**, a blocker of *N*-methyl-D-aspartate (NMDA) receptors, has been used for intractable pain in hospitalized children

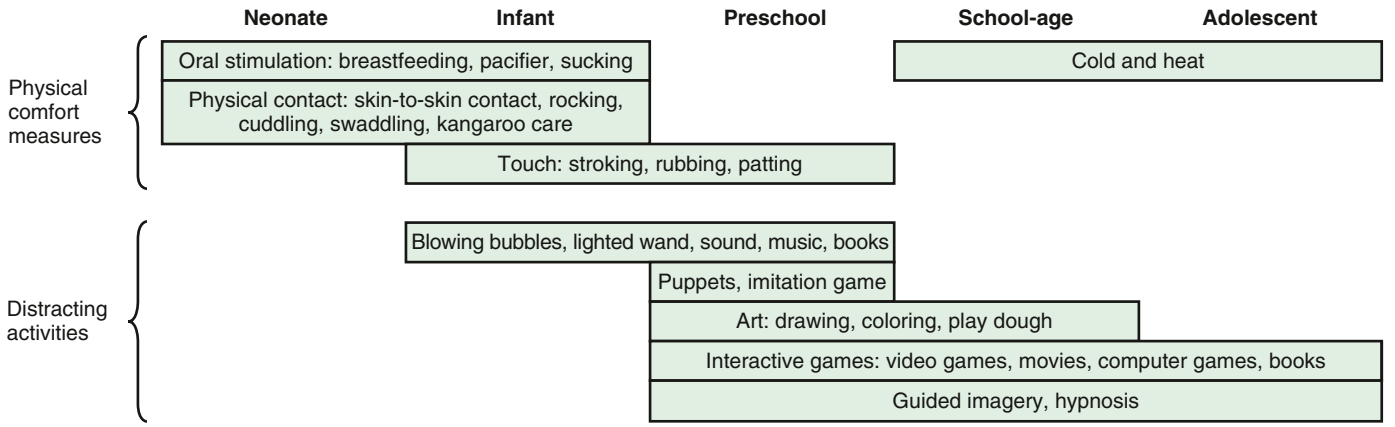

Fig. 93.5 Nonpharmacologic interventions for pediatric pain. *(From Krauss BS, Calligaris L, Green SM, Barbi E. Current concepts in management of pain in children in the emergency department. Lancet. 2016;387:83–92.)*

and in outpatients with severe sickle cell disease–related chronic pain, as well as others in palliative care for whom opioids are not sufficient to reduce pain. Recommended doses for pain management in non-ICU settings are between 0.1 and 0.3 mg/kg/hr. Higher doses may result in increased side effects, sedation with little benefit, and possible ICU admission. Because ketamine can have central hallucinatory effects, such children should be monitored closely.

NONPHARMACOLOGIC TREATMENT OF PAIN

Numerous psychologic and physical treatments for relieving pain, fear, and anxiety as well as enhancing functioning have excellent safety profiles and proven effectiveness and should always be considered for incorporation into pediatric pain treatment (Fig. 93.5). In acute and procedural pain, nonpharmacologic strategies have long been used to help reduce distress in children undergoing medical procedures and surgery. Many of these methods aim to help children shift attention from pain and alter pain perception (e.g., distraction, hypnosis, imagery). Similarly, in the treatment of chronic pain, several strategies, often falling under the umbrella category of **cognitive-behavioral therapies (CBTs)**, have been shown to reduce pain and improve functioning and quality of life. CBT was developed with the goal of modifying social/environmental and behavioral factors that may exacerbate the child's experience of pain and pain-related disability. Meta-analyses of randomized controlled trials (RCTs) of CBT interventions have found large positive effects of psychologic intervention on reductions in pain and/or its deleterious effects in children with headache, abdominal pain, and fibromyalgia, with relative or comparative effectiveness of different interventions examined in areas such as headache and abdominal pain in children. **Biofeedback** and **relaxation therapies** have been found to have superior effects to pharmacologic treatments in reducing headache pain in children and adolescents. Similarly, for recurrent abdominal pain, positive effects for CBT were found relative to attention-control conditions and pharmaceutical, botanical, and dietary interventions (which had very weak evidence). Positive results have even resulted from very brief (three sessions) and remotely delivered (telephone or internet) therapies, with outcomes lasting up to 12 months after intervention.

When deciding how to incorporate nonpharmacologic techniques to treat pain, the practitioner should (1) conduct a thorough assessment of individual, social, and environmental factors that may be contributing to the patient's pain and functioning limitations; (2) based on this assessment, decide whether nonpharmacologic techniques alone may be sufficient as a beginning to treatment or if these treatments should be integrated with appropriate analgesics; (3) give children (and family members) developmentally and situationally appropriate information as to the rationale for treatment selection and what to expect, given the child's medical condition, procedures, and treatments; (4) include patients and their families in decision-making to ensure an appropriate treatment choice and to optimize adherence to treatment protocols; and (5) above all, develop a communication plan among the different care providers, typically with the pediatrician as the case manager, so that the messages to the child and parent are consistent and the modes of therapy are organized into an integrative team approach. Finally, it is important to recognize that in addition to pain, other psychologic disorders (e.g., anxiety disorders, major depression) may affect the presenting pain complaint and may need to be identified and addressed as part of, or separate from, the pain management plan. Individual psychotherapy or psychiatric intervention may be warranted to adequately treat a comorbid disorder.

CBT strategies refer to a range of techniques that teach children (and their caregivers) how to manage pain by learning new ways to think about the pain and how to change behaviors associated with it. Strategies focusing on **cognitions** are typically aimed at enhancing parents' and children's confidence and self-efficacy to handle pain and decrease fear of pain. In addition, pain coping skills may shift the child's attentional focus away from pain and painful stimuli.

The goals of those strategies focusing on **behavior change** are to modify (1) contingencies in the child's environment, such as teaching parents how to respond to pain behaviors in ways that encourage wellness, rather than illness behaviors; (2) the ways parents model reactions to pain or discomfort; (3) child and parent coping techniques when psychosocial distress or problems in social relations exist; and (4) the child's behavioral reactions to situations, such as relaxation and exposure to previously avoided activities. Common examples of these strategies are discussed in the next several paragraphs. Whereas comprehensive CBTs are typically conducted by trained mental health specialists over several sessions, some basic CBT strategies can be briefly and easily introduced by practitioners into most medical settings. If more in-depth CBT treatment is needed, a referral to a qualified mental health specialist with CBT skills is warranted.

Parent and family education and/or **psychotherapy**, particularly within cognitive-behavioral family approaches, is one treatment modality through which these goals are accomplished and has been shown to be effective for treating chronic pain. Parents can learn to cope with their own distress and to understand pain mechanisms and appropriate treatment of pain. Key components include teaching parents to alter family patterns that may inadvertently exacerbate pain through developing behavior plans. Parents are taught to create plans for the child to manage the child's own symptoms and increase independent functioning. Often, adult caregivers (e.g., parents, teachers) need only guidance on developing a behavioral incentive plan to help the child return to school, gradually increase attendance, and receive tutoring after a prolonged, pain-related absence. *Suggested sample brief strategy:* Ask caregivers how they react to the child's pain complaints; assess whether they encourage wellness activities or give attention and "rewards" primarily when the child says he or she does not feel well; and suggest that caregivers respond to the child in ways that encourage wellness, both when complaining and not complaining.

Relaxation training is often employed to promote muscle relaxation and reduction of anxiety, which often accompanies and increases pain. Relaxation training, along with distraction and biofeedback, are treatments often included in CBT, but also are discussed in the literature without mention of CBT.

Controlled breathing and **progressive muscle relaxation** are commonly used relaxation techniques taught to preschool-age and older children. *Suggested sample brief strategy:* Ask the child (or instruct the caregiver to do so) to practice the following and use if pain is coming on: focus on the breath and pretend to be blowing up a big balloon while pursing the lips and exhaling slowly. This is one way to help induce controlled breathing.

Distraction can be used to help a child of any age shift attention away from pain and onto other activities. Common attention sustainers in the environment include bubbles, music, video games, television, the telephone, conversation, school, and play. Asking children to tell stories, asking parents to read to the child, and even mutual storytelling can be helpful distracters. Being involved with social, school, physical, or other activities helps the child in chronic pain to regain function. *Suggested sample brief strategy:* Encourage the child (or instruct the caregiver to do so) to shift attention away from the pain by continuing to engage in other activities and/or think of something else.

Biofeedback involves controlled breathing, relaxation, or hypnotic techniques with a computer synchronized device that provides visual or auditory feedback to the child when the desired action is approximated. Common targets of actions include muscle tension, peripheral skin temperature through peripheral vasodilation, and anal control through rectal muscle contraction and relaxation. Biofeedback also enhances the child's sense of mastery and control, especially for the child who needs more "proof" of change than that generated through hypnotherapy alone.

Hypnotherapy has also been used in the treatment of chronic pain in children, although the evidence for its effectiveness has not been as extensively studied as CBT. Hypnotherapy helps a child focus on an imaginative experience that is comforting, safe, fun, or intriguing. Hypnotherapy captures the child's attention, alters his or her sensory experiences, reduces distress, reframes pain experiences, creates time distortions, helps the child dissociate from the pain, and enhances feelings of mastery and self-control. Children with chronic pain can use *metaphor,* for example, imagining they have overcome something feared because of pain in real life. As the child increases mastery of imagined experiences, the enhanced sense of control can be used during actual pain rehabilitation. Hypnotherapy is best for children of school age or older.

Nonpharmacologic treatments of pain may also be applied to other treatment needs. A child who learns relaxation to reduce distress from lumbar punctures in cancer treatment may also apply this skill to other stressful medical and nonmedical situations, such as stressors caused by school.

Yoga is intended to achieve balance in mind, body, and spirit. **Therapeutic yoga** can be helpful in treating chronic pain; improving mood, energy, and sleep; and reducing anxiety. Yoga involves a series of *asanas* (body poses) oriented to the specific medical condition or symptoms. Some forms of yoga use poses within a movement flow and format. *Iyengar* yoga is an alignment-based system that uses props, such as blankets, bolsters, blocks, and belts, to support the body while the practitioner assumes more healing poses. Yoga promotes a sense of energy, relaxation, strength, balance, and flexibility and, over time, enhances a sense of mastery and control. Within a yoga practice, the child may learn certain types of breathing *(pranayama)* for added benefit. With a focus on body postures or in types of flow yoga, the child learns mindfulness or being present in the moment. By focusing on body and breath, the child can develop strategies to avoid ruminating about the past or worrying about the future.

Mindfulness meditation involves a focus on the present, "in-the-moment" experience using a variety of strategies. Many studies in adults report the value of meditation for chronic pain states and for anxiety and depression. These strategies help children learn how to be mindful and in the present with enhanced parasympathetic control. Many mindfulness smartphone applications are geared to children of different ages, as well as books for parents on how to help their children achieve a mindful state to enhance relaxation. Although there are different schools of mindfulness, such as *Vipassana* (insight-oriented meditation, often using a focus on the breath) and *transcendental* meditation (in which the child learns the use of a silent mantra to facilitate acquiring a deeper inner calmness), the goal is to help the child learn strategies that enhance self-competence in reducing stress and enhancing a state of well-being.

Massage therapy involves the therapist's touching and applying varied degrees of pressure on the child's muscles. Massage is very useful for children with chronic pain and especially helpful for those with myofascial pain. There are several types of massage, including craniosacral therapy. For young children, it can be helpful to have parents learn and perform brief massage on their children before bedtime. Massage therapy likely will not be helpful to or tolerated by the child with sensory sensitivity and sensory aversion.

Physical therapy can be especially useful for children with chronic musculoskeletal pain and for those deconditioned from inactivity. Exercise appears specifically to benefit muscle functioning, circulation, and posture while also improving body image, body mechanics, sleep, and mood. The physical therapist and the child can develop a graded exercise plan for enhancing the child's overall function for the child to continue at home. Research indicates that physical therapy affects central neurobiologic mechanisms that enhance "top-down" pain control.

Acupuncture/acupressure involves the placement of needles or pressure at specific points along a *meridian,* or energy field, after the acupuncturist has made a diagnosis of excess or deficient energy in that meridian as the primary cause of the pain. Acupuncture/acupressure is a feasible, popular part of a pain management plan for children with chronic pain. Acupuncture/acupressure alleviates chronic nausea, fatigue, and several chronic pain states, including migraine and chronic daily headaches, abdominal pain, and myofascial pain. Acupuncture/acupressure also has efficacy in adults with myofascial pain, primary dysmenorrhea, sickle cell crisis pain, and sore throat pain. The acupuncturist must relate well to children so that the experience is not traumatic, because added stress would undo the benefits gained.

Transcutaneous electrical nerve stimulation (TENS) is the use of a battery-operated tool worn on the body to send electrical impulses into the body at certain frequencies set by the machine. TENS is believed to be safe and can be tried for many forms of localized pain. Children often find TENS helpful and effective.

Music therapy and **art therapy** can be especially helpful for young and nonverbal children who would otherwise have trouble with traditional talk psychotherapies. Also, many creative children can more easily express fears and negative emotions through creative expression and, with the therapist's help, learn about themselves in the process. There is also increasing research on the impact of art and music therapy on altering central neural circuits that maintain and enhance pain.

Dance, movement, pet therapies, and **aromatherapy** have also been used and may be helpful, but these have not been as well studied in children for pain control as have other complementary therapies. Often, clinical experience helps guide the pediatrician in the benefits of these therapies with individual patients. For example, pet therapy is gaining favor in hospitals and in stress reduction for sick children. Pets often can become self-regulators for the child with ASD, although the neurobiologic mechanisms are not yet understood.

INVASIVE INTERVENTIONS FOR TREATING PAIN

Various interventional neuraxial and peripheral nerve blocks may have a role in the treatment of pain acutely (e.g., long-bone fracture), perioperatively, and for the patient with chronic pain (e.g., headache, abdominal pain, complex regional pain syndrome [CRPS], or cancer pain). Interventions also provide intraoperative anesthesia and postoperative analgesia (see Chapter 91). Use of interventional procedures varies greatly across institutions; they may be frequently used at some hospitals, whereas other institutions focus mainly on noninterventional treatment plans. Interventional procedures may be useful in some children who have specific types of chronic pain, but their use in children (as widely practiced in adult pain clinics) generally is not

recommended because the pediatric research is insufficient. Therefore the data are largely extrapolated from the adult population. Use of such procedures in children should generally not be considered or undertaken by an adult chronic pain provider who is willing to perform such a procedure on a child or adolescent. Rather, the potential procedure or block should be undertaken only at the direction or guidance of a pediatric pain specialist. Complications and lack of benefit can occur in children, as may occur in adults; however, more harm may be done in the pediatric populations. This is especially true as children and families may "pin their hopes" on a particular intervention "curing their child," when in reality chronic pain is a complex phenomenon that responds best to multidisciplinary management. This does not mean that no block should be recommended in children, but that procedural interventions should be used judiciously, appropriately, and in conjunction with other biopsychosocial treatments by or under the guidance of a pediatric pain expert.

Regional anesthesia provides several benefits, particularly in the acute perioperative setting. As an alternative to or in augmentation of opioid-based pain control, regional anesthesia minimizes opioid requirements and therefore opioid side effects, including nausea, vomiting, somnolence, respiratory depression, pruritus, constipation, and physical dependence. It can provide equal or improved analgesia, as it interrupts nociceptive pathways and may profoundly inhibit endocrine stress responses. Regional anesthesia also results in earlier ambulation in recovering surgical patients, helps prevent atelectasis in the patient with chest pain, and usually results in earlier discharge from the hospital. Theoretically, the interruption of nociceptive pathways in the periphery by regional anesthetics will prevent or reverse the process of amplification of pain signals induced by nociception (e.g., CNS windup, glial cell activation). For postoperative pain, effective regional anesthesia reduces the risks of acute pain evolving to chronic pain. Regional anesthesia is considered safe and effective if performed by trained staff with the proper instruments and equipment. Most frequently, nerve blocks are performed by an anesthesiologist or pain management physician; a few are easily performed by a nonanesthesiologist with appropriate training. The benefits of regional anesthesia are dependent on adequate coverage of the surgical area, the patient and family's expectation of the block, and the expertise of the provider performing the block. When procedures fail to provide adequate analgesia, it can lead to the need to "catch up" with pain control after surgery.

Head and Neck Blocks

Primary pain syndromes of the head, such as trigeminal neuralgia, are distinctly unusual in the pediatric population, and few surgical procedures in the head and neck are amenable to regional anesthesia. Headache disorders, very common in the pediatric age-group, may respond well to regional anesthesia of the greater occipital nerve. However, this is not generally considered a first-line treatment of pediatric headache. The greater occipital nerve (second cervical, C2) provides sensation to much of the cranial structures, from the upper cervical region, the occiput to the apex of the head, or even to the hairline. The greater occipital nerve can be blocked medial to the occipital artery, which can usually be identified at the occipital ridge midway between the occipital prominence and the mastoid process by palpation, Doppler sound amplification, or visualization by ultrasound. The short-term and especially long-lasting effects of nerve blocks for chronic headaches in children have not been documented by research. Studies are needed to determine which children with which types of headaches will benefit most from occipital nerve blocks. Sphenopalatine blocks are increasingly used in the treatment of multiple types of headaches in adults, including migraine and postdural puncture headache (PDPH). There is some evidence to support the benefit of this procedure in children and adolescents. The sphenopalatine ganglion (SPG) is a collection of cells closely related to the trigeminal nerve that plays a role in headache pathology. This block can be performed in a minimally invasive fashion through the nasal cavity. The procedure may be performed either with the use of marketed devices or with the use of cotton-tipped applicators. SPG blocks may be performed with or without fluoroscopic guidance.

Onabotulinum toxin A (Botox) may also be used for the treatment of chronic migraine in children and adolescents. As with many interventions, the available data for benefit of this treatment for pediatric migraine are lacking compared with the adult data. However, many children or adolescents, who may have experienced treatment failure with medical management of headache, may be considered as candidates for the use of Botox.

Upper Extremity Blocks

The brachial plexus block controls pain of the upper extremity. These blocks also protect the extremity from movement, reduce arterial spasm, and block sympathetic tone of the upper extremity. The brachial plexus, responsible for cutaneous and motor innervation of the upper extremity, is an arrangement of nerve fibers originating from spinal nerves C5 through T1, extending from the neck into the axilla, arm, and hand. The brachial plexus innervates the entire upper limb, except for the trapezius muscle and an area of skin near the axilla. If pain is located proximal to the elbow, the brachial plexus may be blocked above the clavicle (roots and trunks); if the pain is located distal to the elbow, the brachial plexus may be blocked at the axilla (cords and nerves). The block may be given as a single injection with a long-acting anesthetic such as bupivacaine or ropivacaine. This may provide up to 12-16 hours of analgesia. Use of a catheter and infusion pump may increase duration and provide continuous analgesia for several days.

Trunk and Abdominal Visceral Blocks

Trunk blocks provide somatic and visceral analgesia and anesthesia for pain or surgery of the thorax and abdominal area. Sympathetic, motor, and sensory blockade may be obtained. These blocks are often used in combination to provide optimal relief. Intercostal and paravertebral blocks may be beneficial in patients for whom a thoracic epidural injection or catheter is contraindicated (e.g., patient with coagulopathy). Respiratory function is maintained, and the side effects of opioid therapy are eliminated.

The intercostal, paravertebral, erector spinae, rectus sheath, and transverse abdominal plane blocks are most useful for pediatric chest and somatic abdominal pain. The celiac plexus and splanchnic nerve block can be useful for abdominal visceral pain, such as that caused by malignancy or pancreatitis. These blocks are best performed by an experienced anesthesiologist, pain physician, or interventional radiologist using ultrasound or CT imaging guidance.

The **intercostal block** is used to block the intercostal nerves, the anterior rami of the thoracic nerves from T1 to T11. These nerves lie inferior to each rib, between the inner and innermost intercostal muscles with their corresponding vein and artery, where they can be blocked, generally posterior to the posterior axillary line. Guidance with either fluoroscopy or ultrasound is often employed to decrease risks associated with this block. With use of ultrasound imaging, the intercostal nerves and the pleura can be identified, which can decrease risks such as pneumothorax or hemothorax that are associated with this procedure. The **erector spinae plane** block has also shown to be effective for blocking several levels of intercostal nerves while avoiding the attendant risks of multilevel intercostal nerve blocks.

The **paravertebral block**, another alternative to intercostal nerve block or epidural analgesia, is useful for pain associated with thoracotomy or with unilateral abdominal surgery, such as nephrectomy or splenectomy. Essentially this block results in multiple intercostal blocks with a single injection. The thoracic paravertebral space, lateral to the vertebral column, contains the sympathetic chain, rami communicantes, dorsal and ventral roots of the spinal nerves, and dorsal root ganglion. Because it is a continuous space, local anesthetic injection will provide sensory, motor, and sympathetic blockade to several dermatomes. The paravertebral block may be performed as a single injection or, for a very prolonged effect, as a continuous infusion over several days or weeks via a catheter. This block is best performed by an anesthesiologist or interventional pain physician under ultrasound guidance.

Ilioinguinal and iliohypogastric nerve blocks are indicated with surgery for inguinal hernia repair, hydrocele, or orchidopexy repair and for chronic pain subsequent to these procedures. The first lumbar (L1) nerve divides into the iliohypogastric and ilioinguinal nerves, which emerge from the lateral border of the psoas major muscle. The iliohypogastric nerve supplies the suprapubic area as it pierces the transversus abdominis muscle and runs deep to the internal oblique muscle. The ilioinguinal nerve supplies the upper medial thigh and superior inguinal region, as it also pierces the transversus abdominis muscle and runs across the inguinal canal. Ultrasound guidance helps ensure success for this nerve block.

The **celiac plexus block** is indicated for surgery or pain of the pancreas and upper abdominal viscera. The celiac plexus, located on each side of the L1 vertebral body, contains one to five ganglia. The aorta lies posterior, the pancreas anterior, and the inferior vena cava lateral to these nerves. The celiac plexus receives sympathetic fibers from the greater, lesser, and least splanchnic nerves, as well as from parasympathetic fibers from the vagus nerve. Autonomic fibers from the liver, gallbladder, pancreas, stomach, spleen, kidneys, intestines, and adrenal glands originate from the celiac plexus. This block is best performed with CT guidance to provide direct visualization of the appropriate landmarks, avoid vascular and visceral structures, and confirm correct needle placement. The close proximity of structures such as the aorta and vena cava make this a technical procedure best performed by an anesthesiologist, interventional pain physician, or interventional radiologist. The evidence for use of this block for chronic pediatric pain is lacking; as such, this block should not be routinely employed in the treatment of chronic noncancer pain.

Nerve blocks have been used for the treatment of *anterior cutaneous nerve entrapment syndrome (ACNES)*. ACNES is characterized by pain associated with use of abdominal muscles. On exam, this can be identified via Carnett sign. Pathology and causation in the pediatric population are not well understood. Treatment may include identification of a specific pain source under ultrasound guidance with infiltration of a local anesthetic or local anesthetic and steroid mixture. Evidence for use of this procedure is limited.

Lower Extremity Blocks

Lumbar plexus and sciatic nerve blocks provide pain control for painful conditions or surgical procedures of the lower extremities, with the benefit of providing analgesia to only one extremity while preserving motor and sensory function of the other. The lumbosacral plexus is an arrangement of nerve fibers originating from spinal nerves L2-L4 and S1-S3. The lumbar plexus arises from L2-L4 and forms the lateral femoral cutaneous, femoral, and obturator nerves. These nerves supply the muscles and sensation of the upper leg, with a sensory branch of the femoral nerve (saphenous nerve) extending below the knee to innervate the medial aspect of the foreleg, ankle, and foot. The sacral plexus arises from L4-S3 and divides into the major branches of the sciatic, tibial, and common peroneal nerves. These nerves in turn supply the posterior thigh, lower leg, and foot. Unlike the brachial plexus block, blockade of the entire lower extremity requires more than one injection because the lumbosacral sheath is not accessible. Separate injections are necessary for the posterior (sciatic) and anterior (lumbar plexus) branches, and the injections can be performed at any of several levels during the course of the nerve, as is clinically expedient. The lumbar plexus can be blocked in the back, resulting in analgesia of the femoral, lateral femoral cutaneous, and obturator nerves. Alternatively, any of these three nerves can be individually anesthetized, depending on the location of the pain. Similarly, the sciatic nerve can be anesthetized proximally as it emerges from the pelvis or, more distally, in the posterior thigh, or its major branches (tibial and peroneal nerves) can be individually anesthetized. These nerve blocks are generally best performed by an anesthesiologist, pain physician, or radiologist.

Table 93.17 Budapest Criteria for Clinical Diagnosis of CRPS

1. **Pain** (ongoing and disproportionate to any inciting event)
2. **Symptoms (reported):** At least one symptom in three out of four of the following categories:
   - *Sensory* – Hyperesthesia and/or allodynia
   - *Vasomotor* – Temperature asymmetry and/or skin color changes and/or skin color asymmetry
   - *Sudomotor/Edema* – Edema and/or sweating changes and/or sweating asymmetry
   - *Motor/Trophic* – Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3. **Signs (examined):** At least one sign in two out of four of the following categories:
   - *Sensory* – Hyperalgesia (to pinprick) and/or allodynia (to light touch and/or temperature sensation and/or deep somatic pressure and/or joint movement)
   - *Vasomotor* – Temperature asymmetry (>1°C) and/or skin color changes and/or asymmetry
   - *Sudomotor/Edema* – Edema and/or sweating changes and/or sweating asymmetry
   - *Motor/Trophic* – Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4. **Diagnosis of exclusion:** No other diagnosis better explains the signs and symptoms.

CRPS, Complex regional pain syndrome
From Davis PJ, Cladis FP, eds. *Smith's Anesthesia for Infants and Children*, 10th ed. Philadelphia: Elsevier; 2022, Box 25.1, p. 583.

Sympathetic Blocks

Sympathetic blocks were once thought to be useful in the diagnosis and treatment of sympathetically mediated pain, CRPS (Table 93.17), and other neuropathic pain conditions (Table 93.18), but large meta-analyses have shown their utility to be minimal. When blocks of the sympathetic plexuses are performed, sympathectomy is obtained

Table 93.18 Examples of Neuropathic Pain Syndromes

PERIPHERAL NERVOUS SYSTEM FOCAL AND MULTIFOCAL LESIONS
Postherpetic neuralgia
Cranial neuralgias (e.g., trigeminal neuralgia, glossopharyngeal neuralgia)
Diabetic mononeuropathy
Nerve entrapment syndromes
Plexopathy from malignancy or irradiation
Phantom limb pain
Posttraumatic neuralgia (e.g., nerve root compression, after thoracotomy)
Ischemic neuropathy
Complex regional pain syndrome types 1 and 2
Erythromelalgia

PERIPHERAL NERVOUS SYSTEM GENERALIZED POLYNEUROPATHIES
Metabolic/nutritional: Diabetes mellitus, pellagra, beriberi, multiple nutritional deficiency, hypothyroidism
Toxic: Alcohol-, platinum-, or taxane-based chemotherapy; isoniazid; antiretroviral drugs
Infective/autoimmune: HIV, acute inflammatory polyneuropathy (Guillain-Barré syndrome), neuroborreliosis (Bannwarth syndrome)
Hereditary: Fabry disease
Malignancy: Carcinomatosis
Others: Idiopathic small fiber neuropathy, erythromelalgia

CENTRAL NERVOUS SYSTEM LESIONS
Spinal cord injury
Prolapsed disc
Stroke (brain infarction, spinal infarction)
Multiple sclerosis
Surgical lesions (e.g., rhizotomy, cordotomy)
Complex neuropathic disorders
Complex regional pain syndrome types 1 and 2

Adapted from Freynhagen R, Bennett MI. Diagnosis and management of neuropathic pain. *BMJ*. 2009;339:b3002.

without attendant motor or sensory anesthesia. Their use for pain management was grounded in the notion that many types of chronic pain were mediated via the sympathetic nerves. This mechanistic model has been proven to be false.

The **stellate ganglion block** was indicated for pain in the face or upper extremity and for CRPS, phantom limb pain, amputation stump pain, or circulatory insufficiency of the upper extremities. The lumbar sympathetic block addressed pain in the lower extremity, CRPS, phantom limb pain, amputation stump pain, and pain from circulatory insufficiency.

The analgesia produced by peripheral sympathetic blocks usually outlives the duration of the local anesthetic, often persisting for weeks or indefinitely. If analgesia is transient, the blocks may be performed with catheter insertion for continuous local anesthesia of the sympathetic chain over days or weeks. Because precise, radiographically guided placement of the needle and/or catheter is required for safety and success, sympathetic blocks are generally best performed by an anesthesiologist, interventional pain physician, or interventional radiologist.

While all these procedures can be considered for the treatment of certain chronic pediatric pain conditions, there is overall a lack of evidence to support routine use in children and adolescents. This information should be used for learning and awareness rather than as a guide map for specific treatment of these conditions. When needed, a dedicated pediatric pain provider should be consulted and these blocks used judiciously when appropriate.

In addition, any time these procedures are considered for the treatment of chronic pain, special consideration should be given to potential risks and complications.

Epidural Anesthesia (Thoracic, Lumbar, and Caudal)

Epidural anesthesia and analgesia are indicated for pain below the clavicles, management of regional pain syndromes, cancer pain unresponsive to systemic opioids, and pain limited by opioid side effects.

The three layers of the spinal meninges—dura mater (outer), arachnoid mater (middle), and pia mater (inner)—envelop the spinal neural tissue. The subarachnoid space contains cerebrospinal fluid between the arachnoid mater and pia mater. The epidural space extends from the foramen magnum to the sacral hiatus and contains fat, lymphatics, blood vessels, and the spinal nerves as they leave the spinal cord. The epidural space separates the dura mater from the periosteum of the surrounding vertebral bodies. In children, the fat in the epidural space is not as dense as in adults, predisposing to greater spread of the local anesthetic from the site of injection.

Epidural local anesthetics block both sensory and sympathetic fibers, and if the local anesthetic is of sufficient concentration, they also block motor fibers. Mild hypotension may occur, although it is unusual in children <6 years of age. Epidural local anesthetics high in the thoracic spine may also anesthetize the sympathetic nerves to the heart (the cardiac accelerator fibers), producing bradycardia. In addition to using local anesthetics, it is routine to use opioids and sometimes α-agonists as adjunctive medications in the epidural space. Clonidine and opioids have been well studied and shown not to be neurotoxic. Side effects of epidural opioid administration include delayed respiratory depression, particularly when hydrophilic opioids such as morphine are used. The risk of this effect requires that children receiving epidural opioids by intermittent injection or continuous infusion be monitored by continuous pulse oximetry and nursing observation, particularly during the first 24 hours of therapy or after significant dose escalations. Respiratory depression occurring after the first 24 hours of epidural opioid administration is distinctly unusual.

Epidural clonidine (an α_2-agonist with μ-opioid analgesic properties) is associated with minimal risk and side effects. Although product labeling indicates use only in children with severe cancer pain, clonidine may be used for treatment of routine postoperative pain as well as pain syndromes such as CRPS. Mild sedation is the most common side effect of epidural clonidine, and it is not associated with respiratory depression.

Because performing epidural blockade is technical and may result in spinal cord injury, it is best done by an anesthesiologist or pain physician skilled in the technique. Caution is advised in the use of epidural anesthesia/analgesia for CRPS in children because no published RCTs have shown these procedures superior to a combination of less invasive physical and psychologic therapy, with or without neuropathic pain-focused medications.

INTRATHECAL ANALGESIA

Intrathecal catheters infused with opioids, clonidine, ziconotide (derived from a marine neurotoxin produced by the cone snail), and local anesthetics are occasionally applicable in pediatric patients with intractable pain from cancer or other life-threatening conditions. Typically, intrathecal catheters are attached to an implanted electronic pump containing a drug reservoir sufficient for several months of dosing. The technique is technical and best performed by an experienced pain management physician or neurosurgeon.

NERVE ABLATION AND DESTRUCTION

In some cases, pain remains refractory despite maximal reliance on oral and IV medications and nerve blockade. In these patients, temporary (pulsed radiofrequency ablation) or permanent neurolytic destruction (phenol or alcohol) of one or more nerves may be performed. The techniques should be carefully weighed against the consideration of permanent nerve destruction in a growing child with decades of life ahead. On the other hand, when pain is severe in life-limiting disease processes, the long-term considerations are less concerning, and these techniques should be discussed with a skilled pain management specialist.

CONSIDERATIONS FOR SPECIAL PEDIATRIC POPULATIONS

Pain Perception and Effects of Pain on Newborns and Infants

Pain may result from a number of circumstances in the newborn period, including acute pain (diagnostic and therapeutic procedures, minor surgery, monitoring), continuous pain (pain from thermal/chemical burns, postsurgical and inflammatory pain), and chronic or disease-related pain (necrotizing enterocolitis, nerve injury, chronic conditions, thrombophlebitis). The most common sources of pain in healthy infants are acute procedures, such as heel lances, surgical procedures, and in males, circumcision.

Many procedures are performed for premature infants in the neonatal intensive care unit (NICU). In the first week of life, approximately 94% of preterm infants <28 weeks gestational age are mechanically ventilated; in these situations, heelsticks and airway suctioning are frequent, yet few of these procedures are preceded by any type of analgesia. Repeated handling and acute pain episodes sensitize the neonate to increased reactivity and stress responses to subsequent procedures. Typical stress responses include increases in heart rate, respiratory rate, blood pressure, and intracranial pressure. Cardiac vagal tone, transcutaneous oxygen saturation, carbon dioxide levels, and peripheral blood flow are decreased. Autonomic signs include changes in skin color, vomiting, gagging, hiccupping, diaphoresis, dilated pupils, and palmar and forehead sweating (see Table 93.4).

Untreated pain in the newborn has serious short- and long-term consequences. There has been a shift in most NICUs to more liberal use of opioids. Nonetheless, **morphine**, the traditional gold standard of analgesia for acute pain, may not be effective and may have adverse long-term consequences. No differences have been found in the incidence of severe intraventricular hemorrhage or in the mortality rate when infants receiving morphine are compared with a placebo group, and there are no changes in assessed pain from tracheal suctioning in ventilated infants receiving morphine compared with those receiving a placebo infusion. Morphine may not alleviate acute pain in ventilated preterm neonates, although there are few data on the effects of morphine and fentanyl in nonventilated newborns. The lack of opioid effects for acute pain in neonates may result from immaturity of opioid receptors; acute pain may cause the uncoupling of μ-opioid receptors in the forebrain. Repetitive acute pain may create central neural changes in the newborn that may have long-term consequences for later pain vulnerability, cognitive effects, and opioid tolerance. Most

Table 93.19 World Health Organization Analgesic Ladder for Cancer Pain

STEP 1
Patients who present with mild to moderate pain should be treated with a nonopioid.

STEP 2
Patients who present with moderate to severe pain or for whom the step 1 regimen fails should be treated with an oral opioid for moderate pain combined with a nonopioid analgesic.

STEP 3
Patients who present with very severe pain or for whom the step 2 regimen fails should be treated with an opioid used for severe pain, with or without a nonopioid analgesic.

neonatologists use opioids in painful situations. Sucrose and pacifiers are also being used in the NICU. The effects of 24% **sucrose** (Sweetease) are believed to be opioid mediated because the effect can be reversed with naloxone. Sucrose, with or without a pacifier, may be effective for acute pain and stress control. Other nonpharmacologic strategies for stress and pain control include infant care by an individual primary nurse, tactile-kinesthetic stimuli (massage), "kangaroo care," and soothing sensorial saturation.

Children With Cancer Pain

The World Health Organization (WHO) proposed an analgesic therapy model for cancer pain known as the *analgesic ladder* (Table 93.19). Designed to guide therapy in care systems with limited access to analgesic experts, this ladder consists of a hierarchy of oral pharmacologic interventions intended to treat pain of increasing magnitude. The hierarchy ignores modalities such as the use of nonconventional analgesics and interventional pain procedures, which physicians in developed countries are often able to prescribe. Nevertheless, because oral medications are simple and efficacious, especially for home use, the ladder presents a framework for rationally using them, before applying other drugs and techniques of drug administration.

Oral medications are the first line of analgesic treatment. Because NSAIDs affect platelet adhesiveness, they are typically not used. As noted earlier, celecoxib may be the exception to this rule. Opioid therapy is the preferred approach for moderate or severe pain. Nonopioid analgesics are used for mild pain, a weak opioid is added for moderate pain, and strong opioids are administered for more severe pain. Adjuvant analgesics can be added, and side effects and comorbid symptoms are actively managed. Determining the type and sources of the pain will help develop an effective analgesic plan. Certain treatments, such as the chemotherapeutic agent vincristine, are associated with neuropathic pain. Such pain might require anticonvulsants or TCAs. Stretching pain from tumor growth within an organ might require strong opioids and/or radiation therapy if the tumor is radiosensitive. Organ obstruction, such as intestinal obstruction, should be diagnosed to relieve or bypass the obstruction.

It is important to consider both pharmacologic and nonpharmacologic strategies (e.g., CBT, family/parent support) to treat pain in children with cancer.

Children with Pain Associated with Advanced Disease

Patients with advanced diseases, including cancer, acquired immunodeficiency syndrome (AIDS), neurodegenerative disorders, and cystic fibrosis, need palliative care approaches that focus on optimal quality of life. Nonpharmacologic and pharmacologic management of pain and other distressing symptoms is a key component. *Palliative care* should be offered to all children with serious diseases, whether or not the diseases are potentially curable or long life expectancy is predicted (see Chapter 8). Examples include young children diagnosed with acute lymphoblastic leukemia (>90% posttreatment life expectancy) and children undergoing organ transplantation. Palliative care in pediatrics connotes treatment that focuses on symptom reduction, quality of life, and good family and clinical team communication. It is not only for patients in hospice care or those at the end of life. Differences in the progression of underlying illness, associated distressing symptoms, and common emotional responses in these conditions should shape individual treatment plans. For end-of-life care, >90% of children and adolescents with cancer can be made comfortable by standard escalation of opioids according to the WHO protocol. A small subgroup (5%) requires enormous opioid dose escalation to >100 times the standard morphine or other opiate infusion rate. Most of these patients have spread of solid tumors to the spinal cord, roots, or plexus, and signs of neuropathic pain are evident. **Methadone** given orally is often used in palliative care, not only end-of-life care, because of its long half-life and its targets at both opioid and NMDA receptors.

The type of pain experienced by the patient (neuropathic, myofascial) should determine the need for adjunctive agents. Complementary measures, such as massage, hypnotherapy, and spiritual care, must also be offered in palliative care. Although the oral route of opioid administration should be encouraged, especially to facilitate care at home, if possible, some children are unable to take oral opioids. Transdermal and sublingual routes, as well as IV infusion with PCA, are likely next choices. Small, portable infusion pumps are convenient for home use. If venous access is limited, a useful alternative is to administer opioids (especially morphine or hydromorphone, but not methadone or meperidine) through continuous SC infusion, with or without a bolus option. A small (e.g., 22-gauge) cannula is placed under the skin and secured on the thorax, abdomen, or thigh. Sites may be changed every 3-7 days, as needed. As noted, alternative routes for opioids include the transdermal and oral transmucosal routes. These latter routes are preferred over IV and SC drug delivery when the patient is being treated at home.

CHRONIC AND RECURRENT PAIN SYNDROMES

Chronic pain is defined as recurrent or persistent pain lasting longer than the normal tissue healing time (3-6 months). Children may experience pain related to injury (e.g., burns) or to a chronic or underlying disease process (e.g., cancer, arthritis), or pain can also be the chronic condition itself (e.g., CRPS, fibromyalgia, functional abdominal pain) (see Chapter 212). During childhood, abdominal, musculoskeletal, and headache pain are the most frequently occurring conditions. However, definitions of chronic pain do not take into account standard criteria for assessing particular pain symptoms or for evaluating the intensity or impact of pain and therefore include individuals with varying symptoms and experiences. Consequently, in epidemiologic surveys, prevalence estimates vary widely. Overall prevalence rates for different childhood pains range from 4% to 88%. An average of 13.5–31.8% of adolescents in a community sample reported having weekly abdominal, headache, or musculoskeletal pains. Most epidemiologic studies report prevalence and do not report the *severity* or impact of the pain. Research indicates that only a subset of children and adolescents with chronic pain (approximately 5%) experience moderate to severe disability, and this likely better represents the estimated population for whom help is needed to treat pain and associated problems.

Neuropathic Pain Syndromes

Neuropathic pain is caused by abnormal excitability in the peripheral or central nervous system that may persist after an injury heals or inflammation subsides. The pain, which can be acute or chronic, is typically described as burning or stabbing and may be associated with cutaneous hypersensitivity **(allodynia)**, distortion of sensation **(dysesthesia)**, and amplification of noxious sensations **(hyperalgesia** and **hyperpathia)**. Neuropathic pain conditions may be responsible for >35% of referrals to chronic pain clinics, conditions that typically include posttraumatic and postsurgical peripheral nerve injuries, phantom pain after amputation, pain after spinal cord injury, and pain caused by metabolic neuropathies (see Table 93.18). Patients with neuropathic pain typically respond poorly to opioids. Evidence supports

the efficacy of antidepressants (nortriptyline, amitriptyline, venlafaxine, duloxetine) and anticonvulsants (gabapentin, pregabalin, oxcarbazepine) for treatment of neuropathic pain (see Table 93.16).

Complex regional pain syndrome is well described in the pediatric population (see Chapter 211 and Table 93.17). **CRPS type 1** is a syndrome of neuropathic pain that typically follows an antecedent and usually minor injury or surgery to an extremity without identifiable nerve injury. It is seen after injury such as sprain or fracture or even in instances as minimal as an IV start. The syndrome of CRPS type 1 includes severe spontaneous neuropathic pain, hyperpathia, hyperalgesia, severe cutaneous allodynia to touch and cold, changes in blood flow (typically extremity cyanosis), and increased sweating. In more advanced cases, symptoms include dystrophic changes of the hair, nails, and skin; immobility of the extremity (dystonia); and muscle atrophy. In the most advanced cases, symptoms include ankylosis of the joints of the extremity. Specific causal factors in CRPS type 1 in both children and adults remain elusive, although coincidental events may be noted. **CRPS type 2** clinically appears the same with respect to symptoms but is associated with a known nerve injury.

Treatment of CRPS in children has been extrapolated from that in adults, with some evidence for efficacy of physical therapy, CBT, nerve blocks, antidepressants, AEDs, and other related drugs. All experts in pediatric pain management agree on the value of aggressive physical therapy, including desensitization. Some centers provide aggressive therapy without the use of pharmacologic agents or interventional nerve blocks. Unfortunately, recurrent episodes of CRPS may be seen in up to 25–50% of patients, particularly adolescent females. Physical therapy can be extraordinarily painful for children to endure; it is tolerated only by the most stoic and motivated patients. If children have difficulty enduring the pain, there is a well-established role for pharmacologic agents, with or without peripheral or central neuraxial nerve blocks, to render the affected limb sufficiently analgesic so that physical therapy can be tolerated. Pharmacologic interventions include the use of AEDs such as gabapentin and/or TCAs such as amitriptyline (see Fig. 93.4). Although there is clear evidence of a peripheral inflammatory component of CRPS, with release of cytokines and other inflammatory mediators from the peripheral nervous system in the affected limb, the use of antiinflammatory agents has been disappointing. Common nerve block techniques include IV regional anesthetics, epidural analgesia, and peripheral nerve blocks. In extreme and refractory cases, more invasive strategies have been reported, including surgical sympathectomy and spinal cord stimulation, although these are not generally recommended in the pediatric population

Although an array of treatments has some benefit, the mainstay of treatment remains **physical therapy** emphasizing desensitization, strengthening, and functional improvement. Additionally, pharmacologic agents and psychologic and complementary therapies are important components of a treatment plan. Invasive techniques, although not curative, can be helpful if they permit the performance of frequent and aggressive physical therapy that cannot be carried out otherwise. A good biopsychosocial evaluation will help determine the orientation of the treatment components. There are insufficient data to indicate the superior value of interventional blocks, such as epidural anesthesia, in children with CRPS over physical and psychologic interventions, with or without pharmacologic support.

Myofascial Pain Disorders and Fibromyalgia

Myofascial pain disorders are associated with tender points in the affected muscles and with muscle spasms (tight muscles). Treatment is targeted at relaxing the affected muscles through physical therapy, Iyengar yoga, massage, and acupuncture. Rarely are pharmacologic muscle relaxants helpful other than for creating tiredness at night for sleep. Dry needling or injections of local anesthetic into the tender points has been advocated, but the data do not support this as a standard treatment. Similarly, although botulinum toxin injections may be used, no data support this practice in children. Often, poor body postures, repetitive use of a body part not accustomed to that movement, or carrying heavy backpacks initiates pain. When it becomes widespread, a diagnosis may be made of **juvenile fibromyalgia**, which may or may not continue to subsequently become adult fibromyalgia. Newer guidelines do not use "tender points" in the diagnosis of fibromyalgia. Instead, diagnosis relies on a model that assesses for widespread pain and symptom severity (see Chapter 211). Likely there are different subtypes of widespread pain syndromes, and physical therapy is a key component of treatment. Psychologic interventions may play an important role to assist the child in resuming normal activities and to manage any psychologic comorbidities. Any pain rehabilitation plan should enhance return to full function. Because there is a high incidence of chronic pain in parents of children presenting with a chronic pain condition, especially fibromyalgia, attention to parent and family

Table 93.20 Clinical Features of Human Disorders Caused by Pathologic Variants in Ion-Channel Genes That Lead to Altered Pain Perception and Are Inherited in a Mendelian Manner

	AFFECTED GENE (PROTEIN)	TYPE AND EFFECT OF MUTATION	MAIN PHENOTYPE	ADDITIONAL FEATURES
Inherited erythromelalgia	*SCN9A* ($Na_v1.7$)	Heterozygous, activating	Onset by age 20 yr; episodic pain triggered by warmth; feet affected more frequently than hands	Erythema of feet
Paroxysmal extreme pain disorder	*SCN9A* ($Na_v1.7$)	Heterozygous, activating	Onset at birth; episodic pain; sacral region is affected most frequently, face is affected more often than the limbs; physical triggers include defecation	Erythema of the sacrum; tonic attacks
Small fiber neuropathy	*SCN9A* ($Na_v1.7$)	Heterozygous, activating	Onset at any age but more common in early adulthood; persistent burning pain; feet affected more frequently than hands	Could be autonomic features
Small fiber neuropathy	*SCN10A* ($Na_v1.8$)	Heterozygous, activating	Persistent burning pain	Could be autonomic features
Familial episodic pain syndrome type I	*TRPA1* (TRPA1)	Heterozygous, activating	Onset at birth or in infancy; episodic chest or arm pain; triggers are hunger and cold	—
Familial episodic pain syndrome type III	*SCN11A* ($Na_v1.9$)	Heterozygous, activating	Onset in first decade; episodic hand and foot pain; triggers are intercurrent illness or exercise	—

Na_v, Sodium ion channel.
Modified from Bennett DLH, Woods CG. Painful and painless channelopathies. *Lancet Neurol*. 2014;13:587–599, Table 1, p. 590.

factors is important. Parent training may entail teaching the parent to model more appropriate pain coping behaviors and to recognize the child's independent attempts to manage pain and function adaptively. Parents may also need referrals to obtain appropriate pain management for their own pain condition.

Pregabalin and duloxetine are FDA approved for management of fibromyalgia in adults; duloxetine is also approved for adolescents ages 13-17. However, the best evidence for the treatment of adolescents with fibromyalgia remains a multimodal approach including CBT and physical therapy. This is generally considered superior to solitary use of pharmacologic agents.

Erythromelalgia

Erythromelalgia in children is generally primary, whereas in adults it may be either primary or secondary to malignancy or other hematologic disorders, such as polycythemia vera (see Chapter 211.5). Patients with erythromelalgia exhibit red, warm, hyperperfused distal limbs. The disorder is usually bilateral and may involve either or both the hands and feet. Patients perceive burning pain and typically seek relief by immersing the affected extremities in ice water, sometimes so often and for so long so that skin pathology results. **Primary erythromelalgia** is caused by a gain of function pathogenic variant (autosomal dominant) in the gene for the NaV1.7 neuronal sodium channel on peripheral C nociceptive fibers, resulting in their spontaneous depolarization, and thus continuous burning pain. The most common pathogenic variant identified is in the *SCN9A* gene, although there are several variants that affect the NaV1.7 channel (Table 93.20). Other ion channel pathologic gene variants are associated with rare pain syndromes (see Table 93.20). Another pathogenic variant (loss of function) in the NaV1.7 channel results in a rare but serious genetic condition, the congenital indifference to pain.

Although some similarities to CRPS may be present in erythromelalgia, there are differences to distinguish the two conditions. CRPS in general is a unilateral phenomenon rather than bilateral. CRPS often presents with a cold, cyanotic limb (although "hot" CRPS with a warm, erythematous limb may occur as well). In addition, erythromelalgia is associated with intermittent pain compared with the more continuous nature and symptoms seen in CRPS. In erythromelalgia, ice water immersion is analgesic, the condition is bilateral and symmetric, and it is associated with hyperperfusion of the distal extremity.

The evaluation of hyperperfused limbs with burning pain should include genetic testing for **Fabry disease (alpha-galactosidase deficiency)** and screening for hematologic malignancies, with diagnosis of primary erythromelalgia being one of exclusion. The definitive treatment of Fabry disease includes enzyme replacement (as disease-modifying treatment) and administration of neuropathic pain medications such as gabapentin, although the success of antineuropathic pain drugs in small fiber neuropathies has not been impressive. The treatment of erythromelalgia is much more difficult. Antineuropathic pain medications (AEDs, TCAs) are typically prescribed but rarely helpful (see Fig. 93.4). Although one might predict that sodium channel–blocking AEDs might be effective in this sodium channelopathy, oxcarbazepine has not proved to be a particularly effective modality. The pain responds well to regional anesthetic nerve blocks, but it returns immediately when the effects of the nerve block resolve. In contrast, in other neuropathic syndromes, the analgesia usually (and inexplicably) persists well after the resolution of the pharmacologic nerve block. Aspirin and even nitroprusside infusions have been anecdotally reported to be of benefit with secondary erythromelalgia but have not been reported to be helpful in children with primary erythromelalgia. Case reports in adults and clinical experience in children suggest that periodic treatment with high-dose **capsaicin cream (8%)** may be effective in alleviating the burning pain and disability of erythromelalgia. Capsaicin (essence of chili pepper) cream is a vanilloid receptor (TRPV1) agonist that depletes small fiber peripheral nerve endings of the neurotransmitter substance P, an important neurotransmitter in the generation and transmission of nociceptive impulses. Once depleted, these nerve endings are no longer capable of generating spontaneous pain until the receptors regenerate, a process that takes many months.

Other Chronic Pain Conditions in Children

A variety of genetic and other medical/surgical conditions are often associated with chronic pain. Examples include Fabry disease, Chiari malformation/syringomyelia, epidermolysis bullosa, juvenile idiopathic arthritis, porphyria, mitochondrial disorders, degenerative neurologic diseases, cerebral palsy, ASD, intestinal pseudoobstruction, inflammatory bowel disease, chronic migraine/daily headaches, and irritable bowel disease. In many cases, treating the underlying disease, such as with enzyme replacement in Fabry disease and in other lysosomal disorders, will reduce what otherwise might be progression of symptoms but may not totally reduce pain and suffering, and other modalities will be needed. Pain that persists and is not well treated can lead to central sensitization and widespread pain, such as seen in children with one pain source who then develop fibromyalgia.

MANAGING COMPLEX CHRONIC PAIN PROBLEMS

Some patients with chronic pain have a prolonged course of evaluation in attempts to find what is expected as the singular "cause" of the pain and thus also undergo many failed treatments (see Chapter 212). Parents worry that the doctors have not yet discovered the cause that may be serious and life threatening, and children often feel not believed, that others perceive they are faking their pain or are "crazy." There may be no identifiable or diagnosable condition, and families may seek opinions from multiple treatment facilities to find help for their suffering child. For some children, what may have begun as an acute injury or infectious event may result in a chronic pain syndrome, with changes in the neurobiology of the pain-signaling system.

In the context of disabling chronic pain, it is very important for the pediatrician to avoid overmedication, because this can exacerbate associated disability. In addition, it is important to maintain an open mind and reassess the diagnosis if the clinical presentation changes. It is essential to communicate to the family that pain has a biologic basis (likely related to neural signaling and neurotransmitter dysregulation) and that the pain is naturally distressing to the child and family. All patients and families should receive a simple explanation of pain physiology that helps them understand the importance of (1) functional rehabilitation to normalize pain signaling, (2) the low risk of causing further injury with systematic increases in normal functioning, and (3) the likely failure of treatment if pain is managed as if it were acute. Because it is counterintuitive for most people to move a part of the body that hurts, many patients with chronic pain have atrophy or contractures of a painful extremity from disuse. Associated increases in worry and anxiety may exacerbate pain and leave the body even more vulnerable to further illness, injury, and disability.

Pain can have a significant impact on many areas of normal functioning and routines for children, and school absenteeism and related consequences of missed schooling are often significant problems. Appropriate assessment and evaluation of the child with chronic pain and the family is the critical first step in developing a treatment plan. For example, a high–academically functioning child might have an acute injury that leads to chronic pain and significant school absenteeism. Although many downstream contributors to pain and disability maintenance can accumulate the more school that is missed, often previously unrecognized focal learning disabilities may become the increasing trigger for a downhill cascade of pain, disability, and school absenteeism. Even for the child with outstanding grades, it may be helpful to learn about the amount of time spent on each subject. As certain subjects become more complicated, such as math, the child with a previously unrecognized math learning disability may be spending hours on math homework each night, even with good grades in math. In this case, the acute illness or injury becomes the "final straw" that breaks down the child's coping and turns the acute pain into a chronic problem.

Interdisciplinary pediatric pain programs have become the standard of care for treating complex chronic pain problems in youth. Although available in many parts of the United States, Canada, Europe, Australia, and New Zealand, the overall number of programs is still small. Therefore many children and adolescents with chronic pain will

be unable to receive specialized pain treatment in their local communities. In recognition of the severity and complexity of pain and disability for some children, different settings and treatment delivery models for providing pain care have been explored. One option is inpatient and day hospital treatment programs, which often address barriers to access to outpatient treatment and coordination of care. In addition, these programs provide an intensive treatment option for children who do not make adequate progress in outpatient treatment or who are severely disabled by pain. Early programs developed in the 1990s focused on CRPS treatment through intensive inpatient rehabilitation and exercise-based programs. Later programs expanded to other clinical populations and broadened the treatment focus to incorporate a range of rehabilitation and psychologic therapies delivered both individually and in groups. The typical length of inpatient admissions for children with chronic pain in such programs is 3-4 weeks, and emerging evidence suggests benefit from these programs. A major problem that limits such care for children with complex chronic disabling pain is the long waiting list for entry into these programs, as well as obtaining financial coverage for the treatment. Additional, more widespread models of care are needed.

Another intervention delivery option is *remote management,* referring to pain interventions used outside the clinic/hospital setting to reach children in their homes or communities. Interventions are typically delivered using some form of technology, such as the internet, or may rely on other media, such as telephone counseling or written self-help materials. Typically, remote management of pain includes monitoring, counseling, and delivery of behavioral and CBT interventions. Internet interventions have received the most research attention to date, with published examples of several different pediatric chronic pain conditions with promising findings for pain reduction. *Telemedicine* may offer additional ways to connect experts in pediatric pain with patients in remote communities. Within any community, the pediatrician will need to locate appropriate referral sources for patients with complex chronic pain. However, although psychologic interventions can be delivered through these telemedicine strategies, the pediatrician is still relied on to obtain the needed biopsychosocial history, complete a thorough physical examination, and provide the pharmacologic management as needed. The pediatrician also communicates with the family to help the child and family understand the pain and how the different pharmacologic and nonpharmacologic treatments will enhance function and alter the long-term neural processes underlying pain.

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Chapter 94

Poisoning

Jillian L. Theobald and Justin N. Corcoran

Poisoning is the leading cause of injury-related death in the United States, surpassing that from motor vehicle crashes. Most of these deaths are unintentional (i.e., not suicide). In adolescents, poisoning is the second leading cause of injury-related death. Of the more than 2 million human poisoning exposures reported annually to the National Poison Data System (NPDS) of the American Association of Poison Control Centers (AAPCC), approximately 50% occur in children <6 years old, with the highest number of exposures occurring in 1- and 2-year-olds. Almost all these exposures are unintentional and reflect the propensity for young children to put virtually anything in their mouth. Fortunately, children <6 years old account for <2% of all poisoning fatalities reported to NPDS.

More than 90% of toxic exposures in children occur in the home, and most involve a single substance. Ingestion accounts for the majority of exposures, with a minority occurring by the dermal, inhalational, and ophthalmic routes. Approximately 40% of cases involve nondrug substances, such as cosmetics, personal care items, cleaning solutions, plants, and foreign bodies. Pharmaceutical preparations account for the remainder of exposures, and analgesics, topical preparations, vitamins, and antihistamines are most commonly reported.

The majority of poisoning exposures in children <6 years old can be managed without direct medical intervention beyond a call to the regional **poison control center (PCC)**. This is because the product involved is not inherently toxic or the quantity of the material is not sufficient to produce clinically relevant toxic effects. However, a number of substances can be highly toxic to toddlers in small doses (Table 94.1). In 2019, carbon monoxide (CO), batteries, and analgesics (mainly opioids) were the leading identifiable causes of poison-related fatalities in young children (<6 years). In addition, anesthetics, antihistamines, chemicals, cough and cold preparations, tobacco/nicotine/e-cigarette products, and hydrocarbons were significant causes of mortality.

Poison prevention education should be an integral part of all well-child visits, starting at the 6-month visit. Counseling parents and other caregivers about potential poisoning risks, poison-proofing a child's environment, and actions in the event of an ingestion diminish the likelihood of serious morbidity or mortality. Poison prevention education materials are available from the American Academy of Pediatrics (AAP) and regional PCCs. Through a U.S. network of PCCs, anyone at any time can contact a regional poison center by calling the toll-free number **1-800-222-1222**. Parents should be encouraged to share this number with grandparents, relatives, babysitters, and any other caregivers.

Product safety measures, poison prevention education, early recognition of exposures, and around-the-clock access to regionally based PCCs all contribute to the favorable exposure outcomes in young children. Poisoning exposures in children 6-12 years are much less common, involving only approximately 10% of all reported pediatric exposures. A second peak in pediatric exposures occurs in adolescence. Exposures in the adolescent age-group are primarily intentional (suicide or abuse or misuse of substances) and thus often result in more severe toxicity (see Chapter 157). Families should be informed and given anticipatory guidance that nonprescription and prescription medications, and even household products (e.g., inhalants), are common sources of adolescent exposures. Although adolescents (age 13-19 years) account for only about 16% of pediatric exposures, they constitute a larger proportion of deaths. Of the 159 poison-related pediatric deaths in 2021 reported to NPDS, 86 were adolescents (2% of all fatalities called in to poison centers). Pediatricians should be aware of the signs of drug abuse or suicidal ideation in adolescents and should aggressively intervene (see Chapter 40).

PREVENTION

Deaths caused by unintentional poisoning among younger children have decreased dramatically over the past 2 decades, particularly among children <5 years old. In 1970, when the U.S. Poison Packaging Prevention Act was passed, 226 poisoning deaths of children <5 years old occurred, compared with only 25 in 2021. Poisoning prevention demonstrates the effectiveness of passive strategies, including the use of child-resistant packaging and limited doses per container. Difficulty using child-resistant containers by adults is an important cause of poisoning in young children today. In 18.5% of households in which poisoning occurred in children <5 years old, the child-resistant closure was replaced, and 65% of the packaging used did not work properly. Almost 20% of ingestions occur from drugs belonging to grandparents, who have difficulty using traditional child-resistant containers and often put their medications in pill organizers that are not childproof.

Even though there has been success in preventing poisoning in young children, there has been a remarkable rise in adolescent poison-related death over the past 20 years. This has mirrored the increasing rate of antidepressant prescriptions written by healthcare providers and the epidemic increase in opioid-related fatalities.

Table 94.1 Common Agents Potentially Toxic to Young Children (<6 yr) in Small Doses*

SUBSTANCE	TOXICITY
Aliphatic hydrocarbons (e.g., gasoline, kerosene, lamp oil)	Acute lung injury
Antimalarials (chloroquine, quinine)	Seizures, dysrhythmias
Benzocaine	Methemoglobinemia
β-Adrenergic receptor blockers†	Bradycardia, hypotension
Calcium channel blockers	Bradycardia, hypotension, hyperglycemia
Camphor	Seizures
Caustics (pH <2 or >12)	Airway, esophageal and gastric burns
Clonidine	Lethargy, bradycardia, hypotension
Diphenoxylate and atropine (Lomotil)	CNS depression, respiratory depression
Ethylene glycol	Altered mental status, seizures
Hypoglycemics, oral (sulfonylureas and meglitinides)	Hypoglycemia, seizures
Imidazolines (oxymetazoline, tetrahydrozoline)	CNS depression, respiratory depression
Laundry detergent packets (pods)	Airway issues, respiratory distress, altered mental status
Lindane	Seizures
Marijuana (cannabis, THC)	Lethargy, seizures, coma
Monoamine oxidase inhibitors	Hypertension followed by delayed cardiovascular collapse
Methyl salicylate	Tachypnea, metabolic acidosis, seizures
Opioids (especially methadone, buprenorphine)	CNS depression, respiratory depression
Organophosphate pesticides	Cholinergic crisis
Phenothiazines (especially chlorpromazine, thioridazine)	Seizures, dysrhythmias
Sulfonylureas (glipizide, glyburide)	Hypoglycemia
Theophylline	Seizures, dysrhythmias
Tricyclic antidepressants	CNS depression, seizures, dysrhythmias, hypotension

*"Small dose" typically implies one to two pills or 5 mL.
†Lipid-soluble β blockers (e.g., propranolol) are more toxic than water-soluble β blockers (e.g., atenolol).
CNS, Central nervous system.

APPROACH TO THE POISONED PATIENT

The initial approach to the patient with a witnessed or suspected poisoning should be no different than that in any other sick child, starting with stabilization and rapid assessment of the airway, breathing, circulation (pulse, blood pressure), and mental state. In any patient with altered mental status, a serum glucose concentration should be obtained early, and naloxone administration should be considered if there is coma or respiratory depression. A targeted history and physical examination serve as the foundation for a thoughtful differential diagnosis, which can then be further refined through laboratory testing and other diagnostic studies.

History

Obtaining an accurate problem-oriented history is of paramount importance. *Intentional* poisonings (suicide attempts, drug abuse/misuse) are typically more severe than unintentional, exploratory ingestions. In patients without a witnessed exposure, historical features such as age of the child (toddler or adolescent), acute onset of symptoms without prodrome, multisystem organ dysfunction, or high levels of household stress should suggest a possible diagnosis of poisoning. In patients with a witnessed exposure, determining exactly what the child was exposed to and the circumstances surrounding the exposure is crucial to initiating directed therapy quickly. For household and workplace products, names (brand, generic, chemical) and specific ingredients, along with their concentrations, can often be obtained from the labels. PCC specialists can also help to identify possible ingredients and review the potential toxicities of each component. Poison center specialists can also help identify pills based on markings, shape, and color. If referred to the hospital for evaluation, parents should be instructed to bring the products, pills, and/or containers with them to assist with identifying and quantifying the exposure. If a child is found with an unknown pill, a list of all medications in the child's environment, including medications that grandparents, parents, siblings, caregivers, or other visitors might have brought into the house, must be obtained. In the case of an unknown exposure, clarifying where the child was found (e.g., garage, kitchen, laundry room, bathroom, backyard, workplace) can help to generate a list of potential toxins.

Next, it is important to clarify the *timing* of the ingestion and to obtain some estimate of how much of the substance may have been ingested. It is better to overestimate the amount ingested to prepare for the worst-case scenario. Counting pills or measuring the remaining volume of a liquid ingested can sometimes be useful in generating estimates. For inhalational, ocular, or dermal exposures, the concentration of the agent and the length of contact time with the material should be determined, if possible.

Symptoms

Obtaining a description of symptoms experienced after ingestion, including their timing of onset relative to the time of ingestion and their progression, can generate a list of potential toxins and help anticipate the severity of the ingestion. Coupled with physical exam findings, reported symptoms assist practitioners in identifying **toxidromes**, or recognized poisoning syndromes, suggestive of toxicity from specific substances or classes of substances (Tables 94.2 to 94.5).

Past Medical and Developmental History

Underlying diseases can make a child more susceptible to the effects of a toxin. Concurrent drug therapy can also increase toxicity because certain drugs may interact with the toxin. A history of psychiatric illness can make patients more prone to substance abuse, misuse, intentional ingestions, and polypharmacy complications. Pregnancy is a common precipitating factor in adolescent suicide attempts and can influence both evaluation of the patient and subsequent treatment. A developmental history is important to ensure that the exposure history provided is appropriate for the child's developmental stage (e.g., report of 6-month-old picking up a large container of laundry detergent and drinking it should indicate a "red flag").

Social History

Understanding the child's social environment helps to identify potential sources of exposure (caregivers, visitors, grandparents, recent parties or social gatherings) and social circumstances (new baby, parent's illness, financial stress) that might have contributed to the ingestion (suicide or unintentional). Unfortunately, some poisonings occur in the setting of serious neglect or intentional abuse.

Table 94.2 Selected Historical and Physical Findings in Poisoning

SIGN	TOXIN
ODOR	
Bitter almonds	Cyanide
Acetone	Isopropyl alcohol, methanol, paraldehyde, salicylates
Rotten eggs	Hydrogen sulfide, sulfur dioxide, methyl mercaptans (additive to natural gas)
Wintergreen	Methyl salicylate
Garlic	Arsenic, thallium, organophosphates, selenium
Mothballs	Camphor, naphthalene
Freshly mowed hay	Phosgene
Carrots	Water hemlock
Gasoline	Petroleum distillates
OCULAR SIGNS	
Miosis	Opioids (except propoxyphene, meperidine, and pentazocine), organophosphates and other cholinergics, clonidine, phenothiazines (typical antipsychotics), sedative-hypnotics, olanzapine
Mydriasis	Anticholinergics (e.g., antihistamines, TCAs, atropine), sympathomimetics (cocaine, amphetamines, PCP), post–anoxic encephalopathy, opiate withdrawal, cathinones, MDMA
Nystagmus	Anticonvulsants, sedative-hypnotics, alcohols, PCP, ketamine, dextromethorphan
Lacrimation	Organophosphates, irritant gas or vapors
Retinal hyperemia	Methanol
CUTANEOUS SIGNS	
Diaphoresis	Cholinergics (organophosphates), sympathomimetics, salicylates, phencyclidine (PCP), withdrawal syndromes
Alopecia	Thallium, arsenic
Erythema	Boric acid, elemental mercury, cyanide, carbon monoxide, disulfiram, scombroid, anticholinergics, vancomycin
Cyanosis (unresponsive to oxygen)	Methemoglobinemia (e.g., benzocaine, dapsone, nitrites, phenazopyridine), amiodarone, silver
Bullae/blisters	Barbiturates, mustard gas, xylazine, snake, spiders
ORAL SIGNS	
Salivation	Organophosphates, salicylates, corrosives, ketamine, PCP, strychnine
Oral burns	Corrosives, oxalate-containing plants
Gum lines	Lead, mercury, arsenic, bismuth
GASTROINTESTINAL SIGNS	
Diarrhea	Antimicrobials, arsenic, iron, boric acid, cholinergics, colchicine, opioid withdrawal
Hematemesis	Arsenic, iron, caustics, NSAIDs, salicylates
Constipation	Lead
CARDIAC SIGNS	
Tachycardia	Sympathomimetics, anticholinergics, antidepressants, antipsychotics, methylxanthines (theophylline, caffeine), salicylates, cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide), withdrawal (ethanol, sedatives, clonidine, opioids), serotonin syndrome, neuroleptic malignant syndrome, MDMA, cathinones
Bradycardia	β Blockers, calcium channel blockers, digoxin, clonidine, organophosphates, opioids, sedative-hypnotics xylazine
Hypertension	Sympathomimetics, anticholinergics, monoamine oxidase inhibitors, serotonin syndrome, nicotine, caffeine, neuroleptic malignant syndrome, clonidine withdrawal
Hypotension	β Blockers, calcium channel blockers, cyclic antidepressants, iron, antipsychotics, barbiturates, clonidine, opioids, arsenic, amatoxin mushrooms, cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide), snake envenomation, xylazine
RESPIRATORY SIGNS	
Depressed respirations	Opioids, sedative-hypnotics, alcohol, clonidine, marijuana, barbiturates, xylazine
Tachypnea	Salicylates, sympathomimetics, caffeine, metabolic acidosis, carbon monoxide, hydrocarbon aspiration
CENTRAL NERVOUS SYSTEM SIGNS	
Ataxia	Alcohols, anticonvulsants, sedative-hypnotics, lithium, dextromethorphan, carbon monoxide, inhalants
Coma	Opioids, sedative-hypnotics, anticonvulsants, antidepressants, antipsychotics, ethanol, anticholinergics, clonidine, GHB, alcohols, salicylates, barbiturates, hypoglycemics, lead, arsenic, rohypnol, carbon monoxide
Seizures	Sympathomimetics, anticholinergics, antidepressants (especially TCAs, bupropion, venlafaxine), cholinergics (organophosphates), isoniazid, camphor, lindane, salicylates, lead, nicotine, tramadol, water hemlock, withdrawal (especially ethanol), strychnine, cocaine
Delirium/psychosis	Sympathomimetics, anticholinergics, LSD, PCP, hallucinogens, lithium, dextromethorphan, steroids, withdrawal, MDMA, cathinones
Peripheral neuropathy	Lead, arsenic, mercury, organophosphates, nicotine
Hypothermia	Carbon monoxide, opioids, oral hypoglycemics, liquor, sedative-hypnotics
Hyperthermia	Antihistamines, amphetamines, salicylates, antidepressants (TCAs), antipsychotics, serotonin syndrome, neuroleptic malignant syndrome, withdrawal (alcohol, baclofen)

GHB, γ-Hydroxybutyrate; LSD, lysergic acid diethylamide; MDMA, 3,4-methylenedioxymethamphetamine (ecstasy); NSAIDs, nonsteroidal antiinflammatory drugs; PCP, phencyclidine; TCAs, tricyclic antidepressants.

Table 94.3 Recognizable Poison Syndromes ("Toxidromes")

	SIGNS						
TOXIDROME	**VITAL SIGNS**	**MENTAL STATUS**	**PUPILS**	**SKIN**	**BOWEL SOUNDS**	**OTHER**	**POSSIBLE TOXINS**
Sympathomimetic	Hypertension, tachycardia, hyperthermia	Agitation, psychosis, delirium, violence	Dilated	Diaphoretic, flushed	Normal to increased		Amphetamines, cocaine, PCP, bath salts (cathinones), ADHD medication
Anticholinergic	Hypertension, tachycardia, hyperthermia	Agitated, delirium, coma, seizures	Dilated	Dry, hot, flushed	Diminished	Ileus, urinary retention	Antihistamines, TCAs, atropine, jimsonweed
Cholinergic	Bradycardia, BP and temp typically normal	Confusion, coma, fasciculations	Small	Diaphoretic	Hyperactive	Diarrhea, urination, bronchorrhea, bronchospasm, emesis, lacrimation, salivation	Organophosphates (insecticides, nerve agents), carbamates (physostigmine, neostigmine, pyridostigmine) Alzheimer medications, myasthenia treatments
Opioids	Respiratory depression, bradycardia, hypotension, hypothermia	Depression, coma, euphoria	Pinpoint	Normal	Normal to decreased		Methadone, buprenorphine, morphine, oxycodone, heroin, etc.
Sedative-hypnotics	Respiratory depression, HR normal to decreased, BP normal to decreased, temp normal to decreased	Somnolence, coma	Small or normal	Normal	Normal		Barbiturates, benzodiazepines, ethanol xylazine
Serotonin syndrome (similar findings with neuroleptic malignant syndrome)	Hyperthermia, tachycardia, hypertension or hypotension (autonomic instability)	Agitation, confusion, coma	Dilated	Diaphoretic	Increased	Neuromuscular hyperexcitability: clonus, hyperreflexia (lower > upper extremities)	SSRIs, lithium, MAOIs, linezolid, tramadol, meperidine, dextromethorphan
Salicylates	Tachypnea, hyperpnea, tachycardia, hyperthermia	Agitation, confusion, coma	Normal	Diaphoretic	Normal	Nausea, vomiting, tinnitus, ABGs with primary respiratory alkalosis and primary metabolic acidosis; tinnitus or difficulty hearing	Aspirin and aspirin-containing products, methyl salicylate
Withdrawal (sedative-hypnotic)	Tachycardia, tachypnea, hyperthermia	Agitation, tremor, seizure, hallucinosis, delirium tremens	Dilated	Diaphoretic	Increased		Lack of access to ethanol, benzodiazepines, barbiturates, GHB, or excessive use of flumazenil
Withdrawal (opioid)	Tachycardia	Restlessness, anxiety	Dilated	Diaphoretic	Hyperactive	Nausea, vomiting, diarrhea	Lack of access to opioids or excessive use of naloxone

ABGs, Arterial blood gases; ADHD, attention-deficit/hyperactivity disorder; BP, blood pressure; GHB, γ-hydroxybutyrate; HR, heart rate; MAOIs, monoamine oxidase inhibitors; PCP, phencyclidine; SSRIs, selective serotonin reuptake inhibitors; temp, temperature; TCAs, tricyclic antidepressants.

Table 94.4 Mini-Toxidromes

TOXIDROME	SYMPTOMS AND SIGNS	EXAMPLES
α_1-Adrenergic receptor antagonists	CNS depression, tachycardia, miosis	Chlorpromazine, quetiapine, clozapine, olanzapine, risperidone
α_2-Adrenergic receptor agonist	CNS depression, bradycardia, hypertension (early), hypotension (late), miosis	Clonidine, oxymetazoline, tetrahydrozoline, tizanidine, dexmedetomidine
Clonus/myoclonus	CNS depression, myoclonic jerks, clonus, hyperreflexia	Carisoprodol, lithium, serotonergic agents, bismuth, organic lead, organic mercury, serotonin or neuroleptic malignant syndrome
Sodium channel blockers	CNS toxicity, wide QRS	Cyclic antidepressants and structurally related agents, propoxyphene, quinidine/quinine, amantadine, antihistamines, bupropion, cocaine
Potassium channel blockers	CNS toxicity, long QT interval	Antipsychotics, methadone, phenothiazines
Cathinones, synthetic cannabinoids	Hyperthermia, tachycardia, delirium, agitation, mydriases	See Chapter 157.

CNS, Central nervous system.
From Ruha AM, Levine M. Central nervous system toxicity. *Emerg Med Clin North Am.* 2015;32(1):205–221, p. 208.

Table 94.5 Predicting Toxicity from Vital Signs

BRADYCARDIA (PACED)
Propranolol (β blockers), poppies (opioids), propoxyphene, physostigmine
Anticholinesterase drugs, antiarrhythmics
Clonidine, calcium channel blockers
Ethanol or other alcohols
Digoxin, digitalis

TACHYCARDIA (FAST)
Free base or other forms of cocaine, Freon
Anticholinergics, antihistamines, antipsychotics amphetamines, alcohol withdrawal
Sympathomimetics (cocaine, caffeine, amphetamines, phencyclidine [PCP]), solvent abuse, strychnine
Theophylline, tricyclic antidepressants (TCAs), thyroid hormones

HYPOTHERMIA (COOLS)
Carbon monoxide
Opioids
Oral hypoglycemics, insulin
Liquor (alcohols)
Sedative-hypnotics

HYPERTHERMIA (NASA)
Neuroleptic malignant syndrome (NMS), nicotine
Antihistamines, alcohol withdrawal
Salicylates, sympathomimetics, serotonin syndrome
Anticholinergics, antidepressants, antipsychotics

HYPOTENSION (CRASH)
Clonidine, calcium channel blockers
Rodenticides (containing arsenic, cyanide)
Antidepressants, aminophylline, antihypertensives
Sedative-hypnotics (xylazine)
Heroin or other opioids

HYPERTENSION (CT SCAN)
Cocaine
Thyroid supplements
Sympathomimetics
Caffeine
Anticholinergics, amphetamines
Nicotine

RAPID RESPIRATION (PANT)
PCP, paraquat, pneumonitis, phosgene
Acetylsalicylic acid (ASA) and other salicylates
Noncardiogenic pulmonary edema, nerve agents
Toxin-induced metabolic acidosis

SLOW RESPIRATION (SLOW)
Sedative-hypnotics (barbiturates, benzodiazepines, xylazine)
Liquor (alcohols)
Opioids
Weed (marijuana)

From Meehan TJ. Approach to the poisoned patient. In: Walls RM, Hockberger RS, Gausche-Hill M, et al., eds. *Rosen's Emergency Medicine*, 9th ed. Philadelphia: Elsevier; 2018, Box 139.6, p. 1816.

Physical Examination

A targeted physical examination is important to identifying the potential toxin and assessing the severity of the exposure. Initial efforts should be directed toward assessing and stabilizing the airway, breathing, circulation, and mental status. Once the airway is secure and the patient is stable from a cardiopulmonary standpoint, a more extensive physical exam can help to identify characteristic findings of specific toxins or classes of toxins.

In the poisoned patient, key features of the physical exam are vital signs, mental status, pupils (size, reactivity), nystagmus, skin, bowel sounds, and muscle tone. These findings might suggest a toxidrome, which can then guide the differential diagnosis and management.

Laboratory Evaluation

A basic chemistry panel (electrolytes, renal function, glucose) is necessary for all poisoned or potentially poisoned patients. Any patient with acidosis (low serum bicarbonate level on serum chemistry panel) must have an anion gap calculated because of the more specific differential diagnoses associated with an elevated **anion gap metabolic acidosis** (Table 94.6). Patients with a known overdose of acetaminophen should have liver transaminases (alanine transaminase [ALT], aspartate transaminase [AST]) and international normalized ratio (INR) assessed. A serum creatinine kinase level is indicated on any patient with a prolonged "down time" to evaluate for **rhabdomyolysis**. A urine pregnancy test is mandatory for all postpubertal female patients. Based

Table 94.6 Laboratory Clues in Toxicologic Diagnosis

ANION GAP METABOLIC ACIDOSIS (MNEMONIC = MUDPILES CAT)
Methanol, metformin
Uremia
Diabetic ketoacidosis
Propylene glycol
Isoniazid, iron, massive ibuprofen
Lactic acidosis
Ethylene glycol
Salicylates
Cellular asphyxiants (cyanide, carbon monoxide, hydrogen sulfide)
Alcoholic ketoacidosis
Tylenol (clinical significance depends upon presence or absence of liver injury), toluene

ELEVATED OSMOLAR GAP
Alcohols: ethanol, isopropyl, methanol, ethylene glycol

HYPOGLYCEMIA (MNEMONIC = HOBBIES)
Hypoglycemics, oral: sulfonylureas, meglitinides
Other: quinine, unripe ackee fruit
Beta Blockers
Insulin
Ethanol
Salicylates (late)

HYPERGLYCEMIA
Salicylates (early)
Calcium channel blockers
Caffeine

HYPOCALCEMIA
Ethylene glycol
Fluoride

RHABDOMYOLYSIS
Neuroleptic malignant syndrome, serotonin syndrome
Statins
Mushrooms (Tricholoma equestre)
Any toxin causing prolonged immobilization (e.g., opioids, antipsychotics) or excessive muscle activity or seizures (e.g., sympathomimetics)

RADIOPAQUE SUBSTANCE ON KUB (MNEMONIC = CHIPPED)
Chloral hydrate, calcium carbonate
Heavy metals (lead, zinc, barium, arsenic, lithium, bismuth)
Iron
Phenothiazines
Play-Doh, potassium chloride
Enteric-coated pills
Dental amalgam, drug packets

KUB, Kidney-ureter-bladder radiograph.

on the clinical presentation and the presumed poison, additional laboratory tests may also be helpful. Acetaminophen is a widely available medication and a commonly detected co-ingestant with the potential for severe toxicity. There is an effective antidote to acetaminophen poisoning that is time dependent. Given that patients might initially be asymptomatic and might not report or be aware of acetaminophen ingestion, an acetaminophen level should be checked in all patients who present after an intentional exposure or ingestion.

For select intoxications (e.g., salicylates, some anticonvulsants, acetaminophen, iron, digoxin, methanol, ethanol, lithium, ethylene glycol, theophylline, CO, lead), **quantitative blood concentrations** are integral to confirming the diagnosis and formulating a treatment plan. However, for most other exposures, quantitative measurement is not readily available and is not likely to alter management. All intoxicant levels must be interpreted in conjunction with the history. For example, a methanol level of 20 mg/dL 1 hour after ingestion may be nontoxic, whereas a similar level 24 hours after ingestion implies a significant poisoning. In general, patients with multiple or chronic exposures to a drug or other chemical will be more symptomatic at lower drug levels than those with a single acute exposure.

Both the rapid urine drug-of-abuse screens and the more comprehensive drug screens vary widely in their ability to detect toxins and generally add little information to the clinical assessment. This is particularly true if the agent is known and the patient's symptoms are consistent with that agent. If a drug screen is ordered, it is important to know that the components screened for, and the lower limits of detection, vary from laboratory to laboratory. In addition, the interpretation of most drug screens is hampered by many false-positive and false-negative results. Many opiate toxicology screens poorly detect hydrocodone and do not detect the fully synthetic opioids at all (e.g., meperidine, methadone, buprenorphine, fentanyl, carfentanil, furanylfentanyl, tramadol). Several common benzodiazepines (e.g., alprazolam and clonazepam) may not be detected; synthetic cannabinoids or "bath salts" may also be missed. The amphetamine screen, on the other hand, is typically overly sensitive and often is triggered by prescription amphetamines and some over-the-counter cold preparations. As such, the urine drug-of-abuse screen is typically of limited utility for the poisoned patient but may serve a useful function for other providers, including psychiatrists, in their evaluation of the adolescent patient. Urine drug-of-abuse screens are potentially helpful in patients with altered mental status of unknown etiology, persistent unexplained tachycardia, and acute myocardial ischemia or stroke at a young age. These screens can also be useful in the assessment of a neglected or abused child. Consultation with a medical toxicologist can be helpful in interpreting drug screens and directing which specific drug levels or other laboratory analyses might aid in patient management.

In the case of a neglected or allegedly abused child, a positive toxicology screen can add substantial weight to a claim of abuse or neglect. In these cases, and any case with medicolegal implications, any positive screen *must* be followed by confirmatory testing (most commonly via gas chromatography/mass spectroscopy), which is considered the gold-standard measurement for legal purposes.

Additional Diagnostic Testing

An electrocardiogram (ECG) is a quick and noninvasive bedside test that can yield important clues to diagnosis and prognosis. Particular attention should be paid to the ECG intervals (Table 94.7). A widened QRS interval, putting the patient at risk for monomorphic ventricular tachycardia, suggests blockade of fast sodium channels. A widened QTc interval suggests effects at the potassium rectifier channels and portends a risk of torsades de pointes (polymorphic ventricular tachycardia).

Further diagnostic testing is based on the differential diagnosis and pattern of presentation. For example, adjunctive chest radiography may reveal signs of pneumonitis (e.g., hydrocarbon aspiration), noncardiogenic pulmonary edema (e.g., salicylate toxicity), or a foreign body. Abdominal radiography is most helpful in screening for the presence of lead paint chips or other foreign bodies. It may detect a *bezoar* (concretion), demonstrate radiopaque tablets, or reveal drug packets in a "body packer."

Table 94.7 Electrocardiographic Findings in Poisoning

PR INTERVAL PROLONGATION
Digoxin
Lithium
Calcium channel antagonists
β-Antagonists
QRS PROLONGATION
Tricyclic antidepressants
Diphenhydramine
Carbamazepine
Cardiac glycosides
Chloroquine, hydroxychloroquine
Cocaine
Lamotrigine
Quinidine, quinine, procainamide, disopyramide
Phenothiazines
Propoxyphene
Propranolol
Bupropion, venlafaxine (rare)
QTc PROLONGATION*
Amiodarone
Antipsychotics (typical and atypical)
Arsenic
Cisapride
Citalopram
Clarithromycin, erythromycin
Disopyramide, dofetilide, ibutilide
Fluconazole, ketoconazole, itraconazole
Methadone
Pentamidine
Phenothiazines
Sotalol

*This is a select list of important toxins; other medications are also associated with QTc prolongation.

PRINCIPLES OF MANAGEMENT

The principles of management of the poisoned patient are supportive care, decontamination, directed therapy, and enhanced elimination. Few patients meet criteria for all these interventions, although clinicians should consider each option in every poisoned patient so as not to miss a potentially lifesaving intervention. Antidotes are available for relatively few poisons (Tables 94.8 and 94.9), thus emphasizing the importance of meticulous supportive care and close clinical monitoring.

Poison control center personnel are specifically trained to provide expertise in the management of poisoning exposures. Parents should be instructed to call the poison control center **(1-800-222-1222)** for any concerning exposure. PCC specialists can assist parents in assessing the potential toxicity and severity of the exposure. They can further determine which children can be safely monitored at home and which children should be referred to the emergency department for further evaluation and care. Although up to one third of calls to PCCs involve hospitalized patients, 86% of PCC calls for exposures in children <6 years old are managed at home. The AAPCC has generated consensus statements for out-of-hospital management of common ingestions (e.g., acetaminophen, iron, calcium channel blockers [CCBs]) that serve to guide poison center recommendations.

Supportive Care

Careful attention is paid first to the "ABCs" of airway, breathing, and circulation; there should be a low threshold to aggressively manage the airway of a poisoned patient because of the patient's propensity to quickly become comatose. Endotracheal intubation is often the only significant intervention needed in many poisoned patients. An important caveat is the tachypneic patient with a clear lung examination and normal oxygen saturation. This should alert the clinician to the likelihood that the patient is compensating for an acidemia. Paralyzing such a patient and underventilating might prove fatal. If intubation is necessary for airway protection or a tiring patient, a good rule of thumb is to match the ventilatory settings to the patient's preintubation minute ventilation.

Hypotensive poisoned patients often are not hypovolemic, and aggressive fluid resuscitation may lead to fluid overload. If hypotension persists after one to two standard boluses of crystalloid, infusion of a direct-acting vasopressor, such as norepinephrine or epinephrine, is preferred. Dysrhythmias are typically managed in the standard manner. The exceptions are for dysrhythmias caused by agents that block fast sodium channels of the heart, for which boluses of sodium bicarbonate are given; dysrhythmias caused by hydrocarbons, which should be treated with β blockers; and an overall avoidance of amiodarone for toxicologic-induced arrythmias.

Seizures should primarily be managed with agents that potentiate the γ-aminobutyric acid (GABA) complex, such as benzodiazepines or barbiturates. Using sodium channel blockers such as phenytoin is likely to be ineffective and potentially harmful. The goal of supportive therapy is to support the patient's vital functions until the patient can eliminate the toxin. Patients with an elevated creatine phosphokinase (CPK) should be aggressively hydrated with crystalloid, with a goal urine output of 1-2 mL/kg/hr and close monitoring of CPK trend.

Decontamination

Most poisonings in children are from ingestion, although exposures can also occur by inhalational, dermal, and ocular routes (Table 94.10). The goal of decontamination is to minimize absorption of the toxic substance. The specific method employed depends on the properties of the toxin itself and the route of exposure. Regardless of the decontamination method used, the efficacy of the intervention decreases with increasing time since exposure. *Decontamination should not be routinely employed for every poisoned patient.* Instead, careful decisions regarding the utility of decontamination should be made for each patient and should include consideration of the toxicity and pharmacologic properties of the exposure, route of the exposure, time since the exposure, and risks vs benefits of the decontamination method.

Dermal and ocular decontamination begins with removal of any contaminated clothing and particulate matter, followed by flushing of the affected area with tepid water or normal saline (NS). Treating clinicians should wear proper protective gear when performing irrigation. Flushing for a minimum of 10-20 minutes is recommended for most exposures, although some chemicals (e.g., alkaline corrosives) require much longer periods of flushing. Dermal decontamination, especially after exposure to adherent or lipophilic (e.g., organophosphates) agents, should include thorough cleansing with soap and water. Water should *not* be used for decontamination after exposure to highly reactive agents, such as elemental sodium, phosphorus, calcium oxide, and titanium tetrachloride. After an inhalational exposure, decontamination involves moving the patient to fresh air and administering supplemental oxygen if indicated.

Gastrointestinal (GI) decontamination strategies are most likely to be effective in the 1-2 hours after an acute ingestion. GI absorption may be delayed after ingestion of agents that slow GI motility (anticholinergic medications, opioids), massive amounts of pills, sustained-release (SR) preparations, and agents that can form pharmacologic bezoars (e.g., enteric-coated salicylates). GI decontamination more than 2 hours after ingestion may be considered in patients who ingest toxic substances with these properties. However, even rapid institution of GI decontamination with activated charcoal will bind only approximately 30% of the ingested substance. GI decontamination should never supplant excellent supportive care and should not be employed in an unstable or persistently vomiting patient. Methods of GI decontamination include induced emesis with ipecac, gastric lavage, cathartics, activated charcoal, and whole-bowel irrigation (WBI). *Of these, only activated charcoal and WBI are of potential benefit.*

Table 94.8 Common Antidotes for Poisoning

POISON	ANTIDOTE	DOSAGE	ROUTE	ADVERSE EFFECTS, WARNINGS, COMMENTS
Acetaminophen	*N*-Acetylcysteine (Mucomyst)	140 mg/kg loading, followed by 70 mg/kg q4h for 17 additional doses (total of 72 hr)	PO	Vomiting (patient-tailored regimens are the norm)
	N-Acetylcysteine (Acetadote)	150 mg/kg over 1 hr, followed by 50 mg/kg over 4 hr, followed by 100 mg/kg over 16 hr	IV	Anaphylactoid reactions (most commonly seen with loading dose) Higher doses of the infusion are often recommended depending on acetaminophen level or degree of injury
Anticholinergics	Physostigmine	0.02 mg/kg over 5 min; may repeat q5-10 min to 2 mg max	IV/IM	Bradycardia, seizures, bronchospasm *Note:* Relatively contraindicated if conduction delays on ECG.
Benzodiazepines	Flumazenil	0.2 mg over 30 sec; if response is inadequate, repeat q1min to 1 mg max	IV	Agitation, seizures from precipitated withdrawal (doses over 1 mg) **Relatively contraindicated for unknown or polypharmacy ingestions**
β Blockers	Glucagon	0.15 mg/kg bolus followed by infusion of 0.05-0.15 mg/kg/hr	IV	Vomiting, relative lack of efficacy
Calcium channel blockers	Insulin	1 unit/kg bolus followed by infusion of 1-10 units/kg/hr	IV	Hypoglycemia Follow serum potassium and glucose closely.
	Calcium salts	Dose depends on the specific calcium salt	IV	
Carbon monoxide	Oxygen	100% FIO_2 by non-rebreather mask (or ETT if intubated)	Inhalation	Some patients may benefit from hyperbaric oxygen (see text).
Cyanide	Hydroxocobalamin (Cyanokit)	70 mg/kg (adults: 5 g) given over 15 min	IV	Flushing/erythema, nausea, rash, chromaturia, hypertension, headache
Digitalis	Digoxin-specific Fab antibodies (Digibind, DigiFab)	1 vial binds 0.6 mg of digitalis glycoside; #vials = digitalis level × weight in kg/100	IV	Allergic reactions (rare), return of condition being treated with digitalis glycoside
Ethylene glycol, methanol	Fomepizole	15 mg/kg load; 10 mg/kg q12h × 4 doses; 15 mg/kg q12h until ethylene glycol level is <20 mg/dL	IV	Infuse slowly over 30 min If fomepizole is not available, can treat with oral ethanol (80 proof)
Iron	Deferoxamine	Infusion of 15 mg/kg/hr (max: 6 g/24 hr)	IV	Hypotension (minimized by titrating dose up slowly)
Isoniazid (INH)	Pyridoxine	Empirical dosing: 70 mg/kg (max dose = 5 g) If ingested dose is known: 1 g per gram of INH	IV	May also be used for *Gyromitra* mushroom ingestions
Lead and other heavy metals (e.g., arsenic, inorganic mercury)	BAL (dimercaprol)	3-5 mg/kg/dose q4h, for the first day; subsequent dosing depends on the toxin	Deep IM	Local injection site pain and sterile abscess, vomiting, fever, salivation, nephrotoxicity *Caution:* Prepared in peanut oil; contraindicated in patients with peanut allergy
	Calcium disodium EDTA	35-50 mg/kg/day × 5 days; may be given as a continuous infusion or 2 divided doses/day	IV	Vomiting, fever, hypertension, arthralgias, allergic reactions, local inflammation, nephrotoxicity (maintain adequate hydration; follow UA and renal function)
	Dimercaptosuccinic acid (succimer, DMSA, Chemet)	10 mg/kg/dose q8h × 5 days, then 10 mg/kg q12h × 14 days	PO	Vomiting, hepatic transaminase elevation, rash
Methemoglobinemia	Methylene blue, 1% solution	0.1-0.2 mL/kg (1-2 mg/kg) over 5-10 min; may be repeated q30-60 min	IV	Vomiting, headache, dizziness, blue discoloration of urine
Opioids	Naloxone	1 mg if patient not likely to be addicted 0.04-0.4 mg if possibly addicted; repeated as needed; may need continuous infusion; higher and prolonged dosing is required for novel potent opioid overdose	IV, intranasal, IO, IM, nebulized	Acute withdrawal symptoms if given to addicted patients May also be useful for clonidine ingestions (typically at higher doses)

Table 94.8 Common Antidotes for Poisoning—cont'd

POISON	ANTIDOTE	DOSAGE	ROUTE	ADVERSE EFFECTS, WARNINGS, COMMENTS
Organophosphates	Atropine	0.05-0.1 mg/kg repeated q5-10 min as needed	IV/ET	Tachycardia, dry mouth, blurred vision, urinary retention
	Pralidoxime (2-PAM)	25-50 mg/kg over 5-10 min (max: 200 mg/min); can be repeated after 1-2 hr, then q10-12h as needed	IV/IM	Nausea, dizziness, headache, tachycardia, muscle rigidity, bronchospasm (rapid administration)
Salicylates	Sodium bicarbonate	Bolus 1-2 mEq/kg followed by continuous infusion	IV	Follow potassium closely and replace as necessary. Goal urine pH: 7.5-8.0
Sulfonylureas	Octreotide and dextrose	1-2 µg/kg/dose (adults 50-100 µg) q6-8h	IV/SC	
Tricyclic antidepressants	Sodium bicarbonate	Bolus 1-2 mEq/kg; repeated bolus dosing as needed to keep QRS <110 msec	IV	Indications: QRS widening (≥110 msec), hemodynamic instability; follow potassium.

BAL, British antilewisite; DMSA, dimercaptosuccinic acid; ECG, electrocardiogram; F_{IO_2}, fraction of inspired oxygen; EDTA, ethylenediaminetetraacetic acid; ET, endotracheal tube; IO, intraosseous; max, maximum; UA, urinalysis.

Table 94.9 Other Antidotes

ANTIDOTES	TOXIN OR POISON
Latrodectus antivenin	Black widow spider
Botulinum antitoxin	Botulinum toxin
Diphenhydramine and/or benztropine	Dystonic reactions
Calcium salts	Fluoride, calcium channel blockers
Intravenous lipid emulsion (ILE)	Local anesthetics; consider for bupropion, calcium channel blockers, β blockers, and type I antidysrhythmics
Protamine	Heparin
Folinic acid	Methotrexate, trimethoprim, pyrimethamine, methanol
Crotalidae-specific Fab antibodies	Rattlesnake envenomation
Sodium bicarbonate	Sodium channel blockade (tricyclic antidepressants, type 1 antiarrhythmics)

Table 94.10 Toxins Associated with Systemic Toxicity After Dermal Absorption

Aniline dyes
Camphor
Dinitrophenol
Hexachlorophene
Hydrofluoric acid
Lindane (γ-benzene hydrochloride)
Organophosphate insecticide
Nerve agents
Nitrobenzene
Organic mercury
Phenol
Thallium

From Shannon MW. Emergency management of poisoning. In: Shannon MW, Borron SW, Burns MJ, eds. *Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose*, 4th ed. Philadelphia: Saunders; 2007, Box 2A-12, p. 28.

Syrup of Ipecac

Syrup of ipecac contains two emetic alkaloids that work in both the central nervous system (CNS) and locally in the GI tract to produce vomiting. Many studies have failed to document a significant clinical impact from the use of ipecac and have documented multiple adverse events from its use. The AAP, the American Academy of Clinical Toxicology (AACT), and the AAPCC have all published statements in favor of *abandoning the use of ipecac.*

Gastric Lavage

Gastric lavage involves placing a large tube orally into the stomach to aspirate contents, followed by flushing with aliquots of fluid, usually water or NS. Although gastric lavage was used routinely for many years, objective data do not document or support clinically relevant efficacy. This is particularly true in children, in whom only small-bore tubes can be used. Lavage is time-consuming and painful and can induce bradycardia through a vagal response to tube placement. It can delay administration of more definitive treatment (activated charcoal) and under the best circumstances, only removes a fraction of gastric contents. *Thus, in most clinical scenarios, the use of gastric lavage is no longer recommended.*

Single-Dose Activated Charcoal

Activated charcoal is a potentially useful method of GI decontamination. Charcoal is "activated" by heating to extreme temperatures, creating an extensive network of pores that provides a very large adsorptive surface area that many (but not all) toxins will bind to, preventing absorption from the GI tract. Charged molecules (i.e., heavy metals, lithium, iron) and liquids do not bind well to activated charcoal (Table 94.11). Administration should also be avoided after ingestion of a caustic substance, as it can impede subsequent endoscopic evaluation. *Charcoal is most likely to be effective when given within 1 hour of ingestion.* A repeat dose of activated charcoal may be warranted in the cases of ingestion of an extended-release product or, more frequently, with significant salicylate poisoning as a result of its delayed and erratic absorption pattern.

The dose of activated charcoal, with or without sorbitol, is 1g/kg in children or 50-100 g in adolescents and adults. Before administering charcoal, one *must* ensure that the patient's airway is intact or protected and that the patient has a benign abdominal examination. In the awake, uncooperative adolescent or child who refuses to drink the activated charcoal, there is little utility and potential morbidity associated

Table 94.11	Substances Poorly Adsorbed by Activated Charcoal

Alcohols
Caustics: alkalis and acids
Cyanide
Heavy metals (e.g., lead)
Hydrocarbons
Iron
Lithium

with forcing activated charcoal down a nasogastric (NG) tube, and such practice should be avoided. In young children, practitioners can attempt to improve palatability by adding flavorings (chocolate or cherry syrup) or giving the mixture over ice cream. Approximately 20% of children vomit after receiving a dose of charcoal, emphasizing the importance of an intact airway and avoiding administration of charcoal after ingestion of substances that are particularly toxic when aspirated (e.g., hydrocarbons). If charcoal is given through a gastric tube in an intubated patient, placement of the tube should be confirmed before activated charcoal is given. Instillation of charcoal directly into the lungs can have disastrous effects. Constipation is another common side effect of activated charcoal, and in rare cases, bowel perforation has been reported.

Cathartics (sorbitol, magnesium sulfate, magnesium citrate) have been used in conjunction with activated charcoal to prevent constipation and accelerate evacuation of the charcoal-toxin complex. There are no data demonstrating their value and numerous reports of adverse effects from cathartics, such as dehydration and electrolyte imbalance.

Whole-Bowel Irrigation

WBI involves instilling large volumes (25 mL/kg/hr in children or 1-2 L/hr in adolescents) of a polyethylene glycol electrolyte solution (e.g., GoLYTELY) to "wash out" the entire GI tract. This technique may have some success for the ingestion of SR preparations, substances not well adsorbed by charcoal (e.g., lithium, iron), transdermal patches, foreign bodies, and drug packets. WBI is most frequently administered to decontaminate the gut of a child whose abdominal radiograph demonstrates multiple lead paint chips. Careful attention should be paid to assessment of the airway and abdominal exam before initiating WBI. WBI should never be given to a patient with signs of obstruction or ileus or with a compromised airway. Given the rate of administration and volume needed to flush the system, WBI is typically administered by NG tube. WBI is continued until the rectal effluent is clear. If the WBI is for a child with ingested paint chips, the end-point will be clearing of the chips from the bowel based on repeat radiographs. Complications of WBI include vomiting, abdominal pain, and abdominal distention. Bezoar formation might respond to WBI but may also require endoscopy or surgery.

Directed Therapy

Antidotal Therapy

Antidotes are available for relatively few toxins (see Tables 94.8 and 94.9), but early and appropriate use of an antidote is a key element in managing the poisoned patient.

Intravenous Lipid Emulsion Therapy

Intravenous lipid emulsion (ILE) therapy is a potentially lifesaving intervention. ILE therapy sequesters fat-soluble drugs, decreasing their impact at target organs; this is known as a "lipid sink." It also enhances cardiac function by supplying an alternative energy source to a depressed myocardium and acting on calcium channels in the heart, increasing myocardial calcium and thus cardiac function. ILE is most effective as a reversal agent for toxicity from inadvertent intravenous (IV) injection of bupivacaine. Using the same 20% lipid solution used for total parenteral nutrition (TPN), a bolus dose of 1.5 mL/kg is given over 3 minutes, followed by an infusion of 0.25 mL/kg/min until recovery or until a total of 10 mL/kg has been infused. *Lipophilic drugs,* those in which the logarithm of the coefficient describing the partition between two solvents (hydrophobic phase and hydrophilic phase) is >2, have the most potential to be bound by ILE. These include but are not limited to CCBs (verapamil, diltiazem), bupropion, tricyclic antidepressants, and refractory β-blocker overdose. Complications associated with ILE include significant lipemia that interferes with serum laboratory tests, pancreatitis, and acute respiratory distress syndrome (ARDS).

Enhanced Elimination

Enhancing elimination results in increased clearance of a poison that has already been absorbed. It is only useful for a few toxins and in these cases is a potentially lifesaving intervention. Methods of enhanced elimination include urinary alkalinization, hemodialysis, and multidose activated charcoal.

Urinary Alkalinization

Urinary alkalinization enhances the elimination of drugs that are weak acids by forming charged molecules, which then become trapped in the renal tubules. Charged molecules, being polar and hydrophilic, do not easily cross cellular membranes; thus they remain in the renal tubules and are excreted. Urinary alkalinization is accomplished by a continuous infusion of sodium bicarbonate–containing IV fluids, with a goal urine pH of 7.5-8. Alkalinization of the urine is most useful in managing salicylate and methotrexate toxicity. Complications of urinary alkalinization include electrolyte derangements (e.g., hypokalemia, hypocalcemia), fluid overload, and excessive serum alkalinization. Serum pH should be closely monitored and not exceed a pH >7.55. Patients typically unable to tolerate the volumes required for alkalinization are those with heart failure, kidney failure, pulmonary edema, or cerebral edema.

Hemodialysis

Few drugs or toxins are removed by dialysis in amounts sufficient to justify the risks and difficulty of dialysis. Toxins amenable to dialysis have the following properties: low volume of distribution (<1 L/kg) with a high degree of water solubility, low molecular weight, and low degree of protein binding. Hemodialysis may be useful for toxicity from methanol, ethylene glycol, salicylates, theophylline, bromide, lithium, and valproic acid. Hemodialysis is also used to correct severe electrolyte disturbances and acid-base derangements resulting from the ingestion (e.g., severe metformin-associated lactic acidosis).

Multidose Activated Charcoal

Whereas single-dose activated charcoal is used as a method of decontamination, multidose activated charcoal (**MDAC**) can help to enhance the elimination of certain toxins. MDAC is typically given as 0.5 g/kg every 4-6 hr (for four doses). MDAC enhances elimination by two proposed mechanisms: interruption of enterohepatic recirculation and "GI dialysis." The concept of GI dialysis involves using the intestinal mucosa as a dialysis membrane and pulling toxins from the bloodstream back into the intraluminal space, where they are adsorbed to the charcoal. The AACT/European Association of Poisons Centres and Clinical Toxicologists position statement recommends MDAC in managing significant ingestions of carbamazepine, dapsone, phenobarbital, quinine, and theophylline. As with single-dose activated charcoal, contraindications to the use of MDAC include an unprotected airway and a concerning abdominal examination (e.g., ileus, distention, peritoneal signs). Thus the airway and abdominal exam *should be assessed before each dose.* A cathartic (e.g., sorbitol) may be given with the first dose, but it should not be used with subsequent doses because of the risk of dehydration and electrolyte derangements. Although MDAC reduces the serum level of an intoxicant quicker than without MDAC, it has not been shown to have a significant impact on outcome.

SELECT COMPOUNDS IN PEDIATRIC POISONING

See other chapters for drug use (Chapter 157) and environmental health hazards (Chapters 757-763).

Pharmaceuticals

Analgesics

Acetaminophen. Acetaminophen (APAP) is the most widely used analgesic and antipyretic in pediatrics, available in multiple formulations, strengths, and combinations. Consequently, APAP is commonly available in the home, where it can be unintentionally ingested by young children, taken in an intentional overdose by adolescents and adults, or inappropriately dosed in all ages. In the United States, APAP toxicity remains the most common cause of acute liver failure and one of the leading causes of death from oral poisonings.

Pathophysiology. APAP toxicity results from the formation of a highly reactive intermediate metabolite, *N*-acetyl-*p*-benzoquinone imine (NAPQI). In therapeutic use, only a small percentage of a dose (approximately 5%) is metabolized by the hepatic cytochrome P450 enzyme CYP2E1 to NAPQI, which is then immediately conjugated with glutathione to form a nontoxic mercapturic acid conjugate. In overdose, glutathione stores are overwhelmed, and free NAPQI is able to combine with hepatic macromolecules to produce hepatocellular necrosis. The single acute toxic dose of APAP is generally considered to be >200 mg/kg in children and >7.5-10 g in adolescents and adults. Repeated administration of APAP at supratherapeutic doses (>90 mg/kg/day for consecutive days) can lead to hepatic injury or failure in some children, especially in the setting of fever, dehydration, poor nutrition, and other conditions that serve to reduce glutathione stores.

Any child with a history of acute ingestion of >200 mg/kg (unusual in children <6 years) or with an acute intentional ingestion of any amount should be referred to a healthcare facility for clinical assessment and measurement of a serum APAP level.

Clinical and Laboratory Manifestations. Classically, four general stages of APAP toxicity have been described (Table 94.12). In the first 24 hours after ingestion, patients are most frequently asymptomatic, although they may have nonspecific symptoms such as nausea/vomiting. Thus the diagnosis of APAP toxicity cannot be based on clinical symptoms alone, but instead requires consideration of the combination of the patient's history, symptoms, and laboratory findings.

If a toxic ingestion is suspected, a serum APAP level should be measured 4 hours after the reported time of ingestion. For patients who present to medical care more than 4 hours after ingestion, a stat APAP level should be obtained. *APAP levels obtained <4 hours after ingestion, unless "nondetectable," are difficult to interpret and cannot be used to estimate the potential for toxicity.* Other important baseline laboratory tests include hepatic transaminases, bilirubin, renal function tests, and coagulation parameters.

Table 94.12 Classic Stages in Clinical Course of Acetaminophen Toxicity

STAGE	TIME AFTER INGESTION	CHARACTERISTICS
I	0-24 hr	Anorexia, vomiting, malaise Laboratory tests typically normal, except for acetaminophen level
II	24-48 hr	Resolution of earlier symptoms; right upper quadrant abdominal pain and tenderness; elevated hepatic transaminases (aspartate > alanine), INR
III	3-5 days	Peak transaminase elevations; development of liver failure, multiorgan system failure, death *or* recovery begins
IV	4 days to 2 wk	Resolution of liver function abnormalities Clinical recovery precedes histologic recovery

Treatment. When considering the treatment of a patient poisoned or potentially poisoned with APAP, and after assessment of the ABCs, it is helpful to place the patient into one of the following four categories:

1. Prophylactic. These patients have a normal AST. If the APAP level is known and the ingestion is within 24 hours of the level being drawn, treatment decisions are based on where the level falls on the Rumack-Matthew nomogram (Fig. 94.1). Any patient with a serum APAP level in the possible or probable hepatotoxicity range per the nomogram should be treated with *N*-acetylcysteine (NAC). This nomogram is only intended for use in patients who present within 24 hours of a single *acute* APAP ingestion with a known time of ingestion. If treatment is recommended, they should receive NAC. Food and Drug Administration (FDA)–approved treatment regimens include a 21-hour protocol for IV administration and a 72-hour protocol for oral administration. Several shorter dosing regimens have been described and may be considered in consultation with a toxicologist. Regardless of treatment duration, serial transaminases and APAP level should be monitored. If the AST becomes elevated while receiving NAC, the patient moves into the next category of treatment (hepatic injury, see later). If AST remains normal but APAP is still present, NAC should be continued until the level is nondetectable. In the case of a patient with a documented APAP level, normal AST, and an unknown time of ingestion, treatment should ensue until the level is undetectable, with normal transaminases.

The importance of instituting therapy with either IV or oral NAC *no later than 8 hours from the time of ingestion* cannot be overemphasized.

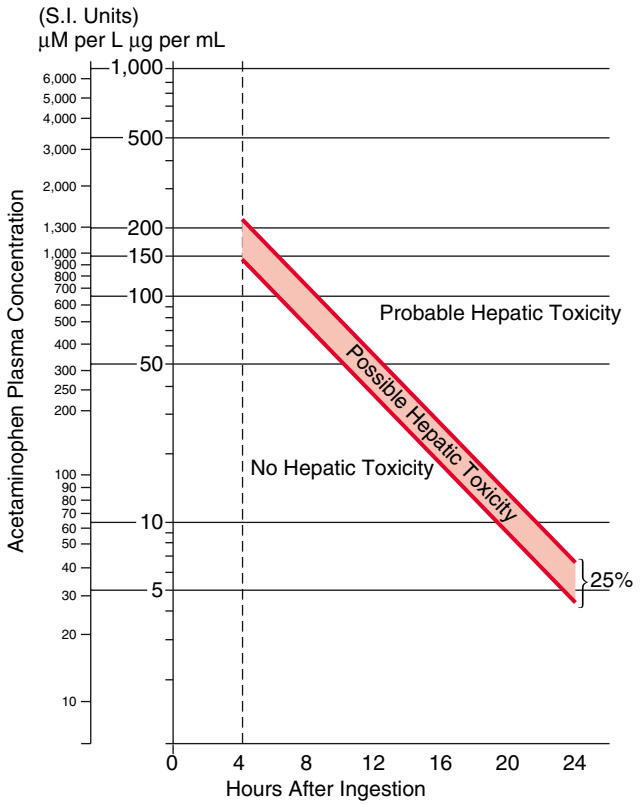

Fig. 94.1 Rumack-Matthew nomogram for acetaminophen poisoning, a semilogarithmic plot of plasma acetaminophen concentrations vs time. *Cautions for the use of this chart:* The time coordinates refer to time after ingestion; serum concentrations obtained before 4 hours are not interpretable, and the graph should be used only in relation to a single acute ingestion with a known time of ingestion. This nomogram is not useful for chronic exposures or unknown time of ingestion and should be used with caution in the setting of co-ingestants that slow gastrointestinal motility. The *lower solid line* is typically used in the United States to define toxicity and direct treatment, whereas the *upper line* is generally used in Europe. *(From Rumack BH, Hess AJ, eds.* Poisindex, *Denver: Micromedix; 1995. Adapted from Rumack BH, Matthew H. Acetaminophen poisoning and toxicity. Pediatrics.1975;55:871–876.)*

No patient, regardless of the size of the ingestion, who receives NAC within 8 hours of overdose should die from liver failure. The longer from the 8 hour-mark that the initiation of therapy is delayed, the greater the risk of acute liver failure. Any patient presenting close to or beyond the 8-hour mark after an APAP overdose should be empirically started on NAC pending laboratory results.

2. Hepatic Injury. These patients exhibit evidence of hepatocellular necrosis, manifested first as elevated liver transaminases (usually AST first, then ALT), followed by a rise in the INR. Any patient in this category requires therapy with NAC (IV or oral). When to discontinue therapy in the clinically well-appearing patient remains controversial, but in general NAC can be discontinued when the transaminases and INR have peaked and are declining significantly (they do not need to be normal). Most patients' liver enzymes will peak 3-4 days after their ingestion.

3. Acute Liver Failure. The King's College criteria are used to determine which patients should be referred for consideration of liver transplant. These criteria are met when a patient exhibits either acidemia (serum pH <7.3) after adequate fluid resuscitation or all three of the following: coagulopathy (INR >6.5), renal dysfunction (creatinine >3.4 mg/dL), and grade III or IV hepatic encephalopathy (see Chapter 412). A serum lactic acid >3 mmol/L (after IV fluids) adds to both sensitivity and specificity of the criteria to predict death without liver transplant. The degree of transaminase elevation does not factor into this decision-making process.

4. Repeated Supratherapeutic Ingestion. APAP is particularly prone to unintentional overdose through the ingestion of multiple medications containing the drug or simply because people assume it to be safe at any dose. Ingestion of amounts significantly greater than the recommended daily dose for several days or more puts one at risk for liver injury. Because the Rumack-Matthew nomogram is not helpful in this scenario, a conservative approach is taken. In the asymptomatic patient, if the AST is normal and the APAP is <10 μg/mL, no therapy is indicated. A normal AST and an elevated APAP warrant NAC dosing for at least long enough for the drug to metabolize while the AST remains normal. An elevated AST puts the patient in the "hepatic injury" category previously described. A patient presenting with symptoms (i.e., right upper quadrant pain, vomiting, jaundice) should be empirically started on NAC pending laboratory results.

NAC is available in oral and IV forms, and both are considered equally efficacious (see Table 94.8 for the dosing regimens of the oral and IV form). The IV form is used in patients with intractable vomiting, those with evidence of hepatic failure, and pregnant patients. Oral NAC has an unpleasant taste and smell and can be mixed in a soft drink or fruit juice or given by NG tube to improve tolerability of the oral regimen. Administration of IV NAC (as a standard 3% solution to avoid administering excess free water, typically in 5% dextrose), especially the initial loading dose, is associated in some patients with the development of anaphylactoid reactions (non–immunoglobulin E mediated). These reactions are typically managed by stopping the infusion; treating with diphenhydramine, albuterol, and/or epinephrine as indicated; and restarting the infusion at a slower rate once symptoms have resolved. IV NAC is also associated with mild elevation in measured INR (range: 1.2-1.5) because of laboratory interference. IV dosing, however, delivers less medication to the liver compared with the oral regimen. As a result, many toxicologists now recommend higher doses of the IV formulation in patients with large overdoses. Transaminases, synthetic function, and renal function should be followed at least daily while the patient is being treated with NAC. Patients with worsening hepatic function or clinical status might benefit from more frequent laboratory monitoring. A patient-tailored approach is now the norm for when to stop NAC therapy, for deciding whom to refer for transplantation evaluation, and often for the dose of IV NAC in patients with either very high APAP levels or signs of injury. Consultation with the regional PCC and medical toxicologist can help streamline the care of these patients, ultimately shortening their length of stay with potentially improved outcomes.

Adjunctive Therapies

Although activated charcoal binds acetaminophen, risks of vomiting associated with large APAP overdoses as well as the likelihood of co-ingestion that may affect mental status must be considered. Activated charcoal may be considered in the first 1-2 hours after ingestion in an alert patient, but its use should not have bearing on the need for NAC. Similarly, hemodialysis is not routinely used in APAP overdose but may be indicated in massive ingestions in consultation with a toxicologist.

Salicylates. The incidence of salicylate poisoning in young children has declined dramatically since APAP and ibuprofen replaced aspirin as commonly used analgesics and antipyretics in pediatrics. However, salicylates remain widely available not only in aspirin-containing products but also in antidiarrheal medications, topical agents (e.g., keratolytics, sports creams), oil of wintergreen, and some herbal products. Oil of wintergreen contains 5 g of salicylate in 5 mL, meaning ingestion of very small volumes of this product has the potential to cause severe toxicity.

Pathophysiology. Salicylates lead to toxicity by interacting with a wide array of physiologic processes, including direct stimulation of the respiratory center, uncoupling of oxidative phosphorylation, inhibition of the tricarboxylic acid cycle, and stimulation of glycolysis and gluconeogenesis. The acute toxic dose of salicylates is generally considered to be >150 mg/kg. More significant toxicity is seen after ingestions of >300 mg/kg, and severe, potentially fatal, toxicity is described after ingestions of >500 mg/kg.

Clinical and Laboratory Manifestations. Salicylate ingestions are classified as acute or chronic, and acute toxicity is much more common in pediatric patients. Early signs of **acute salicylism** include nausea, vomiting, diaphoresis, and tinnitus. Moderate salicylate toxicity can manifest as tachypnea and hyperpnea, tachycardia, and altered mental status. The tachycardia largely results from marked insensible losses from vomiting, tachypnea, diaphoresis, and uncoupling of oxidative phosphorylation. Thus careful attention should be paid to volume status and early volume resuscitation in the significantly poisoned patient. Signs of severe salicylate toxicity include mild hyperthermia, coma, and seizures. **Chronic salicylism** can have a more insidious presentation, and patients can show marked toxicity (e.g., altered mental status, noncardiogenic pulmonary edema, acidemia) at significantly lower salicylate levels than in acute toxicity.

Classically, laboratory values from a patient poisoned with salicylates reveal a primary respiratory alkalosis and a primary, elevated anion gap metabolic acidosis. Early in the course of acute salicylism, respiratory alkalosis dominates and the patient is alkalemic. As the respiratory stimulation diminishes, the patient will move toward acidemia. Hyperglycemia (early) and hypoglycemia (late) have been described. Abnormal coagulation studies and acute kidney injury may be seen but are not common.

Serial serum salicylate levels should be closely monitored (every 2-4 hours initially) until they are consistently downtrending (three consecutive levels <30 mg/dL and decreasing by at least 10–20% on each subsequent measurement). Salicylate absorption in overdose is unpredictable and erratic, especially with an enteric-coated product, and levels can rapidly increase into the highly toxic range, even many hours after the ingestion. The Done nomogram is of poor value and should not be used. Serum and urine pH and electrolytes should be followed closely. An APAP level should be checked in any patient who intentionally overdoses on salicylates, because APAP is a common co-ingestant, and people often confuse or combine their nonprescription analgesic medications. Salicylate toxicity can cause a noncardiogenic pulmonary edema, especially in chronic overdose; consequently, a chest radiograph is recommended in any patient in respiratory distress.

Treatment. For the patient who presents soon after an acute ingestion, initial treatment should include gastric decontamination with activated charcoal. Salicylate pills occasionally form bezoars, which should be suspected if serum salicylate concentrations continue to rise many hours after ingestion or are persistently elevated despite appropriate management. Gastric decontamination is typically not useful after chronic exposure.

Initial therapy focuses on aggressive volume resuscitation and prompt initiation of sodium bicarbonate therapy in the symptomatic patient, even before obtaining serum salicylate levels. Therapeutic salicylate levels are 10-20 mg/dL, and levels >30 mg/dL warrant treatment.

The primary mode of therapy for salicylate toxicity is **urinary alkalinization**. Urinary alkalinization enhances the elimination of salicylates by converting salicylate to its ionized form, "trapping" it in the renal tubules. In addition, maintaining an alkalemic serum pH decreases CNS penetration of salicylates because charged particles are less able to cross the blood-brain barrier. Alkalinization is achieved by administration of a sodium bicarbonate infusion at approximately two times maintenance fluid rates. *The goals of therapy include a urine pH of 7.5-8, a serum pH of 7.45-7.55, and decreasing serum salicylate levels.* In general, the lower the patient's serum pH, the greater the relative amount of salicylate in the uncharged, nonpolar form and the greater amount of salicylate penetration of the blood-brain barrier. Salicylate penetration of the brain leads to severe consequences such as cerebral edema; therefore maintaining alkalemia is imperative. Careful attention should also be paid to serial potassium levels in any patient on a bicarbonate infusion, because potassium will be driven intracellularly, and hypokalemia impairs alkalinization of the urine. For these reasons, potassium is often added to the bicarbonate drip. Repeat doses of charcoal may be beneficial because of the often delayed and erratic absorption of aspirin. Parenteral glucose should be provided to any salicylate-poisoned patients with altered mental status because they may have CNS hypoglycemia (i.e., neuroglycopenia) not seen in a peripheral serum glucose test.

In patients with severe toxicity, hemodialysis may be required. Indications for dialysis include severe acid-base abnormalities (specifically severe acidosis and acidemia), a rising salicylate level (despite adequate decontamination and properly alkalinized urine), pulmonary edema or respiratory failure, cerebral edema, seizures, hepatic failure, and renal failure. Serum salicylate concentrations alone are not a clear indicator of the need for dialysis and should always be interpreted along with the clinical status of the patient.

Ibuprofen and Other Nonsteroidal Antiinflammatory Drugs (NSAIDs). Ibuprofen and other NSAIDs are often involved in unintentional and intentional overdoses because of their widespread availability and common use as analgesics and antipyretics. Fortunately, serious effects after acute NSAID overdose are rare because of their wide therapeutic index.

Pathophysiology. NSAIDs inhibit prostaglandin synthesis by reversibly inhibiting the activity of cyclooxygenase (COX), the primary enzyme responsible for the biosynthesis of prostaglandins. In therapeutic use, side effects include GI irritation, reduced renal blood flow, and platelet dysfunction. To minimize these side effects, NSAID analogs have been developed that are more specific for the inducible form of COX (the COX-2 isoform) than the constitutive form (COX-1). However, overdose of the more selective COX-2 inhibitors (e.g., celecoxib [Celebrex]) is treated the same as overdose of nonspecific COX inhibitors (e.g., ibuprofen) because at higher doses, COX-2–selective agents lose their COX inhibitory selectivity.

Ibuprofen, the primary NSAID used in pediatrics, is well tolerated, even in overdose. In children, acute doses of <200 mg/kg rarely cause toxicity, but ingestions of >400 mg/kg can produce more serious effects, including altered mental status and metabolic acidosis.

Clinical and Laboratory Manifestations. Symptoms usually develop within 4-6 hours of ingestion and resolve within 24 hours. If toxicity does develop, it is typically manifested as nausea, vomiting, and abdominal pain. Although GI bleeding and ulcers have been described with chronic use, they are rare in the setting of acute ingestion. After massive ingestions, patients can develop marked CNS depression, anion gap metabolic acidosis, renal insufficiency, and (rarely) respiratory depression. Seizures have also been described, especially after overdose of mefenamic acid. Specific drug levels are not readily available, nor do they inform management decisions. Renal function studies, acid-base balance, complete blood count (CBC), and coagulation parameters should be monitored after very large ingestions. Co-ingestants, especially APAP, should be ruled out after any intentional ingestion.

Treatment. Supportive care, including use of antiemetics and acid blockade as indicated, is the primary therapy for NSAID toxicity. Decontamination with activated charcoal should be considered if a patient presents within 1-2 hours of a potentially toxic ingestion. There is no specific antidote for this class of drugs. Given the high degree of protein binding and excretion pattern of NSAIDs, none of the modalities used to enhance elimination is particularly useful in managing these overdoses. Unlike in patients with salicylate toxicity, urinary alkalinization is not helpful for NSAID toxicity. Patients who develop significant clinical signs of toxicity should be admitted to the hospital for ongoing supportive care and monitoring. Patients who remain asymptomatic for 4-6 hours after ingestion do not require further medical care but may need psychiatric assessment if their ingestion was intentional.

Prescription Opioids. Opioids are a frequently abused class of medications in both IV and oral forms. The opioid epidemic gripping the United States and other countries is discussed in Chapter 157. Two specific oral opioids, buprenorphine and methadone, merit mention because of potential life-threatening toxicity in toddlers with ingestion of even one pill. Both agents are used in managing opioid use disorder, although **buprenorphine** is the drug of choice. **Methadone** is also widely used in the treatment of chronic pain, meaning multiday prescriptions can be filled. Other agents commonly available in the home include morphine, oxycodone, and hydrocodone, as they are frequently prescribed to patients after injuries or surgical procedures. All of these drugs are also readily available for illicit purchase and potential abuse. Opioids are of great potential toxicity to small children if not dosed appropriately, especially buprenorphine because of its long half-life and high potency.

Pathophysiology. Opioids are well absorbed via multiple routes, including the GI tract, which is the most common route of accidental overdose in young children. At therapeutic dosing, opioids are typically absorbed within a few hours, but absorption may be slowed and symptoms prolonged in overdose. Individual opioids cross the blood-brain barrier to varying degrees. Opioids all undergo hepatic metabolism with renal excretion.

Methadone is a lipophilic synthetic opioid with potent agonist effects at μ-opioid receptors, leading to both its desired analgesic effects and undesired side effects, including sedation, respiratory depression, and impaired GI motility. Methadone is thought to cause QTc interval prolongation through interactions with the human ether-a-go-go–related gene (hERG)–encoded potassium rectifier channel. Its duration of effect for pain control averages only about 8 hours, whereas the dangerous side effects can occur up to 24 hours from the last dose and longer after overdose. Methadone has an average half-life >25 hours, which may be extended to >50 hours in overdose.

Suboxone is a combination of buprenorphine, a potent opioid with partial agonism at μ-opioid receptors and weak antagonism at κ-opioid receptors, and naloxone. Naloxone has poor oral bioavailability but is included in the formulation to discourage diversion for IV use, during which it can precipitate withdrawal. Suboxone is formulated for buccal or sublingual administration; consequently, toddlers can absorb significant amounts of drug even by sucking on a tablet. Buprenorphine has an average half-life of 37 hours.

Clinical and Laboratory Manifestations. In children, opioid ingestions can manifest with the classic toxidrome of respiratory depression, sedation, and miosis. Signs of more severe toxicity can include bradycardia, hypotension, and hypothermia. Many opioids have clinical features that are unique to their chemical structure (Table 94.13). Even in therapeutic use, methadone is associated with a prolonged QTc interval and risk of torsades de pointes. Accordingly, an ECG should be part of the initial evaluation after ingestion of methadone or any unknown opioid. Many prescription opioids, including methadone and buprenorphine, are not detected on routine urine opiate screens, although some centers have added a separate urine methadone screen. Levels of many drugs can be measured, although this is rarely done clinically and is seldom helpful in the acute setting. An exception may be in the cases involving concerns about neglect or abuse, at which point urine for gas chromatography/mass spectroscopy, the legal gold standard, should be sent to confirm and document the presence of the drug.

Treatment. Patients with significant respiratory depression or CNS depression should be treated with the opioid antidote **naloxone**

Table 94.13 Clinical Properties of Select Prescription Opioids

CLINICAL EFFECT	OPIOID
QRS widening, sodium channel blockade	Propoxyphene
QT widening, potassium channel blockade	Methadone
Seizures	Propoxyphene, meperidine
Serotonin syndrome	Meperidine, methadone, tramadol
Hearing loss, ototoxicity	Methadone, hydrocodone

Modified from Nikolaides JK, Thompson TM. Opioids. In: Walls RM, Hockberger RS, Gausche-Hill M, et al., eds. *Rosen's Emergency Medicine*, 9th ed. Philadelphia: Elsevier; 2018, Table 156.2, p. 1944.

(see Table 94.8). In pediatric patients who are not chronically taking opioids, the full reversal dose of 1-2 mg should be used. In contrast, opioid-dependent patients should be treated with smaller initial doses (0.04-0.4 mg), which can then be repeated as needed to achieve the desired clinical response, avoiding abrupt induction of withdrawal. Because the half-life of many opioids is much longer than that of naloxone, patients can require multiple doses of naloxone. These patients may benefit from a continuous infusion of naloxone, typically started at two thirds of the reversal dose per hour and titrated to maintain an adequate respiratory rate and level of consciousness. Patients who have ingested methadone should be placed on a cardiac monitor and have serial ECGs to monitor for the development of a prolonged QTc interval. If a patient does develop a prolonged QTc, management includes close cardiac monitoring, repletion of electrolytes (potassium, calcium, and magnesium), and having a defibrillator readily available should the patient develop torsades de pointes.

Given the potential for clinically significant and prolonged toxicity, any toddler who has ingested methadone, even if asymptomatic, should be admitted to the hospital for at least 24 hours of monitoring. Duration of observation after ingestion of other opioids depends on the half-life and dose of the agent ingested. All such cases should be discussed with a PCC or medical toxicologist before determining disposition.

Cardiovascular Medications

β-Adrenergic Receptor Blockers. β Blockers competitively inhibit the action of catecholamines at the β-adrenergic receptor. Therapeutically, β blockers are used for a variety of conditions, including hypertension, coronary artery disease, tachydysrhythmias, anxiety disorders, migraines, essential tremor, and hyperthyroidism. Because of its lipophilicity and blockade of fast sodium channels, **propranolol** is considered to be the most toxic member of the β-blocker class. Overdoses of water-soluble β blockers (e.g., atenolol) are associated with milder symptoms.

Pathophysiology. In overdose, β blockers decrease chronotropy and inotropy in addition to slowing conduction through atrioventricular (AV) nodal tissue. Clinically, these effects are manifested as bradycardia, hypotension, and heart block. Patients with reactive airway disease can experience bronchospasm as a result of blockade of β_2-mediated bronchodilation. β_2 Blockers interfere with glycogenolysis and gluconeogenesis, which can sometimes lead to hypoglycemia, especially in patients with poor glycogen stores (e.g., toddlers).

Clinical and Laboratory Manifestations. Toxicity typically develops within 6 hours of ingestion, although it may be delayed after ingestion of sotalol or SR preparations. The most common features of severe poisoning are bradycardia and hypotension. Lipophilic agents, including propranolol, can enter the CNS and cause altered mental status, coma, and seizures. Overdose of β blockers with sodium channel–blocking properties (e.g., propranolol) can cause QRS interval widening and ventricular dysrhythmias.

Evaluation after β-blocker overdose should include an ECG, frequent reassessments of hemodynamic status, and blood glucose. Serum levels of β blockers are not readily available for routine clinical use and are not useful in management of the poisoned patient.

Treatment. In addition to supportive care and GI decontamination as indicated, **glucagon** is theoretically the preferred antidote of choice for β-blocker toxicity (see Table 94.8). Glucagon stimulates adenylate cyclase and increases levels of cyclic adenosine monophosphate (cAMP) independent of the β-receptor. Glucagon is typically given as a bolus and, if this is effective, followed by a continuous infusion. In practice, glucagon is often only marginally effective, limited by its proemetic effects, especially at the high doses typically required. Other useful interventions include calcium, vasopressors, and high-dose insulin. Seizures are managed with benzodiazepines, and QRS widening should be treated with sodium bicarbonate. Lipid emulsion therapy (discussed earlier) may be considered in patients with signs of shock who do not respond to conventional treatments. Children who ingest one or two water-soluble β blockers are unlikely to develop toxicity and can typically be discharged to home if they remain asymptomatic over a 6-hour observation period. Children who ingest SR products, highly lipid-soluble agents, and sotalol require longer periods of observation before safe discharge. Any symptomatic child should be admitted for ongoing monitoring and directed therapy.

Calcium Channel Blockers. CCBs are used for a variety of therapeutic indications and have the potential to cause severe toxicity, even after exploratory ingestions. Specific agents include verapamil, diltiazem, and the dihydropyridines (e.g., amlodipine, nifedipine). Of these, diltiazem and verapamil are the most dangerous in overdose because of their higher lipophilicity and direct cardiac suppressant effects.

Pathophysiology. CCBs antagonize L-type calcium channels, inhibiting calcium influx into myocardial and vascular smooth muscle cells. Verapamil works primarily by slowing inotropy and chronotropy and in therapeutic dosing has no effect on systemic vascular resistance (SVR). Diltiazem has effects both on the heart and the peripheral vasculature. The dihydropyridines exclusively diminish SVR. Verapamil and diltiazem can significantly diminish myocardial contractility and conduction, with diltiazem also lowering SVR. By contrast, dihydropyridines will decrease the SVR, leading to vasodilation and reflex tachycardia, although this receptor selectivity may be lost after a large overdose. Because the same L-type calcium channels blocked by CCBs are also on the pancreatic islet cells, any patient significantly poisoned with a CCB may develop hyperglycemia.

Clinical and Laboratory Manifestations. Overdoses of CCBs lead to hypotension, accompanied by bradycardia, normal heart rate, or even tachycardia, depending on the agent. Other rhythm disturbances, including AV block, bundle branch blocks, QT prolongation, and junctional rhythms, may also be seen. A common feature of CCB overdose is the patient exhibiting profound hypotension with preserved consciousness.

Initial evaluation should include an ECG, continuous and careful hemodynamic monitoring, and rapid measurement of serum glucose levels. Both the absolute degree of hyperglycemia and the percentage increase in serum glucose have been correlated with the severity of CCB toxicity in adults. The development of hyperglycemia can even precede the development of hemodynamic instability. Blood levels of CCBs are not readily available and are not useful in guiding therapy.

Treatment. Once initial supportive care has been instituted, GI decontamination should begin with activated charcoal as appropriate. WBI may be beneficial in a stable patient after ingestion of an SR product. Calcium channel blockade in the smooth muscles of the GI tract can lead to greatly diminished motility; thus any form of GI decontamination should be undertaken with careful attention to serial abdominal exams.

Calcium salts, administered through a peripheral IV line as calcium gluconate or a central line as calcium chloride, help to overcome blocked calcium channels. **High-dose insulin euglycemia therapy** is considered the antidote of choice for CCB toxicity. An initial bolus of 1 unit/kg of regular insulin is followed by an infusion at 1-10 units/kg/hr (see Table 94.8). The main mechanism of high-dose insulin euglycemia

is to improve the metabolic efficiency of a poisoned heart that needs carbohydrates for energy (instead of the usual free fatty acids) but has minimal circulating insulin. Blood glucose and serum potassium levels should be closely monitored, and supplemental dextrose may be necessary to maintain euglycemia. Mild hypokalemia may be tolerated, as this reflects intracellular shifting of potassium rather than whole-body potassium depletion; severe hypokalemia (e.g., K <2.8 mEq/L) is treated with IV potassium supplementation.

Additional therapies include judicious IV fluid boluses and vasopressors (often in very high doses). Cardiac pacing is rarely of value. Lipid emulsion therapy (discussed earlier) is a potentially lifesaving intervention, especially for patients poisoned with the more lipid-soluble CCBs, verapamil and diltiazem. In extreme cases an intraaortic balloon pump or extracorporeal membrane oxygenation (ECMO) are potential treatments. Given the potential for profound and sometimes delayed toxicity in toddlers after ingestion of one or two CCB tablets, hospital admission and 12-24 hours of monitoring for all of these patients is strongly recommended.

α_2-Adrenergic Agonists. Although originally intended for use as antihypertensives, the number of **clonidine** and **guanfacine** prescriptions in the pediatric population has greatly increased because of its reported efficacy in the management of attention-deficit/hyperactivity disorder (ADHD), tic disorders, and other behavioral disorders. With this increased use has come a significant rise in pediatric ingestions and therapeutic misadventures. Clonidine is available in pill and transdermal patch forms, while guanfacine is available in pill form.

Pathophysiology. Clonidine, along with the closely related agent guanfacine, is a centrally acting α_2-adrenergic receptor agonist with a very narrow therapeutic index. Agonism at central α_2 receptors decreases sympathetic outflow, producing lethargy, bradycardia, hypotension, and apnea. Toxicity can develop after ingestion of only one pill or after sucking on or swallowing a discarded transdermal patch. Even a "used" transdermal patch might contain as much as one third to one half the original amount of drug.

Clinical and Laboratory Manifestations. The most common clinical manifestations of toxicity are lethargy, miosis, and bradycardia. Hypotension, respiratory depression, and apnea may be seen in severe cases. Very early after ingestion, patients may be hypertensive in the setting of agonism at peripheral α-receptors and resulting vasoconstriction. Symptoms develop relatively soon after ingestion and typically resolve within 24 hours. Serum clonidine concentrations are not readily available and are of no clinical value in the acute setting. Although signs of clinical toxicity are common after clonidine or guanfacine overdose, death is extremely unusual.

Treatment. Given the potential for significant toxicity, most young children warrant referral to a healthcare facility for evaluation after unintentional ingestions of α_2-adrenergic agonists. Gastric decontamination is of minimal value because of the small quantities ingested and the rapid onset of serious symptoms. Aggressive supportive care is imperative and is the cornerstone of management. Naloxone, often in high doses (i.e., 10 mg IV), has shown variable efficacy in treating clonidine toxicity. Other potentially useful therapies include atropine, IV fluid boluses, and vasopressors. Symptomatic children should be admitted to the hospital for close cardiovascular and neurologic monitoring. Also, in a patient receiving chronic clonidine or guanfacine therapy, rapid discontinuation of the drug, or even missing one or two doses, could lead to potentially dangerous elevations in blood pressure.

Digoxin. Digoxin is a cardiac glycoside extracted from the leaves of *Digitalis lanata*. Other natural sources of cardiac glycosides include *Digitalis purpura* (foxglove), *Nerium oleander* (oleander), *Convallaria majalis* (lily of the valley), Siberian ginseng, and the *Bufo marinus* toad. Therapeutically, digoxin is used in the management of heart failure and some supraventricular tachydysrhythmias. Acute overdose can occur in the setting of dosing errors (especially in younger children), unintentional or intentional medication ingestion, or exposure to plant material containing digitalis glycosides. Regarding exposure to such plants, toxicity is unusual unless the poison is concentrated in the form of a tea. Chronic toxicity can result from alteration of the digoxin dose, alteration in digoxin clearance as a result of renal impairment, or drug interactions.

Pathophysiology. Digoxin blocks the sodium-potassium adenosine triphosphatase (Na^+,K^+-ATPase) pump, leading to intracellular loss of K^+ and gain of Na^+ and calcium (Ca^{2+}). This resulting rise in Ca^{2+} available to the contractile myocardium improves inotropy. An increase in myocardial automaticity leads to subsequent atrial, nodal, and ventricular ectopy. Digoxin also affects nodal conduction, leading to a prolonged refractory period, decreased sinus node firing, and slowed conduction through the AV node. Impaired Na^+/K^+ exchange can lead to elevated serum K^+. Overall, digoxin overdose manifests as a combination of slowed or blocked conduction and increased ectopy.

Clinical and Laboratory Manifestations. Nausea and vomiting are common initial symptoms of acute digoxin toxicity, manifesting within 6 hours of overdose. Cardiovascular manifestations include bradycardia, heart block, and a wide variety of dysrhythmias. CNS manifestations consist of lethargy, confusion, and weakness. Chronic toxicity (which is rare in children) is more insidious and may also manifest as altered mental status and visual disturbances.

Initial assessment should include an ECG, serum digoxin level, serum potassium, and kidney function tests. The serum digoxin level should be assessed at least 6 hours after ingestion and carefully interpreted in the setting of clinical symptoms, because the digoxin level alone does not entirely reflect the severity of intoxication. In acute ingestions, serum potassium is an independent marker of morbidity and mortality, with levels >5 mEq/L predicting poor outcomes. In chronic toxicity, serum K^+ concentration is less useful as a prognostic marker and may be altered from concomitant use of diuretics or renal dysfunction.

Digoxin has a very narrow therapeutic index. Therapeutic plasma digoxin concentrations are 0.5-2 ng/mL; a level >2 ng/mL is considered toxic, and >6 ng/mL is considered potentially fatal (in chronic poisonings). As with all serum levels of intoxicants, one must be careful to interpret the number in the context of the scenario of the poisoning and the status of the patient. An acutely poisoned patient may have a very high serum level and minimal to no symptoms, whereas a patient with a chronic or acute-on-chronic poisoning will usually be sicker with a lower serum level.

Numerous drug interactions affect plasma digoxin concentrations. Medications known to increase serum digoxin concentrations include the macrolides, erythromycin and clarithromycin, spironolactone, verapamil, amiodarone, and itraconazole.

Treatment. Initial treatment includes good general supportive care and gastric decontamination with activated charcoal if the ingestion was recent. An antidote for digoxin, digoxin-specific antibody fragments (Fab: Digibind or DigiFab) is available (see Table 94.8). Fab fragments bind free digoxin in both the intravascular and the interstitial spaces to form a pharmacologically inactive complex that is subsequently eliminated renally. Indications for administration of Fab fragments in children are listed in Table 94.14. Atropine is potentially useful in managing symptomatic bradycardia. Although dogma states that patients on digoxin with severe hyperkalemia and QRS widening on the ECG should not receive calcium salts, this has not been supported in the literature. Once stabilized, consultation with a cardiologist is recommended in the management of patients receiving chronic digoxin therapy, because administration of Fab fragments can lead to recurrence of the patient's underlying dysrhythmias or dysfunction.

Iron. Historically, iron was a common cause of childhood poisoning deaths. However, preventive measures such as childproof packaging have significantly decreased the rates of serious iron toxicity in young children. Iron-containing products remain widely available, with the most potentially toxic being adult iron preparations and prenatal vitamins. The severity of an exposure is related to the amount of *elemental iron* ingested. Ferrous sulfate contains 20% elemental iron, ferrous gluconate 12%, and ferrous fumarate 33%. Multivitamin preparations and children's vitamins rarely contain enough elemental iron to cause significant toxicity. Furthermore, nonionic forms of iron, carbonyl iron and iron polysaccharide, also do not cause significant toxicity.

Pathophysiology. Iron is directly corrosive to the GI mucosa, leading to hematemesis, melena, ulceration, and potential perforation.

Table. 94.14 Indications for Administration of Digoxin Antibody Fragments in Children

Ingestion of >0.1-0.3 mg/kg *or* steady-state digoxin concentration >5 ng/mL *PLUS* one of the following: • Rapidly progressive symptoms • Signs of cardioactive steroid intoxication • Potentially life-threatening dysrhythmias or conduction blocks • Serum potassium concentration >5 mEq/L
Co-ingestion of other cardiotoxic drugs with additive or synergistic toxicity
Ingestion of plant known to contain cardioactive steroids *plus* severe dysrhythmias

Modified from Cole JB. Cardiovascular drugs. In: Walls RM, Hockberger RS, Gausche-Hill M, et al., eds. *Rosen's Emergency Medicine*, 9th ed. Philadelphia: Elsevier; 2018, Box 147.4, p. 1879.

Table 94.15 Clinical Manifestations of Iron Toxicity After Acute Overdose

PHASE	CLINICAL FEATURES
1. Gastrointestinal (6 hr)	Vomiting Diarrhea Hematemesis Hematochezia
2. Latent (6-24 hr)	Resolution of GI symptoms Tachycardia Acidosis Depressed mental status
3. Systemic (12-24 hr)	Return of GI symptoms Acidosis Leukocytosis Coagulopathy Renal failure Lethargy or coma Cardiovascular collapse
4. Hepatic (2-5 days)	Fulminant liver failure Coagulopathy
5. Obstructive (3-6 wk)	Pyloric or bowel scarring Obstruction

GI, Gastrointestinal.
Modified from Theobald JL, Mycyk MB. Iron and heavy metals. In: Walls RM, Hockberger RS, Gausche-Hill M, et al., eds. *Rosen's Emergency Medicine*, 9th ed. Philadelphia: Elsevier; 2018, Table 151.2, p. 1913.

Early iron-induced hypotension is caused by massive volume losses, increased permeability of capillary membranes, and vasodilation mediated by free iron. Iron accumulates in tissues, including the Kupffer cells of the liver and myocardial cells, leading to hepatotoxicity, coagulopathy, and cardiac dysfunction. Metabolic acidosis develops in the setting of hypotension, hypovolemia, and iron's direct interference with oxidative phosphorylation and the Krebs cycle. Pediatric patients who ingest >40 mg/kg of elemental iron should be referred to medical care for evaluation, although moderate to severe toxicity is typically seen with ingestions >60 mg/kg.

Clinical and Laboratory Manifestations. Iron toxicity is described in five often-overlapping stages (Table 94.15). Patients who do not develop GI symptoms within 6 hours of ingestion are unlikely to develop serious toxicity. Symptomatic patients and patients with a large exposure by history should have serum iron levels drawn 4-6 hours after ingestion. Serum iron concentrations of <350 µg/dL 4-8 hours after ingestion suggest a low risk of significant toxicity, concentrations of 350-500 µg/dL suggest moderate toxicity, and concentrations of >500 µg/dL indicate that significant toxicity is likely. Additional laboratory evaluation in the ill patient should include arterial or venous blood gas, lactate, CBC, serum glucose level, liver transaminases, and coagulation parameters. Careful attention should be paid to the patient's hemodynamic status. An abdominal radiograph may reveal the presence of iron tablets, although not all formulations of iron are radiopaque.

Treatment. Close clinical monitoring, combined with aggressive supportive and symptomatic care, is essential to the management of iron poisoning. Activated charcoal does not adsorb iron, and WBI remains the decontamination strategy of choice. **Deferoxamine**, a specific chelator of iron, is the antidote for moderate to severe iron intoxication (see Table 94.8). Indications for deferoxamine treatment include a serum iron concentration >500 µg/dL or moderate to severe symptoms of toxicity (e.g., acidosis), regardless of serum iron concentration. Deferoxamine is preferably given by continuous IV infusion at 15 mg/kg/hr. Hypotension is a common side effect of deferoxamine infusion and is managed by slowing the rate of the infusion and administering fluids and vasopressors as needed. Prolonged deferoxamine infusion (>24 hours) has been associated with pulmonary toxicity (ARDS) and *Yersinia* sepsis. The deferoxamine-iron complex can color the urine reddish ("vin rosé"), although the degree of this coloration should not guide therapy. Deferoxamine is typically continued until clinical symptoms and acidosis resolve. Consultation with a PCC or medical toxicologist can yield guidelines for discontinuing deferoxamine.

Oral Hypoglycemics

Oral medications used in the management of type 2 diabetes include sulfonylureas, biguanides (e.g., metformin), thiazolidinediones, and meglitinides. Of these, only the sulfonylureas and meglitinides have the potential to cause profound hypoglycemia in both diabetic and nondiabetic patients. These classes of medications are widely prescribed and thus readily available. In toddlers, unintentional ingestion of a single sulfonylurea tablet can lead to significant toxicity.

Pathophysiology. Sulfonylureas work primarily by enhancing endogenous insulin secretion. In binding to the sulfonylurea receptor, these drugs induce closure of K^+ channels, leading to membrane depolarization, opening of Ca^{2+} channels, and stimulation of Ca^{2+}-mediated insulin release. Even in therapeutic use, the duration of hypoglycemic action can last up to 24 hours.

Clinical and Laboratory Manifestations. Hypoglycemia and symptoms associated with hypoglycemia are the primary clinical manifestations of sulfonylurea toxicity. These signs and symptoms can include diaphoresis, tachycardia, lethargy, irritability, coma, seizures, and even focal neurologic findings. As with other hyperinsulinemic states, sulfonylurea overdoses are associated with a nonketotic hypoglycemia. In the majority of patients, hypoglycemia develops within 6 hours of ingestion but can be delayed up to 16-18 hours after ingestion. Toddlers are particularly susceptible to hypoglycemia during an overnight fast.

Treatment. Patients with symptomatic hypoglycemia should be promptly treated with dextrose. In patients with mild symptoms, oral dextrose may be sufficient. However, patients with severe symptoms or profound hypoglycemia should be treated with a bolus of IV dextrose. Continuous dextrose infusions and repeated IV dextrose boluses should be avoided, if possible, because this can stimulate further insulin release and lead to recurrent and prolonged hypoglycemia. Instead, the preferred antidote for persistent (i.e., requiring ≥2 doses of IV dextrose) sulfonylurea toxicity is **octreotide** (see Table 94.8). Octreotide is a somatostatin analog that inhibits insulin release. Octreotide is given IV or subcutaneously (SC), typically in doses of 1-2 µg/kg (50-100 µg in teens or adults) every 6-8 hours.

Given the potential for significant hypoglycemia, toddlers with witnessed or suspected sulfonylurea ingestions should be admitted to the hospital for serial glucose measurements for at least 12 hours, including an overnight fast. Patients of any age who develop hypoglycemia are also candidates for admission, given the prolonged duration of hypoglycemic activity with these medications. Prophylactic IV dextrose infusions are not recommended because they can mask the symptoms of toxicity and stimulate further insulin secretion. Patients who require IV dextrose and/or octreotide should be monitored until they can demonstrate euglycemia for at least 8 hours off all therapy.

With the increasing numbers of adolescents with type 2 diabetes, pediatricians should be familiar with the toxic effects of **metformin** as well. Although metformin does not cause hypoglycemia, its association with lactic acidosis is well documented (metformin-associated lactic acidosis [MALA]). This state typically arises after a large overdose in which the agent interferes with the liver's ability to clear lactic acid. Dangerously high serum lactate levels can result, leading to hemodynamic instability. Hemodialysis is usually the best option for patients with severe MALA.

Psychiatric Medications: Antidepressants

Selective serotonin reuptake inhibitors (SSRIs; e.g., fluoxetine, sertraline, paroxetine, citalopram) are the most commonly prescribed class of antidepressants. This trend largely results from their wide therapeutic index and more favorable side effect profile compared with older agents such as tricyclic antidepressants (TCAs; amitriptyline, clomipramine, desipramine, doxepin, nortriptyline, imipramine) and monoamine oxidase inhibitors (MAOIs). Other agents include the serotonin-norepinephrine reuptake inhibitors (SNRIs; e.g., venlafaxine) and atypical antidepressants (e.g., bupropion).

Tricyclic Antidepressants. Although now prescribed less often for depression, TCAs remain in use for a variety of other conditions, including chronic pain syndromes, enuresis, ADHD, and obsessive-compulsive disorder. TCAs can cause significant toxicity in children, even with ingestion of one or two pills (10-20 mg/kg).

Pathophysiology. TCAs achieve their desired antidepressant effects primarily through blockade of norepinephrine and serotonin reuptake. TCAs have complex interactions with other receptor types. Antagonism at muscarinic acetylcholine receptors leads to clinical features of the anticholinergic toxidrome. Antagonism at peripheral α-receptors leads to hypotension and syncope. Key to the toxicity of TCAs is their ability to block fast sodium channels, leading to impaired cardiac conduction and arrhythmias.

Clinical and Laboratory Manifestations. Cardiovascular and CNS symptoms dominate the clinical presentation of TCA toxicity. Symptoms typically develop within 1-2 hours of ingestion, and serious toxicity usually manifests within 6 hours of ingestion. Patients can have an extremely rapid progression from mild symptoms to life-threatening dysrhythmias. Patients often develop features of **anticholinergic toxidrome**, including delirium, mydriasis, dry mucous membranes, tachycardia, hyperthermia, urinary retention, and slow GI motility. CNS toxicity can include lethargy, coma, myoclonic jerks, and seizures. Sinus tachycardia is the most common cardiovascular manifestation of toxicity; however, patients can also develop widening of the QRS complex, premature ventricular contractions, and ventricular dysrhythmias. Refractory hypotension is a poor prognostic indicator and is the most common cause of death in TCA overdose.

An ECG can help determine the diagnosis and prognosis of the TCA-poisoned patient (Fig. 94.2; see Table 94.7). A QRS duration >100 msec identifies patients who are at risk for seizures and cardiac arrhythmias. An R wave in lead aVR of ≥3 mm is also an independent predictor of toxicity. Both ECG parameters are superior to measured serum TCA concentrations for identifying patients at risk for serious toxicity, and obtaining levels is rarely helpful in management of the acutely ill patient.

Treatment. Initial attention should be directed to supporting vital functions, including airway and ventilation as needed. Gastric decontamination can be accomplished with activated charcoal in patients who are alert and cooperative without clinical signs of toxicity. Treating clinicians should obtain an ECG as soon as possible and follow serial ECGs to monitor for progression of toxicity. The four primary effects described next may be seen at the bedside.

1. Altered Mental State. TCA-poisoned patients can become deeply comatose relatively quickly, so careful and prompt attention to the airway and placement of an endotracheal tube is of paramount importance.

2. Widened QRS on ECG. TCAs, as well as other agents (e.g., diphenhydramine, cocaine), block the fast Na^+ channels on the myocardial cells, slowing the upstroke of the QRS complex. Because the effect on Na^+ channels is greatest within the first 6 hours, frequent ECGs (i.e., every 20-30 minutes) during this period are important. As the QRS approaches 160 msec, the risk of the patient developing monomorphic ventricular tachycardia rises to 30%. Sodium, usually in the form of sodium bicarbonate, is the antidote of choice. *Indications for sodium bicarbonate include a QRS duration ≥100 msec, ventricular dysrhythmias, and hypotension.* Multiple bolus doses of sodium bicarbonate, 1-2 mEq/kg each, may be needed to narrow the QRS to <100 msec. Some prefer then to place the patient on an infusion of sodium bicarbonate, but this may not be necessary if the QRS is carefully monitored after the initial doses and repeat bolus dosing is provided as needed during the first 6-12 hours. Hypertonic (3%) saline and/or lipid emulsion therapy may be beneficial in refractory cases.

3. Hypotension. A direct-acting vasopressor such as norepinephrine or epinephrine is the agent of choice. Boluses of IV crystalloid fluids should be used with caution to prevent fluid overload.

4. Seizures. Seizures are relatively common and likely the result of multiple factors, including increased synaptic monoamines, sodium channel inhibition, and GABA receptor antagonism. Seizures are typically brief and should be treated with agents targeting the GABA-receptor complex in the brain. Benzodiazepines are the agent of choice.

Asymptomatic children should receive appropriate decontamination and have continuous cardiac monitoring and serial ECGs for at least 6 hours after exposure. If any manifestations of toxicity develop, the child should be admitted to a monitored setting. Children who remain

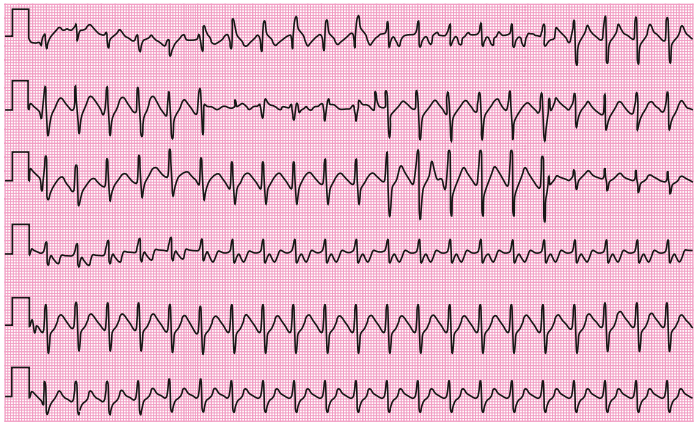

Fig. 94.2 Electrocardiographic findings in tricyclic antidepressant toxicity. Note the tachycardia, widened QRS interval (144 msec), and prominent R wave in lead aVR. These findings are consistent with blockade of fast sodium channels.

completely asymptomatic with normal serial ECGs may be candidates for discharge after that monitoring period.

Selective Serotonin Reuptake Inhibitors. In overdose, SSRIs are considerably less toxic than TCAs. SSRIs are unlikely to cause significant toxicity in exploratory ingestions. Some data suggest that initiating SSRI therapy is associated with an increased risk of suicidal ideation and behavior (see Chapter 40).

Pathophysiology. SSRIs selectively block the reuptake of serotonin in the CNS. In contrast to TCAs and atypical antidepressants, SSRIs do not directly interact with other receptors.

Clinical and Laboratory Manifestations. Although seen more often after therapeutic use or overdose of several serotonergic agents in combination, **serotonin syndrome** has also been described in ingestion of SSRIs alone (Table 94.16). Clinically, serotonin syndrome describes a spectrum of altered mental status, autonomic instability, fever, and neuromuscular hyperactivity (hyperreflexia, tremors, clonus in lower extremities > upper extremities) (Table 94.17). One or all of these signs may be present to varying degrees.

In overdose, the principal clinical manifestations of toxicity are sedation and tachycardia. Cardiac conduction abnormalities (primarily QTc prolongation) and seizures have been described in significant overdoses, especially after ingestions of citalopram. An ECG should be part of the initial assessment after SSRI ingestion. Serum creatine kinase (CK) levels are almost always elevated in a patient with clinically significant serotonin syndrome. The differential diagnosis includes neuroleptic malignant syndrome and malignant hyperthermia (Table 94.18).

Table 94.16 Drugs Associated with Serotonin Syndrome

DRUG TYPE	DRUGS
Selective serotonin reuptake inhibitors	Sertraline, fluoxetine, fluvoxamine, paroxetine, citalopram, escitalopram
Antidepressant drugs	Trazodone, nefazodone, buspirone, clomipramine, venlafaxine, amitriptyline, nortriptyline
Monoamine oxidase inhibitors	Phenelzine, moclobemide, clorgyline, isocarboxazid
Anticonvulsants	Valproate
Analgesics	Meperidine, fentanyl, tramadol, pentazocine
Antiemetic agents	Ondansetron, granisetron, metoclopramide
Antimigraine drugs	Sumatriptan
Bariatric medications	Sibutramine
Antibiotics	Linezolid (a monoamine oxidase inhibitor), ritonavir (through inhibition of cytochrome P450 enzyme isoform 3A4)
Nonprescription cough and cold remedies	Dextromethorphan
Drugs of abuse	Methylenedioxymethamphetamine (MDMA, "ecstasy"), lysergic acid diethylamide (LSD), 5-methoxydiisopropyltryptamine ("foxy methoxy"), Syrian rue (contains harmine and harmaline, both monoamine oxidase inhibitors)
Dietary supplements and herbal products	Tryptophan, *Hypericum perforatum* (St. John's wort), *Panax ginseng* (ginseng)
Other	Lithium

From Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med.* 2005;352:1112–1120.

Treatment. Initial management includes a careful assessment for signs and symptoms of serotonin syndrome and an ECG. Most patients simply require supportive care and observation until their mental status improves and tachycardia, if present, resolves. Management of serotonin syndrome is directed by the severity of symptoms; possible therapeutic interventions include benzodiazepines in mild cases and intubation, sedation, and paralysis in patients with severe manifestations (e.g., significant hyperthermia). Because agonism at the 5-HT_{2A} serotonin receptor is thought to be primarily responsible for the development of serotonin syndrome, use of the 5-HT_{2A} receptor antagonist cyproheptadine has been considered a possible antidote; the efficacy of cyproheptadine in managing serotonin syndrome is not well-supported by the available literature. Furthermore, cyproheptadine should be used with caution when the diagnosis is unclear, as it can worsen anticholinergic toxicity.

Atypical Antidepressants. The atypical antidepressant class includes agents such as venlafaxine and duloxetine (SNRIs), bupropion (dopamine, norepinephrine, and some serotonin reuptake blockade), and trazodone (serotonin reuptake blockade and peripheral α-receptor antagonism). The variable receptor affinities of these agents lead to some distinctions in their clinical manifestations and management.

Clinical and Laboratory Manifestations. In overdose, **venlafaxine** and other SNRIs have been associated with cardiac conduction defects, including QRS and QTc prolongation, and seizures (typically within a few hours of ingestion). **Bupropion** warrants special consideration because it is one of the most common etiologies of toxicant-induced seizures in the United States. After ingestion of SR or extended-release (ER) preparations of bupropion, seizures can occur as late as 18-20 hours after ingestion. In addition, bupropion can cause tachycardia, agitation, and QRS and QTc prolongation. These cardiac effects are thought to result from a reduction in cardiac intracellular coupling caused by inhibition at gap junctions in the heart. Mortality results from not only status epilepticus but also the cardiac conduction disturbances causing ventricular tachycardia and dysrhythmias. In addition to sedation and signs of serotonin excess, trazodone overdose may be associated with hypotension from blockade of peripheral α-receptors.

Treatment. Management is directed at clinical signs and symptoms. QRS and QTc interval prolongation after bupropion poisoning is typically resistant to the standard treatments of sodium bicarbonate and magnesium. Seizures are often brief and self-limited but can be treated with benzodiazepines if necessary. A patient poisoned with bupropion who shows unstable hemodynamics with prolonged ECG intervals or persistent seizure activity after the appropriate therapies should be discussed with a toxicologist for possible lipid emulsion therapy. Because of the potential for delayed seizures, asymptomatic patients who have ingested an SR preparation of bupropion should be admitted to a monitored setting for at least 20-24 hours. Trazodone-associated hypotension typically responds to fluids, though it can require vasopressors in extreme cases.

Monoamine Oxidase Inhibitors. Although now rarely used therapeutically, MAOIs remain important agents given their potential for serious and delayed toxicity. Ingestions of only one or two pills (6 mg/kg) are associated with toxicity in children. Clinical manifestations initially include hypertension, hyperthermia, tachycardia, muscle rigidity, and seizures, followed up to 24 hours later by hemodynamic instability and cardiovascular collapse. *Any child who ingests a MAOI should be admitted to a monitored setting for at least 24 hours, regardless of symptoms.* Management includes blood pressure control, cooling and benzodiazepines for hyperthermia, serial monitoring of CK and renal function, and fluid and vasopressor therapy for hemodynamic instability.

Psychiatric Medications: Antipsychotics

Clinicians are increasingly prescribing antipsychotic medications in the pediatric population. Antipsychotics are usually classified as either typical or atypical. In general, typical agents are associated with more side effects and toxicity than the atypical agents.

Table 94.17 Spectrum of Symptoms of Serotonergic Toxicity

SEVERITY	NEUROMUSCULAR EXCITATION	ALTERED MENTAL STATUS	AUTONOMIC DYSFUNCTION
Mild	Hyperreflexia Tremor Myoclonus	Anxiety Restlessness Insomnia	Diaphoresis Mydriasis Tachycardia
Moderate	Opsoclonus Spontaneous or inducible clonus	Agitation	Hypertension Hyperthermia (<40°C [<104°F]) Hyperactive bowel sounds Diarrhea, nausea, vomiting
Severe	Rigidity Respiratory failure Tonic-clonic seizure	Coma Delirium Confusion	Severe hyperthermia (≥40°C [≥104°F]) Dynamic blood pressure

Adapted from Wang RZ, Vashistha V, Kaur S, Houchens NW. Serotonin syndrome: Preventing, recognizing, and treating it. *Clev Clinic J Med*. 2016;83(11):810–817, Table 2, p. 812.

Table 94.18 Signs and Symptoms of Neuroleptic Malignant Syndrome (NMS)/Serotonin Syndrome/Malignant Hyperthermia

CLINICAL FEATURES	NMS	SEROTONIN SYNDROME	MALIGNANT HYPERTHERMIA
Triggering agent	Neuroleptic	Proserotonergic agent	Succinylcholine or inhaled anesthetic
Onset	Slow (hours to days)	Fast (minutes to hours)	Very fast to fast (minutes to hours)
Duration	Long (days to weeks)	Short (1-2 days)	Short (1-3 days)
Agitation	Sometimes	Yes	No
Confusion	Yes	Sometimes	Unusual
Hyperactivity	No	Yes	No
Bradykinesia/stupor	Yes	No	Unusual
Myoclonus	No	Yes	No
Shivering	No	Yes/sometimes	No
Tremor	Sometimes	Yes	No
Pupils	Mid-sized	Large	Not specific
Hyperreflexia	No	Yes (especially lower extremities)	No
Rigidity	Severe	Sometimes	Severe
Rigidity type	Extrapyramidal (lead pipe)	Pyramidal (clasp-knife)	Generalized
Hyperpyrexia	Yes	Yes	Severe
Tachypnea	Yes	Yes	Yes
Tachycardia	Yes	Yes	Yes (severe)
Hypertension	Sometimes	Yes	Sometimes
Leukocytosis	Yes	Uncommon	Not typical
Elevated creatine phosphokinase	Severe	Mild	Severe

Adapted from Gillman PK. The serotonin syndrome and its treatment. *J Psychopharmacol* 1999;13:100–109; Gillman K; Serotonin toxicity www.psychotropical.com/serotonin-toxicity; and Wappler F, Fiege M, Schulte am Esch J. Pathophysiological role of the serotonin system in malignant hyperthermia. *Br J Anaesth*. 2001;87(5):794–798.

Pathophysiology. *Typical,* or "traditional," antipsychotics (haloperidol, droperidol, thioridazine, chlorpromazine, fluphenazine) are characterized by their antagonism at D_2 dopamine receptors. In therapeutic use, these agents are associated with extrapyramidal symptoms, tardive dyskinesia, and, rarely, development of **neuroleptic malignant syndrome (NMS)** (see Table 94.18). The *atypical* agents (aripiprazole, clozapine, quetiapine, risperidone, ziprasidone) were developed with relatively less dopamine (D_2-receptor) antagonism in the nigrostriatum to avoid these side effects and improve their efficacy in managing the "negative" symptoms of schizophrenia. Instead, these agents have complex and varied interactions with multiple receptor types, including α-receptors, serotonin receptors, muscarinic acetylcholine receptors, and histamine receptors.

Clinical and Laboratory Manifestations. Typical antipsychotic toxicity usually includes sedation, tachycardia, and QTc prolongation. Patients can present with acute dystonia, akathisia, and NMS, although these are seen less frequently in acute overdoses than in therapeutic use. The phenothiazines (e.g., thioridazine) can cause widening of the QRS interval from blockade of fast sodium channels. Clinically, NMS can be difficult to distinguish from serotonin syndrome.

Although the presentation of atypical antipsychotic toxicity can vary based on the receptor affinities of the specific agent, sedation, tachycardia, and QTc prolongation are common. Peripheral α-receptor blockade (e.g., with quetiapine) is associated with hypotension. In therapeutic use, clozapine is associated with agranulocytosis. Atypical antipsychotics that antagonize muscarinic acetylcholine receptors (e.g., olanzapine, quetiapine) may cause symptoms of anticholinergic toxidrome.

Diagnostic testing should include an ECG. Patients with hyperthermia or muscle rigidity should have a serum CK level sent to monitor

for possible rhabdomyolysis. CBC is indicated in patients with fever to evaluate for neutropenia. Antipsychotic levels are not readily available and are not helpful in managing acute poisoning.

Management. Initial management involves assessing and supporting vital functions. In some patients, CNS depression may be so profound as to require intubation for airway control. Acute dystonia is treated with diphenhydramine and benztropine. Management of NMS includes aggressive supportive care, IV fluids, active cooling, benzodiazepines, and bromocriptine or dantrolene in severe cases. QTc prolongation is managed with repletion of electrolytes (especially calcium, magnesium, and potassium), continuous cardiac monitoring, prevention of bradycardia (overdrive pacing, isoproterenol, atropine), and defibrillation if the patient develops torsades de pointes. Delirium associated with anticholinergic toxicity may be managed with benzodiazepines, and a specific antidote (physostigmine) can be considered in consultation with a medical toxicologist (see Table 94.8). Seizures typically are well controlled with benzodiazepines. Hypotension usually responds to boluses of IV fluids, although vasopressor therapy is necessary in some patients.

Household Products

Caustics

Caustics include acids and alkalis as well as a few common oxidizing agents (see Chapter 373). Strong acids and alkalis can produce severe injury even in small-volume ingestions.

Pathophysiology. **Alkalis** produce a *liquefaction necrosis,* allowing further tissue penetration of the toxin and setting the stage for possible perforation. **Acids** produce a *coagulative necrosis,* which limits further tissue penetration, although perforation can still occur. The severity of the corrosive injury depends on the pH and concentration of the product and the length of contact time with the product. Agents with a pH of <2 or >12 are most likely to produce significant injury.

Clinical Manifestations. Ingestion of caustic materials can produce injury to the oral mucosa, posterior pharynx, vocal cords, esophagus, and stomach. Patients can have significant esophageal injury even in the absence of visible oral burns. Symptoms include pain, drooling, vomiting, abdominal pain, and difficulty swallowing or refusal to swallow. Laryngeal injury can manifest as stridor and respiratory distress, necessitating intubation. In the most severe cases, patients can present in shock after perforation of a hollow viscus. Circumferential burns of the esophagus are likely to cause strictures when they heal, which can require repeated dilation or surgical correction and long-term follow-up for neoplastic changes in adulthood. Caustic exposures on the skin or in the eye can cause significant tissue damage.

Treatment. Initial treatment of caustic exposures includes thorough removal of the product from the skin or eye by flushing with water. *Emesis and lavage are contraindicated.* Activated charcoal should not be used because it does not bind these agents, interferes with endoscopy, and can predispose the patient to vomiting and subsequent aspiration. Stridor or other signs of respiratory distress should alert the provider to the need for a thorough evaluation of the airway for potential intubation or surgical airway management. Endoscopy can be performed within 12-24 hours of ingestion in *symptomatic* patients or those with suspected injury based on history and known characteristics of the ingested product. The role of endoscopy is purely diagnostic and is contraindicated in patients with severe oropharyngeal injury with edema and necrosis, evidence of perforation, respiratory distress, or hemodynamic instability, as these patients instead require immediate surgical consultation. Expectant management with a period of nothing by mouth (NPO) and proton pump inhibitor therapy is likely appropriate for most *asymptomatic* patients. Corticosteroids or prophylactic antibiotics are not beneficial.

Pesticides

Cholinesterase-Inhibiting Insecticides. The most commonly used insecticides in agriculture are **organophosphates** and **carbamates**; both are inhibitors of cholinesterase enzymes: acetylcholinesterase (AChE), pseudocholinesterase, and erythrocyte AChE. Most pediatric poisonings occur as the result of unintentional exposure to insecticides in and around the home or farm. The chemical warfare weapons known as "nerve agents" are also organophosphate compounds with a similar mechanism of action but much greater potency.

Pathophysiology. Organophosphates and carbamates produce toxicity by binding to and inhibiting AChE, preventing the degradation of acetylcholine (ACh) and resulting in its accumulation at nerve synapses. If left untreated, organophosphates form an irreversible bond to AChE, permanently inactivating the enzyme. This process, called *aging,* occurs over a variable period, depending on the characteristics of the specific organophosphate. A period of weeks to months is required to regenerate inactivated enzymes. In contrast, carbamates form a temporary bond with the enzymes, typically allowing reactivation of AChE within 24 hours.

Clinical and Laboratory Manifestations. Clinical manifestations of organophosphate and carbamate toxicity relate to ACh accumulation at peripheral nicotinic and muscarinic synapses and in the CNS. Symptoms of carbamate toxicity are usually less severe than those seen with organophosphates. A commonly used mnemonic for the symptoms of cholinergic excess at muscarinic receptors is **DUMBBELS**: diarrhea/defecation, urination, miosis, bronchorrhea/bronchospasm, bradycardia, emesis, lacrimation, and salivation. Nicotinic signs and symptoms include muscle weakness, fasciculation, tremors, hypoventilation (diaphragm weakness), hypertension, tachycardia, and dysrhythmias. Severe manifestations include coma, seizures, shock, arrhythmias, and respiratory failure.

Diagnosis of poisoning is based primarily on history and physical exam findings. Red blood cell cholinesterase and pseudocholinesterase activity levels can be measured in the laboratory. These are only helpful when compared with the patient's known baseline. As such, these assessments are typically limited to farmworkers undergoing ongoing occupational surveillance.

Treatment. Basic decontamination should be performed, including washing all exposed skin with soap and water and immediately removing all clothing. Activated charcoal is unlikely to be of benefit because these are liquids that are rapidly absorbed. Basic supportive care should be provided, including fluid and electrolyte replacement, intubation, and ventilation if necessary. The use of succinylcholine for rapid sequence intubation should be avoided because the same cholinesterase enzymes that are poisoned metabolize this neuromuscular blocking agent, leading to prolonged paralysis.

Two antidotes are useful in treating cholinesterase inhibitor poisoning: atropine and pralidoxime (see Table 94.8). **Atropine**, which antagonizes the muscarinic ACh receptor, is useful for both organophosphate and carbamate intoxication. Often, large doses of atropine must be administered by intermittent bolus or continuous infusion to control symptoms. Atropine dosing is primarily targeted to drying the respiratory secretions. **Pralidoxime** breaks the bond between the organophosphate and the enzyme, reactivating AChE. Pralidoxime is only effective if it is used before the bond ages and becomes permanent. Pralidoxime is not necessary for carbamate poisonings because the bond between the insecticide and the enzyme degrades spontaneously.

Without treatment, symptoms of organophosphate poisoning can persist for weeks, requiring continuous supportive care. Even with treatment, some patients develop a delayed polyneuropathy and a range of chronic neuropsychiatric symptoms.

Pyrethrins and Pyrethroids. Pyrethrins are derived from the chrysanthemum flower and, along with synthetic derivatives, pyrethroids, are the most used pesticides in the home. Although >1,000 pyrethrins and pyrethroids exist, <20 are available in the United States, with **permethrin** being the most common. Exposure to these compounds occurs by inhalation, dermal absorption, or ingestion. Ingestion is the predominant route and typically occurs by eating contaminated foods. Permethrin is also a prescribed medication for the treatment of scabies and lice.

Pathophysiology. Pyrethrins and pyrethroids prolong the open state of the voltage-gated Na^+ channel conduction, which is the main mechanism resulting in its pesticide activity. Pyrethrins have minimal toxicity in mammals because of rapid metabolism, higher affinity for the insect Na^+ channel, and decreased activity at higher temperatures

seen in warm-blooded animals. Because pyrethroids were specifically manufactured to be more stable in the environment, they have a higher likelihood of toxicity.

Clinical and Laboratory Manifestations. Pyrethrin exposures can lead to allergic reactions ranging from dermatitis to urticaria to anaphylaxis. Acute pyrethroid exposure can result in headache, nausea, dizziness, tremors, ataxia, choreoathetosis, loss of consciousness, and seizures. The severity of the symptoms depends on the magnitude of the exposure. Reports of acute lung injury have also occurred after pyrethroid exposures, although this is likely from the other components of the insecticide, such as surfactants and solvents. Paresthesias limited to the cutaneous exposure area can also occur after a dermal exposure. Chronic exposures have not been shown to result in any clinical manifestations. Although one can test for urinary pyrethroid metabolites, this is only useful for monitoring occupational exposure and has no role in the acute exposure.

Treatment. Initial treatment should focus on decontamination, which involves removing all clothing and irrigation of exposed areas. Allergic reactions are treated with oral antihistamines and topical corticosteroids. Systemic toxicity should be treated with excellent supportive care, using benzodiazepines for tremors and seizures.

Hydrocarbons

Hydrocarbons include a wide array of chemical substances found in thousands of commercial products. Specific characteristics of each product determine whether exposure will produce systemic toxicity, local toxicity, both, or neither. Nevertheless, aspiration of even small amounts of certain hydrocarbons can lead to serious, potentially life-threatening toxicity.

Pathophysiology. The most important manifestation of hydrocarbon toxicity is *aspiration pneumonitis* through inactivation of the type II pneumocytes and resulting in surfactant deficiency (see Chapter 446). Aspiration usually occurs during coughing and gagging at the time of ingestion or vomiting after the attempted ingestion of an aliphatic hydrocarbon. The propensity of a hydrocarbon to cause aspiration pneumonitis is inversely proportional to its viscosity and directly proportional to its volatility. Compounds with low viscosity and high volatility, such as mineral spirits, naphtha, kerosene, gasoline, and lamp oil, spread rapidly across surfaces and cover large areas of the lungs when aspirated. Only small quantities (<1 mL) of such chemicals need be aspirated to produce significant injury. Pneumonitis does not result from dermal absorption of hydrocarbons or from ingestion in the absence of aspiration. Gasoline and kerosene are poorly absorbed, but they often cause considerable irritation of the GI mucosa as they pass through the intestines.

Certain hydrocarbons have unique toxicities and can cause symptoms after ingestion, inhalation, or dermal exposures. Several chlorinated solvents, most notably carbon tetrachloride, can produce hepatic toxicity. **Methylene chloride**, found in some paint removers, is metabolized to carbon monoxide. **Benzene** is known to cause cancer, most often acute myelogenous leukemia, after long-term exposure. Nitrobenzene, aniline, and related compounds can produce methemoglobinemia. A number of **volatile** hydrocarbons, including toluene, propellants, refrigerants, and volatile nitrites, are frequently abused by inhalation. Some of these substances, principally the **halogenated** hydrocarbons (which contain a chlorine, bromine, or fluorine), can sensitize the myocardium to the effects of endogenous catecholamines. This can result in dysrhythmias and "sudden sniffing death." Chronic abuse of these agents can lead to cerebral atrophy, neuropsychologic changes, peripheral neuropathy, and kidney disease (see Chapter 157).

Clinical and Laboratory Manifestations. Transient, mild CNS depression is common after hydrocarbon ingestion or inhalation. Aspiration is characterized by coughing, which usually is the first clinical finding. Chest radiographs may initially be normal, but they often show abnormalities within 6 hours of exposure in patients who have aspirated. Respiratory symptoms can remain mild or progress rapidly to ARDS and respiratory failure. Fever and leukocytosis are common accompanying signs in patients with pneumonitis and do not necessarily imply bacterial superinfection. Chest radiographs can remain abnormal long after the patient returns to their clinical baseline. Pneumatoceles can appear on the chest radiograph 2-3 weeks after exposure.

After inhalational exposures to halogenated hydrocarbons, patients can present with ventricular dysrhythmias, often refractory to conventional management. Recurrent inhalation of the aromatic hydrocarbon **toluene** can lead to a type IV renal tubular acidosis.

Treatment. *Emesis and lavage are contraindicated given the risk of aspiration*. Activated charcoal is not useful because it does not bind the common hydrocarbons and can also induce vomiting. If hydrocarbon-induced pneumonitis develops, respiratory treatment is supportive (see Chapter 446). Neither corticosteroids nor prophylactic antibiotics have shown any clear benefit. Standard mechanical ventilation, high-frequency ventilation, and ECMO have all been used to manage the respiratory failure and ARDS associated with severe hydrocarbon-induced pneumonitis.

Patients with dysrhythmias in the setting of halogenated hydrocarbon inhalation should be treated with β blockers (usually esmolol) to block the effects of endogenous catecholamines on the sensitized myocardium.

Toxic Alcohols

Methanol is found in windshield washer fluids, deicers, paint removers, fuel additives, liquid fuel canisters, and industrial solvents. **Ethylene glycol** is found in antifreeze. Unintentional ingestion is the most common exposure in children, and small-volume ingestions of concentrated products can theoretically cause toxicity. The pathophysiology, acid-base derangements, and treatment of both chemicals are similar, although they differ in their primary end-organ toxicity. In both cases the metabolites of the parent compounds are responsible for the serious clinical effects that can follow exposure.

Isopropyl alcohol (rubbing alcohol), found in hand sanitizers, causes intoxication similar to that associated with ethanol but can also cause a hemorrhagic gastritis and myocardial depression in massive ingestions. Unlike ethylene glycol and methanol, isopropyl alcohol is metabolized to a ketone and does not cause a metabolic acidosis. Management is similar to that of ethanol ingestions (see Chapter 157) and is not further discussed here.

Methanol

Pathophysiology. Methanol is oxidized in the liver by alcohol dehydrogenase to formaldehyde, which is further oxidized to formic acid by aldehyde dehydrogenase. Toxicity is caused primarily by formic acid, which inhibits mitochondrial respiration.

Clinical and Laboratory Manifestations. Drowsiness, mild inebriation, nausea, and vomiting develop early after methanol ingestion. The onset of serious effects, including profound metabolic acidosis and visual disturbances, is often delayed up to 12-24 hours as methanol undergoes metabolism to its toxic metabolites. This metabolism is further slowed if *ethanol* has also been ingested, because the liver will preferentially metabolize ethanol. Visual disturbances include blurred or cloudy vision, constricted visual fields, decreased acuity, and the "feeling of being in a snowstorm" and appear only after acidosis is well established. These visual defects may be reversible if treated early, but untreated can lead to permanent blindness. On examination, dilated pupils, retinal edema, and optic disc hyperemia may be noted. Initially, patients have an elevated osmolar gap, then develop an anion gap metabolic acidosis as the parent compound is metabolized to formic acid.

In young children, determining if a significant exposure has occurred is usually difficult based on history. Methanol blood levels are available at some laboratories and should be sent after a concerning exposure. If methanol blood levels are not readily available, estimation of an osmolar gap may be used as a surrogate marker, but a normal osmolar gap does not rule out ingestion of any alcohol. Serum osmolality is measured by the freezing-point depression method and compared with a calculated serum osmolarity.

Treatment. Treatment is as discussed for ethylene glycol toxicity.

Ethylene Glycol

Pathophysiology. Ethylene glycol is oxidized by alcohol dehydrogenase in the liver to glycolaldehyde, which is further converted to

glycolic acid by aldehyde dehydrogenase. Glycolic acid is responsible for the metabolic acidosis and is further metabolized to glyoxylic and then to oxalic acid. Oxalic acid combines with serum and tissue calcium, forming calcium oxalate crystals that deposit throughout the body, especially in the renal parenchyma, leading to acute tubular necrosis.

Clinical and Laboratory Manifestations. Early symptoms include nausea, vomiting, CNS depression, and inebriation. Delayed manifestations include an anion gap metabolic acidosis, hypocalcemia, and acute kidney injury. Even later, patients can develop cranial nerve palsies.

Both ethylene glycol and methanol can produce profound, life-threatening metabolic acidosis and acidemia, with measured serum bicarbonates that may even be nondetectable. The onset of the acidosis is delayed up to 4-12 hours after ethylene glycol ingestion and may be delayed further with any concomitant ingestion of ethanol. Ethylene glycol blood concentrations are technically difficult to perform and are available only at some larger reference laboratories. In the absence of readily available ethylene glycol concentrations, calculation of the osmolar gap may be helpful as a surrogate marker.

Examination of the urine with a Wood lamp is neither sensitive nor specific for ethylene glycol ingestion. The earliest sign on a urinalysis of ethylene glycol poisoning is usually hematuria. Calcium oxalate crystals can be seen on urine microscopy but might not be evident early after exposure. Electrolytes (including calcium), acid-base status, kidney function, and ECG should be closely monitored in poisoned patients.

Treatment. Because methanol and ethylene glycol are rapidly absorbed, gastric decontamination is generally not of value. The classic antidote for methanol and ethylene glycol poisoning was ethanol, a preferential substrate for alcohol dehydrogenase, thus preventing the metabolism of parent compounds to toxic metabolites. **Fomepizole**, a potent competitive inhibitor of alcohol dehydrogenase, has almost entirely replaced ethanol because of its ease of administration, lack of CNS and metabolic effects, and overall excellent patient tolerability profile (see Table 94.8). A serum concentration must be interpreted along with the time removed from exposure. A patient with a methanol level of 20 mg/dL 24 hours after exposure had a much larger dose than a patient with the same level only 1 hour after ingestion. Indications for fomepizole include ethylene glycol or methanol level >20 mg/dL (assuming no ethanol is present), history of potentially toxic ingestion (e.g., any intentional overdose), or history of ingestion with evidence of acidosis. There are few disadvantages to giving the initial dose of fomepizole to patients with a concerning history of ingestion or laboratory findings. Given the dosing schedule of fomepizole (every 12 hours), this strategy buys the clinician time to confirm or exclude the diagnosis before giving a second dose. Adjunctive therapy includes folate (methanol toxicity), pyridoxine (ethylene glycol toxicity), and sodium bicarbonate infusion (if acidemic). If a child has had an unintentional exposure and the toxic alcohol level cannot be obtained, a reasonable approach is to follow serum chemistries every 4 hours until 12 hours after the exposure. If the bicarbonate level on the chemistry panel does not fall in that period, a toxic exposure is unlikely (assuming no ethanol is present).

Hemodialysis effectively removes ethylene glycol, methanol, and their metabolites (except calcium oxalate) and corrects acid-base and electrolyte disturbances. Fomepizole should be given both before and immediately after dialysis. Indications for dialysis include a methanol or ethylene glycol level >50 mg/dL, acidosis, severe electrolyte disturbances, renal failure, and hemodynamic instability. However, in the absence of acidosis and kidney failure, even massive ethylene glycol ingestions have been managed without dialysis. Methanol, however, because its elimination in the setting of alcohol dehydrogenase inhibition is prolonged, often warrants dialysis to remove the parent compound. Therapy (fomepizole and/or dialysis) should be continued until ethylene glycol and methanol levels are <20 mg/dL. Although the visual effects from methanol poisoning are usually permanent, the kidney injury from ethylene glycol injury is not. Patients requiring hemodialysis after ethylene glycol poisoning will almost always recover complete renal function within 2-6 weeks. Consultation with a PCC, medical toxicologist, and nephrologist may be helpful in managing toxic alcohol ingestions.

Plants

Exposure to plants, both inside the home and outside in backyards and fields, is one of the most common causes of unintentional poisoning in children. Fortunately, most ingestions of plant parts (leaves, seeds, flowers) result in either no toxicity or mild, self-limiting effects. However, ingestion of certain plants can lead to serious toxicity (Table 94.19).

The potential toxicity of a particular plant is highly variable, depending on the part of the plant involved (flowers are generally less toxic than the root or seed), the time of year, growing conditions, and the route of exposure. Assessment of the potential severity after an exposure is also complicated by the difficulty in properly identifying the plant. Many plants are known by several common names, which can vary among communities. PCCs have access to professionals who can assist in properly identifying plants. They also are well versed in the common poisonous plants in their service area and the seasons when they are more abundant. For these reasons, consultation with the local PCC may be very helpful in the management of these ingestions.

For potentially toxic plant ingestions, consider decontamination with activated charcoal in patients who present within 1-2 hours of ingestion; otherwise, treatment is primarily supportive and based on symptoms. The most common manifestation of toxicity after plant ingestion is GI upset, which can be managed with antiemetics and fluid and electrolyte support. Table 94.19 outlines management strategies for a few specific toxicities.

Herbal Remedies

Herbal remedies represent a relatively common exposure in children; despite this, reports of life-threatening toxicity are rare.

There are several mechanisms by which herbal remedies may be poisonous. Many herbal remedies are inherently toxic; it is either the dose used or specific processing of the remedy that renders them safe for use. For example, oil of wintergreen used as a liniment contains a high concentration of methyl salicylate, a concerning source of salicylate poisoning in small children. A remedy intended to contain one compound may accidentally contain another; reports exist of contamination of skin creams with mercury, herbal remedies contaminated with lead, and weight loss supplements contaminated with cardioactive steroids. Herbal remedies may interfere with the metabolism of pharmaceuticals; an example is St. John's wort, which by induction of the cytochrome oxidase system (specifically, CYP3A4) may render certain medications less effective.

Management of toxicity associated with herbal remedies remains largely the same as for other organic compounds. Decontamination with activated charcoal should be considered for patients arriving within 1-2 hours of an ingestion. Signs and symptoms should be treated as outlined previously in this chapter, with excellent supportive care and therapy directed toward the suspected toxin. In the rare case of concern for contamination with a heavy metal, specific assays may be obtained for confirmation of exposure. A list of herbal remedies and their associated toxicities are provided in Table 94.20.

In limited cases, specific antidotes are suggested based on the pathophysiologic mechanism. Several plant and animal species contain cardioactive steroids with digoxin-like toxicity. Although digoxin-specific immune fragments are only evidence based for the management of yellow oleander *(Thevetia peruviana)* toxicity, it is reasonable to use this therapy in a critically ill patient who has developed cardiac toxicity or hyperkalemia after ingestion of lily of the valley, squill, or oleander. Several essential oils (pennyroyal oil, clove oil) deplete glutathione as part of their toxic mechanism, and thus treatment with NAC may be of benefit. Gingko causes a depletion of active pyridoxine stores, and thus pyridoxine administration may be helpful in the setting of benzodiazepine-refractory seizures.

Table 94.19 Commonly Ingested Plants with Significant Toxic Potential

PLANT	SYMPTOMS	MANAGEMENT
Autumn crocus (Colchicum autumnale)	Vomiting Diarrhea Initial leukocytosis followed by bone marrow failure Multisystem organ failure	Activated charcoal decontamination Aggressive fluid resuscitation and supportive care
Belladonna alkaloids: jimsonweed (Datura stramonium) Belladonna ("deadly nightshade"; Atropa belladonna)	Anticholinergic toxidrome Seizures	Supportive care, benzodiazepines Consider physostigmine; only use if no conduction delays on ECG
Cardiac glycoside–containing plants (e.g., foxglove, lily of the valley, oleander, yellow oleander)	Nausea Vomiting Bradycardia Dysrhythmias (AV block, ventricular ectopy) Hyperkalemia	Digoxin-specific Fab fragments
Jequirity bean and other abrin-containing species (e.g., rosary pea, precatory bean)	Oral pain Vomiting Diarrhea Shock Hemolysis Renal failure	Supportive care, including aggressive volume resuscitation and correction of electrolyte abnormalities
Monkshood (Aconitum species)	Numbness and tingling of lips/tongue Vomiting Bradycardia	Atropine for bradycardia Supportive care
Oxalate-containing plants: Philodendron, Dieffenbachia, Colocasia ("elephant ear")	Local tissue injury Oral pain Vomiting	Supportive care, pain control
Poison hemlock (Conium maculatum)	Vomiting Agitation followed by CNS depression Paralysis Respiratory failure	Supportive care
Pokeweed	Hemorrhagic gastroenteritis Burning of mouth and throat	Supportive care
Rhododendron	Vomiting Diarrhea Bradycardia	Atropine for symptomatic bradycardia Supportive care
Tobacco	Vomiting Agitation Diaphoresis Fasciculations Seizures	Supportive care
Water hemlock (Cicuta species)	Abdominal pain Vomiting Delirium Seizures	Supportive care, including benzodiazepines for seizures
Yew (Taxus species)	GI symptoms QRS widening Hypotension CV collapse	Supportive care Atropine for bradycardia Sodium bicarbonate does not appear to be effective

AV, Atrioventricular; CNS, central nervous system; CV, cardiovascular; ECG, electrocardiogram; Fab, fragment, antigen binding; GI, gastrointestinal.

Toxic Gases

Carbon Monoxide

Although many industrial and naturally occurring gases pose a health risk by inhalation, the most common gas involved in pediatric exposures is CO. CO is a colorless, odorless gas produced during the combustion of any carbon-containing fuel; the less efficient the combustion, the greater the amount of CO produced. Wood-burning stoves, kerosene heaters, old furnaces, hot-water heaters, closed-space fires, and automobiles are a few of the potential sources of CO.

Pathophysiology. CO binds to hemoglobin with an affinity >200 times that of oxygen, forming carboxyhemoglobin (HbCO). In doing so, CO displaces oxygen and creates a conformational change in hemoglobin that impairs the delivery of oxygen to the tissues, leading to tissue hypoxia. HbCO levels are not well correlated with clinical signs of toxicity, likely because CO interacts with multiple proteins in addition to hemoglobin. CO binds to cytochrome oxidase, disrupting cellular respiration. CO displaces nitric oxide (NO) from proteins, allowing NO to bind with free radicals to form the toxic metabolite peroxynitrite, leading to lipid peroxidation and cellular damage. NO is also a potent vasodilator, in part responsible for clinical symptoms such as headache, syncope, and hypotension.

Table 94.20 Clinical Toxicity of Selected Herbs

COMMON NAME	BOTANICAL NAME	THERAPEUTIC USES	POTENTIAL TOXICITY
Aconite (monkshood, wolfsbane)	*Aconitum* spp.	Sedative, analgesic, antihypertensive	Cardiac arrhythmias
Aloe	*Aloe* spp.	Burns, skin diseases	Nephritis, GI upset
Betel nut	*Areca catechu*	Mood elevation	Bronchoconstriction, oral cancers
Bloodroot	*Sanguinaria canadensis*	Emetic, cathartic, eczema	GI upset, vertigo, visual disturbances
Chaparral (greasewood)	*Larrea tridentata*	Aging, free radical scavenging	Hepatitis
Compound Q	*Trichosanthes kirilowii*	Anthelmintic, cathartic	Diarrhea, hypoglycemia, CNS toxicity
Dandelion	*Taraxacum officinale*	Diuretic, heartburn remedy	Anaphylaxis
Figwort (xuan shen)	*Scrophularia* spp.	Antiinflammatory, antibacterial	Cardiac stimulation
Ginseng	*Panax quinquefolium*	Antihypertensive, aphrodisiac, stimulant, mood elevation, digestive aid	Ginseng abuse syndrome
Goldenseal	*Hydrastis canadensis*	Digestive aid, mucolytic, antiinfective	Uterine, cardiac stimulation; GI upset, leukopenia
Hellebore	*Veratrum* spp.	Antihypertensive	Vomiting, bradycardia, hypotension
Hyssop	*Hyssopus officinalis*	Asthma, mucolytic	Seizures
Juniper	*Juniperus communis*	Hallucinogen	GI upset, seizures, renal injury, hypotension, bradycardia
Kava	*Piper methysticum*	Sedative	Inebriation
Kombucha		Stimulant	Metabolic acidosis, hepatotoxicity, death
Licorice	*Glycyrrhiza* spp.	Indigestion	Mineralocorticoid effects
Lily of the valley	*Convallaria* spp.	Cardiotonic	GI (nausea, vomiting), cardiac arrhythmias
Linn (willow)	*Salix caprea*	Purgative	Hemolysis with glucose-6-phosphate dehydrogenase deficiency
Lobelia (Indian tobacco)	*Lobelia* spp.	Stimulant	Nicotine intoxication
Ma Huang	*Ephedra sinica*	Stimulant	Sympathetic crisis, especially with monoamine oxidase inhibitors
Mandrake	*Mandragora officinarum*	Hallucinogen	Anticholinergic syndrome
Mormon tea	*Ephedra nevadensis*	Stimulant, asthma, antipyretic	Hypertension, sympathomimetic
Nutmeg	*Myristica fragrans*	Hallucinogen, abortifacient	Hallucinations, GI upset
Oleander	*Nerium oleander*	Cardiac stimulant	Cardiac arrhythmias
Passionflower	*Passiflora caeruliea*	Hallucinogen	Hallucinations, seizures, hypotension
Periwinkle	*Vinca* spp.	Antiinflammatory, diabetes	Alopecia, seizures, hepatotoxicity
Pokeweed	*Phytolacca* spp.	Arthritis, chronic pain	GI upset, seizures, death
Sabah	*Sauropus androgynus*	Weight loss, vision	Pulmonary injury
Sage	*Salvia* spp.	CNS stimulant	Seizures
Snakeroot	*Rauwolfia serpentina*	Sedative, antihypertensive	Bradycardia, coma
Squill	*Urginea maritima*	Arthritis, cardiac stimulant	Seizures, arrhythmias, death
Thorn apple (jimsonweed)	*Datura stramonium*	Hallucinations	Anticholinergic
Tonka bean	*Dipteryx odorata*	Anticoagulant	Bleeding diathesis
Valerian root	*Valeriana* spp.	Sedative	Sedation, obtundation
Wild (squirting) cucumber	*Ecballium elaterium*	Constipation, antiinflammatory, rheumatic disease	Airway obstruction
Wormwood (mugwort)	*Artemisia* spp.	Stimulant, hallucinogen	Hallucinations, seizures, uterine stimulation
Yohimbine	*Corynanthe yohimbe*	Aphrodisiac, stimulant	Hypertension, sympathetic crisis

CNS, Central nervous system; GI, gastrointestinal.

From Kingston RL, Foley C. Herbal, traditional, and alternative medicines. In: Shannon MW, Borron SW, Burns MJ, eds. *Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose*, 4th ed. Philadelphia: Saunders; 2007, Table 68.1, p. 1081.

Clinical and Laboratory Manifestations. Early symptoms are nonspecific and include headache, malaise, nausea, and vomiting. These symptoms are often misdiagnosed as indicating flu or food poisoning. At higher exposure levels, patients can develop mental status changes, confusion, ataxia, syncope, tachycardia, and tachypnea. Severe poisoning is manifested by coma, seizures, myocardial ischemia, acidosis, cardiovascular collapse, and potentially death. Physical examination should focus on the cardiovascular and neurologic systems because these are the most detrimentally affected by CO. Emergency department evaluation should include arterial or venous blood gas analysis with HbCO determined by CO-oximetry, CK level in severely poisoned patients, pregnancy test, and ECG and troponin in any patient with cardiac symptoms.

Treatment. Prevention of CO poisoning is paramount and should involve educational initiatives and the use of home CO detectors. Treatment of CO poisoning focuses on the administration of 100% oxygen to enhance elimination of CO. In ambient air the average half-life of HbCO is 4-6 hours. This is dramatically reduced to 60-90 minutes by providing 100% oxygen at normal atmospheric pressures by non-rebreather face mask. Severely poisoned patients might benefit from **hyperbaric oxygen (HBO)**, which decreases the half-life of HbCO to 20-30 minutes and is thought also to decrease the risk of delayed neurologic sequelae. Although the clinical benefits and referral guidelines for HBO therapy remain controversial, frequently cited indications include syncope, coma, seizure, altered mental status, evidence of myocardial ischemia, HbCO level >25% (or >15% in pregnancy), and abnormal cerebellar examination. Consultation with a PCC, medical toxicologist, or HBO facility can assist clinicians in determining which patients could benefit from HBO therapy. Sequelae of CO poisoning include persistent and delayed cognitive and cerebellar effects. HBO advocates believe that the risk of such sequelae is minimized through the delivery of 100% oxygen at 3 atm of pressure. Patients typically receive oxygen, by non-rebreather mask or hyperbaric chamber, for 6 hours.

Hydrogen Cyanide

Pathophysiology. Cyanide inhibits cytochrome-*c* oxidase, part of the electron transport chain, interrupting cellular respiration and leading to profound tissue hypoxia. Patients may be exposed to hydrogen cyanide (HCN) gas in the workplace (manufacturing of synthetic fibers, nitriles, and plastics) by smoke inhalation in a closed-space fire or by ingestion of cassava flour.

Clinical and Laboratory Manifestations. Onset of symptoms is rapid after significant exposure. Clinical manifestations of toxicity include headache, agitation/confusion, sudden loss of consciousness, tachycardia, cardiac dysrhythmias, and metabolic acidosis. Cyanide levels can be measured in whole blood but are not readily available at most institutions. A severe lactic acidosis (lactate >10 mmol/L) in fire victims suggests cyanide toxicity. Impaired oxygen extraction by tissues is implied by elevated mixed-venous oxyhemoglobin saturation, another laboratory finding suggesting cyanide toxicity.

Treatment. Treatment includes removal from the source of exposure, rapid administration of high concentrations of oxygen, and antidotal therapy.

Hydroxocobalamin is the preferred agent for use in known or suspected cyanide poisoning (see Table 94.8). This antidote reacts with cyanide to form the nontoxic cyanocobalamin (vitamin B_{12}), which is then excreted in urine. Side effects of hydroxocobalamin include red discoloration of the skin and urine, transient hypertension, and interference with colorimetric laboratory assays. Other FDA-approved treatments for cyanide poisoning include sodium nitrite and sodium thiosulfate, either alone or in combination. Sodium nitrite induces methemoglobinemia, which may exacerbate symptoms of carboxyhemoglobinemia and thus should be avoided in patients with smoke inhalation.

Miscellaneous Toxic Agents Found in the Home

Nicotine-Containing Products

Nicotine poisoning has become increasingly common with the recent advent of vaporizer ("vaping") and e-cigarette devices (see Chapter 157). Although there are many nicotine-containing products (patches, gums, snuff, chewing tobacco, sprays, lozenges), tobacco cigarettes remain the main source of exposure. Prescription medications (varenicline and cytisine) are available that are partial nicotine receptor agonists. For children, some of the most concerning exposures are from the bottles of liquid nicotine used to refill vaping and e-cigarette devices. These bottles typically do not have childproof caps and contain a large amount of concentrated nicotine.

Pathophysiology. Nicotine acts on nicotinic ACh receptors in the nervous system, neuromuscular junctions, and adrenal medulla, stimulating neurotransmitter release. Nicotine's effects on the dopaminergic reward pathway play a significant role in its addictive properties. The effects of nicotine are dose dependent; at lower doses it primarily acts on the brain, causing stimulation. At higher doses, nicotine overstimulates receptors, leading to inhibition and resulting in neuromuscular and nervous system blockade.

Clinical and Laboratory Manifestations. Clinical effects of nicotine also depend on the dose. At low doses typically achieved through smoking, nicotine results in cognitive and mood enhancement, increased energy, and appetite suppression. Shortness of breath, cough, and fever may be seen with e-cigarette use–associated lung injury (EVALI), an inflammatory response in the lungs triggered by vaping. At higher doses, significant toxicity follows a biphasic pattern, where cholinergic stimulation symptoms predominate and are later followed by inhibition. The first signs of nicotine poisoning are nausea, vomiting, diarrhea, and often muscle fasciculations. Tachycardia and hypertension occur initially, although in severe poisoning these progress to bradycardia, hypotension, coma, and respiratory muscle failure, which typically leads to death if not treated. Serum and urinary levels of nicotine and its metabolite cotinine can be obtained, but these rarely are available in real time and therefore have little effect on diagnosis and management.

Treatment. Treatment of nicotine poisoning focuses on maximizing symptomatic and supportive care. Aggressive airway management should be the priority, especially in severe poisonings, because death usually occurs from respiratory muscle paralysis. IV fluids with escalation to vasopressors should be used for hypotension. Seizures should be managed with benzodiazepines, barbiturates, or propofol.

Single-Use Detergent Sacs

Commonly known as laundry "pods" for clothing, these products resemble candy to many children. When bitten into, a relatively large dose of concentrated detergent is expelled under pressure onto the posterior pharynx and vocal cords. This can lead to stridor and other signs of respiratory distress. Occasionally, and for unknown reasons, these children may also develop altered mental status. Supportive care with attention to any airway and breathing issues is warranted. Admission to the hospital is often indicated. Importantly, these are not considered caustic ingestions; the pH of these products is in the neutral zone. Upper GI endoscopy is rarely indicated. Curiously, laundry detergent ingested from a bottle is rarely of significant concern.

Electric Dishwasher Detergent

Especially when in the form of crystals, these products are highly alkaline (pH >13), and exposure by ingestion can cause significant burns to the vocal cords and GI tract. Admission for expectant management or upper GI endoscopy is usually indicated.

Magnets

Most foreign body ingestions pass through the GI tract once known to have passed into the stomach. However, ingestion of ≥2 magnets (unless very weak refrigerator-style magnets) cause concern for bowel obstruction and perforation (see Chapter 380). Admission for attempted retrieval by endoscopy or clearance by WBI should be considered.

Batteries

Any disk or button-style battery lodged in the esophagus or airway should be considered a true emergency warranting immediate referral

to an endoscopist for removal (see Chapter 373). These batteries can cause necrosis of the tissues in which they are lodged by continued electrical discharge and leaking of their contents (the former is likely the primary method of injury). Mucosal contact for even 2 hours might induce necrosis. Once past the lower esophageal sphincter, button or even larger batteries (e.g., AA, AAA) can usually be allowed to pass through the GI tract with close follow-up.

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