

## PERSPECTIVE

### Background

The nervous system is traditionally divided into central nervous system (CNS) and peripheral nervous system (PNS) components. The PNS can be further subdivided into 12 cranial and 31 spinal nerves. Disorders of the cranial nerves are discussed in Chapter 103. Because diseases of the neuromuscular junction and the myopathies are located distal to the neuron itself, they are also considered separately in Chapter 104. Radiculopathies, which are disorders of the roots of the PNS, are so commonly associated with musculoskeletal neck and back pain that they are mentioned only briefly here and are discussed in detail in Chapter 51.

The simplest approach to diseases of the PNS parallels the CNS model of separating focal from nonfocal disease. In the PNS, the first broad category is the focal group, which can be divided into those with evidence of single versus multiple lesions of peripheral nerves, known respectively as *simple mononeuropathies* and *multiple mononeuropathies* (or *mononeuropathy multiplex*). The second broad category, which constitutes the nonfocal group of peripheral neuropathies, contains the polyneuropathies. These tend to produce bilaterally symmetrical symptoms and signs, reflecting the widespread nature of the underlying pathologic process.

The evaluation of PNS disease involves a goal-directed history and physical examination targeted at answering the following three questions, each of which corresponds to a stratum of the algorithm presented in Fig. 105-1:

1. Are the sensorimotor signs and symptoms symmetrical or asymmetrical?
2. Are the sensorimotor signs and symptoms distal or both proximal and distal?
3. Is the modality involved exclusively motor, sensory, or mixed sensorimotor?

By systematically combining responses to these questions, one can identify seven discrete categories of peripheral neuropathy, each of which contains a finite set of possible diagnoses. Because pure motor or sensory findings tend to occur mainly in an asymmetrical, distal distribution, this is the only category in Figure 105-1 subdivided into pure motor and pure sensory abnormalities.

### Epidemiology

Although Guillain-Barré syndrome (GBS) is the most commonly encountered emergent peripheral neuropathy in devel-

oped countries, its annual incidence is just over 1 to 2 cases per 100,000 population.<sup>1</sup> In contrast to the low incidence of acute peripheral neuropathies, several of which are associated with short-term mortality, the vast majority of peripheral neuropathies seen in the emergency department (ED) are subacute or chronic and are associated not with mortality but with long-term morbidity.

Current estimates suggest that about 1.5% of the U.S. population suffers from peripheral neuropathy.<sup>2</sup> Over 7% of the population has diabetes mellitus, with a prevalence rate of 20% in individuals older than 60 years. Roughly 50% of these individuals have peripheral neuropathy.<sup>3</sup>

## PRINCIPLES OF DISEASE

### Anatomy

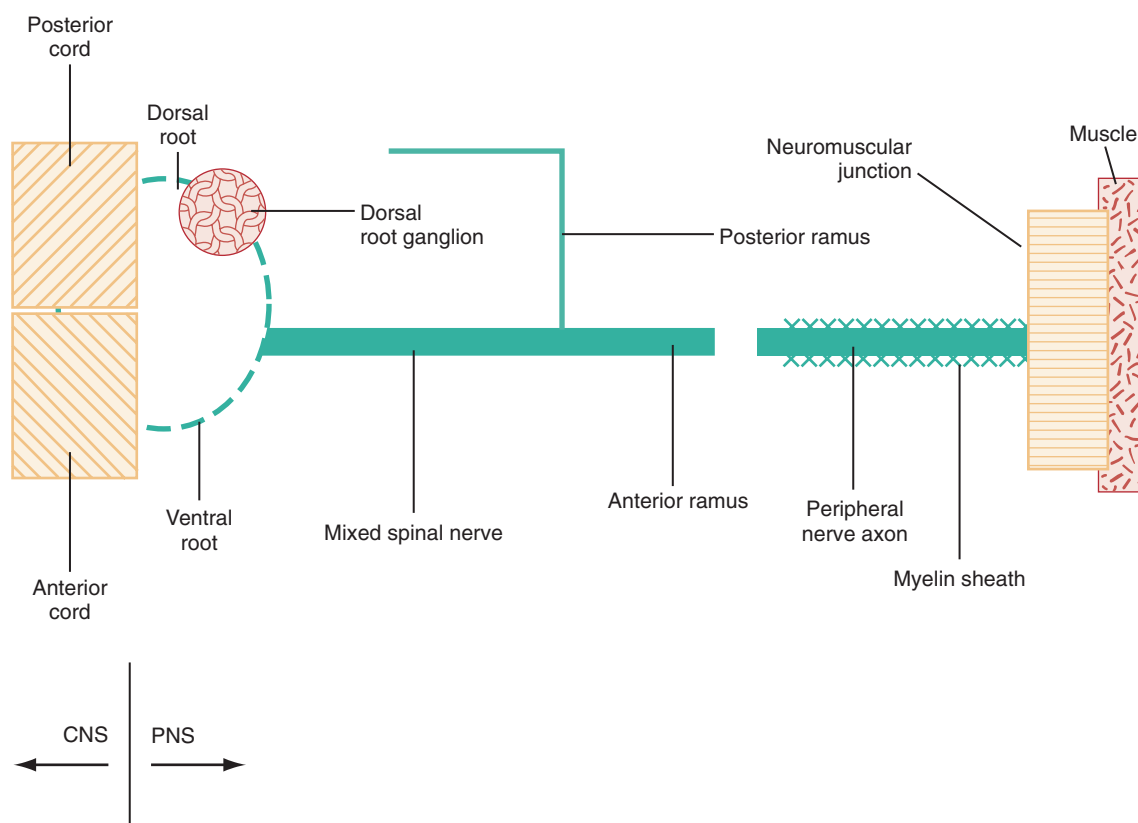
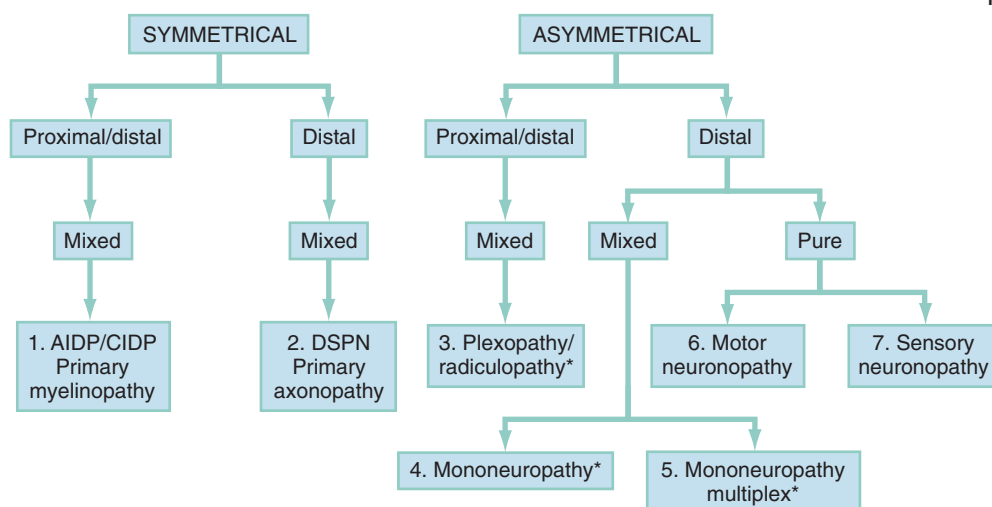
The spinal component of the PNS is shown schematically in Figure 105-2. The anterior and posterior nerve roots exit the spinal cord at each segmental level. Just distal to the dorsal root ganglion they converge to form a mixed (motor and sensory) spinal nerve, of which there are 31 pairs: 8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal. The spinal nerves immediately bifurcate into anterior (ventral) and posterior (dorsal) rami. The posterior ramus travels to the back. The anterior ramus innervates the anterolateral portion of the body and supplies all peripheral nerves for the upper and lower extremities through the brachial and lumbosacral plexus, respectively. Interweaving of fibers occurs within a plexus, producing a mixed sensorimotor innervation of peripheral nerves exiting the plexus.

In addition to the motor and sensory modalities of the PNS, the autonomic nervous system has a peripheral component. Anatomically and functionally, the autonomic nervous system is divided into two parts: a sympathetic (thoracolumbar) component and a parasympathetic (craniosacral) component. Autonomic dysfunction may cause systemic abnormalities, such as orthostasis, or local problems, such as atrophic, dry skin.

### Pathophysiology

The PNS has only three basic responses to a wide array of pathologic stimuli. As shown in Figure 105-2, these are (1) the myelinopathies, where the primary site of involvement is limited to the myelin sheath surrounding the axon; (2) the axonopathies, where the primary site of involvement is the axon, with or without secondary demyelination; and (3)

**Figure 105-1.** An approach to peripheral neuropathy in the emergency department. AIDP, acute inflammatory demyelinating polyneuropathy (Guillain-Barré); CIDP, chronic inflammatory demyelinating polyneuropathy; DSPN, distal symmetrical polyneuropathy. \*A proximal distribution of sensorimotor findings may dominate the clinical picture in patterns 3, 4, and 5, depending on the location of the lesion(s).



**Figure 105-2.** Schematic representation of macroscopic and microscopic anatomy of the peripheral nervous system and its interface with the central nervous system. See text for explanation.

the neuronopathies, where the cell body of the neuron itself is the primary site of involvement, ultimately affecting the entire peripheral nerve. Although overlap occurs, each of these prototypes has a distinctive clinical presentation, electrophysiologic profile, and microscopic appearance.

Electrophysiologic testing, that is, nerve conduction studies (NCSs) and needle electromyography (EMG), detects underlying pathologic abnormalities. Because neither test is readily available in the acute care setting, they are discussed only briefly here. Information gathered from NCSs and EMG can be used to obtain objective information on the anatomic distribution of involvement (symmetrical vs. asymmetrical and distal vs. proximal and distal) and the modalities involved

(sensory, motor, or mixed). NCSs and EMG can also identify the level of the neuraxis affected by the disease process (i.e., root, plexus, or nerve); if the nerve is affected, electrophysiologic testing can help determine whether the lesion is mononeuropathic (either caused by an isolated mononeuropathy or mononeuropathy multiplex) or polyneuropathic. Finally, EMG and NCSs can distinguish axonal from myelinopathic disease, further narrowing the differential diagnosis. Prognosis is determined by the nature of pathologic involvement of the PNS. Primary demyelination spares the axon and thus carries the best prognosis. The prognosis is worse in axonopathies because reestablishing nerve function is dependent on the much slower process of axonal regeneration. Neuronopathies, which begin

**BOX 105-1****CAUSES OF ACUTE, EMERGENT WEAKNESS AND POSSIBLE RESPIRATORY COMPROMISE**

Autoimmune
Demyelinating
Guillain-Barré syndrome
Chronic inflammatory demyelinating polyneuropathy (CIDP)
Myasthenia gravis
Toxic
Botulism
Buckthorn
Seafood
Paralytic shellfish toxin
Tetrodotoxin (puffer fish, newts)
Tick paralysis
Metals
Arsenic
Thallium
Metabolic
Dyskalemic syndromes
Acquired (especially with thyrotoxicosis)
Familial
Hypophosphatemia
Hypermagnesemia
Porphyria
Infectious
Poliomyelitis
Diphtheria

with primary destruction of the nerve cell body, produce pure motor or pure sensory syndromes. Eventually the entire nerve is affected, resulting in the worst prognosis of the three.

### CLINICAL FEATURES

The differential diagnosis for any patient presenting with sensory, motor, or sensorimotor complaints, particularly if localized to the extremities, should include a peripheral neuropathy. Within this group, patients with focal weakness are most concerning because they are at greatest risk for respiratory compromise. **Box 105-1** lists the causes of acute, emergent weakness that may affect respiration. Although several of the disorders listed are myopathies (see Chapter 106) rather than peripheral neuropathies, they are lumped together because it is important to identify patients at risk for respiratory failure early in the course of evaluation.

As soon as the emergent causes of weakness have been excluded—which is possible in the majority of patients—the individuals with focal weakness should be assessed next to exclude CNS disease (e.g., stroke) (see Chapter 99). One can then proceed through the systematic approach to peripheral neuropathy outlined in **Figure 105-1**. Another way to look at the algorithm displayed in **Figure 105-1** is shown in **Table 105-1**, with the distinguishing features of each of the seven peripheral neuropathic patterns described by distribution and modality and represented by a disease prototype.

#### Type 1: Demyelinating Polyneuropathies

The pattern of symmetrical weakness, usually worse distally, accompanied by variable sensory findings is characteristic of acute GBS. This pattern is discussed first because it is the most common cause of weakness associated with acute respiratory failure seen in emergency practice.

**Table 105-1****Patterns and Prototypes of Peripheral Neuropathies**

TYPE	PATTERN DISTRIBUTION	PROTOTYPICAL DISEASE MODALITIES
1	Proximal and distal, symmetrical, sensorimotor polyneuropathy Proximal and distal Motor > sensory	GBS Symmetrical
2	Distal, symmetrical, sensorimotor polyneuropathy Distal Sensory > motor	Diabetic DSPN Symmetrical
3	Proximal and distal, asymmetrical, sensorimotor neuropathy Proximal and distal Sensory and motor	Brachial plexopathy Asymmetrical
4	Distal, asymmetrical, sensorimotor mononeuropathy Distal Sensory and motor	CTS (median mononeuropathy) Asymmetrical
5	Distal, asymmetrical, sensorimotor mononeuropathy multiplex Distal Sensory and motor	Vasculitic mononeuropathy multiplex Asymmetrical
6	Distal, asymmetrical, pure motor neuronopathy Distal Motor	ALS Asymmetrical
7	Distal, asymmetrical, pure sensory neuronopathy Distal Sensory	Pyridoxine toxicity Asymmetrical

ALS, amyotrophic lateral sclerosis; CTS, carpal tunnel syndrome; DSPN, distal symmetrical polyneuropathy; GBS, Guillain-Barré syndrome.

#### Guillain-Barré Syndrome

GBS is a heterogeneous and unpredictable disorder, with marked variation in latency between antecedent infection and symptom onset. The clinical signs, cadence of disease progression, degree of respiratory compromise, laboratory findings, and time required for convalescence are also highly variable. The most common form of GBS is an acute inflammatory demyelinating polyneuropathy (AIDP), comprising 90% of the cases seen in the United States.<sup>1</sup> Less common variants include acute motor axonal neuropathy (AMAN), acute motor and sensory axonal neuropathy (AMSAN), and the Miller Fisher syndrome. AMAN accounts for most of the remaining cases seen in the United States afflicting those of Asian descent. Miller Fisher syndrome is a rare form of GBS characterized by the triad of ophthalmoplegia, ataxia, and areflexia (**Box 105-2**).<sup>1,4</sup>

The majority of patients seek treatment days to weeks after resolution of an upper respiratory or gastrointestinal illness, presenting with progressive, symmetrical distal (and usually to a lesser extent proximal) weakness. Signs and symptoms are usually worse in the lower extremities and are associated with diminution or loss of deep tendon reflexes (DTRs), variable sensory findings, and sparing of the anal sphincter. Up to 32% will have all four extremities affected at the time of presentation and 10% will have weakness that begins in the upper

**BOX 105-2 DEMYELINATING POLYNEUROPATHIES**

Guillain-Barré syndrome  
 Acute inflammatory demyelinating  
 polyradiculoneuropathy (AIDP)  
 Acute motor axonal neuropathy (AMAN)  
 Acute motor and sensory axonal neuropathy (AMSAN)  
 Miller Fisher syndrome  
 Chronic inflammatory demyelinating  
 polyradiculoplexoneuropathy  
 Malignancy  
 HIV  
 Hepatitis B  
 Buckthorn  
 Diphtheria

extremities.<sup>1</sup> However, the ocular muscles are usually spared. Urinary retention secondary to autonomic dysfunction may occur, contributing to a clinical picture easily mistaken for a spinal cord lesion or conus medullaris syndrome.

The most commonly infectious organisms associated with GBS are *Campylobacter jejuni* (in patients with a history of diarrhea), cytomegalovirus, Epstein-Barr virus, and *Mycoplasma pneumoniae*. AIDP is caused in part by macrophage invasion of the myelin sheath. The macrophage is believed to detect antigens in the myelin that are nearly identical to the antigens present on certain infectious organisms.<sup>1,5,6</sup>

In practice, patients with symmetrical weakness of relatively acute onset, decreased or absent DTRs, and variable degrees of sensory loss should be managed as if they have GBS or one of its variants, which places them at risk for respiratory compromise. Conversely, patients with predominantly sensory signs and symptoms are less likely to develop acute respiratory distress and have a more favorable prognosis.<sup>7</sup>

About half of patients with GBS have autonomic dysfunction, experience a peak of disease severity within a week of onset, have some form of cranial nerve involvement (usually VII), and suffer long-term sequelae of their illness. Nearly one third require ventilatory support. Both the mortality and the recurrence rate are about 3%.<sup>8</sup>

In addition to electrophysiologic testing, there are three ancillary tests that may be helpful in the diagnosis of GBS. Cerebrospinal fluid (CSF) analysis is useful when it demonstrates the characteristic picture of markedly elevated protein with only a mild pleocytosis. In the clinical setting of suspected GBS, this finding is highly specific. Early in the disease, however, patients may have normal CSF values. Consequently, a normal CSF cannot be used to exclude GBS because of the limited sensitivity of this test. Selective enhancement of the anterior spinal nerve roots on magnetic resonance imaging (MRI) is suggestive, but not diagnostic, of GBS.<sup>9</sup> The GBS disability score, which combines age, presence or absence of diarrhea, and a score of the patient's ability to ambulate independently at 2 weeks, has been shown to be predictive of prognosis at 6 months, particularly related to independent activity.<sup>10</sup>

**Management.** Individuals with suspected GBS must have their respiratory function tested. A decrease in forced vital capacity (FVC) has been shown to correlate with the need for intubation in patients with GBS. An FVC of less than 20 mL/kg was associated with pending respiratory failure and the need for intubation, whereas patients with an FVC of greater than 40 mL/kg did not require intubation.<sup>11,12</sup> Likewise, patients with a negative inspiratory force (NIF) of less than 30 cm water are more likely to require mechanical ventilation.<sup>12</sup> Other tests, such as the forced expiratory volume in 1 second

(FEV<sub>1</sub>) or peak flow rate (PFR) can also be used to assess respiratory function. Patients unable to perform these tests and those with less than 100% of predicted values should have an arterial blood gas obtained. Evidence of alveolar hypoventilation (elevated carbon dioxide [PCO<sub>2</sub>]) in a patient with an unsecured airway requires a level of intensive monitoring that is impractical in many emergency departments. Therefore, patients with weakness, CO<sub>2</sub> retention, or other evidence of early ventilatory failure should be considered for early, prophylactic intubation.<sup>13</sup>

Among patients with possible GBS who have normal pulmonary function, extensor neck strength can be monitored to predict impending ventilatory failure. Patients with probable GBS should receive neurologic consultation and be admitted to the hospital. Either plasma exchange or intravenous immunoglobulin (IVIG) should be administered. There is sound evidence that both are superior to placebo and that combination or sequential therapy confers no therapeutic advantage over either intervention alone. Plasma exchange is cumbersome and not available at many hospitals. IVIG is more readily available and is usually administered in a dose of 400 mg/kg/day for 5 days. However, IVIG is quite expensive, costing roughly \$50 to \$80 per gram.<sup>14</sup> Although not approved by the Food and Drug Administration, IVIG is supported in certain national guidelines.<sup>15</sup> Corticosteroids are no longer recommended for treatment of GBS.<sup>16</sup> Oral steroids have been shown to delay recovery. Intravenous steroids alone have been shown to impart no benefit, and though the combination of intravenous steroids and IVIG has hastened recovery, there was no effect on long-term outcome.<sup>17-19</sup> The marked elevation in blood pressure seen in some patients with GBS should not be treated because it is typically transient and may be followed by precipitous and unpredictable hypotension.

## Type 2: Distal Symmetrical Polyneuropathies

Most polyneuropathies are characterized by a pattern of distal, symmetrical sensorimotor findings, worse in the lower than upper extremities, with a stocking-glove distribution of sensory abnormalities that gradually diminishes as one moves proximally. The motor findings and loss of DTRs, which lag behind the sensory features, follow a similar pattern of progression from distal to proximal. The diffuse, distal, symmetrical nature of this pattern is most consistent with a toxic-metabolic disease process, as yet unidentified, that causes a length-dependent axonopathy. Distal symmetrical polyneuropathy (DSPN) is the most common type of peripheral neuropathy seen in emergency practice. Only the most common causes of DSPN are discussed, with a more complete listing of causes shown in Box 105-3.

### Diabetic Distal Symmetrical Polyneuropathy

The preponderance of cases of DSPN occur in diabetics, also termed diabetic polyneuropathy. Initial symptoms usually consist of "positive" sensory complaints (e.g., dysesthesias such as tingling or burning) beginning on the plantar surfaces of both feet. At the early stages of a typical DSPN, there may be some asymmetry.<sup>20</sup> At this juncture, it may be impossible to distinguish a focal neuropathic process such as a mononeuropathy from a polyneuropathy, although in this location, prior probability strongly favors a polyneuropathy. As the process advances, the plantar surfaces of both feet become dysesthetic before the dorsum of either foot is involved. Weakness of dorsiflexion of the big toe is usually the first motor sign, followed by weakness of foot dorsiflexion, footdrop, loss of Achilles' reflex, and later a "steppage gait."



**BOX 105-3 DISTAL SENSORIMOTOR POLYNEUROPATHIES**

Diabetes mellitus	Dapsone
Alcoholism	Disulfiram
Neoplastic or paraneoplastic	Isoniazid
Hereditary motor and sensory neuropathies (Charcot-Marie-Tooth)	Metronidazole
Cryptogenic sensorimotor polyneuropathies (CSPN)	Nitrofurantoin
HIV	Paclitaxel (Taxol)
Toxins	Phenytoin
Organic or industrial agents	Statins (HMG-CoA reductase inhibitors)
Acrylamide	Thalidomide
Allyl chloride	Vinca alkaloids (vincristine, vinblastin)
Carbon disulfide	Nutritional
Ethylene oxide	Beriberi (thiamine or vitamin B <sub>1</sub> )
Hexacarbons	Pellagra (niacin, B vitamins)
Methyl bromide	Pernicious anemia (vitamin B <sub>12</sub> )
Organophosphate-induced delayed polyneuropathy (OPIDP)	Pyridoxine deficiency (vitamin B <sub>6</sub> )
Polychlorinated biphenyls (PCBs)	End-organ dysfunction
Trichloroethylene	Acromegaly
Vapor	Chronic pulmonary disease
Metals	Hypothyroidism
Arsenic	Renal failure (uremic neuropathy)
Gold	Paraproteinemias
Mercury (inorganic)	Amyloidosis
Thallium	Monoclonal gammopathy of unknown significance (MGUS)
Therapeutic agents	Multiple myeloma
Amiodarone	Waldenström's macroglobulinemia
Antiretrovirals	Porphyria

HMG-CoA, hydroxymethylglutaryl coenzyme A.

Sensory loss continues to move proximally, and before it reaches the knees, the fingertips are usually involved. DTRs are progressively lost, as is proprioception. If the latter becomes severe, patients may develop sensory ataxia. As the neuropathy continues to progress, sensory abnormalities ultimately involve all modalities and extend to a diamond-shaped periumbilical area. Far advanced disease may affect sensation over the skull vertex and facial midline structures. Atrophy and areflexia occur as weakness worsens. Severely impaired patients may be unable to ambulate or grasp objects. These symptoms have a significant impact on the patient's quality of life, affecting not only physical functioning but emotional, sleep, and social functioning. Many of these patients display signs of depression or anxiety.<sup>21</sup> Polyneuropathies can be difficult to diagnose and are best approached by performing electrodiagnostic studies on patients with a constellation of symptoms and signs suggesting a particular neuropathy.<sup>22</sup>

**Management.** As with virtually all peripheral neuropathies, referral is indicated for management of diabetic DSPNs. If discomfort is severe, the etiology of the neuropathy seems likely to be diabetic, and if referral is delayed, it may be necessary to provide the patient with some symptomatic relief. Because treatment of neuropathic pain has traditionally been linked to etiology rather than an underlying mechanism, the choice of pharmacologic agents is empirical, with substantial practice variation in the United States and worldwide.<sup>23</sup> In the United States the first choice is often a nonsteroidal anti-inflammatory drug, which has little proven efficacy and a high potential for renal impairment.<sup>3</sup> Based on placebo-controlled randomized clinical trials, tricyclic antidepressants and anti-convulsants appear to have the best NNTs (number of patients needed to treat in order to provide at least 50% relief of symptoms in one patient). These are generally in the range 3 to 5,

with confidence intervals whose upper limits reach 10 in some instances.<sup>24</sup> Imipramine or amitriptyline may be started at a dose of 25 mg at bedtime (10 mg in elderly patients) and titrated slowly up to a dose of 300 mg. Carbamazepine at a dose of 200 to 400 mg every 8 hours or gabapentin at a dose of 900 to 3600 mg/day are also effective treatments.<sup>25,26</sup> Tramadol in two studies has shown an NNT below 5.<sup>24</sup> Although tramadol is a mixed opioid, development of dependence in long-term use appears to be uncommon. In a recently published guideline, the following medications were recommended for the treatment of neuropathic pain: gabapentin, opioids, tramadol, and tricyclic antidepressants.<sup>3</sup> Also being used is pregabalin at 150 to 600 mg/day, with a mechanism similar to that of gabapentin, and duloxetine at 60 mg/day, which is a selective serotonin and norepinephrine reuptake inhibitor.<sup>3</sup> Among the selective serotonin reuptake inhibitors (SSRIs), paroxetine and bupropion appear to be effective, but fluoxetine is not.<sup>27</sup> The summary NNT for the SSRIs has a confidence interval that reaches 50, suggesting that, pending further data, these agents should be considered second-line drugs.<sup>24</sup> Topical capsaicin provides relief in some patients, but the burning associated with its application has limited its usage. Improving glycemic control can prevent, diminish, or reverse early diabetic DSPNs. Patients will typically spend over \$1,000 per year for pain relief from diabetic DSPN.<sup>3</sup>

### Alcoholic Distal Symmetrical Polyneuropathy

Although the association between alcoholism and peripheral neuropathy has been well established for centuries, demonstration of a direct neurotoxic effect of alcohol remains elusive. The preponderance of evidence, from both observational studies in humans and experimental data from animal models,

suggests that the association between alcohol and peripheral neuropathy may be confounded by nutritional status (i.e., deficiency states might be the true underlying cause of alcoholic peripheral neuropathy).

The clinical and pathologic picture of alcoholic neuropathy is similar to that of the DSPN of diabetes. However, in alcoholism severe myopathy and cerebellar degeneration often complicate the clinical picture.<sup>28</sup> Autonomic skin changes with atrophy and hair loss accompany the sensorimotor abnormalities. Often other systemic effects of alcoholism are so severe that the patient may not notice the neuropathic symptoms. All patients with suspected alcoholic DSPN should receive dietary supplements and referral for outpatient management.

### Human Immunodeficiency Virus Neuropathies

With the widespread use of highly active and effective anti-retroviral treatment, peripheral neuropathies have become the most common neurologic complication of HIV infection. The typical HIV neuropathy is a DSPN, which appears to be triggered by a combination of dideoxynucleoside therapy and poorly characterized immune-mediated mechanisms associated with HIV.<sup>29,30</sup> These patients require referral for specialized care. In addition to standard therapies for DSPN, lamotrigine has been shown to be moderately effective in the treatment of HIV-associated painful neuropathies.<sup>31</sup>

### Toxic and Metabolic Neuropathies

Many toxic agents and metabolic derangements produce a typical DSPN. [Box 105-3](#) lists some of the most common toxic and metabolic causes of peripheral neuropathy. On the basis of preliminary results from a case-control study, the statins have been added to this list.<sup>32</sup>

## Type 3: Asymmetrical Proximal and Distal Peripheral Neuropathies (Radiculopathies and Plexopathies)

Radiculopathies are discussed in detail in Chapter 103. Plexopathies, which are discussed briefly in this chapter, are uncommon and often the result of trauma ([Box 105-4](#)). Generally, a plexopathy, whether brachial or lumbosacral, is identified by a process of elimination (i.e., a pattern of sensorimotor and reflex abnormalities that fit neither a radicular nor individual peripheral nerve distribution). Although this approach does not exclude a mononeuropathy multiplex on physical examination alone, a careful history should determine whether the patient is at risk for developing a mononeuropathy or plexopathy on the basis of underlying disease.

Most plexopathies are often the result of blunt trauma and are usually seen in young men following motor vehicle accidents. Most present for evaluation several months after injury because of the need to recover from concurrent injuries. Therapeutic intervention is often delayed in order to maximize the potential for spontaneous recovery. Several surgical repairs exist, including neurotization or nerve transfer.<sup>33</sup>

Radiation (actinic) plexopathy occurs after a variable period of latency following treatment, which may extend to 20 years or more. Almost all series include women who received radiation treatment for breast cancer. Among neoplastic causes, most originate from the lung or breast. Patients with probable neoplastic brachial plexopathy need imaging studies and may require immediate radiation therapy. Pain control is the focus of management.

Thoracic outlet syndrome remains a controversial disorder.<sup>34</sup> Although the pendulum has swung over the past 50 years from

### BOX 105-4

#### ASYMMETRICAL PROXIMAL/DISTAL PERIPHERAL NEUROPATHIES

##### Brachial plexopathy

###### Open

- Direct plexus injury (knife or gunshot wound)
- Neurovascular (plexus ischemia)
- Iatrogenic (central line insertion)

###### Closed

- Traction injuries
- “Stingers”
- Traction neurapraxia
- Partial or complete nerve root avulsion
- Radiation
- Neoplastic
- Idiopathic brachial plexitis
- Thoracic outlet

##### Lumbosacral plexopathies

###### Open

###### Closed

- Traction injuries
- Pelvic double vertical shearing fracture
- Posterior hip dislocation
- Retroperitoneal hemorrhage
- Vasospastic (deep buttock injection)
- Neoplastic
- Radiation
- Idiopathic lumbosacral plexitis
- Infectious
- Herpesvirus (sacroccygeal)
- Herpes simplex II
- Herpes zoster
- Cytomegalovirus (CMV) polyradiculopathy (HIV)

a postulated vascular cause to a neurogenic etiology, current evidence supporting the high prevalence of compression of the brachial plexus as a cause of thoracic outlet syndrome is in fact only slightly better<sup>35</sup> than earlier evidence favoring a vascular etiology.<sup>36</sup> Nevertheless, the disorder is currently felt to be most commonly due to compression of the medial or lower portion of the brachial plexus by a cervical rib or fibrous band.<sup>37</sup> The syndrome is characterized by gradually progressive weakness and wasting of median and ulnar hand muscles with ulnar forearm and hand sensory signs and symptoms. Patients with this clinical picture should be referred for NCSs and EMG, which are said to be diagnostic.<sup>37</sup> The treatment of true neurogenic thoracic outlet syndrome requires surgical removal of the rib or aberrant fibrous band to decompress the brachial plexus.<sup>38</sup> An excellent discussion of this entity from a different perspective can be found in Chapter 85.

Because of the complexity of plexopathies, there is no reason to expect that one can or should do more in the ED than localize the probable pathologic process to the brachial or lumbosacral plexus. Depending on severity and suspected etiology, one should either admit or refer the patient to a neurologist with experience in PNS disease.

## Type 4: Isolated Mononeuropathies

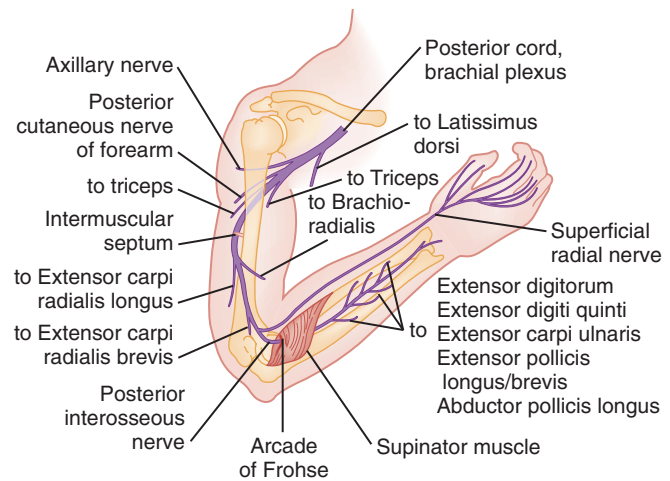
The pattern of asymmetrical, sensorimotor, usually distal, peripheral neuropathy is characteristic of a mononeuropathy. Mononeuropathies are of two main types: isolated and multiple. The isolated mononeuropathies are discussed in this section, while the multiple mononeuropathies, also termed

**BOX 105-5 ISOLATED MONONEUROPATHIES**

Upper extremity
Radial nerve
Axilla
Humerus
Elbow (posterior interosseous neuropathy)
Wrist (superficial cutaneous radial neuropathy)
Ulnar nerve
Axilla
Humerus
Elbow
Condylar groove
Cubital tunnel
Wrist (Guyon's canal)
Hand
Superficial terminal ulnar neuropathy
Deep terminal ulnar neuropathy
Proximal hypothenar
Distal hypothenar
Median nerve
Axilla
Humerus (musculocutaneous mononeuropathy)
Forearm
Anterior interosseus
Pronator syndrome (?)
Wrist (carpal tunnel)
Hand (recurrent motor branch)
Suprascapular mononeuropathy
Axillary mononeuropathy
Lower extremity
Sciatic nerve
Femoral nerve
Iliac compartment (proximal)
Saphenous mononeuropathy (distal)
Lateral femoral cutaneous (meralgia paresthetica)
Peroneal nerve
Common peroneal mononeuropathy (fibular head, popliteal fossa)
Deep peroneal mononeuropathy (anterior compartment)
Tibial nerve
Popliteal fossa (proximal)
Tarsal tunnel (distal)
Sural nerve
Popliteal fossa, calf (proximal)
Fifth metatarsal base (distal)
Plantar nerve
Distal to tarsal tunnel
Interdigital neuropathies (Morton's neuroma)
Obturator mononeuropathy

*mononeuropathy multiplex*, are discussed in the next section, as a type 5 peripheral neuropathy.

Isolated mononeuropathies are usually caused by trauma, either blunt or penetrating (Box 105-5). If the trauma is blunt, the injury may be secondary to compression from an internal or external source. Entrapment neuropathies are a subset of compression neuropathies occurring at anatomic locations where nerves traverse potentially constricting compartments or tunnels.<sup>39</sup> Isolated mononeuropathies may be acute, intermittent, or chronic and continuous. Antecedent peripheral neuropathy may be a risk factor for development of compression neuropathy (so-called double-crush syndrome), particularly in diabetics.<sup>40</sup>



**Figure 105-3.** Radial nerve, major branches, right arm, lateral view. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

### Radial Mononeuropathy

The radial nerve arises from C5-T1 roots. After exiting the brachial plexus, it passes behind the proximal humerus in the spiral groove and takes a lateral (radial) course down the upper arm (Fig. 105-3). At about the level of the antecubital fossa, it bifurcates into the posterior interosseous (pure motor) and superficial radial (pure sensory) nerves.

The radial nerve controls extension of the fingers, thumb, wrist, and elbow (triceps). In contrast to the median and ulnar nerves, the radial nerve provides only *extrinsic* motor innervation to the hand (i.e., it does not supply motor fibers to any muscles that both originate and insert within the hand). In further contrast to the median and ulnar nerves, which supply most of the sensation to the hand, the radial nerve makes a contribution only to a cutaneous dorsal area overlying the first dorsal interosseus muscle, sometimes extending part of the way up the dorsa of the thumb, index, and long fingers.

Radial mononeuropathy caused by involvement at the level of the axilla is uncommon. When it occurs, it is usually associated with other upper extremity mononeuropathies or a brachial plexopathy. Although improper use of crutches may cause this syndrome, it usually occurs after an extended period of unconsciousness during which the arm is positioned in such a way that prolonged, deep compression is applied to the axilla. Axillary radial mononeuropathy is distinguished from the more common humeral form by the finding of triceps involvement in addition to typical wrist and finger drop. Triceps involvement occurs because the innervation to the triceps is proximal to the point where the nerve is most vulnerable as it winds around the humeral shaft (see Fig. 105-3).

Most radial mononeuropathies are due to so-called Saturday night palsies. The euphemism is derived from the association of radial mononeuropathy with improper positioning of the arm during deep, commonly inebriated sleep. Consequently, the radial nerve is trapped for a prolonged period between the humeral shaft and some firm surface, causing an external compression mononeuropathy. “Bridegroom’s palsy” is another eponym for radial mononeuropathy, so named because the radial nerve may be compressed by the bride’s head resting on the bridegroom’s arm during sleep.

Because innervation of the wrist and finger extensors occurs distal to this area of the humeral shaft, findings are characterized by wrist and finger drop and mild numbness over the skin of the first dorsal interosseus muscle. Depending on the level,

degree, and duration of compression, some fascicles of the nerve may remain functional, resulting in a partial radial mononeuropathy. Thus, the superficial radial nerve may remain intact, resulting in no loss of sensation, or loss of wrist and finger extension may be incomplete.

Because the finger drop of radial mononeuropathy places the hand at a mechanical disadvantage, examination of ulnar function by testing interossei may produce false-positive findings of weakness. To adjust for this, the examiner should ask the patient to place the palm on a horizontal supporting surface such as a stretcher. With the fingers extended and no longer “dropped” at the metacarpophalangeal joints, interosseous strength can now be fairly tested. Failure to perform this maneuver may cause misdiagnosis of a simple radial mononeuropathy as a brachial plexopathy in an effort to explain what appears to be radial and partial ulnar nerve involvement.

About 90% of radial nerve palsies occurring during sleep, coma, or anesthesia recover fully, usually within 6 to 8 weeks. Evidence of denervation on EMG studies predicts a slower rate of recovery. Tourniquet injuries to the radial nerve usually recover spontaneously within 2 to 4 months. If axonal degeneration is seen on electrophysiologic testing, recovery may take longer, although virtually all radial mononeuropathies caused by tourniquets eventually resolve. About 75% of radial nerve injuries associated with a closed humeral shaft fracture

recover spontaneously. In contrast, surgical intervention is needed to free the nerve from entrapment associated with complex fractures.

While patients are waiting for spontaneous recovery to occur, the hand should be maintained in about 60 degrees of dorsiflexion. Although a simple dorsal plaster or fiberglass splint treats the wristdrop, atrophy and contractures can be minimized, and function of the hand can be improved if wide rubber bands anchored to the splint at a point proximal to the wrist are attached to individual fingers to provide passive dorsiflexion.

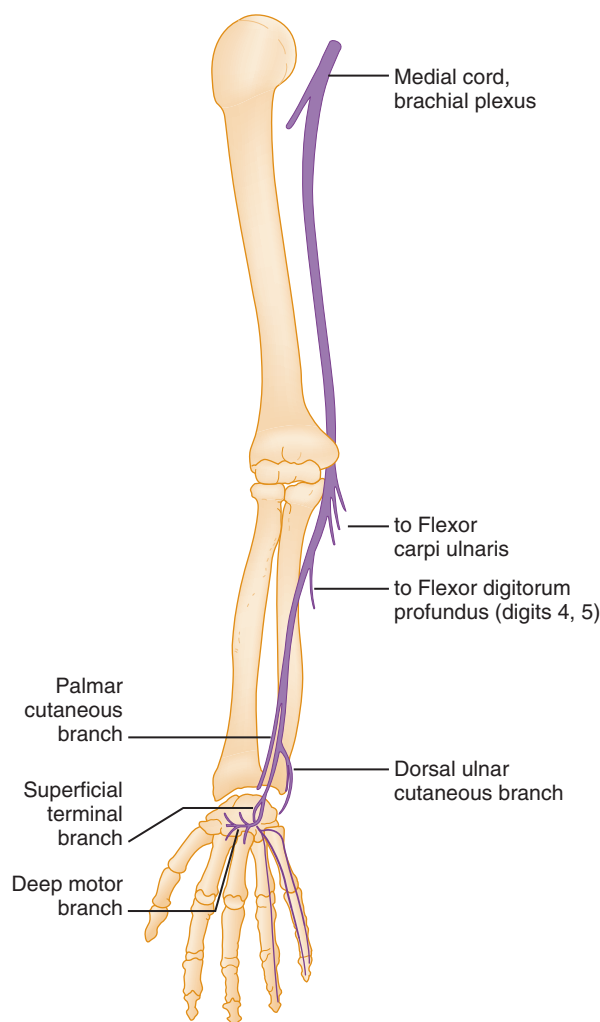
### Ulnar Mononeuropathy

The ulnar nerve includes C7-T1 roots and passes through the brachial plexus to descend medially, without branching, to the ulnar (medial) condylar groove at the elbow. It then enters the cubital canal, where it gives off branches to the ulnar wrist flexor and the deep flexors of the fourth and fifth digits.

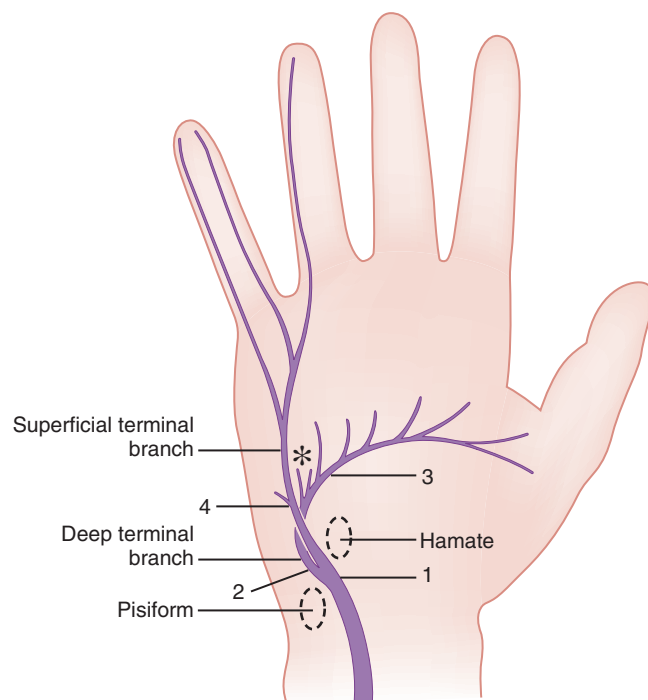
Just proximal to the wrist, two important sensory branches leave the main trunk to supply cutaneous sensation to part of the hand (Fig. 105-4). These are the palmar and dorsal cutaneous branches, which do *not* pass through Guyon’s canal. The palmar branch supplies sensation to the hypothenar eminence and the dorsal branch innervates the ulnar side of the dorsum of the hand, extending out nearly to the tip of the fifth and ulnar half of the fourth digit.

At the wrist, the nerve enters Guyon’s canal (Fig. 105-5) between the pisiform and hook of the hamate, then bifurcates into the superficial terminal sensory branch and the deep motor branch.

The superficial sensory nerve supplies ulnar sensation to the palmar side of the fifth and half of the fourth digit (see Fig. 105-5). The deep motor nerve supplies the hypothenar muscles, then crosses to the radial side of the palm to innervate



**Figure 105-4.** Ulnar nerve, major branches, right arm, anterior view. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)



**Figure 105-5.** Distal ulnar nerve and branches, right hand, palmar view. Numbers indicate four main sites of distal ulnar mononeuropathy in the wrist and hand. \*Denotes hypothenar branches. (From Stewart JD: Focal Peripheral Neuropathies, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)



the ulnar intrinsics (all interossei and the ulnar lumbricals of the fourth and fifth digits), terminating in the first dorsal interosseus. The interossei abduct and adduct the fingers and are all innervated by the ulnar nerve. The lumbrical muscles flex the metacarpal phalangeal joints and are evenly divided between the ulnar (fourth and fifth) and median (second and third) digits. The ulnar nerve can be thought of as the complement to the median nerve in the hand because it supplies all of the muscles and all palmar sensation not innervated by the median nerve.

The ulnar nerve may be injured at two locations near the elbow: in the ulnar condylar groove and distally in the cubital canal. Because the condylar groove is shallow, the ulnar nerve runs superficially in this location and is vulnerable to injury, usually from external pressure or from a fracture or dislocation. The ulnar nerve has a propensity to develop a “tardy ulnar palsy,” occurring years after a traumatic event. Many of these delayed ulnar mononeuropathies can be localized to the elbow on electrophysiologic testing.

Some ulnar mononeuropathies occur secondary to compression just proximal to entry into the cubital canal or are entrapped within the canal itself. Transient symptoms may occur during prolonged flexion or with repeated flexion and extension at the elbow.

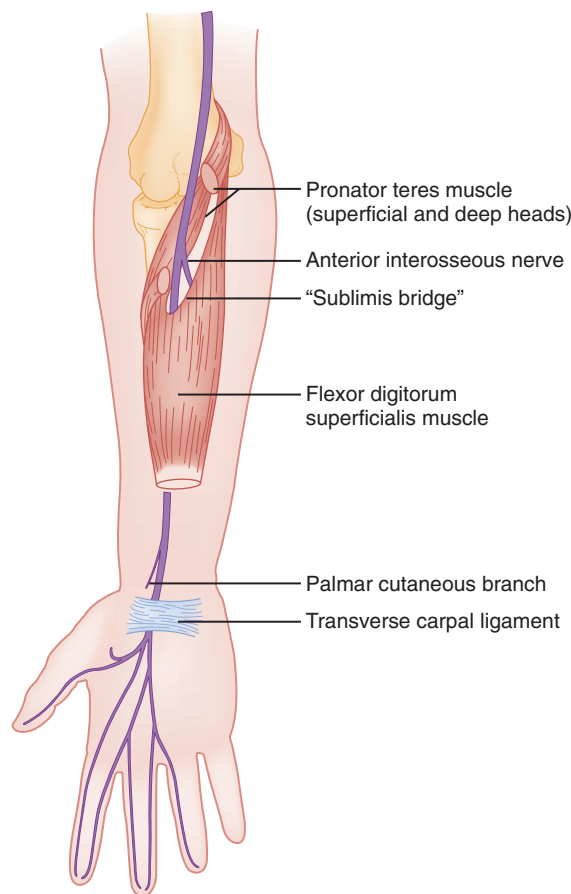
Although distinguishing a condylar from a cubital ulnar mononeuropathy is difficult, it is usually possible to localize the problem to the region of the elbow or the wrist. In addition to prior probability heavily favoring the elbow, the presence of sensory abnormalities in an ulnar distribution in the hand and fingers (i.e., usually including the fifth digit and “splitting” the fourth digit) strongly suggests that the lesion is at the level of the elbow rather than the wrist. The ulnar cutaneous innervation to the hand branches off from the main trunk proximal to the nerve entering Guyon’s canal (see Figs. 105-4 and 105-5). Thus, a lesion at the wrist should not produce sensory abnormalities, whereas one at the elbow would be expected to do so.

Compression of the ulnar nerve within Guyon’s canal is rare. When it does occur, it affects all of the ulnar intrinsics (i.e., the two ulnar [fourth and fifth] lumbricals) and all the interossei. However, the ulnar extrinsics (i.e., the deep flexors of the fourth and fifth digits) are not affected, nor is the ulnar flexor of the wrist. The only sensory abnormalities are those in the distribution of the superficial terminal sensory branch, sparing other areas of ulnar innervation (see Fig. 105-5).

There are three ulnar mononeuropathies that occur distal to Guyon’s canal in the hand. The two most common ones involve the deep terminal branch, either proximal or distal to the separation of the hypothenar branches (see Fig. 105-5). If the lesion is proximal, it produces weakness of all the ulnar innervated muscles of the hand without sensory loss. If it is distal, the hypothenar ulnar intrinsics are spared but the picture is otherwise similar. Usually, this occurs secondary to a laceration or repeated compression in the hand from use of certain tools, a cane, or the handle of a crutch.

Involvement of the superficial terminal branch (see Fig. 105-5) arises as pure sensory loss of the palmar surface of the fifth digit and ulnar half of the fourth digit caused by direct compression of this branch just distal to Guyon’s canal. The dorsal surface of these two digits should have normal sensation except for the distal tips. This configuration of findings is due to the intact innervation provided by the dorsal and palmar cutaneous branches that enter the hand without passing through Guyon’s canal (see Fig. 105-4).

Most ulnar mononeuropathies will spontaneously resolve. However, if muscle atrophy, particularly in the hypothenar area, is detected, then surgery may be considered.<sup>41,42</sup>



**Figure 105-6.** Median nerve, major branches, right arm, anterior view. (From Stewart JD: *Focal Peripheral Neuropathies*, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

### Median Mononeuropathy

The median nerve arises from C5-T1 spinal nerve roots and exits the brachial plexus through the lower trunk (Fig. 105-6). Median mononeuropathy is usually diagnosed as carpal tunnel syndrome (CTS), which is the most common of all entrapment neuropathies. CTS has a prevalence of 3 to 6% in the U.S. population.<sup>43</sup> Although the patient may complain of bilateral symptoms, a careful history usually reveals that symptoms in one hand preceded those in the other. Awakening at night and shaking the hand is a common symptom of CTS. Symptoms are often worsened by activity. For unclear reasons, the pain may spread as high as the arm or shoulder, although the paresthesias are generally confined to the fingers. Many patients on initial questioning state that their entire hand is involved, although this is not supported by careful sensory examination. Complaints that the hands are clumsy or weak, especially when holding a glass or opening a screw-top container, are frequent. The skin of the fingers innervated by the median nerve may be drier and rougher to the touch than the corresponding ulnar skin, depending on the duration of entrapment.<sup>44</sup>

When there is motor involvement in CTS it is confined to the median intrinsics, which innervate the lumbricals (flexion of the metacarpal phalangeal joints), and subserve thumb opposition, abduction, and flexion, known as the LOAF muscles. However, the hallmark of CTS is sensory involvement, with motor abnormalities occurring later. The typical pattern of sensory innervation of the hand by the median, ulnar, and radial nerves shows marked individual variation.

## BOX 105-6

## CONDITIONS ASSOCIATED WITH CARPAL TUNNEL SYNDROME

Acromegaly  
Amyloid  
Diabetes mellitus  
Hypothyroidism  
Obesity  
Pregnancy  
Renal failure  
Rheumatoid arthritis

The most specific finding for CTS is splitting of the fourth digit (i.e., normal sensation of the ring finger on the ulnar palmar side with abnormal sensation on the median [radial] palmar side of the same finger). The most sensitive finding is abnormal sensation of the distal palmar tip of the index finger. If sensory findings are absent in the presence of motor findings consistent with median nerve involvement, it is highly unlikely that the patient has CTS, and an alternative diagnosis should be sought. If neither sensory nor motor symptoms are evident, none of the provocative tests originally reported to reproduce the sensory symptoms of CTS—of which the most common are Tinel's sign (percussion of the median nerve at the wrist) and Phalen's sign (maximal palmar flexion at the wrist)—has shown adequate sensitivity or specificity to determine which patients should be referred for electrodiagnostic studies.<sup>45–47</sup>

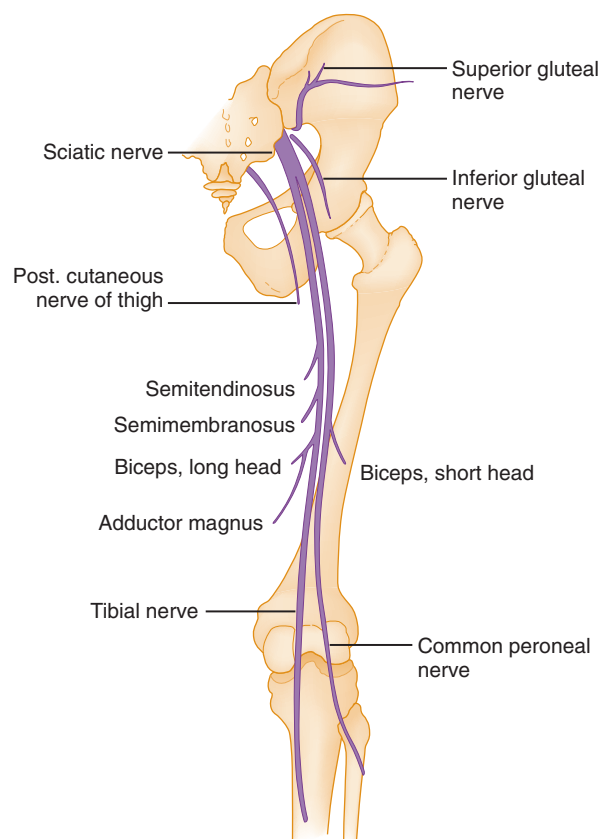
As suggested earlier, the best way to examine patients for sensory findings is to touch the distal palmar tips very lightly, asking the patient whether the sensation feels “abnormal.”

CTS appears to be associated with the conditions listed in Box 105-6. Of these, the two most common are diabetes mellitus and pregnancy. CTS associated with systemic illness is commonly bilateral. Although CTS in pregnancy may be self-limiting, about half the women in one series were still symptomatic at 1-year follow-up.<sup>48</sup> All patients with suspected CTS should be referred for NCSs. However, because of the dissociation between clinical and electrodiagnostic indicators of CTS early in the disease, patients with normal electrodiagnostic findings in the presence of symptoms suggestive of CTS (with or without signs) should have an MRI<sup>49</sup> or sonogram.<sup>50</sup> At present, the sensitivity of MRI is good but its specificity is poor.<sup>51</sup> Ultrasound has been shown to be useful particularly in patients with symptoms and a negative NCS. This is done by measuring the cross-sectional area of the median nerve at the end of the pisiform.<sup>52</sup> Thus, if all diagnostic studies in a symptomatic patient are negative, or if only the MRI result is positive, they should be repeated within a few months if symptoms do not resolve.<sup>44</sup> This recommendation is based on the theory that the CTS will progress over time to the point that an objective indicator such as the NCS will become positive.

Because of the possibility of development of a disabling “median hand” after inadvertent direct injection of the median nerve, one should not inject the carpal tunnel with steroids in the ED. The physician to whom the patient is referred can decide after NCS whether to recommend splinting, injection, or surgical division of the transverse carpal ligament. Endoscopic repair appears to provide excellent results.<sup>53</sup>

### Sciatic Mononeuropathy

The sciatic nerve includes L4-S3 spinal nerve roots that pass through the lumbosacral plexus and divide into two terminal branches: the common peroneal and tibial nerves. The nerve



**Figure 105-7.** Sciatic nerve, major branches, right leg, posterior view. (From Stewart JD: *Focal Peripheral Neuropathies*, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

exits the pelvis through the sciatic notch, passes behind the hip, and remains deep in the thigh until its terminal bifurcation in the proximal popliteal fossa (Fig. 105-7).

Lesions of the sciatic nerve occur with posterior hip dislocation or with virtually any form of penetrating or blunt trauma that causes formation of a buttock hematoma. Other causes include deep gluteal injection and prolonged supine immobilization on a firm surface. Because the sciatic nerve innervates the hamstrings and provides all sensorimotor function distal to the knee, a complete sciatic mononeuropathy is a devastating injury. Ambulation is extremely difficult because of inability to flex the knee and a flail foot (i.e., neither flexion nor extension is possible at the ankle). Fortunately, many sciatic mononeuropathies are incomplete. For unknown reasons, a partial lesion typically involves only the trunk of the sciatic nerve, which subsequently becomes the common peroneal nerve, sometimes making the two difficult to distinguish from one another clinically. On electrophysiologic studies, evidence of involvement of gluteal muscles or of any muscles innervated by the tibial nerve readily distinguishes a partial sciatic mononeuropathy from a lesion of the common peroneal nerve. Treatment of footdrop requires a posterior splint to maintain the ankle at 90 degrees until a brace can be obtained (see later section on “Common Peroneal Mononeuropathy”).

### Lateral Femoral Cutaneous Mononeuropathy

Lateral femoral cutaneous mononeuropathy (meralgia paresthetica) is a common syndrome believed to be caused by injury to this pure sensory nerve as it passes through or over the inguinal ligament, where it may become entrapped or kinked. Along with facial nerve neuropathy, meralgia paresthetica is

one of the most commonly reported mononeuropathies associated with HIV. External pressure and obesity may also contribute to nerve injury, causing numbness and dysesthesia over the skin of the upper lateral thigh. Regression usually occurs spontaneously, but recurrence is common and may require a release procedure for the inguinal ligament.

### Common Peroneal Mononeuropathy

The common peroneal nerve is a continuation of one trunk of the sciatic nerve. It is most vulnerable to injury where it winds around the fibular neck (Fig. 105-8). It then passes through the fibular canal and bifurcates into its terminal branches, the superficial and deep peroneal nerves. The superficial peroneal nerve innervates the peroneal muscles (foot everters) and supplies sensation to the lateral, distal lower leg and dorsum of the foot. The deep peroneal nerve traverses the anterior compartment and supplies innervation to the dorsiflexors of the foot and toes, plus cutaneous sensation between the first and second toes.

Most common peroneal mononeuropathies are idiopathic and thought to be related to compression where the nerve is superficially located lateral to the fibular neck. Because this common neuropathy is often noted on awakening, it may be secondary to position during sleep. Leg crossing may also be a risk factor for development of this mononeuropathy. The most striking feature of a complete common peroneal mononeuropathy is footdrop caused by weakness of foot dorsiflexion. At testing, the everters of the foot are also weak, but the inverters, which are innervated by the tibial nerve, remain strong. This is the single most reliable clinical feature distinguishing sciatic from common peroneal mononeuropathy. Analogous to radial mononeuropathy in the upper extremity, sensory abnormalities in the leg and foot are inconstant and easily overlooked in peroneal mononeuropathy. Most patients

with peroneal palsy recover. Those who do not should be studied electrophysiologically to ensure that the point of compression is not proximal to the fibular neck (i.e., in the popliteal fossa). If the point of peroneal injury appears to be in the region of, or distal to, the fibular neck on EMG, patients whose footdrop does not resolve should be considered candidates for exploration to determine whether the nerve is compressed within the fibular canal.

Treatment of common peroneal palsy may require a posterior splint to maintain the ankle at 90 degrees until the nerve regenerates. This splinting prevents the foot from falling into sustained equinus (plantar flexion), which in turn allows the intermalleolar distance to narrow, effectively locking the talus out of the ankle mortise.

The treatment of isolated mononeuropathies depends on their etiology, location, and natural history of spontaneous recovery. All penetrating neuropathies should have surgical exploration and repair performed. Blunt trauma may cause a mononeuropathy indirectly by entrapment of a nerve within a fracture, hematoma, or compartment, requiring surgical intervention. Alternatively, nerves may be injured at a point where they are superficial, either by a single direct blow or by sustained pressure caused by immobility (pressure palsies). Most of these resolve spontaneously over time, depending on the severity of injury and length of the nerve. If entrapment can be confirmed by imaging or electrophysiologic studies, a release procedure is indicated. In many instances, when there is disagreement between clinical and EMG findings, MRI may be helpful in selecting patients for exploration by visualizing entrapment or traction.<sup>54</sup> Characteristic sonographic findings have also been reported in several mononeuropathies.<sup>55</sup>

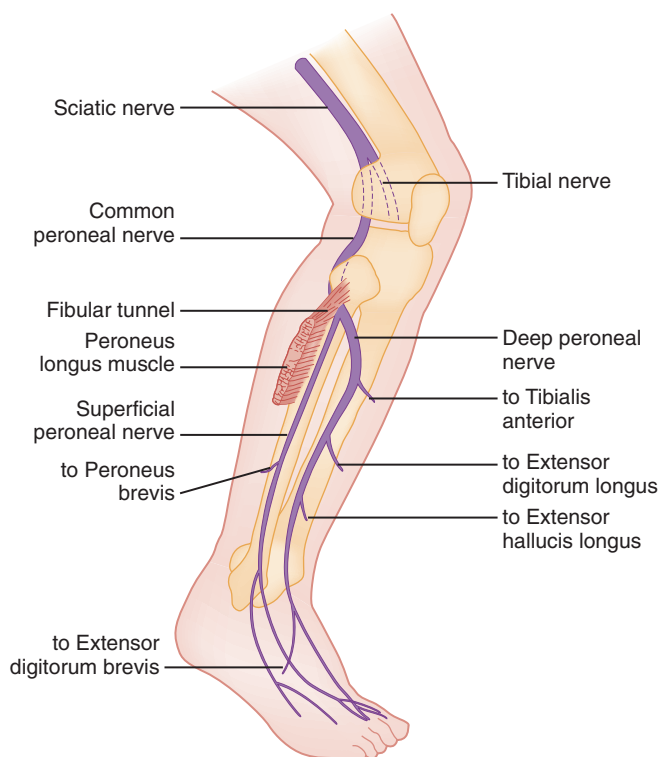
The mononeuropathies that do not require timely surgical exploration should be referred for further workup to confirm the location of the neuropathic lesion.

### Type 5: Mononeuropathy Multiplex

Mononeuropathy multiplex is characterized by an asymmetrical, sensorimotor, usually distal pattern of peripheral neuropathy (Box 105-7). As with isolated mononeuropathies, sensory abnormalities tend to be located in the same general anatomic region as the accompanying motor findings. Whether DTRs are affected depends on which nerves are involved. For example, if the process includes the femoral nerve, the patellar reflex is likely to be diminished or absent.

#### BOX 105-7 MONONEUROPATHY MULTIPLEX

Vasculitis  
 Systemic vasculitis  
   Polyarteritis nodosa  
   Rheumatoid arthritis  
   Systemic lupus erythematosus  
   Sjögren's syndrome (keratoconjunctivitis sicca)  
 Nonsystemic vasculitis  
 Diabetes mellitus  
 Neoplastic  
   Paraneoplastic  
   Direct infiltration  
 Infectious  
   Lyme disease  
   HIV  
 Sarcoid  
 Toxic (lead)  
 Transient (polycythemia vera)  
 Cryoglobulinemia (hepatitis C)



**Figure 105-8.** Common peroneal nerve, major branches, right leg, anterolateral view. (From Stewart JD: *Focal Peripheral Neuropathies*, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2000.)

## Vasculitis

Mononeuropathy multiplex is strongly associated with vasculitis, which is the most common indication for sural nerve biopsy in most series. However, because diabetes mellitus is far more prevalent than vasculitis, the most common cause of mononeuropathy multiplex among ED patients is diabetes.

## Diabetes Mellitus

Although the role of ischemia in diabetic neuropathies is controversial, evidence for a vascular cause is stronger in the asymmetrical diabetic multiple mononeuropathies than in the more common DSPNs seen in diabetes.

## Lyme Disease

The PNS manifestations of Lyme disease can be divided into early and late. The early PNS syndromes commonly include facial nerve involvement (rarely other cranial nerve palsies) and radiculoneuritis. Late PNS involvement occurs as a DSPN, mononeuropathy multiplex, or radiculoneuropathy. The most common neurologic abnormality in Lyme disease is unilateral or bilateral facial nerve palsy, usually occurring within a month of exposure. Patients may also complain of headache and constitutional symptoms. Early in the course of Lyme disease, severe neuritic pain may develop in a radicular distribution, often in or near the dermatome where the tick bite occurred. There may also be associated sensory changes, motor weakness, and decreased reflexes consistent with nerve root involvement. Patients with chronic Lyme disease present with sensory symptoms, particularly distal paresthesias in the lower extremities. Less commonly, they develop a picture consistent with mononeuropathy multiplex or a radiculopathy. The latter is much less severe than the early radiculoneuritis of Lyme disease.

The most useful diagnostic tests for patients with suspected Lyme disease are a serum enzyme-linked immunosorbent assay, Western blot, and CSF examination. CSF abnormalities suggestive of Lyme disease are a lymphocytic pleocytosis, elevated protein, and normal glucose. The CSF is almost always abnormal in early radiculitis, sometimes abnormal with isolated facial palsy, and typically normal in chronic Lyme disease. Facial nerve palsy without CSF abnormalities may be treated with oral doxycycline 100 mg twice a day for 2 weeks. Intravenous ceftriaxone is the drug of choice for all other neurologic syndromes associated with Lyme disease. The adult dosage is 2 g/day, and the pediatric dosage is 75 to 100 mg/kg/day. Treatment with ceftriaxone should be continued for at least 2 weeks.

## Type 6: Amyotrophic Lateral Sclerosis

Although *amyotrophic lateral sclerosis* (ALS) and *motor neuron disease* (MND) are often used synonymously, the latter represents a spectrum of diseases ranging from primary lateral sclerosis, in which degeneration is confined to upper motor neurons, to progressive muscle atrophy, in which only lower motor neurons are involved. ALS, which requires the presence of both upper and lower motor neuron findings, resides in the middle of this spectrum, representing the most common form of MND. The incidence of ALS is 1.5 to 2.5 per 100,000.<sup>56</sup>

In ALS, the primary pathologic process in the PNS component of the disease is a neuronopathy of the anterior horn cell. Because this structure is located proximal to the point where

### BOX 105-8

#### OBJECTIVE CLINICAL FINDINGS CONSISTENT WITH AMYOTROPHIC LATERAL SCLEROSIS

Upper motor neuron signs  
 Hyperreflexia  
 Sustained clonus, especially at ankle  
 Finger flexors and jaw jerk  
 Spasticity, especially of gait  
 Positive Babinski sign  
 Lower motor neuron signs  
 Positive motor phenomena  
 Fasciculations  
 Cramps  
 Negative motor phenomena  
 Asymmetrical distal weakness  
 Atrophy  
 Combined upper and lower motor neuron signs  
 Dysarthria  
 Dysphagia  
 Respiratory compromise

motor and sensory fibers merge to form mixed spinal nerve roots, the signs and symptoms of MND are purely motor (see Fig. 105-2). In the CNS, there is a loss of Betz cells from the motor cortex with secondary degeneration of the corticospinal tracts. Box 105-8 lists some representative upper, lower, and mixed motor signs. Patients typically demonstrate asymmetrical distal weakness without sensory findings. Positive motor phenomena in the form of fasciculations are found in almost all patients at diagnosis but are rarely an initial complaint. Although there is electrophysiologic evidence of autonomic involvement in ALS, this is generally subclinical.

Most patients with an asymmetrical, distal, pure motor neuropathy have ALS, for which only supportive treatment is currently available. However, there are some preliminary studies of recombinant human insulin-like growth factor 1 that have shown marginal improvement in this otherwise fatal disease.<sup>57</sup> All patients in whom this diagnosis is suspected should be referred for electrophysiologic confirmation against standardized criteria. Confirmation is particularly important because multifocal motor neuropathy, a rare disease that masquerades as ALS, responds dramatically to cyclophosphamide and immunoglobulin administration.<sup>58</sup>

## Type 7: Sensory Neuronopathy (Ganglionopathy)

This category of peripheral neuropathy is characterized by a selective or predominant involvement of the dorsal root ganglion, producing a relatively pure sensory syndrome analogous to the pure motor syndrome of ALS. Although all sensory modalities are affected, proprioception is profoundly altered, leading to sensory ataxia and loss of DTRs without weakness. The distribution is typically asymmetrical and distal at the outset, but depending on severity and extent of progression, it may become functionally symmetrical. Sensory ganglionopathies can now be confirmed by MRI of the spinal cord and surrounding areas, showing degeneration of central sensory projections that localize the disease process to the dorsal root ganglion.<sup>59</sup> Some of the more common causes of this type of peripheral neuropathy are listed in Box 105-9.



**BOX 105-9 SENSORY NEURONOPATHIES (GANGLIONOPATHIES)****Herpes**

- Herpes simplex I and II
- Varicella zoster (shingles)

**Inflammatory sensory polyganglionopathy (ISP)****Paraneoplastic****Primary biliary cirrhosis****Sjögren's syndrome (keratoconjunctivitis sicca)****Toxin induced**

- Pyridoxine (vitamin B<sub>6</sub>) overdose
- Metals
  - Platinum (cisplatin)
  - Methyl mercury
- Vitamin E deficiency

**BOX 105-10 ANCILLARY DIAGNOSTIC TESTING IN SUSPECTED PERIPHERAL NEUROPATHY****Obtained in most patients**

- Complete blood count (CBC)
- Erythrocyte sedimentation rate (ESR)
- Glucose
- Creatine kinase (CK)
- Creatinine

**Obtained only if indicated**

- Human chorionic gonadotropin (HCG)
- Magnesium
- Phosphate
- Vitamin B<sub>12</sub>
- Hemoglobin A<sub>1c</sub>
- Serum protein electrophoresis (SPEP) with immune fixation electrophoresis (IFE)
- Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) screen with fluorescent treponemal antibody-absorption (FTA-ABS) test, as appropriate
- Thyroid function
- HIV
- Lyme enzyme-linked immunosorbent assay (ELISA) and Western blot
- Rheumatoid factor and antinuclear antibody
- Blood, urine, hair, or nails for metal, depending on suspected chronicity of exposure
- Specific serum antibodies to components of peripheral nervous system
- Cerebrospinal fluid for cells, protein, Lyme titer
- Electrodiagnostic testing
  - Nerve conduction studies
  - Electromyography
- Neurodiagnostic imaging
  - Magnetic resonance imaging
  - Computed tomography
  - Sonography
- Quantitative sensory testing
- Nerve biopsy
  - Sural
  - Intraepidermal nerve fiber density

**■ ANCILLARY DIAGNOSTIC TESTING**

Relatively few blood tests contribute to the diagnosis of peripheral neuropathy, and only a small number of these are available in the ED. CSF analysis may be helpful in GBS and Lyme disease. Additional tests that may be indicated in patients referred for evaluation are listed in [Box 105-10](#), along with others that may be ordered selectively, depending on the clinical picture. Expensive batteries of tests purporting to measure a wide variety of antibodies to components of peripheral neuropathies are commercially available but have not been shown to be useful as screening tests.

**KEY CONCEPTS**

- In the emergency department, it is not usually possible to arrive at the diagnosis of a specific peripheral neuropathy because of the need for confirmatory ancillary testing that is beyond the scope of emergency practice. Rather, the focus should be on identifying one of seven categorical patterns of peripheral neuropathy, shown in [Figure 105-1](#) and listed in [Table 105-1](#), after other non-PNS causes have been eliminated.
- One of these seven patterns can usually be identified by combining three clinical features that are readily obtainable from a goal-directed history and physical: (1) right-left symmetry or asymmetry, (2) proximal-distal location, and (3) sensorimotor modalities affected. This approach is summarized as an algorithm in [Figure 105-1](#).
- Identification of one of the seven types of peripheral neuropathy determines the need for ancillary diagnostic testing, therapeutic intervention, disposition, and the timing of neurologic referral.
- Respiratory compromise is the primary life-threatening event seen in some peripheral neuropathies; GBS is by far the most common peripheral neuropathic cause of respiratory arrest.
- Any patient with symmetrical weakness, distributed both proximally and distally, with loss or diminution of DTRs and variable sensory abnormalities should be treated as having GBS.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

**PART I**

# Fundamental Clinical Concepts



## CHAPTER 1 Airway

Ron M. Walls

### ■ PERSPECTIVE

Airway management is the cornerstone of resuscitation and is a defining skill for the specialty of emergency medicine. The emergency physician has primary responsibility for management of the airway. All techniques of airway management lie within the domain of emergency medicine. Rapid sequence intubation (RSI) with direct laryngoscopy is the most commonly used method for emergency intubation, but emergency airway management includes various intubation maneuvers, use of ancillary devices, approaches to the difficult airway, and rescue techniques when intubation fails.

Since the first reported use of neuromuscular blocking agents (NMBAs) in the emergency department (ED) by emergency personnel in 1971, there has been progressive sophistication of emergency airway techniques, pharmacologic agents, and special devices used to facilitate intubation.<sup>1,2</sup> In the 1990s, RSI was widely adopted as the method of choice for most emergency intubations in the ED, and increasing attention has focused on identification and management of anticipated difficult intubation.<sup>3,4</sup>

### ■ PATHOPHYSIOLOGY

#### Decision to Intubate

A decision to intubate should be based on careful assessment of the patient with respect to three essential criteria: (1) failure to maintain or protect the airway, (2) failure of ventilation or oxygenation, and (3) the patient's anticipated clinical course and likelihood of deterioration.<sup>5</sup>

#### Failure to Maintain or Protect the Airway

A patent airway is essential for adequate ventilation and oxygenation. If the patient is unable to maintain the airway, patency must be established by artificial means, such as repositioning, chin lift, jaw thrust, or insertion of an oral or nasal airway. Likewise, the patient must be able to protect against aspiration of gastric contents, which carries significant morbidity and mortality. Traditionally, the presence or absence of a gag reflex has been advocated as a reliable indicator of the patient's ability to protect the airway, but the gag reflex is absent in 12 to 25% of normal adults, and there is no evidence that its presence or absence corresponds to airway protective

reflexes or the need for intubation.<sup>6</sup> Testing the gag reflex in an obtunded, supine patient is unlikely to yield useful information with respect to the need to intubate and may precipitate vomiting. The patient's ability to swallow or handle secretions is a more reliable indicator of airway protection.<sup>5</sup> The recommended approach is to evaluate the patient's ability to phonate in response to voice command or query (which provides information about level of consciousness and voice quality), level of consciousness, and ability to manage his or her own secretions (e.g., pooling of secretions in the oropharynx, absence of swallowing spontaneously or to command.) In general, a patient who requires a maneuver to establish a patent airway or who easily tolerates an oral airway probably requires intubation for protection of that airway, unless a temporary or readily reversible condition, such as opioid overdose, is present.

#### Failure of Ventilation or Oxygenation

Ventilatory failure that is not reversible by clinical means or increasing hypoxemia that is not adequately responsive to supplemental oxygen is a primary indication for intubation. This assessment is clinical and includes evaluation of the patient's general status, oxygenation by pulse oximetry, and changes in the ventilatory pattern. Continuous capnography also can be helpful, but is not essential if oximetry readings are reliable. Arterial blood gases (ABGs) generally are not required to determine the patient's need for intubation. In most circumstances, clinical assessment, including pulse oximetry with or without capnography, and observation of improvement or deterioration lead to a correct decision. ABG results are rarely helpful, may cause delay in intubating a deteriorating patient, and may be misleading, so, if obtained, they must be interpreted carefully in the context of the patient's clinical status. Patients who are clinically improving despite severe or worsening ABG alterations may not require intubation, whereas a rapidly tiring patient may require intubation when ABG values are only modestly disturbed or even improving.

Regardless of the underlying cause, the need for mechanical ventilation generally mandates intubation. External mask devices increasingly have been used to provide assisted mechanical ventilation without intubation (see Chapter 2), but despite these advances, most patients who need assisted ventilation or positive pressure to improve oxygenation require intubation.<sup>7</sup>



## Anticipated Clinical Course

Certain conditions indicate the need for intubation even in the absence of frank airway, ventilatory, or oxygenation failure. These conditions are characterized by a moderate to high likelihood of predictable deterioration that would require airway intervention. Intubation may be indicated relatively early in the course of severe cyclic antidepressant overdose. Although the patient is awake, protecting the airway, and exchanging gas well, intubation is advisable to guard against the strong likelihood of clinical deterioration, which can occur relatively abruptly and includes coma, seizure, cardiac dysrhythmia or arrest, and possible aspiration of activated charcoal or gastric contents.

Significant multiple trauma, with or without head injury, may be an indication for intubation.<sup>8,9</sup> Many of these patients are ventilating normally through a patent airway, and oxygen levels frequently are normal or supernormal with supplemental oxygen. Despite this, anticipated deterioration, loss of the ability to protect the airway, the need for invasive and painful procedures, or the need for studies outside the ED (e.g., computed tomography, angiography) may mandate intubation.<sup>10</sup> A patient with penetrating neck trauma may present with a patent airway and adequate gas exchange. Nevertheless, early intubation is advisable with any evidence of vascular or direct airway injury because these patients tend to deteriorate and because increasing hemorrhage or swelling in the neck tends to both compromise the airway and confound later attempts at intubation.<sup>11,12</sup>

Although these indications for intubation may seem quite different and individualized, the common thread is the anticipated clinical course over time. In each circumstance, it can be anticipated that future events will compromise either the patient's ability to maintain and protect the airway or the patient's ability to oxygenate and ventilate. A similar thought process is applied to any patient who will be leaving the ED for diagnostic studies (e.g., angiography) or who may be transported to another facility. If it seems clinically likely that the patient may deteriorate, then "preemptive" intubation is the prudent course.

## CLINICAL FEATURES

### Identification of the Difficult Airway

In most patients, even in the ED's dynamic and unpredictable environment, intubation is technically easy and straightforward. In large ED studies, overall intubation failure rates are less than 1% for medical intubations and less than 3% in trauma patients.<sup>1,13,14</sup> Intubation failure occurs in approximately 1 in 200 to 1 in 2000 elective general anesthesia cases.<sup>3,15,16</sup> Bag-mask ventilation (BMV) is difficult in approximately 1 in 50 general anesthesia patients, and impossible in approximately 1 in 600.<sup>17,18</sup> BMV is difficult, however, in up to one third of patients in whom intubation failure occurs, and difficult BMV makes the likelihood of difficult intubation four times greater and the likelihood of impossible intubation 12 times greater.<sup>17,18</sup> The combination of failure of intubation and failure of BMV in elective anesthesia practice is estimated to be exceedingly rare: 1 in 5000 to 1 in 20,000 elective anesthesia patients.<sup>16,18</sup> These numbers cannot be applied directly to the ED situation, where patient selection cannot occur (as with a preanesthetic visit), but are reassuring in that they indicate a high degree of safety if a preintubation analysis of factors predicting difficult intubation is undertaken.<sup>19</sup>

The emergency nature of the patient's presentation often precludes postponement of the intubation, even for a short

time, but knowledge of the difficulties presented by the patient's airway permits thoughtful planning and preparation for possible intubation failure. Preintubation assessment should evaluate the patient for difficult intubation, difficult BMV, difficult ventilation using an extraglottic device (EGD), such as a laryngeal mask airway, see later discussion) and difficult cricothyrotomy. Knowledge of all four domains is crucial to successful planning.<sup>3,4</sup>

Neuromuscular paralysis should be avoided in patients for whom a high degree of intubation difficulty is predicted, unless the administration of the NMBA is part of a planned approach to the difficult airway. This approach may include use of a *double setup*, in which an alternative approach, such as cricothyrotomy, is simultaneously prepared.

Preintubation evaluation should be as comprehensive as clinical circumstances permit. A systematic approach to the patient is required.

### Difficult Direct Laryngoscopy: LEMON

Most of the difficult airway markers discussed in the anesthesia and emergency medicine literature have not been scientifically validated.<sup>20</sup> Nevertheless, a methodical approach can be used to evaluate the patient, based on the accepted markers of difficult intubation by direct laryngoscopy. One such approach uses the mnemonic *LEMON* (Box 1-1).<sup>3,21</sup>

**L—Look Externally.** The patient first should be examined for external markers of difficult intubation, which are determined based simply on the intubator's clinical impression. For example, the severely bruised and bloodied face of a combative trauma patient, immobilized in a cervical collar on a spine board, might (correctly) invoke an immediate appreciation of anticipated difficult intubation. Subjective clinical judgment can be highly specific (>90%), but insensitive and so must be augmented by other evaluations.<sup>18</sup>

**E—Evaluate 3-3-2.** The second step in the evaluation of the difficult airway is to assess the patient's anatomy to determine his or her suitability for direct laryngoscopy. Direct laryngoscopy requires the ability to visualize the glottis by direct vision through the mouth, using alignment of the oral, pharyngeal, and laryngeal axes. Visualization requires that the mouth open adequately, that the submandibular space be adequate to accommodate the tongue, and that the larynx be positioned low enough in the neck to be accessible. These relationships have been explored in various studies by external measurement of mouth opening, oropharyngeal size, neck movement, and thyromental distance.<sup>22</sup> The "3-3-2 rule" is an effective summary of these geometric evaluations.<sup>3,21</sup> The 3-3-2 rule requires that the patient be able to place 3 of his or her own fingers between the open incisors, 3 of his or her own fingers along the floor of the mandible beginning at the mentum, and 2 fingers from the laryngeal prominence to the floor of the

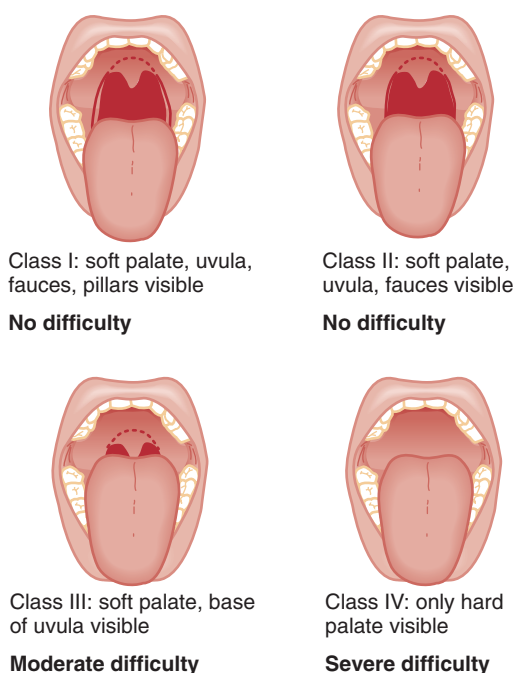
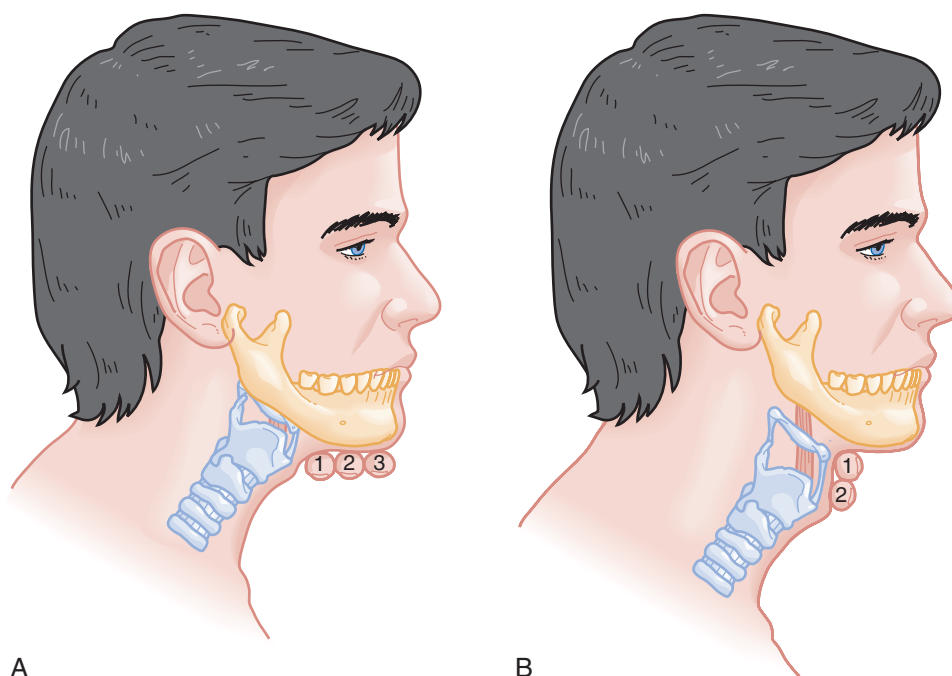
#### BOX 1-1

#### "LEMON" APPROACH FOR EVALUATION OF DIFFICULT DIRECT LARYNGOSCOPY

Look externally for signs of difficult intubation (by gestalt)  
Evaluate the "3-3-2 rule"  
Mallampati  
Obstruction/Obesity  
Neck mobility

Adapted with permission from The Difficult Airway Course: Emergency and Walls RM and Murphy MF [eds]: Manual of Emergency Airway Management, 3rd ed, Philadelphia, Lippincott Williams & Wilkins, 2008.

**Figure 1-1.** Final two steps of the 3-3-2 rule. **A**, Three fingers are placed along the floor of the mouth beginning at the mentum. **B**, Two fingers are placed in the laryngeal prominence (Adam's apple). (Adapted from Murphy MF, Walls RM: Identification of difficult and failed airways. In Walls RM and Murphy MF [eds]: *Manual of Emergency Airway Management*, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, 2008, pp. 81–91. The 3-3-2 Rule is copyrighted © 2004 by The Airway Course and Lippincott Williams & Wilkins, publishers of *The Manual of Emergency Airway Management*.)



**Figure 1-2.** The Mallampati scale assesses oral access for intubation. (From Whitten CE: *Anyone Can Intubate*, 4th ed. San Diego, KW Publications, 2004, with permission.)

mandible (Fig. 1-1). A patient with a receding mandible and high-riding larynx can be impossible to intubate using direct laryngoscopy. Most patients are not sufficiently cooperative for such an evaluation, and the operator compares his or her fingers with the patient's fingers to estimate the sizes for the three tests.

**M—Mallampati Scale.** Oral access is assessed using the Mallampati scale (Fig. 1-2). Visibility of the oral pharynx ranges from complete visualization, including the tonsillar pillars (class I), to no visualization at all, with the tongue pressed against the hard palate (class IV). Class I and class II predict adequate oral

access, class III predicts moderate difficulty, and class IV predicts a high degree of difficulty.<sup>22,23</sup> A recent meta-analysis confirmed that the four-class Mallampati score performs well as a predictor of difficult laryngoscopy (and, less so, difficult intubation), but that the Mallampati score, alone, is not a sufficient assessment tool.<sup>24</sup>

**O—Obstruction or Obesity.** Upper airway (supraglottic) obstruction may make visualization of the glottis, or intubation itself, mechanically impossible. Conditions such as epiglottitis, laryngeal tumor, Ludwig's angina, neck hematoma, or glottic polyps can compromise laryngoscopy, passage of the endotracheal tube (ETT), BMV, or all three. Physical examination for airway obstruction is combined with assessment of the patient's voice to satisfy this evaluation step. There is conflicting evidence regarding whether obesity is itself an independent marker of difficult intubation or whether patients with obesity simply are more likely to have other markers of difficult intubation.<sup>25,26</sup> Regardless, obese patients generally are more difficult to intubate than their non-obese counterparts, and preparations must account both for this, and for the more rapid oxyhemoglobin desaturation and increased difficulty with ventilation using bag and mask or an EGD (see below) that will occur.

**N—Neck Mobility.** Neck mobility is essential for the repositioning of the angled axes of the upper airway in order to permit direct visualization of the glottis. Neck mobility is assessed by having the patient flex and extend the head and neck through a full range of motion. Neck extension is the most important motion, and simple extension may be as effective as the "sniffing" position in achieving an optimal laryngeal view.<sup>27</sup> A recent study also found that the "extension-extension" position, in which the neck is extended on the body (opposite of the sniffing position) with the head extended on the neck, provides superior laryngeal views to the sniffing position.<sup>28</sup> Modest limitations of motion do not seriously impair laryngoscopy, but severe loss of motion, as can occur in ankylosing spondylitis or rheumatoid arthritis, for example, may render laryngoscopy impossible. Cervical spine immobilization in trauma artificially reduces cervical spine mobility and predicts a more difficult laryngoscopy, but direct laryngoscopy is still highly successful in this group of patients.<sup>1</sup>

Identification of a difficult intubation does not preclude use of an RSI technique (see Fig. 1-7). The crucial determination is whether the clinician judges that the patient has a reasonable likelihood of intubation success, despite the difficulties identified, and that ventilation with a bag and mask or an EGD will be successful in the event that intubation fails (hence the value of the BMV and EGD assessments; see Boxes 1-2 and 1-3).

### Difficult Bag-mask Ventilation: MOANS

Attributes of difficult BMV have largely been validated and can be summarized with the mnemonic *MOANS* (see Box 1-2).<sup>3,17,18</sup>

Difficulty with mask seal; obstruction (particularly supraglottic obstruction, but can be present anywhere in the airway) or obesity (because of redundant upper airway tissues, chest wall weight, and resistance of abdominal mass); advanced age (best judged by the physiologic appearance of the patient, but age older than 55 years increases risk); edentulousness (“no teeth”), which independently interferes with mask seal; and stiffness or resistance to ventilation (e.g., asthma, chronic obstructive pulmonary disease, pulmonary edema, restrictive lung disease, term pregnancy) all cause or contribute to increased difficulty with BMV. The difficulty with BMV of the edentulous patient is the basis of the adage: “Remove dentures to intubate, leave them in to bag-mask ventilate.” The wisdom of this approach recently was validated yet again.<sup>29</sup>

### Difficult Extraglottic Device Placement: RODS

Placement of an EGD, such as a laryngeal mask airway, a Combitube, or a similar upper airway device often can facilitate ventilation, and convert a “can’t intubate, can’t oxygenate” situation to a “can’t intubate, can oxygenate” situation, which allows time for more careful planning of the rescue of a failed airway (see following section.) Difficulty achieving placement or ventilation using an EGD is predicted by the mnemonic “RODS.” Fortunately, if the clinician has already performed the LEMON and MOANS assessments, only the “D” for distorted anatomy remains to be evaluated (see Box 1-3).

#### BOX 1-2

#### MOANS MNEMONIC FOR EVALUATION OF DIFFICULT BAG-MASK VENTILATION

**Mask seal**  
**Obstruction or obesity**  
**Aged**  
**No teeth**  
**Stiffness (resistance to ventilation)**

Adapted with permission from The Difficult Airway Course: Emergency and Walls RM and Murphy MF [eds]: Manual of Emergency Airway Management, 3rd ed, Philadelphia, Lippincott, Williams & Wilkins, 2008.

#### BOX 1-3

#### RODS MNEMONIC FOR EVALUATION OF DIFFICULT EXTRAGLOTTIC DEVICE PLACEMENT

**Restricted mouth opening**  
**Obstruction or obesity**  
**Distorted anatomy**  
**Stiffness (resistance to ventilation)**

Adapted with permission from The Difficult Airway Course: Emergency and Walls RM and Murphy MF [eds]: Manual of Emergency Airway Management, 3rd ed, Philadelphia, Lippincott, Williams & Wilkins, 2008.

### Difficult Cricothyrotomy

Difficult cricothyrotomy can be anticipated whenever there is disturbance of the ability to locate and access the landmarks of the anterior airway via the neck. Prior surgery; the presence of hematoma, anatomic disruption, tumor, or abscess; scarring (as from radiation therapy or prior injury); or obesity, edema, or subcutaneous air each has the potential to make cricothyrotomy more difficult. The landmarks for cricothyrotomy are sought and identified as part of the preintubation assessment of the patient.

### Measurement of Intubation Difficulty

The actual degree to which an intubation is “difficult” is highly subjective, and quantification is challenging. Research has relied on laryngoscopic view to characterize the intubation difficulty, and the most widely used system is that of Cormack and Lehane, which grades laryngoscopy according to the extent to which laryngeal and glottic structures can be seen. In grade 1 laryngoscopy, the entire glottic aperture is seen. Grade 2 laryngoscopy visualizes only a portion of the glottis (arytenoid cartilages alone or arytenoid cartilages plus part of the vocal cords). Grade 3 laryngoscopy visualizes only the epiglottis. In grade 4 laryngoscopy, not even the epiglottis is visible.

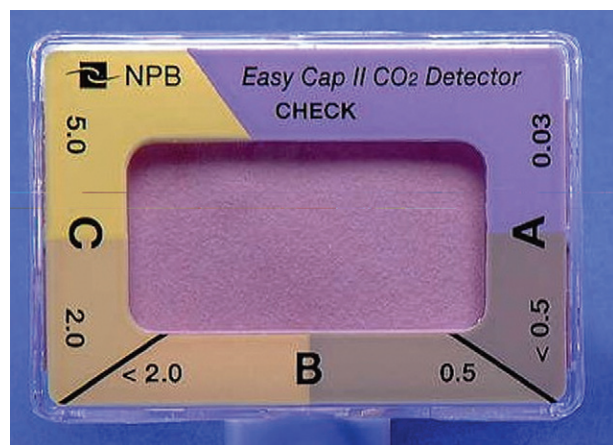
Research conducted on elective anesthesia patients suggests that true grade 4 laryngoscopy, which is associated with impossible intubation, occurs in less than 1% of patients. Grade 3 laryngoscopy, which represents extreme intubation difficulty, is found in less than 5% of patients. Grade 2 laryngoscopy, which occurs in 10 to 30% of patients, can be subdivided further into grade 2a, in which arytenoids and a portion of the vocal cords are seen, and grade 2b, in which only the arytenoids are seen. Intubation failure occurs in 67% of grade 2b cases but in only 4% of grade 2a cases.<sup>30</sup> Approximately 80% of all grade 2 laryngoscopies are grade 2a; the rest are grade 2b. A grade 1 view is associated with virtually 100% intubation success. An alternative system, the POGO (percentage of glottic opening) also has been proposed and validated, but is not widely used or studied.<sup>31</sup>

### Confirmation of Endotracheal Tube Placement

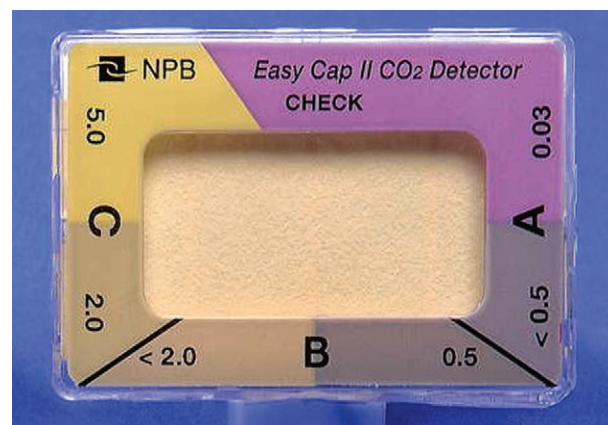
The most serious complication of endotracheal intubation is unrecognized esophageal intubation with resultant hypoxic brain injury. Although direct visualization of the ETT passing through the vocal cords generally is a reliable indicator of tracheal intubation, such clinical anatomic observations are fallible, and additional means are required to ensure correct placement of the tube within the trachea. Traditional methods, such as chest auscultation, gastric auscultation, bag resistance, exhaled volume, visualization of condensation within the ETT, and chest radiography, all are prone to failure as means of confirming tracheal intubation.<sup>32</sup> Other clinical techniques are readily available for detecting tracheal or esophageal intubation.

Immediately after intubation, the intubator should apply an end-tidal carbon dioxide (ETCO<sub>2</sub>) detection device to the ETT and assess it through six manual ventilations. Disposable, colorimetric ETCO<sub>2</sub> detectors are highly reliable, convenient, and easy to interpret, indicating adequate CO<sub>2</sub> detection by color change (Figs. 1-3 and 1-4) (see Chapter 3). ETCO<sub>2</sub> detection is highly reliable in determining tracheal and esophageal intubation in patients with spontaneous circulation.<sup>33</sup> These devices indicate the carbon dioxide content in exhaled





**Figure 1-3.** End-tidal CO<sub>2</sub> detector before application. The indicator is purple, which indicates failure to detect CO<sub>2</sub>. This also is the appearance when the esophagus is intubated.



**Figure 1-4.** Positive detection of CO<sub>2</sub> turns the indicator yellow, indicating tracheal placement of the endotracheal tube.

air either qualitatively or quantitatively. The persistence of detected CO<sub>2</sub> after six manual breaths indicates that the tube is within the airway, although not necessarily within the trachea. Gas exchange is detected with the tube in the main-stem bronchus, the trachea, or the supraglottic space. Correlation of ETco<sub>2</sub> detection with the depth markings on the endotracheal tube (particularly important in pediatric patients) confirms tracheal placement. Rarely, BMV before intubation or ingestion of carbonated beverages may lead to release of CO<sub>2</sub> from the stomach after esophageal intubation, causing a transient false indication of tracheal intubation. Washout of this phenomenon occurs within six breaths, however, so persistence of CO<sub>2</sub> detection after six breaths indicates tracheal intubation.

Although colorimetric ETco<sub>2</sub> measurement is highly sensitive and specific for detecting esophageal intubation, caution is required for patients with cardiopulmonary arrest. Insufficient gas exchange may hamper CO<sub>2</sub> detection in the exhaled air, even when the tube is correctly placed within the trachea.<sup>33</sup> In patients with cardiopulmonary arrest, a CO<sub>2</sub> level greater than 2%, which is the threshold for color change on colorimetric capnometers, should be considered definitive evidence of correct ETT placement, but the absence of such CO<sub>2</sub> cannot be used reliably as an indicator of esophageal intubation. This circumstance arises in approximately 25 to 40% of intubated cardiac arrest patients.<sup>33,34</sup> In all other patients, absence of CO<sub>2</sub> detection indicates failure to intubate the trachea, and rapid reintubation is indicated. When possible, continuous quantitative capnography is more accurate and yields more information than capnometry (including colorimetric devices; see Chapter 3).

The other method of tube placement confirmation is the aspiration technique, which is based on the anatomic differences between the trachea and the esophagus. The esophagus is a muscular structure with no support within its walls. The trachea is held patent by cartilaginous rings. Vigorous aspiration of air through the ETT with the ETT cuff deflated results in occlusion of the ETT orifices by the soft walls of the esophagus, whereas aspiration after tracheal placement of the tube is easy and rapid.

Bulb or syringe aspiration devices may be used in patients with cardiac arrest who have no detectable CO<sub>2</sub>, but although such devices are highly reliable at detecting esophageal intubation (sensitivity > 95%), false-positives, in which a correctly placed tracheal tube is incorrectly identified as esophageal, can occur in up to 25% of cardiac arrest patients.<sup>35</sup> Aspiration

devices may be useful in the out-of-hospital setting when poor lighting hampers colorimetric ETco<sub>2</sub> determination. They also are good backup devices when cardiac arrest confounds attempts to assess placement using ETco<sub>2</sub>. Detection of expired CO<sub>2</sub> is more reliable and should be considered the standard for confirmation of tracheal placement of an ETT and for early detection of accidental esophageal intubation. Aspiration devices have a valuable, but secondary role.

Repeat laryngoscopy generally is insufficient to "confirm" that the tube is through the glottis because error and misinterpretation can occur, especially if the clinician confirming the intubation is the same person who intubated in the first place. The objective instrument (ETco<sub>2</sub>) should be considered correct. Complete obstruction of the trachea or both main stem bronchi, which prevents ventilation of the patient with even small tidal volumes, can lead to failure to detect CO<sub>2</sub> even when the tube is in the trachea. In the absence of known or suggested complete large airway obstruction, however, failure to detect CO<sub>2</sub> should not be ascribed to other causes, such as severe asthma, in which the physician might postulate that adequate CO<sub>2</sub> exchange is not occurring for physiologic reasons. Absent equipment failure, this generally does not occur, and detection failure should be equated with intubation failure.

Accordingly, ETco<sub>2</sub> detection, with aspiration as backup, should be considered the primary means of ETT placement confirmation. Secondary means include physical examination findings, oximetry, and radiography. The examiner should auscultate both lung fields and the epigastric area. Auscultation of typical hollow, gurgling, gastric sounds in the epigastrium is highly suggestive of esophageal intubation and should prompt consideration of immediate reintubation. Diminished or absent breath sounds on one side (usually the left side) indicate main stem bronchus intubation, in the absence of pneumothorax or an alternative cause of unilateral loss of breath sounds. Persistent, obvious leak despite positive ETco<sub>2</sub> detection indicates cuff malfunction or supraglottic placement of the ETT, such that the tube is in the airway, detecting CO<sub>2</sub>, but above the vocal cords. In either case (main stem bronchus intubation or supraglottic intubation), tube malpositioning can be confirmed by inspection of the depth of insertion of the tube, supplemented by chest radiography when needed. If malpositioning is detected, repositioning is indicated.

Pulse oximetry is indicated as a monitoring technique in all critically ill patients, not just those who require intubation. Oximetry is useful in detecting esophageal intubation, but



may not show a decreasing oxygen saturation for several minutes after a failed intubation because of the oxygen reservoir (preoxygenation) created in the patient before intubation.<sup>35</sup> Oximetry may be particularly misleading in a spontaneously breathing patient who has had an inadvertent nasoesophageal intubation and did not have the  $\text{ETCO}_2$  measured. In this case, oxygen saturation may be preserved because of spontaneous respirations, but catastrophe can ensue if the patient is later paralyzed or heavily sedated in the mistaken belief that the tube is in the trachea.

Although chest radiography is universally recommended after ETT placement, its primary purpose is to ensure that the tube is well positioned below the cords and above the carina. A single anteroposterior chest radiograph is not sufficient to detect esophageal intubation, although esophageal intubation may be detected if the ETT is clearly outside the air shadow of the trachea. In cases where doubt persists, a fiberoptic scope can be passed through the ETT to identify tracheal rings, a “gold standard” for confirmation of tracheal placement.

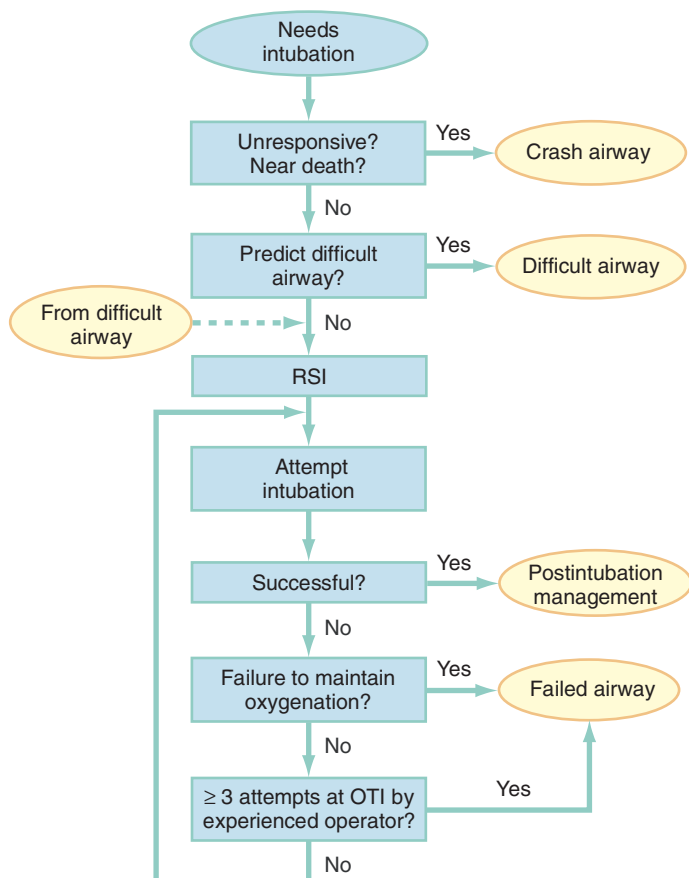
## MANAGEMENT

### Approach to Intubation

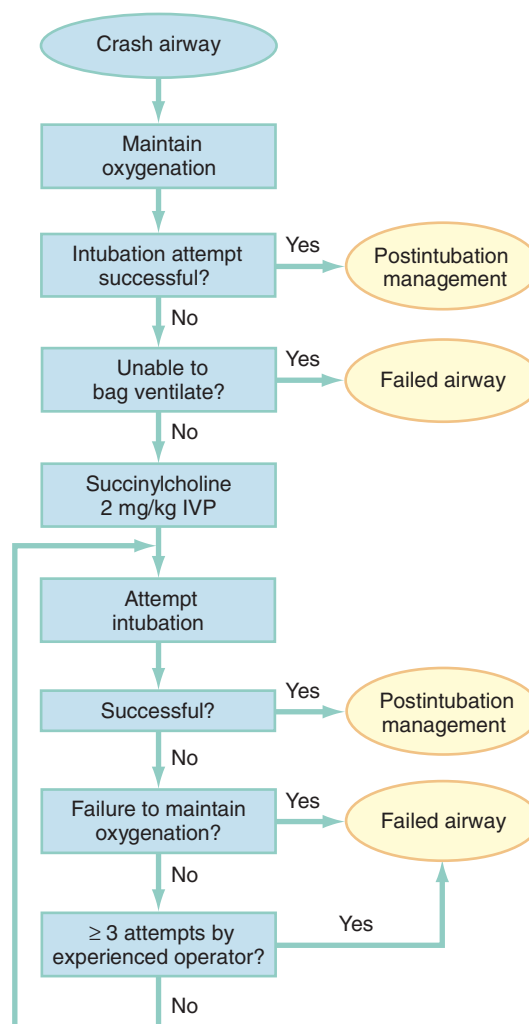
After it is determined that the patient requires intubation, an approach must be planned. Algorithms for emergency airway management have been developed and provide a useful guide,

both for planning intubation and for rescue in the event of intubation failure.<sup>4</sup> The algorithm in Figure 1-5 assumes that a decision to intubate has been made and outlines such an approach. The approach is predicated on two key determinations that must be made before active airway management is begun (see Fig. 1-5). The first determination is whether the patient is in cardiopulmonary arrest or a state near to arrest and is predicted to be unresponsive to direct laryngoscopy. Such a patient (agonal, near death, circulatory collapse) is called a “crash airway” patient for the purposes of emergency airway management and is treated using the crash airway algorithm by immediate intubation without use of drugs, supplemented by a single dose of succinylcholine if the attempt to intubate fails and the patient is felt not to be sufficiently relaxed (Fig. 1-6). Next, it must be determined whether the patient represents a difficult intubation as determined by the LEMON, MOANS, and RODS evaluations. If so, the difficult airway algorithm is used (Fig. 1-7).

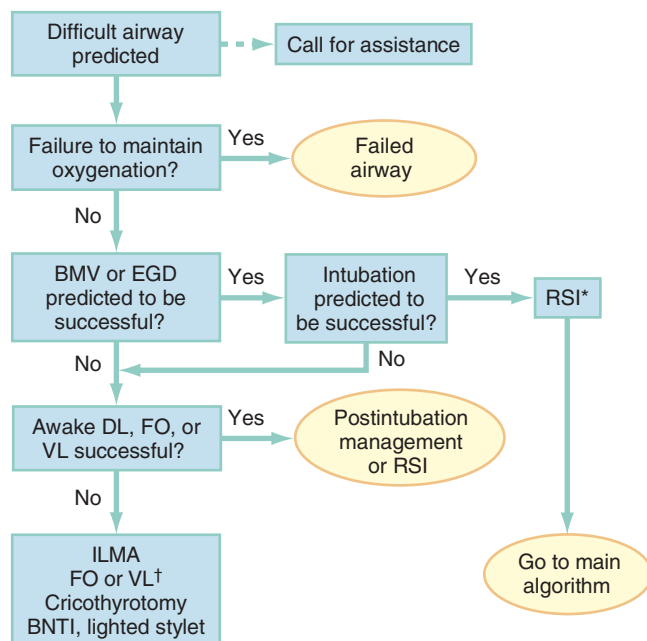
For all other cases, that is, for all patients who require emergency intubation but who have neither a crash airway nor a difficult airway, RSI is recommended. RSI provides the safest and quickest method of achieving intubation in such



**Figure 1-5.** Main emergency airway management algorithm. OTI, orotracheal intubation; RSI, rapid sequence intubation. (Adapted from Walls RM: The emergency airway algorithms. In Walls RM, Murphy MF [eds]: Manual of Emergency Airway Management, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, p. 11, 2008. Copyright © 2008 The Difficult Airway Course: Emergency and Lippincott Williams & Wilkins.)



**Figure 1-6.** Crash airway algorithm. IVP, intravenous push. (Adapted from Walls RM: The emergency airway algorithms. In Walls RM, Murphy MF [eds]: Manual of Emergency Airway Management, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, p. 14, 2008. Copyright © 2008 The Difficult Airway Course: Emergency and Lippincott Williams & Wilkins.)



**Figure 1-7.** Difficult airway algorithm. BMV, bag-mask ventilation; BNTI, blind nasotracheal intubation; DL, direct laryngoscopy; EGD, extraglottic device; FO, fiberoptic laryngoscopy; ILMA, intubating laryngeal mask airway; RSI, rapid sequence intubation; VL, video laryngoscopy. (Adapted from Walls RM: The emergency airway algorithms. In Walls RM, Murphy MF [eds]: Manual of Emergency Airway Management, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, p. 15, 2008. Copyright © 2008 The Difficult Airway Course: Emergency and Lippincott Williams & Wilkins.)

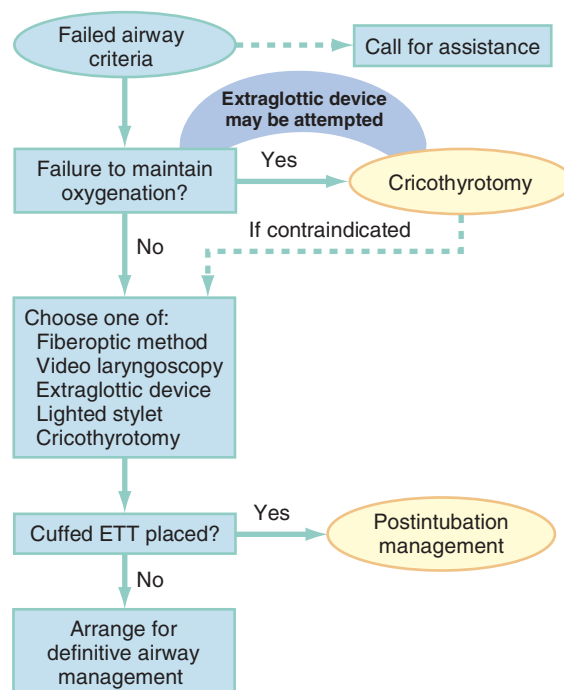
\*May require double set-up.

†If not done earlier.

patients.<sup>1,20,36,37</sup> After administration of the RSI drugs, intubation attempts are repeated until the patient is intubated or a failed intubation is identified. If more than one intubation attempt is required, oxygen saturation is monitored continuously, and if saturation falls to 90% or less, BMV is performed until saturation is recovered for another attempt. If the clinician cannot maintain oxygen saturation with BMV, despite optimal use of a two-person, two-handed technique with an oral airway in place, a failed airway exists. This is referred to as a “can’t intubate, can’t oxygenate” situation. In addition, if three attempts at direct laryngoscopy have been unsuccessful, a failed airway exists because subsequent attempts at laryngoscopy by the same clinician are unlikely to succeed. The three failed laryngoscopy attempts are defined as attempts by an experienced clinician, using best possible patient positioning and technique. A further attempt at direct laryngoscopy by the same clinician or one of equivalent experience is inadvisable, unless the clinician identifies a specific situation on the third laryngoscopy that is amenable to correction, justifying a fourth attempt. Also, if the clinician ascertains after even a single attempt that intubation will be impossible (e.g., grade IV laryngoscopic view despite optimal patient positioning), a failed airway is present. The failed airway is managed according to the failed airway algorithm (Fig. 1-8).

## Difficult Airway

When preintubation evaluation has identified a potentially difficult airway, a different approach is used (see Fig. 1-7).<sup>3,4</sup> The approach is based on the fact that NMBA should not be administered to a patient for intubation unless the clinician believes that (1) intubation is likely to be successful and (2)



**Figure 1-8.** Failed airway algorithm. ETT, endotracheal tube. (Adapted from Walls RM: The emergency airway algorithms. In Walls RM, Murphy MF [eds]: Manual of Emergency Airway Management, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, p. 18, 2008. Copyright © 2008 The Difficult Airway Course: Emergency and Lippincott Williams & Wilkins.)

oxygenation via BMV or EGD is likely to be successful if a first intubation attempt does not succeed and oxygenation is required.

The perception of a difficult airway is relative, and many emergency intubations could be considered “difficult.” The judgment regarding whether to treat the airway as a typical emergency airway or whether to use the difficult airway algorithm is based on the degree of perceived difficulty and the individual circumstances of the case.<sup>38</sup> The LEMON, MOANS, and RODS assessments provide a systematic framework to assist in identifying the potentially difficult airway.

When a difficult airway is identified, the first step is to ensure that oxygenation is sufficient to permit a planned, orderly approach (see Fig. 1-7). If oxygenation is inadequate and cannot be made adequate by supplementation with bag and mask, the airway should be considered a failed airway. The failed airway algorithm should be used because the predicted high degree of intubation difficulty combined with failure to maintain oxygen saturation is analogous to the “can’t intubate, can’t oxygenate” situation. When oxygenation is adequate, the next consideration is whether RSI is appropriate, based on the operator’s assessment of the likelihood of (1) successful ventilation using a bag and mask or an EGD in the event intubation is unsuccessful, and (2) the likelihood of successful intubation by direct laryngoscopy. In some cases, a double setup can be used in which RSI is performed, but all preparations are undertaken for rescue cricothyrotomy before the drugs are administered. If RSI is not advisable, an “awake” technique can be used. In this context, *awake* means that the patient continues to breathe and is able to respond to caregivers. Usually the technique involves sedation and topical anesthesia, often preceded by a drying agent, such as glycopyrrolate.

The awake technique often is direct laryngoscopy, assisted by topical anesthesia and sedation (comparable to that for a painful procedure), with the purpose of ascertaining whether intubation using direct laryngoscopy is possible. If the glottis is adequately visualized, the patient can be intubated at that time, or, in a stable difficult airway situation, the clinician may proceed with planned RSI, now assured of intubation success. Awake laryngoscopy can be performed using a direct laryngoscope, a flexible fiberoptic scope, a videolaryngoscope, or a rigid fiberoptic scope. If the awake laryngoscopy determines that oral intubation using a standard laryngoscope would likely be unsuccessful, the patient is intubated using any of numerous techniques shown in the last box in Figure 1-7. For each of these methods, the patient is kept breathing but variably sedated and anesthetized and each of the methods results in placement of a cuffed ETT in the trachea. The choice among these methods depends on clinician experience and preference, device availability, and patient attributes.

## Failed Airway

Management of the failed airway is dictated by an assessment of whether the patient can be oxygenated.<sup>3,4</sup> If adequate oxygenation cannot be maintained, the rescue technique of first resort is cricothyrotomy (see Fig. 1-8). Multiple attempts at other methods in the context of failed oxygenation delay cricothyrotomy and place the patient at increased risk for hypoxic brain injury. If an alternative device (i.e., an EGD such as a laryngeal mask airway or Combitube) is readily at hand, however, an attempt can be made to use it simultaneously with preparations for immediate cricothyrotomy, as long as initiation of cricothyrotomy is not delayed. Only a single attempt with the EGD is recommended in this circumstance.

If adequate oxygenation is possible, several options are available for the failed airway. In almost all cases, cricothyrotomy is the definitive rescue technique for the failed airway if time (i.e., preservation of oxygenation) does not allow for other approaches or if they fail. The fundamental difference in philosophy between the difficult airway and the failed airway is that the difficult airway is planned for, and the standard is to place a cuffed ETT in the trachea. The failed airway is *not* planned for, and the standard is to achieve an airway that provides adequate oxygenation to avert the immediate problem of hypoxic brain injury. Some of the devices used in the failed airway (e.g., EGDs) are temporary and do not provide airway protection.

## THERAPEUTIC MODALITIES

### Methods of Intubation

Although many techniques are available for intubation of the emergency patient, four methods are most common, with RSI being the most frequently used in nonarrested patients.<sup>1,13,14,39</sup>

### Rapid Sequence Intubation

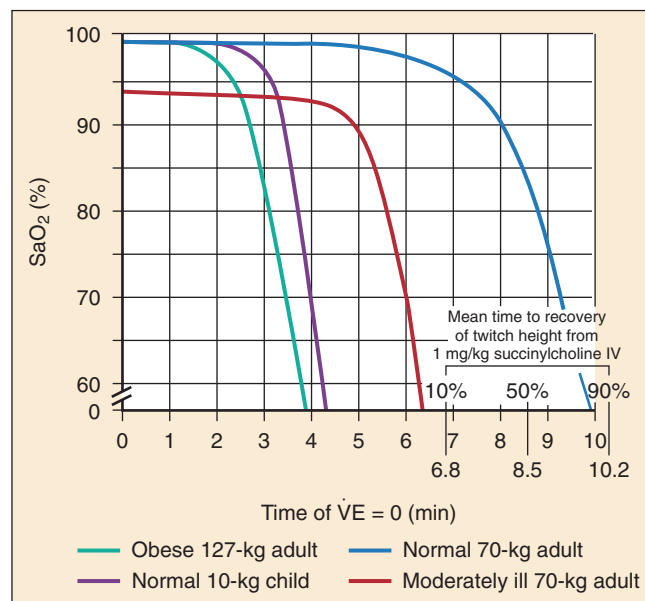
RSI is the cornerstone of modern emergency airway management and is defined as the virtually simultaneous administration of a potent sedative (induction) agent and an NMBA, usually succinylcholine, for the purpose of endotracheal intubation. This approach provides optimal intubating conditions and has long been believed to minimize the risk of aspiration of gastric contents. A systematic review of the literature in 2007 failed to prove that rapid sequence intubation results in a lower incidence of aspiration than other techniques, but the

authors correctly noted that virtually no studies have ever been designed to measure this precise endpoint.<sup>40</sup> RSI is nevertheless the most widely used technique by far for emergency intubation of patients without identifiable difficult airway attributes.<sup>1,13,14</sup>

The central concept of RSI is to take the patient from the starting point (e.g., conscious, breathing spontaneously) to a state of unconsciousness with complete neuromuscular paralysis, then to achieve intubation *without* interposed assisted ventilation. The risk of aspiration of gastric contents is felt to be significantly higher for patients who have not fasted before induction. Application of positive-pressure ventilation can cause air to pass into the stomach, resulting in gastric distention and likely increasing the risk of regurgitation and aspiration.<sup>41</sup> The purpose of RSI is to avoid positive-pressure ventilation until the ETT is placed correctly in the trachea with the cuff inflated. This requires a preoxygenation phase, during which the nitrogen reservoir in the functional residual capacity in the lungs is replaced with oxygen, permitting at least several minutes of apnea (see later discussion) in the normal adult before oxygen desaturation to 90% ensues (Fig. 1-9).<sup>35</sup>

Use of RSI also facilitates successful endotracheal intubation by causing complete relaxation of the patient's musculature, allowing better access to the airway.<sup>19,36,37,42</sup> Finally, RSI permits pharmacologic control of the physiologic responses to laryngoscopy and intubation, mitigating potential adverse effects. These effects include further intracranial pressure (ICP) increase in response to the procedure and to the sympathetic discharge resulting from laryngoscopy (Box 1-4).<sup>43</sup> RSI is a series of discrete steps, and every step should be planned (see Box 1-5).<sup>5</sup>

**Preparation.** In the initial phase, the patient is assessed for intubation difficulty (unless this has already been done), and the intubation is planned, including determining dosages and



**Figure 1-9.** Desaturation time for apneic, fully preoxygenated patients. Children, patients with comorbidity, and obese patients desaturate much more rapidly than healthy, normal adults. The box on the lower right-hand side of the graph depicts time to recovery from succinylcholine, which in almost all cases exceeds safe apnea time. Note also the precipitous decline of oxygen saturation from 90% to 0% for all groups. Modified from Benumof J, et al: Critical hemoglobin desaturation will occur before return to unparalyzed state following 1 mg/kg intravenous succinylcholine. *Anesthesiology* 87:979, 1997.

## BOX 1-4

## PRETREATMENT AGENTS FOR RAPID SEQUENCE INTUBATION\*

**Reactive airways disease:** Lidocaine: 1.5 mg/kg IV, to mitigate bronchospasm. Albuterol 2.5 mg by nebulizer (if time permits and not already given).

**Cardiovascular disease:** Fentanyl: 3 µg/kg to mitigate sympathetic discharge.

**Elevated ICP:** Lidocaine: 1.5 mg/kg IV to mitigate ICP increase in response to airway manipulation. Fentanyl 3 µg/kg to mitigate sympathetic discharge and attendant rise in ICP.

\*Given 3 minutes before induction and paralysis.  
ICP, intracranial pressure.

## BOX 1-5

## THE SEVEN “Ps” OF RSI

1. Preparation
2. Preoxygenation
3. Pretreatment
4. Paralysis with induction
5. Positioning
6. Placement of tube
7. Postintubation management

sequence of drugs, tube size, and laryngoscope type, blade and size. Drugs are drawn up and labeled. All necessary equipment is assembled. All such patients require continuous cardiac monitoring and pulse oximetry. At least one and preferably two good-quality intravenous (IV) lines should be established. Redundancy is always desirable in case of equipment or IV access failure.

**Preoxygenation.** Administration of 100% oxygen for 3 minutes of normal, tidal volume breathing in a normal, healthy adult establishes an adequate oxygen reservoir to permit 8 minutes of apnea before oxygen desaturation to less than 90% occurs (see Fig. 1-9).<sup>35</sup> The time to desaturation to less than 90% in children, obese adults, late-term pregnant women, and patients with significant comorbidity is considerably less. Desaturation time also is reduced if the patient does not inspire 100% oxygen.<sup>44</sup> Nevertheless, adequate preoxygenation usually can be obtained, even in ED patients, to permit several minutes of apnea before oxygen desaturation to less than 90% occurs. In children and adults, preoxygenation is essential to the “no bagging” approach of RSI. If time is insufficient for a full 3-minute preoxygenation phase, eight vital capacity breaths using high-flow oxygen can achieve oxygen saturations and apnea times that match or exceed those obtained with traditional preoxygenation.<sup>45</sup> Preoxygenation of obese patients in the head up position results in significantly longer (approximately 45 seconds) apnea time before critical saturation.<sup>46</sup> Preoxygenation should be done in parallel with the preparation phase and can be started in the field for high risk patients. Oxygen saturation monitors permit earlier detection of desaturation during laryngoscopy, but preoxygenation remains an essential step in RSI.

**Pretreatment.** During this phase, drugs are administered 3 minutes before administration of the succinylcholine and induction agent to mitigate the effects of laryngoscopy and intubation on the patient’s presenting or comorbid conditions. Intubation is intensely stimulating and results in sympathetic discharge (the reflex sympathetic response to laryngoscopy), elevation of ICP in patients with ICP disturbance, and reactive bronchospasm. Bradycardia often occurs in children, particu-

larly young children, but appears multifactorial, likely involving both parasympathetic discharge in response to airway instrumentation and perhaps some contributory effect of succinylcholine.

Pretreatment focuses on three main objectives, in certain at-risk patients. The three groups of patients at risk are those with reactive airways disease, elevated ICP, or a cardiovascular or neurovascular condition or acute event for which an acute elevation in blood pressure and heart rate might be hazardous. Patients with reactive airways disease often experience a worsening of their bronchospasm when intubated. Controversy exists regarding whether albuterol alone, lidocaine alone, or both drugs together are effective in reducing this intubation-related bronchospasm.<sup>47-49</sup> Asthmatic patients being intubated in the ED for status asthmaticus will have received albuterol before intubation, and, pending larger studies, it is reasonable also to administer lidocaine (1.5 mg/kg) as a pretreatment drug in these cases. When an asthmatic patient is being intubated for a condition (e.g., trauma) other than acute asthma, nebulized albuterol and IV lidocaine should be given before intubation, if possible. Patients with significant cardiovascular disease (e.g., ischemic coronary disease) who are being intubated in the ED may benefit from the administration of the synthetic opioid, fentanyl, in a dose of 3 µg/kg to mitigate the release of catecholamines in response to airway manipulation. Similarly, patients with intracranial hemorrhage, elevated ICP, or marked hypertension may benefit from pretreatment with fentanyl.<sup>49</sup> Finally, there is some evidence that patients with elevated ICP may experience less exacerbation of the ICP during intubation if they are pretreated with lidocaine (1.5 mg/kg). These patients, unless hypotensive, should also receive fentanyl (3 µg/kg) to mitigate blood pressure surges that might translate to further increases in ICP. There is evidence supporting the physiologic effects of these agents, but outcome data are lacking. Individualization is necessary, and critical time should not be lost administering pretreatment drugs if the patient requires immediate intubation. Despite the lack of outcome studies, considerable inferential evidence supports this approach, and these agents probably provide protection for vulnerable patients against the adverse hemodynamic and intracranial effects of laryngoscopy and intubation.<sup>49</sup> Although many variations are possible for pretreatment regimens in various conditions, pretreatment can be simplified to these three basic indications (see Box 1-4).

When possible, 3 minutes should elapse between the administration of the pretreatment drug and the administration of the induction drug and NMBA. If time is insufficient to wait 3 minutes, even a reduced time may provide some benefit.

**Paralysis with Induction.** In this phase, a potent sedative agent is administered by rapid IV push in a dose capable of rapidly producing unconsciousness. This is immediately followed by rapid administration of an intubating dose of an NMBA, usually succinylcholine. It is usual to wait 45 seconds from the time the succinylcholine is given to allow sufficient paralysis to occur. (See later discussion of drugs and doses.)

**Positioning.** The patient should be positioned for intubation as consciousness is lost. Usually, positioning involves head extension, often with flexion of the neck on the body, but there is evidence that simple extension of the head alone, or extension of both the head and neck (the extension-extension position) are equivalent or superior.<sup>27,28</sup> (See earlier discussion.) Sellick’s maneuver (application of firm backward-directed pressure over the cricoid cartilage) has long been recommended to minimize the risk of passive regurgitation and, hence, aspiration, but two recent reviews have challenged this premise.<sup>50-52</sup> In addition, there is evidence that Sellick’s maneuver may make laryngoscopy or intubation more difficult



in some patients.<sup>51</sup> Accordingly, Sellick's maneuver should be considered optional, applied selectively, and released or modified to improve laryngeal view or tube passage, as indicated. During this phase after administration of the induction agent and NMBA, although the patient becomes unconscious and apneic, BMV should not be initiated unless the oxygen saturation falls to 90%.

**Placement of Tube.** Approximately 45 seconds after the administration of succinylcholine, the patient is relaxed sufficiently to permit laryngoscopy; this is assessed most easily by moving the mandible to test for absence of muscle tone. The ETT is placed under direct visualization of the glottis. If the first attempt is unsuccessful, but oxygen saturation remains high, it is not necessary to ventilate the patient with a bag and mask between intubation attempts. If the oxygen saturation is approaching 90%, the patient may be ventilated briefly with a bag and mask between attempts to reestablish the oxygen reservoir. When BMV is performed, Sellick's maneuver is advisable to minimize passage of air into the stomach.<sup>41</sup> Sellick's maneuver may be continued or released during repeat laryngoscopy, according to the judgment of the clinician and the glottic view obtained. As soon as the ETT is placed, the cuff should be inflated and its position confirmed as described earlier.

**Postintubation Management.** A chest radiograph should be obtained to confirm that main stem intubation has not occurred and to assess the lungs. There is a trend away from the use of long-acting NMBAs (e.g., pancuronium, vecuronium) toward optimal management using opioid analgesics and sedative agents to facilitate mechanical ventilation.<sup>50</sup> (See Chapter 3.) An adequate dose of a benzodiazepine (e.g., midazolam 0.1–0.2 mg/kg, IV) and an opioid analgesic (e.g., fentanyl, 3–5 µg/kg, IV, or morphine, 0.2–0.3 mg/kg, IV) is given to improve patient comfort and decrease sympathetic response to the ETT. Appropriate use of sedation and analgesia often obviates the need for an NMBA. Table 1-1 presents a sample RSI protocol using etomidate and succinylcholine. “Zero” refers to the time at which the induction agent and succinylcholine are pushed.

Table 1-1

Sample Rapid Sequence Intubation Using Etomidate and Succinylcholine

TIME	STEP
Zero minus 10 min	<b>Preparation</b>
Zero minus 5 min	<b>Preoxygenation</b> 100% oxygen for 3 min <i>or</i> eight vital capacity breaths
Zero minus 3 min	<b>Pretreatment</b> as indicated
Zero	<b>Paralysis with induction</b> Etomidate, 0.3 mg/kg Succinylcholine, 1.5 mg/kg
Zero plus 30 sec	<b>Positioning</b> Sellick's maneuver optional
Zero plus 45 sec	<b>Placement</b> Laryngoscopy and intubation End-tidal carbon dioxide confirmation
Zero plus 2 min	<b>Postintubation management</b> Sedation and analgesia as indicated Initiate mechanical ventilation NMBA only if needed after adequate sedation/analgesia

## Blind Nasotracheal Intubation

Historically, blind nasotracheal intubation (BNTI) was used extensively in the ED and out-of-hospital setting, but has fallen out of favor largely because of the superiority of RSI.<sup>11,53</sup> Success rates have been about 80 to 90%, and high complication rates are reported, most often epistaxis or delayed or incorrect tube placement.<sup>53</sup> Long-term complications (e.g., sinusitis, turbinate destruction, laryngeal perforation) are uncommon and related to multiple attempts or prolonged intubation. Basilar skull fracture and facial trauma have been considered contraindications to nasotracheal intubation because of the risk of entering the cranial vault or increasing the incidence of intracranial infection. These contraindications are not based on scientific study, however, and two small studies failed to detect a difference in complications between orally and nasally intubated facial trauma patients.<sup>54,55</sup> Two other studies compared the success rates of RSI and BNTI performed by physicians or paramedics on helicopter services. Results differed, with one study showing essentially equivalent success rates and the other showing a significant advantage for neuromuscular blockade over BNTI.<sup>56,57</sup> ED studies have shown superiority of RSI over BNTI.<sup>11,39</sup> Also, the incidence and severity of oxygen desaturation are greater in BNTI than with RSI.<sup>58</sup>

BNTI is a valid and useful method of intubation in the out-of-hospital setting and is still widely used by paramedics and other out-of-hospital first responders. In the ED, where NMBAs and RSI are available, BNTI should be considered a second-line approach and reserved for patients in whom the presence of a difficult airway makes RSI undesirable or contraindicated and alternatives (e.g., fiberoptics) are not available. Interestingly, the old recommendation that refrigeration of the tube before use increases success of nasotracheal intubation probably is not true. To the contrary, warming the tube to 40° before use appears to facilitate easy tube passage and reduce the incidence of epistaxis.<sup>59</sup> Similarly, maintaining the head in a neutral position and inflating the ETT cuff to 15 mL in the oropharynx or hypopharynx before attempting to traverse the glottis also improves the success rate.<sup>60</sup> Use of BNTI in the ED has declined sufficiently, and it is doubtful that emergency medicine residents will be adequately trained in the technique.<sup>53</sup>

## Awake Oral Intubation

Awake oral intubation is a technique in which sedative and topical anesthetic agents are administered to permit management of a difficult airway. Sedation and analgesia are achieved in a manner analogous to that for painful procedures in the ED. Topical anesthesia may be achieved by spray, nebulization, or local anesthetic nerve block. After the patient is sedated and topical anesthesia has been achieved, gentle direct, video, or fiberoptic laryngoscopy is performed to determine whether the glottis is visible and intubation possible. The patient may be intubated during the laryngoscopy, or the laryngoscopy may show that oral intubation is possible, permitting safe use of RSI (see earlier discussion).

Awake oral intubation is distinct from the practice of oral intubation using a sedative or opioid agent to obtund the patient for intubation without neuromuscular blockade, which had been a typical ED practice. This latter technique can be referred to as “intubation with sedation alone” or, paradoxically, “nonparalytic RSI.” Proponents of intubation with sedation alone argue that administration of a benzodiazepine, opioid, or both provides improved access to the airway, decreases patient resistance, and avoids the risks inherent

in neuromuscular blockade. This technique actually is more hazardous than RSI, however. Intubating conditions achieved even with deep anesthesia are significantly inferior to the conditions achieved when neuromuscular blockade is used.<sup>36,37,61</sup> The same superiority of neuromuscular blockade-assisted intubation over intubation with sedation alone has been observed in pediatric emergency medicine and in EMS care.<sup>62,63</sup> In general, the technique of administering a potent sedative agent to obtund the patient's responses and permit intubation in the absence of neuromuscular blockade is ill-advised and inappropriate for ETI in the ED, unless it is performed as part of an "awake" intubation as described earlier.

### Oral Intubation without Pharmacologic Agents

The unconscious, unresponsive, near death patient may not require pharmacologic agents for intubation. If the patient is essentially dead, administration of any pharmacologic agent, including an NMBA, may needlessly delay intubation. Even an unconscious patient may retain sufficient muscle tone to render intubation difficult, however. If the glottis is not adequately visualized, administration of a single dose of succinylcholine alone may facilitate laryngoscopy. Success rates for intubating unconscious, unresponsive patients are comparable to those achieved with RSI, presumably because the patient is in a similar physiologic state (i.e., muscle relaxation, no ability to react to laryngoscopy or tube insertion).<sup>1</sup>

## Pharmacologic Agents

### Neuromuscular Blocking Agents

Muscle contraction is the result of membrane depolarization, which causes massive intracellular release of calcium ions from the sarcoplasmic reticulum, leading to active contraction of myofibrils. The inciting incident is the depolarization of portions of the myocyte membrane, called the motor endplates, which are adjacent to the innervating axons. Action potentials conducted down the innervating axons cause release of the neurotransmitter acetylcholine (ACh) from the terminal axon. The ACh traverses the synaptic cleft, binds reversibly to receptors on the motor endplate, and opens channels in the membrane to initiate depolarization.

NMBAs are highly water-soluble, quaternary ammonium compounds that mimic the quaternary ammonium group on the ACh molecule. Their water solubility explains why these agents do not readily cross the blood-brain barrier or placenta. The NMBAs are divided into two main classes. The *depolarizing* agent, succinylcholine, exerts its effects by binding noncompetitively with ACh receptors on the motor endplate and causing sustained depolarization of the myocyte. The other major class of NMBA comprises the *competitive*, or *nondepolarizing*, agents, which bind competitively to ACh receptors, preventing access by ACh and preventing muscular activity. The competitive agents are of two pharmacologically distinct types, steroid-based agents (aminosteroid compounds) and benzylisoquinolines. Each of these basic chemical types has distinct properties, but only the aminosteroid compounds are used in the ED.

**Succinylcholine.** Succinylcholine is a combination of two molecules of ACh. Succinylcholine is rapidly hydrolyzed by plasma pseudocholinesterase to succinylmonocholine, which is a weak NMBA, then to succinic acid and choline, which have no NMBA activity. Pseudocholinesterase is not present at the motor endplate and exerts its effects systemically before the succinylcholine reaches the ACh receptor.<sup>64</sup> Only a small amount of the succinylcholine that is administered survives to

reach the motor endplate. When attached to the ACh receptor, succinylcholine is active until it diffuses away. Decreased plasma pseudocholinesterase activity can increase the amount of succinylcholine reaching the motor endplate, prolonging succinylcholine block, but this is of little significance in the emergency setting because the prolongation of action is rarely significant, reaching only 23 minutes at the extreme.<sup>64,65</sup>

**Uses.** Succinylcholine is rapidly active, typically producing intubating conditions within 60 seconds of administration by rapid IV bolus injection.<sup>37,66</sup> The clinical duration of action before spontaneous respiration is 6 to 10 minutes (see Fig. 1-9).<sup>35</sup> Full recovery of normal neuromuscular function occurs within 15 minutes. The combination of rapid onset, complete reliability, short duration of action, and absence of serious side effects maintains succinylcholine as the drug of choice for most ED intubations.<sup>1,13,50,62</sup> The use of a competitive, or nondepolarizing, NMBA for RSI may be desirable when succinylcholine is contraindicated and in certain other settings.

**Cardiovascular Effects.** As an ACh analogue, succinylcholine binds to ACh receptors throughout the body, not just at the motor endplate. It is difficult to separate the effects of succinylcholine on the heart that are caused by direct cardiac muscarinic stimulation from those caused by stimulation of autonomic ganglia by succinylcholine and from the effects induced by the autonomic responses to laryngoscopy and intubation. Succinylcholine can be a negative chronotrope, especially in children, and sinus bradycardia may ensue after succinylcholine administration. Sinus bradycardia is treated with atropine, if necessary, but is often self-limiting. Some pediatric practitioners recommend pretreatment with atropine for children younger than 1 year old, but there is no evidence for benefit.<sup>67</sup> Other cardiac dysrhythmias, including ventricular fibrillation and asystole, have been reported with succinylcholine, but it is impossible to distinguish the effects of the drug itself from those caused by the intense vagal stimulation and catecholamine release that accompany laryngoscopy and intubation. In addition, many of these catastrophic complications occur in critically ill patients, further confounding attempts to identify whether the illness or any particular drug or procedure is the cause.

**Fasciculations.** The depolarizing action of succinylcholine results in fine, chaotic contractions of the muscles throughout the body for several seconds at the onset of paralysis in over 90% of patients. Muscle pain occurs in approximately 50% of patients who receive succinylcholine. Although it is widely believed that muscle pains are reduced or abolished by prior administration of a defasciculating dose of a competitive NMBA, the evidence is not conclusive.<sup>68</sup> Use of 1.5 mg/kg of succinylcholine results in both less fasciculation and less myalgia than occur with 1 mg/kg.<sup>68</sup>

**Hyperkalemia.** Succinylcholine has been associated with severe, fatal hyperkalemia when administered in specific clinical circumstances (Table 1-2).<sup>69</sup> Although the hyperkalemia occurs within minutes after administration of succinylcholine and may be severe or fatal, the patient's vulnerability to succinylcholine-induced hyperkalemia does not become significant until at least 5 days after the inciting injury or burn. Succinylcholine remains the agent of choice for RSI in acute burn, trauma, stroke, spinal cord injury, and intra-abdominal sepsis if intubation occurs less than 5 days after onset of the condition. If doubt exists regarding the onset time, succinylcholine should be replaced with a competitive NMBA, usually rocuronium. Denervation syndromes (e.g., multiple sclerosis, amyotrophic lateral sclerosis) can be particularly troubling, however, because the risk begins with the onset of the disease and continues indefinitely, regardless of the apparent stability of the symptoms. Patients who have denervation caused by

stroke or spinal cord injury are stabilized after 6 months, and thereafter can receive succinylcholine safely.<sup>65</sup> Potassium release does not occur to any significant extent in the general population. Succinylcholine is not contraindicated in renal failure but probably should not be used in patients with known or presumed hyperkalemia sufficient to manifest on the electrocardiogram. The only published series of patients with hyperkalemia, many of whom had renal failure, failed to show a single adverse event related to succinylcholine administration.<sup>70</sup>

**Increased Intraocular Pressure.** Succinylcholine may cause a modest increase in intraocular pressure and historically has been considered relatively to absolutely contraindicated in penetrating globe injury. There is no published evidence to support this view, however, and several large series show safety when succinylcholine is used in patients with open globes. The admonition to avoid succinylcholine in open globe injuries is unjustified and should be abandoned.<sup>71</sup>

**Masseter Spasm.** Succinylcholine has been reported rarely to cause masseter spasm, primarily in children.<sup>64</sup> The clinical significance of this phenomenon is unclear, but administration of a competitive NMBA terminates the spasm. Severe, persistent spasm should raise suspicion of malignant hyperthermia.

**Malignant Hyperthermia.** Succinylcholine has been associated with malignant hyperthermia, a perplexing syndrome of rapid temperature rise and aggressive rhabdomyolysis. Malignant hyperthermia occurs in genetically predisposed individuals who receive certain volatile anesthetic agents or succinylcholine. The condition is extremely rare and has not been reported in the context of ED intubation. Treatment consists of cessation of any potential offending agents, administration of dantrolene (2 mg/kg IV every 5 min to a maximum dose of 10 mg/kg), and

attempts to reduce body temperature by external means.<sup>72</sup> A national malignant hyperthermia hotline is available for emergency consultation at 1-800-644-9737 (then dial zero).

**Refrigeration.** The standard recommendation to keep succinylcholine refrigerated creates problems related to its storage, timely retrieval, and ready availability on intubation carts or kits in the ED. Succinylcholine undergoes degradation beginning at the time of manufacture, and the rate of this degradation is much lower when the drug is refrigerated. Succinylcholine retains more than 90% of its original activity when stored at room temperature for 3 months; it retains even more if protected from light.<sup>73</sup> Succinylcholine may be kept at room temperature in the ED or EMS setting, provided that a proper inventory control system ensures that all supplies are replaced not more than 3 months after introduction.

**Competitive Agents.** Competitive NMBAs are classified according to their chemical structure. The aminosteroid agents include pancuronium, vecuronium, and rocuronium. Vecuronium neither releases histamine nor exhibits cardiac muscarinic blockade and is an excellent agent for maintenance of neuromuscular blockade when this is desirable. Rocuronium is the best agent for use in RSI when succinylcholine is contraindicated.

**Rapid Sequence Intubation with a Competitive Agent.** Competitive agents, especially vecuronium and rocuronium, have been studied extensively for RSI. Although vecuronium was the first competitive NMBA to establish a role in RSI, it works best when given as a split dose. First, 0.01 mg/kg is administered as a “priming” dose. Three minutes later, 0.15 mg/kg is given for paralysis, which is achieved in about 75 to 90 seconds. Rocuronium bromide (1 mg/kg IV) achieves intubating conditions closely approaching those of succinylcholine, lasts approximately 50 minutes, and has been used in the ED with success (Table 1-3).<sup>61,74</sup>

**Paralysis after Intubation.** After intubation, prolonged paralysis may be desired to optimize mechanical ventilation; however, current management trends are away from the use of prolonged paralysis in favor of deep sedation with analgesia. If neuromuscular blockade is desired, vecuronium (0.1 mg/kg IV) can be given. Longer term neuromuscular blockade must not be undertaken without attention to appropriate sedation and analgesia of the patient.<sup>50</sup> An adequate dose of a benzodiazepine, such as midazolam (0.1–0.2 mg/kg IV), and an opioid analgesic, such as fentanyl (3–5 µg/kg IV) or morphine (0.2–0.3 mg/kg IV), is required to improve patient comfort and decrease sympathetic response to the ETT. Appropriate use

Table 1-2

**Conditions Associated with Hyperkalemia after Succinylcholine Administration**

CONDITION	PERIOD OF CONCERN
Burns >10% BSA	>5 days until healed
Crush injury	>5 days until healed
Denervation (stroke, spinal cord injury)	>5 days until 6 months postinjury
Neuromuscular disease (ALS, MS)	Indefinitely
Intra-abdominal sepsis	>5 days until resolution

ALS, amyotrophic lateral sclerosis; BSA, body surface area; MS, multiple sclerosis.

Table 1-3

**Sample Rapid Sequence Intubation Using Etomidate and Rocuronium**

TIME	STEP
Zero minus 10 min	<b>Preparation</b>
Zero minus 5 min	<b>Preoxygenation</b> 100% oxygen for 3 min <i>or</i> eight vital capacity breaths
Zero minus 3 min	<b>Pretreatment</b> As indicated
Zero	<b>Paralysis with induction</b> Etomidate, 0.3 mg/kg Rocuronium, 1.0 mg/kg
Zero plus 30 sec	<b>Positioning</b>
Zero plus 60 sec	<b>Placement</b> Laryngoscopy and intubation End-tidal carbon dioxide confirmation
Zero plus 2 min	<b>Postintubation management</b> Sedation and analgesia mandatory because of prolonged (45 min) duration of paralysis with rocuronium

of sedation and analgesia often obviates the need for an NMBA. Additional medication may be required if the patient's blood pressure and heart rate indicate excessive sympathetic tone.

## Induction Agents

A patient who presents with any degree of clinical responsiveness, including reactivity to noxious stimuli, requires a sedative or induction agent at the time of administration of any NMBA. Patients who already are deeply unconscious and unresponsive may not require a full dose of an induction agent if the unconscious state is caused by drugs or alcohol (themselves general anesthetic agents.) Patients who are unconscious because of a central nervous system insult should receive an induction agent to attenuate adverse responses to airway manipulation. Induction agents also enhance the effect of the NMBA and improve intubation conditions because the intubation is done at the earliest phase of neuromuscular blockade, and the relaxation effects of the induction agent are additive to those of the NMBA.<sup>75</sup>

**Etomidate.** Etomidate is an imidazole derivative that has been in use since 1972. Its activity profile is similar to that for thiopental, with rapid onset, rapid peak activity, and brief duration, but it is remarkably hemodynamically stable.<sup>76,77</sup> Etomidate has emerged as the agent of choice for ED RSI, and numerous reports attest to its effectiveness and safety.<sup>1,14</sup> The induction dose is 0.3 mg/kg IV. Because etomidate is able to decrease ICP, cerebral blood flow, and cerebral metabolic rate without adversely affecting systemic mean arterial blood pressure and cerebral perfusion pressure, it is an excellent induction agent for patients with elevated ICP, even in cases of hemodynamic instability.<sup>77,78</sup> Etomidate may cause brief myoclonus, but this is of no clinical significance. Etomidate by continuous infusion has been reported to cause suppression of endogenous cortisol production. Recently, controversy has emerged regarding the role of etomidate for intubation of patients with septic shock.<sup>79-81</sup> Several retrospective studies have claimed to demonstrate that etomidate, used in a single dose for intubation, causes suppression of the adrenal response to exogenously administered adrenocorticotrophic hormone, and have attempted to link this to increased mortality.<sup>82,83</sup> Other retrospective studies have shown the opposite.<sup>84,85</sup> Ironically, much of the original criticism of etomidate arose from the belief that adrenocortical response to exogenous corticotropin predicts outcome in patients with septic shock, a belief that has since been abandoned.<sup>86</sup> Also, the most recent and comprehensive study of the role of corticosteroids in septic shock failed to show any benefit, casting further doubt about any possible mortality effect of a single dose of etomidate.<sup>87</sup> Pending a properly constructed, prospective, randomized clinical trial, there is not sufficient evidence to support a recommendation that etomidate not be used in patients with septic shock.<sup>81,88</sup> In fact, etomidate's superior hemodynamic profile makes it an excellent choice in these generally unstable patients.

**Barbiturates.** Although both the thiobarbiturate, sodium thiopental, and the methylated oxybarbiturate, methohexital, have been used as induction agents for RSI, thiopental has been used more widely. The use of these agents has declined significantly, however, with the adoption of newer agents, particularly etomidate and propofol. The rapidly acting barbiturates are highly lipid-soluble and readily cross the blood-brain barrier, acting on the  $\gamma$ -aminobutyric acid receptor neuroinhibitory complex to rapidly depress central nervous system activity. A single dose of 3 mg/kg of thiopental pro-

duces loss of consciousness in less than 30 seconds, has a peak effect at 1 minute, and has a clinical duration of 5 to 8 minutes. Methohexital may have a slightly shorter duration of action but is more prone to cause central nervous system excitatory side effects, such as myoclonus. Thiopental is a negative inotrope and a potent venodilator and should be used with caution in patients whose cardiovascular reserve is diminished. For the same reason, thiopental should be avoided in a hypotensive patient who would not tolerate further compromise of circulation. Thiopental can release histamine and probably should not be used in asthmatic patients.

**Benzodiazepines.** Of the benzodiazepines, only midazolam is suited to use as an induction agent, with a normal induction dose of 0.2 to 0.3 mg/kg IV.<sup>77</sup> In a dose of 0.3 mg/kg IV, midazolam produces loss of consciousness in about 30 seconds and has a clinical duration of 15 to 20 minutes.<sup>89</sup> Midazolam is a negative inotrope comparable to thiopental and should be used with caution in hemodynamically compromised and elderly patients, for whom the dose can be reduced to 0.1 mg/kg or 0.05 mg/kg. Onset is slower at these reduced doses. Much lower doses than indicated are often used in ED intubations, perhaps because practitioners are familiar with the sedation doses, but not the anesthetic induction doses, of midazolam.<sup>90</sup> These inadequate doses reduce the effectiveness of laryngoscopy, do not provide optimal blunting of adverse physiologic effects of laryngoscopy and intubation, and may compromise the patient's amnesia for the intubation. Midazolam may be cerebroprotective, but less so than etomidate or thiopental.

**Ketamine.** Ketamine, a phencyclidine derivative, has been widely used as a general anesthetic agent since 1970. After an IV dose of 1 to 2 mg/kg, ketamine produces loss of awareness within 30 seconds, peaks in approximately 1 minute, and has a clinical duration of 10 to 15 minutes. As a dissociative anesthetic agent, ketamine induces a cataleptic state rather than a true unconscious state. The patient has profound analgesia but may have open eyes. Many protective reflexes, including airway reflexes, are preserved.

The principal uses of ketamine in emergency airway management are for the induction of patients with acute, severe asthma and for hemodynamically unstable trauma patients. Ketamine is exceptionally hemodynamically stable, more so than etomidate, so although either drug is a good choice in the trauma patient, ketamine is probably superior in terms of preserving precarious cardiovascular stability.<sup>89</sup> In patients with status asthmaticus, etomidate or any of most of the other induction agents is acceptable, with the notable exception of sodium thiopental, which releases histamine. Ketamine is a direct bronchodilator and releases catecholamines, so may be useful both for intubation and for intermittent administration as part of sedation for mechanical ventilation in patients with severe asthma, although no outcome studies clearly demonstrate its superiority.

Controversy exists regarding the use of ketamine in patients with elevated ICP because ketamine has been believed to increase cerebral metabolic rate, ICP, and cerebral blood flow.<sup>91</sup> The evidence that ketamine can produce harm in this way is conflicting, however, and its role as an induction agent in trauma is significant because of its superior hemodynamic stability.<sup>10</sup> Because of its tendency to release catecholamines and increase blood pressure, ketamine should probably be avoided in head trauma patients with normal or elevated blood pressure. However, in the hypotensive head trauma patient, ketamine is a reasonable choice for induction.<sup>77</sup> Ketamine tends to produce unpleasant emergence phenomena, especially disturbing or frightening dreams in the first 3 hours after awakening. These reactions, which are more prominent in



adults than in children, in women than in men, in patients receiving larger doses, and in certain personality types, are mitigated by benzodiazepine administration. Patients (e.g., with asthma) who undergo RSI with ketamine should receive a sufficient dose of a benzodiazepine (e.g., 0.05 mg/kg of lorazepam) as part of postintubation management.

## Special Clinical Circumstances

### Status Asthmaticus

Status asthmaticus with supervening respiratory failure is a preterminal event. Respiratory failure in the asthmatic patient is not caused primarily by progressive worsening of the bronchospasm, but rather by eventual exhaustion and fatigue secondary to the effort of breathing against severe airway resistance. All patients who are intubated for status asthmaticus are heavily sedated and receive mechanical ventilation. RSI permits the most rapid attainment of intubation, protects against aspiration, and induces the unconsciousness and motor paralysis necessary for optimal initiation of mechanical ventilation; it is the recommended technique for intubation of a patient in status asthmaticus. Difficult airway considerations are complex in an asthmatic patient because of impending respiratory arrest and the patient's inability to tolerate attempts at awake intubation. Even when a difficult airway is identified in an asthmatic patient, RSI is usually the intubation method of choice, with a double setup for rescue cricothyrotomy when indicated.

The asthmatic patient has highly reactive airways, and steps should be taken to minimize any additional bronchospasm that may occur during intubation. Lidocaine has been shown to suppress the coughing that occurs in response to airway manipulation and may improve ETT tolerance and reduce reactive bronchospasm in asthmatic patients.<sup>48</sup> The balance of evidence suggests that lidocaine (1.5 mg/kg) is indicated as a pretreatment drug before intubation in status asthmaticus and in asthmatic patients being intubated for reasons other than their asthma. High-dose, inhaled beta-agonists may provide maximal protection against reactive bronchospasm during intubation in asthmatics without active bronchospasm, and lidocaine may provide little additional benefit in this setting.<sup>47</sup> This approach has not been tested in patients in status asthmaticus, however. Ketamine has been shown to produce bronchodilation in humans and animal models and may be the ideal induction agent in asthma. Although reports to date have been limited, there is a growing body of experience with ketamine as an induction agent for the emergency intubation of patients with status asthmaticus. Ketamine also has been reported to mitigate bronchospasm in patients who are not intubated and in patients who are already intubated and who are not improving with mechanical ventilation (Table 1-4).

### Hemodynamic Consequences of Intubation

Laryngoscopy and intubation are potent stimuli for the reflex release of catecholamines.<sup>92</sup> This reflex sympathetic response to laryngoscopy (RSRL) produces only modest increases in blood pressure and heart rate and is of little consequence in otherwise healthy patients. The RSRL is of potential clinical significance in two settings: acute elevation of ICP and certain cardiovascular diseases (e.g., intracerebral hemorrhage, subarachnoid hemorrhage, aortic dissection or aneurysm, and ischemic heart disease). In these settings, the reflex release of catecholamines, increased myocardial oxygen demand, and attendant rise in mean arterial blood pressure and heart rate may produce deleterious effects. The synthetic opioids (e.g.,

**Table 1-4** Rapid Sequence Intubation for Status Asthmaticus

TIME	STEP
Zero minus 10 min	<b>Preparation</b>
Zero minus 5 min	<b>Preoxygenation</b> (as possible) Continuous albuterol nebulizer 100% oxygen for 3 min <i>or</i> 8 vital capacity breaths
Zero minus 3 min	<b>Pretreatment</b> Lidocaine, 1.5 mg/kg
Zero	<b>Paralysis with induction</b> Ketamine, 1.5 mg/kg Succinylcholine, 1.5 mg/kg
Zero plus 30 sec	<b>Positioning</b>
Zero plus 45 sec	<b>Placement</b> Laryngoscopy with intubation End-tidal carbon dioxide confirmation
Zero plus 2 min	<b>Postintubation management</b> Sedation and analgesia NMBA only if required after adequate sedation/analgesia In-line albuterol nebulization Additional ketamine as indicated

fentanyl) and beta-adrenergic blocking agents (e.g., esmolol) are capable of blunting the RSRL and stabilizing heart rate and blood pressure during intubation.<sup>92</sup> Lidocaine also has been studied, but the results are contradictory and inconclusive.<sup>93</sup> In patients at risk from acute blood pressure elevation, administration of fentanyl (3 µg/kg) during the pretreatment phase of RSI attenuates the heart rate and blood pressure increase. The full sympatholytic dose of fentanyl is 5 to 9 µg/kg, but if this dose is administered as a single pretreatment bolus, hypoventilation or apnea can occur. The administration of 3 µg/kg is safer and can be supplemented with an additional 3 µg/kg immediately after intubation if full sympathetic blockade is desired or if hypertension and tachycardia ensue, providing evidence of excessive sympathetic activity. Fentanyl should be given as the last pretreatment drug over 60 seconds to prevent hypoventilation or apnea.

### Elevated Intracranial Pressure

When ICP is elevated as a result of head injury or acute intracranial catastrophe, maintenance of cerebral perfusion pressure and avoidance of further increases in ICP are desirable.<sup>43</sup> Significant reductions in mean arterial blood pressure decrease cerebral perfusion pressure by reducing the driving gradient between arterial pressure and ICP, leading to increased cerebral ischemia. Maintenance of the systemic mean arterial blood pressure at 100 mm Hg or greater supports the cerebral perfusion pressure and reduces the likelihood of secondary injury. In addition, cerebral autoregulation may be lost, and increases in systemic blood pressure may lead to corresponding increases in cerebral blood flow and ICP. With elevated ICP, control of the reflex hemodynamic stimulation resulting from intubation is desirable to avoid further elevation of ICP. Fentanyl (3 µg/kg) given as a pretreatment drug is the best choice for this purpose in the emergency setting.<sup>43,94</sup>

Evidence suggests a separate reflex that increases ICP in response to laryngoscopy and intubation, although the precise mechanism is not understood. IV lidocaine reduces ICP and



**Table 1-5** Rapid Sequence Intubation for Elevated Intracranial Pressure

TIME	STEP
Zero minus 10 min	<b>Preparation</b>
Zero minus 5 min	<b>Preoxygenation</b> (as possible) 100% oxygen for 3 min <i>or</i> 8 vital capacity breaths
Zero minus 3 min	<b>Pretreatment</b> Lidocaine, 1.5 mg/kg Fentanyl, 3 µg/kg (slowly)
Zero	<b>Paralysis with induction</b> Etomidate, 0.3 mg/kg Succinylcholine, 1.5 mg/kg*
Zero plus 30 sec	<b>Positioning</b>
Zero plus 45 sec	<b>Placement</b> Laryngoscopy with intubation End-tidal carbon dioxide confirmation
Zero plus 2 min	<b>Postintubation management</b> Sedation and analgesia, consider propofol to permit frequent reexamination NMBA only if required after adequate sedation/analgesia

\*May substitute rocuronium, 1 mg/kg, for succinylcholine.

blunts the ICP response to laryngoscopy and intubation. Lidocaine (1.5 mg/kg IV), administered during the pretreatment phase of RSI, is desirable to blunt the ICP response to laryngoscopy and intubation. Similarly, RSRL and ICP response to laryngoscopy and intubation relatively contraindicate BNTI, which should be undertaken only if RSI is impossible and fiberoptic intubation is not an option.

The physician should choose an induction agent that balances a favorable effect on cerebral dynamics and ICP with a stable systemic hemodynamic profile. At present, etomidate (0.3 mg/kg) probably is the best choice for patients with elevated ICP, although thiopental also is an excellent choice when hypotension is not present (Table 1-5).

### Potential Cervical Spine Injury

Historically, it was believed that oral endotracheal intubation carried an unacceptably high risk of injury to the cervical spinal cord in patients with blunt cervical spine injury and was relatively contraindicated, but this assertion was never subjected to scientific scrutiny. Numerous studies and reports have asserted the safety and effectiveness of controlled, oral intubation with in-line cervical spine immobilization, whether done as an awake procedure or with neuromuscular blockade.<sup>95,96</sup> The evidence favors RSI with in-line stabilization, which provides maximal control of the patient, the ability to mitigate adverse effects of the intubation, and the best conditions for laryngoscopy. In-line stabilization also seems to improve the laryngoscopic view of the larynx compared with conventional tape/collar/sandbag immobilization. The intubating laryngeal mask airway (ILMA) also has been compared with conventional laryngoscopy and may result in less movement of the cervical spine during intubation than that caused by direct laryngoscopy.<sup>97</sup> A comparison of methods on a cadaver model of unstable injury of the third cervical vertebra reinforced the potential role for fiberoptic intubation and raised questions about the safety of the Combitube because of significant cervical spine movement during its placement.<sup>98</sup> Newer devices have also shown promise for safe intubation of patients with cervical spine injury. A fluoroscopic study com-

paring intubation using the Shikani optical stylet (SOS) to that done with direct laryngoscopy showed significantly less cervical spine movement with the SOS, but a slightly longer time (28 sec vs. 17 sec) to achieve intubation.<sup>99</sup> The Airtraq, a single-use intubation device, resulted in better glottic views and more rapid intubation of patients with cervical spine immobilization than direct laryngoscopy using a Macintosh blade.<sup>100</sup> The Glidescope, a video laryngoscope, provides superior glottic views with reduced or comparable cervical spine movement when compared with conventional direct laryngoscopy using the Macintosh blade.<sup>101,102</sup>

Cervical spine immobilization of patients with penetrating head and neck trauma is poorly addressed in the literature. It is not proven whether patients with gunshot or shotgun injuries to the head or neck are at risk of exacerbation of cervical cord injury during intubation, but there is no report of such a patient, with or without clinical evidence of spinal cord injury, who was injured by intubation. If the path of the missile is felt not to involve the bony spinal column and there is no evidence of spinal cord injury, prudence would dictate immobilization of patients with gunshot wounds to the head or neck with a secondary injury mechanism (e.g., fall from height) or with neurologic deficit suggesting spinal involvement.<sup>103</sup> Immobilization for intubation of patients with penetrating injury elsewhere in the body should be directed by the likelihood of secondary injury to the spine from a fall or other event distinct from the wounding.

### Pediatric Intubation

Although many considerations in pediatric intubation are the same as for adults, a few differences exist in regard to airway management. The larynx is higher in the child's neck, causing a more acute angle between the oral pharynx and the larynx. Visualization is aided by gentle posterior pressure on the anterior aspect of the thyroid cartilage. The epiglottis is high and soft, making visualization of the cords more difficult. If the child is very small, the prominent occiput brings the mouth to a position far anterior to the larynx; an assistant can lift the chest gently by grasping both shoulders, immobilizing the head at the same time. The airway in the small child is short, and care must be taken not to intubate either bronchus.<sup>67</sup>

A straight laryngoscope blade is desirable to displace the floppy epiglottis, especially in young children, and positioning for intubation may be different. BNTI is relatively contraindicated in children younger than 12 years old. Although the product insert for succinylcholine now advises against its routine use in pediatric anesthesia because of the risk of hyperkalemia in children with undiagnosed congenital neuromuscular disorders (e.g., muscular dystrophy), it remains the drug of choice for emergency RSI of infants and children.<sup>62</sup> Rocuronium has been used in children, but experience is too limited to recommend that it replace succinylcholine for pediatric RSI in the ED. RSI may be used in children in a similar manner to adults, with two important differences. Excessive bradycardia may be seen with succinylcholine in children younger than 1 year old, but it is not known whether administration of atropine (0.02 mg/kg) during the pretreatment phase prevents any possible adverse outcome. The dose of succinylcholine in infants is 2 mg/kg. Induction agents may be selected using similar criteria as for adults. The major difficulty in intubating children and infants is choosing the correct size of equipment and the correct drug doses for age or size. These obstacles can be overcome by use of a length-based system (Broselow-Luten Color Coding Kids; Vital Signs, Inc., Totowa, NJ), which provides dosing and equipment sizes based on the length of the child. Cricothyrotomy is impossible

in small children, and alternative rescue airway devices (e.g., percutaneous oxygenation via the cricothyroid membrane) are required.

## Other Airway Devices and Techniques

Regardless of the care taken by the intubator and the detailed assessment of the patient before intubation, some intubations are simply unsuccessful or impossible. In most circumstances when intubation is not possible, BMV or ventilation using an EGD provides adequate ventilation and oxygenation until a rescue airway can be established. This underscores the importance of evaluating the patient for ease of intubation, ventilation, and EGD use before deciding on the best approach and initiating the intubation sequence. Over the past 10 years, there has been a revolution in airway management, based primarily on the incorporation of video and fiberoptic technology into laryngoscopes and stylets. In addition, increasing experience with extraglottic devices and other approaches has proved useful both for routine and difficult or failed airways.

### Extraglottic Devices

**Laryngeal Mask Airway.** The laryngeal mask airway (LMA) is an irregular, ovoid, silicone mask with an inflatable rim, connected to a tube that allows ventilation (Fig. 1-10). It is available in both reusable and single-use configurations; single-use models are offered by several manufacturers and are probably equivalent.<sup>104</sup> The mask is inserted blindly into the pharynx, then inflated, providing a seal that permits ventilation of the trachea with minimal gastric insufflation. In elective anesthesia, the LMA has an extremely high insertion success rate and low complication rate, including a low incidence of tracheal aspiration.<sup>105,106</sup> In the emergency setting, studies to date have focused on use during resuscitation from cardiopulmonary arrest, although data are beginning to emerge for use of the LMA as a rescue device in the event of failed intubation and

as an alternative to direct laryngoscopy for intubation or a bag-valve-mask for ventilation.<sup>107</sup> Evaluations of LMA insertion by experienced and inexperienced personnel consistently have shown ease of insertion, high insertion success rates, and successful ventilation.<sup>108</sup> Novice users appear to be able to both ventilate and intubate more easily and successfully with the intubating LMA (ILMA) than by bag-mask ventilation and direct laryngoscopy.<sup>108</sup> The LMA may be a viable alternative to endotracheal intubation for in-hospital or out-of-hospital treatment of cardiac arrest, particularly when responders are inexperienced airway managers. At a minimum, the device may serve a temporizing role equal or superior to BMV until definitive airway management can be achieved. A new form of LMA, the iGel, has a viscous gel within the cuff, so does not require inflation. Initial experience with the device, even with minimally trained novice users, is promising, with high insertion success rates and short insertion times.<sup>109</sup>

The ILMA is designed to facilitate intubation through the mask after correct placement (Fig. 1-11). It differs from the LMA in two main ways: The mask is attached to a rigid, stainless steel ventilation tube that is bent almost to a right angle, and the mask incorporates an epiglottic elevator at its distal end. Placement of the ILMA results in successful ventilation in almost 100% of cases and successful subsequent intubation in 95%.<sup>97,110-112</sup> The ILMA can also be used for both ventilation and intubation in obese patients with similarly high success rates.<sup>113</sup> The ILMA has a special ETT and a stabilizer rod to remove the mask over the ETT after intubation is accomplished, but intubation can be comparably successful with a conventional polyvinylchloride (PVC) endotracheal tube.<sup>114</sup>

The ILMA is a better device than the standard LMA for use in the ED because it facilitates both rescue ventilation and intubation. Intubation through the ILMA has compared favorably in terms of success with direct laryngoscopy and is superior in the hands of relatively novice intubators.<sup>108,110</sup> When the ILMA is placed, intubation can be performed blindly or guided by a lighted stylet or a fiberoptic scope. The ILMA comes only in sizes 3, 4, and 5 and so is not suitable for use in patients weighing less than about 30 kg. For smaller patients, the standard LMA, which has sizes down to size 1 (infant), should be used. Intubation can be achieved through the standard LMA,



**Figure 1-10.** The standard laryngeal mask airway (LMA Classic) is available in sizes from infant to large adult. (Courtesy LMA North America, Inc., San Diego.)



**Figure 1-11.** The intubating laryngeal mask airway is modified to facilitate insertion of an endotracheal tube after placement and ventilation are achieved. The epiglottic elevator (triangle) lifts the epiglottis to allow passage of the special ETT (arrow).

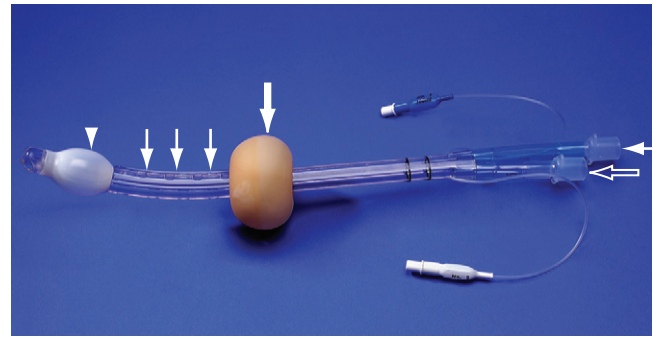
but the success rate is significantly less than with the ILMA. As experience with both the LMA and ILMA grows, it is likely that there will be increasing adoption of the LMA as a primary airway management technique by nonhospital first-responders, and the ILMA is gaining attention as a primary rescue device in the ED.

A new version of the ILMA, the CTrach incorporates fiberoptic bundles and a detachable viewing screen to provide a view of the glottis during intubation. The device performs better than the standard ILMA for first attempt intubation, where it achieves almost 93% success versus approximately 80% for the ILMA in one well-conducted study.<sup>115</sup> Ultimately, though, the ILMA's intubation success rate is so high (on three or fewer attempts) that it is not clear that the CTrach provides additional benefit overall. The view can uncommonly be obscured by secretions, but this is easily solved by removing and reinserting the device, or cleaning it with a swab through the airway lumen.<sup>116</sup> The greatest issue is cost, with the CTrach priced almost five times higher than the corresponding set of standard ILMAs. Whether the additional cost provides additional benefit for application in the ED remains to be seen.

In the ED, the primary use of the LMA or ILMA is as a rescue technique to provide a temporary airway when intubation has failed, bag ventilation is satisfactory, and the patient has been paralyzed or is otherwise in need of immediate airway management. In such cases, the LMA is one of numerous acceptable devices. In the “can’t intubate, can’t ventilate” situation, cricothyrotomy is indicated, but an ILMA may be placed rapidly in an attempt to achieve ventilation (converting the situation to “can’t intubate, can ventilate”) as long as this is done in parallel with preparations for cricothyrotomy and does not delay the initiation of a surgical airway.<sup>107</sup> Availability of the LMA and adequate prior training of the clinician offer a legitimate option for the management of the failed airway, and the ILMA compares well with fiberoptic intubation in terms of successful intubation of difficult airways.<sup>112</sup> The standard LMA may also offer advantages for providing ventilation in unconventional positions, such as when the patient is lying on his or her side.<sup>117</sup> In the out-of-hospital setting, where concerns about esophageal placement of ETTs have focused interest on methods used for airway management, the LMA and Combitube offer excellent placement and ventilation characteristics and may be preferable to endotracheal intubation in this setting, especially when intubation is relatively infrequently performed.<sup>118</sup> If the patient is in a difficult position in terms of intubation access, the LMA may facilitate more rapid ventilation.<sup>119</sup> New LMA devices, from a number of manufacturers, are now available.

**Esophagotracheal Combitube.** The Combitube is a plastic double-lumen tube with one lumen functioning as an airway after esophageal insertion and the other lumen functioning as a tracheal airway (Fig. 1-12). The tube is placed blindly into the esophagus, and proximal and distal balloons are inflated to prevent escape of ventilatory gases through the pharynx to the mouth or nose or down the esophagus. The tube is placed into the esophagus, as designed, almost 100% of the time, but both lumens are patent, so ventilation is still possible if the tube has been placed inadvertently into the trachea.

The Combitube is primarily a substitute for endotracheal intubation for non-ETT-trained personnel, but it also has a role as a primary airway device in place of endotracheal intubation in the out-of-hospital setting.<sup>120</sup> It has been used as a rescue device or as a primary intubating device in difficult airways that have precluded endotracheal intubation or successful LMA placement, both in patients with and those without cardiac arrest.<sup>121,122</sup> Serious complications attributable



**Figure 1-12.** The Combitube is inserted through the mouth blindly, although a laryngoscope can be used, if desired. It seats itself in the esophagus more than 95% of the time, and ventilation is performed through the proximal lumen and side ports (white arrows) after inflation of the two balloons. The lower balloon (triangle) occludes the esophagus. The upper (large) balloon (thick arrow) occludes the oropharynx. If the tube is in the trachea, the alternate lumen (clear arrow) is used for ventilation.

to Combitube use are uncommon.<sup>123</sup> The tube may be difficult to insert blindly when the patient is in cervical spine precautions, raising concerns about first-responder use in trauma patients, but results have been conflicting.<sup>124,125</sup> Standard methods for confirming tube placement, using ET $\text{CO}_2$ , seem to be reliable in identifying whether the tube has been passed into the esophagus or trachea and in confirming the correct ventilation port.

Although the Combitube has provided successful ventilation for several hours, it should be considered a temporizing measure only. Current use in the ED should be restricted to rescue placement after failed oral intubation with adequate BMV or a quick maneuver in the “can’t intubate, can’t oxygenate” patient simultaneous with preparation for a cricothyrotomy (analogous to the use of the ILMA in this situation). The Combitube has virtually no role in the ED as a primary airway management device except in cases of cardiopulmonary arrest when expertise for endotracheal intubation is not available.

### Video Laryngoscopes

New devices incorporate video imaging into modified laryngoscopes to allow superior visualization of the glottis without the need to create a straight-line visual axis through the mouth. The Glidescope uses an extended Macintosh blade with a sharply angulated tip to direct the video camera at the glottis, even in patients with difficult airways (Fig. 1-13). When compared with direct laryngoscopy, the Glidescope provides an equivalent or superior glottic view, and has a very high intubation success rate.<sup>126,127</sup> The Glidescope appears to cause less cervical spine movement than conventional direct laryngoscopy with a Macintosh blade.<sup>101</sup> The C-MAC video laryngoscope (Fig. 1-14) incorporates a complementary-metal-oxide-semiconductor (CMOS) video chip into otherwise conventional laryngoscope blades, to enhance glottic view. Other videolaryngoscopes are available or under development. Overall, videolaryngoscopy offers the promise of transforming laryngoscopy and has the potential to render conventional, direct laryngoscopy obsolete.<sup>128</sup>

### Fiberoptic Intubating Stylets

Several rigid fiberoptic intubating stylets have also been approved and adopted into clinical use.<sup>129</sup> The Shikani Optical Stylet (SOS—Clarus Medical, Minneapolis, Minn.) is the most studied of these. The endotracheal tube is placed over the



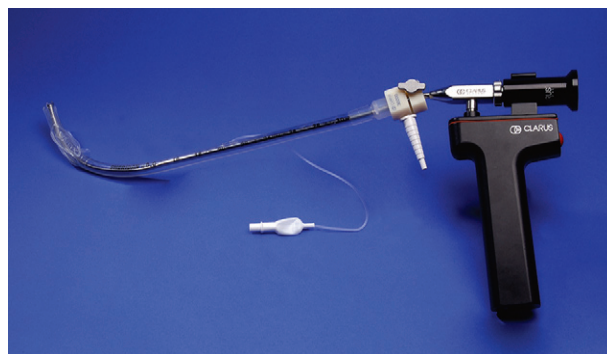


**Figure 1-13.** The GlideScope (Verathon, Inc.) is a video laryngoscope that uses a 50° deflection of the distal tip of the blade (which is otherwise similar to an extended MAC-3 blade) to direct the video camera and light source directly at the glottis without repositioning the head. The endotracheal tube insertion is done under direct vision via the video screen. (From Walls RM, Murphy MF [eds]: *Manual of Emergency Airway Management*, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, p. 171, 2008, with permission.)



**Figure 1-14.** The C-MAC video laryngoscopy (Karl Storz Endoscopy) uses an integrated CMOS video chip to capture a video image from near the distal tip of an otherwise conventional laryngoscope blade. The image is conveyed to a video screen where it is viewed by the intubator. (From Walls RM, Murphy MF [eds]: *Manual of Emergency Airway Management*, 3rd ed. Philadelphia, Lippincott Williams & Wilkins, p. 173, 2008, with permission.)

malleable stylet, then advanced through the mouth in the midline and into the trachea using built-in fiberoptic visualization (Fig. 1-15). The SOS appears to cause less movement of the cervical spine than conventional laryngoscopy during intubation with in-line stabilization.<sup>99</sup> A simpler version, the Levitan scope, uses an LED-illuminated fiberoptic stylet to facilitate intubation by direct laryngoscopy.<sup>128</sup> The device is recommended by the manufacturer to facilitate first-pass success when a limited glottic view is obtained by direct laryngoscopy. In the only study comparing the Levitan scope to the gum-elastic bougie, however, the two devices performed



**Figure 1-15.** The Shikani optical stylet (SOS, Clarus Optical) with endotracheal tube mounted. The eyepiece and battery pack are at the right.



**Figure 1-16.** The Bonfils intubating fiberscope (Karl Storz). The endotracheal tube is mounted on the stylet, and intubation is facilitated through the eyepiece at right.

similarly.<sup>130</sup> The Bonfils intubating fiberscope (Karl Storz Endoscopy of America, Culver City, Calif.) functions as a retromolar intubating stylet (Fig. 1-16). The ETT is loaded directly onto the nonmalleable fiberoptic stylet, then guided along the cheek and directed around posterior to the back molar, then through the glottic aperture by direct fiberoptic visualization.<sup>128,129</sup>

### Flexible Fiberoptic Scopes

Intubation using a flexible fiberoptic scope is increasingly applied to difficult airways in the ED, after many years of use for similar applications in the operating room. The intubating fiberoptic bronchoscope can be passed through the vocal cords under fiberoptic visualization, then can serve as an introducer over which the ETT is passed. Fiberoptic examination facilitates airway assessment for the need for intubation, without definitely committing the patient to intubation, as is the case when an NMBA is administered for RSI. For example, in a patient with smoke inhalation, examination with the fiberoptic scope might identify that intubation is not required, but will also facilitate intubation when it is indicated. Intubation of morbidly obese patients, those with distorted airway anatomy (e.g., penetrating or blunt anterior neck injury), or those with fixed cervical spine deformity, can be achieved using the fiberoptic scope, topical anesthesia, and moderate (procedural level) sedation, thus preserving the patient's ability to breathe until intubation is achieved. The fiberoptic scope also has been used successfully in concert with the ILMA to achieve intubation in difficult cases, including when the cervical spine is immobilized, where it significantly outperforms conventional laryngoscopy.<sup>131</sup>

There is a significant learning curve for flexible fiberoptic intubation, and fiberoptic examination of the upper airway in

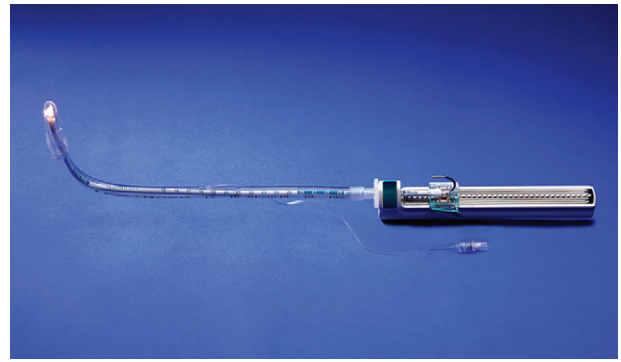
patients with pharyngitis or odynophagia, for example, is helpful, as it requires the same “navigation skills” as are required for intubation. Use of a video attachment for instruction, so that the instructor and learner can simultaneously see the same image appears to enhance learning.<sup>132</sup> Models have been created to allow learners to navigate through a series of openings and around barriers, which also increases subsequent intubation performance.<sup>133</sup>

The role of flexible fiberoptic intubation in the ED is greatly expanding, as obesity increases in the population, and, increasingly, difficult airways are handled in the ED without backup. The transition from fiberoptic to CMOS video technology should make these flexible scopes more durable, less prone to fogging, and less expensive—all desirable attributes for emergency intubation. Emergency physicians should have immediate access to fiberoptic scopes and should endeavor to acquire training and practice in their use. Fiberoptic scopes are of great value in the patient with predicted difficulty in direct laryngoscopy, EGD use, and BMV. The expanding use of video laryngoscopy will redefine the role of flexible fiberoptic scopes, as video laryngoscopy solves many of the difficulties that occur with direct laryngoscopy.

### Other Intubation Techniques

**Retrograde Intubation.** In retrograde intubation, a flexible wire is passed in retrograde fashion through a cricothyroid membrane puncture. The wire is retrieved through the mouth, then used to facilitate intubation by serving as a guide over which the ETT is passed. Purported advantages of retrograde intubation include ease of learning and application to the difficult airway. Although retrograde intubation theoretically may be useful when the upper airway is disrupted by trauma, rendering oral intubation difficult or impossible, it is unlikely to be used in the ED except in circumstances in which alternative devices, such as fiberoptic intubation, Trachlight, Combitube, and cricothyrotomy, are unavailable. Published reports of its use in emergency circumstances have been limited to case reports, very small series, and review articles. It is doubtful whether retrograde intubation would ever be the airway maneuver of first choice in the ED, but it may be a useful consideration in rare, unique difficult airway cases.

**Lighted Stylet.** The lighted stylet is a device that incorporates a handle, a fitting for mounting an ETT, and an intubating stylet with a fiberoptic light mounted on the end (Fig. 1-17). The ETT is mounted as on a conventional intubating stylet, but transillumination of the soft tissues from within the neck permits identification of tracheal entry by the stylet and ETT. The lighted stylet has been used for oral and nasal intubation and has an excellent success rate.<sup>134</sup> The lighted stylet is less stimulating to the heart rate and blood pressure than conventional laryngoscopy and may be useful when sympathetic stimulation is not desirable.<sup>135</sup> Although overall success rates with the Trachlight lighted stylet have been high, it may be more difficult for novice intubators to learn than conventional laryngoscopy, if only minimal manikin training is used.<sup>136</sup> The Trachlight can be used as a primary intubating device or as a rescue device in the “can’t intubate, can ventilate” failed airway. It is not appropriate for the “can’t intubate, can’t ventilate” failed airway, when cricothyrotomy is indicated. As a device for a difficult airway, the lighted stylet can be used as the intubating stylet for a standard oral intubation. The direct illumination by the stylet can aid in visualization during intubation. If direct laryngoscopy is unsuccessful, the first rescue procedure could be an immediate attempt at blind, oral intubation using the lighted stylet, as long as ventilation is possible. There is also some evidence that the Trachlight produces less cervical spine motion than does direct laryngoscopy.<sup>102</sup>



**Figure 1-17.** The Trachlight lighted stylet facilitates placement of the endotracheal tube when the glottis cannot be visualized by direct laryngoscopy. It also is used as a primary intubation device. Here the endotracheal tube is correctly mounted on the stylet.

## Surgical Airway Management

### Needle Cricothyrotomy with Transtracheal Jet Ventilation

Needle cricothyrotomy involves the insertion of a large needle (ideally 10-gauge) through the cricothyroid membrane into the airway. When inserted, the needle is used to ventilate the patient with a standard wall oxygen source. Because of the high-velocity ventilation that ensues through the narrow catheter, this procedure is called *transtracheal jet ventilation*. Transtracheal jet ventilation has been used successfully in humans and has been subjected to various animal experiments to determine its uses and limitations. It rarely has been used in patients in EDs, however, where its role as a rescue device in the “can’t intubate, can’t ventilate” situation is vastly inferior to cricothyrotomy.

The jet ventilator should include a regulator and gauge so that pressures can be monitored and reduced, especially in children (Fig. 1-18). Upper airway obstruction has been considered a contraindication to transtracheal jet ventilation, but ventilation still can be successful, although at the cost of higher intrapleural pressure and possibly pulmonary barotrauma. In general, when upper airway obstruction is present in adults, percutaneous or surgical cricothyrotomy is preferred.

The primary indication for transtracheal ventilation in the ED is the initiation of emergency oxygenation for a pediatric patient who is apneic (either because of the presenting condition or because of administration of an NMBA) and in whom intubation and BMV are impossible. Cricothyrotomy is extremely difficult or impossible in children younger than 10 years old, and transtracheal ventilation should be considered the surgical rescue modality of choice in this age group. For children younger than 5 years old, bag ventilation is used with the percutaneous catheter, and pressurized devices are avoided.<sup>67</sup>

### Cricothyrotomy

Cricothyrotomy is the creation of an opening in the cricothyroid membrane through which a cannula, usually a cuffed tracheostomy tube, is inserted to permit ventilation. The techniques, and variations thereof, are well described elsewhere.<sup>137</sup> When surgical airway management is required, cricothyrotomy is the procedure of choice in the emergency setting, where it is faster, more straightforward, and more likely to be successful than tracheotomy.

Cricothyrotomy is indicated when oral or nasal intubation is impossible or fails and when BMV cannot maintain adequate oxygen saturation (the “can’t intubate, can’t ventilate” situation). Several large series have established that the incidence of cricothyrotomy is approximately 1% of all ED intubations.<sup>1,39</sup>





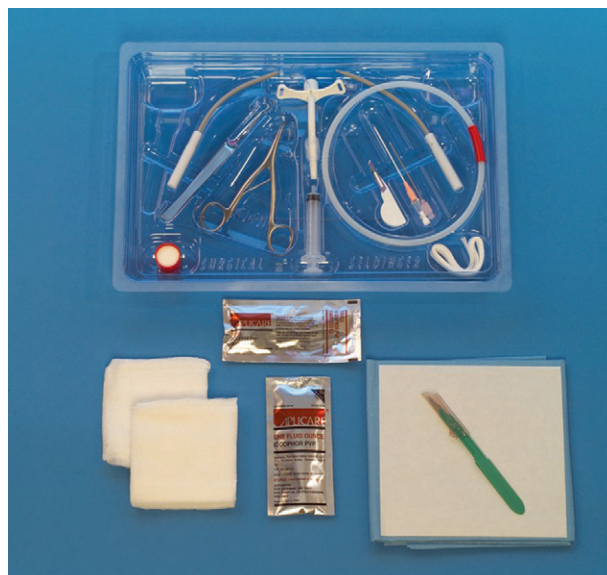
**Figure 1-18.** Transtracheal jet ventilation. High-pressure ventilation tubing (black triangle) attaches to standard wall oxygen outlet at 55 psi. Ventilation block (middle white triangle) is used to control oxygen flow through tubing (top left white triangle) to catheter (lower right triangle), which is inserted in the airway.

Cricothyrotomy is relatively contraindicated by distorted neck anatomy, preexisting infection, and coagulopathy; these contraindications are relative, however, and the establishment of the airway takes precedence over all other considerations. Successful cricothyrotomy after systemic fibrinolytic therapy has been reported.<sup>138</sup> The procedure should be avoided in children younger than 10 years old, in whom anatomic considerations make it exceedingly difficult.<sup>67</sup> Studies suggest that approximately five “practice” cricothyrotomies on a simulator or animal model are sufficient to achieve at least baseline capability with the procedure.<sup>139</sup>

Cricothyrotomies are devices used to perform percutaneous cricothyroidotomy. Percutaneous cricothyrotomy using the Seldinger technique appears comparable to formal open cricothyrotomy in terms of ease of learning and success rates.<sup>140</sup> The safety and effectiveness of other cricothyrotomies are not clearly established. A recently released kit by Portex offers a small red flag indicator to warn when the posterior tracheal wall is touched, but a cadaver study showed that, although the device resulted in somewhat faster placement of an airway than did a Seldinger technique, the incidences of both failure and major complications (posterior airway wall laceration) were unacceptably high, so the device cannot be recommended.<sup>141</sup> Only two percutaneous cricothyrotomy sets on the market currently have the ability to place a cuffed tracheostomy tube. One is a dedicated Seldinger cricothyrotomy set; the other is a combination set that has all necessary equipment for either a Seldinger percutaneous cricothyrotomy or a standard surgical cricothyrotomy (Melker universal cricothyrotomy kit; Cook Critical Care, Bloomington, Ind.) (Fig. 1-19).

## OUTCOMES

Few studies of emergency airway management have characterized complications and outcomes. The largest single-institution series reported a success rate for ED RSI of 99% and a complication rate of 9.3%; most complications were minor.<sup>14</sup> Phase II of the large National Emergency Airway Registry Study (NEAR II) of almost 9000 ED intubations reported success rates of approximately 97% for RSI. The NEAR classification system characterizes potentially adverse occurrences during intubation as “adverse events.”<sup>1,39,142</sup> In the NEAR study, the observed rate of adverse events was approximately



**Figure 1-19.** Melker universal cricothyrotomy kit. (Courtesy of Cook Critical Care.) (Disclosure: The author assisted in the design of this kit and receives a 10–35% royalty on its sales.)

9% in medical patients and 8% in trauma patients, and most of these were minor.<sup>1</sup> No studies have evaluated the long-term outcome of intubated ED patients.

## KEY CONCEPTS

- Knowledge of the clinical course of the patient's condition and anticipation of possible deterioration are crucial to the decision to intubate, especially if the patient is to leave the ED for a time (e.g., interfacility transfer, diagnostic testing).
- Assessment of the patient for potential difficulty with intubation, bag-mask ventilation (BMV), ventilation using an extraglottic device (EGD), and cricothyrotomy is an essential step in planning airway management. The mnemonics LEMON, MOANS, and RODS can serve as useful aids.
- In the absence of a “crash” patient (agonal, unresponsive to laryngoscopy) or a difficult airway, RSI is the airway management method of choice for ED patients.
- Succinylcholine is the NMBA of choice for ED RSI, but it should be avoided in certain patient groups because of risk of significant hyperkalemia.
- Pretreatment drugs given during RSI can mitigate adverse responses to intubation and improve the patient's clinical condition.
- Tube placement confirmation using end-tidal CO<sub>2</sub> (ETco<sub>2</sub>) is essential after intubation, and failure to detect adequate quantities of exhaled CO<sub>2</sub> is evidence of esophageal intubation until proven otherwise.
- Videolaryngoscopy is transforming intubation by eliminating the traditional anatomic barriers to direct laryngoscopy. Emergency practitioners should evaluate video laryngoscopes for incorporation into their practice, both for difficult and routine intubations.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

# Mechanical Ventilation and Noninvasive Ventilatory Support

Megan L. Anderson and John G. Younger

## PERSPECTIVE

Invasive and noninvasive ventilation are essential tools for treatment of critically ill patients. The indications for endotracheal intubation (ETT) and for assisted ventilation in the emergency department (ED) are not always the same. Some patients require support for respiratory failure or as part of comprehensive management of critical illness, while others' cardiopulmonary function may be preserved and assistance is needed primarily for airway protection.

The decision to intubate is discussed in Chapter 1 and in various other places throughout this textbook in the context of individual conditions. This chapter describes the modalities and techniques of mechanical ventilation.

## FUNDAMENTALS

### Invasive Techniques

Once the need for ventilatory support has been identified, three questions must be answered to initiate support: (1) What will constitute a breath—a delivered tidal volume or a delivered airway pressure? (2) To what extent will the patient be allowed to participate in breathing? (3) How will the support be delivered—by endotracheal tube or by some noninvasive means? These three are typically referred to, in order, as the *cycle* or *limit*, the *mode*, and the *method* of mechanical ventilation. Regardless of the specific method used, an oxygenated mixture of gases, usually warmed and humidified, is cyclically forced into the lungs under supra-atmospheric pressure during the inspiratory phase and allowed to exit passively during expiration.

In pressure-limited, or cycled, ventilation, a breath is defined by the peak inspiratory pressure (PIP) that is achieved each cycle. When that pressure is reached, gas insufflation ends, and passive exhalation is permitted; the delivered tidal volume is thus a function of dynamic lung compliance. An advantage of pressure-cycled ventilation is that it serves as an explicit safeguard against iatrogenic, injurious high airway pressures. A significant disadvantage is the possibility of hyper- or hypoventilation in the event of an acute change in lung compliance during therapy.

In volume-cycled ventilation, inhalation ends when a preset tidal volume has been delivered, and inspiratory pressure varies with the inverse of lung compliance. The benefit to this method is the ability to control tidal volume; the risk is poten-

tially high peak pressures when compliance is poor. There is no consensus regarding which approach to positive-pressure ventilation is better; pressure- and volume-cycling are opposite sides of the same coin, and both strategies are used clinically.

The most commonly available modes of positive-pressure ventilation are (1) controlled mechanical ventilation (CMV), (2) assist/control (A/C) ventilation, and (3) synchronized intermittent mandatory ventilation (SIMV), all of which can be supplied through either pressure-cycled or volume-cycled ventilators. Two main factors differentiate these modes from one another: (1) how a breath is *triggered* (at a preset fixed rate or by a patient's inspiratory effort sensed by the ventilator), and (2) the target capacity (pressure or volume) for each breath.

During CMV, the ventilator delivers breaths at a preset rate, regardless of any ventilatory effort made by the patient. A person receiving CMV can neither trigger a breath nor inspire gas spontaneously through the ventilator circuit, so this mode is appropriate only for apneic, pharmacologically paralyzed, and deeply sedated patients. In contrast, a ventilator applying A/C mode continuously monitors the ventilator circuit for either negative pressure or air flow deflections (generated by spontaneous inspiratory effort) and responds with a full breath. In the absence of any such patient effort, the device automatically cycles at a preset minimum "backup" rate. For example, if an A/C ventilator is set to deliver 12 breaths per minute, a breath is provided every 5 seconds in the absence of spontaneous inspiratory effort. Should a patient attempt to inspire, an additional breath is provided and the ventilator's timer resets for another 5 seconds. Thus a patient can breathe at a higher rate than the programmed A/C rate, with an attendant increase in work of breathing. A/C ventilation is a useful initial mode of mechanical ventilation in many ED patients. Commonly encountered disadvantages of this mode include poor tolerance in awake patients (often resulting in frequent elevated airway pressure alarms and underventilation) and worsening of intrathoracic air trapping in patients with chronic obstructive pulmonary disease (COPD).<sup>1</sup>

SIMV is a more complex mode developed to improve patient comfort by facilitating patient-device synchrony. The delivery of a mandatory breath is synchronized as much as possible with a patient's spontaneous respirations, preventing breath *stacking* (i.e., the delivery of a mechanical breath before the previous breath has been completely exhaled). Stacking may result in hyperinflation and barotrauma.<sup>2</sup> If spontaneous breathing occurs at a rate equal to or lower than the preset ventilator rate,

the patient's inspiration, or an elapsed time, triggers the next breath delivery. If the patient's spontaneous breathing is faster than the established SIMV rate, the patient breathes gas from the ventilator circuit and receives a volume consistent with his or her inspiratory effort, in addition to regular breaths at the set tidal volume and rate, which are triggered by the patient and delivered by the ventilator.

Regardless of the ventilatory mode chosen, additional refinements are available and commonly used. The most important of them is positive end-expiratory pressure, or PEEP. PEEP and continuous positive airway pressure (CPAP), a closely related entity, refer to the maintenance of positive airway pressure after the completion of passive exhalation. By convention, PEEP refers to pressure applied during invasive mechanical ventilation, whereas CPAP is the application of positive pressure (invasively or noninvasively) during spontaneous breathing. The terms are occasionally used interchangeably. Acute lung injury and cardiogenic pulmonary edema are characterized by loss of surfactant function. The chief beneficial effect of PEEP or CPAP is to increase functional residual capacity (FRC) by maintaining patency of injured or flooded alveoli that would otherwise collapse at the end of exhalation. Increasing the FRC may improve both oxygenation and lung compliance. One of the potential adverse effects of PEEP is decreased cardiac output.

Pressure support ventilation (PSV) is another adjunct in which breathing is controlled by the patient, and peak pressures are controlled by the ventilator. The primary goal of PSV is to support the patient's spontaneous breathing effort while providing satisfactory oxygenation. PSV provides for the prompt attainment of a preset PIP each time the patient initiates inspiratory effort. Inspiratory time, inspiratory flow rate, and tidal volume (TV) are augmented, whereas inspiratory work of breathing is reduced. The machine likewise senses the end of inspiration or initiation of exhalation, at which time the pressure support ceases, and exhalation is allowed to proceed spontaneously. Increasing levels of PSV decrease the work of breathing.<sup>1</sup> PEEP may be added to PSV, and a manda-

tory ventilation rate can be set in case spontaneous respirations deteriorate, typically using SIMV.

PSV first was used as a weaning tool, but some authorities now recommend it as a primary means of ventilatory support. Careful monitoring is necessary during its use because TV is uncontrolled. Invasive ventilation with PSV is rarely used in the ED, but PSV may be applied noninvasively.

Applied PEEP must be differentiated from *intrinsic* PEEP (iPEEP, or auto-PEEP), which may result from improper assisted ventilation when adequate time is not allowed between breaths for complete exhalation. This circumstance is discussed later.

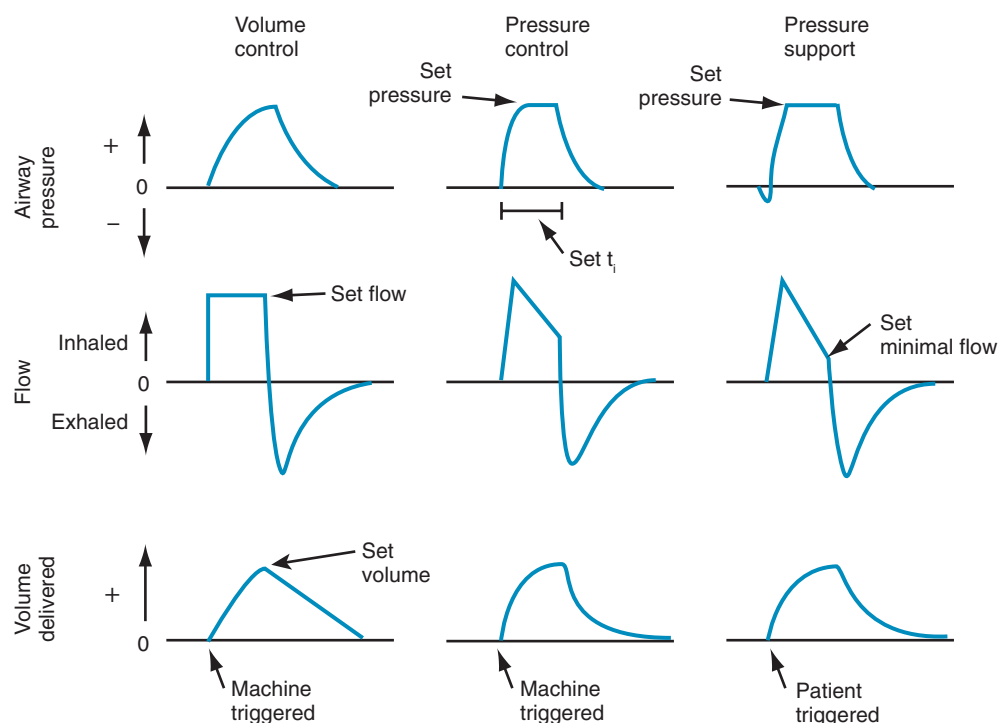
## Noninvasive Techniques

Noninvasive positive-pressure ventilation (NPPV) includes CPAP or biphasic positive airway pressure (BiPAP) and is applied with a face or nose mask. CPAP provides constant pressure throughout the respiratory cycle, and its benefits were discussed earlier in relation to PEEP. BiPAP alternates between higher pressure during inspiration (IPAP) and lower pressure during expiration (EPAP). The machine senses and responds to the patient's respiratory efforts. EPAP splints airways open and prevents alveolar collapse and atelectasis. IPAP decreases the work of breathing and improves TV (Fig. 2-1).

## ■ MANAGEMENT

### Invasive versus Noninvasive Approach

Alert patients with a patent airway and an intact respiratory drive, even if that drive is insufficient, may be candidates for NPPV. Patients most likely to respond to NPPV in the ED are those with more readily reversible causes of their distress, such as COPD exacerbation or cardiogenic pulmonary edema, in which fatigue is a significant factor.<sup>3-6</sup> Patient selection, comprehensive management of the underlying condition, and ongoing monitoring are essential for successful NPPV. NPPV



**Figure 2-1.** Pressure, flow, and waveforms typically encountered during mechanical ventilation in the emergency department. The nature of fresh gas delivery during mechanical ventilation is in part a function of the definition of "breath" (i.e., a delivered volume or delivered pressure) and the means by which that breath is initiated (i.e., by the patient or by a timing decision made by the ventilator). In practice, only a handful of ventilator parameters commonly are managed in the emergency department (the mode, the magnitude of the delivered breath, the rate of delivery, and  $\text{FiO}_2$ ). However, as this figure shows, a number of additional features can be fine-tuned to optimize the effectiveness and comfort of mechanical ventilation in critically ill patients. (Modified from Mason RJ: Murray and Nadel's Textbook of Respiratory Medicine, 4th ed. Philadelphia: Elsevier, 2005.)



has been shown to be a beneficial initial intervention for both congestive heart failure (CHF) and COPD.<sup>7,8</sup> Although studies have significant flaws, they have consistently demonstrated reduced need for intubations in both conditions, as well as a mortality benefit in COPD patients. In COPD, NPPV decreases the work of breathing and splints airways open, improving ventilation-perfusion matching.<sup>7</sup> Predictors for success in COPD include younger age, unimpaired consciousness, less severe acidemia, and prompt response (less than 2 hours), as measured by heart rate, respiratory rate, and gas exchange. Predictors for failure in COPD include a Glasgow Coma Score less than 11, an arterial pH less than 7.25, and tachypnea greater than 30 breaths per minute.<sup>9</sup> In CHF, NPPV reduces work of breathing, improves cardiac output by decreasing preload and afterload, redistributes lung water, and improves ventilation-perfusion matching thereby reducing shunt. However, although symptoms during acute exacerbations of CHF are improved, a mortality benefit has not been detected.<sup>10</sup> Some trials have used NPPV for hypoxemic respiratory failure such as in pneumonia; however, the results are not clearly beneficial.<sup>8,11</sup>

Contraindications to NPPV include severely impaired level of consciousness, cardiac arrest, acute MI, inability to protect airway, apnea, copious secretions, uncontrolled vomiting, upper airway obstruction and facial trauma.<sup>11</sup>

Patients in whom NPPV is initially chosen should be reassessed frequently for progress of therapy, tolerance of the mode of support, and any signs of clinical deterioration that indicate a need for intubation. NPPV is an attractive alternative to ETT because it reduces the risks of airway trauma and ventilator-acquired pneumonia and may be helpful in patients who decline intubation. NPPV also may be considered for a patient whose advanced directives proscribe intubation. An individualized approach is important, and discussion with the patient and family members may be helpful.<sup>12</sup>

### Initial Settings and Ongoing Monitoring

Recommended initial settings for BiPAP ventilators are an IPAP of 8 cm H<sub>2</sub>O and an EPAP of 3 cm H<sub>2</sub>O. Either a face mask or a nose mask can be used. The flow of supplemental oxygen bled into the circuit should be governed by pulse oximetry, as corroborated by arterial blood gas (ABG) results; it is appropriate to initiate therapy with 3 to 5 L/min of supplemental oxygen, but this should be adjusted with each titration of IPAP or EPAP. The ventilator should be in spontaneous mode to support the patient's respiratory effort.

As the patient's response to NPPV and other therapy is monitored (using cardiac and blood pressure monitors, ABGs, and oximetry, and the patient's own voiced assessment of tolerance and progress), support pressures are adjusted. Although this adjustment must be individualized, a reasonable approach for BiPAP support in hypoxemic patients is to increase EPAP in 2-cm H<sub>2</sub>O increments, with IPAP maintained at a fixed interval higher. Hypercapnia can be managed by increasing IPAP in 2-cm H<sub>2</sub>O increments, with EPAP being increased in approximately a 1:2.5 ratio to IPAP.<sup>6,13</sup>

For the intubated patients, initial ventilator settings depend on the goal of the ventilatory intervention (mechanical ventilation, assisted ventilation, or PSV) and on the underlying cause of respiratory insufficiency. The basic parameters to be set in volume-cycled ventilators in CMV, A/C, IMV, and SIMV modes are fraction of inspired oxygen (Fio<sub>2</sub>), TV, rate, and inspiratory/expiratory (I/E) ratio. (The I/E ratio reflects the duration of machine insufflation and the rest periods between them.) If atelectasis is a problem, PEEP should be added; the addition of PEEP may permit the use of more

physiologic Fio<sub>2</sub> values as well. For an apneic or paralyzed patient, CMV, A/C, or IMV mode may be used. For a breathing patient with inadequate ventilatory effort, A/C is usually the best initial approach.

Reasonable initial ventilator settings are a TV of 6 to 8 mL/kg body mass and a rate of 12 to 14 breaths/min. Initial Fio<sub>2</sub> should be set at 1.0 but generally can be adjusted down quickly to maintain an oxygen saturation of 90% or greater. Ventilator settings are adjusted dynamically using pulse oximetry, end-tidal carbon dioxide monitoring, ventilation pressures, clinical status, and ABGs as a guide. PEEP, if indicated, should be initiated at 2.5 to 5 cm H<sub>2</sub>O.

In pressure-cycled ventilators, the rate and Fio<sub>2</sub> are set as described earlier. An inspiratory pressure should be chosen that results in a TV of 6 to 8 mL/kg, usually 25 to 40 cm H<sub>2</sub>O. There are additional specific considerations for many particular conditions (see section on Special Clinical Circumstances).

Mechanical ventilation is a dynamic process that requires constant monitoring and regular adjustment of these parameters. Tachycardia and hypertension can indicate ventilator intolerance and a need for increased sedation or adjustment of the ventilator settings. Bradycardia and ventricular irritability represent hypoxemia until this is disproved. Unless capnometry and pulse oximetry are in use, an ABG should be measured approximately 20 minutes after initiating support. These results indicate the sufficiency of ventilation (using the pH and arterial partial pressure of carbon dioxide, P<sub>a</sub>CO<sub>2</sub>) and oxygenation (using arterial oxygen partial pressure, P<sub>a</sub>O<sub>2</sub>). Adjustments in minute volume (the product of TV and rate) and Fio<sub>2</sub> can be guided by baseline measurements supplemented by ongoing monitoring. To avoid oxygen toxicity, Fio<sub>2</sub> should be reduced to the lowest level that provides acceptable (≥90%) oxygen saturation. In many instances PEEP will allow better oxygenation for a given Fio<sub>2</sub>.

Important ventilator readouts include the PIP and expiratory volume. PIP is among the most frequently referenced measures of ventilatory function during mechanical ventilation. It reflects lung compliance and airway resistance; changes in the magnitude of PIP may reflect any of several potentially detrimental problems related to ventilation.<sup>14</sup> In a practical sense, PIP can be considered an additional vital sign for patients on a ventilator. Acute decreases in PIP reflect inadequate volume delivery to the patient, which may be caused by insufficient gas supply to the ventilator, inadvertent change in settings, a leak in the breathing circuit, unintended extubation, or failure of the ventilator. Increases in PIP may indicate ETT occlusion by secretions in or kinking of the tube, acute bronchospasm, pneumothorax, or conditions causing decreased lung compliance such as the development of worsening pulmonary edema. PIP can serve as a useful measure of effectiveness of therapy in patients with asthma or COPD; as airway resistance lessens, the PIP decreases. High PIP may cause barotrauma and other acute lung injury.<sup>15,16</sup>

Measurement of expiratory volume and expiratory flow allows estimation of the effectiveness of spontaneous respiratory efforts and, by comparing expiratory volume with the set TV, assessment of the effectiveness of ventilation and the integrity of the breathing circuit. The expiratory volume measurement is particularly important in assessing mechanical ventilation in children, who often have air leaks around an uncuffed ETT.

### Patient Treatment

Even if a mechanically ventilated patient's stay in the ED is brief, attention must be paid to ventilatory management. Routine concerns are sedation, neuromuscular paralysis if



necessary, analgesia, and suctioning. Sedation and analgesia should be titrated to provide the greatest patient comfort and ventilation performance. In addition, a rapid and systematic approach should be taken to manage the patient who becomes suddenly difficult to oxygenate or ventilate.

An opioid (e.g., fentanyl or morphine) and a sedative agent (e.g., midazolam by intermittent bolus or infusion, or propofol by infusion) are commonly used for analgesia and sedation. Ketamine can provide both sedation and analgesia and is often used for children and patients with reactive airways disease. Prolonged neuromuscular paralysis can usually be avoided by the use of adequate sedation and analgesia (see Chapter 1). If neuromuscular blockade is required, a competitive, nondepolarizing agent, such as pancuronium, vecuronium, or rocuronium, is often selected.

Endotracheal suctioning should be performed regularly. The appropriate frequency is a balance between the need for clearing secretions (especially in pulmonary edema or asthma) and the disadvantage of interrupting ventilation, which can sacrifice gains in alveolar recruitment by allowing airway pressures to fall, even very briefly, to atmospheric levels. Orally intubated patients should have a bite-block placed to protect the endotracheal tube.

## Complications

PPV is a lifesaving therapy. However, its use is associated with complications that can become quickly life-threatening, and it is important for emergency physicians to be familiar with common problems associated with PPV. Most of these result from changes in thoracic physiology when positive pressure is present for part or all of the respiratory cycle and are outlined in [Box 2-1](#). Many of these are discussed elsewhere in this text.

Acute difficulty with oxygenation or ventilation, or the development of high airway pressures in a previously calm patient, may indicate undersedation or inadequate analgesia. Additional sedation is administered in concert with a systematic search for patient or device-associated abnormalities. The differential diagnosis, after initial acclimatization, includes ETT migration, ETT occlusion, pneumothorax, bronchospasm, pulmonary edema, acute pulmonary embolism, dynamic hyperinflation, abdominal distention, mechanical failure of the ventilator, and patient-ventilator asynchrony.<sup>17</sup> ETT placement can be checked by capnometry, physical examination, and chest radiography. ETT patency should be assessed by passing a suction catheter. In patients with copious secretions,

the existence of a mucous plug acting as a “ball valve” in the endotracheal tube must be considered. This phenomenon presents as a sudden decrease in exhaled volume and elevated PIP, which responds immediately to suctioning but then quickly recurs.

The diagnoses of pulmonary edema, pneumothorax, and bronchospasm can be made clinically, with chest radiography used as an adjunct. Pulmonary embolism in a ventilated patient may be an even more elusive diagnosis than in other ED patients. Abdominal distention should be apparent on physical examination and is relieved by passage of a nasogastric or orogastric tube. Dynamic hyperinflation and ventilator malfunction may be diagnosed by momentarily disconnecting the ventilator. In the former circumstance, allowing full exhalation results in improvement; in the latter, the patient can be ventilated satisfactorily with a bag and 100% oxygen.

Patient-ventilator asynchrony may indicate incorrect ventilator mode selection, improper flow trigger sensitivity for A/C or SIMV modes, dynamic hyperinflation, or poor tolerance of mechanical ventilation despite sedation. In the last case, there is an indication for increased sedation and, if necessary, neuromuscular blockade.

Patients treated in the ED with NPPV generally should not be given sedatives or major analgesics because preservation of respiratory drive is essential to the use of this technique. Small, incremental doses of benzodiazepines for patients who have difficulty tolerating the face mask or nose mask may be useful.<sup>18</sup> Successful application of noninvasive methods is an acquired skill that takes advantage of not just drugs but of a calming bedside approach to frequently terrified patients. The authors' experience suggests that allowing family members to stay at the bedside to offer reassurance is often very helpful during the use of NPPV.

Intrinsic PEEP is an important issue, usually in patients with obstructive lung disease. In these cases, the expiratory flow rate is less than normal because of diminished elastic recoil from small airway obstruction (in emphysema) or because of dynamic airflow obstruction during exhalation (in reactive airway disease), or both. The time needed for intrapulmonary pressures to fall to ambient levels at the end of exhalation is prolonged. In spontaneously breathing intubated patients, iPEEP contributes to respiratory failure because this pressure must be matched by deep negative pressures generated by the respiratory bellows in order to initiate inhalation.<sup>19</sup> In mechanically ventilated patients, failure to anticipate prolonged expiration in patients with chronic obstructive or severe reactive lung disease risks setting a respiratory rate too high to allow complete exhalation. Breath stacking results, and unexpectedly high PIPs, patient distress, and hypotension can occur. In patients with chronic lung disease or severe asthma exacerbations who suddenly develop hypotension or become difficult to mechanically ventilate, an appropriate measure is to temporarily discontinue mechanical ventilation by switching to bag-valve breathing with deliberately prolonged exhalation. If this corrects the problem, then mechanical ventilation can be resumed by either using a slower respiratory rate or often with the aid of a respiratory therapist, customizing the inspiratory/expiratory duty cycle to allow the patient more time to exhale.

## Special Clinical Circumstances

In the following five common clinical indications for mechanical ventilation in the ED, special fine-tuning adjustments to the guidelines offered previously may be appropriate ([Table 2-1](#)).

### BOX 2-1

#### POTENTIAL ADVERSE EFFECTS OF POSITIVE-PRESSURE VENTILATION

- Increased intrathoracic pressure, leading to
  - Decreased venous return to the heart and decreased cardiac output
- Increased ventilation/perfusion ratio
- Air trapping and intrinsic positive end-expiratory pressure (iPEEP)
- Barotrauma
- Nosocomial infections of the lungs and sinuses
- Respiratory alkalosis
- Agitation and increased respiratory distress
- Increased work of breathing due to asynchrony or improperly set triggers

**Table 2-1 General Guidelines for Initial Invasive Ventilator Settings in Various Clinical Settings**

	MODE*	Fio <sub>2</sub> (%)	TV (ML/KG)	RATE (BREATHS/MIN)	I/E RATIO	PEEP (CM H <sub>2</sub> O)
Overdose in otherwise healthy patient	CMV, A/C, IMV, SIMV	100	8–10	10–12	1:2	0–5
Status asthmaticus	CMV, A/C, IMV, SIMV	100	5–10	8–12	1:4	2.5–10 <sup>†</sup>
	PHC <sup>‡</sup> , CMV, IMV, SIMV	100	5–8	6–10	1:4	2.5–10 <sup>†</sup>
COPD exacerbation, respiratory acidosis	CMV, A/C, IMV, SIMV	100	5–10	10–12	1:3–1:4	2.5–10 <sup>†</sup>
	PHC <sup>‡</sup> , CMV, IMV, SIMV	100	5–8	8–12	1:3–1:4	2.5–10 <sup>†</sup>
Cardiogenic pulmonary edema	CMV, A/C, IMV, SIMV	100	8–10	10–12	1:2	2.5–15
ARDS	CMV, A/C, IMV, SIMV	100	6–8	20–25	1:2	2.5–10
	Inverse ratio	100	6–8	8–12	1:1–1:2.1	2.5–5
Hypovolemic shock	CMV, A/C, IMV, SIMV	100	8–10	§	1:2	0–5

\*CMV is the appropriate mode when the patient is apneic or paralyzed.

<sup>†</sup>PEEP in air-trapping diseases should not exceed measured intrinsic PEEP.

<sup>‡</sup>PHC is *permissive hypercapnia*, a ventilatory strategy that can be employed in multiple modes.

<sup>§</sup>Rate should be set based on desired PaCO<sub>2</sub>.

A/C, assist/control (ventilation); ARDS, acute respiratory distress syndrome; CMV, controlled mechanical ventilation; Fio<sub>2</sub>, fraction of inspired oxygen; I/E, inspiratory/expiratory (ratio); IMV, intermittent mandatory ventilation; PEEP, positive end-expiratory pressure; SIMV, synchronized intermittent mandatory ventilation; TV, tidal volume.

When using a pressure-cycled ventilator, set pressures to deliver desired TV. After 20 minutes on initial settings, arterial blood gases should be checked so that settings and down-titrations of Fio<sub>2</sub> can be modified appropriately.

### Acute Exacerbation of Chronic Obstructive Pulmonary Disease

In treating patients with COPD on the ventilator, respiratory acidosis should be corrected gradually over hours. Overcorrection or too-rapid correction of hypercapnia and acidosis may result in metabolic alkalosis, hypokalemia, and hypophosphatemia.<sup>20</sup> Hypoxemia usually is easily correctable by increasing Fio<sub>2</sub>. Target values for PaO<sub>2</sub>, PaCO<sub>2</sub>, and pH should reflect the patient's predicted (or known) baseline function rather than usual "normal" values.

The other major goal in the mechanical ventilation of patients with COPD is normalization of lung volume. Air trapping and resultant iPEEP in a patient with COPD increase the work of breathing and the likelihood of barotrauma with mechanical ventilation. Strategies used to address this problem center on reducing iPEEP. When inadequate expiratory time is allowed in the COPD patient, air trapping is exacerbated with each inspiration; this *dynamic hyperinflation* eventually results in a sufficiently high iPEEP that any additional breath necessarily overinflates the thorax. The immediate remedy for this problem is to disconnect the patient from the ventilator momentarily, allowing complete exhalation. The ongoing solution is to build adequate expiratory time into the ventilator settings. The rate should be kept as low as possible for patients with COPD, and the expiratory time should be maximized by increasing the I/E ratio to 1:3 or 1:4. The TV also should be minimized to reduce exhaled volumes. Often patients with COPD require higher flow rates (≥100 L/min) during inspiration to minimize inspiratory time. This approach allows more of the ventilatory cycle to be spent in exhalation. Each of these modifications in the settings reduces iPEEP.

The iPEEP also may be reduced by the use of bronchodilators and corticosteroids. These agents increase inspiratory muscle strength and reduce the amount of secretions in the bronchial lumen, both of which decrease the work of breathing. Finally, iPEEP can be replaced in part by extrinsic PEEP. PEEP at a level of no more than the measured iPEEP (some authors suggest no more than 85% of iPEEP) unloads the work required to maintain iPEEP and allows the recruitment of the muscles providing the inspiratory effort. A consensus statement has suggested that BiPAP should be the initial ventilatory assistance modality of choice in COPD exacerbation.<sup>19</sup>

### Status Asthmaticus

Interventions aimed at reducing hypercapnia in ventilated patients with status asthmaticus may result in dynamic hyperinflation and barotrauma. The best approach in these patients, similar to that used in COPD, is small TV and high inspiratory flow rates to reduce inspiratory time and peak airway pressures. Airway pressures also can be lowered by *permissive hypercapnia*, which uses a low TV (5–8 mL/kg) and relatively low rates (8–10 breaths/min) to prevent excessive alveolar distention. PaCO<sub>2</sub> is allowed to remain at supranormal values without ventilatory correction. The primary goal of permissive hypercapnia is the reduction of lung volume (and iPEEP) and the risk of barotrauma, while maintaining adequate oxygenation. This approach has not been studied thoroughly under controlled conditions, but permissive hypercapnia has potential applicability in status asthmaticus, acute respiratory distress syndrome, and severe COPD exacerbations.<sup>21</sup> Occasional external chest compression also may be useful in assisting exhalation in asthma. This concept has shown promise in animal and uncontrolled human trials.<sup>22</sup>

### Acute Lung Injury

Acute lung injury (ALI) typically develops over several hours but may become evident in the ED. Pathophysiologically it is characterized by heterogeneous noncardiogenic pulmonary edema and surfactant failure that produces poor lung compliance and hypoxia. Pressure-limited special modes may be the optimal means of ventilating patients with ALI, but these techniques are often unavailable in the ED. On standard ventilators, settings should be adjusted to keep PEEP and Fio<sub>2</sub> as low as possible. Small TV (6–8 mL/kg) and fast rates (20–25 breaths/min) are indicated.<sup>23</sup> Although PEEP is considered primary therapy for ALI, these patients are highly susceptible to barotrauma. The risk of oxygen toxicity in ALI also is high and can be minimized by reducing the inspired oxygen concentration to the lowest level that maintains safe hemoglobin saturation levels. Sustained supraphysiologic oxygen tensions worsen inflammation. Iatrogenic barotrauma includes both mechanically induced tissue injury and the introduction of extrapulmonary air, such as pneumothorax or

## BOX 2-2

## VENTILATOR RECOMMENDATIONS FOR ACUTE LUNG INJURY (ARDSNET REFERENCE)

A/C, volume-cycled ventilation  
 Reduce TV to 6–8 mL/kg ideal body weight  
 Plateau pressures < 30 cm H<sub>2</sub>O (2.9 kPa); may require reducing TV as low as 4 mL/kg  
 Wean Fio<sub>2</sub> to maintain a saturation of 88–95%  
 Strategic use of PEEP to permit lower Fio<sub>2</sub> and reduce risk of oxygen toxicity<sup>24</sup>

A/C, assist/control (ventilation); Fio<sub>2</sub>, fraction of inspired oxygen; PEEP, positive end-expiratory pressure; TV, tidal volume.

pneumomediastinum, due to airspace rupture. Repetitive opening and closing of alveoli lead to shear stress and worsening inflammation. Box 2-2 lists recommendations for minimizing the potential complications of PPV in the setting of ALI; these settings are often appropriate for other applications of mechanical ventilation as well. Collectively, this is often referred to as open lung approach.<sup>25</sup>

### Cardiogenic Shock and Pulmonary Edema

The ventilatory management of pulmonary edema with cardiogenic shock is complicated by the adverse effect of applied PEEP, which is ordinarily a primary mode of therapy for pulmonary edema, on cardiac output. A reasonable compromise is to use only sufficient PEEP to allow titration of the inspired oxygen concentration. Patients in cardiogenic shock require invasive hemodynamic monitoring. Hemodynamic and ventilatory parameters must be followed in tandem to achieve optimal benefit.

Patients with less severe pulmonary edema secondary to CHF often may benefit from noninvasive ventilatory support while receiving appropriate pharmacologic therapy. CPAP and BiPAP have been studied in this setting, and one study indicated that there may be little difference between the two modes in either safety or efficacy.<sup>26</sup>

### Hypovolemic Shock

Appropriate volume resuscitation is the optimal means of managing respiratory compromise after trauma or with other causes of hypovolemic shock (e.g., massive gastrointestinal hemorrhage). PPV may exacerbate hypotension in hypovolemic patients. Patients in shock should be ventilated with 100% oxygen at a rate and TV predicted to produce near-physiologic Paco<sub>2</sub>. PEEP generally should be avoided until circulating volume is restored.

## OUTCOMES

When NPPV is successful (i.e., when ETT-mechanical ventilation is avoided), several potential therapeutic, patient comfort, and fiscal benefits are derived. The advantages of NPPV over ETT-mechanical ventilation include (1) preservation of speech, swallowing, and physiologic airway defense mechanisms; (2) reduced risk of airway injury; (3) reduced risk of nosocomial infection; and (4) decreased length of stay in, and reduced need for admission to, the intensive care unit (ICU) because less weaning and less intensive monitoring are necessary.<sup>18,27-30</sup>

Patients treated with NPPV have an increased risk of pulmonary barotrauma, aerophagia, and pressure stress to the face compared with intubated and ventilated patients. (BiPAP is a

leak-tolerant system so that pressure sores are a much less common complication of extended BiPAP support than of CPAP.) In two series, patients successfully supported in the ED with NPPV usually could be admitted to a telemetry unit instead of an ICU, with significant cost savings.<sup>13,29</sup> Uncontrolled studies without definitive inclusion criteria found NPPV successful in avoiding ETT-mechanical ventilation in 60 to 90% of patients.<sup>3,4</sup> One study<sup>31</sup> showed increased mortality rates from the use of NPPV, which was attributed to a delay in necessary intubation; the study suffered from selection bias, however, and its results have not been corroborated.<sup>6</sup> In a prospective trial of NPPV in acute cardiogenic pulmonary edema, NPPV produced more improvement in subjective dyspnea, tachycardia, and acidosis at 1 hour compared to standard oxygen therapy, but did not produce a difference in mortality at 30 days.<sup>10</sup>

Treatment of mechanically ventilated patients usually extends beyond the ED. Adequate resuscitation and stabilization are the primary ED goals so that more focused therapy of the underlying problems can be pursued in the ICU. Occasionally, patients are extubated in the ED, most often those intubated solely for airway protection when the initial insult has been reversed or adequately tolerated. Adequate ventilatory drive and oxygen must be confirmed before ED extubation; before attempting to discontinue mechanical ventilation, patients should have a respiratory rate less than 30 breaths/minute, PEEP 5 cm H<sub>2</sub>O or less, and Pao<sub>2</sub> greater than 60 mm Hg with Fio<sub>2</sub> less than 60%. NPPV may serve as a bridge between mechanical and spontaneous ventilation.

## KEY CONCEPTS

- Not all patients who require intensive ventilatory support in the ED require endotracheal intubation-mechanical ventilation. Careful patient selection for noninvasive ventilatory support may spare some patients invasive therapy and its attendant risk of complications.
- TV of 6 to 8 mL/kg, rate of 12 to 14 breaths/minute, Fio<sub>2</sub> of 1.0 is a reasonable starting point for mechanical ventilator settings for patients whose primary pathology is not pulmonary. For patients with pulmonary pathology, settings specific for the cause of the patient's respiratory failure should be used, then carefully adjusted based on clinical response.
- Sudden difficulty in the treatment of patients receiving NPPV is usually the result of intolerance, inadequate ventilation or oxygenation, or air trapping. Intolerance should not be assumed until other causes are excluded.
- Sudden difficulty in the treatment of patients receiving mechanical ventilation should prompt a quick and systematic evaluation for tube, ventilator, airway pressures, and physiologic problems; such difficulties must not be automatically assumed to result from undersedation. This frequently starts with disconnecting the ventilator from the tube and temporarily bagging with Fio<sub>2</sub> of 1.0.
- The goal of therapy in many patients is *not* prompt normalization of blood gas parameters but may be relief of significant work of breathing. Slow correction to a patient-specific baseline likely results in significantly better clinical outcomes.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

# Monitoring the Emergency Patient

Michael F. Murphy and Baruch Krauss

## ■ PERSPECTIVE

To *monitor* means to measure or observe a physiologic parameter either continuously or intermittently. Monitoring devices provide a “snapshot in time” and a window into the clinical status of the patient, detecting deterioration, tracking improvement, or measuring the effects of interventions. Monitoring parameters such as clinical observation, routine vital sign measurement, and electrocardiographic monitoring are basic tools in the practice of emergency medicine.

This chapter focuses on the following monitoring modalities: oxygenation monitoring with pulse oximetry, ventilation monitoring with end-tidal carbon dioxide (ETCO<sub>2</sub>) measurement and waveform analysis, and hemodynamic monitoring with noninvasive blood pressure (BP) measurement. Fetal monitoring immediately after maternal trauma is also briefly discussed.

## ■ NONINVASIVE BLOOD PRESSURE MEASUREMENT

Automatic noninvasive BP measurement has become a popular and, if applied appropriately, an accurate method of determining BP. Advantages include more time for staff to attend to other tasks, timed repetition of BP measurements, continuous display of the systolic pressure, and a multiparameter display (e.g., systolic, diastolic, and mean BP; pulse rate).

Two types of noninvasive BP measurement devices are currently available:

1. Cuff-type
2. Radial arterial noninvasive waveform analysis

The noninvasive cuff-type devices use a detection system based on auscultatory, oscillometric, or Doppler principles.<sup>1,2</sup> Automatic oscillometric devices determine BP by electronically determining the pulse amplitude. This method and Doppler are the most accurate of the indirect methods. The cuff is automatically inflated at predetermined intervals to a preset level. As the machine gradually deflates the cuff, it senses the amplitude of the oscillations (pulsations) transmitted to the cuff by movement of the arterial wall under the cuff. An abrupt increase in the magnitude of the oscillation signals an opening of the artery and an increase in volume under the cuff; this is the *systolic pressure*. The magnitude of the oscilla-

tion increases to a peak and then falls rapidly. The point where there is no longer an alteration in the magnitude of the oscillation is the *diastolic pressure*. Some devices calculate the *mean arterial pressure* (MAP); others identify it as the cuff pressure at the point of largest oscillation.<sup>1</sup>

Noninvasive cuff-type oscillometric devices can be cycled every 15 to 20 seconds in the “STAT” mode when necessary to provide rapid but intermittent BP readings.<sup>3</sup> Accuracy during rapid cycling is the same as during less frequent sampling, but to prevent pressure injury from the high frequency of cycling, most cuff-type automatic BP devices revert to the intermittent mode after a brief period of rapid cycling.

The shortcomings of cuff-based noninvasive BP monitoring are those of any cuff measurement technique; patients with obese arms, uncooperative moving patients, and patients with very high or very low BP. Even with these limitations, automatic devices are more accurate and reliable than manual auscultation in patients with very low or high BP because the sensing devices are more sensitive than the human ear.<sup>2</sup> The cycle length of the inflation-deflation sequence of the older devices was exceedingly long and led to frequent failure. The newer devices have rectified this problem.

A newer method of continuous, noninvasive BP monitoring measures radial artery BP and pulse rate every 12 to 15 beats. The Vasotrac (Medwave Inc., Arden Hills, St. Paul, MN) device measures BP and pulse rate and displays a radial arterial pressure waveform.<sup>4</sup> It consists of a reusable circular sensor (diameter 1.20”; width 0.35”) which is strapped over the radial artery at the wrist. The wrist sensor module is designed to measure only the pulsatile energy perpendicular to the artery, using cyclical compression and decompression. The processor requires 12 to 15 consecutive beats without interference (movement artifacts) to obtain adequate energy information to generate the pulsatile calibrated beat.<sup>4</sup>

Although the device is expensive and requires the patient to remain relatively still, a limited number of studies have demonstrated that this noninvasive method of continuous BP measurement is comparable to that provided by an invasive arterial catheter.<sup>4,6</sup>

The most accurate method of measuring BP is with an intra-arterial catheter transduced to an electronic display. The ability to identify beat-to-beat variability, respiratory variation, and longer trends is unsurpassed. In addition, arterial catheter placement enables frequent sampling of arterial blood without additional arterial punctures. Arterial pressure monitoring is



used increasingly in EDs, particularly as lack of available beds in the intensive care unit mandates longer stays in the emergency department (ED) for critically ill patients. The risk of arterial injury or thrombosis related to arterial line insertion is low, but real, and can result in vascular compromise.

Situations when noninvasive BP measurement may prove inadequate and invasive monitoring via an arterial catheter should be considered include

1. Exceedingly high (>250 mm Hg systolic) or low (<80 mm Hg systolic) pressures. Although the invasive methods are also less accurate at these extremes, the error is significantly less than with noninvasive methods.
2. Patients requiring continuous BP monitoring (e.g., rapid antihypertensive therapy with sodium nitroprusside) due to the potential for rapid fluctuations in BP.
3. In impending shock states, the best chance to insert an arterial line may be in the ED while the arterial pulse is still readily palpable, although this should not delay transferring the patient to a more appropriate location for definitive care.
4. Patients with anatomic abnormalities (e.g., no suitable limb to undertake noninvasive measurement, morbidly obese patient).
5. Conditions where frequent arterial sampling is required. The requirement in such cases is for vascular access rather than the monitoring per se. Patients who are ill enough to require frequent arterial sampling usually benefit from continuous arterial BP monitoring.

## ■ BLOOD GAS MONITORING

Although the ability to monitor oxygen utilization at the cellular level might be considered ideal, current technology permits less precise measures of performance. Transcutaneous oxygen and CO<sub>2</sub> monitoring, conjunctival oxygen pressure, pulse oximetry, and ETco<sub>2</sub> monitoring (capnography, capnometry) are all used to indicate the adequacy of pulmonary gas exchange and arterial blood gas [ABG] tensions and to assess ventilatory efficacy.

### Pulse Oximetry

The pulse oximeter provides a rapid, noninvasive, and continuous measurement of arterial oxygen saturation that has become a uniform standard for patient monitoring throughout medicine. Oximeters are easy to use and interpret, pose no risk to the patient, and are relatively inexpensive, although reliable interpretation of the information given by these devices requires an appreciation of the limitations of the technology.<sup>7,8</sup>

Transmission oximetry is the most common type of oximetry used in clinical practice. Transmission oximetry is based on differences in the optical transmission spectrum of oxygenated and deoxygenated hemoglobin. In addition to arterial hemoglobin, other absorbers in the light path include skin, soft tissue, and venous and capillary blood. Pulse oximeters measure the pulse variations in red and infrared (IR) light transmitted through a tissue bed.<sup>9</sup> Data averaged over several arterial pulse cycles are then presented as oxygen saturation as measured using pulse oximetry (SpO<sub>2</sub>).<sup>9</sup> Studies have shown an excellent correlation between arterial hemoglobin oxygen saturation and SpO<sub>2</sub> in patients with normal perfusion.<sup>9,10</sup>

The limitations of oximetry technology are related to alterations in local or systemic perfusion and severe vasoconstriction (e.g., shock, hypothermia), excessive movement, interference with transfer through the nail bed (e.g., from synthetic fingernails or nail polish), and alterations in hemoglobin (e.g., severe

anemia, abnormal hemoglobins). Carboxyhemoglobin (COHb) and methemoglobin (MetHb) contribute to light absorption and cause errors in oximetry readings.<sup>10</sup> The pulse oximeter senses COHb as though it were mostly oxyhemoglobin and provides a falsely high reading. MetHb produces a large pulsatile absorbance signal at both the red and IR wavelengths, which forces the absorbance ratio toward unity, corresponding to an SpO<sub>2</sub> of 85%.<sup>10</sup> Thus, with high levels of MetHb, the SpO<sub>2</sub> is erroneously low when the arterial saturation is above 85% and erroneously high when the arterial saturation is below 85%. Erroneously high readings (about 3–5%) and a higher incidence of failure to detect signals have been reported in dark-skinned races.<sup>9</sup>

Signals tend to be weaker from ears than from fingers, except in hypotension or peripheral vasoconstriction, but ear responses are faster.

Pulse oximetry is particularly useful in the ED evaluation of patients with acute cardiopulmonary disorders such as bronchiolitis, asthma, heart failure, and chronic obstructive pulmonary disease (COPD) and in patients with drug-induced or traumatic alterations in consciousness. It is mandatory in patients undergoing procedural or deep sedation and in those requiring definitive airway management.<sup>11,12</sup> However, it is valuable in any patient for whom continuous knowledge of oxygen levels is helpful in their treatment.<sup>11</sup> Pulse oximetry decreases the frequency with which ABG sampling is required.<sup>11</sup> Continuous monitoring may indicate the insidious development of shock as vasoconstriction and deterioration of signal detection develop. Improvements in pulse oximeter technology have resulted in improved accuracy and reliability during patient motion. In short, this valuable device has become an established component of the monitoring armamentarium of emergency medicine.<sup>13,14</sup>

However, adequate oxygen saturation does not ensure adequate *ventilation*, particularly in patients with decreased levels of consciousness. ETco<sub>2</sub> monitoring is required for accurate assessment of ventilation.

### End-Tidal Carbon Dioxide Monitoring

The concentration of CO<sub>2</sub> in an exhaled breath is intrinsically linked to tissue metabolism, systemic circulation, and ventilation.<sup>15</sup> *Capnography* is the graphic record, represented as a waveform, or *capnogram*, of the instantaneous CO<sub>2</sub> concentrations in respired gases during a respiratory cycle.<sup>16,17</sup> Capnography provides continuous, real-time, breath-to-breath feedback on the clinical status of the patient, allows the clinician to determine the baseline ventilatory status and to track changes over time.<sup>18</sup> Capnography is also a diagnostic monitoring modality because certain disease conditions are associated with characteristic waveforms.<sup>18,19</sup> Although the concentrations of CO<sub>2</sub> can be displayed continuously through the respiratory cycle, by convention only the maximum CO<sub>2</sub> concentration at the end of each tidal breath, the ETco<sub>2</sub>, is ordinarily displayed. *Capnometry* is the quantitative measurement of ETco<sub>2</sub> displayed as a number without a waveform. *Colorimetric* detectors use color scales to estimate ranges of ETco<sub>2</sub>, but are not sufficiently accurate to give quantitative measurements. Their use is therefore limited to confirmation of correct endotracheal tube (ETT) placement and its continuous location in the trachea.

Although originally used during general anesthesia in the operating room, ETco<sub>2</sub> monitoring has become a standard monitoring modality in the ED and nonhospital medical setting.<sup>20,21</sup>

Carbon dioxide monitors are configured as either sidestream or mainstream, depending on the location of the photoelectric

detector or sensor. Mainstream devices measure  $\text{CO}_2$  directly from the airway, with the sensor attached directly to the ETT. Sidestream devices, more commonly used by emergency medical service (EMS) personnel and in the ED, aspirate a sample of gas through tubing into a sensor located inside the monitor, and are used for both intubated and nonintubated patients. They are lightweight and may be integrated into special nasal-oral cannulae that simultaneously sample  $\text{CO}_2$  and deliver low-flow oxygen, allowing for continuous oxygen delivery during procedural sedation and analgesia.

Colorimetric  $\text{CO}_2$  detectors use pH-sensitive filter paper impregnated with metacresol purple, which changes color from purple ( $<4$  mm Hg  $\text{CO}_2$ ) to tan ( $4\text{--}15$  mm Hg  $\text{CO}_2$ ) to yellow ( $>20$  mm Hg  $\text{CO}_2$ ) depending on the concentration of  $\text{CO}_2$ .<sup>15,22,23</sup> (See Chapter 1, Figs. 1-3 and 1-4.) The indicator, housed in a plastic casing, is inserted between the ETT and the ventilator bag and detects changes on a breath-by-breath basis.<sup>16</sup> They are also inexpensive and easy to use, and should be available in every ED and on every EMS unit that performs intubation for confirmation of ETT placement if capnography or capnometry is not available.

In patients with normal cardiopulmonary function, there is a close correlation between alveolar  $\text{CO}_2$  ( $\text{Paco}_2$ ) and arterial  $\text{CO}_2$  ( $\text{Paco}_2$ ). The  $\text{ETCO}_2$  is usually 2 to 5 mm Hg less than the  $\text{Paco}_2$  because of the contribution of physiologic dead space gas to the end-tidal gases.<sup>24</sup> Conditions that affect ventilation-perfusion ratios (including pulmonary embolism), cardiac arrest, hypovolemia, obstructive lung disease, and the lateral decubitus position, can widen the  $\text{Pa-ETCO}_2$  gradient.<sup>25,26,48</sup> Several recent studies, however, have shown high concordance between  $\text{ETCO}_2$  and  $\text{Paco}_2$  in adult asthmatics and in children with moderate and severe respiratory distress from bronchiolitis, asthma, and pneumonia.<sup>27</sup> Although  $\text{ETCO}_2$  may not always accurately reflect the absolute  $\text{Paco}_2$  in critically ill patients, it is still valuable in detecting ventilatory trends and identifying sudden airway events.

Analysis of the shape of the capnogram can yield valuable diagnostic information.<sup>19</sup> A normal capnogram has four phases (Fig. 3-1A). Phase 1-2 represents a  $\text{CO}_2$ -free portion of the respiratory cycle. Most often this is the inspiratory phase, although it may represent apnea or a disconnection of the device from the patient. An elevation of this baseline above zero implies rebreathing of  $\text{CO}_2$ , as in increased dead space in the circuit or contamination of the sensor.<sup>18</sup>

Phase 2-3, the *rapid upstroke* of the curve, represents the transition from inspiration to expiration and the mixing of dead space and alveolar gas. Prolongation of phase 2-3 (Fig. 3-1B) occurs with obstruction to expiratory gas flow (e.g., obstructive lung disease, bronchospasm, kinked ETT) or leaks in the breathing system.

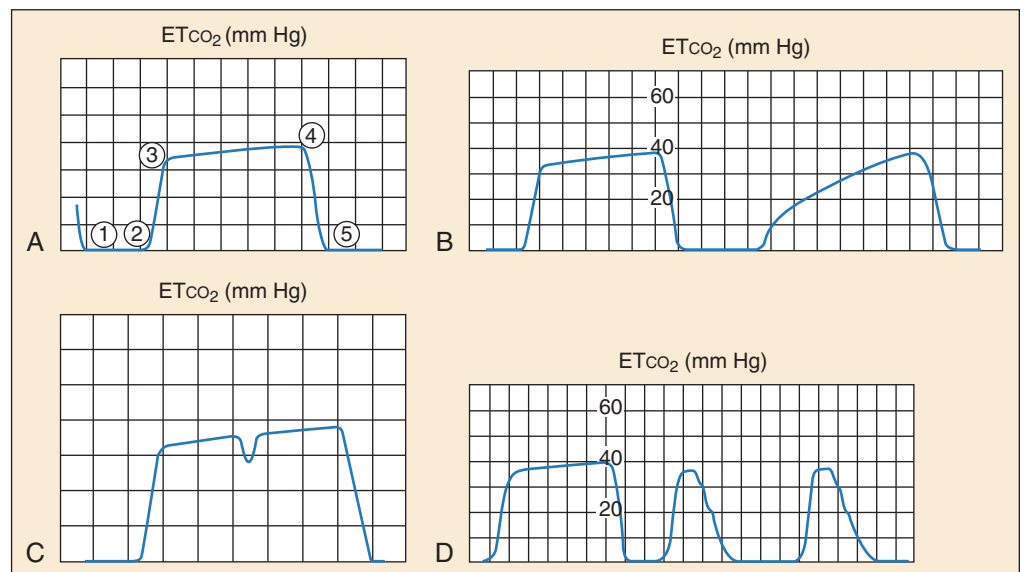
Phase 3-4, the *alveolar plateau*, represents the predominance of  $\text{CO}_2$ -rich alveolar gas in the breath stream and tends to slope gently upward with the uneven emptying of alveoli. *Point 4* (the  $\text{ETCO}_2$ ) represents the maximum  $\text{CO}_2$  concentration in each breath and is the number that appears on the monitor. The slope of this phase can be increased by the same obstructive factors that increase the slope of phase 2-3 and is also a normal physiologic variation in pregnancy.<sup>16</sup> A dip in the plateau indicates a spontaneous respiratory effort during mechanical ventilation, as in hypoxia, hypercarbia, or inadequate anesthesia (Fig. 3-1C).<sup>19,21</sup>

Phase 4-5, the *inspiratory downstroke*, is a nearly vertical drop to baseline. This slope can be prolonged and blend in with the expiratory phase in endotracheal cuff leaks (Fig. 3-1D). Abnormal respiratory patterns that are fast or chaotic limit the usefulness of  $\text{ETCO}_2$  monitoring because characteristic waveform patterns are difficult to discern.

Capnography is used in the ED in many intubated and nonintubated clinical scenarios. It can confirm ETT placement in the trachea, continuously monitor tube position in the trachea during transport, provide qualitative and quantitative methods of assessing cardiac output, gauge effectiveness of cardiopulmonary resuscitation (CPR) during cardiac arrest, determine prognosis in CPR and in trauma, maintain appropriate  $\text{ETCO}_2$  levels in patients with elevated intracranial pressure, estimate  $\text{Paco}_2$  in patients with normal lung function, aid in the detection and diagnosis of pulmonary embolism, assess response to treatment in patients with acute respiratory distress, determine adequacy of ventilation in patients with altered mental status (including drug-induced alterations in consciousness during procedural sedation and analgesia), assess ventilatory status of actively seizing patients, and help detect metabolic acidosis.

Along with visualizing tracheal rings on bronchoscopy, capnography is the other “gold standard” used to confirm intubation of the trachea (see Chapter 1). Misleading  $\text{ETCO}_2$  readings can occur with esophageal intubation after bag or mask ventilation and ingestion of carbonated beverages or antacids.

**Figure 3-1.** (A) Four phases of a normal capnogram. 1-2, The carbon dioxide-free portion of the respiratory cycle. 2-3, The rapid upstroke of the curve, representing the transition from inspiration to expiration and the mixing of dead space and alveolar gas. 3-4, The alveolar plateau, representing the alveolar gas rich in carbon dioxide and tending to slope gently upward with the uneven emptying of the alveoli. 4-5, The respiratory downstroke, which is a nearly vertical drop to baseline.  $\text{ETCO}_2$ , end-tidal carbon dioxide (concentration). (B-D) See text for explanation.



However, detection of  $\text{ETCO}_2$  usually ceases after six breaths and, if capnography is used, the tracings look abnormal.<sup>28</sup>  $\text{ETCO}_2$  is also falsely elevated for 5 to 10 minutes after injection of sodium bicarbonate.<sup>29</sup> In nonarrest settings the  $\text{ETCO}_2$  approaches 100% sensitivity and specificity in confirming correct tube placement and is also useful for monitoring for accidental extubation.

Airway, breathing, and circulatory assessment of critically ill or injured patients can be rapidly determined using  $\text{ETCO}_2$  values and the capnogram.<sup>30</sup> The presence of a normal capnogram denotes a patent airway and spontaneous breathing, and normal  $\text{ETCO}_2$  levels indicate adequate ventilation and perfusion. Capnography can therefore be used to assess critically ill patients (including victims of chemical terrorism with nerve gas exposure) and patients who are actively seizing.<sup>30,31</sup> Unlike pulse oximetry and electrocardiography, capnographic measurement is airway-based and therefore is not subject to motion artifact. It also provides reliable readings in low perfusion states.<sup>32</sup>

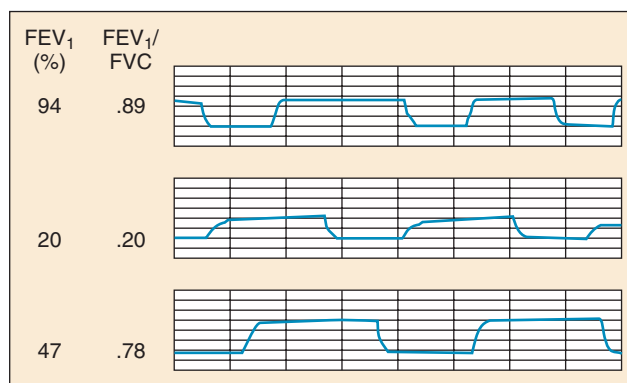
Animal and human studies have shown that  $\text{ETCO}_2$  is a useful noninvasive measurement that is highly correlated with cardiac output and is the earliest indicator of return of spontaneous circulation (ROSC) in CPR.<sup>33-35,40</sup> ROSC is heralded by an almost immediate increase in  $\text{ETCO}_2$  from baseline. Multiple studies showed that  $\text{ETCO}_2$  has prognostic value in terms of mortality during CPR.<sup>35-39</sup> No patient with a mean  $\text{ETCO}_2$  less than 10 mm Hg after 20 minutes of CPR survived, giving  $\text{ETCO}_2$  measurement a high negative predictive value for failure of resuscitation. Despite these promising findings, capnography requires further prospective validation to confirm its utility as a prognostic tool in cardiac arrest.

Capnography is the only ventilation monitoring modality that is accurate and reliable in actively seizing patients.<sup>30,31</sup> Capnographic data (capnogram,  $\text{ETCO}_2$ , respiratory rate) can be used to distinguish among actively seizing patients with apnea (flatline waveform, no  $\text{ETCO}_2$  readings, and no chest wall movement), ineffective ventilation with low tidal volume breathing (small capnograms, low  $\text{ETCO}_2$ ), and effective ventilation (normal capnogram, normal  $\text{ETCO}_2$ ).

Capnography can also rapidly detect the common airway, respiratory, and central nervous system complications associated with the nerve agents in chemical terrorism, including apnea, upper airway obstruction, laryngospasm, bronchospasm, and respiratory failure.<sup>17,30</sup>

Capnography provides dynamic monitoring of ventilatory status in patients with acute respiratory distress, such as from asthma, bronchiolitis, COPD, congestive heart failure, croup, and cystic fibrosis. By measuring  $\text{ETCO}_2$  and respiratory rate with each breath, capnography provides instantaneous feedback on the clinical status of the patient. Respiratory rate is measured directly from the airway by nasal-oral cannulae, providing a more reliable reading than impedance respiratory monitoring. In upper airway obstruction and laryngospasm, for example, impedance monitoring detects chest wall movement, interprets this as a valid breath, and displays a respiratory rate, even though the patient is not ventilating. In contrast, capnography detects no ventilation and shows a flatline capnogram.

Bronchospasm in obstructive lung disease leads to upward slanting of the expiratory plateau of the capnogram (Fig. 3-2, middle panel). Changes in  $\text{ETCO}_2$  over time and the slope of this phase of the capnogram have been shown to correlate well with spirometric measurements (forced expiratory volume in 1 second [ $\text{FEV}_1$ ] and peak expiratory flow rate [PEFR]).<sup>41-43</sup> Capnography has the advantage of being independent of effort, gender, age, and height and is a useful objective measure in asthmatic patients who are unwilling or unable to cooperate



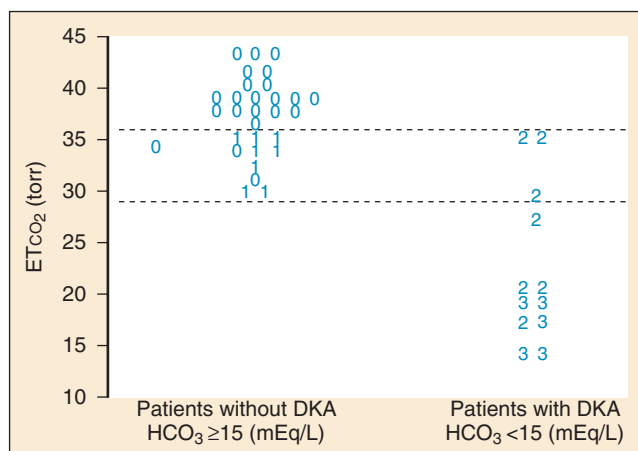
**Figure 3-2.** Capnogram shape in normal subjects (top panel), patients with bronchospasm (middle panel), and those with obstructive and restrictive (bottom panel) lung disease.  $\text{FEV}_1$ , forced expiratory volume in 1 second; FVC, forced vital capacity.

with spirometry (e.g., young children, ventilated patients, and patients in acute respiratory distress). Capnography can also be used to distinguish obstructive from restrictive lung disease.<sup>41</sup> Characteristic capnographic patterns associated with restrictive and obstructive lung disease are shown in Figure 3-2 (bottom panel).

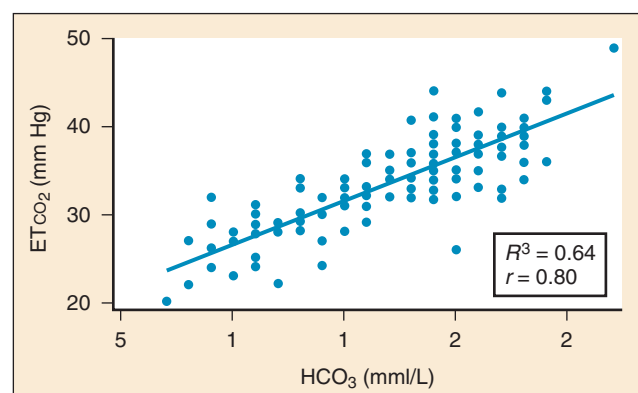
Capnography can also detect the common adverse airway and respiratory events associated with procedural sedation and analgesia.<sup>17</sup> Capnography is the earliest indicator of airway or respiratory compromise and displays an abnormally high or low  $\text{ETCO}_2$  before pulse oximetry detects a falling oxyhemoglobin saturation, especially in patients receiving supplemental oxygen. Both central and obstructive apnea can be almost instantaneously detected by capnography. Capnography may be more sensitive than clinical assessment of ventilation in the detection of apnea. In a recent study, 10/39 (26%) of patients experienced 20-second periods of apnea during procedural sedation and analgesia. All ten episodes of apnea were detected by capnography but not by the anesthesia providers.<sup>44</sup>

Obtunded or unconscious patients, including those with alcohol intoxication, intentional or unintentional drug overdose, and postictal patients (especially those treated with benzodiazepines), may have impaired ventilation. Capnography can differentiate between postictal patients with effective ventilation and those with ineffective ventilation as well as provide continuous monitoring of ventilatory trends over time to identify those patients at risk for respiratory depression and respiratory failure.

In addition to its established uses for assessment of ventilation and perfusion, capnography is a valuable tool for assessing metabolic status. Recent studies have shown that  $\text{ETCO}_2$  and serum bicarbonate ( $\text{HCO}_3^-$ ) are linearly correlated in diabetes and in pediatric gastroenteritis, and  $\text{ETCO}_2$  can be used as an indicator of metabolic acidosis in these patients (Figs. 3-3 and 3-4, respectively).<sup>45,46</sup> As a patient becomes acidotic,  $\text{HCO}_3^-$  decreases and a compensatory respiratory alkalosis develops with an increase in minute ventilation and a resultant decrease in  $\text{ETCO}_2$ . The more acidotic, the lower the  $\text{HCO}_3^-$ ; the higher the respiratory rate, the lower the  $\text{ETCO}_2$ . Furthermore,  $\text{ETCO}_2$  can be used to distinguish diabetics in ketoacidosis (metabolic acidosis, compensatory tachypnea, low  $\text{ETCO}_2$ ) from those who are not (nonacidotic, normal respiratory rate, normal  $\text{ETCO}_2$ ). A similar association between  $\text{ETCO}_2$  and  $\text{HCO}_3^-$  was demonstrated in children with gastroenteritis, in whom an  $\text{ETCO}_2 = 31$  mm Hg is 76% sensitive and 96% specific for the presence of metabolic acidosis (Fig. 3-4).<sup>47</sup>



**Figure 3-3.** Predictive value of end-tidal carbon dioxide ( $\text{ETCO}_2$ ) in detecting metabolic acidosis in diabetics. DKA, diabetic ketoacidosis;  $\text{HCO}_3^-$ , bicarbonate ion.



**Figure 3-4.** End-tidal carbon dioxide ( $\text{ETCO}_2$ )/serum bicarbonate ( $\text{HCO}_3^-$ ) correlation in gastroenteritis.  $r$ , correlation coefficient;  $R^2$ , coefficient of determination for multivariate analysis.

## FETAL MONITORING

Trauma occurs in about 7% of pregnant females.<sup>49</sup> Although maternal mortality rates in trauma do not differ from those for nonpregnant females with comparably severe injury, fetal mortality rates increase over those for pregnant women who have not suffered a traumatic injury. The American College of Obstetricians and Gynecologists recommends that the pregnant patient with a viable fetus undergo fetal monitoring for 2 to 6 hours after an injury characterized with any degree of abdominal jarring.<sup>50</sup>

Fetal monitoring is used by emergency physicians to detect occult fetal distress and inform therapy and referral. Persistent fetal tachycardia, bradycardia, loss of baseline variability or decelerations following uterine contractions (e.g., Braxton Hicks contractions), and uterine hyperactivity require urgent obstetric consultation. Although most emergency medicine residents are trained to recognize the cardiotocographic find-

ings indicative of fetal distress, most EDs do not have this monitoring equipment available. Ultrasound machines are used widely to measure and monitor fetal heart rate.<sup>49</sup>

## CEREBRAL FUNCTION MONITORING

The Bispectral index (BIS) monitors analyses and processes a patient's electroencephalogram during sedation to produce a single number—the Bispectral index. This unitless number, ranging from 0 to 100, is used as an indicator of the depth of sedation, with 0 representing EEG silence and 100 a fully awake adult.<sup>51</sup>

BIS monitoring has been studied in the ED in an attempt to objectify sedation endpoints by titrating to a target BIS score.<sup>52,53</sup> The evidence of its ability to reliably reflect depth of sedation is conflicting, however. More importantly, the threshold beyond which ventilatory compromise occurs has not been determined, further limiting the usefulness of routine BIS monitoring for sedation in the ED.<sup>53-57</sup> Gill and colleagues found that BIS monitoring reliably distinguished patients undergoing procedural sedation and analgesia who were sedated to the point of general anesthesia from those with lesser degrees of sedation but did not discriminate mild-to-moderate sedation or moderate-to-deep sedation.<sup>57</sup> The findings of Miner and coauthors supported this contention in that the assignment of a preprocedural BIS target sedation level of moderate or deep procedural sedation did not influence the level of sedation achieved, the rate of respiratory depression, the occurrence of complications, the time to return of baseline mental status, or the success of the procedure. They concluded that the assignment of a preprocedural target sedation level was not an effective means of changing the outcome of procedural sedation in the ED.<sup>56</sup>

In small pediatric ED studies, however, Agrawal and co-workers<sup>54</sup> and Overly and associates<sup>55</sup> found BIS monitoring correlated with clinical sedation scores. Determination of utility and effectiveness on outcome for children undergoing procedural sedation and analgesia awaits larger trials.

## KEY CONCEPTS

1. Monitoring modalities, when used appropriately, help to identify the effectiveness of interventions, predict deterioration, track the patient's clinical course, and inform clinical decision-making.
2.  $\text{ETCO}_2$  monitoring, especially capnography, supplements oximetry by providing useful information regarding pathologic conditions and response to therapy.
3. Alarm limits should be adjusted to ensure reasonable warnings are delivered, optimally reducing the number of false alarms. Disabling alarms is dangerous.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*



## CHAPTER 4 Shock

Alan E. Jones and Jeffrey A. Kline

### PERSPECTIVE

In philosophic terms, shock can be viewed as a transition between life and death. Whether shock results from hemorrhage, sepsis, or cardiac failure, mortality rates exceed 20%.<sup>1-3</sup> In scientific parlance, shock results from the widespread failure of the circulatory system to oxygenate and nourish the body adequately. In the laboratory the scientist defines the metabolic effect of shock quantitatively, by examining the mechanisms by which shock alters mitochondrial energy transfer, evokes the production of toxic chemicals, and reduces their removal. At the bedside, however, the clinician identifies shock by linking the clinical impression, synthesized from the patient's history of present illness, age, underlying health status, and general appearance, with quantitative data, including vital signs, blood chemistry, urine output, and direct measurements of oxygenation. When the clinical impression and the quantitative data suggest widespread organ hypoperfusion, emergent resuscitation must restore normal tissue oxygenation and substrate delivery to prevent deterioration into systemic inflammation, organ dysfunction, and death.

At the subcellular level, shock first affects the mitochondria. Mitochondria function at the lowest oxygen tension in the body, but paradoxically, they consume almost all the oxygen used by the body. More than 95% of aerobic chemical energy comes from mitochondrial combustion of fuel substrates (fats, carbohydrates, ketones) plus oxygen ( $O_2$ ) into carbon dioxide ( $CO_2$ ) and water ( $H_2O$ ). Mitochondria therefore have been referred to as the “canaries in the coal mine” because they are affected first in conditions of inadequate tissue perfusion.<sup>4,5</sup> When mitochondria have inadequate oxygen, the cell catabolizes fuels to lactate, which inexorably accumulates and diffuses into the blood.

### Classification

For years, shock has been classified into four broad categories based on Blalock's 1940 description: hematologic, neurologic, vasogenic, and cardiogenic.<sup>6</sup> This basic organization scheme remains useful today. [Box 4-1](#) outlines five categories of shock that generally have specific mechanisms and treatments.

### Epidemiology

The epidemiology of shock in the emergency department (ED) context remains speculative because shock is rarely listed as a primary coding diagnosis and depends on defining

criteria. Arterial hypotension, defined as a systolic blood pressure less than 100 mm Hg, is measured at least one time in 19% of ED patients<sup>7</sup>; however, diagnosed traumatic, cardiogenic, or septic shock is less common, constituting about 1 to 3% of all ED visits.

This chapter reviews the metabolic, systemic, and inflammatory responses that occur in all types of circulatory shock and discusses specific pathophysiology of the major causes of shock.

### Specific Causes

#### Hemorrhagic Shock

Hemorrhagic shock results from a rapid reduction in blood volume, which causes baroreceptor activation and leads to vasoconstriction, increased strength of cardiac contraction, and increased heart rate (HR). Cardiovascular response to hemorrhage can vary with underlying cardiopulmonary status, age, and presence of ingested drugs. Responses of HR and blood pressure (BP) are notoriously variable in hemorrhage, so no firm conclusion can be made at the bedside about the presence or absence of hemorrhagic shock simply by evaluating HR and BP.<sup>8</sup> In general, hemorrhage first increases pulse and cardiac contraction, then increases vasoconstriction. Blood loss causes an elevated pulse rate with a slight increase in the diastolic BP, causing the pulse pressure (difference between systolic and diastolic BP) to narrow. As blood loss continues ventricular filling decreases, and cardiac output drops, followed by a reduction in systolic BP. Before the total cardiac output begins to decrease, blood flow to noncritical organs and tissues begins to decrease, and their cells produce and release lactic acid.

Consequently, acidemia often precedes any significant decrease in cardiac output with hemorrhage.<sup>9</sup> However, the blood contains bicarbonate ions that buffer the blood pH, keeping it near neutral, even as lactic acid accumulates in blood. The base deficit, defined as the amount of strong base that would have to be added to a liter of blood to normalize the pH, represents an index of how far the bloodstream has dipped into its reserve of bicarbonate buffer. A normal base deficit is more positive than  $-2$  mEq/L. Accordingly, the arterial and venous blood base deficit can become more negative early in hemorrhage even while blood pH and BP remain in the normal range. The base deficit, therefore, crudely represents the physiologic endpoint that distinguishes trivial blood loss from clinically significant hemorrhage. In addition to

## BOX 4-1

CATEGORIES OF SHOCK ACCORDING TO  
PRIMARY TREATMENT**Causes That Require Primarily the Infusion of Volume**

## Hemorrhagic shock

- Traumatic
- Gastrointestinal
- Body cavity

## Hypovolemia

- Gastrointestinal losses
- Dehydration from insensible losses
- Third-space sequestration from inflammation

**Causes That Require Improvement in Pump Function by  
Either Infusion of Inotropic Support or Reversal of the Cause  
of Pump Dysfunction**

## Myocardial ischemia

- Coronary artery thrombosis
- Arterial hypotension with hypoxemia

## Cardiomyopathy

- Acute myocarditis
- Chronic diseases of heart muscle (ischemic, diabetic, infiltrative, endocrinologic, congenital)

## Cardiac rhythm disturbances

- Atrial fibrillation with rapid ventricular response
- Ventricular tachycardia
- Supraventricular tachycardia

## Hypodynamic septic shock

## Overdose of negative inotropic drug

- Beta-blocker
- Calcium channel antagonist overdose

## Structural cardiac damage

- Traumatic (e.g., flail mitral valve)
- Ventriculoseptal rupture
- Papillary muscle rupture

**Causes That Require Volume Support and  
Vasopressor Support**

## Hyperdynamic septic shock

## Anaphylactic shock

## Central neurogenic shock

## Drug overdose

**Problems That Require Immediate Relief from Obstruction  
to Cardiac Output**

## Pulmonary embolism

## Cardiac tamponade

## Pneumothorax

## Valvular dysfunction

- Acute thrombosis of prosthetic valve
- Critical aortic stenosis

## Congenital heart defects in newborn (e.g., closure of patent ductus arteriosus with critical aortic coarctation)

## Critical idiopathic subaortic stenosis (hypertrophic obstructive cardiomyopathy)

**Cellular Poisons That Require Specific Antidotes**

## Carbon monoxide

## Methemoglobinemia

## Hydrogen sulfide

## Cyanide

chemical buffering, the body responds to small reductions in arterial pH by activating brainstem chemoreceptors, which increase minute ventilation, leading to reduced partial pressure of carbon dioxide in arterial gas ( $P_{aCO_2}$ ).

After approximately one third of the total blood volume is acutely lost, cardiovascular reflexes can no longer sustain ade-

quate filling of the arterial circuit, and frank hypotension supervenes. Arterial hypotension is generally and arbitrarily defined as an arterial BP below 90 to 100 mm Hg. Usually coincident with the development of hypotension, bicarbonate buffers become overwhelmed, and increased alveolar ventilation becomes ineffective, culminating in reduced arterial pH. Hemorrhagic shock causes an activation of the hypothalamic-pituitary-adrenomedullary axis, with release of stress hormones that cause glycogenolysis, lipolysis, and mild hypokalemia. Therefore, in the ED, patients sustaining traumatic hemorrhage generally have an arterial lactate concentration greater than 4.0 mmol/L, a  $P_{aCO_2}$  less than 35 mm Hg, and mild hyperglycemia (150–170 mg/dL) and hypokalemia (3.5–3.7 mEq/L). Although hemorrhagic hypotension reduces lung perfusion, arterial hypoxemia should not be attributed simply to blood loss, but instead should prompt investigation for aspiration, airway obstruction, alveolar consolidation, or lung injury.

The second phase of organ injury from hemorrhagic shock occurs during resuscitation. It has been said that the acute phase of hemorrhage “cocks the gun,” and resuscitation “pulls the trigger” to cause organ injury from hemorrhagic shock. During resuscitation, neutrophils become most aggressive, binding to the lung endothelium and causing capillary leaks that characterize the adult respiratory distress syndrome (ARDS). Inflammatory cytokines are liberated during resuscitation, and membrane injury occurs in many cells. In the liver, damage from inflammation and reactive oxygen species from neutrophils is compounded by persistent microischemia. During resuscitation from hemorrhagic shock, the normal balance of vasodilation by nitric oxide (NO) versus vasoconstriction by endothelins becomes distorted, producing patchy centrilobular ischemic damage in the liver, which may produce an immediate rise in blood transaminase levels. A growing body of evidence suggests that resuscitation from hemorrhage exerts greater injury to the heart than the actual hypotensive insult.<sup>10,11</sup> Depending on the degree of hypotensive insult, the kidney may manifest acute spasm of the preglomerular arterioles, causing acute tubular necrosis. Systemic metabolic changes can impair fuel delivery to the heart and brain, secondary to depressed hepatic glucose output, impaired hepatic ketone production, and inhibited peripheral lipolysis.<sup>12</sup>

**Septic Shock**

Septic shock can be produced by infection with any microbe, although in as many as half of the cases of septic shock, no organism is identified. One of the most well-studied mediators of sepsis is lipopolysaccharide, contained in the outer cell membrane of gram-negative bacteria. Infusion of lipopolysaccharide into humans or animals produces cardiovascular, immunologic, and inflammatory changes identical to those observed with microbial infection. In recent years, multicenter trials of sepsis have suggested the emergence of gram-positive organisms as the chief cause of sepsis in hospitalized patients.<sup>13</sup> Two lines of reasoning imply that gram-positive sepsis will continue to increase in prevalence:

1. More patients are being treated at home for chronic immunocompromising diseases with indwelling catheters, which serve as excellent portals of entry into the vascular space for *Staphylococcus aureus* and coagulase-negative staphylococci.
2. The frequency of community-acquired infections caused by antibiotic-resistant gram-positive organisms has greatly increased in recent years, including infections caused by *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Streptococcus pyogenes*.

Septic shock causes three major effects that must be addressed during resuscitation: relative hypovolemia, cardiovascular depression, and induction of systemic inflammation. Septic shock produces relative hypovolemia from increased venous capacitance, which reduces right ventricular filling. Septic shock often causes absolute hypovolemia from gastrointestinal volume losses, tachypnea, sweating, and decreased ability to drink during development of the illness. Sepsis also induces capillary leak, which leads to relative loss of intravascular volume into third spaces. Recent evidence has shown that septic shock causes myocardial depression simultaneously with vasodepression and capillary leak. Direct measurements of cardiac contractility have shown that cardiac mechanical function becomes impaired early in the course of septic shock, even in the hyperdynamic stages.<sup>14</sup> Multiple mechanisms may explain depressed heart function in sepsis, including actions of specific cytokines (most notably tumor necrosis factor alpha [TNF- $\alpha$ ] and interleukin 1 beta [IL-1 $\beta$ ]),<sup>15</sup> overproduction of NO by nitric oxide synthase (iNOS),<sup>16</sup> and possibly impairment in mitochondrial oxidative phosphorylation<sup>17</sup> coincident with reduced mechanical efficiency.<sup>18</sup> Evidence indicates that circulating mediators, myocardial cellular injury from inflammation, and deranged metabolism interact synergistically to injure the heart during septic shock. Systemic inflammation causes capillary leak in the lung, which may cause alveolar infiltration characteristic of ARDS early in the treatment of septic shock in up to 40% of patients.<sup>13</sup> With the potential for early development of ARDS, more profound ventilation/perfusion ( $\dot{V}/\dot{Q}$ ) mismatching, and pneumonia or pulmonary aspiration, hypoxemia is more severe with septic shock than hemorrhagic shock.

### Cardiogenic Shock

Cardiogenic shock (myocardial pump failure) results when more than 40% of the myocardium undergoes necrosis from ischemia, inflammation, toxins, or immune destruction. Otherwise, cardiogenic shock essentially produces the same circulatory and metabolic alterations observed with hemorrhagic shock. Undoubtedly, impaired baseline cardiac function can contribute to the development of circulatory shock secondary to infection, hemorrhage, or vasodilatory drug overdose. However, when shock results from a pure cardiac cause, severe left ventricular dysfunction is evident on echocardiography early in the course. Patients with severe dysfunction are far more likely to have a cardiogenic cause of shock than patients with normal or moderate left ventricular dysfunction.<sup>19</sup>

### CLINICAL FEATURES

Patients frequently present to the ED in shock with no obvious cause. Rapid recognition of shock requires the integration of information from immediate history and physical examination, and a diagnosis of shock can be strongly supported by the presence of a worsening base deficit or lactic acidosis. In general, patients with shock exhibit a stress response: they appear ill, pale, often sweating, usually tachypneic or grunting, and often with a weak and rapid pulse (Box 4-2). HR can be normal or low in cases of shock, especially when the patient is taking prescribed drugs that depress HR or the circumstance is complicated by profound hypoxemia. BP initially can be normal because of adrenergic reflexes. Although arterial BP as a sole measurement remains an unreliable marker of circulatory status, the finding of a single systolic BP less than 100 mm Hg in the ED is associated with a threefold increase in in-hospital mortality and a tenfold increase in sudden and unexpected death.<sup>7</sup> The HR/systolic BP ratio may provide a

#### BOX 4-2

#### EMPIRICAL CRITERIA FOR DIAGNOSIS OF CIRCULATORY SHOCK\*

Ill appearance or altered mental status  
Heart rate >100 beats/min  
Respiratory rate >20 breaths/min or  $Paco_2$  <32 mm Hg  
Arterial base deficit <-4 mEq/L or lactate >4 mM/L  
Urine output <0.5 mL/kg/hr  
Arterial hypotension >20 minutes duration

\*Regardless of cause. Four criteria should be met.

better marker of shock than either measurement alone; a normal ratio is less than 0.8.<sup>20</sup> Urine output provides an excellent indicator of organ perfusion and is readily available with insertion of a Foley catheter. Measuring urine output, however, requires at least 30 minutes to accurately determine if output is normal (>1.0 mL/kg/hr), reduced (0.5–1.0 mL/kg/hr), or severely reduced (<0.5 mL/kg/hr). Point measurements of the arterial lactate concentration and the base deficit can be rapidly performed and provide accurate assessment of global perfusion status. A lactate concentration greater than 4.0 mM or a base deficit more negative than -4 mEq/L predicts the presence of circulatory insufficiency severe enough to cause subsequent multiple organ failure.<sup>21</sup> Once the empirical criteria for circulatory shock are discovered, the next step is to consider the cause of shock. Figure 4-1 is an algorithm of potential decisions to facilitate diagnosis in a patient with undifferentiated shock.

Use of the history, vital signs and physical examination documented by outside providers represents a valuable insight into a patient's physiologic status prior to any medical intervention and can be useful in ED management. Studies suggest that both medical and trauma patients with hypotension prior to being seen in the ED have a three- to fourfold higher in-hospital mortality rate than patients without hypotension.<sup>22,23</sup>

The primary survey must ensure presence of a patent airway as well as sufficient respiratory effort for adequate oxygenation and ventilation. The physical examination should be performed on an undressed patient and should begin with a quick head-to-toe inspection. Dry mucous membranes suggest dehydration, whereas distended jugular veins suggest cardiac failure or obstruction from pulmonary embolism (PE) or cardiac tamponade. Muffled heart sounds suggest cardiac tamponade, whereas a loud machine-like systolic murmur indicates acute rupture of a papillary muscle or rupture of the interventricular septum. Bilateral pulmonary rales in a patient with a normal rectal temperature help to define the presence of primary left ventricular failure. Wheezing suggests bronchospasm from anaphylaxis or, less likely, cardiac failure or PE. Abdominal tenderness may indicate peritoneal inflammation or occult trauma. Rectal examination may disclose occult gastrointestinal hemorrhage. Rectal temperature should be performed as early as is reasonable on every patient with suspected shock.

The neurologic examination documents responsiveness, cognition, and the presence of any focal deficits. In children, documentation should include level of alertness, response to parents, appropriateness of crying, pupillary function, symmetry of grimace, symmetry of extremity movements, and motor tone in infants.

Laboratory, radiographic, and other ancillary data should be ordered to assess tissue and vital organ perfusion and to diagnose injury from trauma, find the source of infection with sepsis, or identify the cause of cardiac failure. A chest radiograph, electrocardiogram, finger-stick glucose measurement,

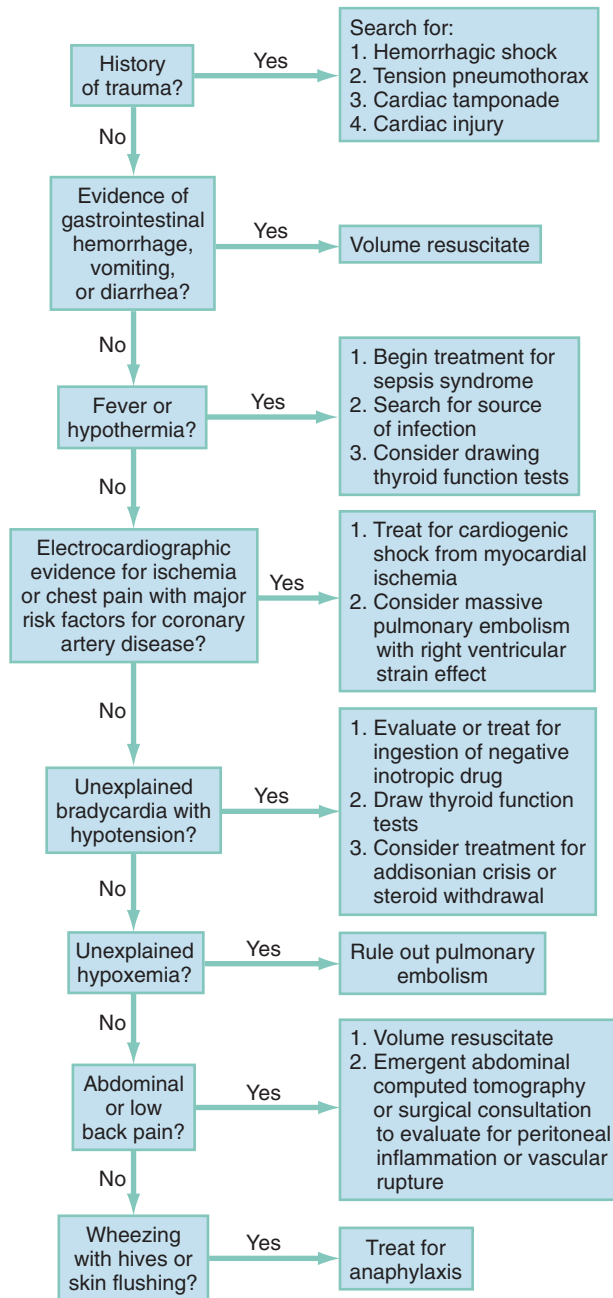


Figure 4-1. Flow diagram to classify undifferentiated shock.

complete blood count (CBC), urinalysis, serum electrolytes, and kidney and liver function tests are all indicated in the ED assessment. Arterial blood gases are ordered for a base deficit calculation and to correlate arterial oxygen partial pressure ( $P_{aO_2}$ ) with that measured by pulse oximetry, when the latter is deemed unreliable. Serum lactate measurement should be performed as early as possible in patients with suspected shock. Either venous or arterial lactate concentrations can be used.<sup>24-27</sup> If peripheral venous lactate is used, time, storage temperature, and tourniquet use have no significant effect on in vitro lactate production by erythrocytes if the measurement is done within 15 minutes after the sample is obtained.<sup>28</sup> Some EDs have bedside ultrasound capability, and both cardiac and abdominal scanning can be rapidly performed at the bedside to screen for inadequate central venous volume, occult hemo-peritoneum, abdominal aortic aneurysm, left ventricular failure, and cardiac tamponade. A systematic ultrasound protocol can significantly improve the physician's ability to accu-

#### BOX 4-3

#### DEFINITIONS AND CRITERIA FOR SEPTIC, HEMORRHAGIC, AND CARDIOGENIC SHOCK

##### Septic Shock

##### Systemic Inflammatory Response Syndrome (SIRS)

Two or more of the following:

1. Temperature  $>38^\circ\text{C}$  or  $<36^\circ\text{C}$
2. Heart rate  $>90$  beats/min
3. Respiratory rate  $>20$  breaths/min or  $P_{aCO_2} <32$  mm Hg
4. White blood cell count  $>12,000/\text{mm}^3$ ,  $<4000/\text{mm}^3$ , or  $>10\%$  band neutrophilia

##### Severe Sepsis

SIRS with suspected or confirmed infection and associated with organ dysfunction or hypotension; organ dysfunction may include presence of lactic acidosis, oliguria, or altered mental status

##### Septic Shock

SIRS with suspected or confirmed infection with hypotension despite adequate fluid resuscitation; septic shock should still be diagnosed if vasopressor therapy has normalized blood pressure

##### Hemorrhagic Shock

##### Simple Hemorrhage

Suspected bleeding with pulse  $<100$  beats/min, normal respiratory rate, normal blood pressure, and normal base deficit

##### Hemorrhage with Hypoperfusion

Suspected bleeding with base deficit  $<-4$  mEq/L or persistent pulse  $>100$  beats/min

##### Hemorrhagic Shock

Suspected bleeding with at least four criteria listed in Box 4-2

##### Cardiogenic Shock

##### Cardiac Failure

Clinical evidence of impaired forward flow of the heart, including presence of dyspnea, tachycardia, pulmonary edema, peripheral edema, or cyanosis

##### Cardiogenic Shock

Cardiac failure plus four criteria listed in Box 4-2

rately diagnose the cause of undifferentiated shock in ED patients,<sup>29</sup> and the finding of hyperdynamic left ventricular function in patients with undifferentiated shock strongly suggests sepsis as the cause.<sup>30</sup>

Consensus definitions of shock show the spectrum of hypoperfusion for the following three common causes of shock (Box 4-3):

1. *Septic shock.* The American College of Chest Physicians, European Society of Intensive Care Medicine, Society for Critical Care Medicine, American Thoracic Society, and the Surgical Infection Society<sup>31</sup> developed international consensus definitions for distinguishing septic shock from its precursor conditions, the systemic inflammatory response syndrome (SIRS), sepsis, and severe sepsis. Although this particular consensus requires persistent hypotension after fluid resuscitation to strictly define septic shock, initiation of treatment for empirically diagnosed severe sepsis or septic shock should not await the onset of hypotension.
2. *Hemorrhagic shock.* The American College of Surgeons has divided hemorrhagic shock into four stages, depending on



the severity of blood loss and the physiologic response to this loss, but such arbitrary divisions are of little value. A more useful approach defines hemorrhagic shock as being present when systemic hypoperfusion manifests as lactic acidosis with organ dysfunction.

3. **Cardiogenic shock.** Cardiogenic shock should be thought to be present whenever cardiac failure (ischemic, toxic, or obstructive) causes systemic hypoperfusion that manifests as lactic acidosis with organ dysfunction.

## ■ MANAGEMENT

### Monitoring Perfusion Status

In the effort to resuscitate a patient with circulatory shock, the clinician must follow specific indices of systemic perfusion and organ function to know if the resuscitation effort is working. In all patients with shock, circulation must be monitored by continuous electrocardiography and pulse oximetry. Cuff sphygmomanometer measurement of BP should be performed frequently during resuscitation. Because cuff sphygmomanometer measurement may be inaccurate in severe hypotensive states, the use of an arterial pressure monitoring line should be considered, especially if vasoactive medications are being administered. BP and HR correlate poorly with cardiac index (CI) in shock and often underestimate the severity of systemic hypoperfusion.<sup>8</sup> Moreover, children with hypovolemic shock frequently demonstrate a normal BP until they rapidly deteriorate.<sup>32</sup> Urine output should be measured as an index of vital organ perfusion (about 1 mL/kg/hr in persons without renal disease). A downward trend of the serum lactate concentration or upward trend of the base deficit, when observed with improving vital signs and urine output, is a reliable gauge of the adequacy of resuscitation and prognosis in shock from any cause.<sup>21,33</sup> A rising lactate concentration (or refractory hypotension with worsening base deficit) despite ongoing resuscitation is a portent of imminent death, and vigorous resuscitation efforts or specific procedural intervention should be instituted.

Most patients with shock can be fully resuscitated with peripheral venous access established with two catheters of at least a size 18 gauge. Monitoring of central venous pressure (CVP) as part of a goal-directed resuscitation may improve outcome in patients with septic shock.<sup>34</sup> Patients with cardiac failure or renal failure may benefit from closer measurement of the CVP and insertion of a central venous catheter. An 8.5-French catheter (Cordis Sheath) allows for accurate measurement of the CVP and insertion of a pulmonary artery catheter or other monitoring device if needed. In children a 3- or 5-French bilumen catheter can be placed in the femoral vein with few complications.<sup>35</sup> To reduce the potential for limb damage from extravasation from a peripheral IV, vasoactive medications are optimally administered through a central venous catheter. If vasoactive medications are administered, additional peripheral intravenous catheters are required for infusion of crystalloid and other treatments. Many patients with renal disease or cancer have indwelling catheters. In patients with empirical criteria for shock, this catheter should be used for IV access, unless satisfactory access has already been established at other anatomic sites. In EDs where the standard practice is not to use these ports at the request of other physicians, a specific hospital policy and training session should be developed to make an exception in the case of circulatory shock. In general, failure to administer fluids rapidly and in sufficient quantity outweighs considerations about preservation of the line for future therapy.

## Quantitative Resuscitation

Quantitative resuscitation (also called goal-directed therapy, goal-oriented resuscitation, or hemodynamic optimization) was first described in 1988 and refers to the practice of resuscitating patients to predefined physiologic endpoints indicating that systemic perfusion and vital organ function have been restored.<sup>36</sup> Since that time many studies have evaluated the efficacy of such a therapeutic approach to shock, and a meta-analysis of these studies confirms its benefit for reducing mortality rates.<sup>37</sup> For many years in the intensive care unit (ICU), physicians have relied on the use of the pulmonary artery catheter (PAC) to help optimize left ventricular filling indices. At present the use of the PAC remains controversial. In the last 5 years, five randomized controlled trials investigating the management of critically ill patients with a PAC have been published.<sup>38-42</sup> None have found a benefit in terms of survival or length of stay. Insufficient data have been published to support the use or avoidance of PACs in ED populations; however, extrapolating from ICU studies, PACs have no role in the management of shock in the ED.

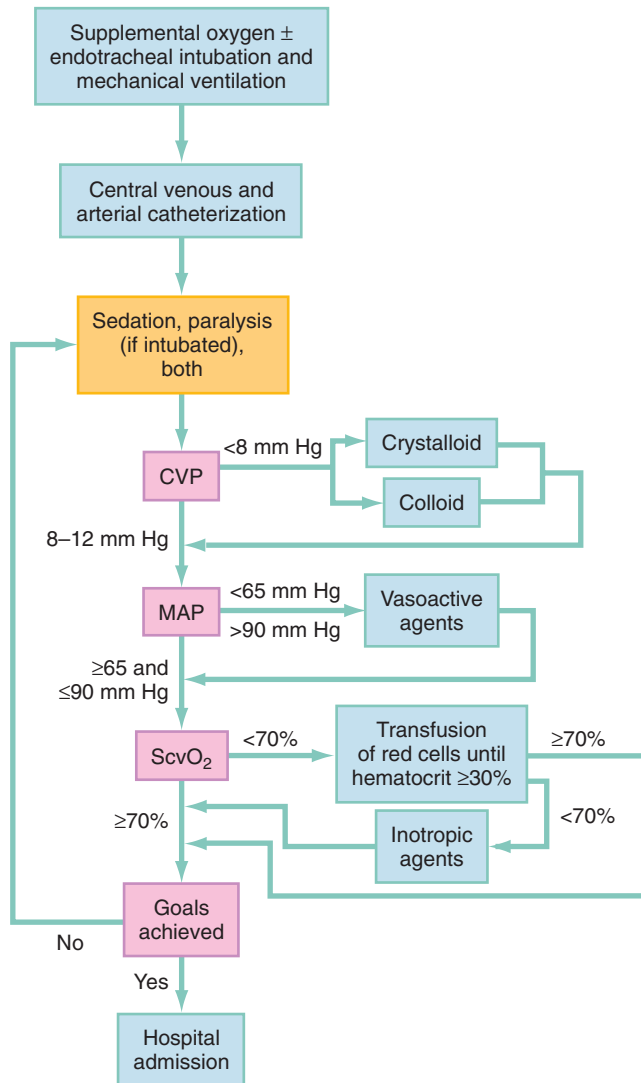
Several alternative methods to the PAC have been proposed as endpoints to resuscitation in the ED. The *lactate clearance* index refers to serial measurements of venous or arterial lactate.<sup>33,43</sup> Lactate clearance involves measuring the blood lactate concentration at two or more times. If the lactate concentration has not decreased by 10% two hours after resuscitation has begun, additional steps must be undertaken to improve systemic perfusion.<sup>43</sup> Resuscitation should continue until the lactate concentration drops below 2 mM/L. Clinical trials are presently investigating the utility of lactate clearance as an endpoint of resuscitation, which will have ramifications for the increasing use of point-of-care lactate testing platforms in the ED.

*Mixed venous oxygen saturation* (Svo<sub>2</sub>) measurements reflect the balance between oxygen delivery and oxygen consumption. Previous studies have suggested that the Svo<sub>2</sub> can be used as a surrogate to CI when targeting normalization of endpoints (Svo<sub>2</sub> = 65% or CI 2.5–3.5 L/min/m<sup>2</sup>) for therapeutic intervention in critically ill patients.<sup>44</sup> Although Svo<sub>2</sub> requires the use of a PAC, the central venous oxygen saturation (Scvo<sub>2</sub>) drawn from the central circulation has been shown to closely parallel the Svo<sub>2</sub>, especially when tracking changes or trends in the values.<sup>45</sup>

Early quantitative resuscitation, which incorporates multiple indices of circulatory and oxygenation status, was shown in one randomized controlled trial to significantly reduce mortality and morbidity rates in ED patients with severe sepsis or septic shock.<sup>34</sup> Patients are resuscitated within the first 6 hours of care to achieve normalization of CVP and mean BP and to maintain a Scvo<sub>2</sub> greater than or equal to 70% (Fig. 4-2). The decrease in mortality rate from this new treatment strategy, termed *early goal-directed therapy*, has been found effective in smaller prospective before-and-after studies of patients with sepsis.<sup>46,47</sup> Large multicenter validation of this resuscitation strategy in sepsis is underway. However, it has not been tested in other causes of shock but shows the value of using defined physiologic endpoints to measure systemic perfusion during resuscitation from shock in the ED. This approach also further substantiates the importance of the first 6 hours of resuscitation.

## Ventilation

Rapid sequence intubation is the preferred method of airway control in most patients with shock (see Chapter 1). Intubation



**Figure 4-2.** Flow diagram outlining the protocol for quantitative resuscitation when treating patients with severe sepsis or septic shock. This protocol outlines specific hemodynamic and physiologic parameters the clinician should seek to achieve within the first 6 hours of care. This protocol is focused on resuscitation and should be used in conjunction with standard clinical care for patients with suspected infection, such as appropriate diagnostic studies to determine the focus of infection and appropriate antimicrobial agents to treat the infection. CVP, central venous pressure; MAP, mean arterial pressure; ScvO<sub>2</sub>, central venous oxygen saturation. (Redrawn from Rivers E, et al: Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 345:1368, 2001.)

prevents aspiration, increases oxygenation, treats acute respiratory failure, provides initial treatment for metabolic or hypercarbic acidemia, and protects the patient who will be sent to an uncontrolled environment (e.g., for tests). Intubation also reduces the work of breathing, which, in the hypoperfused patient, further exacerbates lactic acidemia. Strenuous use of accessory respiratory muscles can increase oxygen consumption by 50 to 100% and decrease cerebral blood flow by 50%.<sup>48,49</sup> More importantly, if the patient has increased airway resistance (e.g., bronchospasm with anaphylaxis) or a decrease in lung compliance (e.g., pulmonary edema, ARDS), a more negative intrathoracic pressure must be generated to fill the lungs with each inspiration. The greater suction effect is also exerted on the left ventricle, impeding its ability to eject and increasing functional afterload. Positive pressure ventilation

#### BOX 4-4

#### CLINICAL MANAGEMENT GUIDELINES FOR FOUR COMMON CAUSES OF SHOCK

##### Hemorrhagic Shock

Ensure adequate ventilation/oxygenation  
Provide immediate control of hemorrhage, when possible (e.g., traction for long bone fractures, direct pressure)  
Initiate judicious infusion of isotonic crystalloid solution (10–20 mL/kg)  
With evidence of poor organ perfusion and 30-minute anticipated delay to hemorrhage control, begin packed red blood cell (PRBC) infusion (5–10 mL/kg)  
With suspected central nervous system trauma or Glasgow Coma Scale score <9, immediate PRBC transfusion may be preferable as initial resuscitation fluid  
Treat coincident dysrhythmias (e.g., atrial fibrillation with synchronized cardioversion)

##### Cardiogenic Shock

Ameliorate increased work of breathing; provide oxygen and positive end-expiratory pressure (PEEP) for pulmonary edema  
Begin vasopressor or inotropic support; norepinephrine (0.5 µg/min) and dobutamine (5 µg/kg/min) are common empirical agents  
Seek to reverse the insult (e.g., initiate thrombolysis, arrange percutaneous transluminal angioplasty)  
Consider intra-aortic balloon pump counterpulsation for refractory shock

##### Septic Shock

Ensure adequate oxygenation; remove work of breathing  
Administer 20 mL/kg of crystalloid or 5 mL/kg of colloid, and titrate infusion to adequate central venous pressure and urine output  
Begin antimicrobial therapy; attempt surgical drainage or débridement  
Begin PRBC infusion for hemoglobin < 8 g/dL  
If volume restoration fails to improve organ perfusion, begin vasopressor support; initial choice includes dopamine, infused at 5–15 µg/kg/min, or norepinephrine, infused at 0.5 µg/min

removes this impedance and can improve ventricular function and cardiac output up to 30%.<sup>48</sup>

#### Volume Replacement

The next imperative in shock is to decide when “the tank is full.” The goal in volume replacement is slightly elevated left ventricular end-diastolic *volume*, which is a difficult measurement to make in the ED. The CVP is most often used to estimate right ventricular filling pressure and is used in some quantitative resuscitation algorithms. Because both ventricles tend to stiffen during shock, a high CVP (10–15 cm H<sub>2</sub>O) is often needed to produce adequate filling volume. It is a long way, however, from the CVP measurement to actual knowledge of left ventricular end-diastolic volume; a presumed adequate CVP must be substantiated by increases in urine output and BP and decreasing lactate concentrations.<sup>50</sup>

#### Treating Specific Causes

Box 4-4 presents the general treatment approach for the four common causes of shock.

## Hemorrhagic Shock

Standard treatment for hemorrhagic shock consists of rapidly infusing several liters of isotonic crystalloid in adults or three successive 20-mL/kg boluses in children. Colloids, including albumin and hydroxyethyl hetastarch (Hespan), can be used as well but at considerable increase in cost and without effect on morbidity or mortality rates.<sup>51</sup> Colloids offer the theoretic advantage of a high osmotic pressure, which should help to maintain a normal intravascular volume after retransfusion from hemorrhage. If criteria for shock persist despite crystalloid infusion (see [Box 4-2](#)), packed red blood cells (PRBCs) should be infused (1–2 units in adults or 5–10 mL/kg in children). Type-specific blood should be used when the clinical scenario permits, but uncrossmatched blood should be used at the earliest opportunity for patients with arterial hypotension and uncontrolled hemorrhage. O-negative blood is used in women of childbearing age and O-positive blood in all others (see Chapter 5). Substantial evidence supports the use of leukodepleted blood, which has been filtered to remove donor neutrophils.<sup>52</sup> Leukodepleted blood is used in countries outside the United States because it produces less retransfusion-related organ damage.<sup>53</sup>

The infusion of hemoglobin-based oxygen carriers as alternatives to PRBCs for resuscitation of hemorrhagic shock have been extensively studied. In a large randomized controlled trial, diaspirin cross-linked hemoglobin, a purified and chemically modified human hemoglobin substrate, was compared with crystalloid for initial resuscitation in the critically injured, and its use resulted in a higher mortality rate at interim analysis, resulting in termination of the trial.<sup>54</sup> Other artificial hemoglobin substitutes may be available in the future but at present show no benefit over PRBCs.

Recent studies have endorsed the concept of either delayed resuscitation or hypotensive resuscitation for hemorrhagic shock. This is discussed in Chapters 34, 42, and 43. Controlling hemorrhage remains the cornerstone of treating hemorrhagic shock, and evidence continues to support immediate surgery when direct vascular control cannot otherwise be obtained (see Chapter 34).

## Septic Shock

Septic shock begins as an infectious nidus, which triggers a domino effect of cellular, microvascular, hematologic, and cardiovascular dysfunction. Treatment begins by establishing adequate ventilation to correct hypoxia and acidosis and to reduce systemic oxygen consumption and left ventricular work. This often requires endotracheal intubation and sedation for mechanical ventilation. The controversy regarding the use of etomidate in patients with septic shock is discussed in Chapter 1.

The second goal is to achieve adequate ventricular filling. The choice of fluids in treating septic shock is probably less important than scrupulous monitoring for adequate tissue perfusion. However, choices for fluid resuscitation should involve consideration of availability and the cost-benefit ratio. Initial volume replacement should include rapid infusion of 20 to 25 mL/kg of crystalloid. If hypoperfusion is persistent, 5- to 10-mL/kg boluses of a colloid should be considered. Blood should be transfused in the ED to restore hematocrit to at least 30 to 35%.

The third directive is to eradicate the infection with antimicrobial therapy and, where necessary, surgical drainage. A recent study reported that in adult patients with septic shock, effective antimicrobial administration within the first hour of documented hypotension was associated with increased sur-

vival to hospital discharge and that each hour delay in antimicrobial administration over the first 6 hours after recognition was associated with an average decrease in survival of 7.6% per hour.<sup>55</sup> The choice of antimicrobial agent can be directed by clinician experience and institutional minimal infective concentration (MIC) data. When no focus can be found in septic shock, a semisynthetic penicillin with a  $\beta$ -lactamase inhibitor, in combination with an aminoglycoside plus vancomycin is a rational empirical choice. When neutropenia is suspected in a patient with sepsis syndrome, the progression to refractory, fatal septic shock can be cataclysmic. Neutropenia is suggested in patients who have recently undergone chemotherapy. Chemotherapy patients with sepsis represent a special challenge because the pathophysiology may be complicated by anemia, thrombocytopenia, dehydration from vomiting, and the effect of adjunctive steroid therapy. Chemotherapy patients often have indwelling catheters, which predisposes them to more unusual causes of sepsis, including gram-positive bacteria and fungi<sup>56</sup> (see Chapter 143).

Septic shock refractory to volume restoration (urine output or BP remains low; lactate increases) requires vasopressor support. The primary goal of vasopressor support is to increase cardiac output and oxygen delivery to vital organs. Norepinephrine (0.5–30  $\mu$ g/min) or dopamine (5–20  $\mu$ g/kg/min) are the first-choice vasopressors for correcting hypotension in septic shock. Norepinephrine is more potent than dopamine and thus may be more effective at reversing hypotension; however, dopamine may be preferred in the setting of inadequate systolic heart function.<sup>57</sup> Dobutamine may also be used with norepinephrine to increase cardiac output and maintain adequate oxygen delivery. A recent multicenter randomized controlled trial of 330 subjects reported that, when simultaneous blood pressure and inotropic support were necessary, there is not a difference in safety or efficacy between epinephrine (0.2  $\mu$ g/kg/min starting dose) alone and norepinephrine plus dobutamine.<sup>58</sup> Many other studies of different vasopressor regimens are ongoing; however, to date there is no definitive evidence to clearly support the use of one vasopressor over another in septic shock.<sup>59</sup>

Drotrecogin alfa activated (or activated protein C), a recombinant human activated protein with anti-inflammatory, antithrombotic, and profibrinolytic properties, has been investigated in large multicenter trials for the treatment of patients with systemic inflammation and organ failure from acute infection.<sup>60</sup> The institution of activated protein C therapy is not part of the routine ED management of sepsis as there is a large window of time for treatment initiation (within 24 hours of meeting criteria). If this therapy is considered, consultation with the ICU physician who will assume care of the patient is recommended because the therapy is continued for 96 hours.

The use of corticosteroids in the treatment of sepsis and septic shock has been investigated with mixed results. The results of two large randomized controlled trials confirm that there is no role for high-dose, short-course corticosteroid therapy in septic shock.<sup>61,62</sup> Recently, two large multicenter randomized trials of low-dose hydrocortisone treatment failed to show survival benefit among all patients with septic shock.<sup>63,64</sup> One of the studies did show a survival benefit to use of low-dose hydrocortisone among patients who did not adequately respond to a corticotropin stimulation test<sup>64</sup>; however, the larger study did not find this survival benefit.<sup>63</sup> Most current guidelines recommend that low-dose hydrocortisone should only be administered to patients receiving chronic steroid replacement and in patients with refractory shock despite adequate fluid and vasopressor support, and corticotropin stimulation testing is no longer considered of value.<sup>57</sup>

## Cardiogenic Shock

The immediate treatment of cardiogenic shock focuses on improving myocardial contractility and pump function. Cardiogenic shock is traditionally defined as the combination of systemic signs of hypoperfusion with arterial systolic BP less than 90 mm Hg (or 30% below a known baseline). If the work of breathing is tiring the patient, if severe pulmonary edema is causing significant hypoxemia, or if respiratory failure is imminent, intubation and mechanical ventilation should be initiated, followed by emergent treatment of bradydysrhythmias or tachydysrhythmias and inotropic support. Barbiturates are not recommended for sedation or anxiety in the intubated patient, because they may have exaggerated negative inotropic effects. Cautious use of benzodiazepines, supplemented by fentanyl for analgesia, is the best approach. Improving perfusion often ameliorates the anxiety and restlessness that accompanies shock states. Etomidate and ketamine have the least risk for hemodynamic compromise and should be used (but in reduced doses) for intubation, accompanied by a full dose of succinylcholine. Prior to administration of vasoactive medications, if hypovolemia is present, it should be corrected by infusing crystalloid or blood products. To improve myocardial contractility, vasopressors or inotropic agents should be administered. The choice of which agent to use depends on signs and symptoms and on the systolic blood pressure (SBP). If the SBP is less than 70 mm Hg and the signs and symptoms of shock are present, norepinephrine is the agent of choice. If the SBP is between 70 and 100 mm Hg and the signs and symptoms of shock are present, dopamine should be used. However, if the SBP is 70 to 100 mm Hg and there are no signs or symptoms of shock, dobutamine is the agent of choice.<sup>3</sup> All of these agents should be started at the same doses used for septic shock. For refractory hypotension and shock, amrinone or milrinone may improve cardiac output, although no empirical evidence is available to support their routine use. Amrinone and milrinone are biperidin derivatives that increase cyclic adenosine monophosphate (cAMP) by inhibiting phosphodiesterase (complex F-III). A loading dose of 0.75 mg/kg for amrinone or 50 µg/kg for milrinone is necessary, followed by a titrated constant infusion for either drug (5–10 µg/kg/min for amrinone and 0.5 µg/kg/min for milrinone).

When pharmacologic support fails to improve indices of perfusion, the next step is to initiate intra-aortic balloon pump

counterpulsation (IABPC). This requires the facilities and personnel of a high-level ICU or coronary care unit (CCU). Controlled trials have shown IABPC to improve short-term survival, improve post-thrombolytic patency rates, and reduce stroke morbidity. IABPC increases cardiac output by a mean of 30% in refractory cardiogenic shock and can prolong survival until interventional procedures can be performed. IABPC may be contraindicated in patients with aortic insufficiency or severe peripheral vascular disease.

The dismal outcome of cardiogenic shock complicating acute myocardial infarction (MI) has been improved in recent years. Evidence suggests that emergent revascularization is not superior to medical management in reducing mortality rates in the short term; however, significant improvements in general mortality rates are seen at both 6 months and 1 year<sup>65,66</sup> (see Chapter 77). At present the management of acute MI with cardiogenic shock proceeds as follows and constitutes optimal therapy: (1) ensure adequate ventilation and oxygenation, (2) treat emergent dysrhythmias, (3) initiate vasopressor/inotropic support, (4) administer aspirin if the patient is not allergic, and (5), heparin anticoagulation and arrangement for emergent percutaneous coronary intervention.

### KEY CONCEPTS

- Circulatory shock can occur with normal arterial blood pressure, and not all patients with arterial hypotension have circulatory shock.
- A base deficit more negative than  $-4$  mEq/L or a serum lactate  $> 4.0$  mmol/L indicates the presence of widespread circulatory insufficiency in suspected shock.
- Urine output is a reliable index of vital organ perfusion in patients with suspected shock.
- Ill patients with tachycardia, a worsening base deficit, and low urine output should be diagnosed with circulatory shock.
- Use of defined physiologic endpoints to measure systemic perfusion during resuscitation (quantitative resuscitation) is a valuable approach to optimal resuscitation in ED patients with shock.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*



## PERSPECTIVE

The era of modern blood transfusion began in the early 1900s with discovery of the ABO red cell antigen system. By World War I it was known that adding citrate enabled the storage of anticoagulated blood. Blood banking in the United States began during the 1930s. Energetic pioneers such as John Lundy of the Mayo Clinic gained a wealth of clinical experience, prompting dissemination of expert-based advice, such as Lundy's recommendation that blood transfusion was appropriate when a patient's hemoglobin (Hgb) was less than 10 g/dL or when a patient lost more than 15% of circulating blood volume. These recommendations were not, however, based on rigorous controlled trials. Rapid expansion of blood banking occurred after World War II, and in subsequent decades research focused on such critical issues as prolonging the storage life of blood products, component therapy, and reducing the risk of transfusion reactions and transfusion-related infections.<sup>1,2</sup>

More recently, at a time when nearly 14 million units of packed red blood cells (PRBCs) are transfused yearly in the United States, attention has turned toward evaluating the efficacy of more restrictive transfusion policies, rethinking the overall risk-benefit ratio of blood products, and developing bloodless alternatives.<sup>1,3-7</sup>

## PATHOPHYSIOLOGIC PRINCIPLES

### Blood Banking<sup>3</sup>

Blood centers, such as those of the American Red Cross and America's Blood Centers, process more than 90% of the units collected in the United States. Traditional allogenic donation methods still predominate, but increasing use is being made of red cell apheresis technology, by which red cells are separated from the blood at the time of collection, with the rest returned to circulation. This allows collection of about two transfusable units during a single donation.

Blood collection bags contain an anticoagulant-preservative of citrate, phosphate, dextrose, and adenine (CPDA-1), ensuring a shelf life (viability of at least 70% of the RBCs 24 hours after infusion) of 35 days and hematocrit of 70 to 80% for PRBCs.<sup>8</sup> Additive solutions (Adsol, Nutricel, Optisol) provide additional nutrients, extending maximum storage to 42 days and lowering viscosity, which makes infusion easier.<sup>9,10</sup>

Storage impairs red cell function. Transfused blood delivers oxygen to the tissues less efficiently. Even though blood is

refrigerated at 1 to 6°C (usually 4°C), cell metabolism continues and changes occur (collectively referred to as the *storage lesion*). Documented alterations are numerous and include a decrease in pH and in the level of 2,3-diphosphoglycerate (2,3-DPG). In addition, the deformability of RBCs makes them, over time, more spherical and rigid, thereby increasing resistance to capillary flow. With time, many of these changes are reversed in vivo. The decrease in 2,3-DPG, for example, results in a left shift in the hemoglobin-oxygen dissociation curve (less oxygen is released at a given partial pressure of oxygen [PO<sub>2</sub>]), but the ability to synthesize 2,3-DPG is regained over the first 24 hours after transfusion.<sup>10</sup> The relationship between overall oxygen transport and oxygen delivery to tissues is complex. Depletion of S-nitrosohemoglobin during storage alters oxygen-dependent regulation of microcirculatory blood flow ("hypoxic vasodilation").<sup>11</sup> There is ongoing debate about whether and when these and other changes are clinically significant, and how they might be overcome.<sup>12-16</sup>

Additional well-established changes include cell leakage of potassium, although the amount ( $\approx 6$  mEq/U<sup>17</sup>) is readily tolerated by most otherwise healthy patients. PRBCs contain essentially no functional platelets or granulocytes.

### Blood Typing

A basic knowledge of compatibility testing allows emergency physicians to order blood bank products and services appropriately. Identified red blood cell (RBC) antigens include the ABO and related carbohydrate antigens (H, P, I, and Lewis), the 48 Rh system antigens, and more than 200 non-ABO/Rh antigens. When a clinician anticipates that transfusion might be indicated, a "type and screen" can be ordered, and a blood specimen from the patient is sent for the following tests: ABO grouping, Rh typing, and an antibody screen for unexpected (non-ABO/Rh) antibodies. Completion of these steps speeds the delivery of crossmatched blood if it is subsequently required.

ABO incompatibility results in acute hemolysis, the most serious transfusion reaction. ABO grouping requires that the recipient's red cells be tested with anti-A and anti-B serum, and that their serum be tested with A and B red cells.<sup>8</sup> Patients form antibodies at about 6 months of age against the A and B antigens they lack. Those with type AB blood form no ABO group antibodies. Patients who are type O have antibodies against both. The major clinically

significant Rh antigen is the D antigen. Rh typing can usually be determined by adding a commercial reagent (anti-D) to recipient RBCs.

The antibody screen identifies clinically significant “unexpected antibodies” in the patient’s serum. These antibodies form when a patient responds to a foreign RBC antigen, usually due to prior exposure, such as with allogenic transfusion, pregnancy, or organ transplant. The antibody screen is performed by mixing commercial RBC reagents (mixtures of red cells expressing clinically significant antigens) with the patient’s serum. The incidence of these unexpected antibodies in the general population is low (<1–2%), but a positive screen mandates further compatibility testing.<sup>10,17</sup>

The type and screen allows quicker selection of appropriate banked blood for complete crossmatch if a transfusion is ordered. Ideally, blood identical to the patient’s own ABO and Rh group is used. Local blood supplies, however, might dictate that a nonidentical, but compatible, unit be used. Patients with blood group AB, for example, can receive blood from any of the ABO groups. Men, and women beyond childbearing age, who are Rh-negative and have no preformed Rh (anti-D) antibodies may receive either Rh+ or Rh– blood. When a blood transfusion is ordered, a formal crossmatch is done by mixing recipient serum with donor RBCs as a final compatibility test prior to transfusion. This can be done using a Coombs test (with serum incubated to 37°C), or the more rapid “immediate spin crossmatch” at room temperature, which will detect only ABO incompatibility. The more thorough Coombs’ test can detect incompatibilities that were missed with the antibody screen.<sup>17</sup>

### Special Clinical Circumstances

To select the most appropriate blood product in the emergency setting, clinicians must consider the patient’s hemodynamic stability and the amount of time available to intervene.<sup>17</sup>

### Universal Donor Group O

Universal (group O) blood is used when RBCs must be given at once to hemorrhaging, unstable patients. Premenopausal females (adults and children) need group O Rh-negative blood, whereas men and all other women may receive O Rh-positive blood, which is more common. Conversely, the “universal” type for fresh frozen plasma (FFP) is type AB, since it contains no antibodies to either A or B antigens.

If the patient’s condition can be initially stabilized with crystalloid infusion, type-specific blood (using ABO and Rh testing) should be available within 15 minutes of receiving a sample of the patient’s blood.

An antibody screen and immediate spin crossmatch take approximately 45 to 60 minutes. The recipient’s serum is screened for unexpected antibodies as described earlier. An “immediate spin crossmatch” is then performed at room temperature if the antibody screen is negative.

If the antibody screen is positive, however, the antibody is identified using more elaborate procedures, and a complete crossmatch (using a Coombs test with incubated serum) is required. This process can take up to several hours.<sup>17</sup>

### Massive Transfusion

Abnormalities from massive transfusion are rarely seen during a patient’s initial resuscitation in the emergency department, but the physician should be aware of potential problems. Massive transfusion has been defined as transfusion equivalent

to the patient’s blood volume with stored RBCs within a 24-hour period.<sup>8</sup>

In addition to storage lesion problems, hypothermia can result when patients receive more than 100 mL/min of cold blood for 30 minutes. This can be prevented by warming the blood to 37°C with a blood warmer. Transiently decreased levels of ionized calcium may result from the citrate preservative. Clinical signs of hypocalcemia include circumoral tingling, skeletal muscle tremors, and QT segment prolongation. Calcium administration is guided by determination of ionized calcium levels and clinical findings.<sup>18</sup>

Dilutional thrombocytopenia may result, but platelet concentrate is not indicated unless there is evidence of microvascular bleeding. If disseminated intravascular coagulation (DIC) develops, platelet concentrate, FFP, and cryoprecipitate may be required.<sup>18</sup>

## Administration

### Legal Aspects

Before a blood product can be infused, two qualified personnel check it at the bedside to prevent a potentially fatal clerical error. This check includes recipient and unit identification, as well as confirmation of compatibility, and the expiration date.<sup>8</sup>

At times a patient may arrive from a transferring facility with typed and crossmatched blood. If the blood is administered immediately in the emergency department, the hospital blood bank is not involved and accepts no responsibility for the blood. If the blood is not used immediately and the blood bank is asked to hold the blood for the patient, it is processed and crossmatched as for other issued blood and quarantined for 24 hours. It can be sent back to the blood bank to have this done only if (1) it has been constantly maintained at a temperature between 1 and 6°C, (2) all container seals are intact, and (3) tubing segments have remained attached to the blood container.<sup>8</sup>

### Infusion Adjuncts

Urgent transfusion situations require flow rates faster than gravity can provide. An administration set with an in-line pump that is squeezed by hand is the simplest method to speed infusion. Pressure bags are also available that completely encase the blood bag and apply pressure evenly to the blood bag surface. If external pressure is anticipated, large-bore needles are recommended for venous access to prevent hemolysis.<sup>8</sup>

If only a small-gauge needle is available, the transfusion may be diluted with normal saline, but this may cause unwanted volume expansion. In elective transfusions, no significant hemolysis occurs when small-gauge needles are used and when the maximum rate of infusion is less than 100 mL/hr.<sup>8</sup>

## MANAGEMENT

### Decision-Making

When considering the use of blood component therapy, the patient’s age, severity of symptoms, cause of the deficit, underlying medical condition, ability to compensate for decreased oxygen-carrying capacity, and tissue oxygen requirements are all considered. Clinical evaluation, including appearance (pallor, diaphoresis), mentation (alert, confused), heart rate, blood pressure, and the nature of the bleeding (active,

controlled, uncontrolled), can be supplemented by laboratory evaluation of Hgb, hematocrit, platelets, and clotting functions.

A review of relevant literature underscores the difficulty of making firm recommendations. Only recently<sup>5,7,19,20</sup> have randomized controlled trials investigated the efficacy of various transfusion triggers in the critical care and surgical setting. The largest randomized trial in adult patients to date, the TRICC (Transfusion Requirements in Critical Care) trial,<sup>5</sup> demonstrated that in the critical care setting, a transfusion threshold of 7 g/dL was as safe as a threshold of 10 g/dL, although subgroup analysis generated some concern that patients with ischemic heart disease may benefit from a higher transfusion threshold.<sup>21</sup> In a large, retrospective analysis of patients hospitalized with acute myocardial infarction, anemia appeared to raise the risk of death, and transfusion for a hematocrit of 33% or less improved overall mortality rates.<sup>22</sup> It is debatable, however, whether these results can be generalized to the emergency department setting. Further research is urgently needed.<sup>1</sup> The list of known and suspected risks associated with transfusion, on the other hand, is long and growing. Recent concerns include Transfusion Related Acute Lung Injury (TRALI) and immune modulation.<sup>23</sup> As a result, recent guidelines generally recommend a “restrictive strategy” for most patients, utilizing transfusion triggers more stringent than those traditionally followed.<sup>24</sup> Recommendations for the use of FFP likewise have long been more expert-based than evidence-based.<sup>25,26</sup>

## Whole Blood

Whole blood is not as economical as component therapy, although there has recently been renewed interest in the benefits of using fresh whole blood in military field hospitals.<sup>16</sup> In the United States it is rarely used.

## Packed Red Blood Cells

PRBCs are given to improve oxygen delivery to tissues at the microvascular level. Controversies regarding efficacy were discussed earlier; absent further research, the recommendations of the American Society of Anesthesiologists seem reasonable: transfusion is rarely needed with a Hgb concentration greater than 10 g/dL and almost always needed when the Hgb is less than 6 g/dL.<sup>27</sup> Patients with a Hgb between 6 and 10 mg/dL require careful clinical judgment. Ischemic heart disease may render patients more intolerant of anemia, although more research is needed to clarify whether transfusion benefits these patients. Lastly, most emergency physicians would still transfuse a patient with ongoing hemorrhage and unstable vital signs despite adequate fluid resuscitation, and would occasionally consider withholding transfusion for Hgb levels even lower than 6 g/dL in a young, healthy, asymptomatic patient without ongoing hemorrhage.

## Artificial Oxygen Carriers

Research into both hemoglobin-based oxygen carriers and perfluorocarbon emulsions is ongoing, but as yet none are approved for general clinical use in the United States. Several problems remain unsolved. Hemoglobin-based carriers, for example, have been found to cause vasoconstriction through nitric oxide (NO) scavenging,<sup>19</sup> endothelin release, and peripheral alpha-adrenergic receptor sensitization. Perfluorocarbon emulsions require relatively high partial pressure of oxygen ( $P_{O_2}$ ) levels. When used clinically, pure oxygen is usually administered to patients.<sup>6</sup>

## Fresh Frozen Plasma

Current practice dictates that FFP be given to patients with evidence of coagulopathy (international normalized ratio [INR] >1.5–2.0) who are either actively bleeding (absolute indication) or require an invasive procedure (relative indication).<sup>28,29</sup> Most clinicians consider active bleeding to include clinically significant hemorrhage, not minor degrees of oozing. If a specific factor deficiency is identified (e.g., hemophilia), targeted replacement of that factor, if available, is more practical. FFP should not be used for volume expansion.

## Platelets

Platelet transfusion is indicated prophylactically when the count is less than 10,000/mL, and this includes a margin of safety, as it appears that hemostasis is well-maintained even at counts of 5000/mL. Platelet counts of 40,000 to 50,000/mL are sufficient to perform invasive procedures.<sup>30</sup> Platelets have traditionally been given to adults in a dose of 6 U of platelet concentrate (i.e., a “six-pack” of platelets), which typically raises the platelet count about 40,000 to 60,000/mL. This practice is not, however, evidence-based.<sup>30</sup> Because hemostasis is maintained with platelet counts as low as 5000/mL, it seems likely that smaller, more frequent platelet transfusions should be equally efficacious, but more cost-effective in hospitalized patients. This may be impractical, of course, in outpatients. An ongoing randomized trial addresses this issue by assigning patients to low-, medium-, and high-dose platelet regimens.<sup>31</sup> Lastly, if immune-mediated consumption is the cause of thrombocytopenia, transfusion is generally ineffective.

## Autotransfusion

Autotransfusion may be used in the emergency setting in the event of severe chest trauma. This strategy has numerous advantages: immediate availability, blood compatibility, elimination of patient-to-patient disease transmission, avoidance of the storage lesion, less risk of circulatory overload, and fewer direct complications (e.g., hyperkalemia, hypothermia, hypocalcemia, and metabolic acidosis). There is also greater acceptability to some patients whose religious convictions prohibit transfusions.<sup>31,33</sup> Widespread use has not occurred, however, because of the limited number of appropriate trauma patients, the training required to operate the equipment, and the time required for equipment setup.<sup>34</sup>

## Therapeutic Modalities

### Packed Red Blood Cells

In acute hemorrhage, PRBCs are used to supplement initial crystalloid replacement. In an average adult, 1 U of PRBCs increases the Hgb by about 1 g/dL or the hematocrit by about 3%.<sup>35</sup> A similar increase in pediatric patients is obtained by administering 3 mL/kg. PRBCs are run through a filter with a large-bore intravenous line with normal saline. Lactated Ringer’s solution can lead to clotting secondary to the added calcium, and hemolysis may result with a hypotonic solution. Medications should not be added to the unit or pushed through the transfusion line unless it has been thoroughly flushed. Most transfusions are given over 60 to 90 minutes (not longer than 4 hours). Unused blood should be returned promptly to the blood bank because any units unrefrigerated for more than 30 minutes are discarded.<sup>8</sup>

## Fresh Frozen Plasma

A unit of FFP typically has a volume of 200 to 250 mL, is ABO compatible, and is given through blood tubing within 2 to 6 hours of thawing.<sup>8</sup> It contains all clotting factors. One unit of activity for any coagulation factor is equal to the clotting activity found in 1 mL of FFP. It should be given in doses calculated to achieve a minimum of 30% of plasma factor concentration, traditionally calculated as 10 to 15 mL/kg of FFP. When used for the urgent reversal of warfarin anticoagulation, 5 to 8 mL/kg of FFP is considered sufficient.<sup>29</sup> Recent research, however, has questioned this,<sup>36</sup> and indicates that screening tests such as INR and activated partial thromboplastin time (aPTT) do not correlate well with clinical risk of bleeding, and large amounts of FFP (possibly as high as 30 mL/kg) may be needed to raise factor levels adequately to achieve hemostasis.<sup>37</sup> The need to correct the INR for invasive procedures such as central line placement has also been questioned.<sup>38</sup>

## Platelets

Crossmatching is unnecessary, but Rh-negative patients should receive Rh-negative platelets because there may be enough cells in the platelet concentrate to cause Rh sensitization. In adults the traditional dose has been 4 to 6 U (a “six pack” of platelets), and in children it is 1 U/10 kg body weight. As noted earlier, however, consider giving smaller, more frequent transfusions in hospitalized patients. In frequently transfused patients it is often desirable to reduce human leukocyte antigen (HLA) sensitization. The use of leukoreduced, HLA-matched, cellular products decreases the risk of HLA antibody-induced immune destruction.<sup>8</sup>

## OUTCOMES

Adverse effects of RBC transfusion can be divided into immune-mediated and non-immune-mediated categories, as well as acute, delayed, and chronic effects.

## Immune-Mediated Adverse Effects

### Acute

**Intravascular Hemolytic Transfusion Reaction.** Intravascular hemolytic transfusion reaction is the most serious transfusion reaction. It is usually the result of ABO incompatibility, most often due to error. The resulting antigen-antibody reaction leads to the intravascular destruction of transfused red cells, producing hemoglobinemia and hemoglobinuria. The onset of symptoms is immediate and may include fever, chills, headache, nausea, vomiting, a sensation of chest restriction, severe joint or low back pain, and a burning sensation at the site of the infusion.<sup>17,39</sup> Clinical effects can include hypotension, DIC, and acute tubular necrosis. Treatment includes stopping the transfusion immediately, replacing all old tubing with new, and initiating vigorous crystalloid fluid therapy. Diuretic therapy should be used to maintain urine output at 1 to 2 mL/kg/hr. Pressor agents may be needed to sustain the blood pressure and protect the kidneys. Blood and urine specimens should be sent to the laboratory, as well as the remainder of the transfusion and the blood tubing. Detecting free Hgb (blood and urine) and a positive Coombs test on post-transfusion, but not pretransfusion specimens confirms the diagnosis.<sup>17</sup>

**Febrile Transfusion Reaction.** This is the most common and least serious transfusion reaction and is defined as a 1°C temperature elevation associated with transfusion that has no other

medical explanation. Reactions are believed to result from antileukocyte antibodies, most commonly as a result of prior transfusion. Treatment is symptomatic with an analgesic-antipyretic and an antihistamine. The use of leukoreduced RBCs can decrease, but not eliminate, the risk of this reaction.<sup>10,17</sup> If a febrile reaction occurs in a first-time transfusion, it should be treated in the same way as an intravascular hemolytic reaction until proven otherwise.

**Allergic Reactions (Urticaria to Anaphylaxis).** Urticaria, or hives, may occur during a transfusion without other signs or symptoms and with no serious sequelae. It is generally attributed to an allergic, antibody-mediated response to a donor's plasma proteins. The transfusion does not need to be stopped, and treatment with an antihistamine is usually sufficient. If the patient has a known history of urticaria, the antihistamine should be administered before the transfusion. Occasionally, full anaphylaxis may be caused by an anti-immunoglobulin A (IgA) reaction to IgA in the donor's blood components. The patient is likely to have a genetic IgA deficiency and display hypotension, respiratory and gastrointestinal symptoms, but no fever. Treatment is with epinephrine and corticosteroids. Future transfusions should be with washed RBCs, and plasma products should be from other IgA-deficient individuals.<sup>10</sup>

**Transfusion-Related Acute Lung Injury.** TRALI, now considered the leading cause of transfusion-related mortality,<sup>40</sup> presents abruptly during, or within 6 hours of, the transfusion of plasma-containing blood products. These include PRBCs, FFP, platelets, and cryoprecipitate. The initial clinical presentation is that of a noncardiogenic pulmonary edema, with dyspnea, hypoxemia, and bilateral infiltrates on chest radiograph. Fever, hypotension, and transient leukopenia may also be seen. Other causes of acute lung injury should be ruled out. The underlying pathophysiologic mechanism is a subject of continuing debate and could involve multiple insults. Proposed theories include a reaction between transfused antibodies and granulocytes in the recipient, as well as the effects of biologically active factors that accumulate in stored blood such as cytokines and lipids.<sup>41</sup> One strategy suggested for reducing TRALI has been to use only male donors for plasma in order to avoid allotypic leukocyte antibodies which can occur in women as a result of prior pregnancies.<sup>42</sup>

Appropriate treatment consists of stopping the transfusion, notifying the blood bank, and providing respiratory support, which may include intubation and mechanical ventilation. It is safe to continue transfusion of blood products from a different donor, if necessary.<sup>43</sup> Complete resolution is typically seen within 48 to 96 hours. Overall prognosis is better than would be expected with many other causes of acute lung injury, with a reported mortality rate of 6% in one series.<sup>44</sup> Survivors rarely show long-term adverse effects.

### Delayed

**Extravascular Hemolytic Transfusion Reaction.** These result from a non-ABO-mediated immune reaction, most often due to an anamnestic response in a patient previously sensitized to red cell antigens by transfusion, pregnancy, or transplant. This prior exposure may result in antibody levels that are too low to detect with the antibody screen. Following repeat exposure from transfusion, however, antibody levels rise, and extravascular hemolysis occurs days to weeks later. Less commonly, primary alloimmunization can occur after transfusion. The patient may have fever, anemia, and jaundice. Symptoms are not usually severe. Rare cases of oliguria or DIC can occur, however. Because the hemolysis is extravascular, hemoglobinemia and hemoglobinuria are typically not present.<sup>10</sup> Many



cases are subclinical, but management may require monitoring of hematologic and renal labs, maintenance of urine output, and additional red cell transfusions. Care is needed for subsequent transfusions to provide antigen-negative blood, which can be discussed with the blood bank.<sup>45</sup>

**Transfusion-Associated Graft-Versus-Host Disease.** This rare, but life-threatening, complication results when transfused lymphocytes proliferate and attack the recipient. Cell-mediated immunodeficiency puts the patient at risk, as does having an HLA type that is identical between donor and recipient (most often among first-degree relatives). Symptoms, which begin 3 to 30 days following transfusion, include fever, erythematous skin rash, diarrhea, elevated liver enzymes, and pancytopenia. The only effective treatment is bone marrow transplant, and most deaths result from coagulopathy or infection. Efforts are therefore directed at prevention by using gamma irradiation of all cellular components, which renders the donor lymphocytes incapable of proliferating. The use of leukocyte-poor components is also advocated. This condition should be kept in mind when considering transfusion in anemic leukemia or lymphoma, especially in patients who have recently received chemotherapy.<sup>10</sup> Consultation with an oncologist prior to transfusion should be strongly considered in these complex cases.

## Non-Immune-Mediated Adverse Effects

### Acute

**Circulatory Overload.** Chronically anemic, normovolemic elderly patients are at greatest risk for developing congestive heart failure with the rapid infusion of blood. Taking 4 hours to infuse a unit and using diuretics (if needed) should prevent this complication.<sup>10</sup>

**Bacterial Contamination.** Bacterial contamination, most commonly with *Yersinia enterocolitica* (which grows well in cool, iron-rich environments), occurs in fewer than 1 per million units of stored RBCs, but typically results in symptoms during

the transfusion, and carries a 60% mortality rate.<sup>23</sup> Risk is higher, however, with platelets, which are stored at a higher temperature, and may occur as frequently as 1 per 1000 to 2000 U.<sup>23</sup> During or after the transfusion, the patient may develop rigors, vomiting, abdominal cramps, fever, shock, renal failure, and DIC. When a septic transfusion reaction is considered, vigorous resuscitative therapy and broad-spectrum antibiotics should be started and the transfusion stopped.<sup>10</sup>

**Other Effects.** Although infrequent, the following complications can occur secondary to multiple-unit transfusions: hypocalcemia, hyperkalemia and acidosis, hypothermia, micro-embolization, and coagulopathies. Treatment is specific to the symptom and problem.

### Chronic

**Risk of Transmission-Transmitted Viruses.** Improved techniques for selecting and testing blood donors have dramatically reduced the risk of viral transmission of disease by transfusion. The blood supply in the United States has never been safer.<sup>23</sup> Current estimates for the risk of acquiring hepatitis C and HIV from transfusion are approaching 1 in 2 million. The risk of hepatitis B infection, however, remains closer to 1 in 200,000 to 500,000.<sup>46</sup> Cytomegalovirus (CMV) can be transmitted by blood transfusion as well. Those at risk include recipients of allogeneic stem cell or solid-organ transplantation, and neonates. CMV-negative blood products should be considered in these patients.<sup>18,23</sup> Recently, West Nile virus has emerged as a risk, although one that varies considerably by geography and season (as high as 1233 per million units in one metropolitan area during the epidemic of 2002).<sup>23</sup> Transfusion-related infection with West Nile virus, however, has been virtually eliminated by the use of system-wide nucleic acid amplification testing.<sup>46</sup>

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## CHAPTER 6 Brain Resuscitation

Robert Silbergleit

### ■ PERSPECTIVE

Recognition of the dominant role of the brain in determining the quality of human life dates back to the dawn of recorded medical history. Until recently, however, medical efforts after cardiac arrest have focused exclusively on cardiac resuscitation. Recent advances in the understanding of the pathophysiologic mechanisms of brain ischemia have encouraged attention to cerebral resuscitation. This chapter reviews the pathophysiology of postischemic encephalopathy and discusses therapies for improving neurologic recovery after cardiac arrest.

### ■ PATHOPHYSIOLOGY

The human brain consists of 10 billion neurons, each with multiple connections to other cells, totaling an estimated 500 trillion synapses. Although the brain constitutes only 2% of body weight, it receives 15% of the body's cardiac output and accounts for 20% of the body's overall oxygen use because of its high metabolic activity. Although no mechanical or secretory work is performed by the brain, energy expenditures include the synthesis of cellular constituents (e.g., an estimated 2000 mitochondria are reproduced each day by each cell) and neurotransmitter substances, the axoplasmic transport of these substances, and the transmembrane pumping of ions.

When the brain is deprived of adequate blood flow, the resulting ischemia is characterized by a bewildering array of inter-related physiologic and cellular responses that ultimately result in neuronal cell death (Fig. 6-1).<sup>1,2</sup> Although this complex cascade of events can be triggered by periods of ischemia lasting only a few minutes, the resulting neuronal death is usually delayed by hours or days. Furthermore, the biology of cerebral cell death after global cerebral ischemia follows (with slight variations) the pattern of delayed cerebral cell death that follows stroke, traumatic brain injury, and other forms of hypoxic or toxic brain injury. Increased understanding of the brain's response to injury during the period between insult and neuronal cell death will eventually allow more specific brain resuscitation therapies.

### ■ MANAGEMENT

Standard management of cardiac arrest and subsequent ischemic brain damage involves restoring cerebral blood flow (CBF) and preventing secondary insult. These treatments have generally not been studied in prospective, randomized

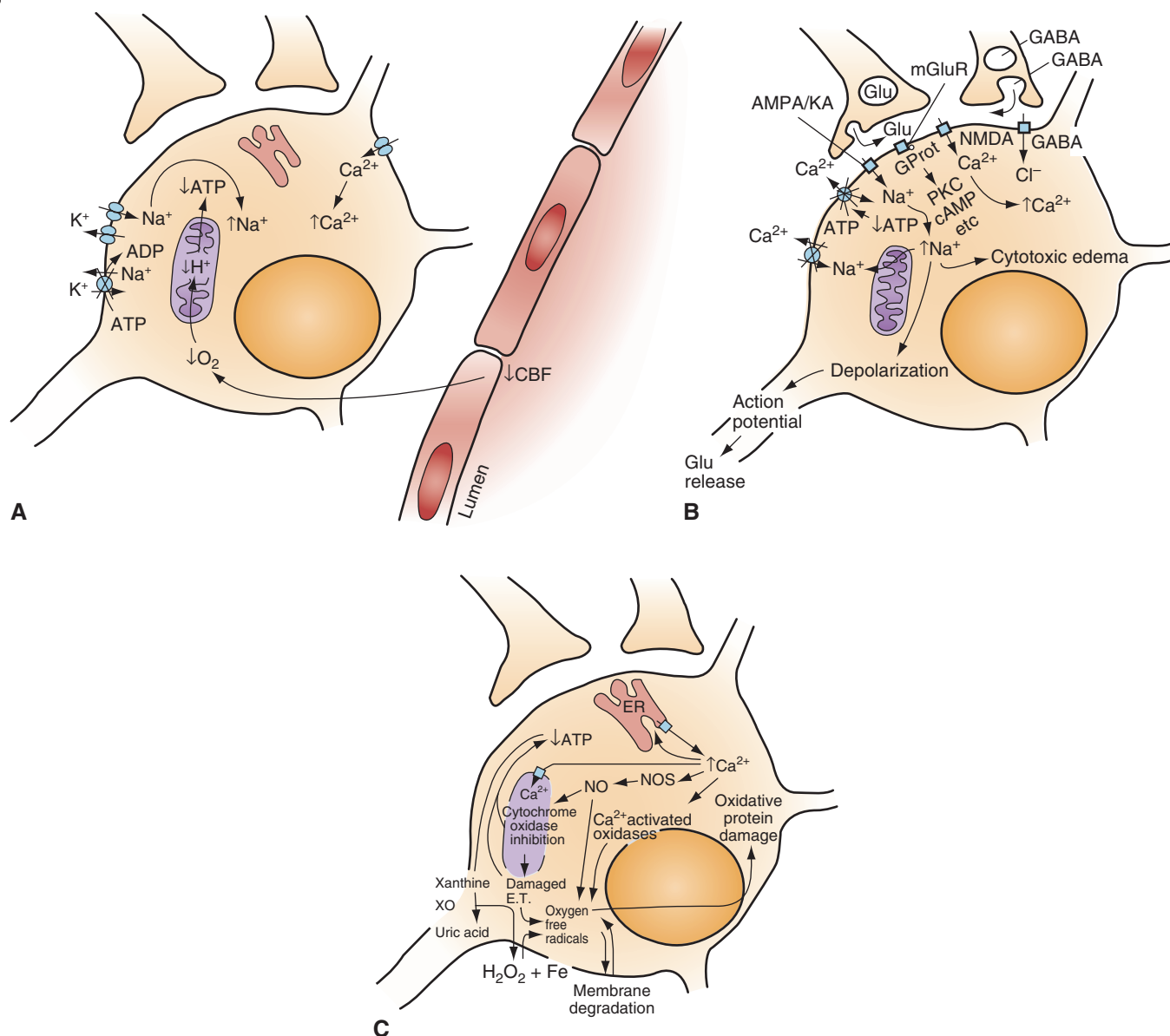
controlled trials, but are supported by clinical experience and limited experimental data. Although proposed and experimental therapies are generally aimed at specific molecular interventions in the pathophysiology of ischemic brain injuries, none of these as yet have proven effective in clinical trials.

### Standard Strategies

#### Return of Spontaneous Circulation

Cardiac resuscitation is the first priority in cerebral resuscitation. The degree of brain injury after cardiac arrest depends on both the duration of complete cerebral ischemia (the “down time,” or time before the initiation of cardiopulmonary resuscitation [CPR]) and the duration of relative ischemia that occurs during CPR and that may occur from cardiogenic shock preceding or subsequent to the period of cardiac arrest.<sup>3</sup> Extensive clinical evidence on hospital discharge rates and neurologic recovery rates supports the concept first proposed nearly 100 years ago that success in resuscitation is inversely proportional to the duration of cardiac arrest. Although duration of arrest generally predicts outcome in the population of patients with sudden cardiac death, it cannot be used reliably to predict the outcome of individual patients. The epidemiology of neurologic outcome of survivors is described in detail in the following section and is influenced by patient comorbidity and other individual characteristics. Depending on their timing and severity, low-flow states, hypotension, or hypoxia preceding cardiac arrest may provide protective preconditioning or may increase the risk of poor neurologic outcome.

The efficacy of closed-chest CPR in generating adequate cerebral perfusion is somewhat controversial. Cardiac output during optimal standard closed-chest CPR has previously been estimated to be only 20 to 30% of normal, but more recent data suggest that higher cardiac outputs are possible in clinical practice.<sup>4</sup> Experimental measurement of CBF during CPR has led to estimates ranging from 1 to 60% of prearrest CBF, depending on the experimental model and technique and on the duration of arrest.<sup>5</sup> Furthermore, the CBF achieved with standard closed-chest CPR is inversely proportional to the duration of cardiac arrest preceding the initiation of CPR.<sup>6</sup> Researchers have obtained 50% of normal (prearrest) CBF in animals when CPR was started within 2 minutes of the onset of ventricular fibrillation, but they obtained only 28% of normal CBF if the circulatory arrest persisted for 5 minutes before



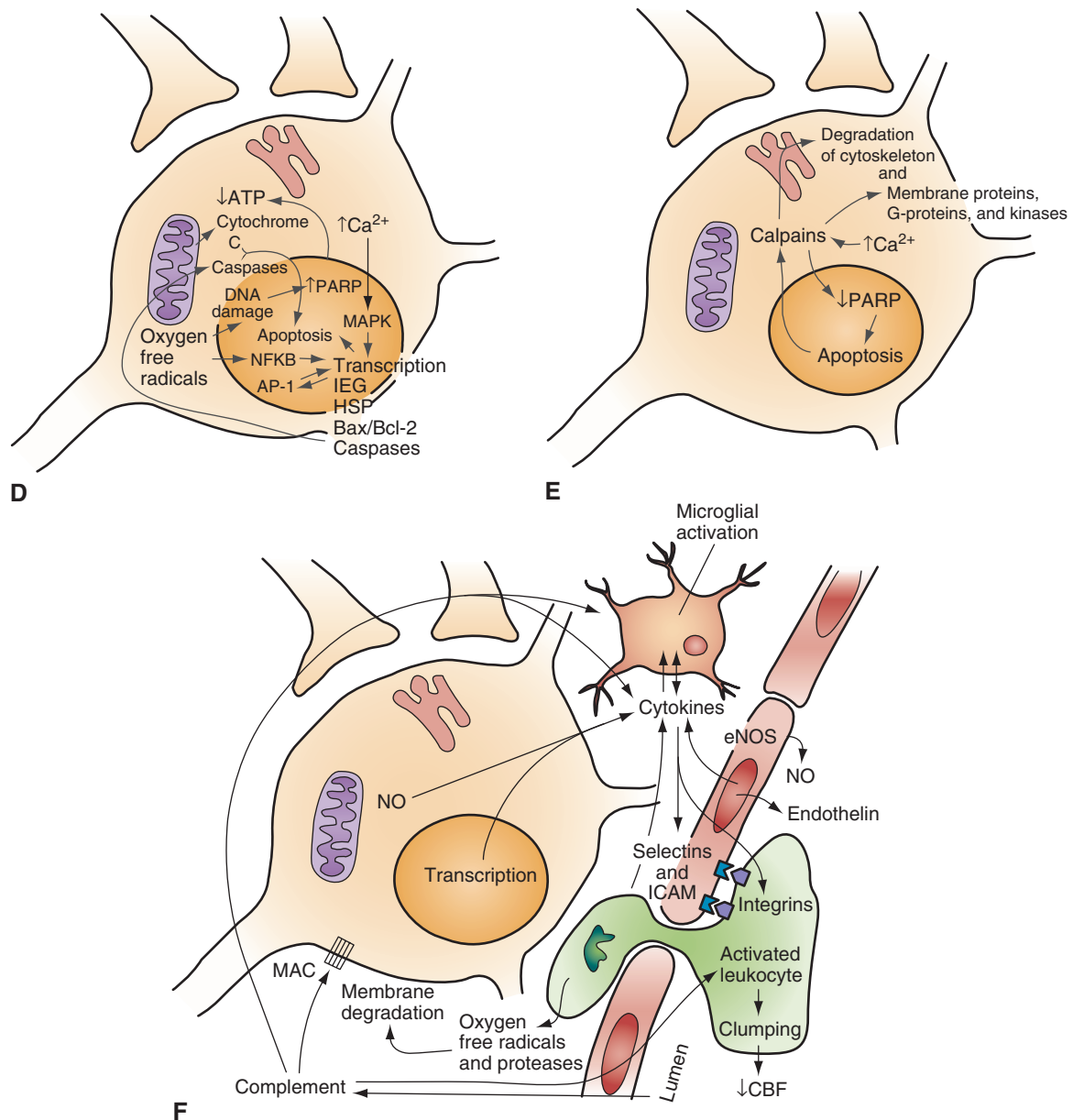
**Figure 6-1.** Synopsis of events contributing to neuron cell death cascade after ischemia. **A**, Decreased cerebral flow (CBF) and arterial oxygen content during ischemia cause decreased adenosine triphosphate (ATP) production, failure of ATP-driven ion pump efflux of potassium ions ( $K^+$ ), and influx of sodium ions ( $Na^+$ ) and calcium ions ( $Ca^{2+}$ ) through voltage-gated channels. ADP, adenosine diphosphate. **B**,  $Na^+$  influx causes depolarization and glutamate (Glu) release, opening Glu receptor  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA) and kainate (KA) channels and exacerbating intracellular  $Na^+$  overload. Increased  $Na^+$  concentration ( $[Na^+]_i$ ) leads to cytotoxic edema. Glu-mediated  $N$ -methyl-D-aspartate (NMDA) channels allow intracellular  $Ca^{2+}$  overload. Insufficient ATP causes failure of energy-dependent  $Ca^{2+}$  pumps, and high  $[Na^+]_i$  prevents removal of  $Ca^{2+}$  by  $Na^+/Ca^{2+}$  exchange pumps.  $\gamma$ -Aminobutyric acid (GABA) release can attenuate excitatory changes by opening a receptor-gated  $Cl^-$ .  $[Ca^{2+}]_i$ ,  $Ca^{2+}$  concentration; cAMP, cyclic adenosine monophosphate; PKC, protein kinase C. **C**, Increased  $[Ca^{2+}]_i$  is amplified by calcium-induced release of  $Ca^{2+}$  from the endoplasmic reticulum (ER). Mitochondria may be injured attempting to buffer increasing  $[Ca^{2+}]_i$ , resulting in further metabolic failure and diminished ATP.  $Ca^{2+}$  activates nitric oxide synthase (NOS), transforming it to nitric oxide (NO), which is amplified by NO activation of NOS. NO contributes to the formation of damaging oxygen free radicals and inhibits mitochondrial cytochrome oxidase function. ATP degradation to xanthine and then uric acid by xanthine oxidase (XO) yields hydrogen peroxide ( $H_2O_2$ ), which reacts with iron to form dangerous oxygen radicals. Oxygen free radicals react with lipids in the cell membrane, which produces membrane degradation and more free radicals. Oxygen free radicals also can damage proteins.

CPR was started. After 10 minutes of arrest, CBF was zero with standard CPR. Although some experimental work suggests that about 20% of normal CBF is necessary to maintain neuronal viability, the real issue is not the degree of biochemical, electric, or physiologic abnormality measured in animal experiments of brain ischemia, but whether functional recovery will occur. Approached from this perspective, clinical evidence overwhelmingly confirms the beneficial effects of CPR in terms of improvement in survival and neurologic recovery.<sup>7,8</sup>

Considerable effort has been directed toward the investigation of improved CPR techniques that will prove to be even more effective for longer periods (see Chapter 7).

#### Treatment of Hypotension, Hypoperfusion, and Hypoxia

Maintaining cerebral oxygen delivery after cardiac resuscitation is a mainstay of therapy. Oxygen delivery requires a sufficiently high cerebral perfusion pressure, a sufficiently low



**Figure 6-1—cont'd D,** Ca<sup>2+</sup> also activates kinase transcription factors, such as mitogen-activated protein kinase (MAPK). Oxygen radicals trigger nuclear factor  $\kappa$  B (NFKB), another transcription factor. Many genes, including immediate early genes (IEG), heat-shock protein (HSP) genes, genes for caspases, and the *Bax/Bcl-2* systems, are activated. IEG products include AP-1, another transcription factor. Mitochondrial release of cytochrome *c*, existing and newly formed caspases, and other factors trigger apoptosis. DNA is damaged by oxygen free radicals and by endonucleases formed in apoptosis. DNA damage activates poly(ADP-ribose) polymerase (PARP), which further depletes ATP stores. **E,** Ca<sup>2+</sup> and apoptosis activate calpains, proteases that degrade a variety of structural elements (e.g., cytoskeletal and membrane proteins), signaling elements (e.g., G-proteins, kinases), and PARP. **F,** Transcription and NO contribute to neuronal expression of cytokines, chemokines, and growth factors. These intercellular signals activate complement, epithelial cells, leukocytes, and microglia. Complement can amplify chemotactic signals, activate microglia directly, or cause cellular damage by creation of the membrane attack complex (MAC). Leukocyte integrins, epithelial cell selectins, and intercellular adhesion molecules (ICAM) allow demargination. Activated leukocytes cause neuronal injury by releasing potent oxidants and protease. Cerebrovascular resistance may be affected by epithelial release of NO and endothelin and by leukocyte clumping. eNOS, endothelial nitric oxide synthase.

cerebrovascular resistance (CVR), and adequate blood oxygen saturation.

Hypotension in the postarrest period can dangerously lower cerebral perfusion pressure. Although CBF is normally independent of perfusion pressure over a wide range of arterial blood pressure, such autoregulation is often lost in the injured brain. As a result, perfusion of ischemic tissue becomes passively dependent on arterial pressure, and hypotension can compromise CBF and result in significant additional brain damage.<sup>3</sup> Therefore, after return of spontaneous circulation

(ROSC), low arterial pressures should be rapidly normalized, using intravascular volume administration and vasopressors as needed. Because elevated arterial pressures may be needed to provide sufficient CBF, hypertension usually should not be treated in the postresuscitation period. Very high blood pressures may require treatment, but specific cutoffs are controversial. Generally, diastolic pressures may be allowed to run as high as 120 mm Hg without requiring treatment. In fact, hypertension is sometimes induced clinically or experimentally with vasopressors in an attempt to raise cerebral perfusion



pressure and improve neurologic recovery.<sup>9</sup> Because it is unproved, and because risks of this therapy include blood-brain barrier disruption and worsening of vasogenic edema, induced hypertension is not currently a standard therapy.

CVR after resuscitation from cardiac arrest is another determinant of CBF and may be affected by hyperventilation and microvascular patency. Although the cerebral circulation may lose its ability to adjust to blood pressure changes after ischemia, attenuated responsiveness to carbon dioxide and oxygen levels in arterial blood can still be present.<sup>10,11</sup> Carbon dioxide is a potent vasoactive agent, and lowering of the arterial carbon dioxide partial pressure ( $P_{aCO_2}$ ) by hyperventilation results in rapid reduction of CBF. Because reductions in CBF reduce total cerebral blood volume, hyperventilation may transiently abort brainstem herniation in the presence of critically elevated intracranial pressure (ICP) until osmotherapy or ventriculostomy can be initiated. When ICP is not elevated, however, the vasoconstriction and increased CVR caused by hyperventilation can cause potentially dangerous reductions in CBF. Although controversy surrounds whether increases in ICP are clinically significant after global ischemia, the measurement of ICP is generally not recommended in the management of adult cardiac arrest survivors.<sup>12</sup> Generally, ventilation to maintain a  $P_{aCO_2}$  between 35 and 40 mm Hg is safe and appropriate. CVR may also be elevated after cardiac arrest by endothelin-induced vasospasm or microvascular occlusion by leukocyte clumping or coagulation. Hemodilution, anticoagulation, and antiplatelet agents have been studied in animals for effectiveness in mitigating microvascular occlusion with mostly negative results.<sup>13</sup> Acute use of these agents to improve microcirculatory flow has not been studied in human cerebral ischemia.

Normal arterial oxygen saturation should be maintained after resuscitation from cardiac arrest. Because the injured brain may not be able to compensate for hypoxia by augmenting CBF, cerebral oxygen delivery may diminish rapidly as the oxygen content of blood decreases. Hyperoxia secondary to the use of 100% oxygen in the immediate postarrest period, however, has also been shown to increase oxidative brain injury in animal models of cardiac arrest and resuscitation.<sup>14</sup> Normoxia or mild hyperoxia ( $P_{aO_2}$  of 80–120 mm Hg) should be maintained using the lowest fraction of inspired oxygen ( $F_{iO_2}$ ) possible. The use of 100% oxygen is appropriate during cardiac arrest, but  $F_{iO_2}$  should be titrated downward shortly after the ROSC. An important clinical trial to compare earlier use of normoxia after ROSC to the more typical prolonged period of postresuscitative hyperoxia has been proposed. Because hypoxia and hypercapnia must be avoided, controlled ventilation is appropriate in the period after resuscitation, with muscle relaxation and sedation if needed.

## Maintenance of Body Temperature

Hyperthermia (or fever) exacerbates brain injury and worsens neurologic outcome.<sup>15,16</sup> Elevated body temperature increases cerebral metabolic demand by 8 to 13% per degree Celsius, escalates glutamate release, increases oxygen free radical production, and increases cytoskeletal and blood-brain barrier breakdown with increased vasogenic edema.<sup>17,18</sup> Core body temperature (usually rectal, bladder, or esophageal) should be accurately measured in patients resuscitated from cerebral ischemia.<sup>19</sup> Hyperthermia may be treated with antipyretics, circulating air or water cooling systems, or evaporative cooling using water mist and fans.<sup>19</sup> Aggressive treatment should, at a minimum, be used to prevent temperature increases in the postischemic period in all patients, and the practice of inducing therapeutic hypothermia is now emerging as a therapy for comatose survivors of cardiac arrest.

## Resuscitative Mild Hypothermia

Hypothermia was first reported more than 50 years ago to have a protective effect in global and focal brain ischemia<sup>20</sup> and ranges from mild (32–34°C) to profound (5°C). The mechanism by which hypothermia conveys protection is uncertain, but several possibilities have been suggested. Hypothermia reduces glutamate release, metabolic demand, free radical formation, and production of inflammatory cytokines.<sup>17</sup> Cell-signaling and genetic responses to cellular injury are also affected by hypothermia, and hypothermia may protect the brain from programmed neuronal cell death.<sup>21,22</sup>

Mild hypothermia is easier to achieve and has fewer adverse effects than lower temperatures, and has consistently been found to be neuroprotective in experimental cerebral ischemia.<sup>21,23</sup> Two multicenter prospective, randomized, controlled trials of mild hypothermia have now shown marked improvements in neurologic outcome in comatose survivors of out-of-hospital cardiac arrest.<sup>24,25</sup> The improvements in neurologic outcome (recovery with minimal or no neurologic deficits at hospital discharge) and in mortality in patients treated with hypothermia in these trials are shown in Table 6-1. In these trials, the number needed to treat in order to have one additional patient with a good neurologic outcome was only about seven. The 2005 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care and the International Liaison Committee on Resuscitation now recommend cooling unconscious adult patients after cardiac arrest to 33°C for 12 to 24 hours.<sup>26,27</sup> Implementation of these guidelines has been slow and represents a failure of clinical translation. Barriers to adoption and the public health impact of widespread use have been reported.<sup>28</sup>

**Table 6-1 Clinical Outcomes in Randomized Controlled Trials of Hypothermia in Comatose Survivors of Cardiac Arrest**

CLINICAL TRIAL	HYPOTHERMIA, N (%)	NORMOTHERMIA, N (%)	P VALUE
<b>HACA<sup>24</sup></b>	<i>N</i> = 137	<i>N</i> = 138	
Good Neurologic Outcome*	75 (55)	54 (39)	<0.01
Death	56 (41)	76 (55)	0.02
<b>Bernard et al.<sup>25</sup></b>	<i>N</i> = 43	<i>N</i> = 34	
Good Neurologic Outcome†	21 (49)	9 (26)	0.05
Death	22 (51)	23 (68)	0.14

\*Good neurologic outcome defined as recovery with no neurologic deficits or with moderate disability but living independently and working at least part time at 6 months.

†Good neurologic outcome defined as recovery with moderate, minimal, or no neurologic deficits at hospital discharge and discharge to home or acute rehabilitation facility.

Mild hypothermia can be induced through a variety of techniques. In both clinical trials of hypothermia after cardiac arrest, hypothermia was achieved by cooling the body surface with ice packs and cooling blankets. Surface cooling is noninvasive, and a variety of specialized devices have been developed to make it less labor intensive and faster,<sup>29,30</sup> but some difficulties inherent with surface cooling are well described.<sup>31</sup> These include slower than desired rates of cooling ( $0.3\text{--}0.6^\circ\text{C/hr} \pm \text{SD } 0.3^\circ\text{C/hr}$ ),<sup>24,25</sup> overshooting and undershooting the temperature target (SD usually  $> 1^\circ\text{C}$ ),<sup>32,33</sup> and uncontrolled rewarming with very frequent rebound hyperthermia.<sup>31</sup> Alternative core cooling methods have been investigated. A promising technique using infusions of ice cold intravenous fluids has been demonstrated and is more effective than would be expected based on the transfer of heat content alone.<sup>34</sup> Although more invasive, endovascular cooling with a heat exchange catheter provides the most rapid cooling ( $1.4\text{--}6.3^\circ\text{C/hr} \pm \text{SD } 0.3^\circ\text{C/hr}$ ) and offers the tightest control of body temperature (SD usually  $< 0.3^\circ\text{C}$ ) at the target temperature and during controlled rewarming.<sup>32,35-37</sup> Designed to induce hypothermia or maintain normothermia in surgical patients, this new type of commercially available device is placed in the inferior vena cava through a femoral introducer and cools or heats passing blood. Endovascular systems promise to be far less nursing labor-intensive than surface cooling because they monitor core temperature and are automatically controlled through a feedback loop. Although temperature control can also be achieved by extracorporeal bypass devices, this is not pragmatic in most circumstances and does not offer the same promise as simpler core cooling techniques. The optimal method of cooling patients resuscitated from cardiac arrest has not been established.

The rate of cooling needed for effective neuroprotection, the optimal duration of cooling, and the best process for rewarming after hypothermia are all unknown.<sup>38</sup> Animal experimentation and the consensus recommendations suggest that cooling should be initiated as early and as rapidly as possible.<sup>26</sup> Cooling may begin during the out-of-hospital phase of resuscitation, and may even be initiated prior to ROSC. In the positive clinical trials, hypothermia at  $33 \pm 1^\circ\text{C}$  was achieved by 2 hours<sup>25</sup> or 8 hours<sup>24</sup> after ROSC and was maintained for either 12 hours<sup>25</sup> or 24 hours.<sup>24</sup> Patients were then allowed to rewarm passively<sup>24</sup> or with a combination of passive and active rewarming.<sup>25</sup> Rebound hyperthermia is common with passive rewarming and must be avoided.<sup>31</sup> Although the clinical trials only enrolled patients resuscitated from cardiac arrest caused by ventricular fibrillation, there is clinical experience with resuscitative hypothermia in patients with cardiac arrest from other causes,<sup>39</sup> and consensus recommendations support its use in such cases.<sup>26</sup>

Cooling of comatose survivors of out-of-hospital cardiac arrest requires a multidisciplinary hospital policy, and should be initiated as early as possible. In hospitals capable of hypothermic resuscitation, cooling is optimally started in the ED and maintained in the ICU.<sup>12</sup> Regardless of cooling technique, patients cooled after cardiac arrest require pharmacologic therapy to prevent shivering because shivering effectively warms the patient. In the two clinical trials, shivering was prevented with a nondepolarizing paralytic, and sedation was maintained with midazolam with or without fentanyl.<sup>24,25</sup> When paralysis is not clinically desirable, it may be possible to sufficiently lower the shivering threshold in awake patients with meperidine, buspirone, dexmedetomidine, or a combination of these.<sup>40,41</sup> Shivering can sometimes also be reduced in a patient cooled by an endovascular catheter even when the core temperature is  $33^\circ\text{C}$  by applying a warming blanket, since surface temperature receptors control thermoregulation to a

much greater extent than core temperature receptors. Other pharmacologic treatments that may be used during induced hypothermia include antipyretics, which lower the core body temperature set point, even in normothermic patients, although to such a small degree that the effect is unlikely to be clinically relevant.<sup>42</sup> More effective pharmacologic lowering of core body temperature is, however, being investigated. Neurotensin is an endogenous neuropeptide involved in thermoregulation that can induce hypothermia and neuroprotection in experimental models of cerebral ischemia.<sup>43</sup>

Clinical trials of mild hypothermia in the resuscitation of patients with acute ischemic stroke,<sup>44</sup> and two new clinical trials of mild hypothermia in adult and pediatric patients with traumatic brain injury<sup>45</sup> are being performed and may expand the indications of this therapy in the future. Ongoing efforts to develop feasible methods of selective cooling of the brain after cardiac arrest,<sup>46,47</sup> and studies of profound systemic hypothermia are still experimental.

### Treatment of Hyperglycemia

Postischemic hyperglycemia has detrimental effects on CBF, metabolism, edema formation, and neurologic outcome. In experimental focal cerebral ischemia, profound hyperglycemia ( $>500\text{ mg/dL}$ ) causes a more pronounced decrease in intracellular pH, increases brain lactate levels, and increases neuronal loss. Increased neuronal damage from hyperglycemia in global cerebral ischemia may also be glutamate-mediated. Observational studies in patients with stroke and survivors of cardiac arrest have shown that hyperglycemia after brain ischemia is strongly associated with worse outcomes in both diabetics and nondiabetics.<sup>48,49</sup> In experimental studies, normoglycemia and mild insulin-induced hypoglycemia have been shown to improve neurologic function after focal and global ischemia. Interestingly, insulin itself may have a neuronal growth-factor-like effect that may theoretically also be neuroprotective. Thus, the best available evidence supports active treatment of hyperglycemia after global brain ischemia, and the administration of glucose should be avoided except in verified hypoglycemia.<sup>50</sup>

### Seizure Management

Seizures may result from global cerebral ischemia and may exacerbate the underlying brain injury. Seizure activity can increase brain metabolism by 300 to 400%, worsening the mismatch between oxygen delivery and demand in the post-arrest period, with greater metabolic failure and neuronal loss and worsened neurologic outcome. Although prevention of seizures has not been proved to improve neurologic recovery, seizures are clearly not desirable in the postischemic period.<sup>12</sup> The prophylactic use of anticonvulsant drugs in patients resuscitated from cardiac arrest is controversial and is not standard care, but it is generally agreed that seizures should be quickly and effectively treated. Common therapeutic agents include benzodiazepines, phenytoin, and barbiturates. Each of these anticonvulsant drugs has also been considered as specific therapy for cerebral ischemia because of the antagonism of excitatory amino acids, sodium channel blockade, or effects on cerebral metabolism. Although these drugs are of proven value as anticonvulsants, other uses in cerebral ischemia are experimental and unproved.

### Immobilization, Sedation, and Head Position

The comatose brain responds to external stimuli (e.g., physical examination, airway suctioning) with increases in cerebral

metabolism. This elevation of regional brain metabolism requires increased regional CBF at a time when the oxygen demand/perfusion ratios may be precariously balanced. Protection from afferent sensory stimuli with administration of titrated doses of sedative-anesthetic drugs and muscle relaxants may prevent oxygen supply/demand imbalance and improve the chances for neuronal recovery.

All activity that increases ICP (e.g., straining, coughing) should be restricted, and tracheal suction should be performed only when necessary and with care. There is no evidence to support the commonly recommended practice of elevating the head of the bed to reduce intracranial venous pressure, and this practice may even be harmful.<sup>51</sup> Torsion or compression of neck veins should be avoided by eliminating compressive dressings and not rotating or flexing the head.<sup>52</sup>

## ■ CLINICAL OUTCOMES

Global cerebral ischemia resulting from a period of cardiac arrest is a frequently fatal and highly morbid condition, but the prognosis for its victims is not universally poor. An increasing body of data is providing more complete and precise estimates of the functional outcomes and quality of life of survivors of cardiac arrest, and the results are better than many physicians assume.

The published experience in Olmsted County, Minnesota, between 1990 and 2000 may represent the best possible outcomes with currently available therapy.<sup>53</sup> First-responders (including police and firefighters) with automated external defibrillators in that county responded to 330 patients with cardiac arrest, 200 (61%) of whom had ventricular fibrillation at presentation. The majority of patients with ventricular fibrillation (145 patients, 44% of all arrests) survived to hospital admission, and 84 patients (25%) were discharged alive. Remarkably, among these 84 survivors, 79 (24% of all arrests) left the hospital neurologically intact.<sup>53</sup>

More typical outcomes were identified by a recent very large cohort study of outcomes in 8091 patients with cardiac arrest in Ontario, Canada.<sup>54</sup> Survival was 5.2% at hospital discharge, and was 4.0% at 1 year. The vast majority of 1-year survivors (3% of all those with cardiac arrest), however, had no or minimal neurologic deficits, and the average quality of life indices of all survivors were as good as those for patients without a history of cardiac arrest.<sup>54</sup> The Ontario experience echoes that of a Portuguese study,<sup>55</sup> but other recent data on 6240 patients from studies in the Netherlands,<sup>56</sup> Norway,<sup>57</sup> and Switzerland<sup>58</sup> all confirm a rate of survival to discharge home with minimal or no deficit of 8% in all out-of-hospital cardiac arrests. Quality of life among long-term survivors of cardiac arrest is consistently high in all of these studies, with low rates of patients in persistent vegetative states or requiring skilled nursing care. Overall, among those surviving to hospital admission, between 14 and 55% of patients will have good long-term neurologic outcomes.<sup>53,55</sup>

Despite these data, nihilism is common among physicians treating patients with cardiac arrest and ischemic brain injury. This may be due, in part, to the fact that most survivors of cardiac arrest are comatose at the time of admission and are without early prognostic findings suggesting which patients will have a favorable outcome. Although predicting the

outcome of coma is difficult, a recent meta-analysis suggests that the absence of pupillary and corneal reflexes at 24 hours and the absence of motor responses at 72 hours on physical examination are the best predictors of a poor neurologic outcome.<sup>59</sup> Nihilism is of particular concern, however, and should be avoided because of the potential for poor prognoses to be self-fulfilling.<sup>59</sup> In the near future, serum biomarkers of brain injury may identify the potential for neurologic recovery early in a patient's course and help guide therapy. Until early predictions of outcome can be accurately made, the emergency physician should consider every survivor of cardiac arrest as having a significant chance of full recovery (14–55%), and should know that bad neurologic outcomes are usually fatal rather than chronically debilitating.

## ■ SUMMARY

Rapidly expanding knowledge about the pathophysiology of postischemic brain injury has stimulated the search for effective cerebral resuscitation therapies. Newly proven therapies like resuscitative hypothermia will continue to be developed and will improve the outcomes of patients with ischemic brain injury in future years. Although experimental work suggests many potentially promising brain resuscitation therapies, attention should also be paid to determining the benefits of existing “standard” therapies.

Because of the complexity and interconnectedness of the pathophysiologic cascades that occur after global cerebral ischemia, it is likely that a multifaceted therapeutic approach or “cocktail,” rather than a single pharmacologic agent, is needed to reduce neurologic damage after cardiac arrest.

It is crucial that the emergency physician recognize that the patient resuscitated from cardiac arrest is, contrary to outward appearance, in a dynamic stage of brain injury. At present, patients must be protected from further brain injury caused by hypotension, hypoperfusion, hypoxia, hyperthermia, hyperglycemia, or seizures. Comatose survivors of out-of-hospital cardiac arrest should now also undergo resuscitative hypothermia. In the future, cerebral resuscitation may also involve other specific pharmacologic interventions to derail the process by which brain cells slowly die after ischemic brain injury.

## KEY CONCEPTS

- Neuronal injury is a dynamic process that continues for hours or days after an ischemic insult to the brain.
- Hypotension, hypoperfusion, and hypoxia must be avoided during brain resuscitation.
- Hyperthermia, hyperglycemia, and seizures should be treated promptly during brain resuscitation.
- Comatose survivors of out-of-hospital cardiac arrest should be rapidly cooled in the ED and maintained at 33°C in an ICU setting for 12 to 24 hours after resuscitation.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

# CHAPTER 7 Adult Resuscitation

Kevin R. Ward and Robert W. Neumar

## ■ PERSPECTIVE

### Epidemiology

It is estimated that between 77,000 and 174,000 patients are treated for out-of-hospital cardiac arrest each year in the United States.<sup>1</sup> The incidence of ventricular fibrillation as the initial rhythm has declined over time and is now estimated to be between 20 and 38%.<sup>1</sup> Epidemiologic data from studies of out-of-hospital cardiac arrest show a wide range of outcomes. Return of spontaneous circulation (ROSC) that takes long enough to result in hospital admission ranges from 9 to 65%, whereas only 1 to 31% (median 6.4%) of patients survive to hospital discharge.<sup>1,2</sup> Of patients surviving to hospital discharge, one third have persistent neurologic deficits, and less than half return to prearrest function. In patients meeting the inclusion criteria of clinical hypothermia trials, favorable outcome was reported in approximately 50% of cardiac arrest survivors who were admitted comatose and treated with hypothermia.<sup>3,4</sup>

## ■ PRINCIPLES OF DISEASE

### Etiology

Understanding the causes of cardiac arrest directs therapy and diagnostic testing during resuscitation and in the immediate postarrest period (Table 7-1). Cardiac arrest from a primary cardiac origin typically presents as ventricular fibrillation (VF) or less often as pulseless ventricular tachycardia (VT). Coronary artery disease is the most common pathologic condition found in patients who die suddenly from VF; autopsy studies show a 75% incidence of previous myocardial infarction (MI) and a 20 to 30% incidence of acute MI.<sup>5</sup> Other anatomic abnormalities associated with sudden cardiac death caused by VF or VT include myocardial hypertrophy, cardiomyopathy, and specific structural abnormalities. Pulseless electrical activity (PEA) and asystole are less common initial presenting rhythms in patients with a cardiac cause of arrest. These rhythms most often occur as a deterioration of VF or VT or develop in response to resuscitation treatments, such as defibrillation.

Primary respiratory failure generally causes initial hypertension and tachycardia, followed by hypotension and bradycardia and progressing to PEA, VF, or asystole. Circulatory obstruction (e.g., tension pneumothorax, pericardial tamponade) and hypovolemia generally present with initial tachycardia and

hypotension, progressing through bradycardia to PEA, but also may deteriorate to VF or asystole.

The most common metabolic cause of cardiac arrest is *hyperkalemia*, which is seen most frequently in patients with renal failure. Hyperkalemia results in progressive widening of the QRS complex, which can deteriorate to VT, VF, asystole, or PEA. Other electrolyte abnormalities (e.g., hypomagnesemia, hypermagnesemia, hypokalemia) may lead to significant dysrhythmias, but the frequency with which they cause cardiac arrest is not documented.

Cardiac arrest from drug toxicity has specific characteristics depending on the drug involved. Specific therapy directed at drug toxicity is essential but may not be immediately effective. Prolonged resuscitation efforts may be needed using a method that provides adequate perfusion.

Electrocution causes cardiac arrest through primary dysrhythmias or apnea. Alternating current in the range of 100 mA to 1 A generally causes VF, whereas currents greater than 10 A can cause ventricular asystole. Lightning produces a massive direct current electrocution that can result in asystole and prolonged apnea.

Hypothermia-induced cardiac arrest can present with any electrocardiogram (ECG) rhythm, and successful resuscitation depends on rapid rewarming, which often requires aggressive and invasive measures (e.g., peritoneal lavage, cardiopulmonary bypass [CPB], open-chest cardiac massage [OCCM]). Drowning is a form of asphyxia usually resulting in bradysystolic arrest. Because drowning often is accompanied by hypothermia, the victim may benefit from prolonged resuscitation efforts similar to resuscitation efforts for hypothermia.

## ■ CLINICAL FEATURES AND MANAGEMENT

Most cardiac arrest cases managed in the emergency department (ED) initially occur outside the hospital. An increasing number of first responders, nontraditional providers, and public venues are being equipped with automated defibrillators. Dramatic resuscitation rates have been achieved when these programs enable providers to deliver countershock within less than 4 to 5 minutes of arrest onset.<sup>6-9</sup> Programs that fail to enable a significant number of patients to be defibrillated within this critical time window have limited or no effect on survival.<sup>10,11</sup>

Advanced life support (ALS) units staffed by paramedics often have standing orders to follow advanced protocols. Because quality of cardiopulmonary resuscitation (CPR) and



Table 7-1

## Common Causes of Nontraumatic Cardiac Arrest

GENERAL	SPECIFIC	DISEASE/AGENT
Cardiac		Coronary artery disease Cardiomyopathies Structural abnormalities Valve dysfunction
Respiratory	Hypoventilation	CNS dysfunction Neuromuscular disease Toxic and metabolic encephalopathies
	Upper airway obstruction	CNS dysfunction Foreign body Infection Trauma Neoplasm
	Pulmonary dysfunction	Asthma, COPD Pulmonary edema Pulmonary embolus Pneumonia
Circulatory	Mechanical obstruction	Tension pneumothorax Pericardial tamponade Pulmonary embolus
	Hypovolemia	Hemorrhage
	Vascular tone	Sepsis Neurogenic
Metabolic	Electrolyte abnormalities	Hypokalemia or hyperkalemia Hypermagnesemia Hypomagnesemia Hypocalcemia
Toxic	Prescription medications	Antidysrhythmics Digitalis beta-blockers Calcium channel blockers Tricyclic antidepressants
	Drugs of abuse	Cocaine Heroin
	Toxins	Carbon monoxide Cyanide
Environmental		Lightning Electrocution Hypothermia or hyperthermia Drowning/near-drowning

CNS, central nervous system; COPD, chronic obstructive pulmonary disease.

time to defibrillation are the two most important determinants of outcome, there is no evidence to support interrupting properly performed advanced measures to transport a patient who is still in cardiac arrest. In cases of cardiac arrest refractory to properly performed advanced measures, the patient may be pronounced dead at the scene if appropriate protocols have been outlined within the system.<sup>12</sup>

Simultaneous assessment and management of cardiac arrest must occur in an orchestrated effort by a health care team led by an emergency physician who can make the ongoing assessment and monitor the efficacy and response to therapeutic interventions. It is often difficult or impossible to determine the cause of cardiac arrest at presentation. Although a differential diagnosis can be formulated based on history, physical examination, and ECG rhythm on arrival, key information often is not available or is unreliable.<sup>13</sup> The differential diagnosis potentially can be narrowed by the patient's age, underlying diseases, and medications.

## History and Physical Examination

Historical information from the family, bystanders, and emergency medical services (EMS) personnel provides key information regarding cause and prognosis. Information surrounding the event includes whether the arrest was witnessed, the time of arrest, what the patient was doing (e.g., eating, exercising, trauma), the possibility of drug ingestion, time of initial CPR, initial ECG rhythm, and interventions by EMS providers. Important past medical history includes baseline health and mental status; previous heart, lung, renal, or malignant disease; hemorrhage; infection; and risk factors for coronary artery disease and pulmonary embolism. The patient's current medications and allergies also should be obtained, if possible.

Physical examination of a cardiac arrest patient is necessarily focused on a few key goals: (1) ensure adequacy of airway maintenance and ventilation, (2) confirm the diagnosis of cardiac arrest, (3) find evidence of cause, and (4) monitor for complications of therapeutic interventions. This examination must occur in descending order of importance, simultaneous with therapeutic interventions, and must be repeated frequently to assess for response to therapy and occurrence of complications (Table 7-2).

*Cardiopulmonary arrest* is defined by the triad of unconsciousness, apnea, and pulselessness. The pulse must be palpated for in a large artery (carotid or femoral). If any question exists as to the diagnosis of pulselessness, CPR should be initiated and pulselessness confirmed by such methods as handheld vascular Doppler ultrasound or end-tidal carbon dioxide monitoring. Rapid bedside ultrasound may confirm loss of cardiac activity, but CPR should not be interrupted to determine this, except in the very late phases of the resuscitation, when termination of resuscitative efforts is contemplated. With sudden onset of circulatory arrest, as in VF, loss of consciousness occurs within 15 seconds, although agonal gasping respirations may persist for several minutes. A brief seizure may result from cessation of cerebral blood flow. Primary respiratory arrest results in transient tachycardia and hypertension that progress to loss of consciousness, bradycardia, and pulselessness, usually within 5 minutes.

After the initial minutes of cardiac arrest, physical examination may provide little evidence of the duration of arrest. Pupils dilate within 1 minute but constrict if CPR is initiated immediately and performed effectively. Dependent lividity and rigor mortis develop after hours of cardiac arrest. Temperature is an unreliable predictor of duration of cardiac arrest because it does not decrease significantly during the first hours of arrest. Moderate to severe hypothermia may cause cardiac arrest or may be caused by prolonged arrest, with opposite prognostic implications.

## Monitoring

Traditional monitoring during CPR has relied on evaluation of the ECG in one or more leads and palpation of carotid or femoral artery pulses. Although the lack of a palpable pulse during CPR may indicate inadequate forward flow, the degree of forward flow cannot be estimated accurately in the presence of a palpable pulse because pressures generated during CPR may be transmitted equally to the venous and the arterial vasculatures. In addition, myocardial blood flow does not depend on the palpated arterial systolic pressure, but rather on the difference between aortic diastolic pressure and right atrial diastolic pressure (coronary perfusion pressure). ECG monitoring during cardiac arrest indicates the presence or absence of electrical but not mechanical activity. Although these two monitoring modalities may be the best attainable in

**Table 7-2 Physical Examination Findings Indicating Potential Cause of Cardiac Arrest and Complications of Therapy**

PHYSICAL EXAMINATION	ABNORMALITIES	POTENTIAL CAUSES
General	Pallor Cold	Hemorrhage Hypothermia
Airway	Secretions, vomitus, or blood  Resistance to positive-pressure ventilation	Aspiration Airway obstruction Tension pneumothorax Airway obstruction Bronchospasm
Neck	Jugular venous distention	Tension pneumothorax Cardiac tamponade Pulmonary embolus
Chest	Tracheal deviation	Tension pneumothorax
Lungs	Median sternotomy scar Unilateral breath sounds  Distant or no breath sounds or no chest expansion  Wheezing  Rales	Underlying cardiac disease Tension pneumothorax Right main stem intubation Aspiration Esophageal intubation Airway obstruction Severe bronchospasm Aspiration Bronchospasm Pulmonary edema Aspiration Pulmonary edema Pneumonia
Heart	Audible heart tones	Hypovolemia Cardiac tamponade Tension pneumothorax Pulmonary embolus
Abdomen	Distended and dull Distended, tympanic	Ruptured abdominal aortic aneurysm or ruptured ectopic pregnancy Esophageal intubation Gastric insufflation
Rectal	Blood, melena	Gastrointestinal hemorrhage
Extremities	Asymmetrical pulses Arteriovenous shunt or fistula	Aortic dissection Hyperkalemia
Skin	Needle tracks or abscesses Burns	Intravenous drug abuse Smoke inhalation Electrocution

certain circumstances, they do not provide reliable information regarding the effectiveness of CPR and interventions or prognosis.

Unfortunately, no ideal monitoring technique provides all the information that might be desired during resuscitation, and even the modalities discussed next are often difficult or impossible to establish or interpret during CPR. A brief overview is provided of coronary perfusion pressure (CPP), end-tidal carbon dioxide (ETCO<sub>2</sub>), and central venous oxygen saturation (ScvO<sub>2</sub>) monitoring, which if available can be used to detect inadequate CPR with high specificity (Table 7-3). In addition, several of these techniques are useful in the immediate post-arrest period.

### Arterial Blood Pressure and Coronary Perfusion Pressure

Successful resuscitation of the arrested heart depends on generating adequate CPP during CPR, which has been directly correlated with myocardial blood flow.<sup>14</sup> Animal and human studies indicate that a minimum CPP of 15 mm Hg is necessary to achieve ROSC if initial defibrillation attempts have failed.<sup>14,15</sup> Unfortunately, CPP monitoring is rarely feasible in ED resuscitations of cardiac arrest patients, because it requires

**Table 7-3 Indicators of Inadequate Blood Flow During Cardiopulmonary Resuscitation**

MONITORING TECHNIQUE	INDICATOR
Carotid or femoral pulse	Not palpable
CPP	<15 mm Hg
ETCO <sub>2</sub>	<10 mm Hg (before vasopressor)
ScvO <sub>2</sub>	<40%

CPP, coronary perfusion pressure; ETCO<sub>2</sub>, end-tidal carbon dioxide partial pressure; ScvO<sub>2</sub>, central venous oxygen saturation.

both an indwelling arterial pressure catheter and a central venous catheter, both transduced properly to provide simultaneous readings.

Invasive arterial blood pressure monitoring alone also may be helpful, but again, establishment of an indwelling arterial pressure catheter often is not feasible during cardiac arrest resuscitation in the ED. Studies have indicated that achievement of an arterial diastolic pressure of 40 mm Hg is highly predictive of ROSC and this relates to the CPP achieved at

such a diastolic pressure.<sup>16</sup> Invasive, arterial pressure monitoring during CPR may also be useful to facilitate distinguishing electromechanical dissociation (EMD) from pseudo-EMD, provide immediate confirmation of ROSC, and assist in serial arterial blood gas monitoring. Although arterial and central venous catheters are most often placed in the postresuscitation phase of care, a significant number of patients initially achieving ROSC will rearrest in the ED, making these modalities helpful at this time in the patient's subsequent resuscitation.

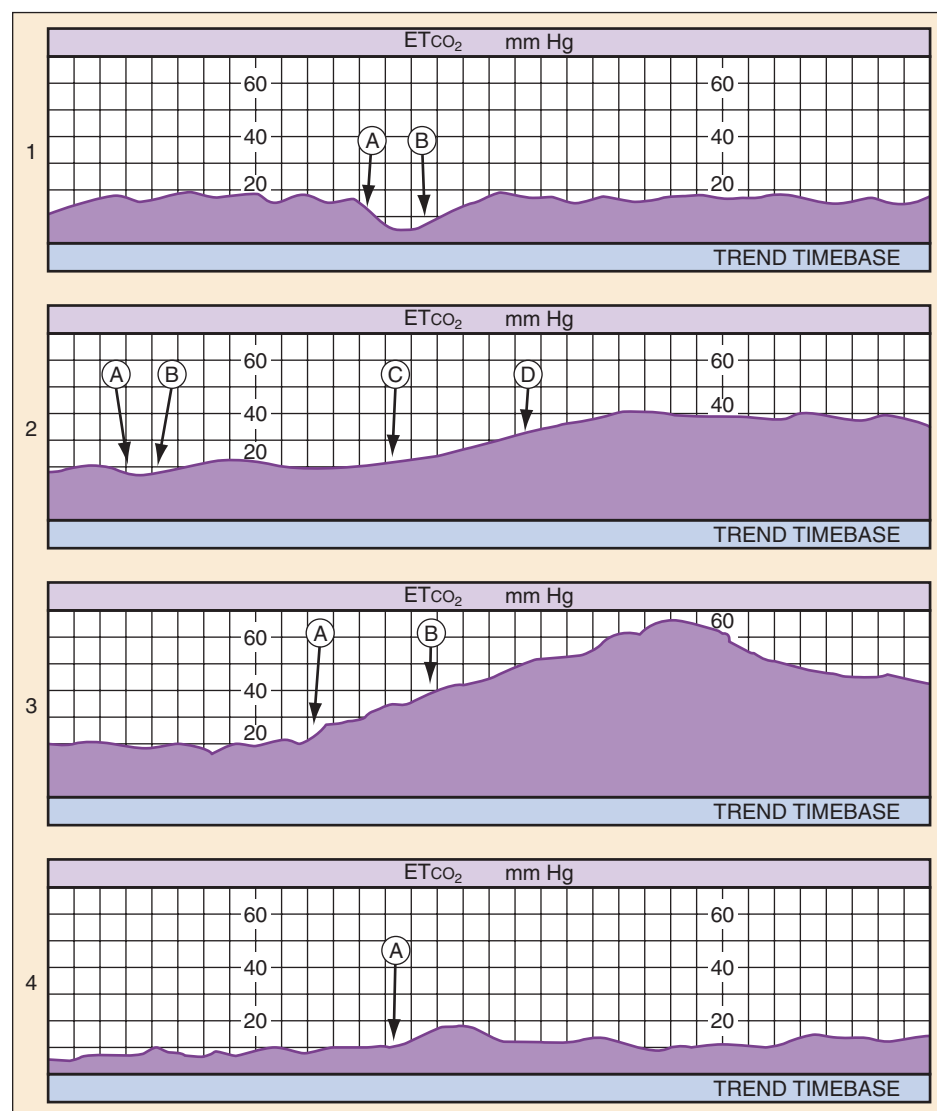
### End-tidal Carbon Dioxide

Experimental and clinical studies have shown that  $ETCO_2$  is a reliable indicator of cardiac output during CPR, but this depends on achieving several conditions during CPR in the out-of-hospital setting or in the ED.  $ETCO_2$  depends on  $CO_2$  production, alveolar ventilation, and pulmonary blood flow (i.e., cardiac output). If ventilation and  $CO_2$  production are held constant, an increase or decrease in  $ETCO_2$  reflects an increase or decrease in cardiac output, respectively. Although  $CO_2$  production during cardiac arrest and CPR probably is not constant, small changes in  $CO_2$  production are not likely to cause appreciable changes in  $ETCO_2$  because of the extremely high mixed-venous  $CO_2$  levels and large dead space created by cardiac arrest and CPR. Administration of sodium bicarbon-

ate ( $NaHCO_3$ ) during CPR may cause a sudden large increase in mixed-venous  $CO_2$ , however, which may produce a variable but transient increase in  $ETCO_2$ . Otherwise, with minute ventilation held constant (a desirable but often unmet goal,) only increased cardiac output during CPR and ROSC significantly increases  $ETCO_2$ .

In addition to correlations with cardiac output, animal and human studies show that  $ETCO_2$  correlates with CPP and cerebral perfusion pressure during CPR.<sup>17,18</sup> This correlation would be predicted based on the known relationship between mean arterial pressure and cardiac output when peripheral vascular resistance (PVR) is constant. With dramatic increases in PVR, however, as may occur with high-dose vasopressor therapy, cardiac output and  $ETCO_2$  may decrease despite increased CPP.

$ETCO_2$  has the potential to guide adjustments in compression force and rate, maximize forward flow, and to detect CPR provider fatigue (Fig. 7-1).<sup>19</sup> Resuscitation after cardiac arrest is likely to fail if  $ETCO_2$  values are less than 10 mm Hg.<sup>20,21</sup> In the absence of high-dose vasopressor therapy,  $ETCO_2$  values less than 10 mm Hg should prompt the clinician to enhance the quality of CPR (either rate or force of compression) or consider more invasive maneuvers such as OCCM if the situation warrants and a good neurologic outcome is believed to be possible.



**Figure 7-1.** Capnogram tracings of end-tidal carbon dioxide pressure ( $ETCO_2$ ) during human cardiopulmonary resuscitation (CPR). **1,** Effect of rescuer fatigue is shown at point A. Point B shows the effect of changing to a fresh rescuer. **2,** Patient with pseudoelectromechanical dissociation. At point A, the patient is pulseless but has a persistent  $ETCO_2$  value of 20 mm Hg without CPR; at point B, CPR is restarted; at point C, dopamine infusion is started; and at point D, CPR is stopped, and a pulse is palpated. **3,** Sudden increase in  $ETCO_2$  (point A) heralds the return of spontaneous circulation; pulses are palpated at point B. **4,** Point A shows a transient increase in  $ETCO_2$  such as occurs during bolus administration of sodium

ETCO<sub>2</sub> monitoring also can aid in the diagnosis and treatment of PEA. Patients in a state of pseudo-EMD (cardiac contraction that does not generate a pulse) may have pulsatile flow that simply cannot be detected by palpation of a pulse. In such circumstances, ETCO<sub>2</sub> levels may be elevated even without compressions. If, for example, the ETCO<sub>2</sub> is 10 mm Hg without compressions, consideration should be given to the possibility the patient has spontaneous circulation but is profoundly hypotensive. In such cases, volume expansion or the use of vasopressors should be considered. ETCO<sub>2</sub> monitoring also is useful in rapidly detecting success of tension pneumothorax decompression, pericardiocentesis for pericardial tamponade, and fluid resuscitation for hypovolemia. ROSC causes immediate and significant increases in ETCO<sub>2</sub> before detection of a pulse by palpation. With the use of ETCO<sub>2</sub> monitoring, interruption of CPR is never necessary except to look for changes in the patient's rhythm.

Finally, ETCO<sub>2</sub> monitoring is valuable in patients after cardiac arrest to detect sudden hemodynamic deterioration. Undetectable ETCO<sub>2</sub> during CPR indicates failure to intubate the trachea, massive pulmonary embolism, or inadequate chest compressions. Undetectable ETCO<sub>2</sub>, even after prolonged cardiac arrest, cannot be attributed to cessation of CO<sub>2</sub> production.

### Central Venous Oxygen Saturation

Scvo<sub>2</sub>, when available, provides an additional method to monitor adequacy of resuscitative measures.<sup>22</sup> The mixed-venous blood oxygen saturation in the pulmonary artery (Svo<sub>2</sub>) represents the oxygen remaining in the blood after systemic extraction. Studies have shown a close correlation between Scvo<sub>2</sub> and Svo<sub>2</sub> during CPR.<sup>23</sup> Because oxygen consumption remains relatively constant during CPR, as does arterial oxygen saturation (Sao<sub>2</sub>) and hemoglobin, changes in Scvo<sub>2</sub> reflect changes in oxygen delivery by means of changes in cardiac output.

Although used primarily in the ICU setting, multilumen oximetric Scvo<sub>2</sub> catheters are placed in the same manner as regular central venous catheters and can be used to monitor Scvo<sub>2</sub> continuously in real time. Scvo<sub>2</sub> values normally range from 60 to 80%. During cardiac arrest and CPR, these values range from 25 to 35%, indicating the inadequacy of blood flow produced during CPR. Failure to achieve a Scvo<sub>2</sub> of 40% or greater has a negative predictive value for ROSC of almost 100%.<sup>22</sup> Scvo<sub>2</sub> also helps to rapidly detect ROSC without interruption of chest compressions. Scvo<sub>2</sub> monitoring also is useful in the postarrest period to help titrate therapy and recognize any sudden deterioration in the patient's clinical condition.

### Echocardiography

The main usefulness of echocardiography is diagnostic, especially in patients with PEA. Echocardiography distinguishes EMD from pseudo-EMD. It also may be helpful in diagnosing mechanical causes of PEA, such as tension pneumothorax, pericardial tamponade, and pulmonary embolism. Echocardiography also is useful in guiding pericardiocentesis. In the postarrest period, echocardiography could prove to be valuable in determining the need for postarrest cardiac intervention or mechanical assistance of the failing heart.

### Laboratory Testing

Intermittent arterial and venous blood sampling for gas or chemistry analysis is of limited utility during CPR. Typical

blood gas findings during CPR are venous respiratory acidosis and arterial respiratory alkalosis. Sao<sub>2</sub> is usually greater than 94% during CPR and of little value in titrating resuscitation therapy except in the case of massive pulmonary embolism or unrecognized esophageal intubation. Although Scvo<sub>2</sub> indicates adequacy of CPR, a single measurement may not be as useful as continuous oximetric Scvo<sub>2</sub> monitoring.

Other laboratory studies during CPR serve more to confirm a diagnosis rather than guide therapy because results are usually available too late to make a difference. Serum electrolytes may be ordered to rule out hyperkalemia, hypokalemia, hypomagnesemia, hypercalcemia, and hypocalcemia; however, empiric therapy should be initiated immediately if a high clinical probability exists. Hemoglobin levels may indicate hemorrhage, but initial hemoglobin may be normal even in acute exsanguinating hemorrhage.

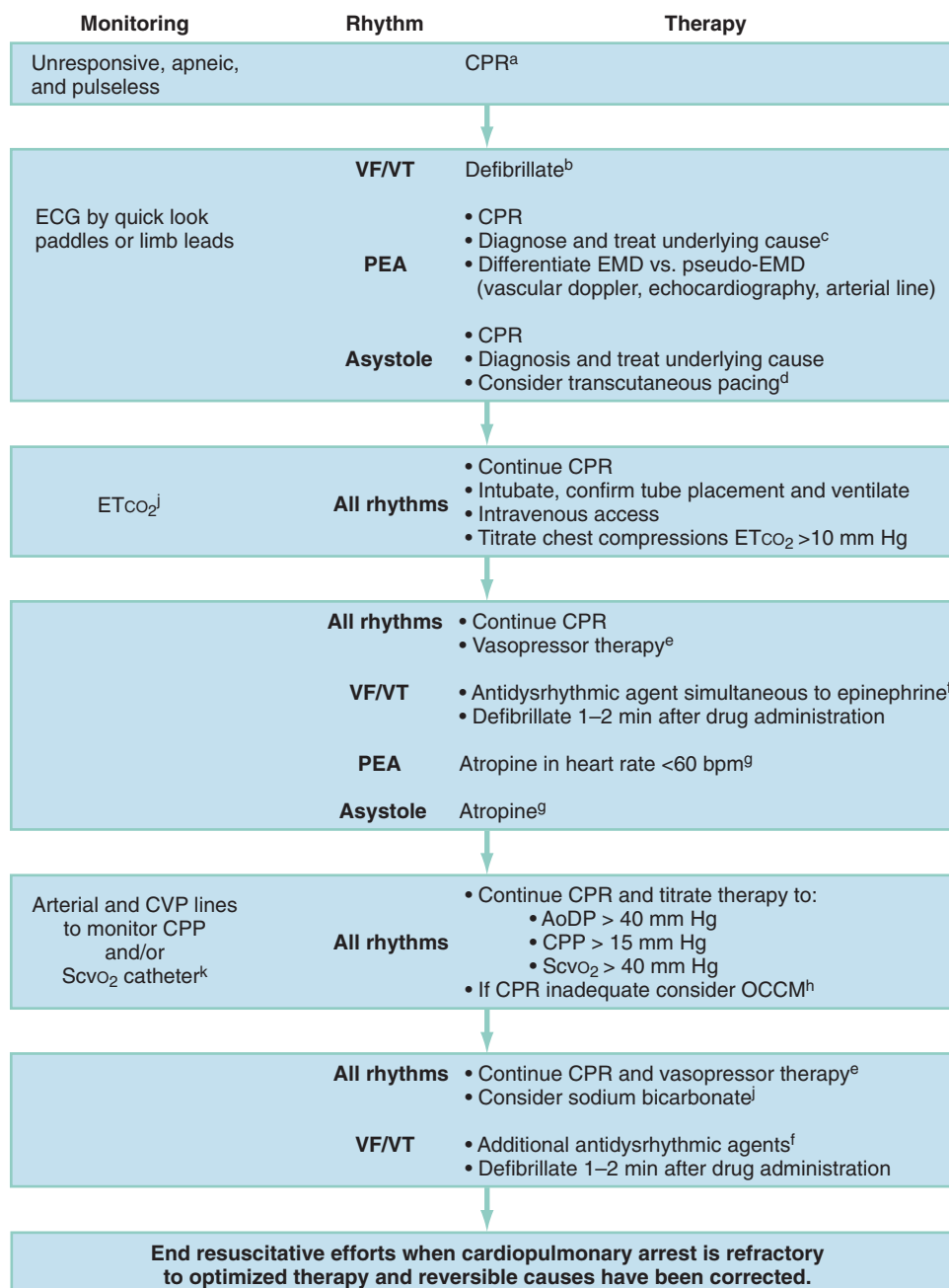
### Resuscitation

Restoration of adequate cardiac function is the defining factor of ROSC, but restoration of normal brain function is the defining factor of successful resuscitation. The likelihood of achieving both of these goals decreases with every minute the patient remains in cardiac arrest. Although many interventions are specific to the presenting ECG rhythm, most therapeutic modalities and monitoring techniques are used in all rhythms, making separate algorithms redundant. In addition, a patient rarely remains in one ECG rhythm during the course of prolonged resuscitation.

Interventions must be performed rapidly and efficiently to maximize the chances of a good neurologic outcome. The quality of CPR is perhaps the most underappreciated component of the resuscitation effort.<sup>24</sup> Important quality performance measures include compression rate (at least 100 per minute), compression depth (4–5 cm), duty cycle (50% of time in compression), full relaxation, and minimum pauses especially before and after defibrillation.<sup>25</sup> Furthermore hyperventilation has been shown to be common and reduces cardiac output during CPR.<sup>26,27</sup> A 30:2 compression-to-ventilation ratio is currently recommended for health care professionals in all adult resuscitation scenarios.<sup>25</sup> Although recent evidence suggests chest-compression-only CPR is effective when performed by bystanders in the out-of-hospital setting, there is inadequate evidence to recommend this as an alternative strategy for health care professionals, except when inadequate personnel are present to provide compressions, ventilation, and other resuscitative activities.<sup>28</sup> Intubation should be performed only when capable personnel are available and without interruption of chest compressions. Use of supraglottic airway adjuncts such as the esophageal tracheal Combitube and laryngeal mask airways may be good alternatives for airway management in the out-of-hospital phase of resuscitation with the main disadvantage being the inability to use the trachea as a route of drug administration. In addition to monitoring specific CPR performance parameters, physiologic monitoring, if available, can help optimize CPR quality for the individual patient (see [Table 7-3](#)). If the inadequacy of CPR is recognized early in the resuscitation despite optimized therapy, the physician in charge may consider more invasive measures such as OCCM if ROSC and a good neurologic outcome are possible. After prolonged arrest, however, clear indications that CPR is inadequate (based on appropriate monitoring techniques) should prompt cessation of resuscitation efforts. [Figure 7-2](#) is an algorithm for management of cardiac arrest. Interventions specific to each rhythm are discussed in the following sections.



# EMERGENCY DEPARTMENT ALGORITHM FOR TREATMENT OF CARDIAC ARREST



**Figure 7-2.** Emergency treatment algorithm for treatment of cardiac arrest. <sup>a</sup>If arrest is witnessed and known to be of short duration, immediate rhythm assessment and defibrillation or ventricular fibrillation/ventricular tachycardia (VF/VT) precede cardiopulmonary resuscitation (CPR). In cases of prolonged untreated VF/VT, 1 to 2 minutes of CPR before defibrillation may enhance the ability to achieve return of spontaneous circulation. EMD, electromechanical dissociation; PEA, pulseless electrical activity. <sup>b</sup>Consider using biphasic defibrillation (120–150 J) vs. monophasic defibrillation (360 J). <sup>c</sup>See Table 7-4. <sup>d</sup>Generally ineffective unless initiated immediately after onset of asystole. <sup>e</sup>Epinephrine, initial dose of 1 mg intravenous (IV) or intraosseous (IO) or 2.5 mg by endotracheal tube (ETT). Repeat every 3 to 5 minutes. Subsequent doses may be increased up to 0.1 mg/kg. An alternative to epinephrine is vasopressin, 40 U IV push. Vasopressin is potentially more effective if the presenting rhythm is asystole. The dose (40 U) can be repeated once in 3 minutes, followed by administration of epinephrine every 3 to 5 minutes. <sup>f</sup>Amiodarone, 300 mg IV push followed by 150 mg every 30 minutes. Alternative antidysrhythmics include lidocaine and bretylium. Magnesium sulfate, 1 to 2 g IV push in torsades de pointes or known hypomagnesemia. <sup>g</sup>Atropine, 1 mg IV push or 2.5 mg by ETT. Repeat dose every 3 to 5 minutes to a total dose of 0.04 mg/kg. <sup>h</sup>Open chest cardiac massage (OCCM) should be considered if (1) there are clear indications of inadequate blood flow during standard CPR, (2) duration of arrest is less than 20 minutes, and (3) the clinician judges that a potential exists for good neurologic outcome. AoDP, aortic diastolic pressure; CPP, coronary perfusion pressure; CVP, central venous pressure; ScvO<sub>2</sub>, central venous oxygen saturation. <sup>i</sup>Sodium bicarbonate, 1 mEq/kg after prolonged rest or high dose of epinephrine. <sup>j</sup>Changes in end-tidal carbon dioxide partial pressure (ETCO<sub>2</sub>) may not be predictive of myocardial blood flow after high-dose vasopressor therapy. <sup>k</sup>Invasive monitoring should be performed only if adequate personnel are available and if it would not delay therapeutic interventions.

## Ventricular Fibrillation and Pulseless Ventricular Tachycardia

VF and pulseless VT are treated identically because they are generally caused by the same mechanisms and respond to the same interventions. Traditional monophasic defibrillators using either a monophasic truncated exponential (MTE) or a monophasic damped sinusoidal (MDS) waveform are rapidly being replaced by defibrillators that use biphasic waveforms. With biphasic defibrillation, the energy required for successful defibrillation, or the “defibrillation threshold,” is less than with monophasic defibrillation. This translates into an increased likelihood of initial defibrillation success and a decreased likelihood of postcountershock myocardial dysfunction. Despite documented advantages of lower defibrillation threshold and reduced myocardial injury using biphasic defibrillation, the data are currently inadequate to conclude that any specific waveform (biphasic or monophasic) is superior in achieving ROSC or survival to hospital discharge. New defibrillation technologies have stimulated reevaluation of optimal defibrillation strategies. Current consensus suggests that the most effective strategy is delivery of single countershocks at optimal energy levels with minimal pauses in CPR both before and immediately afterward.<sup>29</sup> This is facilitated by placement of defibrillation pads early in the resuscitation sequence, thus not requiring a pause while defibrillation paddles and gel pads are placed for each shock. Recommended countershock energies range from 150 to 200 J for biphasic truncated exponential (BTE) waveforms and 120 J for rectilinear biphasic waveforms.<sup>29</sup> Health professionals should be familiar with the manufacturer-recommended countershock energies of the biphasic defibrillator(s) available in their practice setting. The recommended energy for single monophasic defibrillation is 360 J.<sup>29</sup>

A patient who develops VF or pulseless VT while on a cardiac monitor may remain conscious for 15 to 30 seconds. The patient should be encouraged to cough vigorously until a defibrillator is available. If the patient is unresponsive, chest compressions should be initiated immediately and continued until a defibrillator is available. Defibrillation without antecedent CPR is most likely to result in ROSC when administered in the early minutes of arrest. If the duration of untreated arrest is prolonged (>4–5 minutes), a brief period of chest compressions and ventilations (90–180 seconds) before defibrillation has been shown to improve the likelihood of ROSC and survival.<sup>24,30,31</sup> The current consensus favors delivering a single countershock with minimal pause in chest compressions prior to defibrillation.<sup>32</sup> Defibrillation is followed immediately by resumption of chest compressions for 2 minutes prior to rhythm check.<sup>32</sup>

VF and pulseless VT refractory to initial defibrillation should be treated with assisted ventilation and chest compression. Intravenous (IV) access and vasopressor therapy (epinephrine or vasopressin) should be administered and repeated every 3 to 5 minutes. Simultaneous administration of epinephrine and vasopressin does not improve outcome relative to epinephrine alone regardless of presenting rhythm.<sup>33</sup>

Defibrillation attempts should be preceded and followed by minimal interruptions of chest compression.<sup>32</sup> Subsequent therapy for refractory VF and pulseless VT includes continued administration of vasopressors and antidysrhythmic agents, followed by repeated countershocks. Antidysrhythmics should be administered up to their maximum loading dose. The use of magnesium sulfate during VF and pulseless VT is of no proven efficacy except in torsades de pointes and possible hypomagnesemia. Specific indications for NaHCO<sub>3</sub> therapy include hyperkalemia and tricyclic antidepressant overdose. There is no evidence to support use of NaHCO<sub>3</sub> or other

buffers as empiric treatment for metabolic acidosis during cardiac arrest. If a patient is defibrillated into a different pulseless rhythm, such as PEA or asystole, subsequent treatment should be modified to address those specific rhythms.

## Pulseless Electrical Activity

PEA is defined as coordinated electrical activity of the heart (other than VT/VF) without a palpable pulse. This group of dysrhythmias includes EMD, in which no myocardial contractions occur, and pseudo-EMD, in which myocardial contractions occur but no pulse can be palpated. Although distinguishing EMD from pseudo-EMD may be useful in determining cause and guiding treatment, in most cases of primary PEA there is a natural progression from hypotension to pseudo-EMD to EMD.

True EMD is the result of a primary disorder of electromechanical coupling in myocardial cells. It often is associated with abnormal automaticity and conduction resulting in bradycardia and a wide QRS complex. Although the mechanism of uncoupling is unclear, it most often is associated with global myocardial energy depletion and acidosis resulting from ischemia or hypoxia. True EMD typically occurs after defibrillation following prolonged VF and is associated with hyperkalemia, hypothermia, and drug overdose.

Pseudo-EMD caused by global myocardial dysfunction is a transient state in the progression to EMD and has the same etiology. An additional cardiac cause of pseudo-EMD is papillary muscle and myocardial wall rupture, in which the ventricle continues to contract, but forward flow is greatly diminished. Pseudo-EMD also may be caused by primary supraventricular tachycardia. Additional extracardiac causes of pseudo-EMD include hypovolemia, tension pneumothorax, pericardial tamponade, and massive pulmonary embolism. Pseudo-EMD of extracardiac origin most often has narrow-complex tachycardia initially, which can progress to bradycardia with conduction abnormalities and QRS widening.

Treatment of PEA requires all general resuscitation measures, including CPR, intubation with assisted ventilation, IV access, and repeated administration of vasopressors. Initial assessment also should include vascular Doppler ultrasound, echocardiography, or ETco<sub>2</sub> monitoring to distinguish EMD from pseudo-EMD. This is important since volume loading or continuous vasopressor infusion, which is not typically used in routine cardiac arrest resuscitation, may be helpful in cases of pseudo-EMD. PEA thought to result from supraventricular tachycardia should be immediately cardioverted. Atropine should be administered if the heart rate is less than 60 beats/min. These interventions alone are generally inadequate, unless the underlying cause of PEA is primary respiratory arrest or supraventricular tachycardia. Successful resuscitation of patients with PEA hinges on rapid diagnosis and treatment of the underlying cause. Physical examination may provide valuable clues to the underlying cause (Table 7-4). In hypoxia and hypovolemia, the diagnosis is based on response to empirical therapy, whereas other causes, such as pericardial tamponade, tension pneumothorax, and hypothermia, can be definitively diagnosed during resuscitation. Physical examination and monitoring are used to guide ongoing resuscitation efforts.

## Asystole

Asystole represents complete cessation of myocardial electrical activity. Although asystole may occur early in cardiac arrest as a consequence of progressive bradycardia, asystole generally represents the end-stage rhythm after prolonged cardiac arrest caused by VF or PEA. Because the potential exists for an

**Table 7-4** Diagnosis and Treatment of Common Causes of Pulseless Electrical Activity

CAUSE	DIAGNOSIS	PALLIATIVE THERAPY	DEFINITIVE THERAPY
Hypovolemia	Response to volume infusion	Volume infusion, consider OCCM	Hemostasis if hemorrhage
Hypoxia	Response to oxygenation	Oxygenation, assisted ventilation	Treat underlying cause
Cardiac tamponade	Echocardiogram, pericardiocentesis	Pericardiocentesis	Thoracotomy and pericardiotomy
Tension pneumothorax	Asymmetrical breath sounds, tracheal deviation	Needle thoracostomy	Tube thoracostomy
Hypothermia	Rectal temperature		Warm peritoneal or thoracic lavage, OCCM or CPB
Pulmonary embolus	Risk factors or evidence of deep venous thrombosis	OCCM or CPB	Lytic therapy, pulmonary embolectomy
Drug overdose	History of drug ingestion	Drug-specific	Drug-specific
Hyperkalemia	History of renal failure or elevated serum potassium	Calcium chloride, insulin and glucose, sodium bicarbonate	Hemodialysis
Acidosis	Arterial blood gas	Hyperventilation, sodium bicarbonate	Treat underlying cause

CPB, cardiopulmonary bypass; OCCM, open-chest cardiac massage.

organized rhythm or VF to appear as asystole in a single lead (if the rhythm vector is completely perpendicular to the lead vector), asystole always should be confirmed in at least two limb leads. It may be difficult to distinguish between extremely fine VF and asystole. Routine countershock of asystole to treat possible fine VF has not been shown to improve outcome, however.

Treatment of asystole requires all general resuscitation measures, including CPR, intubation with assisted ventilation, IV access, and repeated administration of vasopressors. In one randomized prospective out-of-hospital trial, improved survival to hospital admission and discharge was observed in patients presenting in asystole when two doses of vasopressin (40 IU) were given initially during resuscitation compared with standard-dose epinephrine (1 mg) followed by additional epinephrine if needed.<sup>34</sup> In a more recent study, simultaneous administration of epinephrine and vasopressin did not improve outcome relative to epinephrine alone, regardless of presenting rhythm.<sup>33</sup> Atropine should be administered with the first dose of vasopressor and repeated to a total dose of 0.04 mg/kg. Extensive research has shown that asystole in the out-of-hospital setting seldom responds to pacing. To be effective, pacing must be initiated within several minutes of arrest.

## Postarrest

Resuscitation of a cardiac arrest victim does not end with ROSC. Management includes rapid diagnosis and treatment of the disorders that caused the arrest and the complications of prolonged global ischemia. Simultaneous management of these two entities makes caring for a postarrest patient particularly challenging.

Induction of prolonged therapeutic hypothermia in comatose survivors of cardiac arrest has been shown to improve survival and functional outcome in two prospective randomized clinical trials.<sup>3,4</sup> Both studies enrolled only out-of-hospital patients with witnessed arrest and an initial rhythm of VF. The time to achieve target temperature (32–34°C) ranged from less than 2 hours<sup>3</sup> to a median of 8 hours (interquartile range 4–16 hours),<sup>4</sup> suggesting a broad therapeutic window. Hypothermia was maintained for 12 to 24 hours followed by gradual rewarming over 12 to 24 hours. Although these parameters provide guidelines within which postarrest hypothermia is effective, additional preclinical and clinical data are needed to deter-

mine the optimal temperature, time to achieve target temperature, and duration of therapy. In both studies, the rates of complications were not statistically different between groups. Although there are no absolute contraindications, relative contraindications include severe cardiogenic shock, life-threatening dysrhythmias, uncontrolled bleeding, preexisting coagulopathy, pregnancy, another obvious reason for coma (i.e., drug overdose or status epilepticus), known end-stage terminal illness, and a preexisting do-not-resuscitate status. Thrombolytic therapy does not preclude the use of hypothermia.<sup>4</sup> Finally, although the current data are limited to patients with witnessed VF out-of-hospital cardiac arrest, induced postarrest hypothermia potentially should be effective in patients with other presenting rhythms and cardiac arrest presentations.

When the decision is made to treat the patient with therapeutic hypothermia, cooling efforts should be initiated as soon as possible. Practical methods of rapidly inducing hypothermia include ice packs (applied to the neck, inguinal areas, and axilla), fan cooling of dampened exposed skin, cooling blankets underneath and on top of the patient, and disabling of ventilator warming circuits. Rapid IV infusion of limited volumes (1–2 L) of 4°C saline facilitates rapid cooling, but additional measures are needed to maintain hypothermia. A number of automated surface cooling devices are now available that use chest and thigh pads and continuous temperature feedback from bladder or esophageal temperature probes. More invasive methods, including endovascular venous catheters, are also available and allow for rapid and precise control of temperature, but they require time and additional resources to institute. Shivering, which inhibits cooling, can be prevented with sedation and pharmacologic paralysis. However, prolonged paralysis should be avoided due to the risk of unrecognized seizure activity in postarrest patients. Target core body temperature should be 32 to 34°C and is best monitored by an indwelling temperature-sensitive bladder catheter or esophageal temperature probe.<sup>35</sup>

When the patient is stabilized and cooling efforts are initiated, transfer to a critical care unit should occur as soon as possible. Although the optimal duration of postarrest hypothermia is unknown, target temperature should be actively maintained for 12 to 24 hours followed by gradual rewarming over 8 to 12 hours.<sup>36</sup> Effective application of therapeutic hypothermia in comatose cardiac arrest survivors requires a coordi-

nated interdisciplinary effort and is best carried out using a predetermined goal-directed algorithm developed with input from emergency medicine, cardiology, and critical care physicians and nurses.

A simultaneous immediate concern in a comatose cardiac arrest survivor is whether the patient has an acute coronary syndrome. Diagnosing acute coronary syndrome in an unconscious patient after cardiac arrest presents a unique challenge. A standard 12-lead ECG should be obtained as soon as feasible after ROSC, with a right-sided 12-lead ECG, as indicated. In one study, 50% of patients achieving ROSC after out-of-hospital cardiac arrest were found to have acute coronary occlusion on cardiac catheterization, 10% of whom did not have ST segment elevation.<sup>13</sup>

Immediate percutaneous coronary intervention (PCI) is indicated in patients with ST segment elevation myocardial infarction or new left bundle branch block (LBBB) and can be performed during therapeutic hypothermia.<sup>36-39</sup> Given the potentially high incidence of occult critical coronary stenosis and myocardial ischemia, patients without ECG criteria for PCI represent a greater dilemma. Angioplasty of acute coronary lesions regardless of history or initial postarrest ECG has been shown to be an independent predictor of survival after cardiac arrest.<sup>13</sup> When PCI is indicated but not available, either early transfer of postarrest patients to a center capable of PCI or fibrinolytic therapy should be considered.<sup>40</sup> Relative exclusion criteria for fibrinolytic therapy unique to the postarrest patient include CPR duration greater than 10 minutes and evidence of significant CPR trauma (e.g., pneumothorax, flail chest, pulmonary contusion with hemorrhage). The effects of therapeutic hypothermia on the efficacy and complications of fibrinolytic therapy in postarrest patients have not been formally studied.

Antiplatelet and anticoagulant therapy should be administered to all patients after ROSC, whether or not therapeutic hypothermia is induced, if no evidence of hemorrhage exists and profound hypertension is absent. The choice of antiplatelet and anticoagulant therapy depends in part on the presence of active ischemia, renal function, and plans for acute angioplasty.<sup>41</sup> Although there is no proven benefit from prophylactic antiarrhythmic therapy in postarrest patients, it may be reasonable to continue an infusion of an antiarrhythmic drug that was associated with restoration of a stable rhythm during CPR. Concomitant therapies (e.g., nitrates, beta-blockers) are best performed in conjunction with careful hemodynamic monitoring. If indicated, IV preparations of nitrates and short-acting beta-blockers (e.g., esmolol) should be used because they have a brief duration of action and are easily titrated. Patients with new LBBB, right bundle branch block with left anterior or posterior hemiblock, second-degree type II block, or third-degree block should have transthoracic pacing pads immediately applied if needed. Placement of transvenous pacing catheters also can be considered, but is less often done since transthoracic pacing came into common use.<sup>42</sup>

Inadequate oxygen delivery ( $\text{Do}_2$ ) causes cells to convert to anaerobic metabolism, resulting in increased lactate production (dysoxia). Continued resuscitation efforts to optimize  $\text{Do}_2$  may help to stabilize the patient and potentially prevent subsequent multiorgan dysfunction and recurrent arrest.

During cardiac arrest and CPR,  $\text{Do}_2$  is well below necessary levels. On ROSC, resuscitation efforts should continue to establish adequate  $\text{Do}_2$ . Serum lactate levels provide an indirect measure of whether  $\text{Do}_2$  is adequate to prevent anaerobic metabolism. A single lactate level is almost universally elevated after resuscitation from cardiac arrest. Detection of ongoing lactate production requires following serial lactate levels. Insufficient  $\text{Do}_2$  also causes increased oxygen extrac-

tion, resulting in decreased  $\text{Svo}_2$ . Low  $\text{Svo}_2$  coupled with persistently elevated lactate levels indicates inadequate  $\text{Do}_2$ . Patients subjected to prolonged CPR times or high-dose vasopressor therapy during CPR may develop impaired tissue oxygen extraction.<sup>43</sup> In such patients,  $\text{Svo}_2$  is abnormally high (venous hyperoxia) in the face of inadequate  $\text{Do}_2$  and likely represents a state of severe systemic shunting resulting in an increase in non-nutritive blood flow. Lactate levels in these circumstances continue to be elevated. Thus the combination of sustained elevated lactate levels along with normal or elevated  $\text{Scvo}_2$  levels indicate severe systemic shunting. Treatments for this would include carefully reducing any continuous infusion of vasopressors, more aggressive volume loading, and possibly the use of guided vasodilator therapy to open up underperfused tissue beds.

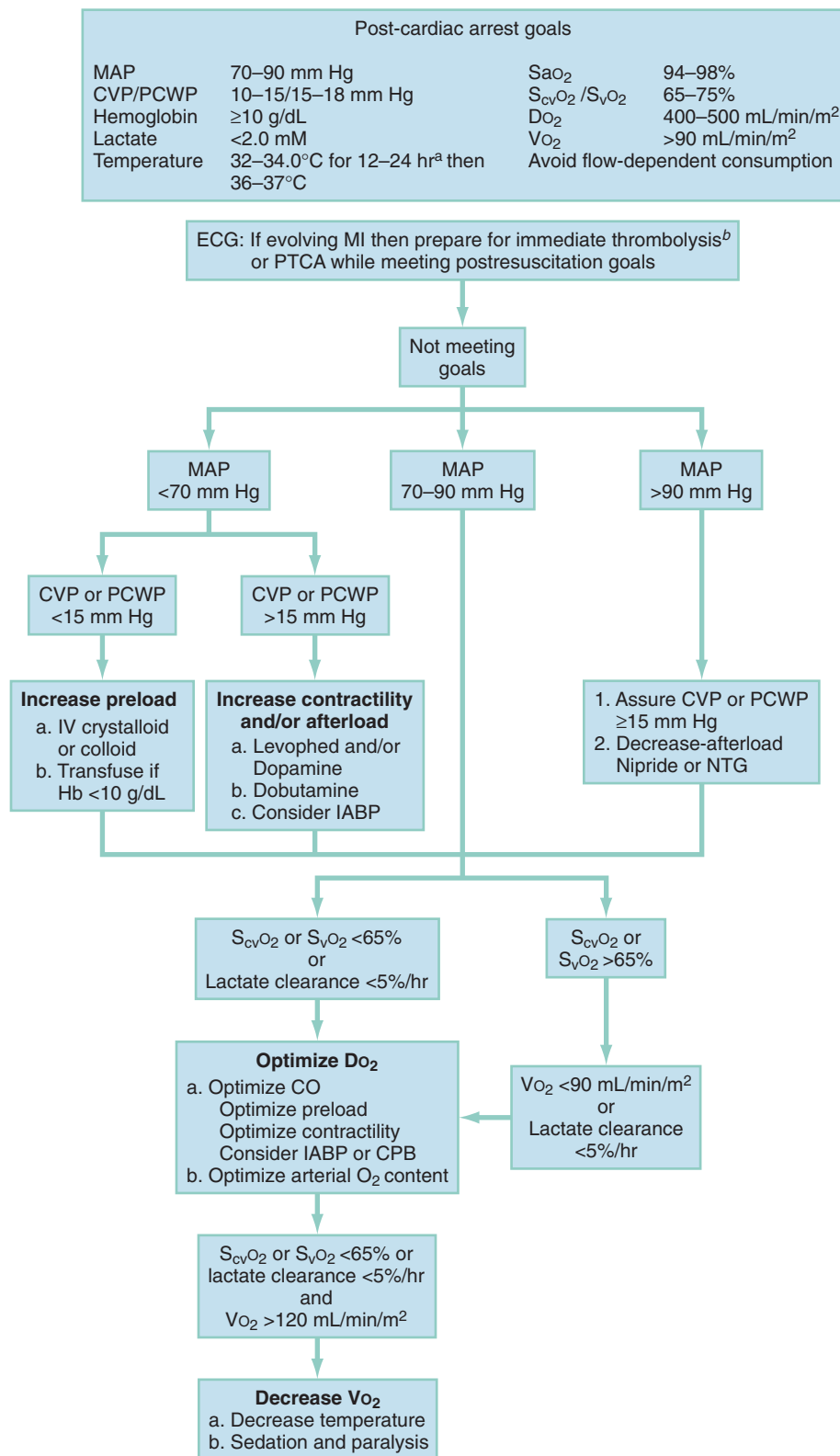
The use of combined hemodynamic and metabolic endpoints to guide resuscitation in the ED has been shown to improve the outcome of patients with septic shock states, but has not been evaluated in the postarrest situation.<sup>44</sup> This strategy may be helpful in this setting, however. It is relatively straightforward and requires only the insertion of a supradiaphragmatic central venous catheter.  $\text{Scvo}_2$  can be used as a reliable surrogate for  $\text{Svo}_2$ , which eliminates the need for a pulmonary artery catheter.<sup>23</sup> If  $\text{Scvo}_2$  is abnormally low (<65%), but hemoglobin and  $\text{Sao}_2$  values are normal, cardiac output is insufficient. Central venous pressure (CVP) should be used to deduce whether inadequate cardiac output is secondary to hypovolemia or impaired myocardial function. Augmenting CVP to levels between 10 and 15 mm Hg ensures adequate preload in most patients. If CVP is adequate and the patient has a mean arterial pressure of at least 70 mm Hg, therapy with an inotropic agent, such as dobutamine, should be initiated while considering reperfusion strategies. CVP measurements may decrease rapidly on initiation of dobutamine therapy. Additional volume expansion while maintaining a hemoglobin value of at least 10 g/dL should be provided as needed to maintain an adequate CVP.

The response to  $\text{Do}_2$ -optimizing interventions can be monitored by continuous or serial  $\text{Scvo}_2$  measurements and serial lactate levels. An increase in  $\text{Scvo}_2$  coupled with a decrease in lactate levels indicates improved  $\text{Do}_2$ . An unchanging  $\text{Scvo}_2$  level indicates the need to continue to increase delivery. Persistently elevated lactate levels and low  $\text{Scvo}_2$  despite maximum pharmacologic support and volume management signal the need for additional interventions to optimize  $\text{Do}_2$  to prevent accumulation of oxygen debt, which will lead to either death or the development of multisystem organ failure. Options to consider include revascularization or mechanical assistance in the form of intra-aortic balloon pulsation or extracorporeal support. The induction of mild hypothermia may assist in lowering the metabolic demands of tissues in the postarrest state. Figure 7-3 provides a goal-directed guide to care of the postarrest patient. Similar options should be considered in a patient with venous hyperoxia and elevated levels of lactate because the combination of these findings indicate severe microvascular dysfunction, which also leads to the accumulation of oxygen debt incompatible with survival. The incidence of this condition may increase with the increased use of potent vasopressors, such as vasopressin.

Systems should ensure prompt transfer of postarrest patients from the ED to the cardiac catheterization laboratory or an intensive care unit, where intensive monitoring can guide subsequent therapy to achieve the optimal patient outcome. Family members should be fully informed of the circumstances and the patient's transfer. Unless prompt transfer to the ICU is anticipated and achieved, postarrest care should begin in the ED.



## GOAL-DIRECTED POST ARREST TREATMENT ALGORITHM



**Figure 7-3.** Goal-directed postarrest treatment algorithm. <sup>a</sup>Therapeutic hypothermia is indicated in comatose survivors of witnessed cardiac arrest that had a presenting rhythm of ventricular fibrillation. It may also be effective in patients resuscitated from other cardiac arrest presentations. Relative contraindications include an unwitnessed cardiac arrest, severe cardiogenic shock, life-threatening dysrhythmias, uncontrolled bleeding, preexisting coagulopathy, pregnancy, another obvious reason for coma (i.e., drug overdose or status epilepticus), known end-stage terminal illness, and a preexisting do-not-resuscitate status. <sup>b</sup>Initiation of therapeutic hypothermia is not a contraindication to thrombolytic therapy. CPB, cardiopulmonary bypass; CVP, central venous pressure; Do<sub>2</sub>, oxygen delivery; ECG, electrocardiogram; Hb, hemoglobin; IABP, intra-aortic balloon pulsation; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; PTCA, percutaneous transluminal angioplasty; SaO<sub>2</sub>, mixed-venous oxygen saturation; Vo<sub>2</sub>, oxygen consumption.

## KEY CONCEPTS

- CPR quality, including minimizing chest compression pauses, is critical to successful resuscitation from cardiac arrest.
- Restoration of adequate cardiac function is the defining factor of ROSC. Restoration of normal brain function is the defining factor of successful resuscitation.
- Resuscitation of a cardiac arrest victim does not end with ROSC. Rapid diagnosis and proper management of the pathologic conditions that precipitated and resulted from the arrest as well as goal-directed hemodynamic management can improve outcome.
- Induced prolonged hypothermia (32–34°C for 12–24 hours) is the first and only post-ROSC intervention shown to improve survival and functional outcome of comatose cardiac arrest survivors.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

# Pediatric Resuscitation

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## CARDIAC ARREST

### Perspective

Cardiac arrest is not rare in pediatric patients, occurring in 2 to 6% of children admitted to a pediatric intensive care unit (PICU)<sup>1,2</sup> and about 16,000 children per year out-of-hospital in the United States (i.e., ≈8-20/100,000 children/year).<sup>3,4</sup> These data suggest that the rate of in-hospital cardiac arrest is about 100-fold higher than that for out-of-hospital arrest.<sup>5</sup>

Although outcomes from pediatric cardiac arrest were once considered dismal,<sup>6,7</sup> more recent data indicate that pediatric cardiopulmonary resuscitation (CPR) is saving lives. As many as two thirds of in-hospital pediatric cardiac arrest patients can be initially resuscitated,<sup>8-12</sup> and over 25% survive to hospital discharge. For out-of-hospital pediatric cardiac arrests, 30% attain return of spontaneous circulation, 24% survive to hospital admission, and 12% survive to discharge.<sup>4</sup> In contrast to previous assertions in the literature, performing CPR in children is not an exercise in futility.<sup>13</sup>

### Etiologic and Pathophysiologic Categories of Cardiac Arrest

Cardiac arrests can result from many pathophysiologic processes. Three common pathways to arrest have been identified: asphyxial, ischemic, and arrhythmogenic. Asphyxial cardiac arrests are precipitated by acute hypoxia or hypercarbia and are the most common in children.<sup>3,10,12</sup> Ischemic arrests are precipitated by inadequate myocardial blood flow, in children most commonly due to shock from hypovolemia, sepsis, or myocardial dysfunction. Finally, arrhythmogenic arrests are precipitated by ventricular fibrillation (VF) or ventricular tachycardia (VT). The immediate cause of arrest in two recent in-hospital studies was arrhythmogenic for 10%, asphyxial for 67%, and ischemic for 61% (many had both asphyxia and ischemia).<sup>10,12</sup> The vast majority of out-of-hospital arrests are also either asphyxial or ischemic, and 5 to 20% are arrhythmogenic.<sup>4,14</sup>

### Distinguishing Principles of Disease

#### Children Are Different

Appropriate pediatric CPR differs from that for adults due to children's differences in anatomy and physiology, as well as the differences in the pathogenesis of cardiac arrest and the common rhythm disturbances for children. In contrast to

adults, children rarely suffer sudden VF cardiac arrest from coronary artery disease. The causes of pediatric arrests are more diverse and are usually secondary to profound hypoxia or asphyxia due to respiratory failure or circulatory shock. Prolonged hypoxia and acidosis impair cardiac function and ultimately lead to cardiac arrest. By the time the arrest occurs, all organs of the body have generally suffered significant hypoxic-ischemic insults.

The use of closed-chest cardiac massage to provide adequate circulation during cardiac arrest was initially demonstrated in small dogs with compliant chest walls.<sup>15</sup> Based on reasonable extrapolation, these investigators felt that closed-chest cardiac massage would be effective with children, but might not be with adults. Therefore, the first patients successfully treated with this technique were children. The presumed mechanism of blood flow was direct compression of the heart between the sternum and the spine in these children with compliant chest walls. Later investigations indicated that blood could also be circulated during CPR by the thoracic pump mechanism. That is, chest compression-induced increases in intrathoracic pressure can generate a gradient for blood to flow from the pulmonary vasculature, through the heart, and into the peripheral circulation. Regardless of mechanism, cardiac output during CPR seems to be greater in children (and immature animals) with compliant chest walls than in adults with less compliant chest walls.<sup>16,17</sup> Interestingly, recent American Heart Association (AHA) National Registry of CPR data indicate that outcomes from in-hospital cardiac arrest are substantially better in infants than older children, perhaps because of superior perfusion during CPR.<sup>9</sup>

### The Four Phases of Cardiac Arrest

Cardiac arrest may be categorized into four "phases," each with unique physiology and treatment strategies: (1) prearrest, (2) no flow (untreated cardiac arrest), (3) low flow (CPR), and (4) postresuscitation.

**The Prearrest Phase.** The prearrest phase is the period before the arrest. Because most out-of-hospital pediatric cardiac arrests are due to progressive asphyxia or ischemia, they can often be prevented by avoiding the precipitating insult. For example, infant and child car seats, and seat belts for older children, can prevent cardiac arrests resulting from motor vehicle collisions. Similarly, fences around swimming pools with self-closing gates can prevent drownings.

Both the BRESUS study in the United Kingdom and the AHA's National Registry of Cardiopulmonary Resuscitation

(NRCPR) data clearly demonstrate that most in-hospital cardiac arrests are asphyxial or ischemic rather than sudden arrhythmia-induced events.<sup>10,18,19</sup> Most importantly, many of these arrests could be prevented by early recognition and treatment of respiratory failure and shock. This information has fueled interest in the development of medical emergency teams (aka rapid response teams) to recognize and treat respiratory failure and circulatory shock before progression to cardiac arrest.<sup>20,21</sup> These issues were appreciated by the founders of the Pediatric Advanced Life Support (PALS) course, which was therefore designed to prevent cardiac arrests by early recognition and treatment of respiratory failure and shock in children.<sup>7</sup> In the *prearrest phase*, hospitalized children at high risk for a cardiac arrest should be in a monitored unit, where prompt diagnosis and treatment is available for respiratory failure, circulatory shock, and life-threatening arrhythmias.

**The No-Flow Phase (Untreated Cardiac Arrest).** Interventions during the *no-flow* phase of untreated pulseless cardiac arrest focus on early recognition of cardiac arrest and initiation of basic and advanced life support. Yet only a third of children with an out-of-hospital cardiac arrest are provided with bystander CPR.<sup>4,14</sup>

According to NRCPR data, 83% of pediatric in-hospital arrests were witnessed, and the children were on monitors.<sup>10</sup> It is becoming increasingly clear that any in-hospital pediatric cardiac arrest that does not occur in a monitored unit should be evaluated as a sentinel event or potentially an avoidable death.

**The Low-Flow Phase (Resuscitation).** During untreated cardiac arrest, circulation has stopped (i.e., the *no-flow* phase). Blood flow during CPR is generated by chest compressions. For children the main mechanism of blood flow is from cardiac compression. The cardiac output depends on the product of the stroke volume and heart rate. The force of compressions is a major determinant of stroke volume, and the rate of compressions is the sole determinant of heart rate. Stroke volume also depends on preload. Therefore, patients with cardiac arrests precipitated by circulatory shock (e.g., hypovolemic or septic shock)

may need additional intravascular volume to generate an adequate stroke volume with chest compressions. Notably, excellent CPR can result in a cardiac output 10 to 25% of that in normal sinus rhythm.

Adequate myocardial blood flow is necessary for return of spontaneous circulation. During CPR, myocardial blood flow depends on coronary perfusion pressure or the “driving pressure” of blood into the coronary arteries from the aorta (i.e., the difference between the aortic and right atrial pressures during the relaxation phase). If the coronary perfusion pressure falls below 15 mm Hg during CPR in adults, the likelihood for a return of spontaneous circulation is substantially decreased.<sup>22</sup> Animal data suggest that outcomes improve as coronary perfusion pressure increases above 25 mm Hg.<sup>23</sup> Moreover, even relatively brief interruptions to chest compressions (e.g., 4-second pauses for two rescue breaths) lead to substantial decreases in the aortic relaxation pressure and coronary perfusion pressure, thereby resulting in inadequate myocardial perfusion<sup>24,25</sup> (Fig. 8-1).

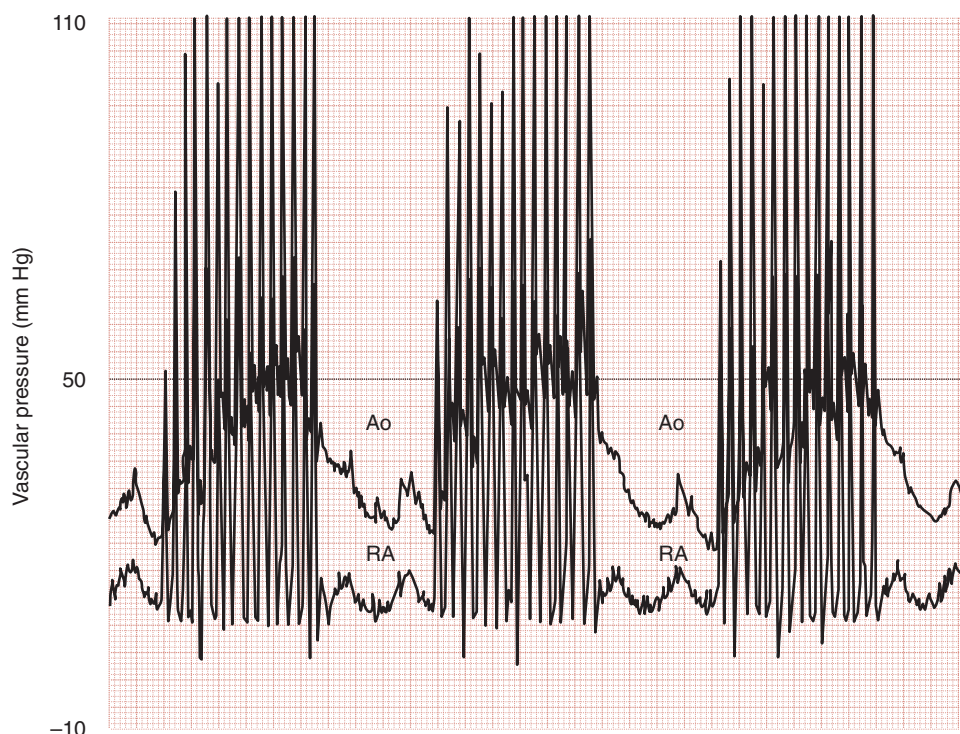
### Circumferential Versus Focal Sternal Compressions

In adults and animal models of cardiac arrest, circumferential CPR (e.g., vest CPR) provides better CPR hemodynamics than two-finger compressions. In smaller infants, the recommended CPR technique is to encircle the chest with both hands and depress the sternum with the thumbs, while compressing the thorax circumferentially (when the resuscitator’s hands are relatively large enough to do so; Fig. 8-2).<sup>14</sup> This “two-thumb” circumferential compression technique results in higher systolic and diastolic blood pressures and a higher pulse pressure than traditional two-finger compression of the sternum.<sup>26,27</sup>

### Chest Compression Rate

Another important determinant of myocardial blood flow is the chest compression rate. Although the optimal chest compres-

**Figure 8-1.** Cerebral perfusion pressure with cardiopulmonary resuscitation. Ao, aorta; RA, right atrium. (Courtesy of University of Arizona, Department of Pediatrics, Division of Pediatric Critical Care.)







**Figure 8-2.** Hand-thumbs encircling technique for chest compression in infants with cardiopulmonary failure. (Reprinted with permission from BLS for Healthcare Providers. Copyright ©2006, American Heart Association, Inc.)

sion rate is unknown, data from large studies of animals have shown that coronary perfusion pressure, cardiac output, and survival are substantially superior, with chest compression rates of 100/minute compared with rates of less than 80/minute.<sup>28,29</sup> In addition, clinical studies in adults have shown that end-tidal carbon dioxide levels, a marker of cardiac output during CPR, were significantly higher with chest compressions at 120/minute versus 80/minute.<sup>30</sup> Because of preferential blood flow to the myocardium and cerebrum compared with the rest of the body during CPR, excellent CPR can provide myocardial blood flow greater than 50% of that in normal sinus rhythm.

Although restoration of coronary perfusion during CPR is critical for successful return of spontaneous circulation, adequate cerebral perfusion is important for mitigating the injurious effects of cerebral anoxia during cardiac arrest. Unlike myocardial blood flow, cerebral blood flow is generated during the compression phase of CPR. Forceful, uninterrupted chest compressions at a rate of 120/minute compared with 60/minute improves both cerebral and coronary perfusion pressures compared with less forceful compressions or compressions at a lower rate.<sup>28,29</sup> In addition, vasoconstrictors, such as epinephrine or vasopressin, preferentially direct the cardiac output during CPR to the coronary and cerebral circulations.

The ultimate goal of CPR is to provide coronary and cerebral perfusion pressure and blood flow to critical organs during the low-flow phase. Excellent quality basic life support with continuous effective chest compressions is the emphasis in this low-flow phase. During this phase, the *only* source of coronary and cerebral perfusion comes from the blood pressure generated by good chest compressions. Providing adequate coronary and cerebral perfusion pressure is critical for successful resuscitation. Any interruption, whether to perform procedures, analyze rhythms, check for pulses, or to change rescuer position for ventilation is potentially harmful.<sup>24</sup> For VF and pulseless VT, rapid determination of electrocardiographic rhythm and prompt defibrillation when appropriate are important. For cardiac arrests due to asphyxia or ischemia, adequate myocardial perfusion and myocardial oxygen delivery with ventilation to match blood flow is important.

Despite evidence-based guidelines, extensive provider training, and provider credentialing in resuscitation medicine, the quality of CPR is typically poor. Slow compression rates, inadequate depth of compression, and substantial pauses are the norm.<sup>31-33</sup> Moreover, observed ventilation rates during pro-

fessional rescuer CPR are often too high, potentially leading to deleterious effects on venous return and outcome.<sup>33,34</sup> The resuscitation mantra must be: *Push hard, push fast, minimize interruptions, allow full chest recoil, and don't overventilate.* This approach can markedly improve myocardial, cerebral, and systemic perfusion, and will likely improve outcomes.<sup>35</sup>

### Chest Compression to Ventilation Ratios

Ideal compression-to-ventilation ratios for pediatric patients are unknown. Physiologic estimates suggest that the amount of ventilation needed during CPR is much less than the amount needed during a normal perfusing rhythm because the cardiac output (and therefore pulmonary blood flow) during CPR is only 10 to 25% of that during normal sinus rhythm.<sup>36</sup> The best ratio of compressions to ventilations depends on many factors, including the compression rate, the tidal volume, the blood flow generated by compressions, and the time that compressions are interrupted to perform ventilations. In a manikin model of pediatric CPR, a chest compression-to-ventilation (CC:V) ratio of 15:2 delivered the same minute ventilation as CPR with a CC:V ratio of 5:1, but the number of chest compressions delivered was 48% higher with the 15:2 ratio.<sup>37,38</sup> The benefits of positive pressure ventilation (increased arterial oxygen content and carbon dioxide elimination) must be balanced against the adverse consequence of impeding circulation because of increases in intrathoracic pressure and venous return to the heart.

For adults, mathematical models of oxygen delivery during CPR suggest the optimal CC:V ratio is approximately 30:2 for two-rescuer health care provider CPR and is closer to 50:2 for single-lay rescuers.<sup>39</sup> Similar mathematical models adjusted to the known physiologic variables in children indicate that CC:V ratios from 10:2 to 30:2 would be reasonable to optimize tissue oxygen delivery during CPR.<sup>40</sup>

The present recommendations for CC:V ratios during CPR are based on rational conjecture from animal, manikin, and mathematical models, as well as educational theory on the retention of skills in adult learners. In the 2005 AHA Guidelines, a universal CC:V ratio of 30:2 is recommended for single-person bystander CPR. For two-rescuer CPR, a 15:2 ratio is recommended for all children beyond the newly born period. For the newly born, a ratio of 3:1 is recommended, resulting in a greater number of ventilations per minute, but nearly the same number of compressions (100/min vs. 90/min).<sup>41</sup> This recommended ratio was arrived at by consensus to balance educational issues (i.e., the benefit to single-rescuer bystanders of remembering only one compression to ventilation ratio of 30:2) with what is known about the physiology of the cardiac and pulmonary circulations of children during cardiac arrest.

### Leaning

Along with the increased recognition that chest compressions are often too slow and too shallow (i.e., not forceful enough), investigators have focused on the problem of leaning during CPR. Leaning, or incomplete decompression of the chest during the relaxation phase of chest compressions, is a well-recognized phenomenon.<sup>42-44</sup> In a manikin study of CPR-trained lay volunteers, Aufderheide observed incomplete chest wall decompression in 6 of 13 resuscitations.<sup>42-44</sup> In a larger observational study of out-of-hospital cardiac arrests, incomplete release in greater than 10% of compressions was observed in 16 of 173 (9%) CPR episodes.<sup>43</sup> Observations during in-hospital pediatric CPR indicate that “leaning” is a common phenomenon, occurring in 23% of chest compressions.<sup>45</sup>

“Leaning” pressures of approximately 15% of body weight may affect intrathoracic pressure and theoretically affect the hemodynamics of CPR.<sup>45-48</sup>

### Real-Time Cardiopulmonary Resuscitation Feedback

In an effort to optimize CPR quality, new technology has been developed that monitors CPR through a force sensor and accelerometer on the chest. This information is transmitted to a defibrillator monitor to provide quantitative verbal feedback to the rescuer on the rate and force of compressions as well as the frequency and volume of ventilations. Recent studies document that poor-quality CPR, as analyzed by a feedback device, reduces the likelihood of defibrillation success,<sup>35</sup> and rescuers can use this type of automated feedback to improve CPR quality and compliance with current guidelines.<sup>49</sup> A recent pilot study suggests that real-time corrective feedback during pediatric CPR can improve CPR performance, but more information on the accuracy and appropriateness of CPR performance targets is warranted.<sup>50</sup> The optimal goals for aortic pressures during pediatric CPR are unknown. Animal data and adult data suggest that a reasonable goal for the aortic diastolic (or relaxation) pressure is greater than 20 to 30 mm Hg.<sup>22,23</sup> Similarly, a reasonable goal for the aortic systolic (or compression) pressure is greater than 50 mm Hg for a newborn, 60 mm Hg for an infant, 70 to 80 mm Hg for a child, and 80 to 90 mm Hg for an adolescent.

### “Hands Only” Bystander Cardiopulmonary Resuscitation

There has been increasing interest in chest compressions alone, or “hands-only” CPR for sudden cardiac arrest. The AHA recently issued a science advisory statement recommending hands-only CPR for adult sudden cardiac arrest.<sup>51</sup> This recommendation specifically excludes pediatric cardiac arrests and arrests secondary to progressive respiratory failure and hypoxia (i.e., asphyxial arrests). Hands-only bystander CPR is the treatment of choice for a bystander without formal CPR training and a CPR-trained bystander who “is not confident in his or her ability to provide rescue breaths with minimal interruptions to chest compressions.” For a CPR-trained bystander who “is confident in his or her ability to provide rescue breaths with minimal interruptions to chest compressions, the bystander should provide either conventional CPR using a 30:2 compression-to-ventilation ratio or hands-only CPR.” Finally, because mouth-to-mouth rescue breathing is a complex psychomotor task that is difficult to teach by telephone, the simpler technique of hands-only CPR is the recommended technique for telephone-directed CPR.

Many animal studies have established that continuous chest compressions without rescue breathing is as effective as chest compressions with rescue breathing for the first several minutes of CPR for VF.<sup>25,52-55</sup> Since oxygenation and ventilation are clearly important for survival from any cardiac arrest, why is rescue breathing not initially necessary for VF? Immediately after an acute fibrillatory cardiac arrest, aortic oxygen and carbon dioxide concentrations do not vary from the prearrest state because there is no blood flow and aortic oxygen consumption is minimal. Therefore, when chest compressions are initiated, the blood flowing from the aorta to the coronary and cerebral circulations provides adequate oxygenation at an acceptable pH. At that time, myocardial and cerebral oxygen delivery is limited more by blood flow than oxygen content. Adequate oxygenation and ventilation can continue without rescue breathing because the lungs serve as a relatively high

oxygen/low carbon dioxide reservoir during the low-flow state of CPR. In addition, ventilation can occur due to chest compression-induced gas exchange and spontaneous gasping during CPR in victims of sudden cardiac arrest. Therefore, arterial oxygenation and pH can be adequate with chest compressions alone in VF arrests.<sup>52,53,56</sup>

Six clinical out-of-hospital studies in adults found that outcomes were as good or better after hands-only bystander CPR as with standard bystander CPR.<sup>57-63</sup> One of these studies was a randomized, controlled prospective study of telephone-directed CPR, whereas the other five were observational studies of outcomes after bystander CPR.<sup>57-63</sup>

### Asphyxia and Pediatric Cardiac Arrest

Chest compression (i.e., hands-only) CPR for children is not recommended. Foregoing ventilation in the pediatric patient is not prudent because respiratory arrest and asphyxia generally precede pediatric cardiac arrest. During asphyxia, blood continues to flow to tissues; therefore, arterial and venous oxygen saturations decrease while carbon dioxide and lactate continue to increase for many minutes before progression to cardiac arrest. In addition, continued pulmonary blood flow before the cardiac arrest depletes the pulmonary oxygen reservoir. In this circumstance, rescue breathing can be life-saving.

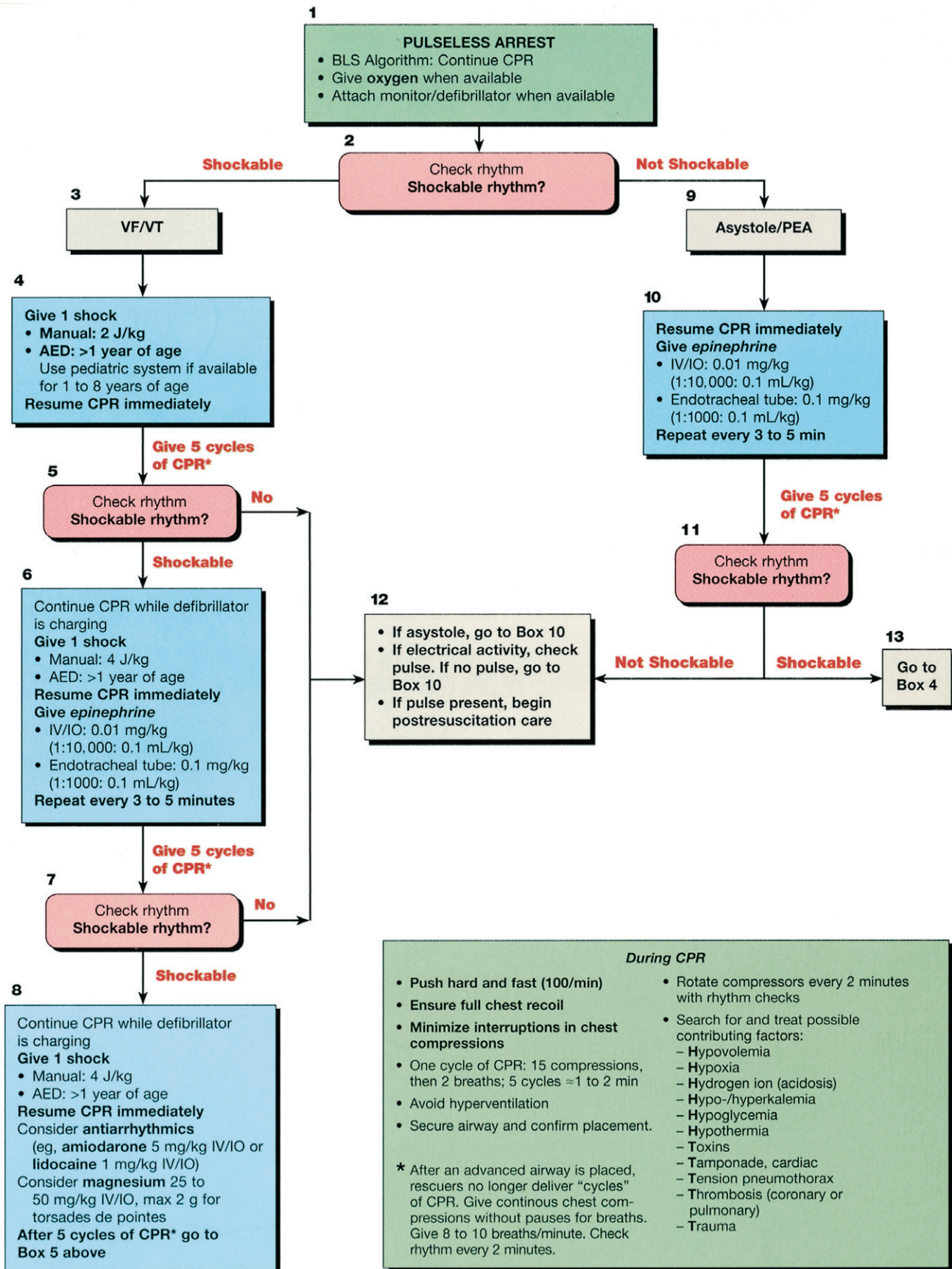
Not surprisingly, animal studies of bystander CPR for asphyxia-precipitated cardiac arrests demonstrate that the addition of rescue breathing to compressions results in much better outcomes than chest compressions alone.<sup>64,65</sup> Chest compressions alone, however, were superior to no CPR at all, even with hypoxia-induced cardiac arrest. These studies support the need for rescue breathing as a critical component of CPR for pediatric asphyxia-precipitated cardiac arrests. However, approximately 10% of both in-hospital and out-of-hospital pediatric cardiac arrests are arrhythmogenic arrests precipitated by VF or VT. For an older child with a sudden collapse from cardiac arrest (i.e., presumed VF or VT), hands-only CPR is a reasonable choice for bystander CPR.

### Advanced Life Support Medications During the Low-Flow Phase of Cardiopulmonary Resuscitation

Figure 8-3 demonstrates a simplified algorithm for pediatric pulseless cardiac arrest. In addition, Table 8-1 lists medicines commonly used during CPR. Table 8-1 also includes the dosage and appropriate indications for these medications.

Although animal studies indicate that epinephrine can improve initial resuscitation success after both asphyxial and VF cardiac arrests, no single medication has been shown to improve survival to hospital discharge outcome from pediatric cardiac arrests. Medications commonly used for CPR in children are vasopressors (epinephrine or vasopressin), calcium chloride, sodium bicarbonate, and antiarrhythmics (amiodarone or lidocaine). During CPR, epinephrine’s alpha-adrenergic effect increases systemic vascular resistance, increasing diastolic blood pressure, which in turn increases coronary perfusion pressure and blood flow and increases the likelihood of the return of spontaneous circulation (ROSC). Epinephrine also increases cerebral blood flow during CPR because peripheral vasoconstriction directs a greater proportion of flow to the cerebral circulation. The beta-adrenergic effect increases myocardial contractility and heart rate and relaxes smooth muscle in the skeletal muscle vascular bed and bronchi, although this effect is of less importance. Epinephrine also changes the character of VF (i.e., higher amplitude, more “coarse”), increasing the likelihood of successful defibrillation.





**Figure 8-3.** Management algorithm for infants and children with cardiopulmonary arrest. AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; IO, intraosseous; IV, intravenous; PEA, pulseless electrical activity; VF, ventricular fibrillation; VT, ventricular tachycardia. Reprinted with permission from Pediatric Advanced Life Support Course Guide. Copyright ©2006, American Heart Association, Inc.

**Table 8-1 Medications Used in the Treatment of Pediatric Patients in Cardiopulmonary Arrest**

DRUG	INDICATIONS/DOSAGE
Adenosine	SVT 0.1 mg/kg IV/IO <i>rapid</i> push (max 6 mg), 2nd dose 0.2 mg/kg IV/IO <i>rapid</i> push (max 12 mg)
Albumin	Shock, trauma, burns 0.5–1 g/kg (10–20 mL/kg of 5% solution) IV/IO <i>rapid</i> infusion
Albuterol	Asthma, anaphylaxis (bronchospasm), hyperkalemia MDI: 4 to 8 puffs INH q 20 min PRN with spacer ( <i>OR</i> ETT if intubated) Nebulizer: 2.5 mg/dose (wt < 20 kg) <i>OR</i> 5 mg/dose (wt > 20 kg) INH q 20 min PRN Continuous nebulizer: 0.5 mg/kg/hr INH (max 20 mg/hr)
Alprostadil (PGE <sub>1</sub> )	Ductal-dependent congenital heart disease (all forms) 0.05–0.1 µg/kg/min IV/IO infusion initially, then 0.01–0.05 µg/kg/min IV/IO
Amiodarone	SVT, VT (with pulses) 5 mg/kg IV/IO <i>load</i> over 20–60 min (max 300 mg), repeat to daily max 15 mg/kg (or 2.2 g) Pulseless arrest (ie, VF/pulseless VT) 5 mg/kg IV/IO <i>bolus</i> (max 300 mg), repeat to daily max 15 mg/kg (or 2.2 g)
Atropine sulfate	Bradycardia (symptomatic) 0.02 mg/kg IV/IO (min dose 0.1 mg, max single dose child 0.5 mg, max single dose adolescent 1 mg), may repeat dose once, max total dose child 1 mg, max total dose adolescent 2 mg 0.04–0.06 mg/kg ETT Toxins/overdose (eg, organophosphate, carbamate) 0.02–0.05 mg/kg (<12 years) <i>OR</i> 0.05 mg/kg (>12 years) IV/IO initially, repeat q 20–30 min until atropine effect (dry mouth, tachycardia, mydriasis) is observed or symptoms reverse
Calcium chloride 10%	Hypocalcemia, hyperkalemia, hypermagnesemia, calcium channel blocker overdose 20 mg/kg (0.2 mL/kg) IV/IO <i>slow</i> push during arrest or if severe hypotension, repeat PRN
Dexamethasone	Croup 0.6 mg/kg PO/IM/IV (max 16 mg)
Dextrose (Glucose)	Hypoglycemia 0.5–1 g/kg IV/IO (D <sub>25</sub> W 2–4 mL/kg; D <sub>10</sub> W 5–10 mL/kg)
Diphenhydramine	Anaphylactic shock 1–2 mg/kg IV/IO/IM q 4–6 hr (max 50 mg)
Dobutamine	Congestive heart failure, cardiogenic shock 2–20 µg/kg/min IV/IO infusion; titrate to desired effect
Dopamine	Cardiogenic shock, distributive shock 2–20 µg/kg/min IV/IO infusion; titrate to desired effect
Epinephrine	Pulseless arrest, bradycardia (symptomatic) 0.01 mg/kg (0.1 mL/kg) 1:10,000 IV/IO q 3–5 min (max 1 mg; 1 mL) 0.1 mg/kg (0.1 mL/kg) 1:1000 ETT q 3–5 min Hypotensive shock 0.1–1 µg/kg/min IV/IO infusion (consider higher doses if needed) Anaphylaxis 0.01 mg/kg (0.01 mL/kg) 1:1000 IM in thigh q 15 min PRN (max 0.5 mg) <i>OR</i> Auto-injector 0.3 mg (wt ≥ 30 kg) IM or Child Jr auto-injector 0.15 mg (wt 10–30 kg) IM 0.01 mg/kg (0.1 mL/kg) 1:10,000 IV/IO q 3–5 min (max 1 mg) if hypotension 0.1–1 µg/kg/min IV/IO infusion if hypotension despite fluids and IM injection Asthma 0.01 mg/kg (0.01 mL/kg) 1:1000 SQ q 15 min (max 0.5 mg; 0.5 mL) Croup 0.25–0.5 mL <i>racemic</i> solution (2.25%) mixed in 3 mL NS INH <i>OR</i> 3 mL 1:1000 INH Toxins/Overdose (e.g., beta-adrenergic blocker, calcium channel blocker) 0.01 mg/kg (0.1 mL/kg) 1:10,000 IV/IO (max 1 mg); if no response, consider higher doses up to 0.1 mg/kg (0.1 mL/kg) 1:1000 IV/IO 0.1–1 µg/kg/min IV/IO infusion (consider higher doses)
Furosemide	Pulmonary edema, fluid overload 1 mg/kg IV/IM (usual max 20 mg if not chronically on loop diuretic)
Hydrocortisone	Adrenal insufficiency 2 mg/kg IV bolus (max 100 mg)
Inamrinone	Myocardial dysfunction and increased SVR/PVR Loading dose: 0.75–1 mg/kg IV/IO slow bolus over 5 min (may repeat twice to max 3 mg/kg), then 5–10 µg/kg/min IV/IO infusion
Ipratropium bromide	Asthma 250–500 µg INH q 20 min PRN × 3 doses



**Table 8-1 Medications Used in the Treatment of Pediatric Patients in Cardiopulmonary Arrest—cont'd**

DRUG	INDICATIONS/DOSAGE
Lidocaine	VF/Pulseless VT, wide-complex tachycardia (with pulses) 1 mg/kg IV/IO bolus Maintenance: 20–50 µg/kg/min IV/IO infusion (repeat bolus dose if infusion initiated >15 min, after initial bolus) 2–3 mg/kg ETT
Magnesium sulfate	Asthma (refractory status asthmaticus), torsades de pointes, hypomagnesemia 25–50 mg/kg IV/IO <i>bolus</i> (pulseless VT) <i>OR</i> over 10–20 min (VT with pulses) <i>OR slow</i> infusion over 15–30 min (status asthmaticus); (max 2 g)
Methylprednisolone	Asthma (status asthmaticus), anaphylactic shock Load: 2 mg/kg IV/IO/IM (max 80 mg); use acetate salt IM Maintenance: 0.5 mg/kg IB/IO q 6 hr (max 120 mg/d)
Milrinone	Myocardial dysfunction and increased SVR/PVR Loading dose: 50–75 µg/kg IV/IO over 10–60 min followed by 0.5–0.75 µg/kg/min IV/IO infusion
Naloxone	Narcotic (opiate) reversal Total reversal required (for narcotic toxicity secondary to overdose): 0.1 mg/kg IV/IO/IM/SQ bolus q 2 min PRN (max 2 mg) Total reversal not required (eg, for respiratory depression associated with therapeutic narcotic use): 1–5 µg/kg IV/IO/IM/SQ; titrate to desired effect Maintain reversal: 0.002–0.16 mg/kg/hr IV/IO infusion
Nitroglycerin	Congestive heart failure, cardiogenic shock 0.25–0.5 µg/kg/min IV/IO infusion, may increase by 0.5–1 µg/kg/min q 3–5 min PRN to 1–5 µg/kg/min (max 10 µg/kg/min) Adolescents: 10–20 µg/min, increase by 5–10 µg/min q 5–10 min PRN to max 200 µg/min
Norepinephrine	Hypotensive (usually distributive) shock (ie, low SVR and fluid refractory) 0.1–2 µg/kg/min IV/IO infusion; titrate to desired effect
Oxygen	Hypoxia, hypoxemia, shock, trauma, cardiopulmonary failure, cardiac arrest Administer 100% O <sub>2</sub> via high-flow O <sub>2</sub> delivery system (if spontaneous ventilations) or ETT (if intubated); titrate to desired effect
Procainamide	SVT, atrial flutter, VT (with pulses) 15 mg/kg IV/IO load over 30–60 min (do not use routinely with amiodarone)
Sodium bicarbonate	Metabolic acidosis (severe), hyperkalemia 1 mEq/kg IV/IO <i>slow</i> bolus Sodium channel blocker overdose (eg, tricyclic antidepressant) 1–2 mEq/kg IV/IO bolus until serum pH is >7.45 (7.50–7.55 for severe overdose) followed by IV/IO infusion of 150 mEq NaHCO <sub>3</sub> /L solution to maintain alkalosis
Sodium nitroprusside	Cardiogenic shock (i.e., associated with high SVR), severe hypertension 1–8 µg/kg/min (wt < 40 kg) <i>OR</i> 0.1 to 5 µg/kg/min (wt > 40 kg) IV/IO infusion
Terbutaline	Asthma (status asthmaticus), hyperkalemia 0.1–10 µg/kg/min IV/IO infusion; consider 10 µg/kg IV/IO load over 5 min 10 µg/kg SQ q 10–15 min until IV/IO infusion is initiated (max 0.4 mg)

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Prospective and retrospective studies indicate that use of high-dose epinephrine in adults or children (0.05–0.2 mg/kg) does not improve survival and may be associated with a worse neurologic outcome.<sup>66–69</sup> A randomized, blinded, controlled trial of rescue high-dose epinephrine versus standard-dose epinephrine following failed initial standard-dose epinephrine for pediatric in-hospital cardiac arrest demonstrated a worse 24-hour survival rate in the high-dose epinephrine group (1/27 vs. 6/23,  $P < 0.05$ ).<sup>70</sup> High-dose epinephrine cannot be recommended for routine use during CPR.

**The Postresuscitation Phase.** The postarrest syndrome is a unique and complex combination of pathophysiologic processes that occurs after successful resuscitation. This postarrest syndrome includes (1) postarrest brain injury, (2) postarrest myocardial dysfunction, (3) systemic ischemia-reperfusion response, and (4) the unresolved pathologic process that caused the cardiac arrest.

Clinical manifestations of postarrest brain injury include coma, seizures, myoclonus, varying degrees of neurocognitive dysfunction (ranging from memory deficits to persistent vegetative state), and brain death. Mild induced hypothermia is the most well-established postresuscitation therapy for adult postarrest brain injury. Two seminal articles established that induced hypothermia (32–34° C) could improve outcome for comatose adults after resuscitation from VF cardiac arrest.<sup>71,72</sup> In both randomized controlled trials, the inclusion criteria were patients *older* than 18 years who were persistently comatose after successful resuscitation from nontraumatic VF. Interpretation and extrapolation of these studies to children are difficult. Fever following cardiac arrest, brain trauma, stroke, and other ischemic conditions is associated with poor neurologic outcome. Hyperthermia following cardiac arrest is common in children.<sup>73</sup> It is reasonable to believe that mild induced systemic hypothermia may benefit children resusci-

tated from nontraumatic cardiac arrest. However, benefit from this treatment has not been rigorously studied and reported in children or in any patients with non-VF arrests. Multicenter trials of induced hypothermia after both in-hospital cardiac arrest and traumatic arrest are ongoing. Emerging neonatal trials of selective brain cooling and systemic cooling show promise for this therapy in neonatal hypoxic-ischemic encephalopathy, suggesting that induced hypothermia may improve outcomes.<sup>74</sup>

Postarrest myocardial dysfunction and hypotensive shock are very common among human survivors of cardiac arrest. For example, Laurent and colleagues reported that 90 of 165 consecutive patients admitted to the ICU after successful resuscitation following an out-of-hospital cardiac arrest needed vasoactive infusions for hypotensive shock.<sup>75</sup> Other studies have similarly demonstrated that left ventricular dysfunction and hypotension are common among adult and pediatric survivors following cardiac arrests and are generally reversible among long-term survivors.<sup>71,72,76-80</sup> Interestingly, postarrest myocardial dysfunction appears to be pathophysiologically similar to sepsis-related myocardial dysfunction, including increases in inflammatory mediator and nitric oxide production.<sup>75,77,78,81,82</sup> Although the optimal management of postarrest hypotension and myocardial dysfunction have not been defined, data suggest that aggressive hemodynamic support may improve outcomes. Controlled trials in animal models have shown that dobutamine, milrinone, or levosimendan can effectively ameliorate postarrest myocardial dysfunction.<sup>83-87</sup> In clinical observational studies, fluid resuscitation has been provided for patients with hypotension and concomitant low central venous pressure, and various vasoactive infusions, including epinephrine, dobutamine, and dopamine, have been provided for the myocardial dysfunction.<sup>71,72,76-80</sup>

*How should patients be treated in the postarrest setting?* An organized multidisciplinary postresuscitation protocol begins before the patient arrives at the hospital, continues in the emergency department (ED), and is tailored in the intensive care unit (ICU). Such a protocol that includes hemodynamic support, induced hypothermia, and percutaneous coronary intervention where indicated appears to improve outcomes in adults.<sup>80</sup> Postarrest myocardial dysfunction and hemodynamic instability are common and should be anticipated. Therefore, continuous electrocardiographic and hemodynamic monitoring should be provided for all patients following successful resuscitation from a cardiac arrest. Furthermore, postarrest echocardiography should be considered for monitoring myocardial function. Reasonable interventions for vasodilatory shock with low central venous pressure include fluid resuscitation and vasoactive infusions. Appropriate considerations for left ventricular myocardial dysfunction include inotropic infusions and afterload reduction.

### Pediatric Ventricular Fibrillation and Ventricular Tachycardia

Although asystole and pulseless electrical activity (PEA) are the most common rhythms seen with in-hospital pediatric cardiac arrest, VF or pulseless VT are not rare.<sup>10</sup> VF/VT may occur as the primary inciting arrest rhythm (i.e., arrhythmogenic arrest) due to a variety of underlying myocardial pathologies (acute infectious cardiomyopathies, congenital heart disease, Wolff-Parkinson-White syndrome, etc.) or electrolyte derangements. Of 1005 pediatric in-hospital cardiac arrests in the NRCPR database, 27% had VF/VT at some point during the resuscitation, 10% as an initial rhythm, an additional 15% as subsequent VF/VT (i.e., some time later during the resuscitation effort), and the timing could not be determined for

2%.<sup>12</sup> Among pediatric cardiac ICU patients, as many as 41% of the arrests have been associated with VF/VT.<sup>88</sup> Asphyxia-associated VF (presumably subsequent VF) is also well documented in pediatric drowning patients.<sup>89</sup>

Traditionally, VF and VT have been considered “good” cardiac arrest rhythms, resulting in much better outcomes than after asystole and PEA. However, NRCPR data establish that survival to discharge was more common among children with *initial* VF/VT than among children with *subsequent* VF/VT (35% vs. 11%; odds ratio 2.6, 95% confidence interval 1.2–5.8).<sup>12</sup> Surprisingly, the subsequent VF/VT group had worse outcomes than children with asystole/PEA (11% vs. 27% survival). These data suggest that outcomes after *initial* VF/VT in children (an arrhythmogenic arrest) are “good,” but outcomes after *subsequent* VF/VT (i.e., VF/VT in the setting of an asphyxial or ischemic arrest) are worse, even compared with initial asystole/PEA without subsequent VF/VT.

### Defibrillation

Defibrillation, defined as termination of VF, is necessary for successful resuscitation from VF cardiac arrest. The goal of defibrillation is return of an organized electrical rhythm with a palpable pulse. When prompt defibrillation is provided soon after the induction of VF in a cardiac catheterization laboratory, the rates of successful defibrillation and survival approach 100%. When automated external defibrillators are used within 3 minutes of adult-witnessed VF, long-term survival can occur in more than 70% of cases.<sup>90,91</sup> In general, the mortality rate increases by 5 to 10% per minute of delay to defibrillation.<sup>92</sup> Provision of high-quality CPR can improve outcomes and save lives. Because pediatric cardiac arrests are commonly due to progressive asphyxia or shock (or both), the initial treatment of choice is prompt CPR, not defibrillation. Therefore, rhythm recognition has been deemphasized in the latest PALS guidelines compared with adult cardiac arrests.<sup>14</sup> This historical emphasis must be balanced against the increasing evidence that VF in children is not rare, outcomes from arrhythmogenic VF arrests are superior to those from other types of cardiac arrests, and that early rhythm diagnosis is necessary for optimal care.

Because of the increasing awareness that “shockable” rhythms are not uncommon in children, greater attention has been focused on the dose for pediatric defibrillation. The recommended shock dose is 2 to 4 J/kg, which is based on animal studies of short-duration VF and a single retrospective study of in-hospital (short duration) VF with 91% (52/57) defibrillation success.<sup>93</sup> More recent piglet and out-of-hospital pediatric data indicate that 2 J/kg is often ineffective at terminating fibrillation.<sup>94,95</sup> In-hospital pediatric defibrillation data also suggest that 2 J/kg is often ineffective at terminating fibrillation.<sup>96</sup> Animal and clinical data suggest that a single pediatric dose of 50 J (i.e., the dose in pediatric AEDs) can be quite effective at terminating fibrillation.

### ■ SPECIAL CONSIDERATIONS: APPARENT LIFE-THREATENING EVENT, SUDDEN INFANT DEATH SYNDROME, AND DISCONTINUATION OF CARDIOPULMONARY RESUSCITATION

#### Sudden Infant Death Syndrome

##### Perspective

Passed in 1974, the Sudden Infant Death Syndrome (SIDS) Act assigned the responsibility for SIDS research to the National Institute of Child Health and Human Development (NICHD)

and provided focus for public information.<sup>97,98</sup> The NICHD established the first nationally recognized definition of SIDS as well as other terms describing infants who present with apnea, periodic breathing, and cardiopulmonary distress.<sup>99</sup>

*Apnea* is a cessation of airflow. The respiratory pause may be central or diaphragmatic (i.e., no respiratory effort), obstructive (usually caused by upper airway obstruction), or mixed. Short (<15 sec) periods of central apnea can be normal at all ages.

*Pathologic Apnea* is an abnormal respiratory pause that is prolonged (>20 sec), or is associated with cyanosis, marked pallor, hypotonia, or bradycardia.

*Apnea of Prematurity (AOP)* is periodic breathing with pathologic apnea in a premature infant. AOP usually ceases by 37 weeks' gestation (menstrual dating) but occasionally persists past term.

*Apnea of Infancy (AOI)* is an unexplained episode of cessation of breathing for 20 seconds or longer or a shorter respiratory pause associated with bradycardia, cyanosis, pallor, or marked hypotonia. This generally refers to infants who are older than 37 weeks' gestational age at the onset of pathologic apnea.

*Periodic Breathing (PB)* is a breathing pattern in which three or more respiratory pauses occur of greater than 3 seconds' duration with less than 20 seconds of respiration between the pause. Periodic breathing may be a normal event.

*Breath-holding Spells* occur when infants perform a Valsalva maneuver in response to pain, fright, crying, coughing, or defecation. During the spell, minute ventilation decreases without any adverse effects. Breath-holding spells, however, if severe and prolonged, may result in cyanosis, unconsciousness, and seizures.

*Apparent Life-threatening Event (ALTE)* is an episode that is frightening to the observer and is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic or pallid but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging. Often the observer fears that the infant has died. Terms for apparent life-threatening events, such as *near-miss SIDS* or *aborted crib death* are no longer used because they imply an unproven, misleading association between an ALTE and SIDS.

*Sudden Infant Death Syndrome (SIDS)* is "the sudden death of an infant under one year of age, which remains unexplained after a thorough case investigation, including performance of a complete autopsy, examination of the death scene, and review of the clinical history."

The National Center for Health Statistics reports that SIDS is the third leading cause of death in infants, accounting for 8% of deaths in children younger than 1 year of age.<sup>100</sup> SIDS may occur at any time during the first 2 years of life, but it is rare (1%) in children younger than 1 month of age and in those older than 1 year of age (2%). Ninety-five percent of SIDS infants die before 6 to 8 months, with a peak occurring between 2 and 4 months of age.<sup>101-104</sup> Some epidemiologic variation occurs among different racial and ethnic groups, with black, Native American, and Alaskan Native infants having rates two to three times higher than the national average.<sup>105-107</sup> Other epidemiologic risk factors include male sex and multiple births.<sup>99,108</sup>

## Distinguishing Principles of Disease

**Risk Factors for Sudden Infant Death Syndrome.** Although a number of risk factors have been studied; the following factors have been

consistently associated with an increased risk of SIDS: maternal smoking during pregnancy, preterm or low birth weight, male gender, prone sleep position, and overheating.<sup>105,108-112</sup>

Approximately 20% of all SIDS cases occur in the preterm population. Compared with age-matched controls, infants born at less than 37 weeks' and less than 33 weeks' gestation are 5 and 16 times, respectively, more likely to die of SIDS.<sup>112</sup>

The most important modifiable *risk factor* for SIDS is prone sleeping. In 1992, the American Academy of Pediatrics (AAP) recommended that infants be placed to sleep in a nonprone position to reduce the risk of SIDS.<sup>113</sup> The "Back to Sleep" (BTS) campaign was initiated in 1994 under the leadership of the NICHD, as a collaborative effort of the U.S. Public Health Service, the AAP, the SIDS Alliance, and the Association of SIDS and Infant Mortality Programs. Since then, the frequency of prone sleeping has decreased 50 to 90% worldwide as has the rate of SIDS.<sup>105,108,109,114-119</sup>

The prevalence of prone sleeping in the United States decreased from 70% in 1992 to 13% in 2004.<sup>105,120</sup> Racial disparities in rates of SIDS deaths have been noted as well as in the prevalence of prone positioning; blacks have a 2.5 times greater risk of SIDS and a prevalence of prone positioning of 21% compared with white infants who have a prone positioning rate of 11%.<sup>105,121,122</sup> Despite the association between prone sleeping and SIDS, some parents continue to place their infant to sleep in the prone position. Many parents and health practitioners do not realize that the supine sleeping position is also associated with other health benefits, such as decreased rates of nasal congestion, otitis media, and fever before the age of 1 month.<sup>123</sup>

The original 1992 recommendation from the AAP identified any nonprone position (supine or side) as reducing the risk for SIDS. Since then, however, studies have demonstrated that side sleeping is less stable, and has a higher risk for SIDS than the supine position.<sup>105,109,124</sup>

Other postnatal factors associated with SIDS include soft sleep surfaces and loose bedding, overheating, and bed sharing.<sup>125-129</sup> Polystyrene bead-filled pillows, soft pillows, quilts, comforters, sheepskin, and porous mattresses have been identified as risk factors for SIDS, particularly when placed under the sleeping infant.<sup>125</sup> Overheating with clothing and blankets, as well as higher room temperatures also increase the risk. Bed sharing may lead to suffocation of an infant by an overlying adult, and the risk of SIDS associated with co-sleeping is greater when the adult is under the influence of alcohol or other mind-altering drugs.<sup>129</sup>

Possible protective factors against SIDS have also been identified. A few retrospective studies have demonstrated a protective effect of breast-feeding; however, other analyses have failed to confirm the association after adjustment for confounding variables. Thus, the Task Force on Infant Sleep Position and Sudden Infant Death Syndrome does not recommend breast-feeding as a strategy for reducing SIDS.<sup>130</sup> Other studies have demonstrated a lower incidence of SIDS among infants who use pacifiers, possibly by stenting of the airway. Conversely, the use of pacifiers is associated with an increased susceptibility to otitis media, an increased rate of dental malocclusion, and a shorter duration of breast-feeding. Additional outcome studies are therefore required before specific recommendations regarding pacifiers can be made.<sup>108,109</sup>

The AAP Task Force on SIDS has made the following recommendations to reduce the risk of SIDS in the general population: (1) parents should place infants in the supine position for sleep (wholly on the back), and side sleeping is no longer recommended; (2) parents should not place infants to sleep on waterbeds, sofas, soft mattresses, or other soft surfaces; (3) soft

materials should not be placed in the infant's sleeping environment; (4) smoking in pregnancy should be discontinued as smoking has proven to be a major risk factor for SIDS; (5) bed sharing and co-sleeping may be hazardous and should be avoided; (6) parents should consider offering a pacifier at nap time and bed time; (7) overheating should be avoided; (8) parents should avoid using commercially available devices to prevent SIDS as none of the devices has been adequately safety tested; (9) parents should not use home monitors to reduce the risk of SIDS as home monitoring has no effect on the incidence of SIDS; and (10) parents should place the infant in the non-prone position while the infant is awake to prevent positional plagiocephaly.<sup>109</sup>

**Pathophysiology and Etiology of Sudden Infant Death Syndrome.** The pathophysiology of SIDS is multifactorial and includes genetic factors that may change an infant's response to environmental or infectious stressors, maturational factors that affect the infant's control of homeostatic mechanisms, and environmental factors, such as exposure to infection or being placed in the prone position.<sup>105,108,131</sup> This construct has been termed "the triple-risk theory,"<sup>105,132,133</sup> which suggests that when these factors combine, selected infants succumb to SIDS.

Genetic factors have not been fully defined, but recent data suggest multiple polymorphisms influence autonomic nervous system development and the ability of SIDS infants to respond to infectious or environmental stressors.<sup>105,131</sup> These reports suggest that SIDS infants have a delayed or deficient arousal response. Arousal is affected by gestational and postnatal age, and the arousal threshold is significantly elevated at 2 to 3 months, when the rate of SIDS is highest.<sup>134</sup>

Prone sleeping may further impair arousability. Prone sleep positions also cause a reduction in vasomotor tone with a lower resting blood pressure, a higher peripheral skin temperature, and a faster heart rate. A combination of sleep-induced reduction in vasomotor control with a reduction in central venous return and cardiac distension may trigger a brainstem-mediated bradycardia. Decreased central venous return compromises pulmonary perfusion and causes worsening hypoxia.<sup>135,136</sup> Prone positioning may exacerbate the rebreathing of exhaled gases trapped in soft bedding material, leading to hypercarbia and worsening hypoxia.<sup>137,138</sup>

**Diagnosis of Sudden Infant Death Syndrome.** The diagnosis of SIDS is made at autopsy after postmortem evaluation fails to reveal another cause of death. Autopsies of SIDS victims demonstrate the effects of chronic hypoxemia, but no specific findings are pathognomonic of SIDS.<sup>108,139-141</sup>

Guidelines are available for the diagnosis of SIDS by autopsy as well as for the on-scene investigation.<sup>141-144</sup> If a suspected SIDS death has occurred, a thorough investigation of the death scene may identify contributing factors, such as accidental asphyxiation or hyperthermia. Any findings suggestive of child abuse should be reported, although fewer than 5% of SIDS victims are discovered to have died of child abuse. However, in families with recurrent unexpected deaths, the estimated association increases to 55%.<sup>103,145</sup> Most investigations of the history, home circumstances, and postmortem examination are negative for child neglect or abuse. Child protection is rarely needed, but an investigation should be initiated if there is a recurrence of SIDS or an ALTE with a second baby.<sup>103</sup>

**Management of Sudden Infant Death Syndrome.** In the management of a SIDS case, the death scene investigation should delineate the location and position of the infant, the room temperature, type of surface, presence of soft toys, pillows, bedding materials, and the general condition of the house.

**Nonhospital Medical Considerations and Emergency Department Management of Sudden Infant Death Syndrome.** Nonhospital medical care providers and emergency physicians may be involved in the resuscitation

of infants who are apparent SIDS victims. In a study of apparent SIDS victims (cardiopulmonary arrest after being placed to nap by a caregiver) in Los Angeles and Orange Counties, California, all 113 infants with apparent SIDS ultimately died,<sup>146</sup> including the 30% of infants whose final diagnosis was not SIDS. Nonhospital management centers on the delivery of cardiopulmonary life support and rapid transport to the ED. These nonhospital providers may be faced with the complex decision to begin resuscitation and transport infants with possible SIDS or declare the infant with signs of death in the field.<sup>146,147</sup> Currently, no national guidelines are available for termination of resuscitation in the field for children; local practices dictate declaration of death without resuscitation as well as termination of resuscitation. Nonhospital providers generally feel uncomfortable in making the decision to terminate resuscitation, and patients are often transported to the ED for care.

Because CPR is unsuccessful in the majority of cases, the emergency physician must provide supportive care for the family. When the cause of death is unknown, appropriate samples (blood, urine, etc.) should be obtained. An autopsy should be performed on all SIDS deaths by a competent and experienced pathologist.<sup>52</sup>

**Psychosocial Considerations for Sudden Infant Death Syndrome.** The emergency physician and pediatrician must address psychosocial considerations in any SIDS case. The physician should be direct when informing parents that their child has died. The word *dead* or *died* should be used instead of confusing euphemisms as *passed on*.<sup>148-151</sup> Parents universally experience intense guilt, and siblings may also have guilt over the loss of their brother or sister. Additionally, parents may further intensify the guilt by accusing one another of not taking adequate care of the infant. The police investigation may arouse suspicion in neighbors and friends and leave the parents and caretakers socially alienated. The overall toll of guilt and social alienation is enormous, and the effects are manifested in increased rates of miscarriage, divorce, and infertility after a SIDS death. The outcome of SIDS for the family depends on the support they receive. Thus, the team approach, which includes the nurse, social worker, chaplain, emergency physician, and pediatrician, may provide comfort and information to the grieving family. The emergency physician and the pediatrician must recognize that they can play a pivotal role in helping the family to adjust to their loss, initiate the process of grieving, and educate the family about SIDS prevention.<sup>152,153</sup> The AAP and the American College of Emergency Physicians have outlined recommendations for emergency physicians in a joint policy statement entitled "Death of a child in the emergency department." Recommendations for emergency physicians caring for families can be found in Table 8-2.<sup>151</sup>

Health care providers may also experience guilt, self-reproach, and sadness after a SIDS death. Although the likelihood of survival for infants who present with SIDS is infinitesimally small, health care providers may require opportunities to openly express and work through these tumultuous emotions.

## ■ APPARENT LIFE-THREATENING EVENTS

### Perspective

#### Epidemiology of Apparent Life-Threatening Event

Children with ALTE account for 0.8% of all ED visits of those younger than 1 year of age, and 2% of pediatric hospitalizations. Generally, children with ALTE are younger than 1 year, with a median age of 2 to 3 months. Most studies also demonstrate a male predominance as high as 2:1.<sup>154,155</sup>



**Table 8-2 Recommendation for Emergency Physicians in Caring for Families of Children Who Have Died in the Emergency Department**

- Use a family-centered and team-oriented approach when a child dies in the ED.
- Provide personal, compassionate, and individualized support to families while respecting social, religious, and cultural diversity.
- Notify the child's primary care physician of the death and, as appropriate, work with the primary care physician in follow-up of postmortem examination results.
- Organize resources and staff to provide a coordinated response to a child's death, such as working with the primary care physician to notify subspecialty physicians of the death of their patient; identifying and reporting cases of child maltreatment; working with staff to provide resources to families for follow-up care and grief counseling; facilitating organ procurement; and assisting in critical stress management for prehospital and ED staff.

ED, emergency department.

Adapted from The American College of Emergency Physicians and the American Academy of Pediatrics Policy recommendations in the policy statement "Death of a child in the emergency department." *Ann Emerg Med* 40:409, 2004.

## Distinguishing Principles of Disease

### Pathophysiology and Etiology of an Apparent Life-Threatening Event

ALTE is a description of a characteristic clinical presentation; therefore, the pathophysiology of an ALTE has not been clearly defined. Children with ALTE pose a diagnostic and therapeutic challenge to emergency physicians because the cause of such events is diverse and ranges from minor to life-threatening. In addition, studies of children with ALTE reveal that in 50% of the cases, a definitive diagnosis will not be made.<sup>156,157</sup>

The etiology of ALTE is extensive (Table 8-3) and includes infection (sepsis, respiratory syncytial virus, or other respiratory viruses, pertussis, or central nervous system infection), gastroesophageal reflux disease (GERD) with or without obstructive apnea, congenital malformations (tracheomalacia, vascular rings, pulmonary slings), seizure disorder, cardiac dysrhythmias, congenital cardiac malformations, metabolic derangements (hypoglycemia), and child abuse.<sup>157</sup> A number of authors suggest clues to the various categories of diagnoses; however, many of the signs and symptoms of these conditions overlap.

ALTE may be a manifestation of child abuse, possibly from a smothering attempt, an intentional poisoning, or "shaken baby" syndrome.<sup>158,159</sup> The AAP Committee on Child Abuse and Neglect outlines certain circumstances that should alert the emergency physician to the possibility of intentional suffocation in children with ALTE (Table 8-4).<sup>103</sup> Injury associated with head trauma or child abuse may be difficult to distinguish in the absence of a reliable history. Intoxication, either accidental or intentional, as in Munchausen syndrome by proxy, can produce subsequent hypoventilation, hypoxia, cardiopulmonary arrest, and death.

In a retrospective study of 196 infants that presented with an ALTE, the discharge diagnoses included seizure (25%), GERD (18%), febrile convulsion (12%), bronchiolitis (9%), apnea (9%), pertussis (6%), choking (5%), upper respiratory tract infections (4%), cyanotic episode (2%), gastroenteritis (2%), asthma (1%), head injury (1%), feeding difficulties (1%), urinary tract infection (1%), and breath-holding (1%).<sup>160</sup>

Since GERD is physiologic and occurs in most infants, establishing the diagnosis of GERD does not prove that it is the cause of an ALTE.

An ALTE may be the first manifestation of an epileptic seizure, but the diagnosis is often difficult. A transient episode of apnea may be the only manifestation of a partial seizure, and the interictal electroencephalogram is characteristically normal. Seizures may be the cause for up to 11% of ALTEs, and a normal interictal electroencephalogram does not exclude seizures as the precipitating factor.<sup>161</sup>

**Table 8-3 Etiologies of Apparent Life-Threatening Event**

Cardiac
Dysrhythmias
Congenital heart disease
Child Abuse
Physical abuse
Munchausen syndrome by proxy
Gastrointestinal
GERD
Congenital malformations
Infectious
Meningitis/encephalitis
Pertussis
Respiratory syncytial virus
Sepsis
Metabolic
Hypoglycemia
Hypocalcemia
Hyponatremia
Inborn errors of metabolism
Neurologic
Seizure
CNS tumor
Arnold-Chiari malformations
Subdural or epidural hematoma
Respiratory
Foreign body aspiration
Obstructive sleep apnea
Respiratory infection
Other
Breath-holding spells
Vasovagal syncope
Drug/toxin exposure

CNS, central nervous system; GERD, gastroesophageal reflux disease.

QT prolongation has been associated with ALTE. Thus, an electrocardiogram is often recommended as an initial screen for differentiating an ALTE in the ED.<sup>162</sup>

Overall, the most common causes include GERD, seizure, and lower respiratory tract infection, accounting for 50% of the diagnoses associated with ALTE.

### Management of an Apparent Life-Threatening Event

The infant who presents with a history of an ALTE may look well and act normally at the time of the evaluation by the nonhospital medical provider or the emergency physician. However, infants who are judged by nonhospital personnel to have choked, turned blue, or are showing other signs suggestive of a possible ALTE should be considered seriously ill and transported to the ED for evaluation.<sup>157</sup> Fifty percent of children who present to the ED after an ALTE have an entirely

Table 8-4

**American Academy of Pediatrics Recommendations for Circumstances That Could Indicate Intentional Suffocation Versus Sudden Infant Death Syndrome**

Previous recurrent cyanosis, apnea or ALTE, while in care of the same person  
 Age at death greater than 6 months  
 Previous unexpected or unexplained deaths of one or more siblings  
 Simultaneous or nearly simultaneous death of twins  
 Previous death of infants, under the care of the same unrelated person  
 Discovery of blood on the infant's nose or mouth in association with ALTE

ALTE, apparent life-threatening event.

Adapted from Hymel KP and the American Academy of Pediatrics Committee on Child Abuse and Neglect and National Association of Medical Examiners:

Distinguishing sudden infant death syndrome from child abuse fatalities. *Pediatrics* 118:421, 2006.

normal clinical examination, and the final diagnosis often correlates poorly with the presenting signs and symptoms, which often includes cyanosis, breathing difficulties, abnormal movements, loss of consciousness, vomiting, pallor, and choking.<sup>157</sup>

In the ED, resuscitation must be the initial focus. Airway, breathing, and circulation should be stabilized. A complete history should be taken and a physical performed. If possible, the physician should obtain a detailed description of the infant at the time of discovery (especially the color and muscle tone of the infant), the duration of the episode, the resuscitation measures used, and the infant's response to the resuscitation measures. Other questions that may be pertinent include the following: Was the infant awake or sleeping? Were there symptoms of airway obstruction? Does the infant have any history or symptoms suggestive of GERD? Did the event occur after feeding? Did the episode occur after vigorous crying (suggestive of breath-holding)? Is there any family history of SIDS, apnea, or unexplained sibling death?

During the physical exam, the physician should note the presence of stridor or wheezing. The skin should be examined for suspicious bruising (patterned bruises or truncal bruising suggestive of child abuse), the extremities for abnormalities (fractures, burns, healing wounds, or other signs of unusual injury), and the eyes for pupillary changes or retinal hemorrhages (shaken baby syndrome). A recent study demonstrated that a dilated fundoscopic examination in 128 patients who presented with an ALTE-detected retinal hemorrhages in 1.4% of the patients and helped detect child abuse in 2.3% of the patients.<sup>159</sup> Thus, in addition to obtaining a detailed family and social history, it may be prudent to conduct a dilated fundoscopic exam in children who present to the ED after an ALTE.

The ED evaluation of children presenting with ALTE must be tailored to the child's history and physical examination but often includes laboratory and radiographic studies. Laboratory evaluation may include complete blood count, serum glucose, electrolytes, blood and urine cultures if the child is younger than 1 month of age or febrile, a toxicology screen, and an electrocardiogram.<sup>163</sup> The infants may also undergo a screen for inborn errors of metabolism, chest radiograph, computed tomographic scan of the head, and lumbar puncture depending on signs and symptoms at presentation, although few diagnostic tests are positive.<sup>163-165</sup>

Inpatient evaluation often includes electroencephalogram, an evaluation for GERD (24-hour pH probe and barium esophagram), polysomnography for sleep disorders, and possibly flexible and rigid laryngoscopy.

The outcome of an ALTE depends on the underlying cause. In a retrospective patient review of 196 ALTE patients, there were no deaths.<sup>160</sup> The follow-up revealed a high percentage of asthma and seizures, as well as GERD requiring Nissen fundoplication. Infants who survive an ALTE generally do well

in follow-up. However, some rare complications do occur, including pulmonary edema, aspiration pneumonia, and neurologic sequelae secondary to hypoxia.<sup>166</sup>

Based on the results of a study of 59 infants with ALTE, Claudius and Keens developed a clinical decision rule suggesting that infants younger than 1 month of age and those with recurrent ALTE should be admitted for evaluation, but other well-appearing children with ALTE may be discharged with close follow-up.<sup>167</sup> Fu and Moon suggest other conditions under which it may be safe to discharge a patient with an ALTE, and these include the following: (1) the episode is brief, nonsevere, and self-resolving; (2) the cause is probably a nonprogressive condition such as GERD; and (3) the infant has no comorbidities and is well-appearing.<sup>154</sup> It should be noted, however, that none of these proposed criteria has been adequately validated in clinical trials to determine which patients may be safely discharged from the ED. Multiple studies show that 84% of cases of ALTE are admitted for evaluation and monitoring.

**Home Monitoring.** Monitoring devices measure chest wall movement and heart rate. Parents must learn about equipment maintenance, interpretation of alarms, and CPR. Technical support should be available to the parents 24 hours a day. Parents may misinterpret alarms when they sound, and the majority of alarms that parents felt required resuscitation were associated with normal electrocardiograms. Due to the lack of demonstrated efficacy and the frequency of false alarms, a great deal of controversy is associated with the use of home monitoring. In fact, the AAP Committee on Fetus and Newborn SIDS and home monitoring does not recommend home cardiorespiratory monitoring to prevent SIDS, since studies show that SIDS death is not reduced by home monitor use. Home monitors, however, may be warranted for premature infants with an ALTE, especially those younger than 43 weeks postmenstrual age or those with extreme episodes.<sup>168</sup> Both pediatricians and emergency physicians should be consulted about monitor alarms. Admission to the hospital for further care may be prudent if the event was associated with the infant changing color or the infant required vigorous resuscitation.

**When Should Cardiopulmonary Resuscitation Be Discontinued?** Several factors determine the likelihood of survival after cardiac arrest, including the mechanism of the arrest (e.g., traumatic or asphyxial), location (out-of-hospital vs. in-hospital, ward vs. PICU), response (e.g., monitored vs. unmonitored, witnessed vs. unwitnessed), and underlying pathophysiology (e.g., cardiomyopathy, congenital defect, single-ventricle physiology, drug toxicity or metabolic derangement). Additionally, discontinuation of resuscitation in the nonhospital setting is further complicated because emergency medical service providers are not comfortable making this decision before transport to the hospital.<sup>97</sup> These factors should all be considered before deciding to terminate resuscitative efforts.

Continuation of CPR has been considered futile beyond 15 to 20 minutes of CPR or when more than two doses of epinephrine are needed.<sup>169-181</sup>

**Future Directions.** New epidemiologic initiatives, such as the National Registry for Cardiopulmonary Resuscitation for in-hospital cardiac arrests and the large-scale, multicenter National Heart, Lung, and Blood Institute Resuscitation Outcome Consortium for out-of-hospital arrests, are providing new data to guide our resuscitation practices and generate

hypotheses for new approaches. Innovative technical advances, such as directive and corrective real-time feedback, can increase the likelihood of effective basic life support and skill sorely lacking in many resuscitative efforts today. In addition, team dynamic training and debriefing can rapidly identify weaknesses and improve operational performance.<sup>182</sup> Simulation technology will be increasingly used for effective team training to provide excellent resuscitations<sup>183</sup> and improve outcomes.

## KEY CONCEPTS

- Excellent CPR is the foundation for successful resuscitation from cardiac arrest; without it all other subsequent interventions are rendered meaningless. The mantra for excellent CPR is: "Push Hard, Push Fast, Allow Full Chest Recoil, and Minimize Interruptions." This "new emphasis" on CPR is intended to enhance CPR performance so that more lives can be saved.
- The thumb-encircling technique is recommended over the two-finger technique for chest compression in infants.
- Prospective and retrospective studies indicate that use of high-dose epinephrine in adults or children does not improve survival and may be associated with a worse neurologic outcome.
- Despite the dramatic decline in the incidence of SIDS in the past several decades, SIDS remains the leading cause of postneonatal mortality in the United States, accounting for one-third of all such deaths and is the third most common cause of infant deaths.
- Emergency physicians may play a key role in SIDS education and prevention. Parents must be taught the importance of the supine sleeping position, smoking cessation, and the elimination or avoidance of co-sleeping, overheating, and soft or loose bedding material.
- The team approach that combines the efforts of the nurse, social worker, chaplain, emergency physician, and pediatrician may help the family to adjust to their loss, initiate the process of grieving, and counsel the family about SIDS.
- Although the infant who presents with a history of an ALTE may look well and act normally at the time of the evaluation by the nonhospital medical provider or the emergency physician, these infants and children generally require admission and monitoring, as the final diagnosis and the presenting symptoms often correlate poorly.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## CHAPTER 9 Neonatal Resuscitation

Suzan S. Mazor and Eileen J. Klein

### ■ PERSPECTIVE

Approximately 10% of newborns require some resuscitative assistance at birth, and approximately 1% require extensive resuscitative measures.<sup>1</sup> Appropriate equipment and preparation, knowledge of neonatal physiology and response to stress, and skill in performing the necessary procedures are essential to successful resuscitation. Preparation for neonatal resuscitation requires an understanding of how it differs from pediatric and adult resuscitation, as follows:

1. Newborns have rapidly changing cardiopulmonary physiology, their own range of normal vital signs (Table 9-1), and unique responses to stress.<sup>2,3</sup>
2. The approach to newborn resuscitation focuses almost *entirely* on respiratory, not cardiac, management.
3. Because of their small size, infants require special equipment.

### ■ PATHOPHYSIOLOGY

#### Transition from Fetal to Extrauterine Life

The successful transition from the fetal to the extrauterine environment requires two major cardiorespiratory changes: (1) removal of fluid from unexpanded alveoli to allow ventilation and (2) redistribution of cardiac output to provide lung perfusion. Failure of the development of either adequate ventilation or adequate perfusion leads to shunting, hypoxia, and ultimately reversion to fetal physiology.<sup>2</sup>

In utero, the pulmonary alveoli are filled with pulmonary fluid. Removal of this fluid is partially accomplished by vaginal delivery, which compresses the fluid into the bronchi, trachea, and pulmonary capillary bed. Most pulmonary fluid is removed by the first few breaths; the amount of fluid removed depends on the forcefulness of these breaths. Expansion of alveoli requires the generation of high intrathoracic pressures and the presence of surfactant to maintain alveolar patency. The quality of the first few breaths is crucial to the establishment of adequate ventilation.

The fetal lung is poorly perfused. Because the pulmonary arterial bed is intensely vasoconstricted, the fetal lung receives only 40% of the right ventricular cardiac output; most of the right ventricular output is shunted from the pulmonary artery through the ductus arteriosus to the descending aorta. After the first few breaths, with exposure to diffused alveolar oxygen, pulmonary vascular resistance decreases. The fetal shunt through the ductus arteriosus reverses as systemic vascular

resistance increases; then the shunt ceases by 15 hours of age as the ductus also constricts. This reversal of flow allows all right ventricular output to perfuse the lungs. If hypoxia or severe acidosis occurs, however, the muscular pulmonary vascular bed constricts again, and the ductus may reopen. The reinstitution of fetal circulation, with its attendant shunting, leads to ongoing hypoxia and is termed *persistent fetal circulation*. Resuscitation facilitates the first few breaths, prevents and reverses ongoing hypoxia and acidosis, and assists the newborn in the transition to extrauterine life.

#### Neonatal Responses

##### Hypoxia

The newborn's clinical response to severe hypoxia is unique.<sup>4</sup> In utero or intrapartum asphyxia (pathologic lack of oxygen to the fetus before or during delivery) precipitates a sequence of events termed *primary apnea* and *secondary apnea*. After initial hypoxia, the infant gasps rapidly, followed by cessation of respirations (primary apnea) and a decreasing heart rate (HR). At this point, only simple stimulation and oxygen are needed to reverse bradycardia and assist the development of ventilation. With ongoing asphyxia, however, the infant takes several final deep, gasping respirations, followed by secondary apnea, worsening bradycardia, and decreasing blood pressure; in this case more vigorous and prolonged resuscitation is needed to restore ventilation and an adequate circulation. Apnea in the newborn should be assumed to be secondary apnea and treated rapidly with ventilatory assistance.

The presence of respirations *may not* ensure adequate ventilation. In addition, signs of hypoxia (e.g., cyanosis, lethargy, unresponsiveness) may have other causes. Bradycardia in the newborn (HR < 100 beats/min) almost always reflects inadequate ventilation and oxygenation. *Bradycardia is a major indicator of hypoxia.*<sup>5-7</sup>

##### Hypothermia

The newborn's inability to maintain body temperature (36.5–37°C) has severe physiologic consequences. The newborn cannot generate heat by shivering, cannot retain heat because of low fat stores, and has a relatively large surface-to-volume area. In addition, the newborn is at risk for heat loss because of a high metabolic rate, wet amniotic fluid covering, and exposure to a relatively cool environment, especially in contrast to intrauterine temperature. The body temperature easily decreases, and low body temperatures can lead to meta-



**Table 9-1 Normal Vital Signs in the Newborn**

WEIGHT	HEART RATE (BEATS/MIN)	RESPIRATORY RATE (BREATHS/MIN)	SYSTOLIC BLOOD PRESSURE (MM HG, MEAN)
≥3 kg (full term)	>100 (100–180)	40–80	60–70 (45–55)
<3 kg (premature)	>100 (100–180)	40–80	40–60 (35–45)

bolic acidosis, increased oxygen consumption, hypoglycemia, and apnea.<sup>2,8</sup> Some studies have suggested that selective cerebral hypothermia in asphyxiated infants may protect against brain injury, but there is not enough evidence to implement such a therapy until further study is performed.<sup>9–13</sup> Currently there is insufficient data to recommend routine use of hypothermia after resuscitation of infants with possible asphyxia.<sup>1</sup>

### Hypoglycemia

The newborn is at risk for developing hypoglycemia (defined as glucose level < 40 mg/dL if the newborn weighs > 2.5 kg or < 30 mg/dL if < 2.5 kg) when stressed because of poor glycogen stores and immature liver enzymes. Hypoglycemia is common in premature or small-for-gestational-age infants and in infants born to diabetic mothers. It also develops in response to respiratory illness, hypothermia, asphyxia, and sepsis. Hypoglycemia may be asymptomatic or may cause an array of symptoms, including apnea, color changes, respiratory distress, lethargy, jitteriness, seizures, acidosis, and poor myocardial contractility.<sup>14</sup> Low blood glucose has been associated with adverse neurologic outcomes in both animal and clinical studies.<sup>15,16</sup>

## ■ INDICATIONS FOR RESUSCITATION

Any infant born outside of the controlled environment of the delivery room should be considered in need of resuscitation.<sup>17</sup> Minimal intervention may be required, but a standardized approach as described in this chapter should be followed. Some specific conditions increase the likelihood that resuscitation will be required. Premature infants pose a special problem because of their immature lungs and susceptibility to hypothermia. Adequate ventilation and warming are essential to a successful resuscitation.

The presence of meconium in the amniotic fluid at delivery indicates that the infant has been stressed before delivery and warrants special consideration in resuscitation. When delivered, a nonvigorous infant with meconium in the amniotic fluid must have the trachea suctioned before other steps in resuscitation to prevent aspiration of meconium.

Medications given to the mother or illicit drugs taken before delivery can lead to respiratory depression in the newborn. Maternal opioid administration or opioid use should be considered in any newborn with isolated respiratory depression. Naloxone reverses respiratory depression caused by opioids. Naloxone may have a shorter half-life than the original maternal opioid; so the neonate should therefore be monitored closely for recurrent apnea or hypoventilation, and subsequent doses of naloxone may be required.<sup>1</sup> Use of naloxone may precipitate acute withdrawal in infants who have prolonged intrauterine opioid exposure.<sup>18,19</sup> Therefore, in infants whose

mothers may have had long-term opioid exposure, support of ventilation may be preferable to reversal using naloxone.

Hemorrhage caused by abruptio placentae, placenta previa, trauma, or other complications can lead to respiratory depression and shock. Hemorrhage is one of the few situations in which fluid resuscitation is required.

No reliable set of parameters has been identified for newborns who should not receive resuscitative efforts.<sup>20</sup> Currently, resuscitation is not recommended for neonates with confirmed gestational age less than 23 weeks; those with birth weight less than 400 g; and those with confirmed anencephaly, trisomy 13, or trisomy 18.<sup>1,21,22</sup> In the out-of-hospital setting or in the emergency department, every attempt should be made to stabilize the neonate until it is clear that attempted or continued resuscitation would not improve the patient's chance of survival. Infants with no signs of life (no heart beat and no respiratory effort) after 10 minutes of resuscitation show either a high mortality or severe developmental delay. After 10 minutes of continuous and adequate resuscitative efforts, discontinuation may be justified if there are no signs of life.<sup>23,24</sup>

Few situations require deviations from the approach described here. The presence of meconium may require intervention after delivery. Other anatomic anomalies require special care and include diaphragmatic hernia, meningomyelocele, abdominal anomalies (e.g., gastroschisis, omphalocele), and upper airway obstructive lesions (e.g., bilateral choanal atresia, Pierre Robin sequence).

## ■ SPECIFIC DISORDERS

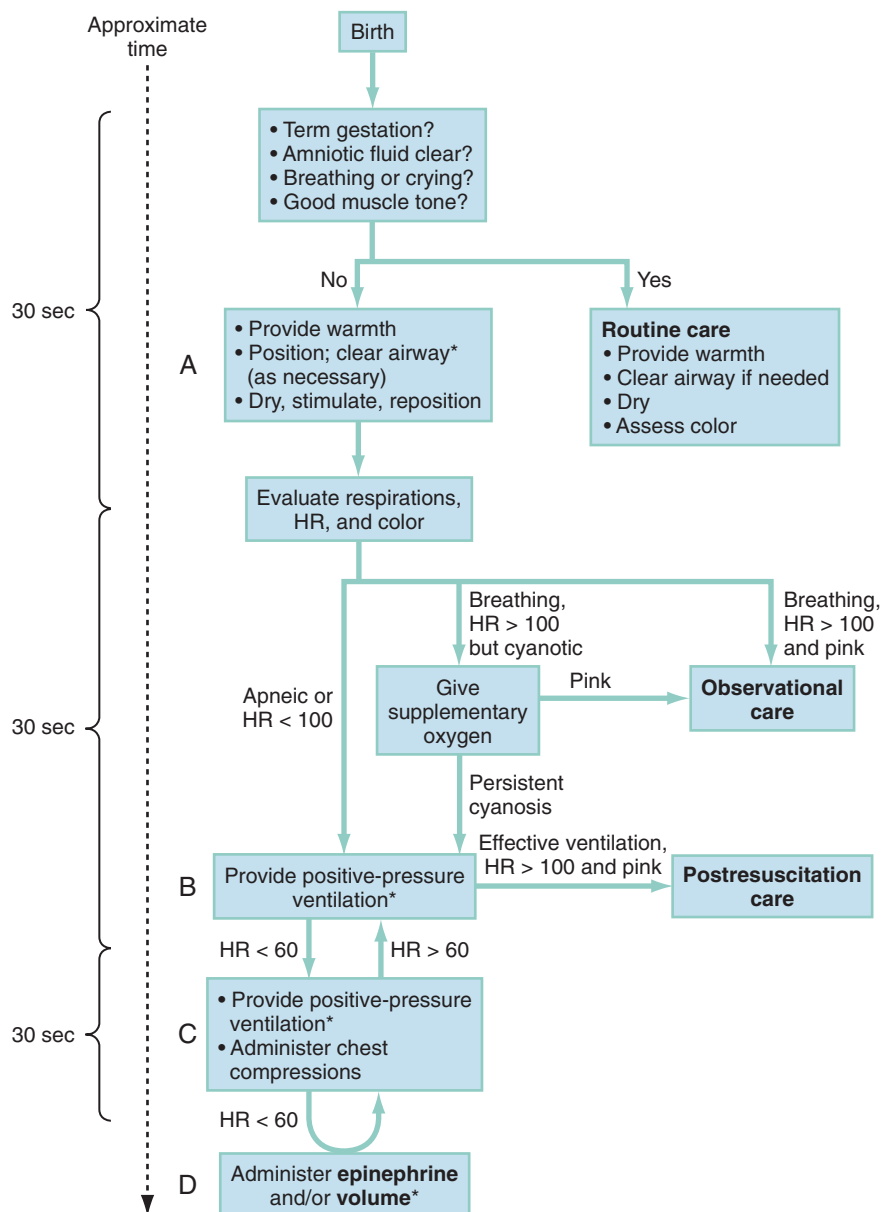
### Meconium Aspiration

Meconium in the amniotic fluid is a sign of in utero distress, and the presence of thick or particulate meconium before or at delivery should raise concern about the potential for aspiration. Aspiration of meconium and its consequences can be avoided by rapid intervention to avoid aspiration. Previous recommendations included suctioning meconium from the infant's airway after delivery of the head but before delivery of the shoulders (intrapartum suctioning). However, evidence from a large multicenter trial did not show benefit from intrapartum suctioning.<sup>25</sup> Therefore, current recommendations no longer advise routine intrapartum suctioning for infants born to mothers with meconium-stained fluid. Decision to perform endotracheal intubation with tracheal suctioning after delivery of the infant should be made based on the vigor of the infant, rather than on the consistency of the meconium (e.g., thick or particulate vs. thin). Infants with meconium-stained fluid and with any of the following are candidates for tracheal suctioning: (1) absent or depressed respirations, (2) poor muscle tone, or (3) HR less than 100 beats/min.<sup>21,22,26</sup> In such newborns, a meconium aspirator should be attached to the endotracheal tube (ETT) and connected to wall suction at 100 mm Hg or less. The ETT is withdrawn as suction is being applied. The ETT with meconium aspirator serves as the ideal suction catheter. Because of its narrower width, a suction catheter placed in the ETT does *not* suction meconium effectively. Reintubation and suction should be repeated until the meconium clears. Two passes are usually sufficient. When these steps are completed, the resuscitation should continue, beginning with the steps at the top of the neonatal flow algorithm (Fig. 9-1).

### Anatomic Anomalies

The neonate should be intubated as soon as possible if a prenatal diagnosis of diaphragmatic hernia was made or if a diaphragmatic hernia is diagnosed on chest radiograph. Bag-mask

**Figure 9-1.** Neonatal flow algorithm.\*Endotracheal intubation may be considered at several steps. (From American Heart Association, American Academy of Pediatrics, Pediatrics 117:e1029, 2006. © Copyright 2006 American Academy of Pediatrics.)



ventilation distends the stomach and worsens respiratory distress because of the presence of the stomach in the chest cavity.

Infants with meningomyelocele should not be placed on their backs to avoid pressure on the defect, but on their stomachs or sides. The resuscitation should be conducted in this position if possible. The spinal defect should be covered with warm sterile gauze pads soaked in warm sterile saline and covered with a plastic covering. Infants with gastroschisis or omphalocele should be resuscitated as needed; in the same manner as for patients with meningomyelocele, the defect should be covered with an occlusive plastic covering to decrease water and heat loss.

Because newborns are obligate nose breathers, bilateral choanal atresia causes upper airway obstruction and respiratory distress. It is diagnosed by the inability to pass a catheter through either nare into the oropharynx. An oral airway bypasses the obstruction. Patients with Pierre Robin sequence have small jaws and large tongues leading to upper airway obstruction. A nasal or oral airway should be able to bypass the

obstruction; if not, intubation may be necessary. It is technically difficult to intubate a patient with Pierre Robin sequence, so a laryngeal mask airway (LMA) may be placed instead.<sup>27</sup> Consultation with anesthesiology may be needed.

## ■ PREPARATION

To maximize the effectiveness of resuscitation, the emergency department should have a prestocked drug pack, standardized equipment (Box 9-1), and staff familiar with newborn resuscitation.<sup>4,22,20,28</sup> The pediatric Broselow Emergency Tape has a section that can be used to determine equipment size and drug dosages for newborn resuscitation for infants weighing greater than or equal to 3 kg.<sup>29,30</sup>

It is crucial to use universal precautions and to wear gown, gloves, and eye protection during neonatal resuscitation. For adequate preparation, the heat source must be turned on early, and the resuscitation table must be warm when the newborn is placed on it. Equipment of proper size is essential, especially respiratory equipment because it is most likely to be

**BOX 9-1 EQUIPMENT NEEDED FOR NEONATAL RESUSCITATION**

1. Gown, gloves, and eye protection (universal precautions)
2. Blankets (to warm and dry infant)
3. Radiant warmer
4. Bulb syringe
5. Suction and suction catheters (French #5, #8, and #10)
6. Self-inflating bags (450 and 750 mL)
7. Masks (premature, newborn, and infant sizes)
8. Laryngoscope with straight blades (No. 0 and 1)
9. Endotracheal tubes with stylets (2.5, 3, and 3.5 mm)
10. Scissors and tape to stabilize endotracheal tube
11. Meconium aspirator
12. Umbilical catheters (French #3.5 and #5)
13. Hemostats, sterile drapes and gloves, povidone-iodine solution, scalpel, umbilical tape, suture, and three-way stopcock for umbilical vessel catheterization

**BOX 9-2 MATERNAL HISTORY QUESTIONS**

1. What is the estimated gestational age?
2. Is this a multiple gestation?
3. Is meconium present?
4. Is there a history of vaginal bleeding?
5. Were medications given or drugs taken?

used, and ventilation is the key to most resuscitative efforts. Appropriately sized self-inflating devices and ventilation masks decrease complications from overventilation and prevent injury or inability to ventilate because of improper mask fit.

If available, additional information may be helpful in preparing for resuscitation (Box 9-2). The estimated gestational age provides information about possible prematurity and associated complications. Multiple births require more equipment and personnel, and the newborns are at greater risk for prematurity and its complications. Meconium present in the amniotic fluid may require suctioning of the neonate's trachea after delivery. A history of maternal vaginal bleeding increases the likelihood of hypovolemic shock and respiratory distress in the newborn. A history of medication administration or drug use may provide clues to the cause of respiratory depression in the neonate.

**MANAGEMENT**

An organized approach is key to successful resuscitation outside and inside the delivery room. The American Heart Association and the American Academy of Pediatrics have published a neonatal flow algorithm (see Fig. 9.1)—a stepwise approach to neonatal resuscitation. These steps are discussed in this section.<sup>1</sup>

**Dry, Warm, Position, Suction, Stimulate, Assess Need for Further Intervention**

To prevent complications caused by hypothermia, all newborns should be dried off as soon as possible after delivery and placed under a radiant heat source. Wet blankets should be replaced after drying with dry, preferably warm blankets. Next, the neonate should be positioned to maximize air entry and avoid obstruction of airflow. Because of the infant's relatively large occiput and anterior airway, an open airway is best

**Table 9-2 Apgar Score**

SIGN	0	1	2
Heart rate (beats/min)	Absent	Slow (<100)	>100
Respirations	Absent	Slow, irregular	Good, crying
Muscle tone	Limp	Some flexion	Active, good flexion
Reflex irritability	No response	Grimace	Cough, sneeze
Color	Blue, pale	Pink body, blue hands/feet	Pink

achieved with the neck in slight extension. The slightly extended position is best accomplished by placing a rolled diaper or small towel *under the infant's shoulders*. Placement under the neck is not useful, and a towel that is too large and under the shoulders leads to hyperextension at the neck and possible airway occlusion.

If meconium is present and the newborn has poor respirations, poor tone, or bradycardia (HR < 100 beats/min), the trachea should be suctioned with an ETT before any other intervention. If no meconium is present, the newborn may be suctioned with bulb or mechanical suction (<100 mm Hg wall suction). The mouth should be suctioned first, followed by the nose. The mouth is suctioned first to avoid aspiration of material if the infant takes in a breath after suctioning of the nose. Vigorous or deep suctioning can lead to a vagal response, with subsequent bradycardia, or to apnea, and should be avoided.<sup>31</sup>

Usually these measures adequately stimulate the infant to breathe effectively and may be the only measures needed to resuscitate a newborn. If adequate respirations are not present at this point, stimulation of the infant is needed; this is best done by flicking the soles of the feet and rubbing the back. It is important to avoid stimulation that is too vigorous because it does not aid in initiation of respirations and may stress the newborn. If stimulation is not effective in initiating respirations, bag-mask ventilation is required followed by intubation if necessary.

The Apgar score, comprising HR, respiratory effort, muscle tone, reflex irritability, and color, has been used as a prognostic indicator in newborns (Table 9-2). The Apgar score is not useful in resuscitation management, however.<sup>32</sup> Muscle tone and reflex irritability do not aid in the assessment of the newborn during resuscitation.<sup>32</sup> HR, respiratory effort, and color are the important indicators of hypoxia and should be monitored continuously. Further resuscitative efforts are required if respiratory effort is insufficient, HR is less than 100 beats/min, or central cyanosis is present.

**Oxygen, Ventilation, Intubation**

Any infant who is cyanotic or appears to be in respiratory distress (grunting, nasal flaring, tachypnea) should be given 100% oxygen. If the infant is apneic, appears to be in severe respiratory distress, has an HR of less than 100 beats/min, or has central cyanosis despite oxygen administration, bag-mask ventilation (with a manometer, if available) should be initiated. Although resuscitation with 100% oxygen is recommended, especially for hypoxia, more recent studies support the effectiveness of room air if 100% oxygen is not available for bag-mask ventilation.<sup>21,22,33-36</sup> The initial breaths require higher pressure (30–40 mm Hg) to remove lung fluid and to get the chest to rise. Subsequent breaths generally require 20 mm Hg.

Excessive pressures, more than is needed to achieve chest rise should be avoided since barotraumas may result. The primary measure of adequate initial ventilation is a prompt improvement in HR. An appropriately sized mask with a good seal (covering the mouth and nose, but not the eyes), proper positioning of the infant, and use of appropriate pressure to attain chest wall movement are essential for effective ventilation. The newborn should be ventilated at 40 to 60 breaths/min, unless blood gases dictate otherwise. If bag-mask ventilation is required for more than 2 minutes, an orogastric tube should be placed to prevent respiratory compromise from stomach distention.<sup>4</sup>

Endotracheal intubation may be indicated at several points during neonatal resuscitation: when tracheal suctioning for meconium is needed, if bag-mask ventilation is ineffective or prolonged, when chest compressions are performed, and for extremely low-birth-weight infants or infants with anatomic anomalies (e.g., diaphragmatic hernia). Box 9-1 lists the equipment needed for endotracheal intubation. Confirmation of proper ETT placement should include detection of expired carbon dioxide.<sup>37-40</sup>

Acute deterioration (bradycardia, decreased oxygen saturation) after intubation should suggest one of the following problems (DOPE)<sup>41</sup>:

1. **Dislodgment:** The ETT is no longer in the trachea (right main stem bronchus or esophagus).
2. **Obstruction:** Secretions are obstructing airflow through the ETT.
3. **Pneumothorax**
4. **Equipment:** Oxygen is not being delivered to the patient (check equipment).

If the patient acutely deteriorates after intubation, the equipment should be checked quickly; if no explanation is obvious, the patient should be extubated and ventilated with a self-inflating resuscitator (bag-mask ventilation device). Time should not be wasted adjusting or suctioning the ETT if the patient is bradycardic. If unequal breath sounds are present after extubation, or if the patient is not improving with effective ventilation, needle aspiration of the chest should be considered for treatment of a possible pneumothorax.

The LMA has been shown effective for ventilating full-term newborns<sup>42-44</sup>; however, there are limited data on LMA use in preterm infants.

## Chest Compressions

Bradycardia (HR < 100 beats/min) is the major indicator of hypoxia. Most infants respond promptly to effective ventilation with 100% oxygen. If a neonate has an HR of less than 60 beats/min despite oxygen and adequate ventilation (good air movement and chest rise) for at least 30 seconds, chest compressions should also be provided.<sup>1,22</sup> Chest compressions should be performed at a rate of 90/min, with 30 breaths/min for a total of 120 events/min. The preferred method for performing chest compressions is as follows:

The fingers of both hands encircle the chest and support the back. The thumbs of both hands are placed side by side or one over the other on the sternum just below the nipple line. The depth of compression is one third the anteroposterior diameter of the chest.

Respirations, HR, and color should be reassessed about every 30 seconds, and coordinated chest compressions and ventilation should continue until the spontaneous HR is greater than or equal to 60 beats/min.<sup>1</sup>

## Medications

Few neonates require the use of medications during resuscitation.<sup>45</sup> Medications are indicated for bradycardia or asystole that does not respond to effective ventilation and chest compressions, and for hemorrhage (maternal, fetal, or placental) that requires fluid resuscitation.<sup>46</sup> Naloxone may be needed for respiratory depression caused by maternal ingestion of opioids before delivery.

The only medications that should be used during the early phase of neonatal resuscitation are oxygen, epinephrine, and volume expanders (Table 9-3). Albumin has been removed as an initial resuscitation drug but may be used in the postresuscitation phase. Dopamine should be reserved for prolonged resuscitation. Naloxone should be used only after the neonate is adequately ventilated. Sodium bicarbonate should not be used in most resuscitations; it may be beneficial in the rare instance of a prolonged resuscitation when metabolic acidosis has been documented and ventilation is adequate.<sup>47</sup> No current evidence supports the use of atropine or calcium in neonatal resuscitation.

Vascular access is a challenge in neonatal resuscitation. The preferred route of immediate vascular access is the umbilical vein because it is easily identified and cannulated. Because of

**Table 9-3 Resuscitation Medications**

MEDICATION	CONCENTRATION	DOSE	ROUTE	CONSIDERATIONS
Oxygen	100%		Blowby, ET	
Epinephrine	1:10,000	0.01–0.03 mg/kg (0.1–0.3 mL/kg)	IV (preferred), ET	
Naloxone	0.4 mg/mL	0.1 mg/kg (0.25 mL/kg)	IV, IM, IO, SQ	
Glucose	D <sub>10</sub> W	2–4 mL/kg	IV	Avoid higher concentrations
Volume expanders*	Whole blood	10 mL/kg	IV	Give over 5–10 min; repeat as needed
	Normal saline	10 mL/kg	IV	
	Ringer's lactate	10 mL/kg	IV	
Dopamine	Concentration varies among institutions.	Continuous IV infusion at 5 µg/kg/min Increase to 20 µg/kg/min as needed		

\*5% albumin/saline no longer recommended for use during initial resuscitation efforts.

D<sub>10</sub>W, 10% dextrose in water; ET, endotracheal; IM, intramuscular; IV, intravenous; SQ, subcutaneous.



potentially serious complications (infection, portal vein thrombosis), the umbilical vein cannula should be removed immediately after stabilization after other access (e.g., umbilical artery catheterization) has been attained. Other routes include peripheral veins and the femoral vein. Intraosseous access can be problematic in neonates (especially premature infants) because of bone fragility and the small size of the intraosseous space.<sup>22</sup> If vascular access cannot be achieved, some drugs (e.g., lidocaine, epinephrine, atropine) can be given through the ETT. The medication should be injected directly into the ETT, followed by several positive-pressure ventilations.<sup>4,41</sup>

### Oxygen

The first resuscitation medication that should be used is 100% oxygen. Indications for oxygen use include central cyanosis and respiratory distress (nasal flaring, grunting, tachypnea, apnea).

### Epinephrine

Epinephrine is indicated for asystole, and for an HR less than 60 beats/min despite effective ventilation with 100% oxygen and chest compressions. Although epinephrine may be given by ETT, the preferred administration route is intravenous (IV). The IV dose is 0.01 to 0.03 mg/kg or 0.1 to 0.3 mL/kg of 1:10,000 solution. Repeat doses may be given every 3 to 5 minutes.<sup>22,48,49</sup> If the endotracheal route is used, doses of 0.01 or 0.03 mg/kg will likely be ineffective. While access is being obtained, administration of up to 0.1 mg/kg through the ETT may be considered, but the safety and efficacy of this practice have not been evaluated.<sup>1</sup>

### Naloxone

Respiratory depression induced by opioids given or taken within 3 to 4 hours of delivery can be reversed with naloxone. If respiratory depression is present, and if it is unclear whether the mother took opioids before delivery, reversal with naloxone may be attempted. The dose is 0.1 mg/kg IV, IO, SQ, or intramuscularly (IM). Administration of naloxone by ETT is not recommended in newborn resuscitation.<sup>1</sup> The duration of action of naloxone is 1 to 4 hours, depending on route of administration. Repeat dosing may be necessary, and the patient should be monitored carefully. Naloxone is not always needed in a newborn with respiratory depression. It may precipitate withdrawal seizures in an infant born to a drug-addicted mother.<sup>19,49</sup> The priority of care is support of ventilation with bag-mask device and intubation, if necessary. Naloxone should be considered only after ventilatory support is achieved.

### Glucose

Hypoglycemia should be considered in a neonate undergoing resuscitation. Hypoglycemia is diagnosed with a rapid bedside glucose or serum glucose measurement. Treatment is indicated only for documented hypoglycemia: glucose less than 40 mg/dL in a full-term infant (>2.5 kg) and less than 30 mg/dL in a premature infant (<2.5 kg). Hypoglycemia is treated with 2 to 4 mL/kg of 10% dextrose in water (D<sub>10</sub>W). Higher concentrations of glucose (e.g., 25% dextrose in water, D<sub>25</sub>W) are hyperosmolar and should be avoided. Repeat glucose measurement should be obtained 10 to 20 minutes after glucose administration.

### Volume Expanders

Volume expanders are indicated when acute bleeding is evident with signs of hypovolemia (pallor despite oxygenation, weak pulses with a good HR, poor response to resuscitation), or the newborn appears to be in shock.<sup>21,22</sup> Volume expanders include whole blood (Rh-negative type O blood crossmatched with the mother's blood), normal saline, or Ringer's lactate solution. Whole blood is preferred in the setting of significant blood loss but may be difficult to obtain quickly. Normal saline and Ringer's lactate (e.g., isotonic crystalloid solutions) should be readily available and may be considered the fluid of choice overall for volume expansion. Expanders are given in small IV boluses of 10 mL/kg over 5 to 10 minutes. When resuscitating premature infants, rapid administration of volume expanders should be avoided, as this has been associated with intraventricular hemorrhage.<sup>1</sup> Higher volume (e.g., 20 mL/kg) fluid boluses are recommended for older infants. Boluses may be repeated several times, guided by patient assessment. The use of albumin 5% with saline is currently not recommended for the initial resuscitation.

### Dopamine

Dopamine is indicated only when signs of shock (e.g., poor peripheral perfusion, thready pulses) are still present despite adequate volume replacement. Given as a continuous infusion beginning at 5 µg/kg/min, dopamine may be increased to 20 µg/kg/min as necessary.

## ■ DISPOSITION

Early consultation with a neonatologist can assist in the resuscitation and postresuscitation phases of care. When the neonate has been stabilized, monitoring of oxygenation, ventilation, perfusion, temperature, and glucose must continue. Preparations should be made for transport of the newborn to a neonatal intensive care unit. A transport team with personnel skilled in neonatal resuscitation should be employed. Ideally, before transport, parents should see and touch (and hold if medically appropriate) their newborn.

### KEY CONCEPTS

- The necessary equipment must be readily available for neonatal resuscitation in the emergency department.
- Preparation is most effective with an adequate maternal and prenatal history.
- The neonatal flow algorithm provides a guide for management.
- Drying, warming, positioning, and stimulating the infant are usually sufficient resuscitative measures in most deliveries.
- Endotracheal suctioning for neonates at risk for meconium aspiration is reserved for nonvigorous infants.
- Transport of the neonate to a neonatal intensive care unit allows continued treatment.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## CHAPTER 10 Fever in the Adult Patient

Frederick C. Blum

### ■ PERSPECTIVE

#### Epidemiology

Fever is part of the presenting complaint in 6% of all adult (aged 18–65) visits to the emergency department (ED), 10 to 15% of all elder (older than 65 years) patient visits, and 20 to 40% of all pediatric visits.<sup>1,2</sup> Morbidity and mortality rates vary dramatically with age. Younger adults with fever usually have benign self-limited disease with less than 1% mortality. The challenge in this group is to identify the rare meningitis or septic conditions when confronted with a predominance of self-limited viral and focal bacterial diseases. Patients older than 65 years, or those with chronic disease who present with fever, represent a group at high risk for serious disease. Morbidity and mortality rates in this group are significant. Between 70 and 90% are hospitalized, and 7 to 9% die within 1 month of admission. Infection is the most common cause of fever in these patients, and most of these infections are bacterial in nature. Three body systems: the respiratory tract, the urinary tract, and the skin and soft tissue, are the target for more than 80% of these infections.<sup>3</sup> The relative mortality and morbidity for any given infection are much higher in the geriatric population. For example, elders are at 5 to 10 times greater risk for urinary tract infections and 15 to 20 times for appendicitis.<sup>4,5</sup> Even viral illnesses that are generally not fatal, such as influenza, can be highly lethal in elder persons.

#### Pathophysiology

Body temperature is normally controlled within a narrow range by the preoptic area of the hypothalamus. This range is usually between 36.0 and 37.8°C (96.8–100.4°F). There is a circadian rhythm within this range, with lower temperatures in the morning and higher temperatures in the late afternoon. Fever occurs when this normal range is reset to a higher value. Fever is typically defined as a core temperature greater than 38.0°C (100.4°F). Fever should not be confused with hyperthermia. Hyperthermia is an elevation of the temperature related to the inability of the body to dissipate heat. Almost all cases of temperatures higher than 41.0°C (105.8°F) are due to hyperthermia rather than to fever.

In the anterior hypothalamus, neurons directly sense the blood temperature. Temperature is subsequently controlled by a combination of vasomotor changes, shivering, changes in metabolic heat production, and behavioral changes.

Fever may be produced by a number of endogenous and exogenous substances referred to as *pyrogens*. Endogenous

pyrogens include a variety of cytokines released by leukocytes in response to infectious and inflammatory and neoplastic processes. Exogenous pyrogens include a large number of bacterial and viral products and toxins. Toxins induce fever by stimulating cells of the immune system to release endogenous pyrogens. These cytokines, such as interleukin-1 (IL-1), IL-6, tumor necrosis factor, and interferon, travel to the hypothalamus and induce the production of prostaglandin E<sub>2</sub> (PGE<sub>2</sub>).

PGE<sub>2</sub> raises the set point of the temperature range by a combination of effects including peripheral vasoconstriction, increased metabolic heat production, shivering, and behavioral changes that conserve heat. Fever is maintained as long as the levels of endogenous pyrogens and PGE<sub>2</sub> are high. Cyclooxygenase inhibitors, such as aspirin, decrease fever by blocking the production of PGE<sub>2</sub>. Age, malnutrition, and chronic disease may also blunt the febrile response.

Moderate elevations of the body temperature may serve to aid the host defense by increasing chemotaxis, decreasing microbial replication, and improving lymphocyte function. Elevated temperatures directly inhibit the growth of certain bacteria and viruses.<sup>5</sup>

Fever also results in certain increased costs to the host including increased oxygen consumption, metabolic demands, protein breakdown, and gluconeogenesis. These costs are particularly problematic in elders, who typically have a smaller margin of reserve for any given body system. It is well established that the ability to develop fever in elders is somewhat impaired. Older individuals also are known to have lower baseline temperatures than younger adults.<sup>6</sup> It has not been proved that treatment of fever with antipyretics has a beneficial effect on outcome or prevents complications.

The initial step in the process of fever is the resetting of the thermostatic set point in the hypothalamus to a higher temperature while actual body temperature remains normal. This mismatch of the thermostat with the “sensed” body temperature causes the patient to feel chilled (chills). If the chills are reported to a caregiver and the skin is touched or the temperature is taken, it is usually noted to be normal or minimally elevated. The patient remains chilled until the body temperature rises. At this point, the patient feels eutermic (but may feel fatigued or ill), but to the caregiver, the skin temperature or thermometer reading is now elevated. This sequence of chills followed by febrile illness is the basis of the (incorrect) popular belief that getting chilled leads to infection (classically pneumonia). When the thermostatic set point is reduced to normal, the patient suddenly feels hot and

**Table 10-1 Differential Diagnoses—Infectious Causes**

ORGAN SYSTEM	CRITICAL DIAGNOSES	EMERGENT DIAGNOSES	NONEMERGENT DIAGNOSES
Respiratory	Bacterial pneumonia with respiratory failure	Bacterial pneumonia, peritonsillar abscess, retropharyngeal abscess, epiglottitis	Otitis media, sinusitis, pharyngitis, bronchitis, influenza, tuberculosis
Cardiovascular		Endocarditis, pericarditis	
Gastrointestinal	Peritonitis	Appendicitis, cholecystitis, diverticulitis, intra-abdominal abscess	Colitis/enteritis
Genitourinary		Pyelonephritis, tubo-ovarian abscess, pelvic inflammatory disease	Cystitis, epididymitis, prostatitis
Neurologic	Meningitis, cavernous sinus, thrombosis	Encephalitis, brain abscess	
Skin and soft tissue		Cellulitis, infected decubitus ulcer, soft tissue abscess	
Systemic	Sepsis/septic shock, meningococemia		

sweats until the body temperature falls to match the (now normal) set point.

## ■ DIAGNOSTIC APPROACH

### Differential Considerations

The complete differential diagnosis for the patient presenting to the ED with fever is extensive. The major infectious and noninfectious causes are summarized in [Table 10-1](#) and [Box 10-1](#), respectively. The vast majority of serious causes are infectious in origin. Immediate threats to life result from decompensated shock (usually septic), respiratory failure (related to shock or pneumonitis), or central nervous system infection (meningitis). Some critical noninfectious causes of fever also exist (see [Box 10-1](#)), but these are relatively rare and frequently do not occur with fever as the primary symptom.

#### BOX 10-1

#### DIFFERENTIAL DIAGNOSIS—NONINFECTIOUS CAUSES OF FEVER

##### Critical Diagnoses

Acute myocardial infarction  
Pulmonary embolism/infarction  
Intracranial hemorrhage  
Cerebrovascular accident  
Neuroleptic-malignant syndrome  
Thyroid storm  
Acute adrenal insufficiency  
Transfusion reaction  
Pulmonary edema

##### Emergent Diagnoses

Congestive heart failure  
Dehydration  
Recent seizure  
Sickle cell disease  
Transplant rejection  
Pancreatitis  
Deep vein thrombosis

##### Nonemergent Diagnoses

Drug fever  
Malignancy  
Gout  
Sarcoidosis  
Crohn's disease  
Postmyocardiotomy syndrome

### Rapid Assessment and Stabilization

Patients with life-threatening signs and symptoms, including significant alterations in mental status, respiratory distress, and cardiovascular instability, may require rapid, vigorous treatment. Prompt airway management and initiation of monitoring, intravenous access, fluid resuscitation, supplemental oxygen, and respiratory support are often necessary despite incomplete information concerning the cause of the fever. Sustained temperatures above 41.0° C are rare but can be damaging to neural tissue and require rapid cooling (e.g., misting, fans, cooling blankets).

In the younger, otherwise healthy patient with fever, immediate threats to life such as toxic or septic shock, meningitis, meningococemia, and peritonitis should be considered and treated empirically.

In the older, chronically ill population with fever, most of the serious illnesses originate from infections in the respiratory tract, the genitourinary tract, and the skin and soft tissues. Meningitis, although less common, can also be a significant cause of morbidity and mortality in this group.

### Pivotal Findings

Although the differential diagnosis of fever is broad, most of the treatable causes are of infectious origin. Up to 85% of these may be diagnosed by careful history and physical examination alone. Age and the presence of underlying medical conditions can substantially influence the evaluation and subsequent decision-making regarding management.

In younger and otherwise healthy adults, self-limited, localized bacterial infections or benign systemic viral infections are usually the cause of their fever. The challenge with this group is to identify the rare life-threatening illness, such as meningococemia, meningitis, or systemic methicillin-resistant *Staphylococcus aureus* (MRSA) infection.

In the older or chronically ill population, fever is frequently a sign of severe illness. Usually, the cause is infectious. Eighty percent have respiratory infections, urinary tract infections, or soft tissue infections as the cause. Infections such as meningitis, cholecystitis, appendicitis, and diverticulitis may arise with atypical signs and symptoms in elderly or immunosuppressed patients. In this population, subtle changes in behavior may be the only sign of severe infection. Abnormal vital signs, especially significant tachypnea and hypotension, may portend a complicated and severe course. Seventy-five percent of the cases of functional decline in nursing home patients are due to infection.<sup>6,7</sup>

## History

The *onset* of the fever, its *duration* and *magnitude*, and any *associated symptoms* help identify possible causes and severity of illness. Localizing symptoms such as dysuria or productive cough are especially helpful. The *timing* of the fever and its *patterns* may implicate certain diseases (e.g., malaria). *Recent or remote travel*, *chronic illnesses*, past surgeries, hospitalizations, and treatment modalities may raise the suspicion of exotic or nosocomial infections. The presence of cardiac valves or any prosthetic or indwelling device may be critical to the diagnosis.<sup>8</sup> With the emergence of community-acquired MRSA, it is important to seek a history of skin infections in close family members or other close contacts. MRSA should also be considered in military personnel, prisoners, and persons involved in competitive sports that involve close contact.<sup>9,10</sup>

Also important is a list of all the patient's medications, including any antipyretic medication. Family members are frequently an important source of information in elder and very young patients. They are often the first to notice a functional decline in the patient, such as difficulty ambulating, anorexia, decreased activity, or new urinary incontinence. A decline in mental status in the older patient may be the only clue to the presence of significant infection. The patient's baseline mental function must rely on the reports of others who know the patient well.

Atypical symptoms are common in elder patients. Pneumonia or urinary tract infection in the older patient may be heralded by only a change in mental status, difficulty ambulating, or some other functional decline. Dysuria, frequency, and flank pain often are absent entirely in elders with urinary tract infection. Patients with pneumonia may inconsistently present with productive cough or shortness of breath. Other frequent but nonspecific symptoms include anorexia, weight loss, weakness, lethargy, nausea, and recurrent falls.<sup>8,9</sup> A history of cancer with recent chemotherapy or radiation therapy may be a clue to leukopenia or other immunodepressed states.<sup>4</sup>

## Physical Examination

The presence and magnitude of fever is an important element of the examination, but the elder, very young, or chronically ill patient may not mount a febrile response to significant infection. Temperatures may fluctuate, and rechecks may be necessary.

Rectal temperatures are the most accurate. Axillary and tympanic temperatures often are unreliable. Oral temperatures may be transiently distorted by recent ingestion of hot or cold liquids, smoking, or hyperventilation. Rectal temperatures are typically 0.7 to 1.0°C higher than oral temperatures.

Fever is inconsistently associated with tachycardia and tachypnea. The heart rate may increase by 10 beats/min for each 0.55°C (1°F) degree rise in temperature. Relative bradycardia may be caused by medication such as beta-blockers, but can suggest factitious or drug-related fevers, typhoid fever, brucellosis, or leptospirosis. Frank bradycardia may occur with rheumatic fever, Lyme disease, viral myocarditis, and endocarditis. The respiratory rate may increase 2 to 4 breaths per minute per degree Celsius. More significant tachypnea may be due to respiratory infection or the acidosis related to shock.

In many patients, the examination is directed by the patient's localization of symptoms. The head and neck examination focuses on treatable foci of infection such as otitis media, sinusitis, pharyngitis, peritonsillar abscess, retropharyngeal abscess, and dental infections. A muffled, "hot potato" voice with severe sore throat may be a clue to adult epiglottitis or

upper airway abscess. Funduscopy rarely may reveal evidence of disseminated candidiasis, miliary tuberculosis, endocarditis, toxoplasmosis, or leukemia.

The neck is examined for lymphadenopathy, masses, or thyroid pathology (thyromegaly or mass). Nuchal rigidity or pain on forward flexion of the neck is assessed but may not be prominent in the very young, or in a debilitated or elder patient, even if meningitis is present. Conversely, cervical arthritis or Parkinson's disease may cause preexisting nuchal rigidity.

The lungs are examined for rales, pleural rubs, or dullness to percussion. Localized rales or rhonchi may be more subtle clues to the presence of pneumonia. The presence of concomitant chronic obstructive pulmonary disease or congestive heart failure, as well as poor respiratory effort, may hamper the diagnosis of pneumonia in elders. The heart is examined for pericardial rubs or new murmurs.

The abdominal examination may be deceptively benign in older patients, patients with diabetes, or patients taking immunosuppressives or steroids.<sup>10</sup> When indicated by history or other findings, a rectal examination is performed to check for evidence of enteritis, perirectal abscess, or prostatitis. The external genitalia examination may reveal evidence of Bartholin's abscess, urethral or vaginal discharge, or evidence of epididymitis or orchitis.

Females with appropriate symptoms should have a pelvic examination to evaluate for pelvic inflammatory disease or tubo-ovarian abscess. The skin and extremities should be evaluated for rash, petechiae, joint inflammation, or evidence of soft tissue infection. In the absence of trauma, tenderness over the long bones or the spine may be evidence of osteomyelitis or neoplastic processes. Elders and bedridden patients should be checked for the presence of pressure sores or decubitus ulcers.<sup>3</sup>

## Ancillary Testing

The two most important ancillary tests, especially in elder patients, are urinalysis and chest radiography. Chest radiographs are often helpful in the diagnosis of pulmonary infection but may be difficult to interpret in the patient with concurrent chronic obstructive pulmonary disease, congestive heart failure, dehydration, or other chronic lung disease. The urinalysis, although not foolproof, is highly accurate for urinary tract infection, especially in men. Although the white blood cell count is almost universally used in the evaluation of febrile patients, it lacks the sensitivity and specificity to be of discriminatory value. The white blood cell count may incorrectly indicate serious infection when none is present or may be normal in the presence of life-threatening infection.<sup>11</sup> Other indirect tests of infection and inflammation, such as the erythrocyte sedimentation rate, are also plagued with irregular sensitivity and poor specificity and should be used sparingly. Gram's stain of appropriate specimens may be helpful, and cultures may be ordered, although the results do not influence emergency evaluation and treatment. With the emergence of MRSA, it has become increasingly important to obtain cultures from soft tissue skin abscesses in patients considered at risk for MRSA infection. In elder or chronically ill patients with fever of unknown source, blood and urine cultures are frequently appropriate. Outpatient blood cultures should rarely, if ever, be done. A patient ill enough to require blood cultures generally requires hospitalization and empirical antibiotic coverage. Cerebrospinal fluid evaluation should be considered when mental status changes or if headache, meningismus, or other unexplained neurologic symptoms are present and cannot be clearly accounted for by infection outside the central



nervous system. Thyroid function studies may be helpful when thyroid storm is suspected.

Plain films of the abdomen are rarely indicated or helpful. Abdominal computed tomography (CT) is helpful if appendicitis, diverticulitis, cholecystitis, or intra-abdominal abscess is suspected. Ultrasonography may be helpful in the patient with potential cholecystitis.

Cranial CT scanning may be indicated prior to lumbar puncture in patients with focal neurologic findings or an embolic source, such as suspected endocarditis, to exclude mass lesions such as tumor or brain abscess. This test should not delay antibiotics in patients with suspected meningitis.

Other ancillary testing is directed by the findings of the history and physical examination.

## ■ DIFFERENTIAL DIAGNOSIS

The differential diagnoses of infectious causes of fever are summarized in [Table 10-1](#). The differential diagnoses of non-infectious causes of fever are listed in [Box 10-1](#).

## ■ EMPIRICAL MANAGEMENT

Patients with temperatures greater than 41.0° C require prompt and vigorous treatment with antipyretics and possibly external cooling measures. Temperatures above this range can result in damage to neuronal tissue. There is no evidence for improved outcome by routine use of antipyretic therapy, such as acetaminophen, in patients without extreme temperature elevation, but it is not harmful, and patients often feel better when their temperature declines. Achieving a normal or near-normal temperature is not necessary as a criterion for discharge, however. Patients with signs and symptoms of shock require prompt and vigorous treatment (see Chapter 4). Patients with evidence of respiratory failure from shock or pneumonia require ventilatory support. Soft tissue infections of the head and neck may compromise the airway because of mechanical obstruction. These may require acute intervention to provide a secure airway.

In many cases, early empirical antibiotic therapy is appropriate. The choice of antibiotics is based on the likely cause of

the fever as well as concomitant conditions such as absolute neutropenia and end-stage renal disease. If a specific infection is identified, antibiotic therapy should be specific to that infection. In the absence of a clear source of infection, broad-spectrum coverage of gram-positive and gram-negative aerobic and anaerobic bacteria is indicated.

## ■ DISPOSITION

Localized bacterial infections can most frequently be treated with outpatient oral antibiotics. Relatively young, healthy patients with systemic viral illness can be treated as outpatients. These illnesses are often accompanied by vomiting and poor oral intake, and treatment in the ED with antipyretics, anti-nausea medications, and intravenous hydration may help prepare the patient for a successful outpatient course.

When no clear infection is identified in older patients or those with chronic illness such as diabetes or chronic renal failure, admission to the hospital often is necessary to further elucidate the possible causes of the presentation. In this subset of patients, a diligent search for evidence of bacterial infection is required. Also, admission to an inpatient unit or ED observation unit may be advisable when fever or other systemic symptoms accompany a suspected MRSA infection. In patients with unexplained severe febrile illness, blood and urine cultures and broad-spectrum antibiotics are indicated to treat possible life-threatening infection, until a specific disease process or pathogen is identified. Indwelling devices, such as percutaneous intravenous access ports, frequently require culture and may need to be removed. Neutropenic patients with fever require prompt treatment with broad-spectrum parenteral antibiotics pending results of cultures. Patients with unstable vital signs or life-threatening infections may require admission to a special care unit if they cannot be adequately stabilized in the ED prior to admission.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## PERSPECTIVE

*Weakness* is a subjective term that can be used to describe many symptoms that can relate to a variety of disease states. *Webster's Dictionary* definition for *weak* is “lacking strength, deficient in physical vigor, not able to sustain or exert much weight, pressure, or strain.” However, when a patient uses the term *weakness*, he or she might be describing symptoms beyond the loss of muscle power. Malaise, frailty, fatigue, pain, dizziness, and alteration of mental status might all be described as weakness.

This chapter focuses on the evaluation and treatment of patients complaining of the acute onset of generalized, diffuse, and symmetrical weakness. Discussion regarding chronic neurologic conditions, localized weakness, space-occupying lesions, and traumatic injury can be found elsewhere.

## Epidemiology

No research data are currently available specifically related to the presenting complaint of “weakness” in the emergency department (ED). Because this complaint can originate from derangements in multiple organ systems, it is difficult to get a true estimate of its frequency in the ED setting.

Acute neuromuscular weakness is a relatively rare entity. Poliomyelitis has been eradicated in Western Europe and North America, and there has been a dramatic decrease in the incidence of this disease worldwide (1187 cases in 2007 per the World Health Organization).<sup>1</sup> The most common cause of acute symmetrical weakness in industrialized countries is Guillian-Barré syndrome, with an annual incidence of 2 cases per 100,000 in the United States. To put this in perspective, the incidence of diabetes mellitus is 740 cases per 100,000.<sup>2</sup> New infectious causes of acute symmetrical weakness have emerged in the past few decades including West Nile virus and HIV.

## Pathophysiology

The key differentiation is whether the patient has actual, quantitative, muscle weakness. If so, the nervous system is involved, often with dysfunction of the motor unit. In contrast, the complaint of weakness in the absence of decreased strength on examination suggests a disease process outside of the nervous system. These two broad categories of weakness will be examined in turn.

## Neuromuscular Weakness

Muscle contraction is the result of a series of signals that originate in the cerebral cortex. Upper motor neurons (UMN) originate in the motor strip, anterior to the central sulcus, and travel in the pyramidal system. They descend the spinal column in the lateral corticospinal tract on the side opposite their origin in the brain. The UMN then synapses with the lower motor neuron (LMN) in the anterior horn of the spinal cord, which in turn carries the signal to the muscle bundle. The LMN (peripheral nerve) releases acetylcholine into the synaptic cleft, which then depolarizes the motor endplate and results in muscle contraction. This series of events depends on the presence of myelin insulating the nerves, the function of calcium and sodium channels, and the presence of acetylcholinesterase. Neuromuscular weakness can be caused by lesions or derangements at any level of this cascade of events.

## Non-neuromuscular Weakness

A patient's complaint of weakness often stems from a non-neuromuscular cause. The patient's age, underlying health status, current symptom complex, and examination findings help narrow the differential diagnosis. Infectious, cardiovascular, endocrine, metabolic, and toxicologic causes of the patient's complaint need to be considered.

## DIAGNOSTIC APPROACH

### Pivotal Findings

#### History

A clear description of the symptoms is crucial to clarifying whether the patient is experiencing neuromuscular weakness. Does the patient describe a decrement in function? For example, is the patient unable to climb stairs because of leg weakness or because of shortness of breath and fatigue? The former case is likely to be due to neuromuscular weakness; the latter may be related to compromised cardiovascular function or another systemic process.

It is important to obtain the time course of symptoms, severity, and their progression or worsening. The distribution (proximal, distal, generalized) of weakness, fluctuations in function, and alleviating or aggravating factors (activity, rest) are also

important factors. The presence or absence of bladder and bowel dysfunction, sexual dysfunction, paresthesias or altered sensation, and muscle pain or spasm should also be elicited. Recent history of infectious illness, trauma, new medications, exposure to toxins, alcohol and drug use should also be considered. Table 11-1 lists a few of the serious causes of acute neuromuscular weakness with their distinguishing characteristics and management.

The patient's age, comorbidities, and overall vigor or frailty should be taken into account. A thorough review of organ systems should be performed. The presence or absence of fever, infectious symptoms, fatigue, chest discomfort, dyspnea, malaise, abdominal discomfort, alteration of bowel habits, especially melena or hematochezia, and headache should be elicited. Careful medication review, especially of diuretics, beta-blockers, and psychotropic medications, may suggest

**Table 11-1 Neuromuscular Diseases: A Brief Description**

DISEASE	MECHANISM	HISTORICAL FEATURES/EXAM FINDINGS	ED MANAGEMENT
<b>Botulism</b> Toxin 12–72 hr postingestion	Neurotransmission Toxin prevents release of acetylcholine at the neuromuscular junction	Ingestion of contaminated canned goods 50% have GI symptoms Postural hypotension Diplopia, blurred vision, ptosis, facial weakness, dysphagia, respiratory compromise, then limb weakness	Supportive care, ICU admission Notify Health Dept/CDC Trivalent antitoxin (May try guanidine hydrochloride, facilitates release of acetylcholine from nerve endings; anticholinesterase drugs not helpful)
<b>Myasthenia Gravis</b> Idiopathic	Neurotransmission Decreased number of functioning acetylcholine receptors	Mild infection may exacerbate symptoms Fluctuating weakness; easy fatigability of voluntary muscles; cranial nerves involved with ptosis and diplopia in >25%; normal pupillary responses; normal sensation; normal reflexes Improves with rest May have a coexisting thymoma (CXR, chest CT)	Supportive care, ICU admission Neurology consult Edrophonium/neostigmine test Bedside spirometry Measure serum acetylcholine receptor antibody levels Tx: Anticholinesterase drugs—neostigmine; pyridostigmine
<b>Organophosphate/Carbamate Poisoning</b> Immediate–3 wk	Neurotransmission Cholinergic crisis from inhibition of acetylcholine Neuropathy (weeks after exposure)	History of insecticide exposure Gastrointestinal symptoms, agitation, miosis, paralysis, diaphoresis, muscle weakness, bradycardia Cramping muscle pain, distal numbness and paresthesias, progressive muscle weakness; decreased reflexes; can develop flaccid/wasted leg muscles	Decontamination Supportive care, ICU admission Atropine Pralidoxime (2-Pam)
<b>Tetanus</b> Toxin 3 wk 10–60% fatality	Neurotransmission Toxin interferes with release of inhibitory transmitters including GABA; results in motor nerve hyperactivity	Immunization status History of cutaneous infection Trismus, laryngospasm, painful muscle spasms and rigidity (opisthotonos), autonomic instability	Supportive care, ICU admission Débridement of wounds Tetanus immunoglobulin Penicillin for the infection High-dose benzodiazepines Neuromuscular blockade
<b>Tick Paralysis</b> Toxin 2–7 days Rocky Mountain wood tick and the American dog tick are most common in the USA	Neurotransmission Toxin reduces motor neuron action potential and the action of acetylcholine	History of outdoor activities/tick bite Progressive, ascending, flaccid weakness over several hours may lead to respiratory failure; may present as acute ataxia without muscle weakness; decreased or absent reflexes; ophthalmoplegia and bulbar palsy can occur	Removal of the embedded tick (look at the hairline/in the scalp) Supportive care Full recovery if tick removed; 10% fatality if not recognized
<b>Ciguatoxin</b> Toxin 12–24 hr; neurologic symptoms can last months	Neuropathy Toxin causes cell membrane excitability and instability	History of ingestion of large, tropical fish Diarrhea, abdominal pain, nausea, and vomiting are followed by painful paresthesias, ataxia, altered hot/cold perception, myalgias, bradycardia, and hypotension Rarely, death occurs through respiratory failure	Supportive care, ICU admission Atropine for bradycardia Hydration IV mannitol can be helpful
<b>Diphtheria</b> Toxin 2 wk–3 mo after infection	Neuropathy Lower motor neuron	Immunization status History of throat infection with pseudomembrane; cutaneous infection Palatal weakness, impaired pupillary responses, generalized sensorimotor polyneuropathy; respiratory failure; motor weakness of the proximal muscle groups and extending distally	Supportive care, ICU admission Equine diphtheria antitoxin Erythromycin or penicillin G for 14 days to halt toxin production, treat localized infection and prevent transmission of organisms Immunization

**Table 11-1 Neuromuscular Diseases: A Brief Description—cont'd**

DISEASE	MECHANISM	HISTORICAL FEATURES/EXAM FINDINGS	ED MANAGEMENT
<b>Gullian-Barré Syndrome</b> Idiopathic 1–4 wk 75% recover 5% fatality	Neuropathy Lower motor neuron Immune-mediated polyneuropathy Multiple variants	May have a history of infection; viral infection; <i>Campylobacter jejuni</i> in 15–40% Symmetrical ascending motor neuropathy; decreased/absence reflexes; mild sensory involvement; autonomic dysfunction; can progress to respiratory compromise	Lumbar puncture: CSF with elevated protein but normal WBC Bedside spirometry Plasmapheresis and IVIG Consider ICU admission Neurology consult
<b>Transverse Myelitis</b> Idiopathic, postinfectious, autoimmune Rapid onset (hours–days)	Neuropathy Upper motor neuron Axonal demyelination	Loss of spinal cord functions with symptoms depending on the level of the lesion; thoracic is most common Acute, focal back pain; distal muscle weakness; abnormal sensation; urinary retention/loss of bowel control; muscles may be flaccid; decreased or absent reflexes initially Differentiate from spinal cord compression, trauma or infarct; may be the first sign of multiple sclerosis	Supportive care, ICU admission if C-spine level for respiratory support Spine radiograph to evaluate for bony lesion Stat MRI/CT myelogram Decompress bladder
<b>Electrolyte Imbalance</b>	Myopathy	History of nausea/vomiting/diarrhea History of renal failure, alcohol dependence, new medication Ascending symmetric muscle weakness with normal to diminished reflexes	ECG Electrolyte panel: Na, K, Cl, PO <sub>4</sub> , Ca, and Mg Renal function Correct the abnormality; close hemodynamic monitoring
<b>Polymyositis</b> Autoimmune	Myopathy	History of connective tissues disorders or cancer Progressive at a variable rate; muscle weakness and wasting; ascending pattern with proximal limb and girdle muscle involvement; muscle pain; dysphagia; respiratory difficulty; can have an erythematous periorbital and eyelid rash (dermatomyositis)	Elevated CPK, rhabdomyolysis rare Normal ESR Supportive care Corticosteroids

Adapted and expanded from LoVecchio, et al: Approach to generalized weakness and peripheral neuromuscular disease. Emerg Med Clin North Am 15:605, 1997.

CDC, Centers for Disease Control and Prevention; CPK, creatine phosphokinase; CSF, cerebrospinal fluid; CT, computed tomography; CXR, chest radiograph; ESR, erythrocyte sedimentation rate; GABA,  $\gamma$ -aminobutyric acid; GI, gastrointestinal; ICU, intensive care unit; IVIG, intravenous immunoglobulin; MRI, magnetic resonance imaging; WBC, white blood cell count.

electrolyte disturbances or generalized medication side effects.

In adults older than age 50, particularly women, the complaint of generalized weakness should prompt consideration of cardiac ischemia.

In adults older than age 65, a complaint of weakness may be the only symptom of a serious infection, electrolyte disturbance, or cardiovascular compromise. When this complaint is combined with a recent fall, altered mental status, or urinary incontinence, urosepsis should be considered. When this complaint is accompanied by the report of poor sleep, dyspnea, or decreased exercise tolerance, acute coronary syndrome or heart failure should be considered. Consideration should be given to situational orthostasis resulting in a sensation of weakness accompanied by a presyncopal feeling; examples include postprandial hypotension and post-tussive or micturition near-syncope.

### Examination

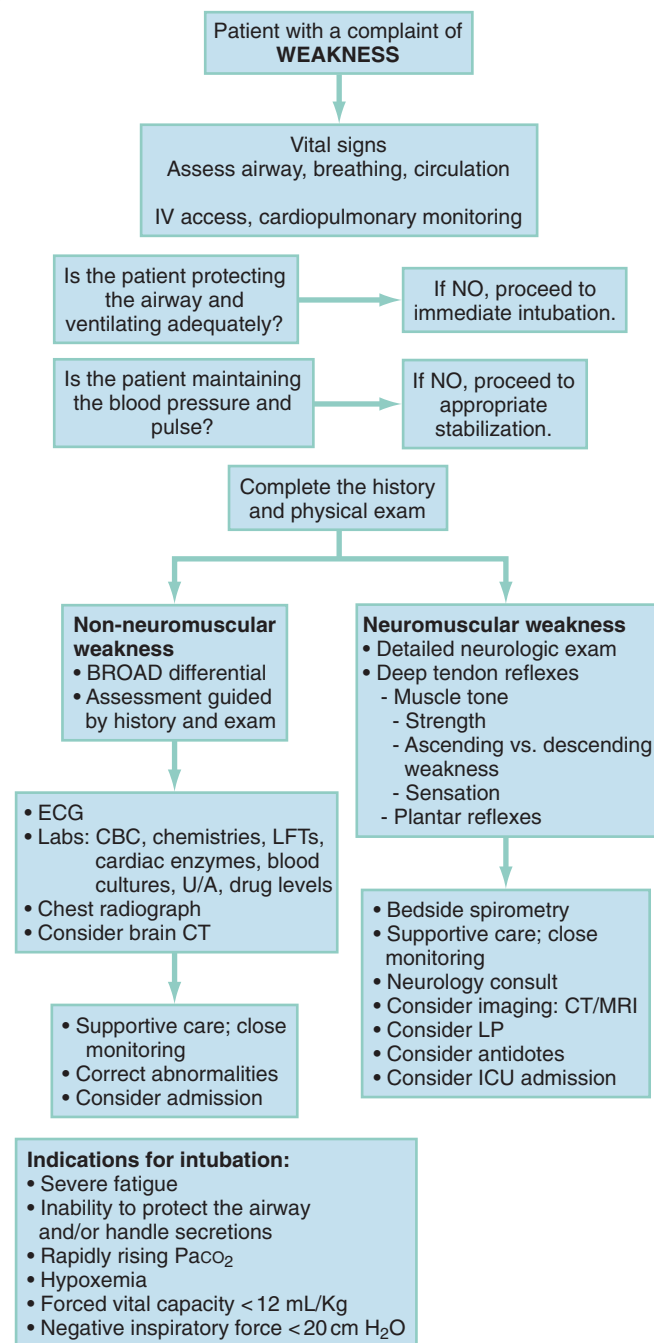
Fever, hypotension, tachycardia, or tachypnea may provide clues regarding the source of the patient's complaint (Table 11-2). If severe weakness is present, an assessment of the patient's ability to maintain the airway and the adequacy of respiration is indicated (Fig. 11-1).

The neurologic exam should focus on clarifying if the patient is experiencing true loss of strength along with the distribution of the deficits (Table 11-3). A complete examination, including cranial nerves, and gait, where possible, is helpful. The motor exam should be systematic and thorough. Muscle bulk, strength, tone, and the presence or absence of abnormal movements should be noted. Sarcopenia (age-associated loss of muscle mass and function) is normal in the older adult. In this situation, the loss of power is uniform in all limbs. Walking on heels, toes, and in tandem is a good test of strength as well as coordination and proprioception. Gait apraxia has a wide differential and should prompt investigation for cerebellar abnormality; normal pressure hydrocephalus should be considered in the patient who has simultaneous incontinence and decreased cognitive function. Fine muscle fasciculations typically point to an LMN disorder, whereas spasticity, greater in the flexors than extensors, is seen in UMN lesions.

### Ancillary Testing

Patients presenting with weakness can have myriad underlying abnormalities. Although testing will be guided by the history and exam, virtually all patients require a complete blood count to evaluate for anemia or blood loss and serum electrolytes, glucose, and creatinine. An electrocardiogram





**Figure 11-1.** Diagnostic management algorithm. CBC, complete blood count; CT, computed tomography; ECG, electrocardiogram; ICU, intensive care unit; LFTs, liver function tests; LP, lumbar puncture; MRI, magnetic resonance imaging; PaCO<sub>2</sub>, arterial partial pressure of carbon dioxide; U/A, urinalysis.

may indicate cardiac ischemia or hypo- or hyperkalemia. In patients with infectious symptoms and in elders with nonlocalized symptoms, a chest radiograph and urinalysis are helpful. Computed tomography or magnetic resonance imaging of the brain or spine are not generally indicated in the absence of focal findings, altered mental status, history of cancer, or anticoagulation with (even minor) trauma. Lumbar puncture can help confirm central nervous system infection when suggested, or Guillain-Barré syndrome when protein levels are elevated and a white blood cell count of 10 or fewer per milliliter strongly supports the diagnosis.

Any patient who appears to have respiratory compromise or for whom Guillain-Barré syndrome or myasthenia gravis is possible should undergo bedside spirometry. A forced vital capacity (FVC) of less than 10 to 12 mL/kg or a negative inspiratory force (NIF) of less than 20 cm H<sub>2</sub>O is an indication for respiratory support. An arterial blood gas test for carbon dioxide tension or capnography may also be helpful.

## ■ DIFFERENTIAL DIAGNOSIS AND INITIAL MANAGEMENT

The differential diagnosis of weakness is very broad, and at times, a definitive diagnosis is impossible in the span of an ED visit. Ensuring appropriate disposition and follow-up is particularly important in these patients.

In a patient with neuromuscular weakness, the respiratory drive is preserved, but the ability to ventilate adequately can be impaired and the patient may complain of dyspnea. Patients with rapid progression of weakness may require early airway intervention and mechanical ventilation. Warning signs of worsening respiratory status include the inability to lift the head, ineffective cough, alteration of the voice, and difficulty controlling secretions. As a crude measure of vital capacity, the patient's inability to count to 20 in a single exhalation suggests that the FVC is compromised; when the patient can only count to 10, the FVC can be estimated at 1 L and preparations to intubate should be made. About 30% of patients with Guillain-Barré syndrome require mechanical ventilation, and several studies have demonstrated that an elective, controlled intubation leads to better outcomes in terms of ventilation-associated pneumonia and total time on the ventilator<sup>3</sup> (Fig. 11-2).

Patients with neuromuscular weakness increase their respiratory rate to compensate for low tidal volumes, and the PaCO<sub>2</sub> is maintained within the normal range. If the patient develops muscle fatigue or increased muscle weakness, the PaCO<sub>2</sub> will rise and respiratory failure can occur quickly. In this situation, intubation, usually using a rapid sequence technique, is indicated. Succinylcholine should be avoided when a progressive denervation syndrome is suggested.<sup>4</sup> The up-regulation and redistribution of acetylcholine receptors on denervated myocytes that occurs with succinylcholine can lead to significant hyperkalemia with administration of this drug (see Chapter 1). In addition, autonomic instability in these patients can make intubation challenging; the physician should anticipate the possibility of labile blood pressures and bradycardia.<sup>5</sup> Bradycardia responds to atropine administration, and the blood pressure should be closely monitored but not necessarily treated as it can fluctuate rapidly.

## Special Situations

### Myasthenia Gravis: Myasthenic Crisis versus Cholinergic Crisis

Myasthenia gravis is discussed in detail in Chapter 106. *Myasthenic crisis* refers to a rapid worsening of neuromuscular function with respiratory compromise. It occurs in approximately 15% of patients with this disease and can be triggered by infection ( $\approx$  30% of cases), change in medications, metabolic derangement, or physical stress; a third of the time no cause is found.<sup>6</sup> A crisis can be precipitated by a recent change in the dose of the patient's anticholinesterase inhibitor, recent initiation or tapering of corticosteroids, and recent initiation of several commonly used medications (aminoglycoside and quinolone antibiotics, beta-blockers, and antiarrhythmic agents). Myasthenic crisis is associated with prolonged hospitalization and intubation periods of 1 to 3 weeks.

**Table 11-2 Vital Signs: Weakness**

VITAL SIGNS	ELEVATED	DECREASED	POTENTIAL INTERVENTIONS / ANCILLARY TEST
Heart rate	Arrhythmia Blood loss Dehydration Hyperthyroidism Pain Serious infection	Electrolyte imbalance Medication effect (BB, CCB)	ECG Fluid bolus and reevaluate Orthostatic blood pressure/pulse Rate control based on ECG findings Antibiotics if infection suspected
Blood pressure	Hyperthyroidism Medication noncompliance Pain	Arrhythmia Blood loss Dehydration Medication effect (BB, CCB) Serious infection	ECG Fluid bolus and reevaluate Orthostatic blood pressure/pulse Pressors
Respiratory rate	Serious infection COPD/Asthma	Impending respiratory failure	Bronchodilators CXR Respiratory support: oxygen, BiPAP, intubation
Temperature	Serious infection Medication effect	Serious infection Environmental exposure	Antipyretics/cooling measures Passive rewarming ECG Infectious workup
Oxygen saturation	N/A	Serious infection COPD/asthma Impending respiratory failure	Bronchodilators CXR Respiratory support: oxygen, BiPAP, intubation

BB, beta-blocker; BiPAP, Bi-level positive airway pressure; CCB, calcium channel blocker; COPD, chronic obstructive pulmonary disease; CXR, chest radiograph, ECG, electrocardiogram.

**Table 11-3 Physical Examination: Localizing Neuromuscular Lesions**

LOCATION OF LESION	DEEP TENDON REFLEXES	MUSCLE TONE	PLANTAR REFLEXES	STRENGTH
Upper motor neuron	Increased	Normal (Increased/spastic as disease progresses)	Upgoing	Weak/paralysis
Lower motor neuron	Decreased or absent	Decreased/flaccid (may see fasciculations)	Normal or absent	Weak/paralysis
Neuromuscular junction	Normal or decreased	Decreased/flaccid	Normal or absent	Variable weakness pattern
Muscle	Normal or decreased	Decreased/flaccid	Normal or decreased	Constant/progressive Proximal > distal

**Non-neuromuscular**

**Critical:** Hemodynamic instability  
Myocardial infarction  
Arrhythmia  
Severe infection/sepsis  
Respiratory failure  
Hyperkalemia

**Emergent**

Acute anemia  
Dehydration  
Metabolic disorder  
Hypothyroidism  
Diabetes  
Electrolyte imbalance

**Other**

Fatigue  
Psychiatric (anxiety, depression)  
Rheumatologic (fibromyalgia; SLE)  
Malignancy  
Renal or hepatic disease  
Metabolic disease  
Alcoholism and other toxin-related disease  
Malingering

**Neuromuscular**

**Critical:** Potential for respiratory compromise  
Rabies  
Botulism  
Tetanus  
Organophosphate poisoning  
Myasthenia gravis crisis

**Emergent**

Guillain-Barré syndrome  
Transverse myelitis  
Impingement syndromes  
Spinal cord infarction  
Electrolyte imbalance

**Other**

Lambert-Eaton syndrome  
ALS  
Paraneoplastic syndrome  
Diphtheria  
Porphyria  
Drugs and toxins  
Tick paralysis  
Poliomyelitis

**Figure 11-2.** Differential diagnosis algorithm: Weakness.

*Cholinergic crisis* results from an excess of cholinesterase inhibitor medication that produces a flaccid muscle paralysis and generalized weakness. Respiratory failure may be present with or without other cholinergic symptoms.

These two forms of crisis can be difficult to distinguish but are managed similarly with a focus on airway protection and ensuring adequate ventilation. Potential triggers for the crisis should be sought, and because many of these patients are on immunosuppressive medications, infection should be strongly considered. An urgent neurology consultation may be helpful, and an edrophonium challenge test may be performed if a myasthenic crisis is suggested (see Chapter 106).

### Older Adults and Frailty

In the older adult with a complaint of weakness, an accurate history can be difficult to obtain. In addition, comorbidities and polypharmacy can often complicate the presentation in these patients.

Frailty is a biologic syndrome defined by decreased reserve and resistance to stressors and is an independent predictor of future functional decline, falls, hospitalization, and mortality.<sup>7,8</sup> Hallmarks of this syndrome include generalized muscle weakness, poor endurance, weight loss, low physical activity, and slow gait speed. The prevalence of frailty in community-dwelling persons older than age 65 is approximately 7% and it increases with age and female gender.

Older adults with disability, frailty (as measured by their functional status, grip strength, and ability to ambulate), and comorbid chronic illness are at high risk for poor outcome after the ED visit.<sup>9</sup> A thorough evaluation with attention to potential life-threatening conditions and a low threshold for admission and further evaluation is warranted in this population.

One year post-ED visit with hospitalization, mortality in this population is in the range of 25%.

### ■ DISPOSITION

Most patients presenting to the ED with a complaint of weakness have a non-neuromuscular cause for their complaint. The history, exam, and results of ancillary testing dictate treatment and disposition of these patients.

Those patients who present with acute symmetrical neuromuscular weakness require a thorough evaluation with particular attention to their airway and ventilation. Disposition decisions should be made in conjunction with neurology consultation, and admission to the intensive care unit for close respiratory monitoring should be considered.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## ■ PERSPECTIVE

An estimated 7.5 million patients with dizziness are seen each year in ambulatory care settings. It is one of the most common principal complaints in the emergency department.<sup>1</sup> Benign paroxysmal positional vertigo, felt to be caused by loose particles in the semicircular canals, is the most common cause of vertigo with an incidence estimated to be 107 cases per 100,000 population per year.<sup>2</sup> Dizziness in older persons is associated with a variety of cardiovascular, neurosensory, and psychiatric conditions and with the use of multiple medications.<sup>3</sup> Among patients older than 60 years, 20% have experienced dizziness severe enough to affect their daily activity.<sup>4</sup> In a study of 1000 outpatients, dizziness was the third most common complaint. *Vertigo* is defined more clearly as a sensation of disorientation in space combined with a sensation of motion. In 1921, Bárány published the first detailed description of benign paroxysmal positional vertigo.

A complaint of “dizziness” is an imprecise term. The emergency department physician may believe that the patient will be difficult to interview and that the condition will be problematic to diagnose and treat. But in reality, most of these patients have an organic basis for symptoms that can be successfully identified and treated. The diagnostic process is consistently based on two basic concepts: deciding whether the patient has true vertigo and, if vertigo exists, deciding whether the cause is central or peripheral.<sup>5</sup>

## Pathophysiology

The maintenance of equilibrium and awareness of the body in relationship to its surroundings depend on the interaction of three systems: visual, proprioceptive, and vestibular. The eyes, muscles, joints, and otic labyrinths continuously supply information about the position of the body. Visual impulses, mediated through the higher brain centers, provide information about body position in space. Impulses from proprioceptors of the joints and muscles supply data about the relative positions of the parts of the body. Impulses from the neck are of special importance in relating the position of the head to the rest of the body. The sense organs of the visual, vestibular, and proprioceptive systems are connected with the cerebellum by way of the vestibular nuclei in the brainstem. Any disease that interrupts the integration of these three systems may give rise to symptoms of vertigo and disequilibrium.

The vestibular apparatus helps maintain head position and stabilize head movement. It is housed in the inner ear, or laby-

rinth, which lies embedded in the petrous portion of the temporal bone, where it is vulnerable to trauma; blood-borne toxins; and infections in nearby structures, including the middle ear and meninges. The vestibular apparatus consists of three semicircular canals with their cristae and two otolithic structures: the utricle and saccule. The semicircular canals provide information about movement and angular momentum; the otoliths provide information about the orientation of the body with respect to gravity.

The semicircular canals are paired structures that normally respond to motion in a symmetrical manner. With inner ear disease, the resting discharge or the discharge stimulated by motion can be altered in one ear. This alteration produces asymmetrical responses and results in the perception of vertigo. Freely moving debris within the semicircular canals can produce positional vertigo as the debris moves under the influence of gravity.

Impulses leave the vestibular apparatus by the vestibular part of the acoustic nerve (cranial nerve VIII), enter the brainstem just below the pons and anterior to the cerebellum, and proceed to the four vestibular nuclei of the brainstem and to the cerebellum. From there, impulses travel along two pathways that contribute to the clinical manifestations of vertigo: the medial longitudinal fasciculus and the vestibulospinal tract. In individuals with healthy vestibular systems, these connections allow the eyes to compensate for body movement in different directions and to maintain a visual axis that is stable with respect to the environment.

Nystagmus occurs when the synchronized vestibular information becomes unbalanced. Typically, it results from unilateral vestibular disease, which causes asymmetrical stimulation of the medial and lateral rectus muscles. This unopposed activity causes a slow movement of the eyes toward the side of the stimulus, regardless of the direction of deviation of the eyes. The cerebral cortex then corrects for these eye movements and rapidly brings the eyes back to the midline, only to have the process repeated.

By convention, the direction of nystagmus is denoted by the direction of the fast “cortical” component. Nystagmus caused by vestibular disease tends to be unidirectional and horizontal. If the nystagmus is vertical, a central lesion (either brainstem or cerebral) is usually the cause.

The vestibular nuclei send information to the lateral vestibulospinal tract, where they connect with motor neurons that supply the muscles of the extremities. This phenomenon explains the false steps or other body movements made by people with a defective vestibular apparatus who are



attempting to correct for an imagined change in position. Connections between the vestibular nuclei and the autonomic system account for the perspiration, nausea, and vomiting that commonly accompany an attack of vertigo. Connections between the vestibular nuclei and the cerebellum account for the modulating influence of this organ on motor activity.

## ■ DIAGNOSTIC APPROACH

### Differential Considerations

Patients use the term *dizzy* to describe a variety of experiences, including sensations of motion, weakness, fainting, light-headedness, unsteadiness, and depression. To clarify the picture, it is often helpful to have patients describe the sensation without using the word *dizzy*. True vertigo may be defined as a sensation of disorientation in space combined with a sensation of motion. There is a hallucination of movement either of the self (subjective vertigo) or the external environment (objective vertigo). Descriptions of light-headedness or feeling faint are more consistent with presyncope. The differential diagnosis for these patients should include dysrhythmias, myocardial infarction, sepsis, hypovolemia, drug side effects, and pulmonary embolism. For some patients, dizziness is simply a metaphor for malaise, representing a variety of other causes, such as anemia, viral illness, or depression. The primary focus of this chapter is to review the evaluation of the vertiginous patient.

If the patient has true vertigo, the clinician must determine whether the cause is a peripheral lesion (e.g., of the inner ear) or a central process, such as cerebrovascular disease or a neoplasm. In most cases, peripheral disorders are benign, and central processes have more serious consequences. Occasionally, as in the case of a cerebellar hemorrhage, immediate therapeutic intervention is indicated. Acute suppurative labyrinthitis is the only cause of peripheral vertigo that requires urgent intervention. [Box 12-1](#) lists causes of vertigo and identifies the peripheral, central, and systemic diagnoses. [Table 12-1](#) summarizes the different characteristics of peripheral and central vertigo.

### Pivotal Findings

#### History

The medical history is the most important source of information. A first key question is, “Does true vertigo exist?” Does the patient have a sensation of disorientation in space or a sensation of motion? The sensation of spinning usually indicates a vestibular disorder. Some nausea, vomiting, pallor, and perspiration accompany almost all but the mildest forms of vertigo. The presence of these symptoms without vertigo should suggest a different cause. The labyrinth has no effect on the level of consciousness. The patient should not have an associated change in mentation or syncope. A sensation of imbalance often accompanies vertigo, but true instability, disequilibrium or ataxia makes a higher likelihood of a central process.<sup>6</sup>

Because nystagmus accompanies acute vertigo, it is often helpful to ask members of the patient’s family if they have noted any unusual eye movements during the dizzy spells. This question is especially important in children unable to offer a concise history.<sup>7</sup> Occasionally, the patient may be able to describe a flickering or oscillating visual field immediately after a change in position, such as rolling over in bed. In addition, interviewing family and other witnesses can often uncover

## BOX 12-1 CAUSES OF VERTIGO

### Peripheral Causes

Foreign body in ear canal  
Cerumen or hair against tympanic membrane  
Acute otitis media  
Labyrinthitis (suppurative, serous, toxic, chronic)  
Benign positional vertigo  
Ménière’s disease  
Vestibular neuronitis  
Perilymphatic fistula  
Trauma (labyrinth concussion)  
Motion sickness  
Acoustic neuroma\*

### Central Causes

Infection (encephalitis, meningitis, brain abscess)  
Vertebral basilar artery insufficiency  
Subclavian steal syndrome  
Cerebellar hemorrhage or infarction  
Vertebral basilar migraine  
Post-traumatic injury (temporal bone fracture)  
Postconcussive syndrome  
Temporal lobe epilepsy  
Tumor  
Multiple sclerosis  
Cervical spine muscle and ligamentous injury

### Systemic Causes

Diabetes mellitus  
Hypothyroidism

\*Cause of peripheral vertigo that proceeds centrally.

**Table 12-1** Characteristics of Peripheral and Central Vertigo

CHARACTERISTIC	PERIPHERAL	CENTRAL
Onset	Sudden	Gradual or sudden
Intensity	Severe	Mild
Duration	Usually seconds or minutes; occasionally hours, days (intermittent)	Usually weeks, months (continuous) but can be seconds or minutes with vascular causes
Direction of nystagmus	One direction (usually horizontorotary), never vertical	Horizontal, rotary, or vertical (different directions in different positions)
Effect of head position	Worsened by position, often single critical position	Little change, associated with more than one position
Associated neurologic findings	None	Usually present
Associated auditory findings	May be present, including tinnitus	None

evidence suggesting seizures, syncope, or imbalance unrelated to feelings of vertigo.

The *time of onset* and the *duration of vertigo* are important clues to the cause. Episodic vertigo that is severe, lasts several hours, and has symptom-free intervals between episodes sug-

gests a peripheral labyrinth disorder. Vertigo produced primarily by a change in position also suggests a peripheral disorder. Vestibular neuronitis and benign positional vertigo fit this pattern.

The presence of *auditory symptoms* suggests a peripheral cause of the vertigo, as in middle and inner ear problems, or a peripheral cause that progresses centrally, such as an acoustic neuroma. The abnormally hearing ear is usually the side of end-organ disturbance. Progressive unilateral hearing loss of several months' duration may be the earliest symptom of an acoustic neuroma. Tinnitus occurs in most patients with acoustic neuroma and, along with vertigo, is what often prompts patients to seek medical attention. Hearing loss, vertigo, and tinnitus form the characteristic triad of Ménière's disease.

*Are there associated neurologic symptoms?* The patient or family members should be questioned about the time of onset of ataxia or gait disturbances. Ataxia of recent and relatively sudden onset suggests cerebellar hemorrhage or infarction in the distribution of the posterior inferior cerebellar artery or the superior cerebellar artery. The salient feature of chronic cerebellar disorders is a slowly progressive ataxia. True ataxia may be difficult to discern from the unsteadiness that occurs when a patient with significant vertigo attempts to walk.

Vertiginous symptoms are common after head injury. The presence of recent head or neck trauma should be explored because vertiginous symptoms are common after both.<sup>8,9</sup> Head injury can cause vertigo occasionally from intercerebral injury and more commonly from labyrinth concussion. Neck injury can cause vertigo from strain of muscle proprioceptors. In addition, vertebral artery injury has been seen resulting from activities such as chiropractic manipulation and even hair shampooing with marked hyperextension in a salon.<sup>10</sup>

It has clearly been shown that isolated vertigo can be the only initial symptom of cerebellar and other posterior circulation bleeds, transient ischemic attacks (TIAs), and infarction.<sup>11-13</sup> One study showed that emergency physicians often did not make the correct diagnosis in patients with validated strokes or TIAs that presented with only vertigo.<sup>6</sup> Risk factor assessment and symptom patterns can be extremely helpful in deciding which patients warrant imaging and admission. Older age, male sex, hypertension, coronary artery disease, diabetes mellitus, and atrial fibrillation put patients at higher risk. In addition, frequent episodes lasting only minutes or prolonged episodes of a day or more are more often associated with central processes.<sup>6,11,12</sup> A recent retrospective study showed emergency physicians often failed to chart triggers and duration of dizziness, information that could potentially lead to increased likelihood of a more serious cause of symptoms.<sup>14</sup>

**Past Medical History.** Many medications have direct vestibulotoxicity. The most commonly encountered are the aminoglycosides, anticonvulsants, alcohols, quinine, quinidine, and minocycline. In addition, caffeine and nicotine can have wide-ranging autonomic effects that may exacerbate vestibular symptoms. The history of past and present illnesses should be explored, with specific questioning about the existence of diabetes, drug or alcohol use, and the risk factors mentioned earlier.

### Physical Examination

**Vital Signs.** In some cases, pulses and blood pressure should be checked in both arms. Most patients with subclavian steal syndrome, which also can cause vertebrobasilar artery insufficiency, have pulse or systolic blood pressure differences between the two arms.

**Head and Neck.** Carotid or vertebral artery bruits suggest atherosclerosis. The neck is auscultated along the course of the

carotid artery from the supraclavicular area to the base of the skull.

Vertigo can be caused by impacted cerumen or a foreign object in the ear canal. Accumulation of fluid behind the eardrum as a result of a middle ear infection may cause mild vertigo, as can occlusion of the eustachian tubes associated with an upper respiratory tract infection. A perforated or scarred eardrum may indicate a perilymphatic fistula, especially if the history includes previous trauma.

Examination of the eyes is key in assessing a patient with vertigo or disequilibrium. The focus is on any pupillary abnormalities indicating third cranial nerve or descending sympathetic tract involvement or optic disk signs of early increased intracranial pressure. Extraocular movements should be assessed carefully. Relatively subtle ocular movement abnormalities can be the only clue to a cerebellar hemorrhage. A sixth cranial nerve palsy ipsilateral to the hemorrhage may result from early brainstem compression by the expanding hematoma. Internuclear ophthalmoplegia is recognized when the eyes are in a normal position on straight-ahead gaze, but on eye movement the adducting eye (cranial nerve III) is weak or shows no movement while the abducting eye (cranial nerve VI) moves normally, although often displaying a coarse nystagmus. This finding indicates an interruption of the medial longitudinal fasciculus on the side of the third cranial nerve weakness. It indicates brainstem pathology and is virtually pathognomonic of multiple sclerosis.

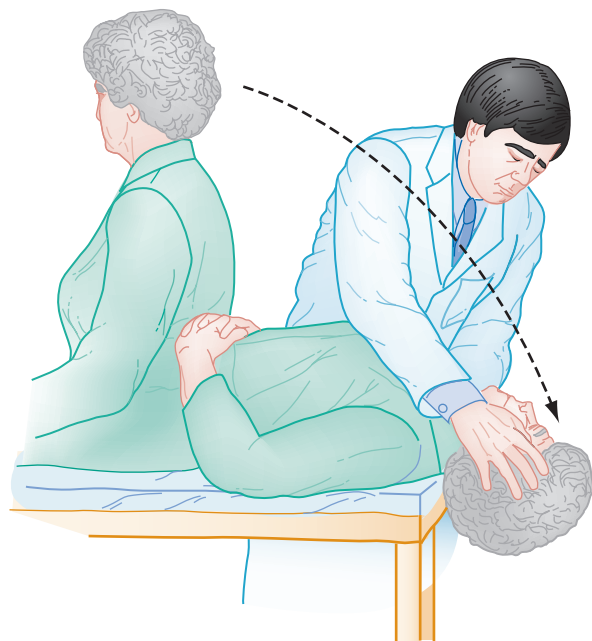
Abnormal nystagmus is the cardinal sign of inner ear disease and the principal objective evidence of abnormal vestibular function. In nystagmus, the patient has difficulty maintaining the conjugate deviation of the eyes or has a postural control imbalance of eye movements.

The abnormal jerk nystagmus of inner ear disease consists of slow and quick components. The eyes slowly "drift" in the direction of the diseased, hypoactive ear, then quickly jerk back to the intended direction of gaze. Positional nystagmus, induced by rapidly changing the position of the head, strongly suggests an organic vestibular disorder. The characteristics of nystagmus are one of the most valuable tools for distinguishing peripheral from central causes of vertigo (Table 12-2).

**Positional Testing.** If nystagmus is not present at rest, positional testing can be helpful in determining its existence and characteristics. In the Hallpike maneuver, the patient is moved quickly from an upright seated position to a supine position, and the head is turned to one side and extended (to a head-down posture) approximately 30° from the horizontal plane off the end of the stretcher. The eyes should be observed for nystagmus and the patient queried for the occurrence of symp-

**Table 12-2** Distinguishing Characteristics of Nystagmus with Central and Peripheral Vertigo

CHARACTERISTIC	CENTRAL	PERIPHERAL
Direction	Any direction	Horizontal or horizontorotary
Laterality	Unilateral or bilateral	Bilateral
Position testing effects:		
Latency	Short	Long
Duration	Sustained	Transient
Intensity	Mild	Mild to severe
Fatigability	Nonfatigable	Fatigable
Effect of visual fixation	Not suppressed, may be enhanced	Suppressed



**Figure 12-1.** Testing for positional vertigo and nystagmus.

toms. This test should be repeated with the head turned to the other side. Positive elicitation of symptoms and signs to one side or the other generally indicates vestibular pathology on that same side. This test should be performed with caution if vertebrobasilar insufficiency (VBI) is suggested because sudden twisting movements theoretically might dislodge atheromatous plaques (Fig. 12-1).

**Neurologic Examination.** The presence of cranial nerve deficits suggests a space-occupying lesion in the brainstem or cerebellopontine angle. The corneal reflex is a sensory cranial nerve V and motor cranial nerve VII circuit. Its diminution or absence can be one of the early signs of an acoustic neuroma. Vertigo caused by eighth cranial nerve involvement is likely to be accompanied by a unilateral hearing loss. Patients cannot hear a tuning fork when it is held alongside the affected ear, but they can hear it when it is held against the mastoid process. Involvement of the eighth cranial nerve suggests an acoustic tumor. Seventh cranial nerve involvement causes facial palsy that affects the entire side of the face. In supranuclear facial paralysis, the forehead is spared because these muscles receive bilateral cortical innervation.

The patient should be evaluated specifically for evidence of cerebellar dysfunction. This examination must be performed in bed and standing because truncal ataxia may be occult on testing of limbs in bed and may become obvious only when the patient has to sit, stand, or walk unaided. Dysmetria is the inability to arrest a muscular movement at the desired point. Dysmetria should be assessed using finger-to-finger/finger-to-nose pointing, and dysdiadochokinesia (an inability to perform coordinated muscular movement smoothly) is assessed with rapid alternating movements. The gait must be evaluated when the patient gives a history suggesting ataxia, although examination may be impossible during an attack of vertigo. Any marked abnormality (e.g., consistent falling or a grossly abnormal gait) should suggest a central lesion, especially in a patient whose vertiginous symptoms have subsided. The main features of a cerebellar gait are a wide base (separation of legs), unsteadiness, irregularity of steps, tremor of the trunk, and lurching from side to side. The unsteadiness is most prominent on arising quickly from a sitting position, turning quickly,

or stopping suddenly while walking. Patients with gait ataxia cannot perform heel-to-toe walking.

### Ancillary Testing

Most routine laboratory testing is not helpful in the evaluation of a vertiginous patient. A finger-stick blood glucose test should be performed in most cases because hypoglycemia can present as vertigo.<sup>15</sup> Blood counts and blood chemistries are sometimes helpful when it is difficult to distinguish whether “dizziness” is vertigo or near-syncope. An electrocardiogram should be obtained if there is any possibility of myocardial ischemia.

**Radiologic Imaging.** If cerebellar hemorrhage, cerebellar infarction, or other central lesions are suggested, emergent computed tomography (CT) or magnetic resonance imaging (MRI) of the brain is indicated. MRI, when available, has become the diagnostic modality of choice when cerebellar processes other than acute hemorrhage are possible. MRI is particularly useful for the diagnosis of acoustic neuromas and for sclerotic and demyelinating lesions of the white matter, as seen in multiple sclerosis. Acute vertigo by itself does not usually warrant urgent CT or MRI in all patients, particularly patients in whom a clear picture of peripheral vertigo emerges. But as mentioned earlier, many studies strongly support the use of imaging in patients of advanced age or at risk for cerebrovascular disease.<sup>6,11,12,16</sup>

Conventional angiography or magnetic resonance angiography can be used in cases of suspected VBI to document the presence of vascular disease. It is used most often in patients with changing neurologic signs and symptoms, suggesting impending posterior circulation occlusion.

Audiology and electronystagmography are helpful in the follow-up evaluation of a vertiginous patient. Audiology can locate the anatomic site of a lesion causing vertigo. Electronystagmography is a collection of examinations that, when abnormal, suggest vestibular dysfunction but do not yield the specific diagnosis.

### ■ DIFFERENTIAL DIAGNOSIS

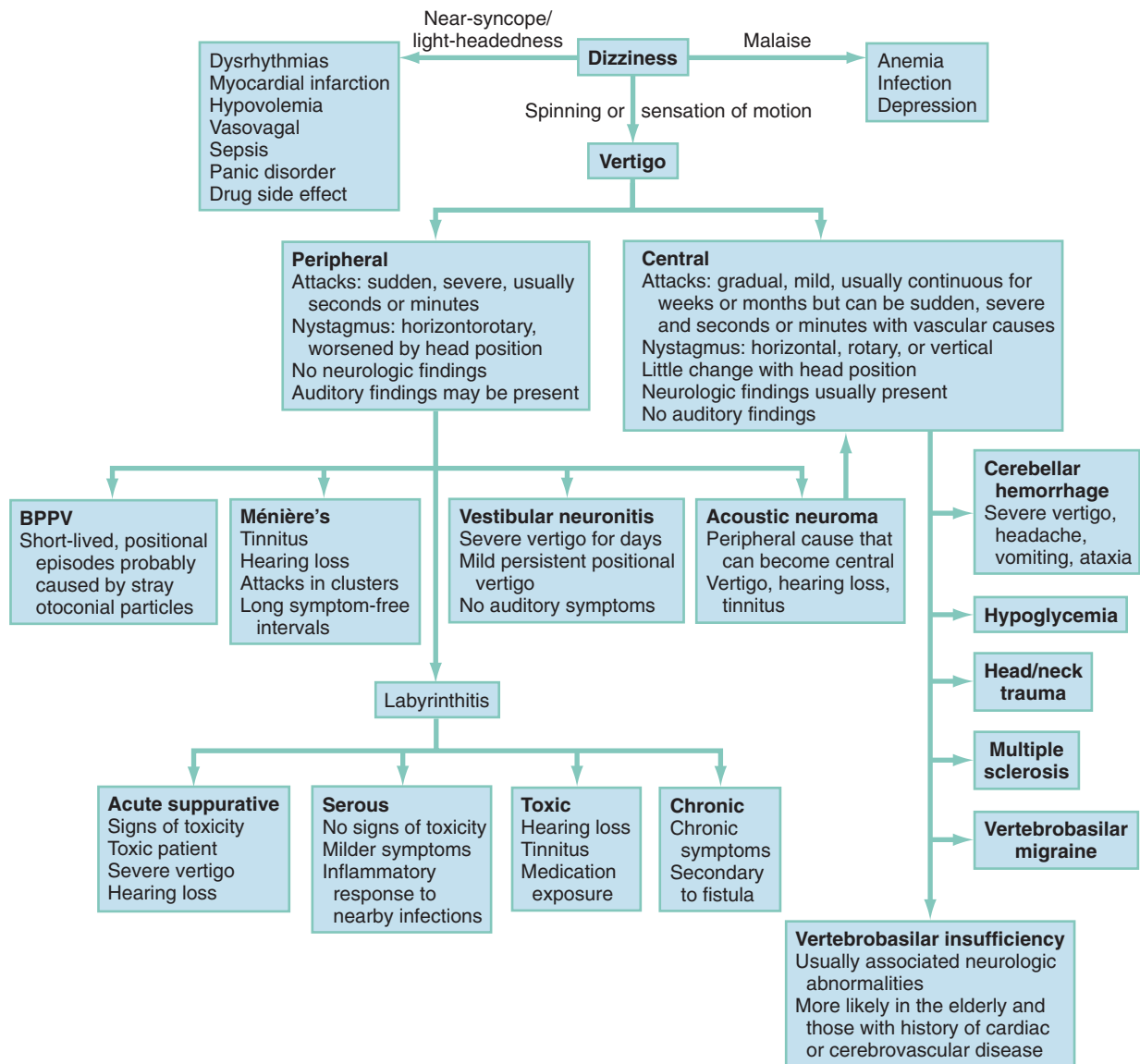
The differential diagnosis for other peripheral, central, and systemic causes of vertigo is large (see Box 12-1). More detailed information is given on selected causes in Table 12-3, including the most common peripheral causes of true vertigo: benign positional vertigo, labyrinthitis, Ménière’s disease, and vestibular neuronitis.

### Diagnostic Algorithm

Most cases of vertigo are of peripheral origin and are not usually life-threatening. The diagnostic approach must focus on identifying entities that either immediately or in the near future can lead to death or significant morbidity (Fig. 12-2).

### ■ MANAGEMENT

Management is based on an accurate diagnosis that distinguishes the serious central causes of vertigo from the less serious, albeit more debilitating, peripheral causes (Fig. 12-3). Any suggestion of cerebellar hemorrhage should warrant immediate imaging with CT or MRI and neurosurgery consultations. VBI should be considered in any patient of advanced age or at high risk of cerebrovascular disease with isolated, new-onset vertigo without an obvious cause.<sup>6,11,17,18</sup> Because of the possibility of progression of new-onset VBI in the first 24 to 72 hours, hospital or observation unit admission and consid-



**Figure 12-2.** Diagnostic algorithm for dizziness and vertigo. BPPV, benign paroxysmal positional vertigo.

eration of early magnetic resonance angiography probably are warranted, even in a stable patient. Changing or rapidly progressive symptoms should raise awareness of impending posterior circulation occlusion. If CT or MRI excludes hemorrhage as the source of the patient's symptoms, an immediate neurologic consultation, emergency angiography, and possibly anticoagulation are indicated.

Acute bacterial labyrinthitis requires admission, intravenous antibiotics, and, occasionally, surgical drainage and débridement. In cases of toxic labyrinthitis, the offending medication should be discontinued immediately.

Some cases of Ménière's disease have been treated successfully by vasodilation and diuretic therapy. Diets low in sodium and caffeine and cessation of smoking also have been helpful. Chemical ablation of vestibular function with gentamicin and streptomycin is an option in severe Ménière's disease. In one small controlled study, corticosteroids were more effective than placebo in treating the acute symptoms of vestibular neuritis.

The treatment of acute attacks of vertigo caused by peripheral disorders is symptomatic. Intravenous diazepam in 2- to

5-mg doses is extremely effective in stopping vertigo. It has a sedative effect that acts on the limbic system, the thalamus, and the hypothalamus. Outpatient treatment with diazepam can be continued at doses of 5 to 10 mg three times daily.

The neurons involved in vestibular reactions are mediated by acetylcholine. Anticholinergic drugs or antihistamines with anticholinergic activity are extremely useful in treating vertigo. Meclizine hydrochloride (Antivert) is usually prescribed as 25 mg every 8 hours, but has a wide therapeutic margin and can be taken much more frequently to control symptoms. Diphenhydramine hydrochloride (Benadryl), 25 to 50 mg every 6 to 8 hours, and dimenhydrinate (Dramamine, Gravol) are also effective, but are more sedating than meclizine. Either drug also can be given intravenously. Transdermal scopolamine has shown disappointing results for treatment of peripheral vertigo but may be considered a third-line or fourth-line option. Promethazine hydrochloride (Phenergan), 25 mg orally or rectally every 6 to 8 hours, is effective because of its strong antiemetic and mild anticholinergic properties; it also can be used intravenously in doses of 12.5 to 25 mg. Buccal



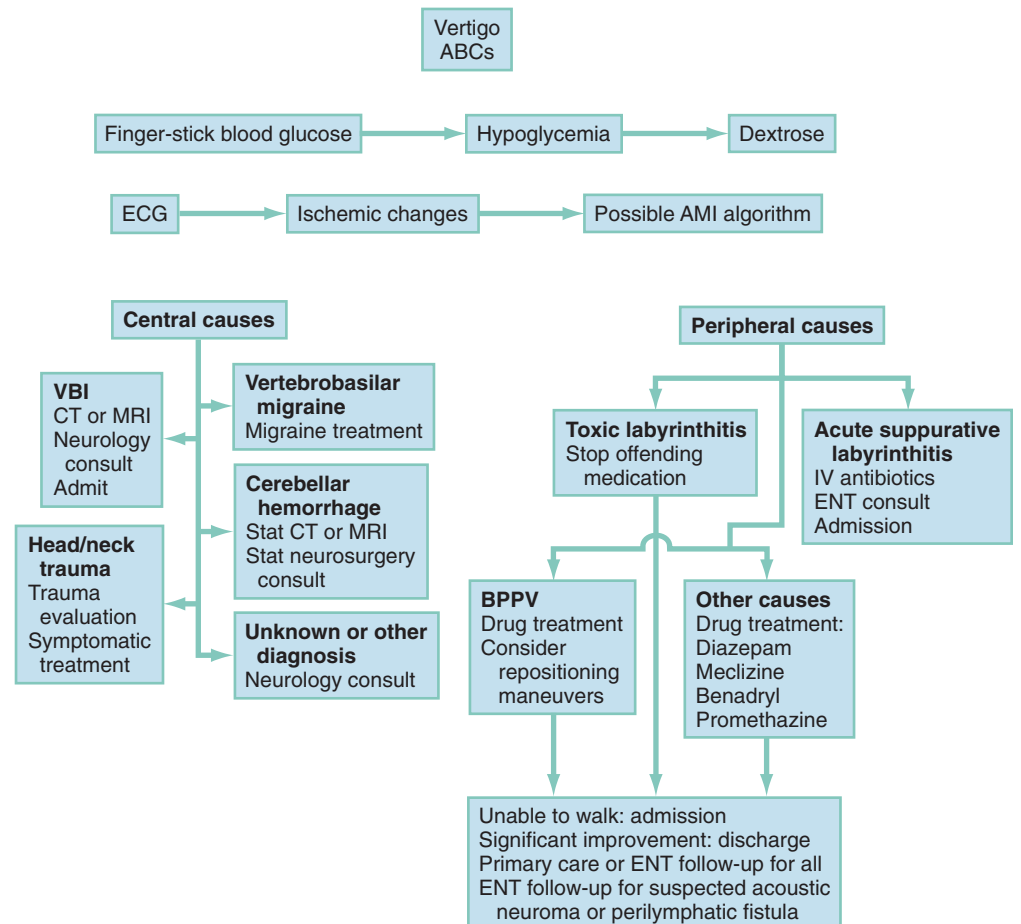
**Table 12-3 Differential Diagnosis of Patients with True Vertigo**

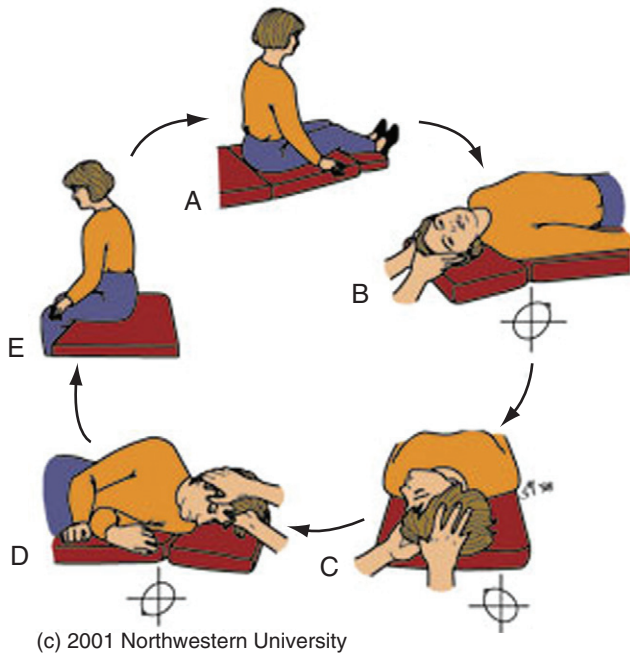
CAUSE	HISTORY	ASSOCIATED SYMPTOMS	PHYSICAL
<b>Peripheral</b>			
1. Benign paroxysmal positional vertigo	Short-lived, positional, fatigable episodes	Nausea, vomiting	Single position can precipitate vertigo. Horizontorotary nystagmus often can be induced at bedside.
2. Labyrinthitis			
A. Serous	Mild to severe positional symptoms. Usually coexisting or antecedent infection of ear, nose, throat, or meninges	Mild to severe hearing loss can occur	Usually nontoxic patient with minimal fever elevation
B. Acute suppurative	Coexisting acute exudative infection of the inner ear. Severe symptoms	Usually severe hearing loss, nausea, vomiting	Febrile patient showing signs of toxicity. Acute otitis media
C. Toxic	Gradually progressive symptoms: Patients on medication causing toxicity	Hearing loss that may become rapid and severe, nausea and vomiting	Hearing loss. Ataxia common feature in chronic phase
3. Ménière's disease	Recurrent episodes of severe rotational vertigo usually lasting hours. Onset usually abrupt. Attacks may occur in clusters. Long symptom-free remissions	Nausea, vomiting, tinnitus, hearing loss	Positional nystagmus not present
4. Vestibular neuronitis	Sudden onset of severe vertigo, increasing in intensity for hours, then gradually subsiding over several days. Mild positional vertigo often lasts weeks to months. Sometimes history of infection or toxic exposure that precedes initial attack. Highest incidence is found in third and fifth decades	Nausea, vomiting. Auditory symptoms do not occur	Spontaneous nystagmus toward the involved ear may be present.
5. Acoustic neuroma	Gradual onset and increase in symptoms. Neurologic signs in later stages. Most occur in women between 30 and 60	Hearing loss, tinnitus. True ataxia and neurologic signs as tumor enlarges	Unilateral decreased hearing. True truncal ataxia and other neurologic signs when tumor enlarges. May have diminution or absence of corneal reflex. Eighth cranial nerve deficit may be present.
<b>Central</b>			
1. Vascular disorders			
A. Vertebrobasilar insufficiency	Should be considered in any patient of advanced age with isolated new-onset vertigo without an obvious cause. More likely with history of atherosclerosis. Initial episode usually seconds to minutes	Often headache. Usually neurologic symptoms including dysarthria, ataxia, weakness, numbness, double vision. Tinnitus and deafness uncommon	Neurologic deficits usually present, but initially neurologic examination can be normal.
B. Cerebellar hemorrhage	Sudden onset of severe symptoms	Headache, vomiting, ataxia	Signs of toxicity. Dysmetria, true ataxia. Ipsilateral sixth cranial nerve palsy may be present.
C. Occlusion of posterior inferior cerebellar artery (Wallenberg's syndrome)	Vertigo associated with significant neurologic complaints	Nausea, vomiting, loss of pain and temperature sensation, ataxia, hoarseness	Loss of pain and temperature sensation on the side of the face ipsilateral to the lesion and on the opposite side of the body, paralysis of the palate, pharynx, and larynx. Horner's syndrome (ipsilateral ptosis, miosis, and decreased facial sweating)
D. Subclavian steal syndrome	Classic picture is syncopal attacks during exercise, but most cases present with more subtle symptoms.	Arm fatigue, cramps, mild light-headedness may be only other symptoms than vertigo	Diminished or absent radial pulses in affected side or systolic blood pressure differentials between the two areas occur in most patients.

**Table 12-3 Differential Diagnosis of Patients with True Vertigo—cont'd**

CAUSE	HISTORY	ASSOCIATED SYMPTOMS	PHYSICAL
2. Head trauma	Symptoms begin with or shortly after head trauma. Positional symptoms most common type after trauma. Self-limited symptoms that can persist weeks to months	Usually mild nausea	Occasionally, basilar skull fracture
3. Neck trauma	Usual onset 7–10 days after whiplash injury. Symptoms may last weeks to months. Episodes seconds to minutes when turning head	Neck pain	Neck tenderness, pain on movement, and positional nystagmus and vertigo when head is turned to side of the whiplash
4. Vertebrobasilar migraine	Vertigo almost always followed by headache. Patient has usually had similar episodes in past. Most patients have a family history of migraine. Syndrome usually begins in adolescence	Dysarthria, ataxia, visual disturbances, or paresthesias usually precede headache	No residual neurologic or otologic signs are present after attack.
5. Multiple sclerosis	Vertigo presenting symptoms in 7–10% and appears in the course of the disease in a third. Onset may be severe and suggest labyrinth disease. Disease onset usually between ages 20 and 40. Often history of other attacks with varying neurologic signs or symptoms	Nausea and vomiting, which may be severe	May have horizontal, rotary, or vertical nystagmus. Nystagmus may persist after the vertiginous symptoms have subsided. Bilateral internuclear ophthalmoplegia and ataxic eye movements suggest multiple sclerosis.
6. Temporal lobe epilepsy	Can be initial or prominent symptom in some patients with the disorder	Memory impairment, hallucinations, trancelike states, seizures	May have aphasia or convulsions
7. Hypoglycemia	Should be considered in diabetics and any other patient with unexplained symptoms	Sweating, anxiety	Tachycardia, mental status change may be present.

**Figure 12-3.** Management algorithm for vertigo. AMI, acute myocardial infarction; BPPV, benign paroxysmal positional vertigo; CT, computed tomography; ECG, electrocardiogram; ENT, ear, nose, and throat; MRI, magnetic resonance imaging.





**Figure 12-4.** The Epley maneuver for benign paroxysmal peripheral vertigo, also known as the particle repositioning or canalith repositioning procedure. Image used with permission of (<http://www.dizziness-and-balance.com/disorders/bppv/bppv.html>) Timothy C. Hain, Professor of Neurology, Feinberg School of Medicine, Northwestern University, <http://www.dizziness-and-balance.com/disorders/bppv/bppv.html>.

prochlorperazine (Compazine, Stemetil) also has been shown to be a safe and effective treatment for vertigo. Avoidance of stimulants (e.g., caffeine, pseudoephedrine, nicotine) may ease symptoms in some cases. In addition, canalith repositioning procedures, such as the Epley and Semont maneuvers,

have been shown to be extremely effective in treating benign paroxysmal positional vertigo.<sup>19-21</sup> The Epley maneuver involves sequential movement of the head into four positions, staying in each position for approximately 30 seconds, as demonstrated in Figure 12-4. One study has even shown these maneuvers have resulted in long-term efficacy in successful symptom treatment.<sup>22</sup>

One of the most useful tools the physician has is patient reassurance. Most patients with vertigo have self-limited disease processes that have a specific organic cause. By combining patient education and reassurance with judicious use of medications, the treatment of a dizzy patient can be rewarding for the patient and the physician.

## ■ DISPOSITION

Documented or suggested cerebellar hemorrhage or infarction, VBI, and acute bacterial labyrinthitis require workup and hospitalization. In patients older than age 55 years, particularly patients with vascular disease, admission for observation and imaging of cerebral vasculature is often warranted. Most younger patients with peripheral causes of vertigo can be discharged from the emergency department after symptoms are controlled. Some patients may have such severe symptoms (e.g., vomiting, inability to walk) despite a trial of medication that they require admission for intravenous hydration and observation. All discharged patients should receive primary care; neurology; or a follow-up consult with an ear, nose, and throat specialist. This follow-up is especially important for possible cases of acoustic neuroma and toxic labyrinthitis.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

J. Stephen Huff

## ■ PERSPECTIVE

The term *confusion* connotes an alteration in higher cerebral functions, such as memory, attention, or awareness. Confusion is a symptom, not a diagnosis. Clinical jargon includes “altered mental status,” “delta MS” (change in mental status), “altered mentation,” and “change from baseline.” Additionally, the ability to sustain and focus attention is impaired. Symptoms of confusion may fluctuate, as may the level of consciousness. Implicit in the definition is a recent change in behavior. Chronic mental status changes such as dementia typically have a different clinical chronology. Other forms of altered mentation include states of diminished alertness on the coma spectrum; these presentations may result from some of the same pathophysiologic processes causing confusion and are discussed in Chapter 15. Confusion may range in severity from a mild disturbance of short-term memory to a global inability to relate to the environment and process sensory input. This extreme state is termed *delirium*. Delirium has two subtypes: hyperactive and hypoactive.<sup>1</sup> Hyperactive delirium is characterized as an acute confusional state associated with increased alertness, increased psychomotor activity, and disorientation and is often accompanied by hallucinations. In hypoactive delirium (sometimes referred to as quiet delirium), the confusional state is present but the patient has a reduction in alertness and behavior. Confusion has many causes, and an orderly approach is necessary to discover the causative diagnosis.

## Epidemiology

Physicians underestimate the incidence of confusion in patients.<sup>2,3</sup> Often, confusion is accepted as an incidental or secondary component of another condition. A patient with injuries from a motor vehicle crash or with dyspnea may be confused, but the primary condition overshadows the underlying abnormal mental status. When confusion exists as an isolated or unexplained finding, it is more likely to receive full and immediate consideration by the clinician. Confusion is estimated to occur in 2% of emergency department (ED) patients, 10% of all hospitalized patients, and 50% of elderly hospitalized patients.<sup>2,4</sup>

## Pathophysiology

Conceptually, consciousness may be divided into elements of alertness or arousal and elements constituting content of consciousness. Confusion is largely a problem of the content

portion of consciousness. Many different clinical processes may disrupt optimal cortical functioning and result in confusion. The pathophysiology is not straightforward. Widespread cortical dysfunction is thought to result from substrate deficit (hypoglycemia or hypoxemia), neurotransmitter dysfunction, or circulatory dysfunction. Compounding this problem is the idea that the reserve of central nervous system (CNS) function varies from individual to individual; individuals with a pre-existing impairment may become confused after even minor changes in their normal state.

## ■ DIAGNOSTIC APPROACH

### Differential Considerations

The observation of acute confusion prompts a search for an underlying cause. Four groups of disorders encompass most causes of diffuse cortical dysfunction: (1) systemic diseases secondarily affecting the CNS, (2) primary intracranial disease, (3) exogenous toxins, and (4) drug withdrawal states (Box 13-1).<sup>1</sup> Focal cortical dysfunction, such as from tumor or stroke, typically does not cause confusion, although exceptions are encountered. Likewise, subcortical or brainstem dysfunction most frequently results in a diminished level of alertness and consciousness, not confusion.

### Rapid Assessment and Stabilization

Most patients with acute confusion do not require immediate interventions. Three crucial exceptions are hypoglycemia, hypoxemia, and shock. A complete set of vital signs, including temperature and oxyhemoglobin saturation, and a bedside blood glucose level should be determined promptly for all confused patients. Oral or intravenous glucose therapy is indicated if low blood glucose is discovered. Supplemental oxygen and intravenous fluid are administered as necessary.

Patients should be protected from harming themselves or others. Close observation may need to be supplemented by medications or physical restraint. Family members may offer valuable assistance in observing and comforting the patient.

In a patient with abnormal or unstable vital signs, initial diagnostic and management efforts are directed toward treatment of the systemic condition. A confused patient with acute pulmonary edema, hypoxia, and confusion obviously requires evaluation and treatment of the pulmonary edema, not a screening test for cognitive functioning.



**BOX 13-1 MAJOR CATEGORIES: DIFFERENTIAL CONSIDERATIONS**

Primary intracranial disease  
 Systemic diseases secondarily affecting the central nervous system  
 Exogenous toxins  
 Drug withdrawal

**BOX 13-2 FINDINGS THAT MAY HELP DIFFERENTIATE BETWEEN ORGANIC AND FUNCTIONAL CAUSES OF CONFUSION**

Organic	Functional (psychiatric)
History	History
Acute onset	Onset over weeks to months
Any age	Onset ages 12 to 40 years
Mental status examination	Mental status examination
Fluctuating level of consciousness	Alert
Disoriented	Oriented
Attention disturbances	Agitated, anxious
Poor recent memory	Poor immediate memory
Hallucinations: visual, tactile, auditory	Hallucinations: most commonly auditory
Cognitive changes	Delusions, illusions
Physical examination	Physical examination
Abnormal vital signs	Normal vital signs
Nystagmus	No nystagmus
Focal neurologic signs	Purposeful movement
Signs of trauma	No signs of trauma

Generally, in patients with schizophrenia and other psychiatric disorders, tests of cognition, orientation, and attention are normal unless the condition is severe. The term *psychosis* implies a disorder of reality testing and thought organization severe enough to interfere with normal daily functioning. Psychosis is a nonspecific syndrome, and careful evaluation is required to differentiate between psychiatric and organic origins (e.g., drug intoxication or other systemic process) (Box 13-2).

### Pivotal Findings

A patient with an altered state of consciousness including confusion is evaluated by taking a focused history and conducting a pertinent examination, performing rapid bedside screening investigations, and observing the response to certain therapies (e.g., dextrose or naloxone). Additional evaluation may include laboratory testing and diagnostic imaging with various modalities. Useful information that provides the diagnosis or strongly suggests the etiology is found roughly in descending order from the patient's history, the examination including results of rapid bedside testing, and the response to ED therapies; the results of laboratory testing and diagnostic imaging are less often useful.<sup>5</sup>

### History

Confusion is often reported by family members or caregivers; frequently the patient is not aware of the confusion and seem-

<b>ORIENTATION TO TIME</b> "What is the date?"
<b>REGISTRATION</b> "Listen carefully. I am going to say three words. You say them back after I stop. Ready? Here they are . . . HOUSE (pause), CAR (pause), LAKE (pause). Now repeat those words back to me." [Repeat up to 5 times, but score only the first trial.]
<b>NAMING</b> "What is this?" [Point to a pencil or pen.]
<b>READING</b> "Please read this and do what it says." [Show examinee the words on the stimulus form.] <b>CLOSE YOUR EYES</b>

**Figure 13-1.** Mini-mental state examination sample items. (Reproduced by special permission of the Publisher, Psychological Assessment Resources, Inc., 16204 North Florida Avenue, Lutz, Florida 33549, from the Mini Mental State Examination, by Marshal Folstein and Susan Folstein. Copyright © 1975, 1998, 2001 by Mini Mental LLC, Inc. Published 2001 by Psychological Assessment Resources, Inc. Further reproduction is prohibited without permission of PAR, Inc. The MMSE can be purchased from PAR, Inc., by calling (800) 331-8378 or (813) 968-3003.)

ingly glosses over problems. Families may articulate the complaint as confusion but also may describe rambling, disorientation, speaking to persons not there, the patient's inability to find his or her way around familiar surroundings, or simply "not being right." An essential goal of the history is to determine when the patient last exhibited "normal" thinking and behavior.

Attention deficit is the common denominator in confusional states. The initial task in evaluating the patient is to define the symptoms and severity of confusion. The specific behaviors that are of concern to the patient or caregivers should be defined. Often, the family is the most valuable source for information; a physician or other caregiver with an established relationship with the patient also may be helpful. The duration of the confusion, any recent changes in medications, and recent illnesses are important points in the clinical history. Hallucinations are not unique to psychiatric illness and can commonly occur in confusion states, especially delirium. Hallucinations in delirium tend to be visual (with or without auditory components), powerful, fleeting, and poorly organized. A history of medication or substance abuse and any recent changes, especially cessation of benzodiazepines or ethanol, should be sought.

### Physical Examination

The patient's confusion may be obvious at the bedside. In other cases, confusion may be subtle, and informal assessment of mental status and cognitive abilities may fail to detect it. The mini-mental state examination (MMSE) (Fig. 13-1) commonly is recommended as a screening instrument but is used infrequently in the ED because of the time required to administer it.<sup>6,7</sup> A more rapidly performed screening tool, the Quick Confusion Scale (QCS; Fig. 13-2), has been developed and tested in ED patients.<sup>8-10</sup> This tool objectively measures elements of the patient's mental status in 2 to 3 minutes and correlates well with the MMSE.<sup>9,11</sup> The tasks measured by either the MMSE or the QCS require adequate attention on

Figure 13-2. Quick Confusion Scale.

ITEM	SCORE (highest number in category indicates correct response; decreased scoring indicates increased number of errors)	WEIGHT	SCORE
What year is it now?	0 or 1 (score 1 if correct; 0 if incorrect)	x2	
What month is it?	0 or 1 (score 1 if correct; 0 if incorrect)	x2	
Repeat phrase and remember it: "John Brown, 42 Market Street, New York"			
About what time is it? (answer correct if within the hour)	0 or 1 (score 1 if correct; 0 if incorrect)	x2	
Count backwards from 20 to 1	0, 1, or 2 (score 2 if correct; 1 if 1 error; score 0 if more than 2 errors)	x1	
Say the months in reverse	0, 1, or 2 (score 2 if correct; 1 if 1 error; score 0 if more than 2 errors)	x1	
Repeat the memory phrase (each underlined portion is worth 1 point)	0, 1, 2, 3, 4, 5 (score 5 if correctly performed; each error drops score by one)	x1	
TOTAL			_____

Final score is sum of the totals; score less than 15 suggests the presence of altered cognition and need for further assessment.

the part of the patient. If the patient's attention span is greatly impaired, detailed testing may be impossible. Digit repetition forward (five or six digits) and backward (four digits) is a brief screen for attention function. Alternatively, spelling a commonly used word backward ("world" is frequently used) measures a patient's ability to concentrate. Screening tests may detect confusion not obvious in casual conversation, identifying the need for further investigations.<sup>12,13</sup>

The physical examination may suggest a cause for confusion such as congestive heart failure or pneumonia. A fever suggests an infection as the cause of altered mental status and should prompt a search for the source, particularly urinary tract infection in the elder patient. Any new focal neurologic findings suggest a possible mass lesion or stroke and should trigger neuroimaging. In this regard, testing of gait and tandem gait, if possible, may be invaluable. Aphasia, fluent or nonfluent, is a focal sign suggesting a lesion in the dominant cerebral hemisphere. In confusional states, speech may be abnormal and is often incoherent, and the rate of speech may be either rapid or slowed. Involuntary movements, such as asterixis or tremor, may be present. The various toxidromes may assist in the identification of an intoxication or drug effect as the cause of confusion.

### Laboratory Tests

The results of the history and physical examination frequently guide the clinician in the choice of laboratory tests most likely to yield valuable diagnostic information. Pulse oximetry may reveal hypoxia, or bedside glucose testing may reveal hypoglycemia or hyperglycemia. In the presence of a fever, chest radiography and urinalysis often reveal the source of the infection causing the altered mentation. In elder patients, urinalysis should be performed whether or not fever is present. Other

tests commonly available in the ED and useful in the evaluation of a confused patient are serum electrolyte testing (especially sodium) and electrocardiography. Electrocardiography is indicated in elderly patients because myocardial infarction may present as confusion. The complete blood count, although commonly performed, is unlikely to provide useful diagnostic clues. Arterial blood gas testing is rarely indicated or useful, unless pulse oximetry is not reliable.

If common and simple tests do not suggest a solution, more complex testing should be initiated in the ED, observation unit, or inpatient service. The clinical situation and overall condition of the patient determine the speed and direction of evaluation. Additional laboratory work is often of decreasing yield but may reveal the cause of confusion. Serum ammonia, calcium, thyroid function, and selected drug and toxicologic testing may be ordered in this second tier of evaluation. Blood and urine cultures should be obtained in the febrile patient when hospital admission is anticipated and a clear infectious source is not evident. Paracentesis or thoracentesis may be appropriate if ascites or pleural effusion is present. Cranial computed tomography (CT) scanning is usually done to screen for CNS lesions in the absence of another identified source for the confusion. Focal findings on CT increase the yield of this test, but unanticipated abnormalities are often found on neuroimaging. Lumbar puncture may discover or exclude CNS infection if no other source has been identified. Cerebrospinal fluid examination may clarify a diagnosis of bacterial meningitis, encephalitis, aseptic meningitis, or subarachnoid hemorrhage. If the cause of confusion remains unclear or if the patient is unable to function safely in his or her current environment, admission may be necessary for additional ongoing assessment, including diagnostic testing not usually available in the ED, such as magnetic resonance imaging or electroencephalography.<sup>5</sup>

**BOX 13-3 CRITICAL AND EMERGENT DIAGNOSES****Critical**

Hypoxia/diffuse cerebral ischemia  
 Respiratory failure  
 Congestive heart failure  
 Myocardial infarction  
 Shock  
 Systemic processes  
 Hypoglycemia  
 CNS infections  
 Hypertensive encephalopathy  
 Elevated intracranial pressure—medical and surgical origin

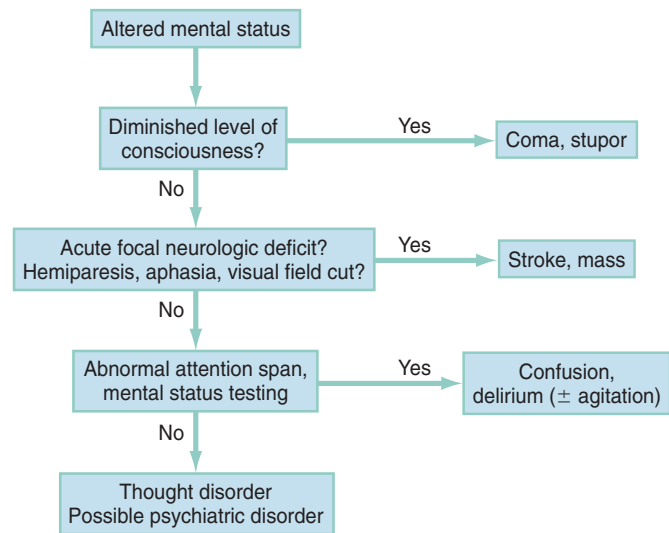
**Emergent**

Hypoxia/diffuse cerebral ischemia  
 Severe anemia  
 Systemic diseases  
 Electrolyte and fluid disturbance  
 Endocrine disease  
 Thyroid  
 Adrenal  
 Hepatic failure  
 Nutrition/Wernicke's encephalopathy  
 Sepsis, infection  
 Intoxications and withdrawal  
 CNS sedatives  
 Ethanol  
 Other medication side effects, particularly anticholinergics  
 CNS disease  
 Trauma  
 Infections  
 Stroke  
 Subarachnoid hemorrhage  
 Epilepsy/seizures  
 Postictal state  
 Nonconvulsive status epilepticus  
 Complex partial status epilepticus  
 Neoplasm

*Note:* These represent a partial diagnosis; causes are myriad. "Critical" in this case means conditions that need immediate assessment and correction within moments, such as oxygenation and ventilation problems or hypoglycemia. Because confusion represents CNS failure, other problems may be considered critical as well and may require intensive care unit admission, depending on severity. CNS, central nervous system.

**■ DIFFERENTIAL DIAGNOSIS**

Certain critical and emergent diagnoses require prompt recognition to prevent morbidity or mortality (Box 13-3). The diagnosis of confusion implies the exclusion of other states of altered mental status, such as coma and decompensated psychiatric syndromes. A new focal neurologic deficit points to a focal defect of the CNS, which is less likely to cause the global cortical dysfunction necessary for confusion. Stroke rarely causes confusion, but resulting disturbances in speech or understanding may mimic a confusional state. The diagnosis of stroke is relatively straightforward if a new motor deficit is present. Occasionally, other focal neurologic abnormalities may mimic a confusional state. A person with a new visual field deficit and visual neglect may have difficulty ambulating in familiar surroundings and be labeled as confused, but this



**Figure 13-3.** Diagnostic algorithm for confusion.

reflects focal neurologic injury and not a confusional state from global CNS dysfunction. Careful assessment of mental status assists in resolving the diagnostic dilemma. Frontal lobe dysfunction from stroke, subdural hematoma, or tumor may result in personality changes and the report of "confusion" by family or friends.

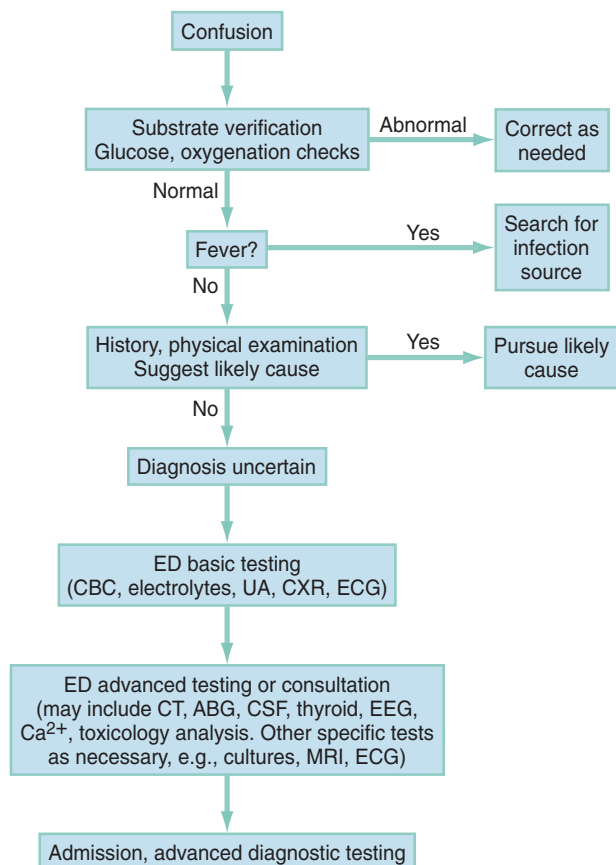
Altered mental status may be divided into three different categories depending on the findings of diminished level of consciousness, acute focal neurologic deficit, or abnormal attention span. Placement into one of these categories may guide the differential assessment and therapy (Fig. 13-3).

**■ EMPIRICAL MANAGEMENT**

Ideally, treatment is directed at the underlying cause of the confusion. Investigations continue until a likely diagnosis is discovered or consultation and admission are deemed necessary (Fig. 13-4). Many febrile patients are found to have a systemic infectious cause of the confusion. Urinary tract infections and pneumonia are the more common sources, but soft tissue infections also warrant consideration. CNS infections are encountered less frequently but have potentially devastating consequences if not recognized promptly. Antibiotic treatment for coverage of common causes of meningitis may be considered in ill febrile patients while definitive evaluation is in progress.

Postictal confusion is common in patients with seizures but should improve within 20 to 30 minutes. If the patient remains unconscious or confused after a seizure, the possibility of ongoing or intermittent seizure activity (i.e., nonconvulsive seizures) should be considered. Nonconvulsive status epilepticus, an epileptic twilight state, is unusual but does occur, and may be particularly difficult to recognize in the elderly<sup>14</sup> (see also Chapter 15).

Sometimes it may be necessary to treat confusion or agitation for patient safety. Environmental manipulations, such as dim lighting or psychosocial support, may be helpful. Confinement or physical restraint may be necessary at times for patient safety; institutional guidelines should be followed. Benzodiazepines or butyrophenones may be used if necessary to decrease agitation. These medications may alter mental status further, making evaluation more difficult.



**Figure 13-4.** Management algorithm for confusion. ABG, arterial blood gas; CBC, complete blood count; CT, computed tomography; CSF, cerebrospinal fluid; CXR, chest x-ray; ECG, electrocardiogram; MRI, magnetic resonance imaging; UA, urinalysis.

## DISPOSITION

Most patients presenting with confusion are admitted to the hospital or ED observation unit for additional diagnostic procedures, extended observation, and treatment. Exceptions include patients with rapidly resolved confusional states after treatment for insulin-induced hypoglycemia, after generalized seizures of known origin, or after recovering from self-limiting intoxicants or withdrawal states, such as those related to ethanol or recreational drugs. These patients may be observed and then discharged after successful identification and resolution of acute confusional state. Unresolved confusion or unexplained findings on repeat mental status screen should prompt admission or careful reevaluation before considering discharge.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*



# Depressed Consciousness and Coma

Jeremy L. Cooke

## PERSPECTIVE

### Epidemiology

Depressed consciousness is a common presenting complaint in the emergency department (ED). It represents a spectrum of disease that ranges from sleepiness or decreased alertness to frank coma. The majority of cases of depressed consciousness and coma are caused by metabolic or systemic derangements, and the remainder are caused by structural lesions.<sup>1</sup> The differential diagnosis for depressed level of consciousness often overlaps that for confusion (see Chapter 13).

### Pathophysiology

*Consciousness* includes the properties of *arousal*, which is defined as the awareness of one's self or surroundings, and *cognition*. *Cognition* is the combination of *orientation*, the accurate perception of what is experienced, *judgment*, the ability to process input data to generate more meaningful information, and *memory*, the ability to store and retrieve information. The *ascending reticular activating system* (ARAS) is the neuroanatomic structure primarily responsible for arousal. It is located in the paramedian tegmental zone in the dorsal part of the brainstem (Fig. 14-1). The input of somatic and sensory stimuli to the cerebral cortex is controlled by the ARAS and functions to initiate arousal from sleep. The brain's cognition centers are located primarily in the cerebral cortex.

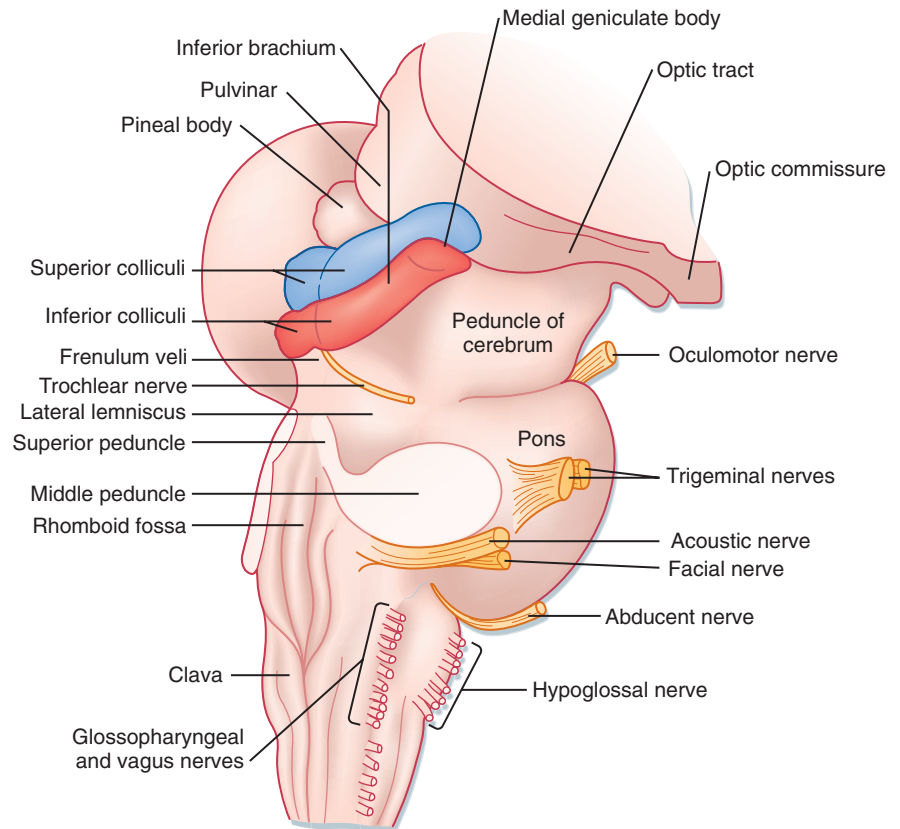
Insults to the cerebral cortex or brainstem can each independently cause depressed consciousness or coma. These structures are vulnerable to metabolic derangements, toxins, or mechanical injury. Typically, both cerebral hemispheres need to be affected to induce coma and this also depends on the size and speed of progression of the insult. Localized, unilateral lesions in the cerebral cortex usually do not induce depressed consciousness or coma even if other cognitive functions are impaired. In contrast, a completely intact brainstem is necessary for arousal. Small focal lesions in the brainstem can affect the ARAS. If the ARAS is impaired, the cerebral cortex cannot be aroused and depressed consciousness or coma occurs.

Potential causes of depressed consciousness can be broken down into a few general categories. Metabolic or systemic causes of coma can include hypoxia, hypoperfusion, infection, toxic drug effects, or electrolyte disturbances. Hypoxia can be the result of congestive heart failure (CHF), pulmonary embolism, carbon monoxide poisoning, or severe pulmonary com-

promise such as occurs in chronic obstructive pulmonary disease (COPD), cystic fibrosis, and asthma. The various causes of shock can result in hypoperfusion states leading to depression of consciousness. These include anaphylactic, septic, hypovolemic, cardiogenic, and neurogenic origins of shock. Each type of shock has its own special characteristics, which are detailed in other chapters. Infection, both systemic (sepsis) and focal, can be another general cause of depressed consciousness. This is particularly true if central nervous system (CNS) structures are involved as in meningitis, encephalitis, or CNS abscess. Toxic drug effects ranging from recreational drug use and intentional overdoses to therapeutic doses with adverse side effects are common general causes of depressed consciousness seen in the ED. In the elderly, adverse side effects from prescription medications are common. In addition, electrolyte and glucose abnormalities can be caused by multiple conditions, including diabetes, renal dysfunction, malignancy, and medication interactions or dosing errors.

Structural causes of coma and depressed consciousness are those most commonly arising from head trauma, stroke, tumor, or infection. Traumatic causes can include subdural and epidural hematomas, intraparenchymal or subarachnoid hemorrhage, or simply contusion or concussion. Strokes occur with embolic, thrombotic, or hemorrhagic mechanisms, but it is extremely unusual for ischemic (i.e., nonhemorrhagic) stroke to depress consciousness unless a massive insult to both hemispheres has occurred (e.g., diffuse, severe cerebral edema after a massive infarct). Depression of consciousness with CNS infections may be caused by mass effect and is common with severe bacterial meningitis, cerebral abscess or empyema, or parasitic mass. Malignancies, whether primary or metastatic, can cause depressed consciousness if their mass effect is sufficient or if surrounding edema develops rapidly.

Special consideration should be given to specific populations of patients. The elderly, in particular, are susceptible to alterations in therapeutic medication dosage and drug-drug interactions. Even seemingly minor infections, such as urinary tract infections, upper respiratory infections, or viral gastroenteritis, may cause altered mental status (see Chapter 13), depressed consciousness, or coma. In addition, immunocompromised patients such as those with AIDS or those undergoing chemotherapy treatment for transplants, malignancy, or immunologic disease are vulnerable to a multitude of opportunistic infections not commonly seen in the general patient population.



**Figure 14-1.** Brainstem anatomy. (Adapted from Adams J: Emergency Medicine. Fig. 89-1. Philadelphia, Elsevier. Copyright © 2008.)

## Clinical Evaluation

The clinical evaluation and stabilization of patients with depressed consciousness occur simultaneously with the diagnosis in the ED. The differential diagnosis of depression of consciousness is extensive but can be greatly simplified by focusing attention on the distinguishing characteristics of the available patient history and physical examination (Boxes 14-1 and 14-2).<sup>2</sup> Approaching the patient's presentation systematically, beginning with a broad differential diagnosis, usually allows development of a short list of likely diagnoses early in the encounter.

## History

Chief complaints relating to depressed consciousness vary widely. Family members may report the patient as being more difficult to arouse from sleep or less interactive. Often, family members or friends have alerted emergency medical services after the patient is "found down" and unarousable even with vigorous stimulation.

Family members, caregivers, or friends often can provide information that is unobtainable or unreliable from the patient who presents with depressed consciousness. They usually have some knowledge regarding the patient's past medical history, which may include diabetes, liver or renal disease, vascular disease such as hypertension, stroke or transient ischemic attacks, malignancy, seizures, immunocompromised states such as HIV, sickle cell disease or a history of organ transplant, or psychiatric illness. Symptoms in the hours to days preceding the occurrence of depressed consciousness are important. Specifically, the patient may have complained of headache, focal weakness or numbness, incoordination, or vision disturbances. The patient may have experienced nausea, vomiting, or fever. There may be a history of a traumatic fall or exposure to drugs or toxins. Family members may also be

### BOX 14-1

### STRUCTURAL ETIOLOGY OF ALTERED MENTAL STATUS AND COMA

#### Trauma

- Subdural hematoma
- Epidural hematoma
- Cerebral concussion/contusion

#### Stroke Syndromes

- Embolism
  - Cardiac (atrial fibrillation, endocarditis)
  - Paradoxical (fat embolus)
- Thrombosis
  - Cerebral venous sinus thrombosis
- Hemorrhage
  - Subarachnoid hemorrhage (SAH)
  - Pontine hemorrhage
  - Cerebellar hemorrhage
  - Intracerebral hemorrhage

#### Tumor

- Brainstem tumors
- Metastatic disease
- Angiomas
- Pituitary apoplexy
- Acute hydrocephalus

#### Infection

- Subdural empyema/abscess

able to relay additional diagnostic clues such as rate of onset or waxing-waning characteristics of the patient's symptoms.

Causes of depression of consciousness vary with patient age (Box 14-3). The elderly are particularly vulnerable to infec-

**BOX 14-2 METABOLIC/SYSTEMIC ETIOLOGY OF ALTERED MENTAL STATUS AND COMA****Hypoxia**

Severe pulmonary disease (hypoventilation)  
 Severe anemia  
 Environmental/toxin  
 Methemoglobinemia  
 Cyanide  
 Carbon monoxide  
 Decreased atmospheric oxygen (high altitude)  
 Near-drowning

**Disorders of Glucose**

Hypoglycemia  
 Chronic alcohol abuse and liver disease  
 Excessive use of insulin or other hypoglycemic agents  
 Insulinoma  
 Hyperglycemia  
 Diabetic ketoacidosis  
 Nonketotic hyperosmolar coma

**Decreased Cerebral Blood Flow**

Hypovolemic shock  
 Cardiac  
 Vasovagal syncope  
 Arrhythmias  
 Myocardial infarction  
 Valvular disorders  
 Congestive heart failure  
 Pericardial effusion/tamponade  
 Myocarditis  
 Infectious  
 Septic shock  
 Bacterial meningitis  
 Vascular/hematologic  
 Hypertensive encephalopathy  
 Pseudotumor cerebri  
 Hyperviscosity (sickle cell, polycythemia)  
 Hyperventilation  
 Cerebral lupus vasculitis  
 Thrombotic thrombocytopenic purpura  
 Disseminated intravascular coagulation

**Metabolic Cofactor Deficiency**

Thiamine (Wernicke-Korsakoff syndrome)  
 Pyridoxine (isoniazid overdose)  
 Folic acid (chronic alcohol abuse)  
 Cyanocobalamin  
 Niacin

**Electrolyte/pH Disturbances**

Acidosis/alkalosis  
 Hyponatremia/hyponatremia\*  
 Hypercalcemia/hypocalcemia  
 Hypophosphatemia  
 Hypermagnesemia/hypomagnesemia

**Endocrine Disorders**

Myxedema coma, thyrotoxicosis  
 Hypopituitarism  
 Addison's disease (primary or secondary)  
 Cushing's disease  
 Pheochromocytoma  
 Hyperparathyroidism/hypoparathyroidism

**Endogenous Toxins**

Hyperammonemia (liver failure)  
 Uremia (renal disease)  
 Carbon dioxide narcosis (pulmonary disease)  
 Porphyria

**Exogenous Toxins**

Alcohol  
 Ethanol, isopropyl alcohol, methanol, ethylene glycol  
 Acid poisons  
 Salicylates  
 Paraldehyde  
 Ammonium chloride  
 Antidepressant medications  
 Lithium  
 Tricyclic antidepressants (TCAs)  
 Selective serotonin reuptake inhibitors (SSRIs)  
 Monoamine oxidase inhibitors (MAOIs)  
 Stimulants  
 Amphetamines/methamphetamines  
 Cocaine  
 Over-the-counter sympathomimetics  
 Narcotics/opiates  
 Morphine  
 Heroin  
 Codeine, oxycodone, meperidine, hydrocodone  
 Methadone  
 Fentanyl  
 Propoxyphene  
 Sedative-hypnotics  
 Benzodiazepines  
 Barbiturates  
 Rohypnol  
 Bromide

**Hallucinogens**

Lysergic acid diethylamide (LSD)  
 Marijuana  
 Mescaline, peyote  
 Mushrooms  
 Phencyclidine (PCP)

**Herbs/plants**

Aconite  
 Jimson weed  
 Morning glory

**Volatile substances**

Hydrocarbons (gasoline, butane, toluene, benzene, chloroform)  
 Nitrites  
 Anesthetic agents (nitrous oxide, ether)

**Other**

γ-Hydroxybutyrate (GHB)  
 Ketamine  
 Penicillin  
 Cardiac glycosides  
 Anticonvulsants  
 Steroids  
 Heavy metals  
 Cimetidine  
 Organophosphates

**Disorders of Temperature Regulation/Environmental**

Hypothermia  
 Heat stroke  
 Malignant hyperthermia  
 Neuroleptic malignant syndrome  
 High-altitude cerebral edema (HACE)  
 Dysbarism

**Primary Glial or Neuronal Disorders**

Adrenoleukodystrophy  
 Creutzfeldt-Jakob disease  
 Progressive multifocal leukoencephalopathy  
 Marchiafava-Bignami disease  
 Gliomatosis cerebri  
 Central pontine myelinolysis

**Other Disorders of Unknown****Etiology**

Seizures  
 Postictal states  
 Reye's syndrome<sup>†</sup>  
 Intussusception<sup>†</sup>

\*Can be associated with dilution of formula in infant feeding.

<sup>†</sup>Prominent in the pediatric population.

tious etiologies, medication changes, and alterations in their living environments. Young adults and adolescents are more likely to present after recreational drug use or trauma. Accidental toxic ingestions are often seen in younger children. In infants, infectious causes of depressed consciousness are most common; however, trauma secondary to physical abuse and metabolic derangements from inborn errors of metabolism can be seen.<sup>3</sup>

**Physical Examination**

The severity of presenting symptoms dictates the speed needed for stabilization and diagnosis. After necessary stabilization measures have been instituted (e.g., intubation of the frankly comatose patient), a systematic examination is conducted. Level of consciousness is determined by the patient's ability to speak in full, coherent sentences and to respond

**BOX 14-3****COMMON AGE-RELATED ETIOLOGY OF ALTERED MENTAL STATUS****Infant**

Infection  
Trauma/abuse  
Metabolic

**Child**

Toxic ingestion

**Adolescent/Young Adult**

Toxic ingestion  
Recreational drug use  
Trauma

**Elderly**

Medication changes  
Over-the-counter medications  
Infection  
Alterations in living environment  
Stroke

appropriately to the examiner. A rapid, directed neurologic screening examination can determine whether the patient has a significant focal motor deficit. The presence of a distinctive odor on the breath, although uncommon, can cue the examiner to the presence of alcohol, ketones (diabetic/alcoholic ketoacidosis), or bitter almonds (cyanide toxicity). Undressing the patient promptly and completely permits evaluation for signs of trauma or skin lesions suggesting overwhelming infection.

Vital signs are paramount in the initial assessment of all patients. Significant hypotension with depressed consciousness suggests shock, and both causes and therapy should be addressed immediately. Late-stage, severe elevation in intracranial pressure (ICP) can cause bradycardia and hypertension. Tachycardia and hypotension can be the result of primary cardiac, infectious, or toxic/metabolic causes. Both hypothermia and hyperthermia can result in altered mental status whether from infectious, structural, or toxic/metabolic causes. Hyperventilation, Kussmaul's or Cheyne-Stokes breathing, agonal breathing, apnea, or other alterations in respiratory patterns can suggest primary CNS abnormalities or toxic/metabolic derangements.

Immediately after an assessment of the patient's vital signs, a head-to-toe physical examination is performed.<sup>4</sup> A methodical and complete head and neck examination is conducted, with particular emphasis on examination of the pupillary reflexes and eye movements (see later discussion) and any indications of head trauma (hemotympanum, scalp hematoma). The mucous membranes may suggest specific toxidromes.

Examination of the neck should focus on evidence of infection, including nuchal rigidity, lymphadenopathy, or fluctuance. The cervical spine should be immobilized if there are signs of neck trauma, such as cervical spine tenderness, or evidence of blunt external trauma. Stridor indicates respiratory distress typically from infection, edema, or foreign body aspiration.

Chest examination focuses on pulmonary function, infection, cardiac output, and the presence of injury. Potentially helpful abdominal findings include ascites, hepatosplenomegaly, ecchymosis, or striae. Gross blood, purulent drainage, or retained foreign bodies should be sought on genitourinary and rectal examination. In the absence or presence of signs of

**BOX 14-4****GLASCOW COMA SCALE**

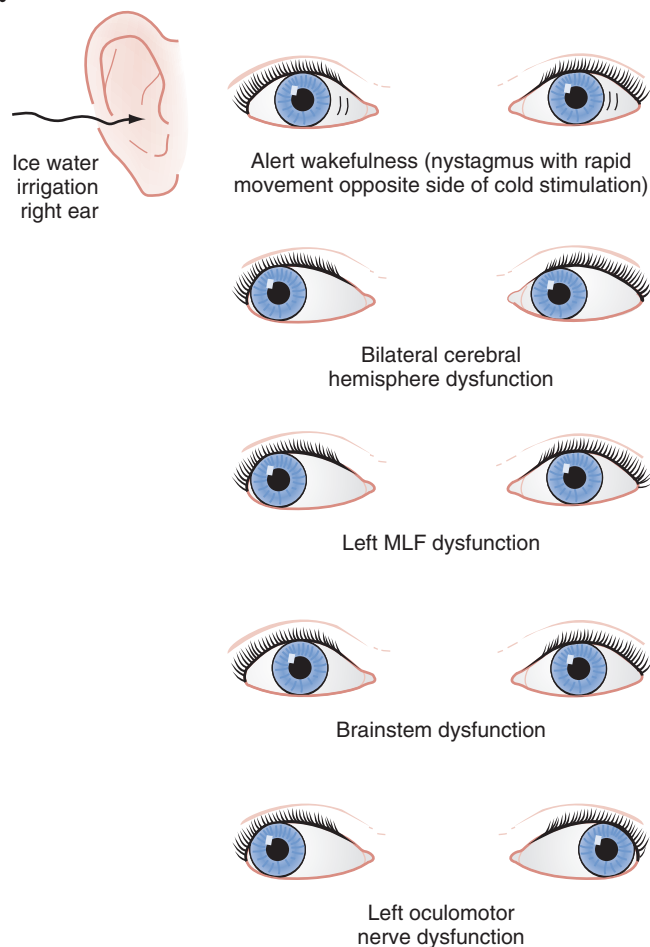
		Score
Eye Opening	Spontaneous	4
	To voice	3
	To pain	2
	None	1
Verbal Response Adult	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible words	2
	None	1
	Pediatric	Appropriate
Cries, consolable		4
Persistently irritable		3
Restless, agitated		2
None		1
Motor Response	Obeys commands	6
	Localizes pain	5
	Withdraws to pain	4
	Flexion to pain	3
	Extension to pain	2
	None	1

trauma, lesions on the skin such as rashes, signs of drug use (needle "tracks" or medication patches), or embolic phenomena can be differential clues.

A systematic neurologic examination, with particular attention paid to the eyes, is the most useful tool in differentiating a structural from a systemic or metabolic etiology of depressed consciousness or coma. A head-to-toe approach is a proven strategy. This should include evaluation of the patient's Glasgow Coma Scale (GCS) (Box 14-4), level of alertness, cranial nerves, strength, reflexes, and cerebellar functions with emphasis on gait, pronator drift, finger-to-nose, heel-to-shin, rapid alternating movements, and Romberg testing. A change of two or more points in serial GCS testing represents a significant change in the patient's level of consciousness.

Discovery of a focal neurologic deficit is suggestive of a structural etiology. Particular attention should be paid to a focused eye examination during which a helpful amount of information can be obtained. Unilateral dilatation of a pupil ("blown pupil") and loss of reactivity in a comatose patient are ominous signs of uncal herniation requiring immediate neurosurgical consultation and intervention. Papilledema in the setting of increased ICP or retinal hemorrhage associated with trauma can be found on funduscopic examination. The eye examination should also include testing of eye movements, which are coordinated by the medial longitudinal fasciculus located in the brainstem and ocular centers located in the cerebral cortex. Cranial nerves III, IV, and VI are responsible for control of the extraocular muscles. Cranial nerve III paralysis results in a persistently abducted eye, whereas a persistently adducted eye is caused by paralysis of cranial nerve VI. In the setting of trauma, a unilateral third cranial nerve palsy suggests an ipsilateral compressive lesion such as seen with epidural hematoma. Cranial nerve VI palsies are often nonlocalizing as the nerve has a long intracranial course and compressive forces from intracranial mass effects (tumor, traumatic hematoma, increased ICP, etc.) may compromise cranial nerve function anywhere in its course. Horizontal disconjugate gaze is an important finding and is commonly seen in patients who are sedated, drowsy, or intoxicated. Disconjugate gaze found





**Figure 14-2.** Oculocephalogyric (caloric) responses to various central nervous system pathologic conditions. MLF, medial longitudinal fasciculus.

in the vertical plane is usually more serious and suggests cerebellar or pontine dysfunction.

Oculocephalic (doll's eyes) and oculovestibular reflex testing are useful in looking at the functional integrity of the brainstem. These tests, if negative, make structural lesions in the brainstem very unlikely as the source of the patient's altered mental status.

If there are no contraindications, such as suspected cervical spine injury, oculocephalic testing is accomplished by observing the patient's eye movements while the head is turned from side to side. Patients who exhibit a maintained forward gaze despite head turning ("doll's eyes reflex") are unlikely to have a brainstem-mediated cause of coma. If the eyes remain in a fixed position within the orbits, turning in unison with the head, brainstem dysfunction is suggested. Oculovestibular or "cold water caloric" testing is a more sensitive test for brainstem involvement and cannot voluntarily be resisted (Fig. 14-2). After elevation of the patient's head to 30° (this can be done in patients whose cervical spine is not cleared by placing the bed in the reverse Trendelenburg position), 10 to 30 mL of ice water is used to irrigate the external auditory canal. Tympanic membrane perforation and cerumen impaction should be ruled out prior to performing this test. In patients who have an intact brainstem, the response is a slow conjugate deviation of gaze toward the side of the cold water stimulus lasting 30 to 120 seconds. The reflex is short-lived and followed by corrective fast beats of nystagmus toward the midline. This corrective nystagmus is described by the mnemonic

COWS, which stands for "cold-opposite, warm-same." If there is no response to the irrigation, brainstem dysfunction is possible.

### Diagnostic Algorithm

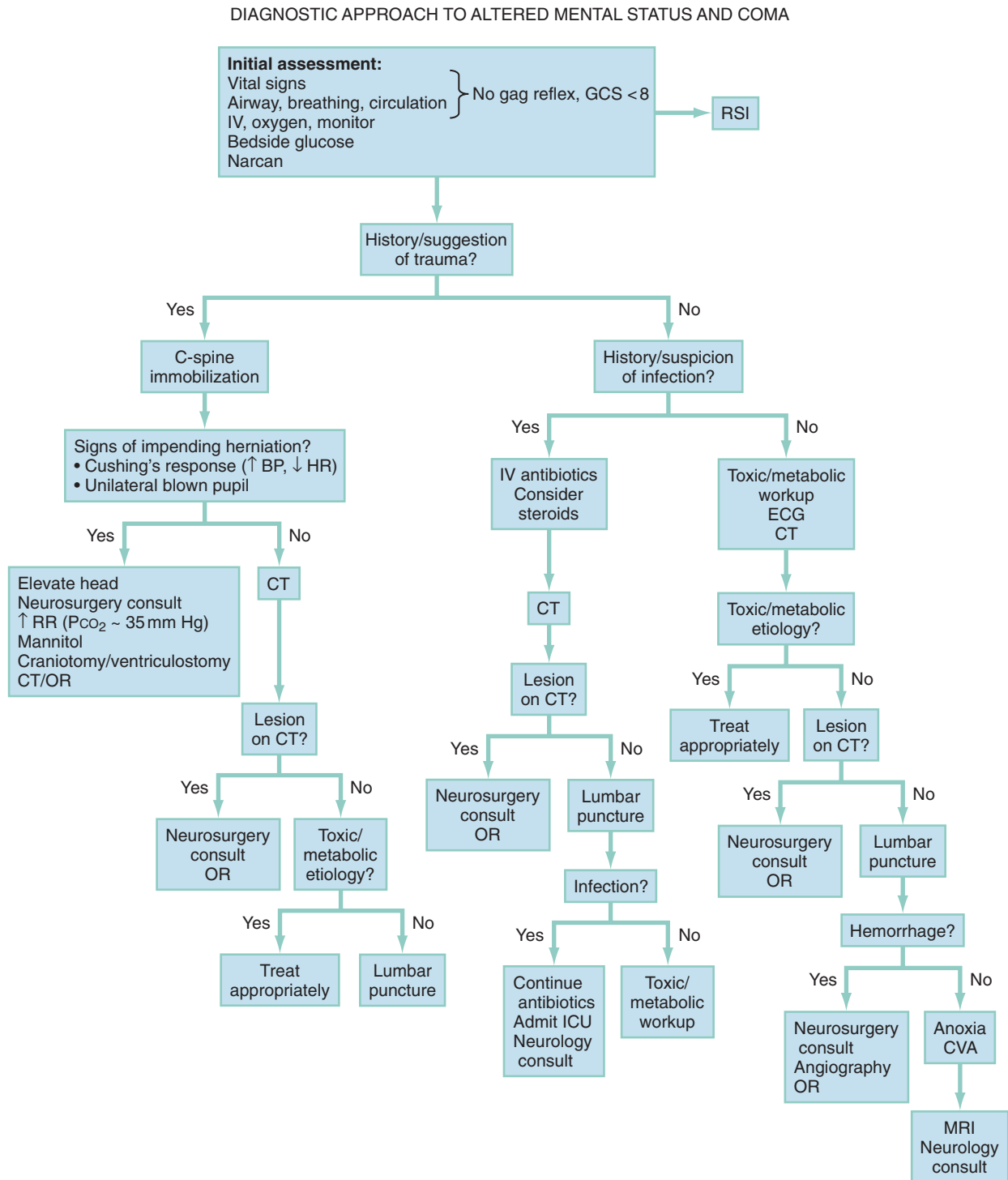
Information gathered from the history and physical examination of the patient with depressed consciousness must be used to direct the approach to diagnostic testing (Fig. 14-3). Most often, this information points toward a systemic or metabolic rather than a structural etiology. Neuroimaging studies are performed early in patients with suggested structural causes, but should not precede treatment of quickly reversible conditions such as possible opioid overdose or hypoglycemia.

Systemic or metabolic causes of depressed consciousness and coma are most often found on analysis of laboratory studies. Bedside glucose testing definitively confirms or excludes hypoglycemia. Serum electrolytes identify derangements in sodium,  $\text{CO}_2$ , or the anion gap. Changes in serum calcium can be a marker for metastatic disease. A urine dip test is a quick way to identify infection, ketones, or spilling of glucose. Urinalysis itself provides valuable information regarding volume status (specific gravity), infection, and the possible presence of calcium oxalate crystals in the setting of ethylene glycol ingestion. Urine drug testing may be helpful if another cause is not forthcoming.

Although an elevated white blood cell count can be a marker for infection, it is nonspecific and rarely helpful. An abnormally low white blood cell count, however, suggests an immunocompromised state and should urgently direct clinical investigation toward an infectious etiology. Thrombocytopenia can be a marker for sepsis or intracranial hemorrhage and may sound a cautionary note against an invasive procedure such as obtaining central venous access or performing a lumbar puncture. Elevated results from serum coagulation studies can be a marker for bleeding tendencies or liver disease. Serum ammonia levels are controversial and have not been shown to be a reliable marker in the setting of depressed consciousness. Thyroid function studies can reveal myxedema coma from hypothyroidism. When CNS pathology such as infection or hemorrhage is suggested but not seen on neuroimaging studies, cerebrospinal fluid analysis is undertaken.

Noncontrast computed tomography (CT) of the brain is the preliminary imaging modality of choice in the setting of depressed consciousness and coma. In the majority of ED settings, it is quickly available, making it more suitable for the patient with borderline stability. It is sufficiently sensitive to detect most intracranial hemorrhages that are large enough to cause coma. Contrast-enhanced CT may be used if a tumor or infection is possible. Linear artifacts created by the thick skull base can limit the view of the posterior fossa on CT. For this reason, magnetic resonance imaging of the brain is generally more useful for identifying structural lesions in this region; however, this modality is less feasible in most ED settings due to its cost and limited availability. Angiography may be available in larger tertiary care centers for use in the diagnosis or treatment of intracerebral aneurysms or arteriovenous malformations after initial identification of an intracranial hemorrhage on noncontrast CT.

Plain radiography may identify severe pneumonia or acute respiratory distress syndrome, or it may rarely reveal specific types of heavy-metal ingestions such as mercury, iron, or lead in the pediatric population. Electrocardiograms can point to certain ingestions (tricyclic antidepressants, etc.), electrolyte abnormalities (potassium, calcium, etc.), or hypothermia. If nonconvulsive status epilepticus is suggested, or if a patient with status epilepticus has required neuromuscular blockade,



**Figure 14-3.** Algorithm for diagnostic approach to altered mental status and coma. BP, blood pressure; C-spine, cervical spine; CT, computed tomography; CVA, cerebrovascular accident; HR, heart rate; ICU, intensive care unit; IV, intravenous; OR, operating room; RR, respiration rate; RSI, rapid sequence intubation. (Adapted from Adams J: Emergency Medicine. Fig. 89-2. Philadelphia, Elsevier. Copyright ©2008.)

continuous electroencephalographic monitoring, if available, can provide key information about the patient's status and guide therapy.

### Empirical Management

Initial establishment of airway, breathing, and circulation (ABCs) is of primary importance in stabilizing the patient with

altered mental status. Initiation of IV access combined with the administration of oxygen and continuous telemetry monitoring should happen concomitantly within the first few minutes of the patient's arrival.<sup>5</sup> In patients with a GCS score lower than 8, definitive airway control should be obtained unless the coma is readily reversible (e.g., hypoglycemia, opioid overdose). Patients with possible increased ICP should receive lidocaine prior to rapid sequence intubation (see

Chapter 1). Trauma patients require spinal immobilization in addition to indicated fluid resuscitation.

Reversible causes of the patient's condition should be sought concomitantly with initial stabilization. Administration of the components of the "GI cocktail," which include dextrose, naloxone, and thiamine, can quickly reverse the alterations in mental status caused by hypoglycemia, narcotic overdose, and thiamine deficiency, respectively. Further therapy and workup will be dictated by the patient's history and physical examination. Specific attention should be given to identifying the focal neurologic abnormalities, including pupillary reflexes and pathologic eye movements that suggest mass effect or depressed brainstem function, prompting neuroimaging and evaluation by a neurosurgeon. Empirical administration of mannitol is indicated when there is evidence of transtentorial herniation in this setting. Ventriculostomy and ICP monitoring are commonly performed by the neurosurgeon in the ED. In trauma patients with suspected epidural hematoma who have evidence of brain herniation, the use of burr holes in the skull on the side of the dilated pupil may be a last resort. In patients with compromised brainstem function who lack evidence of herniation, a workup to investigate possible exposure to toxins or metabolic imbalances should proceed while supportive care is provided. Brain tissue is considered to be unsalvageable in patients who have not received sedative medications, are normothermic, and demonstrate lack of brainstem reflex activity.

In patients who demonstrate normal brainstem function, the workup proceeds as supportive care is provided. When an infectious cause is suggested, empirical administration of a broad-spectrum antibiotic should not be delayed for lumbar puncture or other diagnostic tools. Lesions or masses found on brain imaging should prompt evaluation by a neurosurgeon and, if indicated, early operative intervention. In patients in whom a toxic ingestion is possible, activated charcoal is of no proven benefit in most cases and gastric emptying is rarely indicated (see Chapter 145). Specific toxin antidotes, if indicated, can be given, with consultation with a local or regional poison center when required. Early hemodialysis after consultation with a nephrologist should also be considered in patients who have toxic or metabolic abnormalities amenable to this therapy.

The vast majority of patients who present with depressed consciousness or coma require admission to the hospital for further treatment and workup. Some patients who have returned to their baseline mental status after reversal of hypoglycemia or opioid overdose may be suitable for discharge directly from the ED or ED observation unit after a period of observation. Patients with alcohol or recreational drug intoxication and no other discernible cause of altered mental status can be discharged when they are clinically sober.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## CHAPTER 15 Seizures

Ana M. Davitt and Charles V. Pollack, Jr.

### ■ PERSPECTIVE

*Seizure* is defined as abnormal neurologic functioning caused by abnormally excessive activation of neurons, either in the cerebral cortex or in the deep limbic system. *Epilepsy* is defined as recurrent unprovoked seizures due to a genetically determined or acquired brain disorder<sup>1</sup>; it is not an appropriate term for seizures that occur intermittently and predictably after a known insult, such as alcohol intoxication and withdrawal.

Presentation to the emergency department (ED) with a generalized convulsive seizure prompts immediate concern for airway protection and stabilization, followed by a focused search for the cause. Nonconvulsive seizures, which are much less common, may be relatively obscure in their presentation, more diverse in their etiology, and are sometimes more difficult to recognize and control acutely.

### Epidemiology and Classification

It is estimated that 6% of the U.S. population experience at least one nonfebrile seizure during their lifetime; the annual incidence among adults is 84 per 100,000 population, and more than half of these individuals develop epilepsy.<sup>2</sup> In one study, approximately 1% of ED visits were for seizure-related complaints.<sup>3</sup> Nearly half of these patients had alcohol or low antiepileptic drug levels implicated as contributing factors.

Seizures can be classified as primary or secondary (the latter also termed *reactive*), as generalized or focal (partial), or as convulsive or nonconvulsive. Table 15-1 shows the distribution of seizures in a typical population of patients. A generalized seizure is defined as abnormal neuronal activity in both cerebral hemispheres. Seizures may be divided into tonic-clonic, absence, and myoclonic. Partial seizures or focal seizures usually involve one hemisphere. They are divided into simple partial (in which consciousness is maintained), complex partial (in which consciousness is lost), and those that become secondarily generalized. Some seizures are impossible to classify because of inadequate or inaccurate description of the ictal activity.<sup>2,3</sup>

Status epilepticus is defined as at least 30 minutes of persistent seizures or a series of recurrent seizures without intervening return to full consciousness,<sup>4</sup> although several authors have proposed shortening the time criterion from 30 minutes to 5 minutes.<sup>5</sup>

Secondary seizures may occur as a result of a vast array of injuries and of illnesses such as intoxication or poisoning,

encephalitis, encephalopathy, organ failure, other metabolic disturbances, infections of the central nervous system, cerebral tumors, pregnancy, and, paradoxically, supratherapeutic levels of anticonvulsants.

Seizures in children follow a different distribution, primarily because of the relatively high incidence of febrile seizures and the frequently uncertain observational history of possible ictal activity. Febrile seizure is the most common pediatric seizure, occurring in 2 to 5% of children between 6 months and 5 years of age; 20 to 30% of those children have at least one recurrence. It is important to differentiate between febrile seizure and seizure with fever.<sup>6</sup> First-time seizures in infants younger than 6 months may indicate significant underlying pathology and warrant a full assessment.<sup>7</sup>

### Pathophysiology

Seizures occur when the abnormal increased electrical activity of the initiating neurons activates adjacent neurons and propagates until the thalamus and other subcortical structures are similarly stimulated. At a cellular level, the pathophysiology is not well understood, although recent research in specific epilepsy syndromes is elucidating possible mechanisms. Investigation of rare inherited epilepsy syndromes has identified mutations in neuronal ion channel proteins, limiting intracellular passage of potassium. Given that the potassium current is the primary force behind repolarization of membranes, depolarization is prolonged in these patients, leading to an increase in neuronal hyperexcitability.<sup>1</sup> Other studies have found that malformations of cortical development and glial cells may play a role in epileptogenesis.<sup>1</sup>

Clinical seizure activity typically, but not always, reflects the initiating focus. When the ictal discharge extends below the cortex to deeper structures, the reticular activating system in the brainstem may be affected, altering consciousness. In generalized seizures, the focus is often deep and midline, which explains the prompt loss of consciousness and bilateral involvement. Seizures are typically self-limited; at some point the hyperpolarization subsides and the bursts of electrical discharges from the focus terminate. This cessation may be related to reflex inhibition, neuronal exhaustion, or alteration of the local balance of neurotransmitters.

Partial seizures may represent a similar pathophysiologic process in which less recruitment occurs and the ictal activity does not cross the midline. Because of the more limited focus of abnormal activity, convulsive motor activity may not be the predominant clinical manifestation.<sup>3</sup>



## ■ DIAGNOSTIC APPROACH

### Differential Considerations

Because an incorrect diagnosis is expensive and involves loss of driving privileges and exposure to potentially toxic medicines, the first diagnostic task is to determine whether the patient is having a “true” seizure.<sup>8</sup> Ictal activity can be irrefutably verified only by electroencephalography (EEG). Other abnormal movements and states of consciousness, including pseudoseizures, can be confused with ictal activity. Other disorders mimicking seizures are listed in Table 15-2.<sup>7</sup>

Syncopal, whether vasodepressive (vagal syncope), orthostatic, or dysrhythmia related, can be confused with seizures by observers. A sudden loss of consciousness followed by abnormal movements can be ictal or syncopal in origin, hence

the consideration “fit versus faint.” One video analysis of 56 brief syncopal episodes showed myoclonic activity in 90% of patients, together with frequent head turns, upward gaze, oral automatisms, and righting movements. These are likely a transient response by the brain to sudden deprivation of blood flow. Generally, ictal tonic-clonic movements are more forceful and prolonged than the “twitches” sometimes associated with fainting. In addition, most generalized seizures are characterized by a postictal state (an important exception being atonic drop attack ictus), which syncope patients do not manifest.<sup>9</sup>

The cause of an unwitnessed, unprovoked loss of consciousness with a fall, after which the patient presents to the ED, may be difficult to determine. Suggestions of an ictal diagnosis include retrograde amnesia, loss of continence, and evidence of tongue biting.<sup>10</sup> If blood was drawn by emergency medical service personnel soon after a true seizure, it often demonstrates a metabolic acidosis that has resolved by the time a repeat analysis is performed in the ED.

Table 15-1

**Classification of Seizures in a General Adult Population**

SEIZURE TYPE	PERCENTAGE
<b>Generalized</b>	
Tonic-clonic	35
Absence	1
Myoclonic	<1
Others	2–3
<b>Partial</b>	
Simple partial	3
Complex partial	11
Secondarily generalized	27
Mixed partial	12
Unclassified	9

### Rapid Assessment and Stabilization

The patient who arrives with a history of possible seizure activity should be placed in a monitored area of the ED and prepared for prompt physician examination.<sup>4</sup> An IV line or saline lock catheter should be placed in case anticonvulsants are emergently indicated. Blood glucose is checked at the bedside, and a thorough list of all medications currently being used by the patient is obtained.

If the patient is seizing in the ED, the first step is to confirm that a pulse is present and that the “seizure” activity is not the result of cerebral hypoxia from lack of blood flow. After this, attention is paid to protecting and maintaining the airway, including use of a nasopharyngeal airway and ready availability of oxygen and suction. The patient should be protected from self-injury during this time.<sup>11</sup>

Table 15-2

**Differential Considerations for the Diagnosis of Seizure\***

DISORDER	CLASSIFICATION	ICTAL-LIKE MANIFESTATIONS
Syncopal	Vasodepressive vs dysrhythmogenic (including long QT syndrome) vs orthostatic Preictal or postictal twitching	“Fit vs. faint”
Hyperventilation syndrome		Mood disturbances Posturing of extremities
Prolonged breath-holding	More typical in children	Tonic-clonic movements Loss of urinary continence
Toxic and metabolic disorders	Alcohol abuse/withdrawal Hypoglycemia Phencyclidine Tetanus Strychnine and camphor Extrapyramidal reactions	Delirium tremens, blackout Abnormal behavior Buccolingual spasms Myotonic spasms Myotonic spasms Posturing, deviation of eyes
Nonictal CNS events	Transient ischemic attacks Transient global amnesia Hemiparetic migraine Carotid sinus hypersensitivity Narcolepsy	Drop attacks, “fit vs. faint” Similar to postictal state, absence status Todd’s paralysis Drop attacks, “fit vs. faint” Drop attacks, “fit vs. faint”
Movement disorders	Hemiballismus, tics	Convulsions
Psychiatric disorders	Fugue state Panic attacks	Similar to postictal state, absence status Twitching, altered mental state
Functional disorders	Pseudoseizure	May closely resemble ictal activity; patients may have both true seizures and pseudoseizures

\*Electroencephalography provides the definitive diagnosis in unclear cases.  
CNS, central nervous system.

A pulse oximeter should be applied and oxygen administered as necessary. Optimally, the patient is turned on his or her side to protect the airway from aspiration. If the patient is immobilized on a spine board after trauma, the entire board is tipped up to one side. Preparation should be made for endotracheal intubation in case anticonvulsant drugs fail to terminate the seizure. While these procedures are accomplished, an assistant should be establishing IV access.<sup>11</sup>

Hypoglycemia is the most common metabolic cause of seizure activity. The only treatment required for the patient may be administration of IV glucose. *Prolonged* seizure activity may also *cause* hypoglycemia, so that the cause-and-effect relationship may sometimes be reversed and further therapy is required. Benzodiazepines are the optimal first-line agents for stopping seizure activity in patients of all ages. Available agents include lorazepam (Ativan), diazepam (Valium), and midazolam (Versed). All three are efficacious in terminating seizure activity (see Table 15-3 for doses), but if IV access cannot be achieved, diazepam may be given rectally, endotracheally, or intraosseously; rectal diazepam stops seizures in 70% of patients, compared with 60 to 80% for IV dosing.<sup>12</sup> Midazolam can be given intramuscularly, and recent research shows that buccal midazolam works in children.<sup>13</sup> If IV access is obtained, however, lorazepam is the agent of choice for

initial management of status epilepticus, particularly because its longer half-life leads to less recurrence of seizures.<sup>14</sup> Lorazepam is also specifically recommended for alcohol withdrawal seizures, again due to its longer duration of action.<sup>15</sup>

If benzodiazepines do not abort seizure activity, the airway should be reevaluated. If the patient's ability to protect the airway is compromised or oxygen saturation remains persistently below 90%, emergent intubation should be performed. If the seizure has not terminated 5 to 7 minutes after benzodiazepine administration, or if the maximum dose of lorazepam (0.1 mg/kg) or diazepam (0.15 mg/kg)<sup>16</sup> has been reached, a second drug should be given.<sup>16</sup> Use of maximal doses of benzodiazepines may require intubation and ventilatory support. Phenytoin is recommended as second-line therapy for adults with persistent seizure activity.<sup>16</sup> The prodrug, fosphenytoin, can be administered more quickly, can be given intramuscularly, and has less tendency to cause hypotension, but is significantly more expensive.<sup>17</sup> (See Table 15-3).<sup>18,19</sup> Second-line therapy for children is phenobarbital. Third-line therapy is phenytoin for children and phenobarbital for adults.<sup>20-23</sup> IV valproic acid is safe<sup>24</sup> and should be considered for patients who are on chronic valproic therapy and whose levels are subtherapeutic.<sup>25</sup> If a patient's seizures are refractory to benzodiazepines, consider isoniazid overdose as the cause. Pyridoxine

**Table 15-3 Drugs and Dosages for Abortive Treatment of Seizures in the Emergency Department\***

DRUG	ADULT DOSE	PEDIATRIC DOSE	COMMENTS
Glucose	50 mL of 50% glucose	0–1 month: 2 mL/kg IV of D10W 1 month–2 years: 2 mL/kg IV of D25W >2 years: 2 mL/kg IV of D50W	1 month–2 years: 2 mL/kg IV of D25W
Magnesium sulfate		6 g over 15–20 min followed by 2 g/hr	First-line therapy for eclamptic seizures
Diazepam	0.2 mg/kg IV at 2 mg/min up to 20 mg	0.2–0.5 mg/kg IV/IO/ET <i>or</i> 0.5–1.0 mg/kg PR up to 20 mg	Monitor airway protection and respiratory drive
Lorazepam	0.1 mg/kg IV at 1–2 mg/min to up to 10 mg	0.05–0.1 mg/kg IV	Monitor airway protection and respiratory drive
Midazolam	0.1 mg/kg given at 1 mg/min up to 10 mg IV 0.2 mg/kg IM 0.5 mg/kg buccal	0.15 mg/kg IV, then 2–10 mcg/kg/min	Monitor airway protection and respiratory drive
Phenytoin	20 mg/kg IV at ≤40 mg/min	20 mg/kg IV at 1 mg/kg/min	During infusion patient should have continuous cardiac and blood pressure monitoring
Fosphenytoin	15–20 mg/kg IV at 100–150 mg/min <i>or</i> 20 mg/kg IM	20–25 mg/kg IV, then up to 3 mg/kg/min IV up to 159 mg/min IV	Level of monitoring directed by patient's status, not drug use
Propofol	3–5 mg/kg initial dose, then 1–15 mg/kg/hr infusion		Used for status epilepticus; intubation required
Phenobarbital	20–30 mg/kg IV at 60–100 mg/min or as single IM dose		Intubation may be required
Valproate	20 mg/kg PR or 10–15 mg/kg IV (initial dose)		Maximum dosage 60 mg/kg/day Dilute 1:1 with water; onset is slow
Pentobarbital	5 mg/kg IV at 25 mg/min, then titrate to EEG		Intubation, ventilation, and pressor support are required
Isoflurane	Via general endotracheal anesthesia		Monitor with EEG

\*Although alternative routes of administration (e.g., IO, PR) have not all been studied in adults, appropriate weight or length based on dosing by pediatric guidelines can be used when the clinical situation dictates.

EEG, electroencephalogram; ET, endotracheal; IM, intramuscular; IO, intraosseous; IV, intravenous; PR, rectal administration.

is the only fully effective pharmacologic treatment for toxic isoniazid seizures, although benzodiazepines have been shown to suppress seizure activity in some cases.<sup>26</sup> In seizing females of childbearing age, eclampsia should be considered; in this case, intravenous magnesium (6 g) is the drug of choice. (See Chapter 177.) Approximately 10% of patients will have a second seizure despite magnesium; these patients should get a second 2-g bolus of magnesium.<sup>27</sup> If the eclamptic patient continues seizing, magnesium dosing should be repeated; refractory eclamptic seizures can also respond to benzodiazepines or barbiturates with or without phenytoin. Children and psychiatric patients at risk for water intoxication should be considered potential candidates for hypertonic saline therapy, after laboratory confirmation of hyponatremia.

Patients who remain unresponsive to the third-level choice of pharmacologic intervention are by definition in *refractory* status epilepticus. Further choices for therapy at that juncture are general anesthetic doses of midazolam or propofol, barbiturate coma and isoflurane anesthesia; all of which mandate endotracheal intubation.<sup>22,23,29</sup> A neuromuscular blocking agent is administered concomitantly to reduce the metabolic burden and potential hyperthermia that can ensue from prolonged status seizures. Anesthetic dosing of midazolam is 0.2 to 0.3 mg/kg bolus, then 0.05 to 2.0 mg/kg/hr, and for propofol it is 2 to 4 mg/kg, then 1 to 15 mg/kg/hr. Both drugs are usually well-tolerated and can be titrated to effect, although propofol is preferable because of its rapid onset and offset of action, which allows the patient to be “awakened” intermittently for examination in the event that continuous EEG monitoring is not available.<sup>16</sup>

## Pivotal Findings

When the patient is stabilized with a secure airway and ictal activity is controlled, attention is turned to gathering more complete data.

## History

History taking in the patient with seizure is directed by two main questions. First, “Was the incident truly a seizure?” This is important because of the broad differential diagnosis for seizures (see Table 15-2) and the notoriously inaccurate descriptions of seizure-like activity from laypersons.<sup>10</sup> In general, however, ictal events have six properties:

1. *Abrupt onset*: Generalized seizures typically occur without an aura.
2. *Brief duration*: Seizures rarely last longer than 90 to 120 seconds, although bystanders typically overestimate the duration.
3. *Altered mental status*: Present by definition, except for simple partial seizures.
4. *Purposeless activity*: For example, automatisms and undirected tonic-clonic movements.
5. *Unprovoked*: Especially with regard to emotional stimuli; fever in children and substance withdrawal in adults are notable exceptions.
6. *Postictal state*: An acute confusional state that typically occurs with all seizures except simple partial and absence.

Information regarding focality of onset, loss of bowel or bladder control, or tongue biting should also be elicited.

The second question to direct the history is, “Does this patient have a history of seizures?” If he or she does have a documented history of seizures, ED evaluation may be limited to a thorough history and consideration of measurement of

anticonvulsant drug levels. History should focus on intercurrent illness or trauma, drug or alcohol use, potential adverse drug-drug interactions with anticonvulsants, medication compliance, a recent change in anticonvulsant dosing regimens, or a change in ictal pattern or characteristics.<sup>2,11</sup>

Supratherapeutic and toxic levels of some anticonvulsants such as phenytoin and carbamazepine, whether attained chronically or after acute overdose, may *cause* seizures. If empiric anticonvulsant therapy is indicated before the serum level is available, only 50% of a full loading dose should be given unless the patient is known reliably not to be taking anticonvulsant medication.

If the patient does not have a history of seizures and the description of the event is truly consistent with a seizure, the history should focus on potential underlying medical, toxicologic, or neurologic causes.

A personal history from the patient, close friend, relative, or medical record may reveal potential ictogenic factors such as recent or remote head trauma, developmental abnormalities, metabolic diseases, drug or alcohol abuse, sleep deprivation, pregnancy, recent travel, previous seizures, or use of herbal supplements. When no witness or family member is available, extensive questioning must await clearance of the postictal confusional state.

## Physical Examination

The physical manifestations of convulsive ictal activity include hypertension, tachycardia, and tachypnea from sympathetic stimulation. These signs typically resolve quickly after the seizure activity ceases. With more prolonged convulsions, skeletal muscle damage, lactic acidosis, and, rarely, frank rhabdomyolysis may ensue. Autonomic discharges and bulbar muscle involvement may result in urinary or fecal incontinence, vomiting (with significant aspiration risk), tongue biting, and airway impairment. All of these signs are helpful discriminators in the differential evaluation of seizure-like spells.

After the seizure activity has ceased, resting vital signs should be evaluated. Fever and underlying infection can cause seizures, although there may be a low-grade temperature elevation immediately after a convulsive generalized seizure. Tachypnea, tachycardia, or an abnormal blood pressure that persists beyond the immediate postictal period may indicate toxic exposure, hypoxia, or a central nervous system lesion. Pertinent physical findings may include nuchal rigidity, stigmata of substance abuse, lymphadenopathy suggestive of HIV disease or malignancy, dysmorphic features, or skin lesions. The examination should also focus on potential adverse sequelae of convulsive seizures, such as head trauma, tongue injury, posterior shoulder dislocation, or back pain.

Finally, a complete neurologic examination must be performed. A persistent focal deficit after a seizure (e.g., Todd's paralysis) often indicates the focal origin of the event but also can be evidence of an underlying stroke. The patient should be carefully examined for papilledema; elevated intracranial pressure can both cause and result from ictal activity. Failure to note steady improvement of postictal depression of consciousness suggests the possibility of an underlying encephalopathy or nonconvulsive status epilepticus.

## Ancillary Testing

**Laboratory.** Routine screening studies such as a complete blood count and chemistry profile have little use in the neurologically normal, otherwise healthy, postictal patient with a known seizure disorder for whom a reliable history can be obtained.

Table 15-4

**Indications for Emergent Head CT for New-Onset Seizure Patients**

Acute intracranial process is suspected  
 History of acute head trauma  
 History of malignancy  
 Immunocompromise  
 Fever  
 Persistent headache  
 History of anticoagulation  
 New focal neurologic examination  
 Age older than 40 years  
 Focal onset before generalization  
 Persistently altered mental status

CT, computed tomography.

Bedside blood glucose is measured early. Anticonvulsant levels are appropriate in patients known or thought to be taking anticonvulsant medication. Febrile patients are evaluated for the source of the fever. For medically ill adults (e.g., diabetic patients, cancer patients, patients with liver disease, patients taking medications that can affect serum electrolyte levels) and in those presenting with a first-time seizure, appropriate chemistry studies are ordered, including electrolytes and liver function tests.<sup>8</sup> Directed toxicologic screens should be obtained if substance abuse is possible. Serum sodium should be evaluated, particularly if mental status remains altered after apparent recovery from the postictal state. Pregnancy testing is useful if eclampsia is possible. If there is *any* suggestion of meningitis or subarachnoid hemorrhage, lumbar puncture should be performed, with a preceding cranial computed tomography (CT) scan.<sup>30</sup>

**Imaging.** In the fully recovered patient without headache and with fully normal mental status and neurologic examination who has had a single, brief seizure, a cranial CT scan can be obtained in the ED or at a follow-up visit at the discretion of the treating physician.<sup>4,29</sup> Table 15-4 lists the circumstances under which a head CT is recommended in the ED due to a higher likelihood of discovering an acute abnormality.<sup>4</sup>

The literature on this issue for first-time nonfebrile seizures in children is also inconclusive.<sup>31</sup> Cranial CT is indicated in any age group when there is a possibility of head trauma, elevated intracranial pressure, intracranial mass, persistently abnormal mental status or focal neurologic abnormality, or HIV disease.

**Electroencephalography.** EEG is not consistently available in the ED. It may be particularly useful in specific cases, such as the diagnosis of nonconvulsive status epilepticus, to monitor seizure activity after intubation and neuromuscular blockade,

and to help differentiate seizures from other similar presentations. In general, EEGs are most appropriate for the follow-up evaluation of first-time seizures without clear cause after a complete ED evaluation.<sup>19</sup>

## ■ MANAGEMENT

Usually, an acute seizure self-terminates or can be pharmacologically terminated before a need arises for active airway management. Rapidly reversible ictal insults (e.g., hypoglycemia, hypoxemia, isoniazid ingestion) should be considered and, if found, treated. Primary abortive therapy in the ED is accomplished as described earlier. Although a number of newer antiepileptic medications have become available, their therapeutic purpose is directed toward chronic rather than acute seizures.<sup>32</sup>

Identifying a new-onset seizure in the ED generates consideration for further management. The choice to initiate anticonvulsant therapy depends on the risk of seizure recurrence and any underlying predisposing disease, and the risk of initiating anticonvulsant therapy is typically not made by the emergency physician. The initiation of anticonvulsant therapy after a single seizure is an issue of considerable controversy and should be undertaken in consultation with the neurologist who will be following the patient after discharge from the ED.<sup>33,34</sup> Prompt treatment of any apparent ictal source discovered in the ED, however, is always appropriate.

## ■ DISPOSITION

Disposition plans must be individualized according to the findings of the ED evaluation and the presence or absence of underlying disease. One quarter of adult patients presenting with seizure-related complaints have new-onset seizures.<sup>3</sup> Almost half of them require admission, most because of abnormal CT scans or persistent focal abnormalities; 95% of those who retrospectively required admission were correctly identified by using an ED evaluation consistent with that recommended previously. Patients may be discharged home with early referral to a neurologist if they have a normal neurologic exam, no comorbidities, no known structural brain disease, do not require the use of an antiepileptic drug in the ED, and are felt to be sufficiently resourceful and reliable to comply with follow-up instructions.<sup>4</sup> Patients discharged home from the ED should receive appropriate state-specific guidance regarding driver's license privileges and information for prompt follow-up with a neurologist.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*



## CHAPTER 16 Headache

Christopher S. Russi

### ■ PERSPECTIVE

#### Epidemiology

Up to 85% of the U.S. adult population complains of significant headaches at least occasionally, and 15% does so on a regular basis. Headache as a primary complaint represents between 3 and 5% of all emergency department (ED) visits. The vast majority of patients who have the primary complaint of headache do not have a serious medical cause for the problem. Tension headache accounts for approximately 50% of patients presenting to the ED, another 30% have headache of unidentified origin, 10% have migraine-type pain, and 8% have headache from other potentially serious causes (e.g., tumor, glaucoma). It is estimated that less than 1% of patients who present to the ED with headache have a life-threatening organic disease.<sup>1</sup> The percentages can create a false sense of security, and headache is disproportionately represented in emergency medicine malpractice claims. Although still rare, the most commonly encountered life-threatening cause of severe sudden head pain is subarachnoid hemorrhage (SAH); approximately 20,000 potentially salvageable cases of SAH present to EDs each year. It is estimated that between 25 and 50% of these are missed on the first presentation to a physician.<sup>2</sup> The other significant, potentially life-threatening causes of headache occur even less frequently. Meningitis, carbon monoxide poisoning, temporal arteritis, acute angle-closure glaucoma, intracranial hemorrhage (ICH), cerebral venous sinus thrombosis, and increased intracranial pressure can often be linked with specific historical elements and physical findings that facilitate their diagnosis.

#### Pathophysiology

The brain parenchyma is insensitive to pain. The pain-sensitive areas of the head include the coverings of the brain—the meninges—and the blood vessels, both arteries and veins supplying the brain, and the various tissues lining the cavities within the skull. The ability of the patient to specifically localize head pain is often poor. Much of the pain associated with headache, particularly with vascular headache and migraines, is mediated through the fifth cranial nerve. Such pain may proceed back to the nucleus and then be radiated through various branches of the fifth cranial nerve to areas not directly involved. A specific inflammation in a specific structure (e.g., periapical abscess, sinusitis, or tic douloureux) is much easier to localize than the relatively diffuse pain that may be generated by tension or traction headaches. Pains in the head and

neck may easily overlap. They should be thought of as a unit when considering complaints of headache.

### ■ DIAGNOSTIC APPROACH

#### Differential Considerations

The differential diagnosis of headache is complex because of the large number of potential disease entities and the diffuse nature of many types of pain in the head and neck region (Table 16-1). However, in evaluating the patient with a headache complaint, the top priority is to exclude intracranial hemorrhage (SAH and ICH), meningitis, encephalitis, and mass lesions. Carbon monoxide is an exogenous toxin, the effects of which may be reversible by removing the patient from the source and administering oxygen. Carbon monoxide poisoning is a rare example of a headache in which a simple intervention may quickly improve a critical situation. On the contrary, returning the patient to the poisoned environment without a diagnosis could be lethal.

#### Rapid Assessment and Stabilization

If the patient presents in a critical or comatose state, initial stabilization, including airway management, is undertaken as indicated, preceded by a neurologic examination if at all possible. For purposes of the initial assessment, headache can be divided into two categories: accompanied by altered mental status and without altered mental status. Whenever a patient's mental status is impaired, brain tissue is initially assumed to be compromised. The principles of care centered on cerebral resuscitation address the seven major causes of evolving brain injury: lack of substrate (glucose, oxygen), cerebral edema, intracranial mass lesion, endogenous or exogenous toxins, metabolic alterations (fever, seizure), ischemia, or elevated intracranial pressure.

#### Pivotal Findings

##### History

The history is the pivotal part of the workup for the patient with headache (Table 16-2).

1. The patient should be asked to describe the *pattern and onset of the pain*. Patients often relate frequent and recurrent headaches similar to the one they have

**Table 16-1 Differential Diagnosis**

ORGAN SYSTEM	CRITICAL DIAGNOSES	EMERGENT DIAGNOSES	NONEMERGENT DIAGNOSES
Neurologic, CNS, vessels	Subarachnoid hemorrhage	Shunt failure Traction headaches Tumor/other masses Subdural hematomas	Migraine, various types Vascular, various types Trigeminal neuralgia Post-traumatic Postlumbar puncture Headaches
Toxic/metabolic Environmental Collagen vascular disease Eye/ENT	Carbon monoxide poisoning Temporal arteritis	Mountain sickness  Glaucoma/sinusitis	Dental problems/temporomandibular joint disease Tension headaches Cervical strain Cluster/histamine headaches
Musculoskeletal Allergy Infectious disease	Bacterial meningitis/encephalitis	Brain abscess	Febrile headaches/nonneurologic source of infection
Pulmonary/O <sub>2</sub>		Anoxic headache Anemia	
Cardiovascular Unspecified		Hypertensive crisis	Hypertension (rare) Effort-dependent/coital headaches

CNS, central nervous system; ENT, ear, nose, and throat.

**Table 16-2 Significant Symptoms**

SYMPTOM	FINDING	POSSIBLE DIAGNOSES
Sudden onset of pain	Lightning strike or thunder clap with any decreased mentation, any positive focal finding or intractable pain	Subarachnoid hemorrhage
“Worst headache of their life”	Associated with sudden onset	Subarachnoid hemorrhage
Near syncope or syncope	Associated with sudden onset	Subarachnoid hemorrhage
Increase with jaw movement	Clicking or snapping. Pain with jaw movement	Temporomandibular joint disease
Facial pain	Fulminant pain of the forehead and area of maxillary sinus. Nasal congestion	Sinus pressure or dental infection
Forehead or temporal area pain (or both)	Tender temporal arteries	Temporal arteritis
Periorbital or retro-orbital pain	Sudden onset with tearing	Temporal arteritis or acute angle-closure glaucoma

on this ED visit. A marked variation in headache pattern can signal a new or serious problem. The rate of onset of pain may have significance. Pain with rapid onset of a few seconds to minutes is more likely to be vascular in origin than pain that developed over several hours or days.

Almost all studies dealing with subarachnoid bleeding report that patients moved from the pain-free state to severe pain within seconds to minutes. The “thunder clap” or “lightning strike” headache is a real phenomenon, and this response to questioning may lead to the correct diagnosis of subarachnoid hemorrhage, even if the pain is improving at the time of evaluation.<sup>3</sup>

2. The patient’s *activity at the onset of the pain* may be helpful. Certainly, headaches that come on during severe exertion have a relationship to vascular bleeding, but again, there is enough variation to make assignment to any specific cause highly variable. The syndrome of coital or postcoital headache is well known, but coitus is also a common time of onset for SAH. These headaches require the same evaluation on initial presentation as any other exertion-related head pain. If the patient can recall the precise activity in

which he or she was engaging at the time of the onset of the headache (e.g., “I was just getting up out of the chair to answer the doorbell”), sudden onset is extremely likely and evaluation for SAH is warranted.

3. If the patient or nonhospital medical personnel can relate a *history of head trauma*, the differential diagnosis and emergent causes have narrowed significantly. The considerations now focus on epidural and subdural hematoma, traumatic SAH, skull fracture, and closed-head injury (i.e., concussion and diffuse axonal injury).
4. Toxoplasmosis, cryptococcal meningitis, and abscess are considered higher in the differential in patients with a *history of HIV or immunocompromised state*. Although such entities are rare, it is important to remember that this subset of patients may have serious disease without typical signs or symptoms of systemic illness (e.g., fever and meningismus).
5. The *intensity of head pain* is difficult to quantify objectively. Almost all patients who present to the ED consider their headache to be “severe.” Use of a pain scale of 1 to 10 may help differentiate patients initially but has more value in monitoring their response to therapy.

6. The *character of the pain* (i.e., throbbing, steady), although sometimes helpful, may not be adequate to differentiate one type of headache from another.
7. The *location of head pain* is helpful when the patient can identify a specific area. It is useful to have the patient point or try to indicate the area of pain and the emergency physician to then properly examine that area. Unilateral pain is more suggestive of migraine or a localized inflammatory process in the skull (e.g., sinus) or soft tissue.<sup>4</sup> Occipital headaches are classically associated with hypertension. Certainly, temporal arteritis, temporomandibular joint disease, dental infections, and sinus infections frequently have a highly localized area of discomfort. Meningitis, encephalitis, SAH, and even severe migraine, although intense in nature, are usually more diffuse in their localization.
8. *Exacerbating or alleviating factors* may be important. Patients whose headaches rapidly improve when they are removed from their environment may have carbon monoxide poisoning. Most other severe causes of head pain are not rapidly relieved or improved when patients get to the ED. Headaches on awakening are typically described with brain tumors. Intracranial infections, dental infections, and other regional causes of head pain tend not to be improved or alleviated before therapy is given.
9. *Associated symptoms and risk factors* may relate to the severity of headache but rarely point to the specific causes (Box 16-1). Nausea and vomiting are completely nonspecific. Migraine headaches, increased intracranial pressure, temporal arteritis, and glaucoma can all manifest with severe nausea and vomiting, as can some systemic viral infections with headache. Such factors may point toward the inten-

sity of the discomfort but are not specific in establishing the diagnosis.

10. *A prior history of headache*, although helpful, does not rule out current serious problems. It is extremely helpful, however, to know that the patient has had a workup for severe disease. Previous ED visits, computed tomography (CT) magnetic resonance imaging, and other forms of testing should be inquired about. Patients with both migraine and tension headaches tend to have a stereotypical recurrent pattern. Adherence to these patterns is also helpful in deciding the degree to which a patient's symptoms are pursued.

### Physical Examination

Physical findings associated with various forms of headache are listed in Table 16-3.

### Ancillary Testing

The vast majority of headache patients do not require additional testing (Table 16-4). The single largest consistent mistake made by emergency physicians in the workup of the headache patient is believing a single CT scan clears the patient of the possibility of SAH or other serious intracranial disease. The CT scan can miss 6 to 8% of patients with SAH, especially in patients with minor (grade I) SAH, who are most treatable.<sup>5</sup> The sensitivity of CT for identifying SAH is reduced by nearly 10% for symptom onset greater than 12 hours and by almost 20% at 3 to 5 days. The basic approach to integrating CTs and lumbar puncture in the assessment of headache is outlined in Figure 16-1.<sup>6,8,9</sup>

## BOX 16-1 RISK FACTORS ASSOCIATED WITH POTENTIALLY CATASTROPHIC ILLNESS

1. Carbon monoxide poisoning
  - a. Breathing in enclosed or confined spaces with engine exhaust or ventilation of heating equipment
  - b. Multiple family members with the same symptoms
  - c. Pattern of recurrence in one setting (where the exposure is occurring), relief when not in that setting
  - d. Wintertime and working around machinery or equipment producing carbon monoxide (furnaces, etc.)
2. Meningitis/encephalitis/abscess
  - a. History of sinus or ear infection or recent surgical procedure
  - b. Immunocompromised state
  - c. General debilitation with decreased immunologic system function
  - d. Acute febrile illness—any type
  - e. Extremes of age
  - f. Impacted living conditions (e.g., military barracks, college dormitories)
  - g. Lack of primary immunizations
3. Temporal arteritis
  - a. Age > 50
  - b. Females > males 4:1
  - c. History of other collagen vascular diseases (e.g., systemic lupus)
  - d. Previous chronic meningitis
  - e. Previous chronic illness such as tuberculosis, parasitic infection, fungi
4. Glaucoma—sudden angle-closure
  - a. Not associated with any usual or customary headache pattern
  - b. History of previous glaucoma
  - c. Age > 30
  - d. History of pain increasing in a dark environment
5. Increased intracranial pressure
  - a. History of previous benign intracranial hypertension
  - b. Presence of a cerebrospinal fluid shunt
  - c. History of congenital brain or skull abnormalities
6. Cerebral venous sinus thrombosis
7. Intracranial hemorrhage (ICH)
  - a. Subarachnoid hemorrhage (SAH)
    - i. Sudden severe pain. "Worst headache of life."
    - ii. Acute severe pain following sexual intercourse or straining (i.e., heavy lifting)
    - iii. History of SAH or cerebral aneurysm
    - iv. History of polycystic kidney disease
    - v. Family history of subarachnoid hemorrhage
    - vi. Hypertension—severe
    - vii. Previous vascular lesions in other areas of the body
    - viii. Young and middle-aged
  - b. Subdural hematoma (SDH)
    - i. History of alcohol dependency with or without trauma
    - ii. Current use of anticoagulants
  - c. Epidural hematoma (EDH)
    - i. Traumatic injury
    - ii. Lucid mentation followed by acute altered mentation or somnolence
    - iii. Anisocoria on physical examination

**Table 16-3 Pivotal Findings on Physical Examination**

SIGN	FINDING	POSSIBLE DIAGNOSES
General appearance	Alteration of mental status—nonfocal	Meningitis/encephalitis Subarachnoid hemorrhage Anoxia
	Alterations of mental status with focal findings	Increased CSF pressure Intraparenchymal bleed Tentorial herniation Stroke
	Severe nausea/vomiting	Increased CSF pressure Acute angle-closure glaucoma Subarachnoid hemorrhage
Vital signs	Hypertension with normal heart rate or bradycardia	Increased CSF pressure Subarachnoid hemorrhage Tentorial herniation Intraparenchymal bleed
	Tachycardia	Anoxia/anemia Febrile headache Exertional/coital headaches
	Fever	Febrile headaches Meningitis/encephalitis Temporal arteritis
HEENT	Tender temporal arteries	Temporal arteritis
Fundi—loss of spontaneous venous pulsations or presence of papilledema	Increased CSF pressure	Mass lesions Subarachnoid hemorrhage Acute angle-closure glaucoma
	Subhyaloid hemorrhage	
	Acute red eye (severe ciliary flushing) and poorly reactive pupils	Tentorial pressure cone Mass effect (i.e., subdural, epidural, tumor, intraparenchymal hemorrhage)
	Enlarged pupil with third nerve palsy	Stroke (rare) Subdural hematoma, epidural hematoma, hemiplegic or anesthetic migraine (rare)
Neurologic	Lateralized motor or sensory deficit	Acute cerebellar hemorrhage Acute cerebellitis (mostly children) Chemical intoxication—various types
	Acute cerebellar ataxia	

CSF, cerebrospinal fluid; HEENT, head, eyes, ears, nose, and throat.

**Table 16-4 Diagnostic Adjuncts in Headache Assessment**

TEST	FINDING	DIAGNOSIS
Erythrocyte sedimentation rate (ESR)	Significant elevation	Temporal arteritis
ECG	Nonspecific ST-T wave changes	Subarachnoid hemorrhage Increased CSF pressure
CBC	Severe anemia	Anoxia
CT—head	Increased ventricular size	Increased CSF pressure
	Blood in subarachnoid space	Subarachnoid hemorrhage
	Blood in epidural or subdural space	Epidural/subdural hematoma
	Bleeding into parenchyma of brain	Intraparenchymal hemorrhage
	Areas of poor vascular flow	Pale infarct
Lumbar puncture/CSF analysis	Structural/mass lesion	Traction headache secondary to mass effect
	Increased pressure	Pseudotumor cerebri Mass lesions Shunt failure
	Increased protein	Tumor/other structural lesions
	Increased RBCs	Subarachnoid hemorrhage
	Increased WBCs	Infection
	Positive Gram's stain	Infection
	Decreased glucose	Infection

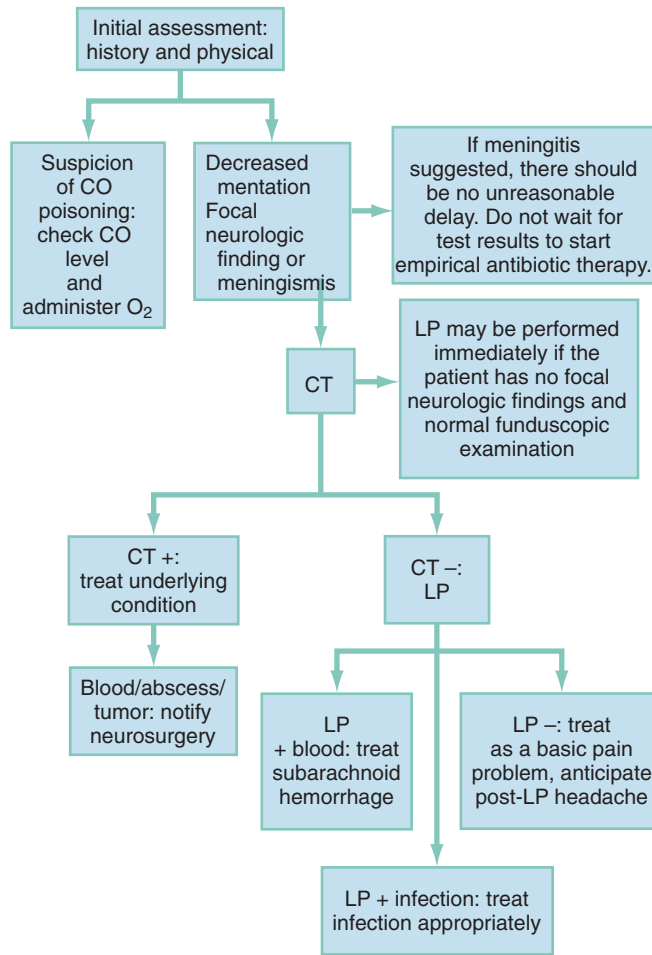
CBC, complete blood count; CSF, cerebrospinal fluid; CT, computed tomography; ECG, electrocardiogram; RBC, red blood cell; WBC, white blood cell.



**Table 16-5** Causes and Differentiation of Potentially Catastrophic Illness Presenting with Nontraumatic Headache

DISEASE ENTITIES	PAIN HISTORY	ASSOCIATED SYMPTOMS	SUPPORT HISTORY	PREVALENCE	PHYSICAL EXAMINATION	USEFUL TESTS	ATYPICAL OR IMPORTANT ASPECTS
Carbon monoxide poisoning	Usually gradual, subtle, dull, nonfocal throbbing pain	May wax and wane as they leave and enter the involved area of carbon monoxide. Throbbing may vary considerably	Exposure to engine exhaust, old or defective heating systems, most common in winter months	Rare	No focal neurologic findings. May need cognitive testing	Carbon monoxide level, cognitive testing	May improve on the way to the hospital. Occurs in groups, may involve entire families or groups of people exposed to the carbon monoxide
Subarachnoid hemorrhage	Sudden onset, “thunder clap” or “lightning strike,” severe throbbing	When ever altered mental status is present, the outcome is decidedly worse	History of polycystic kidney disease. History of chronic hypertension	Uncommon	Frequently decreased mentation—meningismus, increased blood pressure, decreased pulse, venous pulsations, rarely subhyaloid hemorrhage	CT. Lumbar puncture	If CT positive, immediate involvement of neurosurgery. If CT negative, lumbar puncture
Meningitis/encephalitis/abscess	Gradual—as general symptoms increase, headache increases—nonfocal	Decreased mentation prominent, irritability prominent. With abscess, focal neurologic findings may be present	Recent infection Recent facial or dental surgery or other ENT surgery	Uncommon	Fever—late in course, decreased spontaneous venous pulsations	CT. Lumbar puncture	When such infection suspected, treat. Do not delay antibiotics and steroids awaiting laboratory results
Temporal arteritis	Often pain developing over a few hours from mild to severe. Virtually always focal in nature	Decreased vision, nausea, vomiting intense—may confuse diagnosis	Age over 50. Other collagen vascular diseases or inflammatory diseases	Uncommon	Tender temporal arteries	Sedimentation rate	Usually unrelated and rapidly progressive
Acute angle-closure glaucoma	Sudden in onset	Nausea, vomiting, decreased vision	History of glaucoma. History of pain going into dark area	Rare	“Steamy” cornea. Midposition pupil poorly reactive. Acute red eye	Measurement of intraocular pressure	Rapid intervention with medications required—if no relief, immediate surgery may be required
Increased intracranial pressure syndromes	Gradual, dull, nonfocal	Vomiting, decreased mentation	History of CSF shunt or other congenital brain or skull abnormality	Uncommon	Papilledema. Loss of spontaneous venous pulsations	CT. Shunt function study. If OK, lumbar puncture	Shunt failure or other cause of significant increased CSF pressure requires involvement of neurosurgery

CSF, cerebrospinal fluid; CT, computed tomography; ENT, ear, nose, and throat.



**Figure 16-1.** Initial assessment and treatment of headache. CO, carbon monoxide; CT, computed tomography; LP, lumbar puncture.

Obtaining cerebrospinal fluid should not delay antimicrobial treatment if intracranial infection is suggested. Intravenous antibiotics should precede lumbar puncture. Abnormal mental status, signs of increased intracranial pressure, papilledema focal findings on the neurologic examination, or any other indication suggestive of focal intracranial lesion requires CT before lumbar puncture.

## ■ DIFFERENTIAL CONSIDERATIONS

Certain historical and physical findings can help the emergency physician decide whether the patient falls into an “all clear” or a “warning signal” group. In the warning group, further investigation and testing should be performed on all patients who present with any of the following: (1) sudden onset of headache, (2) “the worst headache ever,” (3) decreased

or altered mental status, (4) true meningismus, (5) unexplained fever or bradycardia, (6) focal neurologic deficits on examination, (7) symptoms refractory to treatment or worsening under observation, (8) new onset of headache with exertion, or (9) history of HIV. These patients have the highest risk for significant disease.

In addition, a group of reliable “all clear signals” indicates patients who do not require further investigation when *all* are present: (1) previous identical headaches, (2) normal alertness and cognition by both examination and history of the event, (3) normal examination of the neck showing no meningismus, (4) normal vital signs, (5) normal or nonfocal neurologic examination, and (6) improvement under observation or with treatment.

Sequential evaluation and assessment of data are ongoing processes. Patients should be reevaluated while in the ED, and inconsistent findings may require a rapid review of the situation and rethinking of the diagnosis (Table 16-5).<sup>7</sup>

## ■ MANAGEMENT

### Empirical

Patients with headache represent a spectrum of disease. Patients with headache need to receive triage for evaluation according to their symptoms. Clearly, patients with abnormal vital signs or altered mental status require evaluation before patients with less severe symptoms. If history and physical examination point toward potentially lethal causes, however, effort should be made to establish the diagnosis rapidly with ancillary testing. Pain treatment should be started early. The pain medication of choice depends on the particular patient, underlying vital signs, allergies, and general condition; but relief of pain is still an essential part of the physician’s job and should have little effect on the diagnostic workup.

### Specific

Specific management for headache is described in Chapter 101. The challenge in emergency medicine, however, is to eliminate life-threatening causes of headache and to treat the patient’s pain.

## ■ DISPOSITION

Most patients presenting with headache are discharged from the ED with appropriate analgesia and follow-up. These represent patients in the all-clear category or those found to have no serious disease after a careful evaluation and testing. Any patients in whom warning findings are noted require more extensive assessment.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## CHAPTER 17 **Dyspnea**

Sabina Braithwaite and Debra Perina

### ■ PERSPECTIVE

*Dyspnea* is the term applied to the sensation of breathlessness and the patient's reaction to that sensation. It is an uncomfortable awareness of breathing difficulties that in the extreme manifests as "air hunger." Dyspnea is often ill defined by patients, who may describe the feeling as shortness of breath, chest tightness, or difficulty breathing. Dyspnea results from a variety of conditions, ranging from nonurgent to life-threatening. Neither the clinical severity nor the patient's perception correlates well with the seriousness of underlying pathology and may be affected by emotions, behavioral and cultural influences, and external stimuli.<sup>1,2</sup>

The following terms may be used in the assessment of the dyspneic patient:

*Tachypnea*: A respiratory rate greater than normal. Normal rates range from 44 cycles/min in a newborn to 14 to 18 cycles/min in adults.

*Hyperpnea*: Greater than normal minute ventilation to meet metabolic requirements.

*Hyperventilation*: A minute ventilation (determined by respiratory rate and tidal volume) that exceeds metabolic demand. Arterial blood gases (ABG) characteristically show a normal partial pressure of oxygen ( $P_{O_2}$ ) with an uncompensated respiratory alkalosis (low partial pressure of carbon dioxide [ $P_{CO_2}$ ] and elevated pH).

*Dyspnea on exertion*: Dyspnea provoked by physical effort or exertion. It often is quantified in simple terms, such as the number of stairs or number of blocks a patient can manage before the onset of dyspnea.

*Orthopnea*: Dyspnea in a recumbent position. It usually is measured in number of pillows the patient must use to lie in bed (e.g., two-pillow orthopnea).

*Paroxysmal nocturnal dyspnea*: Sudden onset of dyspnea occurring while reclining at night, usually related to the presence of congestive heart failure.

### Epidemiology

Dyspnea is a common presenting complaint among emergency department patients of all ages. Causes vary widely and may be due to a benign, self-limited condition or significant pathology that can produce long-term morbidity and premature mortality.

### Pathophysiology

The actual mechanisms responsible for dyspnea are unknown. Normal breathing is controlled both centrally by the respiratory control center in the medulla oblongata, as well as peripherally by chemoreceptors located near the carotid bodies, and mechanoreceptors in the diaphragm and skeletal muscles.<sup>3</sup> Any imbalance between these sites is perceived as dyspnea. This imbalance generally results from ventilatory demand being greater than capacity.<sup>4</sup>

The perception and sensation of dyspnea are believed to occur by one or more of the following mechanisms: increased work of breathing, such as the increased lung resistance or decreased compliance that occurs with asthma or chronic obstructive pulmonary disease (COPD), or increased respiratory drive, such as results from severe hypoxemia, acidosis, or centrally acting stimuli (toxins, central nervous system events). Pulmonary stretch receptors also are thought to play a role.

### ■ DIAGNOSTIC APPROACH

#### Differential Considerations

Dyspnea is subjective and has many different potential causes.<sup>5</sup> The differential diagnosis list can be divided into acute and chronic causes, of which many are pulmonary. Other etiologies include cardiac, metabolic, infectious, neuromuscular, traumatic, and hematologic (Table 17-1).

### Pivotal Findings

#### History

*Duration of Dyspnea*. Chronic or progressive dyspnea usually denotes primary cardiac or pulmonary disease.<sup>6</sup> Acute dyspneic spells may result from asthma exacerbation; infection; pulmonary embolus; intermittent cardiac dysfunction; psychogenic causes; or inhalation of irritants, allergens, or foreign bodies.

*Onset of Dyspnea*. Sudden onset of dyspnea should lead to consideration of pulmonary embolism (PE) or spontaneous pneumothorax. Dyspnea that builds slowly over hours or days may represent a flare of asthma or COPD; pneumonia; recurrent, small pulmonary emboli; congestive heart failure; or malignancy.

**Table 17-1 Differential Diagnoses for Acute Dyspnea**

ORGAN SYSTEM	CRITICAL DIAGNOSES	EMERGENT DIAGNOSES	NONEMERGENT DIAGNOSES
Pulmonary	Airway obstruction Pulmonary embolus Noncardiogenic edema Anaphylaxis Ventilatory failure	Spontaneous pneumothorax Asthma Cor pulmonale Aspiration Pneumonia	Pleural effusion Neoplasm Pneumonia (CAP score $\leq 70$ ) COPD
Cardiac	Pulmonary edema Myocardial infarction Cardiac tamponade	Pericarditis	Congenital heart disease Valvular heart disease Cardiomyopathy
<b>Primarily Associated with Normal or Increased Respiratory Effort</b>			
Abdominal		Mechanical interference Hypotension, sepsis from ruptured viscus, bowel obstruction, inflammatory/infectious process	Pregnancy Ascites Obesity
Psychogenic			Hyperventilation syndrome Somatization disorder Panic attack
Metabolic/endocrine	Toxic ingestion DKA	Renal failure Electrolyte abnormalities Metabolic acidosis	Fever Thyroid disease
Infectious	Epiglottitis	Pneumonia (CAP score $\leq 70$ )	Pneumonia (CAP score $\leq 70$ )
Traumatic	Tension pneumothorax Cardiac tamponade Flail chest	Simple pneumothorax, hemothorax Diaphragmatic rupture	Rib fractures
Hematologic	Carbon monoxide poisoning Acute chest syndrome	Anemia	
<b>Primarily Associated with Decreased Respiratory Effort</b>			
Neuromuscular	CVA, intracranial insult Organophosphate poisoning	Multiple sclerosis Guillain-Barré syndrome Tick paralysis	ALS Polymyositis Porphyria

ALS, amyotrophic lateral sclerosis; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; DKA, diabetic ketoacidosis.

**Positional Changes.** Orthopnea can result from left-sided heart failure, COPD, or neuromuscular disorders. One of the earliest symptoms seen in patients with diaphragmatic weakness from neuromuscular disease is orthopnea.<sup>7</sup> Paroxysmal nocturnal dyspnea is most common in patients with left-sided heart failure,<sup>6</sup> but also can be found in COPD. Exertional dyspnea commonly is associated with COPD, but also can be seen with poor cardiac reserve and abdominal loading. Abdominal loading, caused by ascites, obesity, or pregnancy, leads to elevation of the diaphragm, resulting in less effective ventilation and dyspnea.

**Trauma.** Dyspnea can result from trauma, causing fractured ribs, flail chest, hemothorax, pneumothorax, diaphragmatic rupture, pericardial effusion, cardiac tamponade, or neurologic injury.

## Symptoms

Patient descriptions of dyspnea vary significantly and generally correlate poorly with severity. Fever suggests an infectious cause. Anxiety may point to panic attack or psychogenic dyspnea, if no organic cause can be isolated. PE or myocardial infarction may present with isolated dyspnea or with associated chest pain, particularly if the pain is constant, dull, or visceral.<sup>8,9</sup> If the pain is sharp and worsened by deep breathing but not by movement, pleural effusion and pleurisy or pleural irritation from pneumonia or PE are possible. Spontaneous pneumothorax also may produce sharp pain with deep breathing that is not worsened by movement.

## Signs

Physical signs in dyspneic patients may be consistent with specific illnesses (Table 17-2). Physical findings found in specific diseases also can be grouped as presenting patterns (Table 17-3).

## Ancillary Studies

Specific findings obtained from the history and physical examination should be used to determine which ancillary studies are needed (Table 17-4). Bedside oxygen saturation determinations, or selective use of ABGs when oximetry is not reliable, are useful in determining the degree of hypoxia and the need for supplemental oxygen or assisted ventilation. An additional resource for quickly assessing ventilatory status is non-invasive waveform capnography. Using both the end-tidal CO<sub>2</sub> value and the shape of the waveform itself can be helpful in assessing the adequacy of ventilations as well as potential causes of the dyspnea (See Chapter 3). An electrocardiogram may be useful if the etiology is cardiac or suggests acute pulmonary hypertension.

Serum electrolytes may suggest less common possible causes, such as hypokalemia, hypophosphatemia, diabetic ketoacidosis, or hypocalcemia. A complete blood count may identify severe anemia or thrombocytopenia associated with sepsis. The white blood cell count is not sufficiently sensitive or specific to be of discriminatory value. Cardiac markers and D-dimer assay may be useful in pursuing etiologies such as



**Table 17-2 Pivotal Findings in Physical Examination**

SIGN	PHYSICAL FINDING	DIAGNOSES TO CONSIDER
Vital signs	Tachypnea Hypopnea Tachycardia Hypotension Fever	Pneumonia, pneumothorax Intracranial insult, drug/toxin ingestion PE, traumatic chest injury Tension pneumothorax Pneumonia, PE
General appearance	Cachexia, weight loss Obesity Pregnancy Barrel chest “Sniffing” position “Tripoding” position Traumatic injury	Malignancy, acquired immune disorder, mycobacterial infection Hypoventilation, sleep apnea, PE PE COPD Epiglottitis COPD/asthma with severe distress Pneumothorax (simple, tension), rib fractures, flail chest, hemothorax, pulmonary contusion
Skin/nails	Tobacco stains/odor Clubbing  Pallid skin/conjunctivae Muscle wasting Bruising  Subcutaneous emphysema Hives, rash	COPD, malignancy, infection Chronic hypoxia, intracardiac shunts or pulmonary vascular anomalies Anemia Neuromuscular disease Chest wall: rib fractures, pneumothorax Diffuse: thrombocytopenia, chronic steroid use, anticoagulation Rib fractures, pneumothorax, tracheobronchial disruption Allergic reaction, infection, tick-borne illness
Neck	Stridor  JVD	Upper airway edema/infection, foreign body, traumatic injury, anaphylaxis Tension pneumothorax, COPD or asthma exacerbation, fluid overload/CHF, PE
Lung examination	Wheezes  Rales Unilateral decrease  Hemoptysis Sputum production Friction rub Abnormal respiratory pattern (e.g., Cheyne-Stokes)	CHF, anaphylaxis Bronchospasm CHF, pneumonia, PE Pneumothorax, pleural effusion, consolidation, rib fractures/contusion, pulmonary contusion Malignancy, infection, bleeding disorder, CHF Infection (viral, bacterial) Pleurisy Intracranial insult
Chest examination	Crepitance or pain on palpation Subcutaneous emphysema Thoracoabdominal desynchrony Flail segment	Rib or sternal fractures Pneumothorax, tracheobronchial rupture Diaphragmatic injury with herniation; cervical spinal cord trauma Flail chest, pulmonary contusion
Cardiac examination	Murmur S <sub>3</sub> or S <sub>4</sub> gallop S <sub>2</sub> accentuation Muffled heart sounds	PE PE PE Cardiac tamponade
Extremities	Calf tenderness, Homans' sign Edema	PE CHF
Neurologic examination	Focal deficits (motor, sensory, cognitive) Symmetrical deficits Diffuse weakness  Hyporeflexia Ascending weakness	Stroke, intracranial hemorrhage causing central abnormal respiratory drive; if long-standing, risk of aspiration pneumonia Neuromuscular disease Metabolic or electrolyte abnormality (hypocalcemia, hypomagnesemia, hypophosphatemia), anemia Hypermagnesemia Guillain-Barré syndrome

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; JVD, jugular venous distention; PE, pulmonary embolism.

cardiac ischemia or PE. Amino-terminal pro-B-type natriuretic peptide (NT-proBNP) analysis adds both diagnostic and prognostic value for several causes of dyspnea, including heart failure, PE, and ischemic cardiac disease.<sup>9-11</sup> Combinations of specific serum markers can also help define pathology.<sup>12-14</sup> Specialized tests, such as ventilation-perfusion scans, chest computed tomography, pulmonary angiography, or, rarely, conventional pulmonary angiography, may confirm the diagnosis of PE.<sup>15</sup> If dyspnea is believed to be upper airway in origin, direct or fiberoptic laryngoscopy or a soft tissue lateral radiograph of the neck may be useful.

## ■ DIFFERENTIAL DIAGNOSIS

The range and diversity of pathophysiologic states that produce dyspnea make a simple algorithmic approach difficult.<sup>16</sup> After initial stabilization and assessment, findings from the history, physical examination, and ancillary testing are collated to match patterns of disease that produce dyspnea. This process is updated periodically as new information becomes available. Table 17-3 presents recognizable patterns of disease for common dyspnea-producing conditions, along with specific associated symptoms.

**Table 17-3 Diagnostic Table: Patterns of Diseases Often Resulting in Dyspnea**

DISEASE	HISTORY: (DYSPNEA)	ASSOCIATED SYMPTOMS	SIGNS AND PHYSICAL FINDINGS	TESTS
Pulmonary embolism	HPI: abrupt onset, pleuritic pain, immobility (travel, recent surgery) PMH: malignancy, DVT, PE, hypercoagulability, oral contraception, obesity	Diaphoresis, exertional dyspnea	Tachycardia, tachypnea, low-grade fever	ABG (A-a gradient), D-dimer ECG (dysrhythmia, right heart strain) CXR (Westermark sign, Hampton's hump) V/Q, spiral CT, MRV Pulmonary angiogram Ultrasound positive for DVT CXR, CBC, sputum and blood cultures
Pneumonia	Fever, productive cough, chest pain	Anorexia, chills, nausea, vomiting, exertional dyspnea, cough	Fever, tachycardia, tachypnea, rales or decreased breath sounds	ABG if hypoxia suspected Waveform capnography if altered mental status
Bacterial	SH: tobacco use			
Viral	Exposure (e.g., influenza, varicella)			
Opportunistic	Immune disorder, chemotherapy			
Fungal/parasitic	Exposure (e.g., birds), indolent onset	Episodic fever, nonproductive cough		
Pneumothorax	Abrupt onset ± trauma, chest pain, thin males more likely to have spontaneous pneumothorax	Localized chest pain	Decreased breath sounds, subcutaneous emphysema, chest wall wounds or instability	CXR: pneumothorax, rib fractures, hemothorax
Simple Tension	Decompensation of simple pneumothorax	Diaphoresis	Above JVD, tracheal deviation, muffled heart sounds, cardiovascular collapse	Ultrasound positive for pneumothorax Clinical diagnosis: requires immediate decompression. May verify using bedside ultrasound
COPD/asthma	Tobacco use, medication noncompliance, URI symptoms, sudden weather change PMH: environmental allergies FH: asthma	Air hunger, diaphoresis	Retractions, accessory muscle use, tripodding, cyanosis	CXR: rule out infiltrate, pneumothorax, atelectasis (mucus plug) Waveform capnography
Malignancy	Weight loss, tobacco or other occupational exposure	Dysphagia	Hemoptysis	CXR, chest CT: mass, hilar adenopathy, focal atelectasis
Fluid overload	Gradual onset, dietary indiscretion or medication noncompliance, chest pain PMH: recent MI, diabetes, CHF Abrupt onset, exposure to allergen	Worsening orthopnea, PND	JVD, peripheral edema, S <sub>3</sub> or S <sub>4</sub> gallop, new cardiac dysrhythmia, hepatojugular reflux	CXR: pleural effusion, interstitial edema, Kerley B lines, cardiomegaly ECG: ischemia, dysrhythmia NT-proBNP
Anaphylaxis		Dysphagia	Oral swelling, stridor, wheezing, hives	

ABG, arterial blood gas; CBC, complete blood count; CHF, congestive heart failure; CT, computed tomography; CXR, chest x-ray; DVT, deep vein thrombosis; ECG, electrocardiogram; FH, family history; HPI, history of present illness; JVD, jugular venous distention; MI, myocardial infarction; MRV, magnetic resonance venography; NT-proBNP, amino-terminal pro-brain natriuretic peptide; PE, pulmonary embolism; PMH, past medical history; PND, paroxysmal nocturnal dyspnea; SH, social history; URI, upper respiratory infection.

**Table 17-4 Ancillary Testing in the Dyspneic Patient**

CATEGORY	TEST	FINDINGS/POTENTIAL DIAGNOSES
Laboratory	Pulse oximetry, selective ABG use	Hypoxia, hyperventilation (muscular weakness, intracranial event)
	Waveform capnography	CO <sub>2</sub> retention (COPD, sleep apnea), obstructive or restrictive pulmonary pattern Metabolic versus respiratory acidosis (DKA, ingestions) A-a gradient (PE) Elevated carboxyhemoglobin (inhalation injury or CO poisoning)
	Complete blood count	WBC Increase: infection, stress demargination, hematologic malignancy Decrease: neutropenia, sepsis Hgb/Hct: anemia, polycythemia Smear: abnormal Hgb (i.e., sickling), inclusions Platelets: thrombocytopenia (marrow toxicity)
	Chemistry	BUN/Cr: acute/chronic renal failure K/Mg/Phos: low levels resulting in muscular weakness Glucose: DKA D-dimer: abnormal clotting activity NT-proBNP: heart failure, PE Troponin: cardiac ischemia or infarct
Cardiac	ECG	Ischemia, dysrhythmia, S <sub>1</sub> Q <sub>3</sub> T <sub>3</sub> (PE), right heart strain
	Echocardiogram	Pulmonary hypertension, valvular disorders Wall motion abnormalities related to ischemia, intracardiac shunts
Radiologic	Chest radiograph	Bony structures: fractures, lytic lesions, pectus, kyphoscoliosis Mass: malignancy, cavitory lesion, infiltrate, foreign body Diaphragm: eventration, elevation of hemidiaphragm, bowel herniation Mediastinum: adenopathy (infection, sarcoid), air Cardiac silhouette: enlarged (cardiomyopathy, fluid overload) Soft tissue: subcutaneous air Lung parenchyma: blebs, pneumothorax, effusions (blood, infectious), interstitial edema, local consolidation, air bronchograms, Hampton's hump, Westermarck's sign
	V/Q scan	PE
	Pulmonary angiogram	PE, intervention (thrombolysis)
	CT	Mass lesion, adenopathy, trauma, PE
	MRI	PE, bony and soft tissue lesions, vascular abnormality
	Soft tissue neck radiograph	Epiglottitis, foreign body
	Ultrasound	Pneumothorax, pleural effusion, impaired cardiac function or pericardial effusion
	Fiberoptic	Mass lesion, foreign body
	Bronchoscopy	Intervention (stenting, biopsy)
	Laryngoscopy	Mass lesion, edema, epiglottitis, foreign body

A-a, alveolar-arterial; ABG, arterial blood gas; BUN, blood urea nitrogen; CHF, congestive heart failure; CO, carbon monoxide; COPD, chronic obstructive pulmonary disease; Cr, creatinine; CT, computed tomography; DKA, diabetic ketoacidosis; ECG, electrocardiogram; MRI, magnetic resonance imaging; NT-proBNP, amino-terminal pro-brain natriuretic peptide; PE, pulmonary embolism; V/Q, ventilation-perfusion; WBC, white blood cell.

## Critical Diagnoses

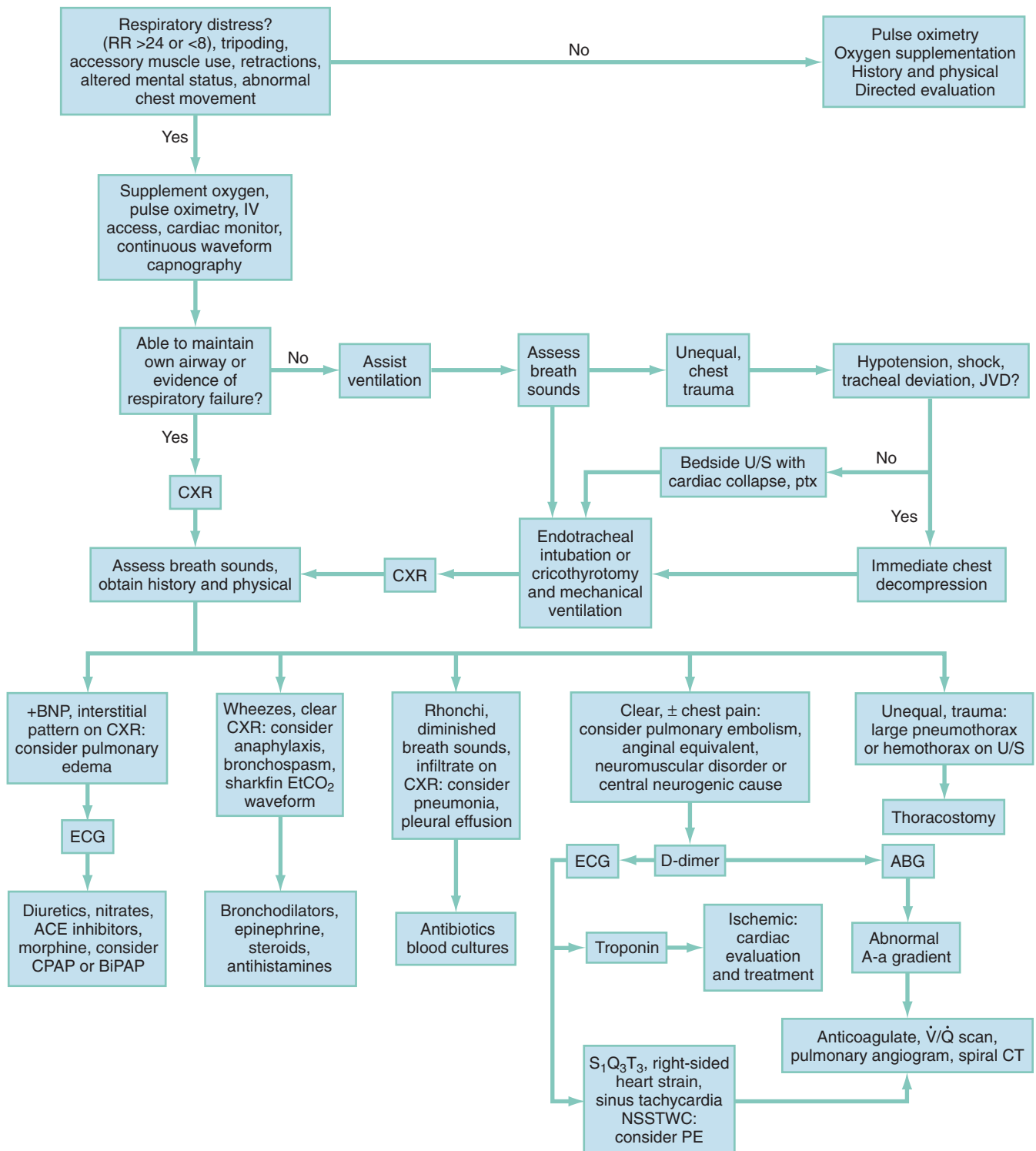
Several critical diagnoses should be promptly considered to determine the best treatment options to stabilize the patient. Tension pneumothorax is such a critical diagnosis. If a dyspneic patient has diminished breath sounds on one side, ipsilateral hyper-resonance, severe respiratory distress, hypotension, and oxygen desaturation, prompt decompression of presumptive tension pneumothorax is necessary. Bedside ultrasonography may assist in confirming pneumothorax. If obstruction of the upper airway is evidenced by dyspnea and stridor, early, definitive assessment and intervention must occur in the emergency department or operating room. Complete obstruction by a foreign body warrants the Heimlich maneuver until the obstruction is relieved or the patient is unconscious, followed rapidly by direct laryngoscopy. Congestive heart failure and pulmonary edema can produce dyspnea and respiratory failure and should be treated as soon as possible if severe.<sup>17</sup> Significant dyspnea and wheezing can be seen in anaphylaxis and must be treated promptly to prevent further deterioration. Severe bronchospastic exacerbations of asthma at any age may lead rapidly to respiratory failure and arrest and

should receive vigorous attention, including continuous or frequent administration of a beta-agonist aerosol.<sup>18</sup> As mentioned earlier, waveform capnography is a valuable tool for assessing the severity and determining the cause of respiratory distress.

## Emergent Diagnoses

Asthma and COPD exacerbations can result in marked dyspnea with bronchospasm and decreased ventilatory volumes.<sup>19</sup> Sudden onset of dyspnea with a decreased oxygen saturation on room air accompanied by sharp chest pain may represent PE.<sup>15</sup> Dyspnea accompanied by decreased breath sounds and tympany to percussion on one side is seen with spontaneous pneumothorax. Dyspnea associated with decreased respiratory effort may represent a neuromuscular process, such as multiple sclerosis, Guillain-Barré syndrome, or myasthenia gravis.<sup>14</sup> Unilateral rales, cough, fever, and dyspnea usually indicate pneumonia.

Figure 17-1 provides an algorithm for assessment and stabilization of a dyspneic patient. The initial division is based on the degree of breathing effort associated with the symptoms.



**Figure 17-1.** Rapid assessment and stabilization of a dyspneic patient. ABG, arterial blood gas; ACE, angiotensin-converting enzyme; BiPAP, biphasic positive airway pressure; BNP, B-type natriuretic peptide; CO, carbon monoxide; CPAP, continuous positive airway pressure; CT, computed tomography; CXR, chest x-ray; ECG, electrocardiogram; EtCO<sub>2</sub>, end-tidal carbon dioxide; IV, intravenous; JVD, jugular venous distention; NSSTWC, nonspecific ST wave changes (on ECG); PE, pulmonary embolism; RR, respiratory rate; V/Q, ventilation-perfusion ratio; U/S, ultrasound.

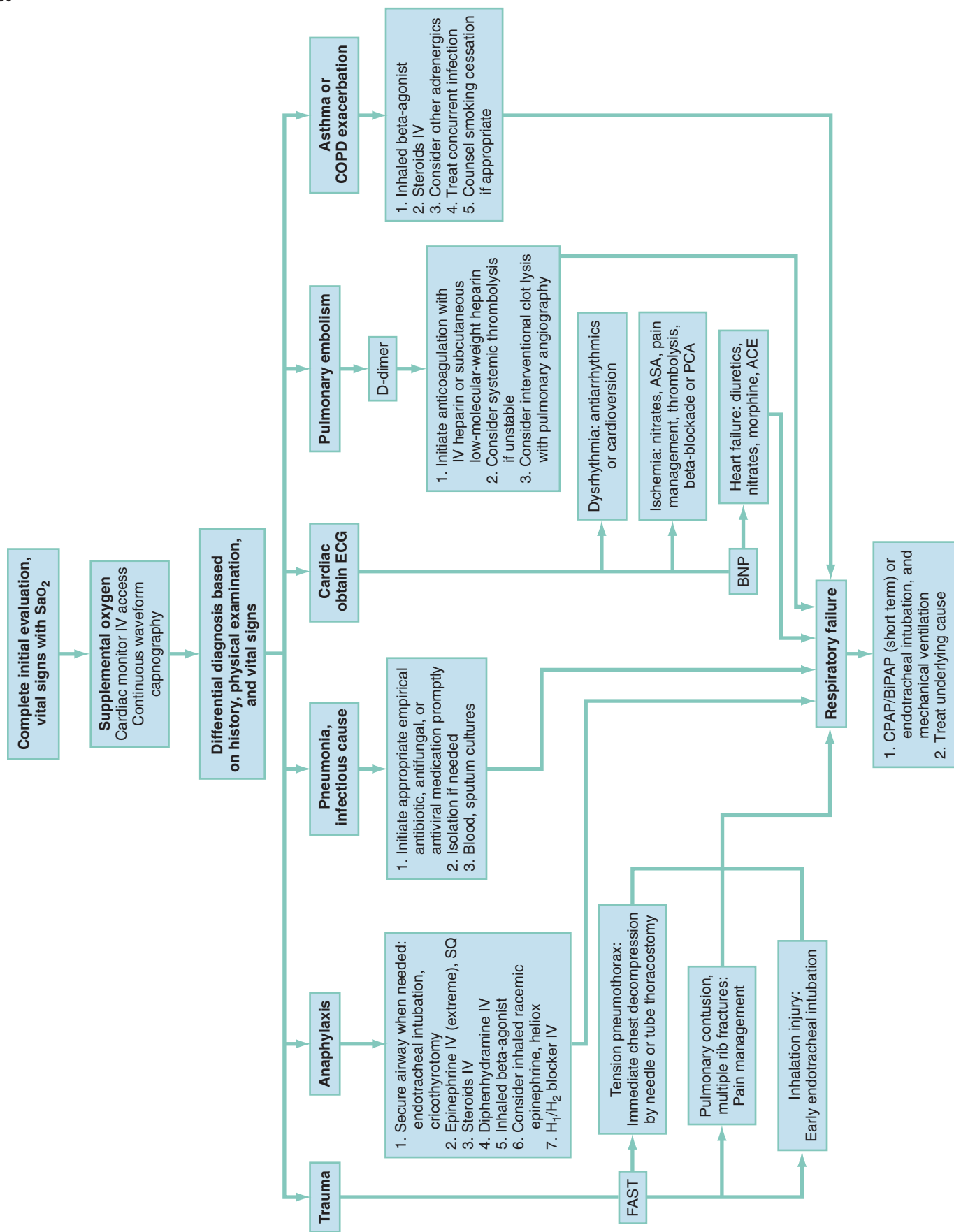
The most critical diagnoses must be considered first and appropriate intervention taken as necessary.

All patients experiencing dyspnea, regardless of possible cause, should be promptly transported to the treatment area. Bedside pulse oximetry should be obtained, and the patient should be placed on a cardiac monitor. If the pulse oximetry is less than 98% saturated on room air, the patient should be placed on supplemental oxygen either by nasal cannula or

mask depending on the degree of desaturation detected. If necessary, the patient should be intubated, and breathing should be assisted with manual or mechanical ventilation.

When the airway has been secured, rapid assessment of the patient's appearance and vital signs can help determine the need for further stabilization. Decreased mental alertness, inability to speak in more than one-word syllables, or certain types of body positioning, signal the presence of significant





**Figure 17-2.** Clinical guidelines for emergency department management of dyspnea. ACE, angiotensin-converting enzyme; ASA, acetylsalicylic acid; COPD, chronic obstructive pulmonary disease; CPAP/BiPAP, continuous positive airway pressure/biphasic positive airway pressure; ECG, electrocardiogram; IV, intravenous; PCA, patient-controlled analgesia; SQ, subcutaneous.

respiratory distress and the need for rapid intervention. After stabilization has occurred, the cause of the dyspnea can be further investigated.

### ■ EMPIRICAL MANAGEMENT AND DISPOSITION

The management algorithm for dyspnea (Fig. 17-2) outlines the approach to treatment for most identifiable diseases. Unstable patients or patients with critical diagnoses must be stabilized and may require admission to an intensive care unit. Emergent patients who have improved in the emergency department may be admitted to an intermediate care unit. Patients diagnosed with urgent conditions in danger of dete-

rioration without proper treatment or patients with severe comorbidities, such as diabetes, immunosuppression, or cancer, may also require admission for observation and treatment.

Most patients in the nonurgent category can be treated as outpatients if good medical follow-up can be arranged. If dyspnea persists despite therapy and no definitive cause has been delineated, the best course of action is hospitalization for observation and ongoing evaluation. If no definitive diagnosis can be obtained and the symptoms have abated, the patient may be discharged with good medical follow-up and instructions to return if symptoms recur.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*

## CHAPTER 18 Chest Pain

James E. Brown and Glenn C. Hamilton

### ■ PERSPECTIVE

Nearly 6 million patients present to the emergency department (ED) each year with complaints of chest pain, constituting 5% of all patients seen in EDs in the United States.<sup>1</sup> Chest pain is a symptom caused by several life-threatening diseases and has a broad differential diagnosis. It is complicated by a frequent disassociation between intensity of symptoms and signs and seriousness of underlying pathology.

### Epidemiology

The epidemiology of the critical diagnoses causing chest pain varies widely. Acute coronary syndromes (ACS), aortic dissection, pulmonary embolism (PE), pneumothorax, pericarditis with tamponade, and esophageal rupture are potentially catastrophic causes of chest pain. Due to its high incidence and potential lethality, ACS is the most significant potential diagnosis in the ED. Of all deaths in the United States, 36% are attributed to cardiovascular diseases; these account for approximately 870,000 deaths per year.<sup>2</sup> Historically, emergency physicians misdiagnose 3 to 5% of myocardial infarctions (MIs), accounting for 25% of malpractice losses in emergency medicine.<sup>3,4</sup> Thoracic aortic dissection has an incidence of 0.5 to 1 per 100,000 population with a mortality rate exceeding 90% if misdiagnosed. The true incidence of PE is unclear, with estimates of 70 per 100,000. This equates to approximately 100,000 PE cases per year in the United States.<sup>5</sup> Although the incidence of tension pneumothorax is also unclear, the incidence of spontaneous pneumothorax ranges from 2.5 to 18 per 100,000 total patients. The total incidence of esophageal rupture is 12.5 cases per 100,000 persons. The true incidence of pericarditis is unknown, but is diagnosed in 1 of every 1000 hospital admissions.<sup>6</sup> Up to 5% of ED chest pain patients without acute ST elevation MI may have pericarditis.<sup>7</sup>

### Pathophysiology

Afferent fibers from the heart, lungs, great vessels, and esophagus enter the same thoracic dorsal ganglia. Through these visceral fibers, each organ produces the same indistinct quality and location of pain. The quality of visceral chest pain varies widely and is described as “burning,” “aching,” “stabbing,” or “pressure.” Since dorsal segments overlap three segments above and below a level, disease of a thoracic origin can produce pain anywhere from the jaw to the epigastrium. Radi-

ation of pain is caused by somatic afferent fibers synapsing in the same dorsal root ganglia as the thoracic viscera. This stimulation can “confuse” the patient’s central nervous system into misperceiving that the pain originates in the arms or shoulders.

### ■ DIAGNOSTIC APPROACH

#### Differential Considerations

Due to the indistinct nature of visceral pain, the differential diagnosis of chest pain is broad and includes many of the most critical diagnoses in medicine and many nonemergent conditions (Table 18-1).

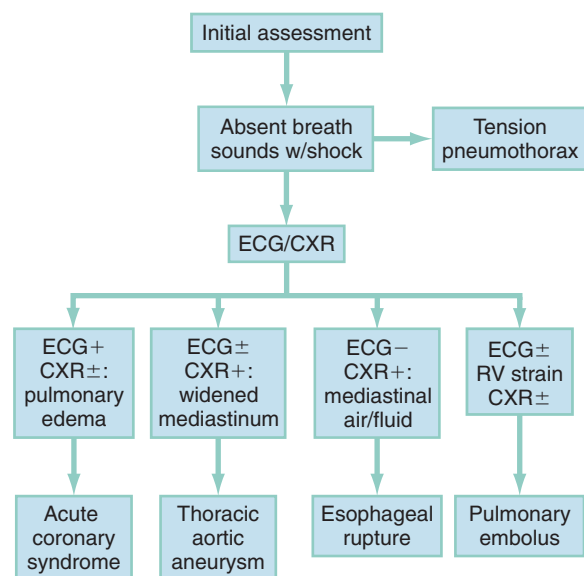
#### Rapid Stabilization and Assessment

The initial questions are, “Must I intervene immediately?” and “What are the life-threatening possibilities in this patient?” The answers are usually apparent within the first few minutes after assessing the patient’s appearance and vital signs. One of the critical diagnoses is tension pneumothorax. If a patient presents with chest pain, respiratory distress, shock, and unilateral reduction or absence of breath sounds, immediate intervention with needle or tube thoracostomy is required. Additionally, patients with severe derangements in vital signs require stabilizing treatment during a search for the precipitating cause. Patients who present with respiratory distress require immediate intervention and lead the emergency physician to consider a more serious cause of the pain (Fig. 18-1; also see Chapter 17).

All patients, except those with obvious benign causes of chest pain, must have an electrocardiogram (ECG) within minutes of reporting their pain. This ECG should be read for acute MI by the emergency physician as soon as it is completed. Patients with positive ECG findings and those considered at high risk are triaged directly to the treatment area and monitored. Symptomatic derangements in vital signs are addressed. If vital signs are stable, a focused history and physical examination are performed. Most patients also require a chest radiograph to evaluate the chest pain. If a cardiac cause is suggested and vital signs are stable, pain relief with nitroglycerin (0.4 mg sublingual every 3–5 minutes) may be appropriate. Aspirin (81–325 mg) is a consideration for patients without hemorrhagic disorders, known allergies, or vascular dissections. Clopidogrel (loading dose 300 mg) or other anti-

**Table 18-1** Differential Diagnosis of Chest Pain

ORGAN SYSTEM	CRITICAL DIAGNOSES	EMERGENT DIAGNOSES	NONEMERGENT DIAGNOSES
Cardiovascular	Acute myocardial infarction Acute coronary ischemia Aortic dissection Cardiac tamponade	Unstable angina Coronary spasm Prinzmetal's angina Cocaine-induced pericarditis or myocarditis	Valvular heart disease Aortic stenosis Mitral valve prolapse Hypertrophic cardiomyopathy
Pulmonary	Pulmonary embolus Tension pneumothorax	Pneumothorax Mediastinitis	Pneumonia Pleuritis Tumor Pneumomediastinum
Gastrointestinal	Esophageal rupture (Boerhaave)	Esophageal tear (Mallory-Weiss) Cholecystitis Pancreatitis	Esophageal spasm Esophageal reflux Peptic ulcer Biliary colic
Musculoskeletal			Muscle strain Rib fracture Arthritis Tumor Costochondritis Nonspecific chest wall pain
Neurologic			Spinal root compression Thoracic outlet Herpes zoster Postherpetic neuralgia
Other			Psychologic Hyperventilation

**Figure 18-1.** Initial assessment of critical diagnoses. CXR, chest x-ray; ECG, electrocardiogram; RV, right ventricular.

platelet agents may also be an alternative. Patients with low voltage on the ECG, diffuse ST segment elevation, elevated jugular venous pressure on examination,<sup>8</sup> and signs of shock should undergo prompt bedside cardiac ultrasound.

### Pivotal Findings

The broad and complex nature of chest pain defies application of a simple algorithm. An organized approach to a patient with chest pain is essential, however, to ensure that all causes are evaluated appropriately. The history and physical examination

are key to diagnosis. Information pertinent to the differential diagnosis is obtained by the history, physical examination, and ECG in 80 to 90% of patients.

### History

1. The patient is asked to describe the character of the pain or discomfort. Descriptions such as “squeezing,” “crushing,” or “pressure” lead the emergency physician to suspect a cardiac ischemic syndrome, although cardiac ischemia can also be characterized by nonspecific discomfort, such as “bloating” or “indigestion.” “Tearing” pain that may migrate from the front to back or back to front is the classic description in aortic dissection. “Sharp” or “stabbing” pain is seen more in pulmonary and musculoskeletal diagnoses. Patients complaining of a “burning” or “indigestion” type of pain may initially be thought to have a gastrointestinal etiology, but due to the visceral nature of chest pain, all causes of pain may present with any of the preceding descriptions. Of note, descriptors may vary among ethnic groups, and, for example, “sharp” may mean “severe.”
2. Additional history about the patient’s activity at the onset of pain may be helpful. Pain occurring during exertion suggests an ischemic coronary syndrome, whereas progressive onset of pain at rest suggests acute MI. Pain of sudden onset is more typical with aortic dissection, PE, or pneumothorax. Pain after meals is more indicative of a gastrointestinal cause.
3. The severity of pain is commonly quantified using a 1-to-10 pain scale. Alterations in pain severity are documented at times of onset, peak, present, and after intervention.
4. The location of the discomfort is described. Pain that is localized to a small area is more likely to be somatic versus visceral in origin. Pain localized at the periphery of the



chest is more likely with a pulmonary rather than cardiac etiology. Lower chest or upper abdominal pain may be of cardiac or gastrointestinal origin.

5. Any description of radiation of pain should be noted. Transthoracic pain through to the back should suggest aortic dissection or gastrointestinal causes, especially pancreatitis or posterior ulcer. Inferioposterior myocardial ischemia may also present primarily as thoracic back pain. Radiation to the arms, neck, or jaw increases the likelihood of cardiac ischemia.<sup>9,10</sup> Pain located primarily in the back, especially interscapular back pain that migrates to the base of the neck, suggests aortic dissection.<sup>11</sup>
6. Duration of pain is another important historical factor. Pain that lasts a few seconds is rarely of cardiac origin.<sup>12</sup> Pain that is exertional but lasts for only a few minutes after rest may be a manifestation of cardiac ischemia.<sup>9</sup> Pain that is maximal at onset may be due to aortic dissection.<sup>11</sup> Pain that is not severe and persists over the course of days is less likely to be of serious origin than pain that is severe or has a stuttering or fluctuating course.
7. The clinician should consider aggravating or alleviating factors. Pain that worsens with exertion and improves with rest is more likely related to coronary ischemia.<sup>9</sup> Pain related to meals is more suggestive of a gastrointestinal cause. Pain that worsens with respiration is seen more often with pulmonary, pericardial, and musculoskeletal causes.
8. Other associated symptoms may suggest the visceral nature of the pain (Table 18-2). Diaphoresis should lead to an increased clinical suspicion for a serious or visceral cause. Hemoptysis, a classic PE sign, is rarely seen.<sup>13</sup> Near-syncope and syncope lead to higher likelihood of a cardiovascular cause or PE. Dyspnea is seen in cardiovascular and pulmonary disease. Nausea and vomiting may be seen in cardiovascular and gastrointestinal complaints.
9. A history of prior pain and the diagnosis of that episode can facilitate the diagnostic process, but the physician must be wary of prior presumptive diagnoses that may be misleading. A prior history of cardiac testing, such as stress testing, echocardiography, or angiography, may be useful in determining if the current episode is suggestive of cardiac disease. Similarly, patients with previous spontaneous pneumothorax or PE<sup>14</sup> are at increased risk of recurrence.
10. The presence of risk factors for a particular disease is primarily of value as an epidemiologic marker for large population studies (Box 18-1). In the ED, presence of risk factors in an individual patient without established disease has minimal or no effect on the clinical likelihood (pretest probability) of a specific disease process.

## Physical Examination

Specific findings may be found in a variety of causes (Table 18-3).

## Ancillary Studies

The two most commonly performed studies in patients with chest pain are the chest radiograph and 12-lead ECG (Table 18-4). An ECG should be performed within 10 minutes of arrival in all patients with chest pain in whom myocardial ischemia is a possibility.<sup>15,16</sup> This generally includes all male patients 33 years old and older and female patients over the age of 39 who complain of pain from the umbilicus to the mandible unless a noncardiac cause is readily apparent. Rapid acquisition of the ECG facilitates the diagnosis of acute MI

**Table 18-2 Significant Symptoms of Chest Pain**

SYMPTOM	FINDING	DIAGNOSIS
Pain	Severe, crushing, pressure, substernal, exertional, radiation to jaw, neck, shoulder, arm	Acute MI Coronary ischemia Unstable angina Coronary spasm
	Tearing, severe, radiating to or located in back, maximum at onset, may migrate to upper back or neck	Aortic dissection
	Pleuritic	Esophageal rupture Pneumothorax Cholecystitis Pericarditis Myocarditis
	Indigestion or burning	Acute MI Coronary ischemia Esophageal rupture Unstable angina Coronary spasm Esophageal tear Cholecystitis
Associated syncope/near-syncope		Aortic dissection PE Acute MI Pericarditis Myocarditis
Associated dyspnea (SOB, DOE, PND, orthopnea)		Acute MI Coronary ischemia PE Tension pneumothorax Pneumothorax Unstable angina Pericarditis
Associated hemoptysis		PE
Associated nausea/vomiting		Esophageal rupture Acute MI Coronary ischemia Unstable angina Coronary spasm Esophageal tear Cholecystitis

DOE, dyspnea on exertion; MI, myocardial infarction; PE, Pulmonary embolism; PND, paroxysmal nocturnal dyspnea; SOB, shortness of breath.

and expedites the National Heart, Lung, and Blood Institute's recommended "door to treatment" times from arrival to percutaneous coronary intervention (PCI) or thrombolytic therapy in acute MI. Patients with a new injury pattern on ECG (Table 18-5) or new ischemic ECG changes should have appropriate therapy instituted at this point (Fig. 18-2; see also Chapter 77). An ECG showing right ventricular strain pattern, in the appropriate setting, should raise the clinical suspicion for PE. Diffuse ST segment elevation helps make the diagnosis of pericarditis.

A chest radiograph is performed for patients with a possibly serious cause of chest pain. Pneumothorax is definitively diagnosed at this point. A wide mediastinum or ill-defined aortic knob increases the clinical suspicion for acute aortic dissection. Pleural effusion, subcutaneous air, or mediastinal air-fluid

**Table 18-3 Pivotal Findings in Physical Examination**

SIGN	FINDING	DIAGNOSES	SIGN	FINDING	DIAGNOSES
Appearance	Acute respiratory distress	PE Tension pneumothorax Acute MI Pneumothorax	Cardiovascular examination	Significant difference in upper extremity blood pressures	Aortic dissection
	Diaphoresis	Acute MI Aortic dissection Coronary ischemia PE Esophageal rupture Unstable angina Cholecystitis Perforated peptic ulcer		Narrow pulse pressure New murmur	Pericarditis (with effusion) Acute MI Aortic dissection Coronary ischemia
Vital signs	Hypotension	Tension pneumothorax PE Acute MI Aortic dissection (late) Coronary ischemia Esophageal rupture Pericarditis Myocarditis	Pulmonary examination	S <sub>3</sub> /S <sub>4</sub> gallop	Acute MI Coronary ischemia Pericarditis
	Tachycardia	Acute MI PE Aortic dissection Coronary ischemia Tension pneumothorax Esophageal rupture Coronary spasm Pericarditis Myocarditis Mediastinitis Cholecystitis Esophageal tear (Mallory-Weiss)		Pericardial rub Audible systolic “crunch” on cardiac auscultation (Hamman’s sign) JVD	Esophageal rupture Mediastinitis Acute MI Coronary ischemia Tension pneumothorax PE Pericarditis
	Bradycardia	Acute MI Coronary ischemia Unstable angina	Abdominal examination	Unilateral diminished/absent breath sounds Pleural rub Subcutaneous emphysema	Tension pneumothorax Pneumothorax PE Tension pneumothorax Esophageal rupture Pneumothorax Mediastinitis
	Hypertension	Acute MI Coronary ischemia Aortic dissection (early)		Rales	Acute MI Coronary ischemia Unstable angina
	Fever	PE Esophageal rupture Pericarditis Myocarditis Mediastinitis Cholecystitis	Extremity examination	Epigastric tenderness	Esophageal rupture Esophageal tear Cholecystitis Pancreatitis Pancreatitis
	Hypoxemia	PE Tension pneumothorax Pneumothorax		Left upper quadrant tenderness Right upper quadrant tenderness	Cholecystitis
			Neurologic examination	Unilateral leg swelling, warmth, pain, tenderness, or erythema Focal findings Stroke	PE Aortic dissection Acute MI Coronary ischemia Aortic dissection Coronary spasm

JVD, jugular venous distention; MI, myocardial infarction; PE, pulmonary embolism.

**BOX 18-1 RISK FACTORS ASSOCIATED WITH POTENTIALLY CATASTROPHIC CAUSES OF CHEST PAIN**

Acute coronary syndromes Past or family history of coronary artery disease Age Men >33 years Women >40 years Diabetes mellitus Hypertension Cigarette use/possible passive exposure Elevated cholesterol (LDL)/triglycerides Sedentary lifestyle Obesity Postmenopausal Left ventricular hypertrophy Cocaine abuse Pulmonary embolism Prolonged immobilization Surgery >30 minutes in last 3 mo Prior deep vein thrombosis or pulmonary embolus Pregnancy or recent pregnancy Pelvic or lower extremity trauma Oral contraceptives with cigarette smoking Congestive heart failure Chronic obstructive pulmonary disease Obesity Past medical or family history of hypercoagulability	Aortic dissection Hypertension Congenital disease of the aorta or aortic valve Inflammatory aortic disease Connective tissue disease Pregnancy Arteriosclerosis Cigarette use Pericarditis or myocarditis Infection Autoimmune disease (e.g., systemic lupus erythematosus) Acute rheumatic fever Recent myocardial infarction or cardiac surgery Malignancy Radiation therapy to mediastinum Uremia Drugs Prior pericarditis Pneumothorax Prior pneumothorax Valsalva's maneuver Chronic lung disease Cigarette use
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**Table 18-4 Ancillary Testing of Patients with Chest Pain**

TEST	FINDING	DIAGNOSIS
ECG	New injury	Acute MI
	New ischemia	Aortic dissection Coronary ischemia Coronary spasm
	RV strain	PE
	Diffuse ST segment elevation	Pericarditis
CXR	Pneumothorax with mediastinal shift	Tension pneumothorax
	Wide mediastinum	Aortic dissection
	Pneumothorax	Esophageal rupture Pneumothorax
	Effusion	Esophageal rupture
	Increased cardiac silhouette Pneumomediastinum	Pericarditis Esophageal rupture Mediastinitis
ABG	Hypoxemia, A-a gradient	PE
$\dot{V}/\dot{Q}$ scan or spiral CT	High probability or any positive in patient with high clinical suspicion	PE

ABG, arterial blood gas; CT, computed tomography; ECG, electrocardiogram; MI, myocardial infarction; RV, right ventricular.

level may be seen in esophageal rupture. Increased cardiac silhouette may indicate pericarditis or cardiomyopathy.

Pneumomediastinum is seen with esophageal rupture and mediastinitis. A serum D-dimer assay may help discriminate patients with PE from those with a possible gastrointestinal cause. A low serum D-dimer in a patient without a high pretest

**Table 18-5 Electrocardiogram Findings in Ischemic Chest Pain**

Classic myocardial infarction	ST segment elevation (>1 mm) in contiguous leads; new LBBB; Q waves $\geq 0.04$ sec duration
Subendocardial infarction	T wave inversion or ST segment depression in concordant leads
Unstable angina	Most often normal or nonspecific changes; may see T wave inversion
Pericarditis	Diffuse ST segment elevation; PR segment depression

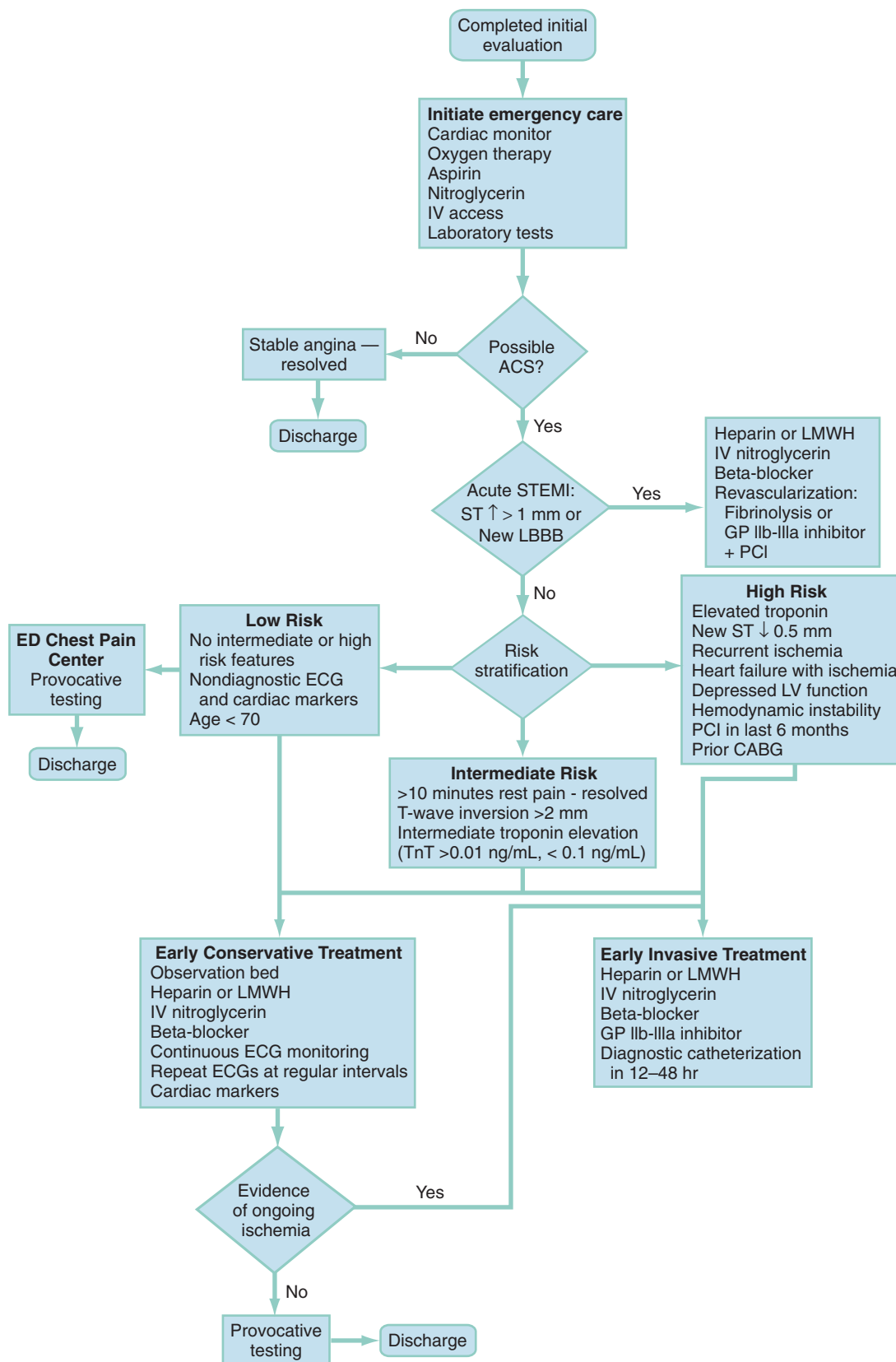
LBBB, left bundle-branch block.

probability of PE effectively excludes the diagnosis.<sup>13,17,18</sup> (see Chapter 87.)

Patients at high pretest probability for PE should undergo diagnostic imaging (multidetector computed tomography [CT], or, less commonly, pulmonary angiography or a ventilation-perfusion lung scan).<sup>19</sup> High pretest probability warrants initiation of anticoagulation (heparin or low-molecular-weight heparin) therapy in the ED before the imaging study, in the absence of a contraindication.

Patients with suspected thoracic aortic dissection may be evaluated by CT angiography, transesophageal echocardiography, or magnetic resonance imaging. Selection of imaging modality depends on patient status and availability of the testing equipment.<sup>20</sup>

CT with a 64 or higher detector scanner has the potential to rule out all of the life-threatening causes of chest pain. Although the “triple rule out” of ACS, PE, and thoracic dissection are the causes most commonly discussed, pneumothorax, mediastinitis, and pericardial effusions are also diagnosed with CT.<sup>21,22</sup>



**Figure 18-2.** Clinical guidelines for emergency department management of chest pain of myocardial ischemic origin. ACS, acute coronary syndrome; CABG, coronary artery bypass graft; ECG, electrocardiogram; GP, glycoprotein; IV, intravenous; LBBB, left bundle-branch block; LMWH, low-molecular-weight heparin; LV, left ventricular; MI, myocardial infarction; PCI, percutaneous coronary intervention; ST, echocardiographic peak; STEMI, ST segment elevation myocardial infarction; TnT, troponin T. (Adapted from Gibler WB, Cannon CP, Blonikals AL, et al: Practical implementation of the guidelines for unstable angina/non-ST-segment elevation myocardial infarction in the emergency department: A scientific statement from the American Heart Association Council on Clinical Cardiology (Subcommittee on Acute Cardiac Care), Council on Cardiovascular Nursing, and Quality of Care and Outcomes Research Interdisciplinary Working Group, in Collaboration with the Society of Chest Pain Centers. *Circulation* 111:2699, 2005.)



**Table 18-6** Causes and Differentiation of Potentially Catastrophic Illness Presenting with Central Chest Pain or Discomfort

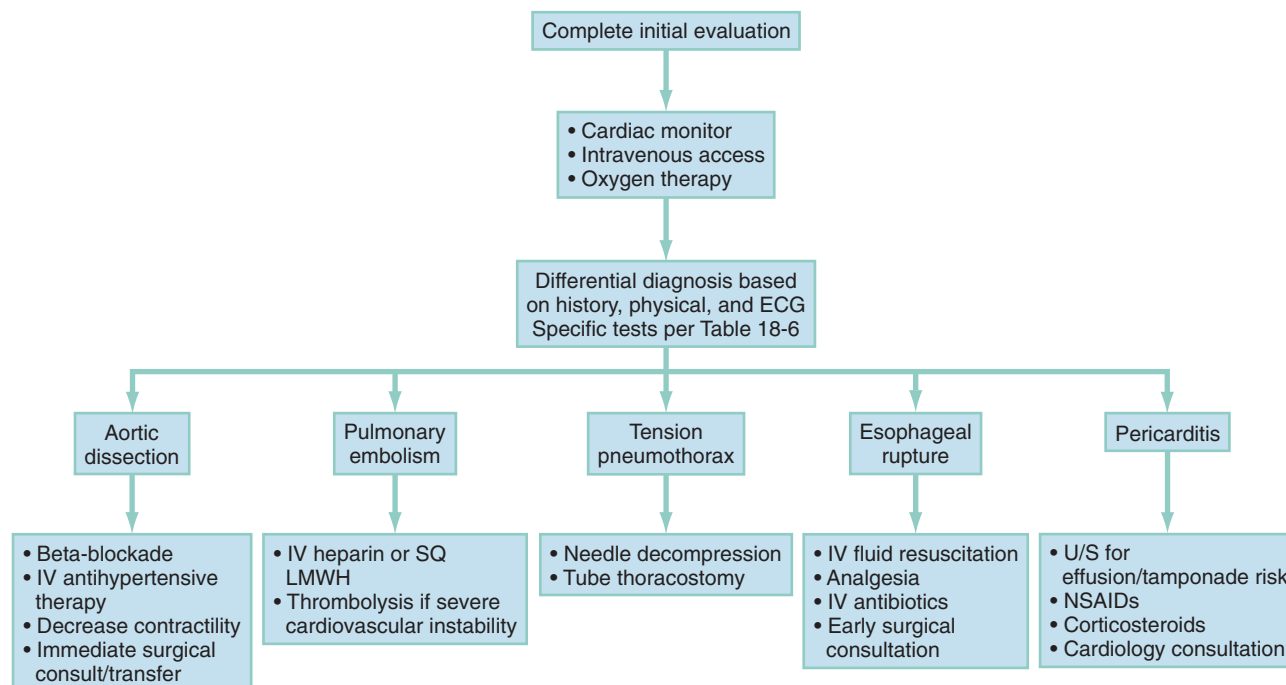
	PAIN HISTORY	ASSOCIATED SYMPTOMS	SUPPORTING HISTORY	PREVALENCE IN EMERGENCY DEPARTMENT	PHYSICAL EXAMINATION	USEFUL TESTS	ATYPICAL OR ADDITIONAL ASPECTS
Myocardial Infarction	Discomfort is usually moderately severe to severe and rapid in onset. May be more “pressure” than pain. Usually retrosternal, may radiate to neck, jaw, both arms, upper back, epigastrium, and sides of chest (left more than right). Lasts more than 15–30 min and is unrelieved by NTG	Diaphoresis, nausea, vomiting, dyspnea	May be precipitated by emotional stress or exertion. Often comes on at rest. May come on in early awakening period. Prodromal pain pattern often elicited. Previous history of MI or angina. Age >40 years, positive risk factors, and male sex increase possibility	Common	Patients are anxious and uncomfortable. Blood pressure usually is elevated, but normotension and hypotension are seen. The heart rate is usually mildly increased, but bradycardia can be seen. Patients may be diaphoretic and show peripheral poor perfusion. There are no findings for MI, although S <sub>3</sub> and S <sub>4</sub> heart sounds and new murmur are supportive	ECG changes (new Q waves or ST segment–T wave changes) occur in 80% of patients. CK-MB and troponins are helpful if elevated, but may be normal	Pain may present as “indigestion” or “unable to describe.” Other atypical presentations include altered mental status, stroke, angina pattern without extended pain, severe fatigue, syncope. Elderly may present with weakness, congestive heart failure, or chest tightness. 25% of nonfatal MIs are unrecognized by patient. The pain may have resolved by the time of evaluation
Unstable Angina	Changes in pattern of preexisting angina with more severe, prolonged, or frequent pain (crescendo angina). Pain usually lasts >10 min. Angina at rest lasting 15–20 min or new-onset angina (duration <2 mo) with minimal exertion. Pattern of pain change important in gauging risk for AMI. Unpredictable responses to NTG and rest	Often minimal. May have mild diaphoresis, nausea, dyspnea with pain. Increasing pattern of dyspnea on exertion	Not clearly related to precipitating factors. May be a decrease in amount of physical activity that initiates pain. Previous history of MI or angina. Over 40 years old, presence of risk factors, and male sex increase probability	Common	Nonspecific findings of a transient nature, may have similar cardiac findings as in MI, especially intermittent diaphoresis	Often no ECG or enzyme changes. Variant angina (Prinzmetal’s) has episodic pain, at rest, often severe, with prominent ST segment elevation	May be pain-free at presentation. Full history is essential. Fewer than 15% of patients hospitalized for unstable angina go on to acute MI. May respond to NTG. May manifest similarly to non–Q wave infarction

<b>Aortic Dissection</b>	90% of patients have rapid-onset severe chest pain that is maximal at beginning. Radiates anteriorly in chest to the back interscapular area or into abdomen. Pain often has a “tearing” sensation, and may migrate	Neurologic complications of stroke, peripheral neuropathy, paresis or paraplegia, abdominal and extremity ischemia possible	Median age 59 years. History of hypertension in 70–90% of patients. 3:1 ratio males to females. Marfan’s syndrome and congenital bicuspid aortic valves have increased incidence	Rare	Often poorly perfused peripherally but with elevated BP. In 50–60% of cases, there is asymmetrical decrease or absence of peripheral pulses. 50% of proximal dissections cause aortic insufficiency. Other vascular occlusions: coronary (1–2%), mesentery, renal, spinal cord. New-onset pericardial friction rub or aortic insufficiency murmur supportive of diagnosis	ECG usually shows left ventricular hypertrophy, nonspecific changes. Chest film shows abnormal aortic silhouette (90%). Aortic angiography has diagnostic accuracy of 95–99%. Transesophageal echocardiogram, CT, MRI most useful in screening	Rare for patient to present pain-free. May present with neurologic complications. Physical examination findings may be minimal. Dissection into coronary arteries can mimic MI. Ascending aortic aneurysms are more often approached surgically. Descending are generally managed medically
<b>Pulmonary Embolism</b>	Pain is more often lateral-pleuritic. Central pain is more consistent with massive embolus. Abrupt in onset and maximal at beginning. May be episodic or intermittent	Dyspnea and apprehension play a prominent role, often more than pain. Cough accompanies about half the cases  Hemoptysis occurs in <20%. Anginal-like pain may occur in 5%	Often some period of immobilization has occurred, e.g., postoperative. Pregnancy, oral contraceptives, heart disease, and cancer are all risk factors. Previous DVT or PE is the greatest risk factor	Uncommon in ambulatory patients, but common in departments with high volumes of elderly or medically complex patients	Patients are anxious and often have a respiratory rate >16/min. Tachycardia, inspiratory rales, and an increased pulmonary second sound are common. Fever, phlebitis, and diaphoresis are seen in 30–40% of patients. Wheezes and peripheral cyanosis are less common	Arterial blood gases show $PO_2$ < 80 mm Hg in 90%. Widened A-a gradient is helpful. Chest film is usually normal, although 40% show some volume loss, oligemia, or signs of consolidation due to pulmonary infarction. Lung perfusion scan rules out, if truly negative	Patients may present with dyspnea with or without bronchospasm. Acute mortality rate is 10%. Emboli usually from lower extremities above knee, prostate/pelvis venous plexus, right heart. May be subtle cause of COPD exacerbation

**Table 18-6** Causes and Differentiation of Potentially Catastrophic Illness Presenting with Central Chest Pain or Discomfort—cont'd

	PAIN HISTORY	ASSOCIATED SYMPTOMS	SUPPORTING HISTORY	PREVALENCE IN EMERGENCY DEPARTMENT	PHYSICAL EXAMINATION	USEFUL TESTS	ATYPICAL OR ADDITIONAL ASPECTS
Pneumothorax	Pain is usually acute and maximal at onset. Most often lateral-pleuritic, but central pain can occur in large pneumothorax	Dyspnea has a prominent role. Hypotension and altered mental states occur in tension pneumothorax	Chest trauma, previous episode, or asthenic body type	Infrequent	Decreased breath sounds, increased resonance on percussion. Elevated pressure in neck veins occurs in tension pneumothorax	Chest film definitive. Inspiratory and expiratory films may enhance contrast between air and lung parenchyma. Tension pneumothorax should be diagnosed on physical examination	May be subtle in COPD, asthma, cystic fibrosis. Can be complicated by pneumomediastinum
Esophageal Rupture	Pain usually is preceded by vomiting and is abrupt in onset. Pain is persistent and unrelieved, localized along the esophagus, and increased by swallowing and neck flexion	Diaphoresis, dyspnea (late), shock	Older individual with known gastrointestinal problems. History of violent emesis, foreign body, caustic ingestion, blunt trauma, alcoholism, esophageal disease	Rare	Signs of lung consolidation, subcutaneous emphysema may be present	Chest film usually has mediastinal air, a left-sided pleural effusion, pneumothorax, or a widened mediastinum. pH of pleural effusion is <6.0. Diagnosis supported by water-soluble contrast esophagram or esophagoscopy	Patient may present in shock state. This entity often considered late in differential diagnostic process
Pericarditis	Dull, aching recurrent pain unrelated to exercises or meals. Or it may be a sharp, stabbing, pleuritic-type pain that does not change with chest wall motion. May be severe. Not relieved by NTG	Dyspnea, diaphoresis	Pain is often worse when supine, but improves sitting up. Often preceded by viral illness or underlying disease (SLE or uremia)	Rare	Friction rub may be heard, often fleeting, position-dependent (50% of patients).	ECG pattern typical for ST segment elevation across the precordial leads. Erythrocyte sedimentation rate may be elevated	More common in 20- to 50-year-olds. May have associated tachycardias, ventricular dysrhythmias. Idiopathic most common (80%). Treated with aspirin, NSAID

AMI, acute myocardial infarction; CK-MB, an isoform of creatine kinase; COPD, chronic obstructive pulmonary disease; CT, computed tomography; DVT, deep vein thrombosis; ECG, electrocardiogram; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug; NTG, nitroglycerin; PE, pulmonary embolus; SLE, systemic lupus erythematosus.



**Figure 18-3.** Clinical guidelines for emergency department management of chest pain from potentially catastrophic nonmyocardial origins. ECG, electrocardiogram; IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs; SQ, subcutaneous; LMWH, low-molecular-weight heparin; U/S, ultrasound.

Laboratory testing is useful in the evaluation of ACS. Creatine kinase (CK) is associated with multiple false-positive results and has no use in the evaluation of unstable angina. CK-MB, an isoform of CK, is more specific for cardiac ischemia. Evaluating this enzyme produces fewer false-positive results, and peak sensitivity approaches 98%. Sensitivity at 4 hours is, however, only about 60%. CK-MB isoforms improve sensitivity at 4 hours to 80%, approaching 93% at 6 hours. The current universal definition of MI places CK and CK-MB in a secondary role to troponins.<sup>23</sup>

Troponins (I and T), when elevated, identify patients with ACS who have the highest risk for an adverse outcome.<sup>23,24</sup> Sensitivity for acute MI at 4 hours is 60%, rising to nearly 100% by 12 hours.<sup>25,26</sup> Elevated troponin in the correct clinical setting is synonymous with acute MI and is embedded in the universal definition of MI.

## ■ DIAGNOSTIC TABLE

After the patient is stabilized and assessment has been completed, the findings are matched to the classic and atypical patterns of the seven potentially critical diseases causing chest pain. This matching process is continual while evaluating the patient and monitoring the response to therapy. Any inconsistency in findings with the primary working diagnoses requires

a rapid review of the pivotal findings and the potential diagnoses (Table 18-6).

## ■ MANAGEMENT AND DISPOSITION

The management of ACS is discussed in Chapter 76. Figure 18-3 outlines the approach to treatment of critical noncardiac diagnoses. Patients with critical diagnoses generally are admitted to the intensive care unit. Patients with emergent diagnoses typically are admitted to the hospital, most often on telemetry units. Patients with nonemergent diagnoses are most frequently treated as outpatients. Hospitalization is required in certain circumstances, particularly when patients have other comorbid conditions.

Frequently, no definitive diagnosis is established. Any patient with almost any type of chest pain may be having coronary ischemia, PE, or aortic dissection. When a clear pattern does not emerge to allow the emergency physician to make an alternative diagnosis confidently, continued evaluation, hospitalization, or observation admission may be the best course.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*



## CHAPTER 19 Syncope

Robert A. De Lorenzo

### ■ PERSPECTIVE

*Syncope* is the sudden transient loss of consciousness with a loss of postural tone. It is a common presenting complaint in the emergency department (ED). Despite improved understanding of risk and outcomes, consensus on diagnostic approach and disposition remains elusive. This is in part due to its varied causes and lack of definitive diagnostic studies, and in part because of confusion and lack of standard terminology to describe the disorder.<sup>1</sup> Diagnostic accuracy relies largely on the synthesis of patient risk factors and reported symptoms, with limited reliance on the physical examination and ancillary testing.

### Epidemiology

The prevalence of syncope in the general population is approximately 19%.<sup>2</sup> Patients present to the ED at a rate of 2.8 visits per 1000 population, which accounts for 0.8% of ED visits.<sup>2,3</sup> Approximately 32% of these patients are admitted, and syncope accounts for 1 to 6% of all hospitalized patients.<sup>2,4</sup> Persons aged 65 years and older account for 80% of such admissions.<sup>5</sup> In the pediatric population, 15% experience at least one episode of syncope.<sup>6</sup>

Risk factors for syncope include cerebrovascular disease, cardiac medications, and hypertension.<sup>7</sup> Most causes of syncope are benign and have favorable outcomes. Patients with pre-existing cardiovascular disease and syncope from any cause are at the greatest short- and long-term risk of mortality.<sup>4,8</sup> Syncope from cardiovascular causes carries a long-term hazard ratio of death of 2.41 when adjusted for age and sex.<sup>8</sup> In contrast, there is no increased risk of cardiovascular morbidity or mortality associated with syncope from neurocardiogenic, orthostatic, and medication-related syncope.<sup>8</sup> Recurrence of syncope may be as high as 50% and is not correlated with age or sex.<sup>2</sup>

Benign causes of syncope predominate in adolescents and young adults. Approximately 30% of athletes dying during exercise, however, have had a prior episode of syncope as a sentinel event.<sup>9</sup> Prospective outcome studies in children are lacking, but most reports suggest that mortality rates are very low.<sup>9</sup> Significant trauma may result from syncope and can contribute to increased risk of mortality and morbidity, particularly in the elderly.<sup>10,11</sup> The overall U.S. medical cost of syncope is estimated at \$2.4 billion annually.<sup>12</sup>

### Pathophysiology

The final common pathway resulting in syncope is dysfunction of either both cerebral hemispheres or the brainstem (reticular activating system), usually from acute hypoperfusion. Reduced blood flow may be regional (cerebral vasoconstriction) or systemic (hypotension).<sup>13</sup> Loss of consciousness results in loss of postural tone, with the resulting syncopal episode. Less severe derangements may result in sensations of presyncope or light-headedness. In this fashion, presyncope and syncope may be considered on a continuum with shared etiologies and mechanisms. By definition, syncope is transient; therefore, the cause of central nervous system (CNS) dysfunction must likewise be transient.<sup>8,14</sup> Persistent causes of significant CNS dysfunction result in coma or depressed consciousness (See Chapter 14).

Hypoperfusion resulting in approximately 35% or more reduction in cerebral blood flow usually produces unconsciousness, and any mechanism that adversely affects the components of perfusion (cardiac output, systemic vascular resistance, blood volume, regional vascular resistance) can cause or contribute to syncope. Other mechanisms of CNS dysfunction resulting in syncope include hypoglycemia, toxins, metabolic abnormalities, failure of autoregulation, and primary neurologic derangements.

### ■ DIAGNOSTIC APPROACH

#### Differential Considerations

The potential causes of syncope are numerous and can be categorized according to their primary mechanism (**Box 19-1**). The first differential diagnostic consideration is to distinguish syncope from other causes of an apparent sudden loss of consciousness, especially seizure and uncommon disorders such as cataplexy. When syncope has been established as the working diagnosis, the life-threatening causes, primarily cardiovascular in origin, are considered first. The principal serious causes of syncope are dysrhythmias and myocardial ischemia.<sup>15</sup> Cerebrovascular disease, principally subarachnoid hemorrhage, is less frequently encountered, but equally serious. Toxic-metabolic abnormalities may induce syncope through alterations in blood pressure or cardiac rhythm. Structural cardiac lesions, such as critical aortic stenosis, and sudden

**BOX 19-1 CAUSES OF SYNCOPE****Focal Hypoperfusion of CNS Structures**

Cerebrovascular disease  
Hyperventilation  
Subclavian steal  
Subarachnoid hemorrhage  
Basilar artery migraine  
Cerebral syncope

**Systemic Hypoperfusion Resulting in CNS Dysfunction**

Outflow obstruction  
  Mitral, aortic, or pulmonic stenosis  
  Hypertrophic cardiomyopathy  
  Atrial myxoma  
  Pulmonary embolism  
  Pulmonary hypertension  
  Cardiac tamponade  
  Congenital heart disease  
Reduced cardiac output  
  Tachycardia  
    Supraventricular tachycardia  
    Ventricular tachycardia  
    Ventricular fibrillation  
    Wolff-Parkinson-White syndrome  
    Torsades de pointes  
  Bradycardia  
    Sinus node disease  
    Second-degree and third-degree A-V block  
    Prolonged Q-T syndrome  
    Pacemaker malfunction  
    Implanted cardioverter-defibrillator malfunction  
Other cardiovascular disease  
  Aortic dissection  
  Myocardial infarction  
  Cardiomyopathy

Vasomotor—neurally mediated (reflex vasodepressor)  
  Neurocardiogenic (vasovagal)  
  Emotion  
  Pain  
  Situational  
Carotid sinus sensitivity  
  Necktie syncope  
  Shaving syncope  
Miscellaneous reflex  
  Tussive, sneeze  
  Exercise/postexercise  
  Gastrointestinal—swallowing, vomiting, defecation  
  Postmicturition  
  Elevated intrathoracic pressure (weightlifting)  
Other causes of hypoperfusion  
  Orthostatic hypotension—volume depletion  
  Anemia  
  Drug-induced

**CNS Dysfunction with Normal Cerebral Perfusion**

Hypoglycemia  
Hypoxemia—asphyxiation  
Seizure  
Narcolepsy  
Psychogenic  
  Anxiety disorder  
  Conversion disorder  
  Somatization disorder  
  Panic disorder  
  Breath-holding spells  
Toxic  
  Drugs  
  Carbon monoxide  
  Other agents  
  Undetermined causes

CNS, central nervous system.

interruption of right ventricular outflow by pulmonary embolism can also cause sudden loss of consciousness.<sup>14</sup> Dissection of the thoracic aorta rarely manifests primarily as syncope, but is potentially catastrophic.<sup>15</sup>

**Pivotal Findings**

The majority of cases of syncope arise from benign causes, so the evaluation is largely focused on excluding serious pathology. Young, healthy patients with clearly benign syncope may require no formal diagnostic evaluation other than a thorough history and physical examination.<sup>16,17</sup> The yield of an electrocardiogram (ECG) is generally low; however, it is recommended because it is noninvasive and relatively inexpensive.<sup>18</sup> The clinical examination alone can suggest the diagnosis in 45% of cases.<sup>19</sup> Nevertheless, up to 50% of patients may not have a clear diagnosis for their syncope after an initial evaluation in the ED.<sup>19</sup>

**Symptoms**

Symptoms can often suggest the diagnosis, although the value of the history diminishes in older patients.<sup>20</sup> The patient is asked to describe the *character* of the syncopal event.<sup>14</sup> Witnesses may be able to supplement and corroborate the patient's incomplete recall, and that history should be solicited. Key characteristics include the rate of onset (gradual or abrupt),

position on symptom onset (e.g., standing, sitting, or supine), and duration and rate of recovery. Abrupt onset, occurrence while sitting or supine, and duration of more than a few seconds are usually ascribed to serious, often cardiac, causes of syncope.<sup>15</sup> Similarly, incomplete or near-syncope may be less serious, but at least one study suggests that onset associated with a prodrome or presyncope may herald cardiac origin.<sup>20</sup> The diagnostic approach to presyncope, however, is the same as for syncope.

Additional history regarding the events *preceding* the syncope is helpful.<sup>14</sup> Occurrence during significant exertion suggests outflow obstruction, whereas after exercise or a prolonged exposure to heat stress suggests orthostasis. The myriad mechanisms that may mediate a neurocardiogenic response (e.g., vagal stimulation), including significant emotional events, micturition, eating, bowel movements, emesis, and movement or manipulation of the neck causing stimulation of the carotid sinus, must be addressed. Occurrence in supine position or the presence of acute palpitations is relatively specific for syncope of cardiac origin.<sup>20</sup> Seizures may be preceded by an aura.

Events *during* the syncopal episode do not usually clarify the cause.<sup>14</sup> Tonic-clonic movements, related to inadequate cerebral perfusion, can occur in any form of syncope, including benign neurocardiogenic syncope, and must be differentiated from the prolonged activity with subsequent postictal depression of consciousness seen in seizure disorders (see Chapter

15). Trauma from a fall or other mechanism may mask the underlying syncope that caused the incident.<sup>11</sup>

The postsyncope events should be queried. Symptoms consistent with a postictal state are characteristic of seizures. Initial vital signs and cardiac monitoring by nonhospital medical providers may provide clues to primary cardiac dysrhythmias.

*Associated symptoms* can offer potentially important clues.<sup>15</sup> Chest pain or shortness of breath can suggest myocardial ischemia, aortic dissection, or pulmonary embolism. Diaphoresis and light-headedness are nonspecific, but if prominent and accompanied by a graying of vision may suggest orthostasis or vasovagal causes. Tongue biting and incontinence of urine or stool suggest seizures.

The *past medical history* is critical in stratifying risk.<sup>4,20</sup> Prior coronary artery or cerebrovascular disease, diabetes, hypertension, or other significant chronic disease increases the risk of mortality after syncope.<sup>7</sup>

Certain *medications* are well established to be associated with syncope (Box 19-2). QT interval-prolonging agents, beta-blockers, insulin, and oral hypoglycemics, in particular, deserve attention because of the likelihood of repeated syncope without careful medication monitoring.<sup>7</sup>

## Signs

The physical examination focuses primarily on the elements affecting the cardiovascular and neurologic systems.<sup>20</sup> Specific findings are detailed in Table 19-1. Signs of orthostasis should be sought in all cases where this mechanism is suggested.<sup>21</sup> Carotid massage to detect carotid sinus hypersensitivity is both safe and occasionally revealing; it is probably underutilized. Rectal examination for gross blood or melena is recommended if anemia or gastrointestinal bleed is possible.

## Ancillary Studies

The chief diagnostic adjunct in evaluating syncope is the 12-lead ECG (Table 19-2). It is warranted in all cases of syncope

except in young, otherwise healthy patients with a clear history and setting for benign neurocardiogenic (vasovagal) syncope.<sup>16,17</sup> Although the yield is low, the ECG is noninvasive and relatively inexpensive, and may be revealing.<sup>18</sup> New ischemic ECG changes are indicative of acute coronary ischemia and

### BOX 19-2

### MEDICATIONS THAT MAY INDUCE SYNCOPE

Cardiovascular  
 β-Blockers  
 Vasodilators (α-blockers, calcium channel blockers, nitrates, hydralazine, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, phenothiazines, phosphodiesterase inhibitors)  
 Diuretics  
 Central antihypertensives (clonidine, methyldopa)  
 Other antihypertensives (guanethidine)  
 Q-T prolonging (amiodarone, disopyramide, flecainide, procainamide, quinidine, sotalol)  
 Other antidysrhythmics  
 Psychoactive  
 Anticonvulsants (carbamazepine, phenytoin)  
 Antiparkinsonian agents  
 Central nervous system depressants (barbiturates, benzodiazepines)  
 Monoamine oxidase inhibitors  
 Antidepressants  
 Narcotic analgesics  
 Sedating and nonsedating antihistamines  
 Cholinesterase inhibitors (donepezil, tacrine, galantamine)  
 Drugs with other mechanisms  
 Drugs of abuse (cannabis, cocaine, alcohol, heroin)  
 Digitalis  
 Insulin and oral hypoglycemics  
 Neuropathic agents (vincristine)  
 Nonsteroidal anti-inflammatory drugs  
 Bromocriptine

**Table 19-1 Directed Physical Examination in Syncope**

SYSTEM	PIVOTAL FINDING	SIGNIFICANCE
Vital signs	Pulse rate and rhythm	Tachycardia, bradycardia, other dysrhythmias
	Respiratory rate and depth	Tachypnea suggests hypoxia, hyperventilation, or pulmonary embolus
	Blood pressure	Shock may cause decreased cerebral perfusion; hypovolemia or medication use may lead to orthostasis
Skin	Temperature	Fever from sepsis may cause volume depletion and orthostasis
	Color, diaphoresis	Signs of decreased organ perfusion
	HEENT	Signs of trauma
HEENT	Tenderness and deformity	Increased intracranial pressure, head injury
	Papilledema	Ketones from ketoacidosis
	Breath	
Neck	Bruits	Identify presence of cerebrovascular disease
	Jugular venous distention	Infection, left heart failure from myocardial ischemia, tamponade, pulmonary embolism
Lungs	Breath sounds, crackles, wheezes	Infection, left heart failure from myocardial ischemia, rarely pulmonary embolism
Heart	Systolic murmur	Aortic stenosis, hypertrophic cardiomyopathy
	Rub	Pericarditis, tamponade
Abdomen	Pulsatile mass	Abdominal aortic aneurysm
Rectum	Stool for gross blood or melena	Anemia, GI bleed
Pelvis	Uterine bleeding, adnexal tenderness	Anemia, ectopic pregnancy, hypovolemia
Extremities	Pulse equality in upper extremities	Subclavian steal, thoracic aortic dissection
Neurologic	Mental status, focal neurologic findings	Seizure, stroke, or other primary neurologic disease

HEENT, head, eyes, ears, nose, and throat.

**Table 19-2 Ancillary Studies in Syncope**

STUDY	INDICATION
12-Lead ECG/limb-lead ECG monitoring	Cardiac dysrhythmia, ischemia, cardiomyopathy
Orthostatic vital signs	Orthostatic hypotension or bradycardia
Hemogram	Anemia
Electrolytes, serum	Metabolic abnormality, especially hyponatremia, hyper- or hypokalemia
Glucose, serum or blood	Hypoglycemia
D-dimer, serum	Pulmonary embolism
Cardiac enzymes, serum	Myocardial infarction
$\beta$ -hCG	Pregnancy
Toxicologic screen	Drug-related syncope
Arterial blood gas	Acid-base disturbance
Chest x-ray	Thoracic aortic dissection
Cranial CT/MRI	New-onset or focal seizure, trauma, intracranial hemorrhage
Echocardiogram	Cardiac outflow obstruction, tamponade, thoracic dissection
Ventilation-perfusion scan	Pulmonary embolism
CT pulmonary angiogram	Pulmonary embolism, thoracic aortic dissection
Abdominal ultrasound /CT	Abdominal aortic aneurysm
Pelvic ultrasound	Ectopic pregnancy
<b>Tests Usually Performed as Part of an Inpatient or Outpatient Evaluation</b>	
Holter or loop ECG	Dysrhythmia
Echocardiogram	Cardiomyopathy, valvular disease
Exercise/ $^{99m}\text{Tc}$ sestamibi ECG	Myocardial ischemia
Electrophysiologic study	Dysrhythmia
Carotid ultrasound	Stroke, TIA
Head-up tilt-table test	Orthostatic hypotension
Electroencephalogram	Seizures

CT, computed tomography; ECG, electrocardiogram; hCG, human chorionic gonadotropin; MRI, magnetic resonance imaging; TIA, transient ischemic attack.

warrant appropriate therapy. Dysrhythmias and shortened PR or prolonged QT intervals may be identified on the 12-lead ECG. A right bundle branch block in association with ST elevation in leads  $V_1$  through  $V_3$  suggests Brugada's syndrome.<sup>22</sup> Unanticipated cardiac hypertrophy may be revealed. Continuous limb-lead ECG monitoring in the ED may also identify transient dysrhythmias. An ECG showing right ventricular strain pattern may suggest pulmonary embolism, whereas diffuse ST elevation or electrical alternans help diagnose pericarditis associated with pericardial tamponade.

Routine blood, serum, and urine studies have limited utility in the evaluation of syncope and are generally unrewarding.<sup>23</sup> When suggested by the history and physical examination, however, selective use of the hemogram, serum electrolytes and glucose, urine drug screen, and pregnancy test may identify or exclude some uncommon causes of syncope. Radiographic studies including cranial computed tomography offer limited yield in most cases of syncope, and unless abnormalities are identified on neurological examination, are not routinely indicated.<sup>24</sup>

In otherwise healthy patients for whom a benign dysrhythmia, such as rapid supraventricular tachycardia or atrial fibrillation, is suggested, Holter or preferably event ECG monitoring may be helpful. In patients with significant underlying cardiac disease or when a significant dysrhythmia is a possible cause of the syncope, echocardiography, continuous monitoring, or cardiovascular stress-testing may be helpful in the inpatient or ED observation unit setting. Depending on the results of initial evaluation, electrophysiologic studies, or magnetic resonance imaging may be indicated. Electroencephalography has a low yield unless seizure is suggested. Tilt table testing, although infrequently used in the United States, may have diagnostic value in elderly patients and children in whom chronic orthostatic hypotension is possible.

**Table 19-3 Critical Diagnoses to Consider in Syncope**

Myocardial infarction
Life-threatening dysrhythmias
Thoracic aortic dissection
Critical aortic stenosis
Hypertrophic cardiomyopathy
Pericardial tamponade
Abdominal aortic aneurysm
Pulmonary embolism
Subarachnoid hemorrhage
Stroke
Toxic-metabolic derangements
Severe hypovolemia or hemorrhage

Although not technically an ancillary study, formal psychiatric evaluation deserves mention as a potential diagnostic tool in syncope.<sup>25</sup> In patients with compatible symptoms and signs or negative medical evaluation and recurrent episodes of syncope, psychiatric evaluation may be revealing.

## ■ DIAGNOSTIC ALGORITHM

The critical diagnoses to consider are listed in [Table 19-3](#).

The emergent causes of syncope are protean and are included in [Box 19-1](#). Many other causes such as neurocardiogenic and reflex-mediated syncope have benign mechanisms.

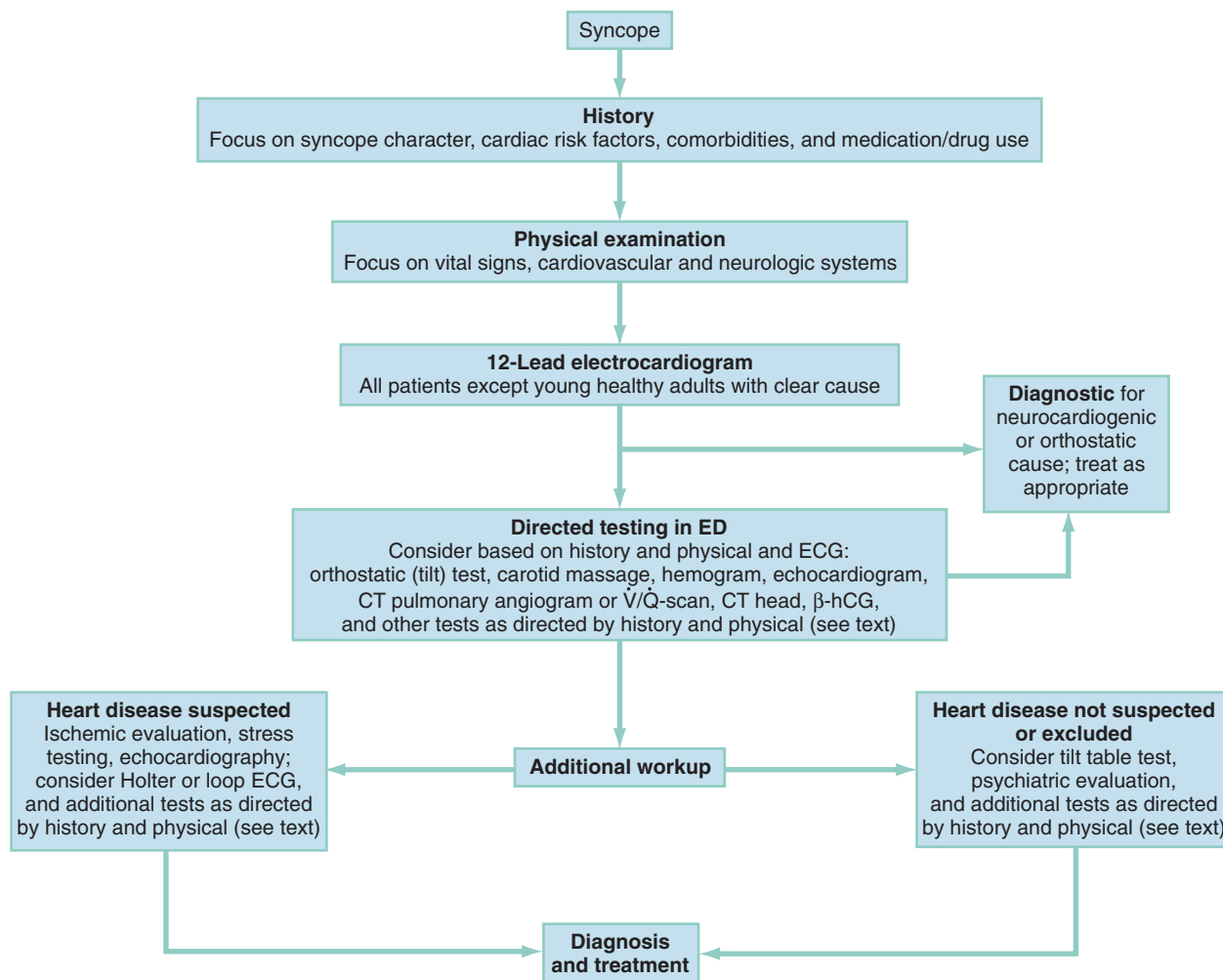
After stabilization and assessment, the clinical features coupled with onset and recovery suggest the cause ([Table 19-4](#)). A logical approach to the history, physical examination, and diagnostic testing is depicted in [Figure 19-1](#). The emphasis is on risk stratification since short-term mortality risk in syncope



**Table 19-4 Clinical Features of Common and Serious Causes of Syncope**

CAUSE	ONSET AND RECOVERY	FEATURES
Dysrhythmia	Abrupt onset; rapid recovery	Past cardiac history, risk factors for CAD more common in elderly; implanted pacemaker or cardioverter-defibrillator
Cardiac outflow obstruction	Exertion causes abrupt symptoms; rapid recovery with rest	Murmurs not always audible; mechanical valves warrant close monitoring
Myocardial infarction	Exertion or at rest; recovery often incomplete with chest pain persisting	Past cardiac history, risk factors for CAD; chest pain and shortness of breath common but frequently absent in diabetics and the elderly
Pulmonary embolism	Abrupt onset; recovery often incomplete with dyspnea persisting	Chest pain, dyspnea, hypercoagulable state, DVT, pregnancy
Thoracic aortic dissection	Spontaneous; recovery often incomplete with chest or upper back pain persisting	Tearing chest pain; associated with hypertension, Marfan syndrome, cystic medial necrosis
Abdominal aortic aneurysm	Spontaneous onset; recovery often incomplete with abdominal pain persisting	Abdominal or low back pain; associated with peripheral vascular disease
Pericardial tamponade	Penetrating chest trauma or thoracic cancers	Beck's triad of hypotension, JVD, muffled heart sounds
Anomalous left coronary artery	Onset with exercise, Valsalva maneuver	Left coronary artery arises from pulmonary artery; usually detected in childhood
Subarachnoid hemorrhage	Rapid onset; sentinel event may resolve	Focal neurologic findings; "thunderclap" worst headache; nuchal rigidity
Vertebrobasilar insufficiency	Posture change or neck movement	Vertigo, nausea, dysphagia, dysarthria, blurry vision common associated symptoms
Hypovolemia	Bleeding, emesis, heat stress, dehydration; gradual onset	Orthostatic hypotension
Anemia	Bleeding, often occult or gradual from menses or gastrointestinal sources; iron deficiency or decreased red blood cell production	Orthostatic hypotension commonly associated
Hypoglycemia	Gradual onset; incomplete spontaneous recovery common	Diabetes, ingestion or injection of hypoglycemics or insulin; diaphoresis, anxiety, jitteriness
Hypoxemia	Usually gradual onset; spontaneous recovery if asphyxiating circumstance is reversed	Carbon monoxide, natural gas, sewer gas, bleach-ammonia mix
Subdural hematoma	Onset with or after trauma (which may be trivial in high-risk patients)	Elderly, alcoholics, patients on anticoagulants at greater risk
Air embolus	Diving	Hyperbaric oxygen a key treatment
Pulmonary hypertension	Associated with myocardial infarction or pulmonary embolus	Risk factors for myocardial infarction or pulmonary embolism
Drug syncope	Medication associated with syncope	Consider illicit and alternative drug use; elderly at risk for polypharmacy and drug interactions
Ruptured ectopic pregnancy	Patient often unaware of pregnancy	Abdominal pain, abnormal tenderness; positive $\beta$ -hCG test
Seizure	Abrupt or with aura; postictal state common	Past history common
Carotid sinus sensitivity	Carotid sinus sensitivity; rapid onset and recovery	Shaving, necktie, sudden neck movement; carotid massage may provoke symptoms
Reflex syncope	Gastrointestinal, genitourinary, or thoracic stimulation	Urination, defecation, cough, eating, swallowing, weightlifting
Neurocardiogenic (vasovagal)	Emotion, pain are common triggers; upright posture; gradual onset; rapid recovery once supine	Prodrome of light-headedness, graying or blurring of vision, nausea, sweats common
Hyperventilation	Emotion, pain; gradual onset; patient often unaware of rapid respirations	Perioral tingling, carpopedal spasms, extremity numbness
Narcolepsy	Often spontaneous	Known history
Basilar artery migraine	Specific triggers often known to patient	Visual prodrome often absent; more common in young women; vertigo and nausea common
Trigeminal or glossopharyngeal neuralgia	Sudden onset; specific triggers often known to patient	Lancinating pain in characteristic location
Subclavian steal	Moving affected arm	Thoracic outlet syndrome
Psychogenic	Variable	Anxiety or psychiatric history; diagnosis by examining symptom pattern and excluding organic cause
Breath-holding	Deliberate breath-holding	Usually toddlers or young children
Drop attack	Unpredictable	Not true syncope—no loss of consciousness; usually elderly; loss of tone, ataxia, vertigo

CAD, coronary artery disease; DVT, deep vein thrombosis; hCG, human chorionic gonadotropin; JVD, jugular venous distention; TIA, transient ischemic attack.



**Figure 19-1.** Management algorithm for patients with syncope.

is related to structural cardiac disease, heart failure, and dysrhythmias.<sup>26</sup>

## ■ EMPIRICAL MANAGEMENT

### Rapid Assessment and Stabilization

Syncope is by definition a transient event so most patients are asymptomatic on presentation. Patients with significantly abnormal vital signs, recurrent syncope, or associated symptoms of a concerning nature such as chest pain or shortness of breath should undergo rapid evaluation.

### Diagnosis and Management

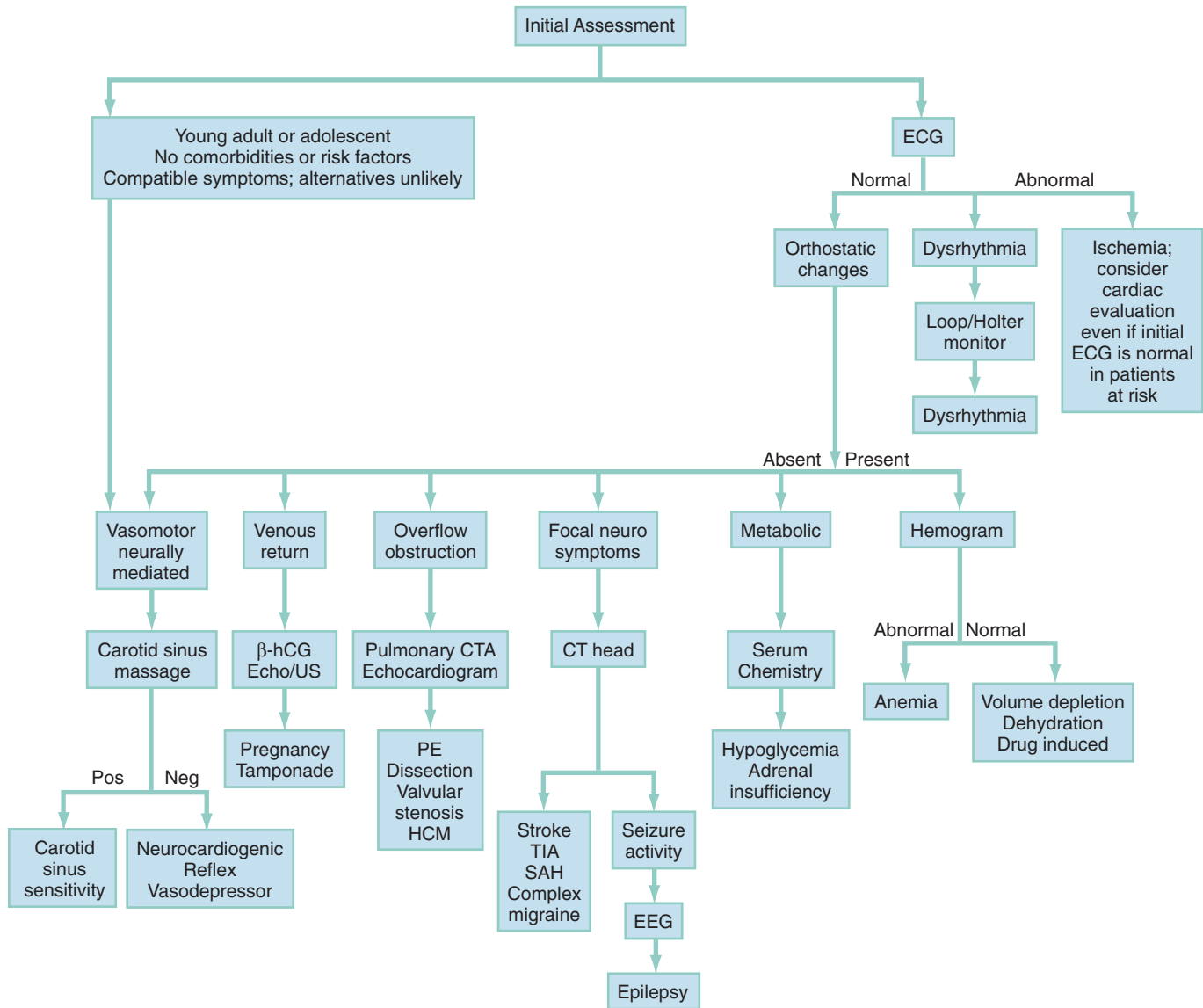
Most patients presenting with syncope require confirmatory bedside diagnostic evaluation. The 12-lead ECG is the principal tool for evaluating cardiac causes of syncope. Orthostatic vital signs, although unreliable as an evaluation of volume status, may be helpful when positional changes are accompanied by typical presyncopal symptoms and a significant fall in heart rate or blood pressure.<sup>23</sup> A schematic of selected diagnostic testing strategies for syncope is depicted in **Figure 19-2**.

Patients with critical diagnoses are generally admitted to the intensive care unit (ICU). Those with emergent diagnoses are typically admitted to telemetry units. Patients with nonemergent diagnoses can be treated as outpatients.

Several scoring systems aid in the admission decision-making process, most notably the San Francisco Syncope Rule.<sup>27</sup> In essence, this guideline suggests that in the absence of abnormal ECG findings, shortness of breath, hypotension (systolic < 90 mm Hg), anemia (hematocrit < 30%), or a history of congestive heart failure, the patient is at sufficiently low risk to consider outpatient disposition. The San Francisco Syncope Rule as well as other proposed rules, however, require external validation before widespread application.<sup>4,28-31</sup>

Hospitalization is required for patients with chest pain, unexplained shortness of breath, a history of significant congestive heart failure, or valvular disease.<sup>14,18,32</sup> Patients with ECG evidence of ventricular dysrhythmias, ischemia, significantly prolonged QT interval, or new bundle branch block are also admitted.<sup>14,17,18</sup> The clinician should consider monitoring patients with any of the following indications: age older than 45 years, preexisting cardiovascular or congenital heart disease, family history of sudden death, serious comorbidities such as diabetes, or exertional syncope.<sup>17,18,23,32</sup>

The ED evaluation of syncope is often inconclusive. After a history, physical examination, and 12-lead ECG, up to 50% of patients do not have a firm diagnosis.<sup>19,32</sup> Patients younger than 45 years and without worrisome symptoms, signs, or ECG findings are generally at lower risk for adverse outcome and may often be treated as an outpatient. Discharged patients should be warned of the hazards of recurrent syncope occurring during activities such as driving or working at heights.<sup>17</sup>



**Figure 19-2.** Diagnosis algorithm for syncope.

*The references for this chapter can be found online by accessing the accompanying Expert Consult website.*