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Coma is a presenting symptom in approximately 0.5-1% of emergency department (ED) admissions,[1] although the only paper addressing frequency of coma in the ED dates from 1934, citing coma as the presentation in 3% of admissions to the ED.[2] A more recent retrospective analysis found alteration of mental status in between 4% and 10% of ED patients.[3] Disturbances of level of consciousness may be caused by a wide variety of disorders, ranging from systemic disorders to structural central nervous system (CNS) disorders.

—The Editor

Coma: A Systematic Approach to Patient Evaluation and Management

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Definitions

A diminished level of consciousness, encompassing terms such as drowsiness, stupor, and coma, must be distinguished from clouding of consciousness, or confusional states, which entail content of consciousness. Confusion represents the inability to maintain a coherent sequence of thoughts, usually accompanied by inattention and disorientation. There is reduced memory, awareness, mental clarity, and coherence. This is more a disorder of the content of consciousness. Confusional states may be produced by many of the same medical disorders that produce diminished consciousness.

Definitions are, of necessity, inexact. For purposes of documentation it always is desirable to confirm and document specifics regarding what the patient is able to do at any given time. Establishing a baseline and describing changes in the patient's condition mandates this. Terms such as stupor, obtundation, and lethargy have been used so inexactly that they often have little meaning. For purposes of discussion, the following terms have been used, although objective assessments of patient capabilities and mental status always are preferable.

Clouding of consciousness represents a disturbance characterized by impaired capacity to think clearly and to perceive, respond to, and remember stimuli.

Delirium represents a state of disturbed consciousness with motor restlessness and disorientation. Delusions and hallucinations may be present. It is an acute confusional state, with maximal duration of symptoms lasting for days. Emotional lability

and impaired short-term memory are present, with disturbance of all higher cortical functions. Fever, tachycardia, and hypertension are common.

Obtundation is a state in which a patient is awake but not alert. Psychomotor retardation is present.

Drowsiness or lethargy is a disorder that simulates light sleep. The patient is arousable by touch or noise and can maintain alertness for a period of time.

Stupor is a state in which the patient can be aroused only by vigorous stimuli. Efforts to avoid stimulation are displayed. The patient exhibits little or no spontaneous activity, and shows little motor or verbal activity once aroused.

Coma indicates a state in which the patient is not arousable at all to verbal or physical stimuli, and no attempt is made to avoid painful or noxious stimuli. This has been subdivided further into light coma, in which patients respond to noxious stimuli with a variety of protective reflexes, and deep coma, in which patients do not respond at all.[4]

Coma Scales. Several methods have been proposed to assess objectively the level or grade of consciousness. Scales that assign points do not correlate with any specific terms cited above, which are subjective by necessity.

The most widely used mathematical scale to assess the patient with altered level of consciousness is the Glasgow Coma Scale (GCS). First described in 1974, it is a simple, reproducible scoring system used in trauma patients to define the level of responsiveness.[5] (*See Table 1.*) A GCS score of 8 or lower has been used as an alternative definition of coma. An advantage of the test is that a patient's neurologic status can be followed in an objective way. Its reproducibility is variable. It has been criticized because of the absence of brain stem signs in the evaluation.[6] However, because of its ease, familiarity, and widespread acceptance, the GCS continues to be the standard coma scoring system in the United States. Other named scales for the assessment of the comatose patient include the Liege coma scale, Swedish Reaction Level Scale, and the Apache II scale.

The Swedish Reaction Level Scale (RLS 85) has been proposed for use in patients whose assessment of eye opening may be difficult because of eye swelling, or whose verbal response may be difficult due to intubation. (*See Table 2.*) It has been shown to correlate with the GCS.[7]

The AVPU scale has been utilized by some because of its simplicity:

A= alert and aware
V= responds to verbal stimuli
P= responds to painful stimuli
U= unresponsive.

Pathophysiology

Consciousness has two easily assessable components: arousal and awareness. Most simply put, arousal implies the appearance of being awake. Wakefulness and alertness are maintained by a system of upper brain stem and thalamic neurons, the reticular activating system (RAS), with its connections to the cerebral hemispheres. For this reason, reduced consciousness results from depression of either the RAS or of neuronal activity in both cerebral hemispheres. An intact brain stem is necessary for arousal to occur, and a patient who looks awake generally has an intact brain stem.

The RAS is located ventral to the ventricular system in the pons, and extends continuously up to the posterior hypothalamus and thalamus. Even small lesions in the pons are capable of inducing coma. The RAS acts as a gateway for stimuli to the cerebral cortex and as a trigger for arousal from sleep. Therefore, when the RAS is dysfunctional, the cerebral cortex cannot be aroused and coma occurs.

Alternatively, coma can occur due to failure of cognition in the cerebral cortex. Awareness, as opposed to arousal, arises from brain activity in the cerebral cortex. Awareness constitutes

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Table 1. Glasgow Coma Scale

EYE OPENING	TALKING	MOTOR	SCORE
Does not open eyes	Makes no noise	No motor response to pain	1
Opens eyes with pain	Moans, makes unintelligible sounds	Exterior response (decerebrate)	2
Opens eyes with loud verbal command	Talks, but nonsensical	Flexor response (decorticate)	3
Opens eyes on own	Seems confused, disoriented	Moves part of body but does not remove noxious stimulus	4
	Alert and oriented	Pushes away noxious stimulus	5
		Follows simple motor commands	6

sensation, emotion, volition, and thought. Since awareness cannot be well localized, a unilateral cortical lesion cannot abolish it. There must be diffuse, bilateral, cortical lesions or extensive lesions disrupting traffic between the thalamus and the cortex to produce a vegetative state in which patients appear awake but are unaware of their surroundings. Bilateral cortical disease usually is secondary to toxic/metabolic derangement, and alteration in consciousness is dependent upon the size of injury and the speed with which it progresses. Unilateral hemispheric diseases, therefore, do not cause coma unless the brain stem fails. For these reasons, focal neurologic signs are expected to be absent or not prominent, except occasionally due to hypoglycemia.

Table 3 contrasts findings in patients with coma of brain stem origin with those in patients with coma from hemispheric origin.

The RAS may be disrupted or suppressed anatomically by a variety of mechanisms: Intrinsic brain stem lesions directly may compress or destroy RAS fibers, as with pontine hemorrhage, trauma, degenerative diseases, or tumor. The RAS may be disrupted by torque to the brain stem, as from a sudden blow to the head.

Infratentorial lesions may displace posterior fossa contents through the tentorial notch or the foramen magnum, as with cerebellar hemorrhage or posterior fossa tumors.

Supratentorial pressure may result from lesions that displace tissue and result in decreased perfusion and compression of brain stem structures or of the opposite hemisphere, as with subdural hematoma, intracranial hemorrhage, epidural hematoma, tumor, or brain abscess. Supratentorial lesions are a more common cause of coma than subtentorial lesions. In the uncal herniation syndrome, the most common of the herniation syndromes, the medial temporal lobe shifts to compress the upper brain stem. Typically, the ipsilateral third cranial nerve is compressed. Hemiparesis contralateral to the mass may develop from compression of the descending motor tracts in the ipsilateral cerebral peduncle, prior to their crossing in the medulla.

Any disturbance in the RAS, whether structural or functional, may produce a state resembling physiologic sleep that is not interrupted by the normal sleep-ending stimuli of pain or verbal command. Therefore, in brain stem coma, the patient is unresponsive and appears asleep. In hemispheric coma, the patient is awake and unresponsive.

Initial Assessment of the Comatose Patient

The key question in the diagnostic approach to the patient with diminished level of consciousness (LOC) is whether the patient's altered LOC is due to toxic/metabolic causes or whether there is structural CNS disease. Structural lesions, in general, are diagnosed more urgently because of the possibility of life-saving surgical intervention. In approximately 15% of cases, coma is caused by structural lesions.[4] Conversely, toxic-metabolic causes require supportive care until a definitive diagnosis is made and appropriate medical therapy can be instituted.

History. Clinicians must be able to perform a focused history and rapid neurologic examination that screens for most common abnormalities. Since people in coma cannot answer questions or follow commands, it becomes necessary to eliminate many parts of the neurologic examination and to seek historical data from friends, family, or other sources.

Specific questions should include the rate of onset of neurologic or behavioral changes. Abrupt onset favors the diagnosis of CNS hemorrhage or ischemia, or a cardiac cause inducing abrupt loss of cerebral perfusion. Gradual onset over days favors a metabolic problem such as hypercalcemia, diabetic emergency, or electrolyte disturbance.

Any history of trauma or ongoing medical illness, including prescribed and available medications, should be sought. Over-the-counter medications, salicylates, anticoagulants, hypoglycemic agents, antidepressants, anti-epileptic drugs, opioids, neuroleptics, steroids, or anticholinergic agents are all of potential significance in the patient with altered mental status. Any mydriatic or miotic agent can affect the neurologic examination.[8]

Suicidal ideation, past attempts at self-harm, and any history of substance abuse are critical considerations.

The setting in which the patient was found may be a clue to exposure to products of combustion or to extremes of temperature. Changes in activities of daily living or recent alteration in neurologic status may be reported from others. The social history may indicate substance abuse or HIV risk.

The patient's belongings should be searched for pill bottles. The patient may have a Medic Alert bracelet indicating prior seizure disorder, diabetes, or renal failure.

Physical Examination. The focus of the examination is to distinguish metabolic causes for coma from structural ones, since the former generally require supportive medical care, whereas the latter may require urgent surgical intervention. Specific signs

of brain stem herniation, including respiratory pattern, motor posturing, pupillary abnormalities, and extra-ocular muscle assessment, are critical to recognize, as rapid diagnosis of intracranial mass lesions may be life-saving.

The Role of Vital Signs in the Comatose Patient. Vital signs should be taken, including an accurate core temperature utilizing a probe that reads under 34°C, if necessary. Hypothermia is suggestive of sepsis, hypothyroidism, hypoglycemia, or environmental exposure. Hyperthermia or hyperpyrexia is suggestive of CNS infection, sepsis, serotonin syndrome, neuroleptic malignant syndrome, heat stroke, thyrotoxicosis, stroke, or exposure to certain toxins, such as salicylates, anticholinergics, or sympathomimetics.[8]

Systolic blood pressure of over 200 mmHg, with a diastolic of over 130 mmHg, is suggestive of intracranial hemorrhage, thyrotoxicosis, or exposure to sympathomimetic agents. Bradycardia is suggestive of increased intracranial pressure, hypothyroidism, or exposure to toxins such as calcium channel blockers or beta-blocking medications. The patient's breath may suggest fetor hepaticus, uremia, acetone, or alcohol.

Slow respiratory rate suggests opiate or sedative-hypnotic poisoning. Rapid respiratory rate or hyperventilation may be an indicator of hypoxemia or acidosis. Table 4 gives a differential diagnosis of abnormal respiratory rate in the unresponsive patient.

Certain respiratory patterns classically have been described in comatose states. Cheyne-Stokes Respiration (CSR) is a pattern of periodic breathing in which phases of hyperpnea alternate with apnea. It occurs in some mild drug intoxications, as part of the aging process, and in a variety of states associated with prolonged circulation time, including congestive heart failure, and during sleep in some normal persons. CSR requires generally intact brain stem function. The presence of CSR in the comatose patient implies bilateral dysfunction of the cerebral hemispheres or diencephalon.[9]

Central neurogenic or primary hyperventilation (CNH) has been described in low midbrain and middle pons lesions. Hyperventilation in a comatose patient usually implies some sort of acidosis, perhaps from diabetic ketoacidosis or lactic acidosis, or from some ingested toxin such as methanol, aspirin, or ethylene glycol. (*See Table 4.*)

Other brain stem respiratory patterns have been described. Apneustic breathing represents a pause at full inspiration, signifying an upper pons lesion. This long pause, also called inspiratory cramp, with a prolonged exhalation, typically is repeated 5-6 times per minute. Clusters of breaths may follow each other in a disorderly fashion with high medullary or lower pons lesions. Ataxic breathing, or Biot's respiration (*see Table 5*), has a completely irregular pattern in which deep and shallow breaths occur randomly, indicative of a medullary disorder. These patterns are unusual; the importance to the emergency physician is to recognize brain stem disorders and to pursue diagnoses aggressively. Patients with apneustic breathing or ataxic breathing require intubation.[10]

Other Physical Findings. The patient should be fully exposed. Skin findings such as cyanosis, pallor, needle tracks, uremic frost, or icterus should be noted. Petechiae may suggest meningococcemia or Rocky Mountain spotted fever.

Table 2. Swedish Reaction Level Scale (RLS85)

SCORE	DESCRIPTION
1	**Alert—**No delay of response
2	**Drowsy or confused—**Responsive to light stimulation
3	**Drowsy or confused—**Responsive to strong stimulation **Mental responsiveness—**At least one of the following: words, orienting, eye movements, obeying of commands, warding off pain
4	**Unconscious—**Localizes but does not ward off pain
5	**Unconscious—**Withdrawing movements on pain stimulation
6	**Unconscious—**Stereotyped flexion movements on pain stimulation
7	**Unconscious—**Stereotyped extension movements on pain stimulation
8	**Unconscious—**No response to pain stimulation

Examination of the head should concentrate on evidence for trauma, such as hemotympanum, CSF rhinorrhea or otorrhea, mastoid ecchymosis (Battle's sign), or depressed skull fracture. The patient may have evidence of shunt placement or prior surgery. Funduscopic examination may show hemorrhage or papilledema. Occasionally, subhyaloid hemorrhages can been seen behind the vitreous humor along the edge of the optic disc. This finding is pathognomonic for subarachnoid hemorrhage.

If the cervical spine can be cleared of injury by imaging or by history, meningeal signs may be assessed for evidence of subarachnoid hemorrhage. The neck should be examined for thyroidectomy scar as a possible clue for myxedema coma.

The abdominal examination may reveal ascites or organomegaly suggestive of hepatic encephalopathy. Table 5 summarizes clues to coma based upon the physical examination.

The Neurologic Examination. Given that the region of the nervous system affected in a comatose patient is in the brain stem or above, the neurologic examination should be focused and will differ from that of the awake, conversant patient.

In the alert patient, the mental status examination evaluates speech flow and content; memory; orientation to person, place, and time; and thought process. The patient may be asked to count backward from 20, then by serial 3s or 7s. Memory may consist of recent recall of three unrelated objects.

In the unresponsive patient, posture should be observed. If the patient is in a comfortable-appearing position, the brain stem probably is functioning well. Spontaneous reflexes should be noted. Coughing, sneezing, or hiccuping carries a less positive prognosis.[10]

The mental status examination in the comatose patient is an assessment of the patient's response to auditory, visual, and noxious stimuli. Stimuli may range from verbal stimuli to more noxious stimuli, such as tickling the nasopharynx with a cotton swab.

Two specific patterns of motor activity are notable: Decorticate posturing consists of upper extremity adduction with flexion

Table 3. Clinical Clues in Differentiating Brain Stem and Hemispheric Coma

	BRAIN STEM COMA	HEMISPHERIC COMA
TYPE OF UNRESPONSIVENESS		
	Looks asleep	Looks awake (i.e., eyes open)
BODILY POSITION		
	Looks unnatural	Looks natural (i.e., appears to be a comfortable posture)
RESPIRATION		
	Apneustic or ataxic	Normal or Cheyne-Stokes
SPONTANEOUS REFLEXES		
	Yawning or sneezing not seen Coughing, swallowing, or hiccuping does not rule out brain stem coma	Yawning or sneezing may be seen
PUPILLARY FUNCTION		
	Tends to be abnormal (e.g., unilateral fixed, dilated pupil)	Pupils tend to show normal responsiveness to light
EYE MOVEMENT		
	Caloric testing elicits no response	Caloric testing reveals slow phase without fast phase Spontaneous roving conjugate movements indicate brain stem disinhibition due to hemispheric coma

at the elbows, wrists, and fingers. There is lower extremity extension and internal rotation. This indicates disease of the diencephalon. Decerebrate posturing consists of upper extremity adduction, extension, and pronation. Lower extremity extension is present. There is internal rotation and extension of all four limbs. This posture indicates that the vestibular nuclei in the medulla and the vestibulospinal tracts are intact.

While these postures do not have localizing value in human patients, in general, patients with decorticate posturing in response to pain have a better prognosis than do those with decerebrate posturing.

Formal strength testing is impossible in comatose patients, but deep tendon reflexes and resistance to passive manipulation still can be tested in the usual manner. The degree to which movement is purposeful should be recorded. A purely local withdrawal reflex from noxious stimulation of the lower extremity produces triple flexion: dorsiflexion of the ankle with flexion of the knee and hip. To look for purposeful withdrawal, the stimulus should be applied to a location where triple flexion would be an inappropriate response. For example, pinching the skin of the anterior thigh would elicit hip extension as a purposeful movement, while hip flexion would represent purely reflex withdrawal. In both upper and lower extremities, reflex withdrawal produces limb adduction. Therefore, to differentiate reflex withdrawal from purposeful movement, the noxious stimulus should be applied to the medial aspect of the limb.[11] Abduction of a limb is a purposeful mediated cortical response. Triple flexion withdrawal of the lower extremity is a spinal cord-mediated reflex.

The cranial nerve examination of the patient in coma should concentrate on the eyes. Although visual acuity cannot be tested, testing of field defects may be performed by assessing response to visual threat. A finger or small object introduced suddenly into the visual field may elicit a response.

Pupillary reflexes can be tested in the same manner as in an awake person. Pupillary abnormalities or focal neurologic findings suggest an intracranial cause for coma. A unilateral fixed, dilated pupil often is taken to be a sign of brain herniation, with the causative mass usually on the same side as the pupillary abnormality. Consider the possibility of topically applied mydriatic agents in an alert patient or, alternatively, compression of CN III by a posterior communicating artery aneurysm. This finding in a comatose patient suggests the need for urgent computed tomography (CT) to assess for space-occupying lesions such as hemorrhage, abscess, or tumor. Pinpoint pupils may result from opiates other than meperidine or from pontine lesions. Finally, pupillary dilatation may be elicited from a painful stimulus below the neck, as with pinching (ciliospinal reflex).

Eye movements are the cornerstone of the neurologic examination of the comatose patient, as they closely approximate the ascending RAS anatomically. These can be assessed by activating certain specific reflexes. Cranial nerves III, IV, and VI enter and exit the brain stem at the lower pontine to upper midbrain levels, closely associated with the RAS, making testing of extraocular movements critical. Extraocular movement testing permits evaluation of the cortex, and of the medial longitudinal fasciculus in the brain stem, as evidenced by the function of cranial nerves III, IV, and VI. If the patient's eyes rove spontaneously and conjugately, the brain stem probably is intact. A persistently adducted eye indicates paresis of cranial nerve VI, while an abducted eye indicates cranial nerve III dysfunction. Dysconjugate gaze in the horizontal plane may be observed in various sedated states, including alcohol intoxication. Dysconjugate gaze in the vertical

plane may be caused by pontine or cerebellar lesions and is termed skew deviation. Conjugate eye movements or horizontal roving imply an intact midbrain and pons. Ocular bobbing may indicate bilateral pontine damage, cerebellar hemorrhage, or metabolic derangement.[4] Typical ocular bobbing with pontine lesions is characterized by conjugate downward jerks followed by slow but conjugate return to the midposition.[12]

The oculocephalic reflex, or doll's eye reflex, is tested by turning the patient's head from side to side. This should be performed only if there is no chance of a traumatic injury to the cervical spine. Imaging of the cervical spine may have to be performed to rule out injury. A positive doll's eye test occurs when the eyes do not turn with the head; in other words, it appears that the patient is maintaining fixation on a single point in space. The eyes appear to be moving relative to the head in the direction opposite to the head movement. This reflex usually is suppressed in conscious patients, and is a normal finding in comatose patients. Absence of this reflex in a comatose patient indicates dysfunction somewhere in the reflex pathway. The abnormality may be in the afferent limb, from the labyrinth and vestibular nerve, or from neck proprioceptors. Alternatively, the lesion may be in the efferent limb, including the medial longitudinal fasciculus (MLF), cranial nerves III and VI, or in the muscles they innervate. The function of the MLF is to coordinate head, neck, and eye movement while receiving input from the horizontal semicircular canals. It extends the eyes' input from the superior colliculus high in the midbrain into the cervical spinal cord. Finally, the dysfunction may be in the connecting pathways in the pons and medulla. An intact doll's eye reflex demonstrates the functional integrity of the brain stem, and the cause for coma should be sought elsewhere.

An alternative to doll's eye reflex testing is the vestibulo-ocular reflex, commonly referred to as cold calorics. This may be performed if trauma is suspected, as the test does not entail moving the patient's neck. The patient is placed supine, with the head or upper body tilted forward so that the neck forms an angle of 30° with the horizontal. This isolates endolymph movement to the horizontal semicircular canal. The tympanic membrane is examined to verify that it is intact prior to the test. A syringe is filled with 25-50 cc of ice water with a small catheter attached, and the water forcefully is injected against the tympanic membrane. This stimulus should have the same effect on the horizontal semicircular canal as sustained turning of the head in the opposite direction, resulting in sustained deviation of the eyes toward the ear being stimulated. Movement begins typically 10-30 seconds after the ice water is introduced. There are several possible results from the test:

1. Absence of this reflex indicates dysfunction of the pons, medulla, or, less commonly, cranial nerves III, VI, or VIII.

2. Normally, this reflex produces deviation of the eyes toward the stimulated ear. There is nystagmus, with the fast component away from the stimulated ear. Bilateral tonic deviation of the eyes toward the stimulus should last 30-120 seconds and indicates an intact brain stem. Absence of the quick, corrective nystagmus indicates damage to the cerebral hemispheres. A normal response in a comatose patient raises the suspicion of psychogenic coma. While the eyes deviate toward the side of the cold water infusion, a mnemonic for the nystagmus is that the rapid nystagmus is away from the side of the ice water infusion, with the slow tonic deviation toward the stimulated side: COWS (cold opposite, warm same).

3. If both eyes deviate tonically toward the side of the cold-water infusion, the brain stem is intact, but the source of coma may be from cerebral hemisphere dysfunction, failing to correct eye position with rapid nystagmus.

4. Movement of only one eye ipsilateral to the stimulus signifies internuclear ophthalmoplegia—a brain stem structural lesion.

Benzodiazepenes, barbiturates, and alcohol may affect reflex eye movements, although they leave pupillary responsiveness intact.

Table 4. Causes of Abnormal Ventilation in Unresponsive Patients

I. HYPERVENTILATION

A. Metabolic acidosis

1. High anion gap
   - Diabetic ketoacidois
   - Hyperglycemic hyperosmolar non-ketotic coma
   - Lactic acidosis
   - Uremia
   - Alcoholic ketoacidosis
   - Acid poisons: Ethylene glycol, methyl alcohol, paraldehyde, salicylates
   - Other toxins: Iron, toluene, INH (isoniazid)
2. No anion gap
   - Diarrhea
   - Pancreatic drainage
   - Carbonic anhydrase inhibitors
   - Acetazolamide, NH4 Cl ingestion
   - Renal tubular acidosis
   - Ureteroenterostomy
   - Hypoaldosteronism

B. Respiratory alkalosis

- Hepatic failure
- Sepsis
- Pneumonia
- Anxiety (hyperventilation syndrome)

C. Mixed acid-base disorders (metabolic acidosis and respiratory alkalosis)

- Salicylate overdose
- Sepsis
- Hepatic failure

II. HYPOVENTILATION

A. Acute (uncompensated)

- Sedative drugs
- Opiate poisoning
- Brain stem injury
- Neuromuscular disorders
- Chest injury
- Acute pulmonary disease

B. Chronic pulmonary disease

Table 5. Pertinent Physical Examination in the Comatose Patient

AREA	FINDINGS	COMMENT/INTERPRETATION
Vital signs	Blood pressure—hypotension	Decreased perfusion can result in depressed mental status Suggests hypovolemic, cardiogenic, or septic shock
	Blood pressure—hypertension	Systolic pressures > 200 mmHg, diastolic > 130 mmHg suggests intracranial hemorrhage, thyrotoxicosis, exposure to sympathomimetic agents, hypertensive encephalopathy. Intracranial hemorrhage is the first consideration.
	Respiratory rate—tachypnea	A sign of hypoxemia, brain stem herniation, or metabolic acidosis
	Respiratory rate—bradypnea	Associated with opiate or sedative-hypnotic poisoning
	Respiratory pattern	Look for CSR, CNH, ataxic or Biot's breathing
Airway	Ensure patency and protection; breath odor may suggest cause	Essential examination to anticipate need for airway management Unique breath odors: alcohol, fetor hepaticus, ketones, uremia
Skin	Cyanosis, pallor, jaudice, petechiae/ purpura, surgical scars, needle tracks	Full exposure necessary to look for wide variety of visual clues
Head	Palpation for trauma, previous craniotomy, or ventricular shunt	External injury may reflect acute internal damage or prior hematoma, tumor, or hydrocephalus.
ENT	Signs of infection, hemotympanum, tongue lacerations	May reveal signs of meningitis, basilar skull fracture, or recent seizure
Eyes	Pupillary changes	May be significant in identifying brainsteam dysfunction from structural cause; reactivity usually preserved in metabolic causes
	Eye movement	Conjugate roving eye movement connotes intact brain stem. Oculocephalic testing may assist in locating level of structure damage.
	Funduscopy	Papilledema, subhyaloid hemorrhage, findings of HTN or DM
Neck	Rigidity	Assess after cervical spine clearance (historical or imaging) Nuchal rigidity is meningitis or SAH until proven otherwise.
Lung	Varied	Findings consistent with acute or chronic hypoxia source or acute infection.
Cardiovascular	Varied	Possible murmurs (embolic), dysrhythmias (cerebral perfusion pressure); AI murmur may accompany aortic dissection
Neurologic	Level and content of consciousness	
	Posture	Posture (decorticate, decerebrate) may indicate neurologic level of injury.
	Movement	Movement—specifically looking for purpose (e.g., protective) and asymmetry and spontaneous patterns (e.g., subtle seizure activity)
	Deep tendon reflexes	Reflect spinal cord function; asymmetry may be useful

Key: CSR = Cheyne-Stoke's respiration; CNH = central neurogenic hyperventilation; ENT = ear, nose, and throat; HTN = hypertension; DM = diabetes mellitus ; SAH = subarachnoid hemorrhage

In the setting of trauma, CN VI palsy may result from a brain stem lesion, peripheral nerve injury with or without basilar skull fracture, or from lateral rectus muscle entrapment.[13] Because of the close proximity of these structures, a traumatic lesion to the brain stem at the level of the sixth nerve may be accompanied by pyramidal tract signs, as well as a seventh nerve palsy.[14]

Cranial nerves V and VII can be assessed in comatose patients by testing corneal reflexes and by observing facial grimacing in response to noxious stimulation, such as supraorbital pressure. Cranial nerves IX and X can be assessed by testing the gag reflex, although this may be absent in 20% of normal subjects.[11]

Classically, patients with progressive metabolic encephalopathy or transtentorial herniation of the brain stem demonstrate a rostrocaudal deterioration. This may be identifiable through four functional levels: diencephalon, midbrain, pons, and medulla. Those patients who are functioning at the highest level (diencephalon) have the best prognosis. (*See Table 6.*) A mnemonic for functions tested is SPERM: State of consciousness; Pupils and their reactivity; Eye movements; Respiratory pattern; and Motor response.

Emergency Management of the Comatose Patient

As with any medical emergency, establishment of an airway is paramount. Any patient with a GCS of less than 9 should under-

Table 6. Physical Signs of Coma by Level

SIGN	DIENCEPHALON	MIDBRAIN	PONS	MEDULLA OBLONGATA
Level of consciousness	Drowsiness to obtundation	Light coma	Deep coma	Deep coma
Pupil reactivity & size	Small reactive pupils 2-3 mm in diameter	Unreactive, dilated pupils (midposition, fixed)		
		Tectal pupils large, fixed	Midposition pupils or pinpoint pupils	Unreactive pupils
Oculocephalic reflex	Eye movement in opposite direction of head turning	No eye movement, may be dysconjugate	No eye movement	No eye movement
Oculovestibular reflex	Eye movement toward irrigated ear	Abduction of ipsilateral eye or no eye movement	No eye movement	No eye movement
Respiratory pattern	Sighing or Cheyne-Stokes respiration	Hyperventilation, rarely Cheyne-Stokes respiration	Hyperventilation or apneustic breathing	Ataxic or cluster breathing
Motor response	Withdrawal or decorticate posturing	Decerebrate posturing	Decerebrate posturing or flaccid (lower pons)	No response

go intubation. Patients should be placed on oxygen and fully undressed. If there is any suspicion of cervical spine (C-spine) injury, the C-spine should be immobilized. The neck cannot be moved until there is unimpeachable historical or radiographic evidence that the patient did not sustain neck trauma.

Most causes for coma are non-traumatic and involve medical management and supportive care with specific care dictated by diagnosis. Ventilation and establishment of circulation are paramount. While detailed trauma management is outside the purview of this article, supportive care for the trauma patient includes airway management, including intubation and ventilation, blood and fluid resuscitation, control of external bleeding, and control of agitation.

Primary brain injury occurs with the initial insult, and is best delineated in the ED by CT. Secondary brain injury is defined as those processes that occur later that contribute to overall traumatic brain injury: from decreased cerebral blood flow, elevated intracranial pressure, hemorrhage, and failure to adequately address shock.[15,16] It now is recognized that excessive hyperventilation causing constriction of cerebral blood vessels may be a factor in reducing cerebral blood flow, especially if the pCO_2 is decreased below 25 mmHg.[17,18] Hyperventilation should be viewed as a temporizing measure only in the face of worsening neurologic status, with close monitoring and return of the pCO_2 to 30-35 mmHg as soon as possible.[19] Mannitol 0.25-1 g/kg has an onset of action of osmotic diuresis within 30 minutes, and may be viewed as another temporizing measure in the ED. Steroids such as dexamethasone have a role in vasogenic cerebral edema, as from tumor, but no role in the management of head injury.[20,21] The mean arterial blood pressure should be maintained at 90 mmHg. If there are signs of herniation, any potentially surgical lesion should be identified as rapidly as possible. Otherwise, treatment for elevated intracranial pressure entails elevation of the head of the bed to 30°, adequate volume resuscitation, and maintenance of arterial oxygenation.

The Coma Cocktail

Exposure to drugs and toxins is reported to occur in approximately 2 million Americans annually.[22] As well, one report identified 29 patients with hypoglycemia out of 340 consecutive paramedic calls for patients with altered mental status.[23] There has been ongoing interest in the use of the "coma cocktail" in patients with altered consciousness. This has dated from the 1960s when analeptic agents such as doxapram hydrochloride, picrotoxin, nikethimide, caffeine, and physostigmine were administered to combat CNS depression. Analeptics have fallen out of favor since they have been demonstrated to increase morbidity and mortality, largely because of their induction of seizures.[24,25] Physostigmine usage empirically is mentioned only to be condemned. Proposed components of a reasonable coma cocktail are reviewed in turn.[26]

Intravenous Glucose. Early use of 25-50% dextrose should be considered to prevent the sequelae from prolonged neuroglycopenia. A normal or elevated bedside glucose test strip is a valid reason to withhold glucose administration in the comatose patient. The prompt response of coma with dextrose confirms hypoglycemia and may obviate the need for any further diagnostic testing. It is notable that patients with poorly controlled diabetes mellitus may experience symptoms of hypoglycemia at greater glucose concentrations than non-diabetics—at average

levels of 77 mg/dL in one report.[27] At equilibrium, one ampule of 50% dextrose in water, or 25 grams, should raise the serum glucose of a 70-kg patient acutely by approximately 60 mg/dL if it distributes into total body water prior to any metabolism. A much higher rise in serum glucose has been demonstrated, however, of 165 mg/dL when 25 grams of dextrose was administered to adult patients.[28] There have been reports that hyperglycemia adversely affects outcomes after ischemic injury,[29-31] perhaps related to elevated lactate levels in ischemic tissue. Since even mild degrees of hyperglycemia may result in accentuated neurologic damage from an ischemic insult, it has been proposed that empiric administration of glucose should be avoided in patients at risk for cerebral ischemia. This may include those with acute stroke, cardiac arrest, or severe hypotension.[32] It is logical to rapidly and accurately detect hypoglycemia prior to the administration of 50% dextrose in water to a patient with diminished level of consciousness.[33]

Thiamine. Thiamine functions as a co-factor in enzymes in the Kreb's cycle and the pentose phosphate pathway. Thiamine requirements, therefore, are dependent upon glucose intake. It is prudent to administer 100 mg of thiamine intravenous (IV) or intramuscular (IM), as acute Wernicke's encephalopathy has been described following glucose loading.[34] Although Wernicke's initial case descriptions in 1861 included two alcoholics, this encephalopathy has been recognized in non-alcoholic individuals at risk for malnutrition, including those patients with hyperthyoid state, neoplasia, anorexia nervosa, hyperemesis gravidarum, acquired immunodeficiency syndrome,[35,36] and a variety of gastrointestinal disorders. Ataxia, vertical and horizontal nystagmus, confusion, hypotension, and ophthalmoplegia are characteristic, but not all are reversible later with thiamine.[37] Thiamine uptake into cells is slower than the entrance of dextrose into cells, so it makes little sense to withhold hypertonic dextrose until thiamine administration.[38] Furthermore, the IV route has been demonstrated to be safe.[39] In fact, since patients who truly need thiamine tend to be malnourished with little muscle mass, the IM route of administration is best avoided.[33]

Narcotic Antagonists. Naloxone is a pure narcotic antagonist, competitively blocking sites used by narcotic agents. A rapid response to naloxone may obviate the need for airway management. Dosage should be 0.1 mg/kg in children, 2-4 mg IV in adults up to a total dose of 4-6 mg. Patients who have exposure to long-acting narcotics such as methadone will require hospitalization. An hourly infusion rate should deliver a dose of naloxone that is equal to the initial dose required to produce arousal.[40] Patients who have consumed shorter-acting narcotics may benefit from an observation stay, due to the short half-life (20-30 minutes, with duration of effects 45-70 minutes) of naloxone. The occasional cases of pulmonary edema or ventricular dysrhythmias seen after opioid reversal are felt to be due to surges in catecholamine levels that may follow naloxone administration.[41] Naloxone has been demonstrated to be safe when used in the pre-hospital setting.[42] Because of the risk of precipitating withdrawal, a low initial dose of 0.1-0.3 mg has been proposed initially to reverse respiratory depression.[40]

Nalmefine is a pure opiate antagonist that is structurally similar to naloxone. A 2-mg IV dose has been shown to prevent respiratory depression from fentanyl challenge in volunteers for up to eight hours after administration.[43] It has been demonstrated to be safe in children.[44]

Flumazenil is a centrally acting benzodiazepene antagonist. It competitively blocks benzodiazepene activation of gamma aminobutyric acid synapses. The empiric use of flumazenil in the comatose patient is to be condemned because of the risk of seizures in patients chronically using benzodiazepenes, as well as patients who may have coingested cyclic antidepressants. It has use in isolated benzodiazepene overdose, in which flumazenil may reverse coma within 1-2 minutes. Fatalities from benzodiazepene overdose are rare and usually associated with aspiration.[45,46] Airway management may be preferable to administration of flumazenil in this instance, as seizures may be difficult to control because of the presence of a benzodiazepene antagonist. There may be a subset of patients who safely may receive empiric flumazenil: those whose clinical picture is consistent with isolated benzodiazepene ingestion, with no suggestion of stimulant or antidepressant exposure, no history of underlying seizure disorder, and no long-term benzodiazepene use.[47] The dose of flumazenil is 0.3 mg over 1 minute IV, followed by 0.3 mg every minute up to a total dose of 1 mg. So long as this dose is not exceeded, no more than 50% of benzodiazepene receptors will be occupied by this drug.[48]

Ancillary Diagnostic Testing

Testing in the ED. A bedside glucose level should be obtained for all patients presenting with coma. Hypoglycemia has been associated with a variety of focal deficits and neurologic findings, including hemiplegia[49] and decerebrate[50] and decorticate[51] posturing. Pulse oximetry should be obtained for all patients with disturbed level of consciousness.

Urine easily is tested in the ED for infection, hyperglycemia, or presence of ketones.

An electrocardiogram may give evidence for the cause of coma, if characteristic alterations in electrolytes such as calcium or potassium are present. Specific evidence for hypothermia (Osborn J waves) or tricyclic antidepressant poisoning (widened QRS interval, terminal rightward QRS axis) are present.

Other testing must involve the hospital laboratory. A bicarbonate level or arterial blood gas should be obtained to assess for acidosis and for retention of carbon dioxide. Lactic acidosis from a seizure will normalize within one hour of the seizure, but may give a clue to a postictal state.

Venous or arterial carbon monoxide levels may be obtained, especially if there is a discrepancy between measured and calculated oxygen saturation. A history may indicate whether the patient lives alone, whether other people at home have become sick, or whether the patient had suicidal intent.

Thyroid function tests may be performed if myxedema is a consideration. A sensitive thyroid-stimulating hormone (TSH) test is most critical and should be available within 1-2 hours. Free T_4 and T_3 levels may be helpful to confirm diagnosis of thyroid dysfunction. Toxicologic screening should be focused, based upon clinical findings and vital signs.

Urinalysis may demonstrate hyperglycemia from hyperosmolar coma. Microscopy may indicate calcium oxalate crystals from ethylene glycol poisoning, or leukocytes, bacteria, and nitrites suggestive of urosepsis.

A head CT scan should be ordered when there is no evidence of metabolic cause for coma. If there is a suspicion for intracranial hemorrhage or for trauma, this study should be ordered early. Magnetic resonance imaging (MRI) may be more sensitive for brain stem lesions, but its utility is limited by availability. In the absence of herniation, the most likely cause for brain stem dysfunction is a toxin. CT can delineate surgical mass lesions, midline shift, and compression of cisterns. (*See Table 7.*)[17]

MRI is the most sensitive test for diagnosing diffuse axonal injury (DAI), which occurs in deeper cerebral white matter, where shear forces cause mechanical disruption of axons.[17] Although this injury is not amenable to surgery, its presence indicates that a patient is more likely to develop persistent vegetative state or persistent coma.[52,53] While MRI may demonstrate punctate areas of bleeding below the level of CT detection, its value in the evaluation of trauma is limited by availability. As well, acute brain injury amenable to surgery is well-defined by CT. MRI has value in diagnosis of extra-cranial and intra-cranial arterial dissections. Non-hemorrhagic brain lesions often are more readily identifiable by MRI. The depth of lesions in white matter, midbrain, and the brain stem can be assessed.[54,55]

A lumbar puncture (LP) should be considered for diagnosis of infection or subarachnoid hemorrhage. Head CT should, in general, precede LP to diagnose a mass lesion that could predispose the patient to herniation and which might be diagnostic of the patient's coma. Negative imaging and metabolic work-up in the setting of brain stem failure implies a vascular event, such as basilar artery occlusion. Figure 1 summarizes a suggested overall diagnostic and therapeutic approach to the patient in coma.

Electroencephalography (EEG) is of limited utility in the emergency setting, but occasionally may be useful in the diagnosis of status epilepticus. Electrical seizures without corresponding motor movements make EEG the diagnostic modality of choice in this setting. It may be of prognostic utility when performed 6-72 hours after anoxic injury. Malignant EEG findings indicate a poor prognosis for recovery, including most patients with intact brain stem reflexes.[56,57]

Somatosensory evoked potentials are most useful in predicting a poor or fatal outcome. They are a more specific marker than the EEG, with few false positives. The bilateral absence of an evoked response after one week is a reliable predictor of failure to regain consciousness.[57,58]

Causes of Coma

There are numerous causes for coma, which should be classified into two broad categories: toxic-metabolic and structural.

Toxic causes for coma may include the following: alcohols, such as ethyl, isopropyl, and methyl; barbiturates; anti-cholinergics; bromides; carbon monoxide; opiates; anticonvulsants; tranquilizers; cyanide; phenothiazines; cyclic antidepressants; sympathomimetics, including cocaine, amphetamines; sedative-hypnotics; salicylates; hallucinogens; heavy metals.

Metabolic causes for coma include any disorder that induces hypoxia or hypercapnea. Acidosis, hyper- and hyponatremia, and hypo- and hypercalcemia must be considered. Hepatic failure, including Reye's syndrome, may induce altered consciousness. Endocrine abnormalities, such as myxedema, Addisonian crisis, hypoglycemia, and hyperosmolarity, must be considered. Wernicke's encephalopathy occurs in a variety of malnourished states. Overwhelming sepsis, meningitis, peritonitis, and encephalitis are among infectious causes to be considered.

Structural causes for coma may be divided into supratentorial disorders and infratentorial. Supratentrorial causes include bilateral cerebral disease, concussion, contusion, postictal states, hypertensive encephalopathy, encephalitis, meningitis, subarachnoid hemorrhage, generalized increased intracranial pressure, and unilateral cerebral disease causing herniation such as infarction, hemorrhage, tumor, and abscess. Infratentorial lesions that may cause coma include pontine hemorrhage, cerebellar hemorrhage, basilar artery occlusion, brain stem tumors, or traumatic hemorrhage in the posterior fossa.

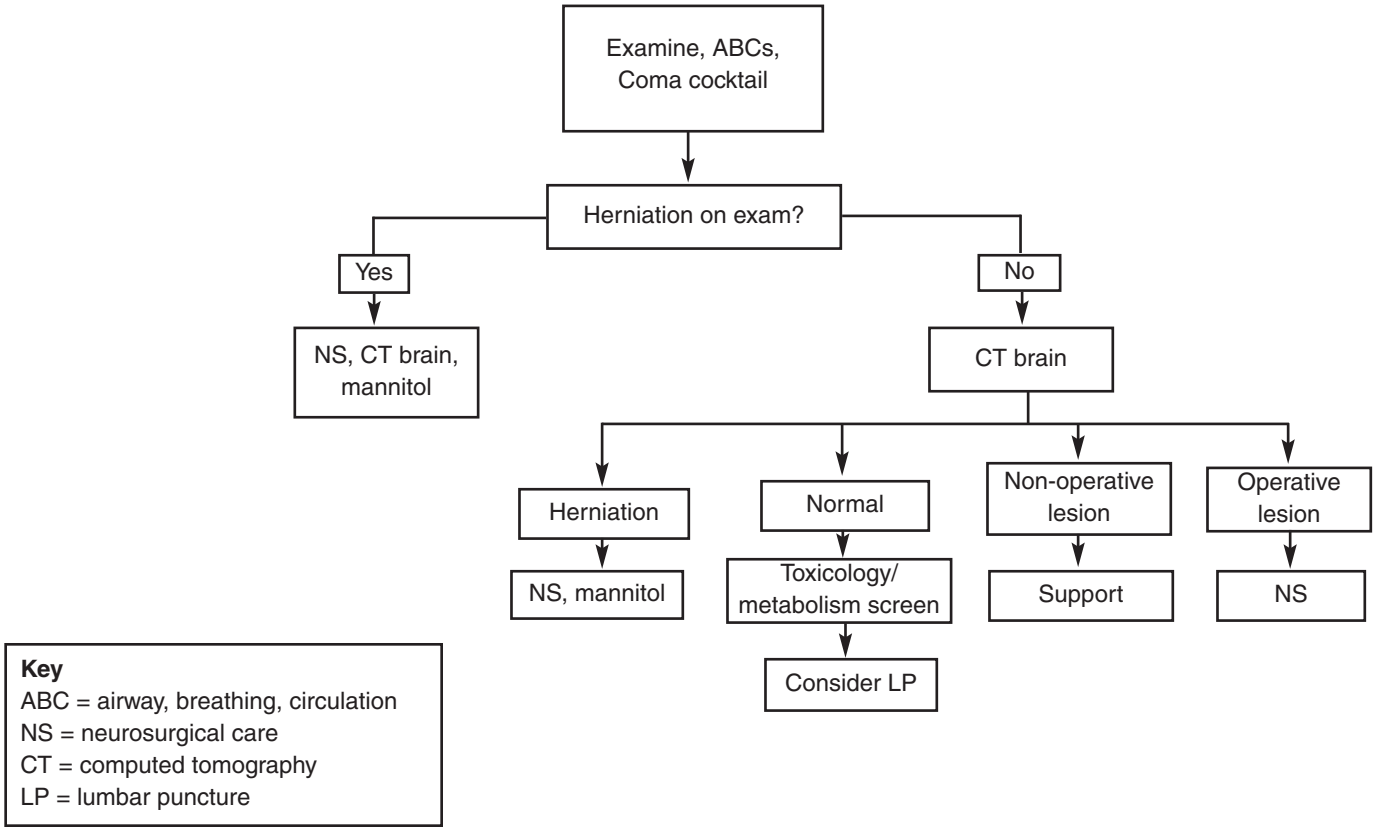
Table 7. Marshall Classification System for Cranial CT Imaging in Patients with Traumatic Brain Injury

CATEGORY	DEFINITION
Diffuse Injury I	No visible pathology on cranial CT scan
Diffuse Injury II	Cisterns are visible with midline shift 0-5 mm, and/or 1. lesion densities present; 2. high- or mixed-density, lesion present, but < 25 mL in volume; 3. bone fragments or foreign bodies present
Diffuse Injury III	Cisterns compressed or absent with midline shift 0-5 mm, no high- or mixed-density lesions > 25 mL in volume
Diffuse Injury IV	Midline shift > 5 mm, no high- or mixed-density lesions > 25 mL in volume
Evacuated mass lesion	Any lesion surgically evaluated
Nonevacuated mass lesion	High- or mixed-density lesion > 25 mL, not surgically evacuated

Specific Scenarios Causing Coma that Require Specific Consideration

Myxedema. The hypothyroid crisis of myxedema coma is a life-threatening manifestation of the hypothyroid state. Myxedema coma can be defined as severe thyroid deficiency contributing to a decreased level of consciousness.[59] The diagnosis is largely a clinical one made in the context of hypothermia, hypoventilation, stupor, and abnormal TSH and free thyroxine. Altered mental status and a precipitating event such as infection or trauma may

Figure 1. Shortened Coma Protocol



be present. Levothyroxine or liothyronine (T_3), hydrocortisone, and supportive care in the form of airway management, antibiotics, or rewarming techniques may be life-saving.[60,61]

Subarachnoid Hemorrhage. Subarachnoid hemorrhage may present as coma. It is important to note that the sensitivity of CT in the diagnosis of SAH approximates 93%, and declines with degree of anemia and time from the initial bleed. Lumbar puncture still is the gold standard for diagnosis if the CT is negative.[62] A history of sickle cell disease, polycystic kidney, use of sympathomimetic agents, Ehlers-Danlos disease, or Marfan's syndrome may yield clues.[63] Referral for neurosurgical management is mandatory.

Elevated intracranial pressure may cause brain shift and compression through the tentorial opening, inducing brain herniation. When cardiorespiratory centers in the brain stem are compressed, respiratory arrest and cardiovascular collapse may ensue. Large hematomas must be evacuated surgically. Mannitol 0.5-1.0 gm/kg may serve as a temporizing measure to lower intracranial pressure until more definitive therapy can be accomplished. Neurological outcome was shown to improve and mortality to be reduced in patients with subdural hematomas if operative drainage and control of hemorrhage was achieved within 4 hours of injury.[64]

Brain edema is typically maximal 24-48 hours after injury.[65] Proposed mediators of injury have included excretory amino acids, oxygen radical molecules, and nitrous oxide released from injured vascular endothelium.[66] Iron released from extravasated blood promotes oxidant reactions.[67] Blood in the interstitial space also triggers an inflammatory immune response regulated by local cytokines.[68] Management of cerebral edema was discussed earlier.

Conditions that Mimic Coma

Catatonia is a hypomobile syndrome associated with major psychosis. Patients appear awake, but make no voluntary movements. Characteristically, there is a "waxy flexibility," in which limbs maintain their posture when placed by their examiner. It occurs chiefly in elderly patients as a manifestation of severe or vegetative depression. The catatonic patient usually becomes responsive after an injection of amobarbital, distinguishing this from severe abulia.[10]

Hysterical or conversion pseudocoma may entail voluntary attempts to appear comatose. Patients actively may resist eyelid opening, or may respond to visual threats. Mild stimulation, such as tickling the nose with cotton, should be employed instead of painful stimuli.

Akinetic mutism or abulic state describes a patient who shows long delays between any stimulus, such as a pinch or a question, and a reaction. Movement and speech are markedly deficient, but spontaneous visual tracking always is intact.[69] Abulia denotes a form of this disorder of lesser severity. The slowness applies to verbal output as well as motor response. This is considered to be the opposite of ebullience, and in severe cases is called akinetic

Table 8. Glasgow Outcome Scale Score

CATEGORY	DESCRIPTION
1	Dead
2	Vegetative state: No meaningful responsiveness; cannot obey simple commands or communicate
3	Severe disability: Dependent on others for daily activities; cannot function independently because of significant physical or cognitive impairment
4	Moderate disability: Able to function independently but cannot return to preinjury level of functioning because of physical or cognitive deficits.
5	Good recovery: Able to resume all preinjury functions, although slight physical or cognitive impairments may lead to a lower level of functioning.

mutism.[10] This results from frontal lobe disease, and may be caused by underlying disorders such as hydrocephalus, frontal meningioma, cerebral trauma, intracerebral hemorrhages, or cerebral infarctions in the distribution of both anterior cerebral arteries. Investigation includes CT or MRI.

Locked-in syndrome is caused by damage to the corticospinal, corticopontine, and corticobulbar tracts. Since the patient cannot move, this has been misdiagnosed as coma. However, extraocular movements are intact. Testing for this motor function establishes that, in fact, the patient is alert—with implications for what should be said in the patient's presence. Communication may be via eye blinks or vertical eye movement. Causes include high cervical spine transection, spinal cord contusion, infarction or hemorrhage of the pons.[70]

Psychogenic unresponsiveness occurs rarely, and should be diagnosed only after organic causes for coma have been ruled out. A conversion reaction is the most common etiology and occurs in patients with depressive states, neuroses, or hysteric personalities. In this dissociative state, psychological stress is translated into neurologic symptomatology, such as loss of vision, loss of movement, or unresponsiveness. Once true coma has been ruled out, there have been strategies adduced to give the patient a way out of the situation while maintaining his or her dignity.[10]

The Role of Hypothermia in Future Therapy

The induction of moderate hypothermia has improved the outcome of patients successfully resuscitated after a cardiac arrest, even when the patient remains comatose after resuscitation.[71] The target temperature is 32-34° C for 24 hours.[72] One study compared neurologic outcome in patients subjected to hypothermia within 12 hours of return of spontaneous circulation (ROSC) vs. patients maintained at normothermia after ROSC. Threshold neurologic recovery was defined as discharge to home or to a rehabilitation facility. The hypothermic group had a significantly higher percentage of patients who achieved neurologic recovery.[73]

Prognosis for Coma

The ability to assess prognosis and predict outcome has value in making decisions about triage, transfer, and resource utilization. A good clinical outcome generally is defined as moderate disability or good recovery. A poor outcome has grouped severe disability, persistent vegetative state, and death. As many as 30-40% of survivors of severe brain injury will remain in prolonged states of severely reduced consciousness.[69]

In one review of 500 patients who sustained nontraumatic, anoxic brain injury, 16% of patients had a good outcome, 11 % were left with severe disability, and 73% never improved beyond a vegetative state. Of the patients in coma after one week, only 7% improved to a good recovery or moderate disability. None of the patients who were in a coma at two weeks improved beyond severe disability.[74] The Glasgow Outcome Coma Scale categorizes patient functioning into five categories, and generally is applied to patients who have sustained traumatic brain injury (TBI). (*See Table 8.*)[75] Therapy does make a difference in the management of coma. From 1966 to 1991, mortality from severe TBI fell from approximately 50% to 25% without a corresponding increase in the number of patients left with severe disability.[76,77]

A meta-analysis was performed in 1998 of 33 studies, which predicted a poor clinical outcome following anoxic brain injury nearly 100% of the time with:

- no pupillary reaction after 72 hours;
- absent motor response to pain after 72 hours;
- burst suppression or isoelectric pattern on electroencephalogram (EEG) within the first week;
- absence of early cortical responses to median nerve somatosensory evoked potentials within the first week.[78]

The presence of confounding factors, such as intoxication or shock, may make accurate and reliable prediction of outcome impossible in the comatose patient in the emergency setting.

Persistent Vegetative State and Brain Death

Patients in a persistent vegetative state represent those patients who have suffered an anoxic brain injury and who have progressed to a state of wakefulness without awareness. First described in 1972, it currently is defined as patients with:

- no evidence of awareness of self or environment and an inability to interact with others;
- bowel and bladder incontinence;
- hypothalamic and brain stem autonomic function preservation to permit survival with medical and nursing care;
- maintainence of intermittent wakefulness and sleep-wake cycles;
- no evidence of language comprehension or expression;
- no evidence of reproducible, purposeful, or sustained behavioral responses to visual, auditory, noxious, or tactile stimuli;
- possible preservation of cranial nerves and spinal reflexes.[79-81]

Persistent vegetative state is judged to be permanent after three months if from a non-traumatic source. At any given time, there are as many as 10,000-25,000 adult patients and 4000-10,000 children in this category in this country.[82] However, reliable neurologic markers presaging neurologic recovery or failure

to recover have not been identified,[83] and recovery of consciousness has been reported in 37 patients 12 months postinjury who were vegetative at three months.[84]

Brain death is defined as the cessation of cerebral and brain stem function. The patient must be normothermic and non-drugged, with no contributing metabolic derangements.[81] Spinal reflexes may persist, such as the triple flexion response at the hip, knee, and ankle, but there is no respiratory drive. The Uniform Determination of Death Act in the United States mandates irreversible cessation of all functions of the entire brain and brain stem. It has been accepted by 44 states and the District of Columbia.[85] The apnea test requires serial measurement of arterial pCO_2, which can be measured at the bedside. The premise is to document apnea using acute hypercarbia to maximally stimulate the respiratory centers. When a determination of death is made according to accepted medical and legal standards, organs can be harvested for transplantation and life support measures removed.[86]

In some cases patients who meet brain death criteria may be potential organ donors. While death clearly has implications for family members, resource utilization, and organ donation, brain death probably cannot be determined in the ED. Disorders such as hypothermia and barbiturate intoxication can produce a flat EEG. Serum chemistry may give the clinician a sense of poor clinical outcome, for example if serum lactate is greater than 16 mmol/L.[87] Serum concentrations of neuron-specific enolase and S-100 protein have shown promise, but cannot replace clinical evaluation at this time.[88,89]

Conclusions

Disorders of consciousness may be the manifestation of a wide variety of medical and traumatic illnesses. It is incumbent upon the emergency physician to resuscitate these patients aggressively, to identify those with a surgically correctable lesion, to provide supportive medical care, and to rapidly identify those patients who may benefit from surgical intervention.

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Physician CME Questions

101. Confusion represents the inability to maintain a single coherent thought.
   A. True
   B. False

102. Which Glasgow Coma Score has been cited for purposes of defining coma requiring intubation?
   A. Less than 3
   B. 5
   C. Less than 9
   D. 12
   E. 14

103. Reduced consciousness may result from depression of:
   A. The reticular activating system
   B. The right cerebral hemisphere
   C. Both cerebral hemispheres
   D. Small lesions in the pons
   E. A, C, and D are correct.

104. Focal neurologic signs may be present in coma due to:
   A. myxedema.
   B. opiate poisoning.
   C. hypoglycemia.
   D. uremia.
   E. salicylate poisoning.

105. Which of the following may cause coma by disrupting the reticular activating system?
   A. Intrinsic brain stem lesions such as pontine hemorrhage, trauma, degenerative diseases, or tumor
   B. Trauma from torque to the brain stem, as from a sudden blow to the head
   C. Infratentorial lesions such as cerebellar hemorrhage or posterior fossa tumors
   D. Supratentorial pressure from subdural hematoma, intracranial hemorrhage, epidural hematoma, tumor, or brain abscess
   E. All of the above

106. Supratentorial lesions are more common than subtentorial ones as a cause for coma.
   A. True
   B. False

107. In the assessment of whether coma is caused by toxic/metabolic vs. structural pathology, which of the following is true?
   A. Structural lesions generally are diagnosed more urgently because of the possibility of life-saving surgical intervention.
   B. In approximately 15% of cases, coma is caused by structural lesions.
   C. Toxic-metabolic causes require supportive care until a definitive diagnosis is made and appropriate medical therapy can be instituted.
   D. All of the above are true.

108. In the evaluation of the comatose patient, which element of the history would be of *least* significance?
   A. The rate of onset of neurologic or behavioral changes
   B. Any history of trauma or ongoing medical illness, including prescribed and available medications available to the patient
   C. Suicidal ideation, past attempts at self-harm, and any history of substance abuse
   D. Family history of hypertension or heart disease
   E. The setting in which the patient was found

109. In the evaluation of vital signs in the comatose patient, which is *false*?
   A. Hypothermia is suggestive of sepsis, hypothyroidism, hypoglycemia, or environmental exposure.
   B. Hyperthermia or hyperpyrexia is suggestive of CNS infection, sepsis, serotonin syndrome, neuroleptic malignant syndrome, heat stroke, thyrotoxicosis, stroke, or exposure to certain toxins.
   C. Bradycardia is suggestive of thyrotoxicosis or exposure to sympathomimetic agents.
   D. Systolic blood pressure of over 200 mmHg, with a diastolic of over 130 mmHg is suggestive of intracranial hemorrhage, thyrotoxicosis, or exposure to sympathomimetic agents.
   E. Slow respiratory rate suggests opiate or sedative-hypnotic poisoning.

110. In the evaluation of the eyes of a comatose patient, which of the following is/are true?
   A. Pupillary abnormalities or focal neurologic findings suggest an intracranial cause for coma.
   B. A unilateral fixed, dilated pupil may be a sign of brain herniation, with the causative mass usually on the same side as the pupillary abnormality.
   C. Pupillary reflexes can be tested in the same manner as in an awake person.
   D. Pinpoint pupils may result from opiates other than meperidine or from pontine lesions.
   E. All of the above are true.

In Future Issues:

CNS Manifestations of Drug Toxicity

Emergency Medicine Reports CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- be educated about how to correctly perform necessary diagnostic tests;
- take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;
- apply state-of-the-art therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed;
- understand both likely and rare complications that may occur;
- and provide patients with any necessary discharge instructions.

CME Answers

101. B	106. A
102. C	107. D
103. E	108. D
104. C	109. C
105. E	110. E

CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to evaluate their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. *After completing this activity, you must complete the evaluation form that will be provided at the end of the semester and return it in the reply envelope provided to receive a certificate of completion.* When your evaluation is received, a certificate will be mailed to you.

Emergency Medicine Reports
The Practical Journal for Emergency Physicians

Coma: Patient Evaluation and Management

Glasgow Coma Scale

EYE OPENING	TALKING	MOTOR	SCORE
Does not open eyes	Makes no noise	No motor response to pain	1
Opens eyes with pain	Moans, makes unintelligible sounds	Exterior response (decerebrate)	2
Opens eyes with loud verbal command	Talks, but nonsensical	Flexor response (decorticate)	3
Opens eyes on own	Seems confused, disoriented	Moves part of body but does not remove noxious stimulus	4
	Alert and oriented	Pushes away noxious stimulus	5
		Follows simple motor commands	6

Swedish Reaction Level Scale (RLS85)

SCORE	DESCRIPTION
1	**Alert—**No delay of response
2	**Drowsy or confused—**Responsive to light stimulation
3	**Drowsy or confused—**Responsive to strong stimulation **Mental responsiveness—**At least one of the following: words, orienting, eye movements, obeying of commands, warding off pain
4	**Unconscious—**Localizes but does not ward off pain
5	**Unconscious—**Withdrawing movements on pain stimulation
6	**Unconscious—**Stereotyped flexion movements on pain stimulation
7	**Unconscious—**Stereotyped extension movements on pain stimulation
8	**Unconscious—**No response to pain stimulation

Glasgow Outcome Scale Score

CATEGORY	DESCRIPTION
1	Dead
2	Vegetative state: No meaningful responsiveness; cannot obey simple commands or communicate
3	Severe disability: Dependent on others for daily activities; cannot function independently because of significant physical or cognitive impairment
4	Moderate disability: Able to function independently but cannot return to preinjury level of functioning because of physical or cognitive deficits.
5	Good recovery: Able to resume all preinjury functions, although slight physical or cognitive impairments may lead to a lower level of functioning.

Clinical Clues in Differentiating Brain Stem and Hemispheric Coma

	BRAIN STEM COMA	HEMISPHERIC COMA
TYPE OF UNRESPONSIVENESS		
	Looks asleep	Looks awake (i.e., eyes open)
BODILY POSITION		
	Looks unnatural	Looks natural (i.e., appears to be a comfortable posture)
RESPIRATION		
	Apneustic or ataxic	Normal or Cheyne-Stokes
SPONTANEOUS REFLEXES		
	Yawning or sneezing not seen Coughing, swallowing, or hiccuping does not rule out brain stem coma	Yawning or sneezing may be seen
PUPILLARY FUNCTION		
	Tends to be abnormal (e.g., unilateral fixed, dilated pupil)	Pupils tend to show normal responsiveness to light
EYE MOVEMENT		
	Caloric testing elicits no response Spontaneous roving conjugate movements indicate brain stem disinhibition due to hemispheric coma	Caloric testing reveals slow phase without fast phase

Causes of Abnormal Ventilation in Unresponsive Patients

I. HYPERVENTILATION

- **A. Metabolic acidosis**
  - 1. High anion gap
    - • Diabetic ketoacidois
    - • Hyperglycemic hyperosmolar non-ketotic coma
    - • Lactic acidosis
    - • Uremia
    - • Alcoholic ketoacidosis
    - • Acid poisons: Ethylene glycol, methyl alcohol, paraldehyde, salicylates
    - • Other toxins: Iron, toluene, INH (isoniazid)
  - 2. No anion gap
    - • Diarrhea
    - • Pancreatic drainage
    - • Carbonic anhydrase inhibitors
    - • Acetazolamide, NH4 CI ingestion
    - • Renal tubular acidosis
    - • Ureteroenterostomy
    - • Hypoaldosteronism
- **B. Respiratory alkalosis**
  - • Hepatic failure
  - • Sepsis
  - • Pneumonia
  - • Anxiety (hyperventilation syndrome)
- **C. Mixed acid-base disorders (metabolic acidosis and respiratory alkalosis)**
  - • Salicylate overdose
  - • Sepsis
  - • Hepatic failure

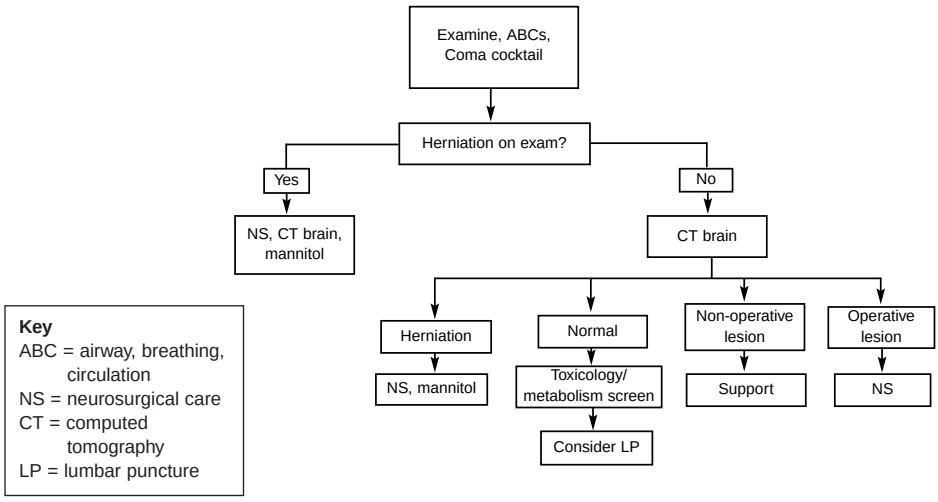
II. HYPOVENTILATION

- **A. Acute (uncompensated)**
  - • Sedative drugs
  - • Opiate poisoning
  - • Brain stem injury
  - • Neuromuscular disorders
  - • Chest injury
  - • Acute pulmonary disease
- **B. Chronic pulmonary disease**

Marshall Classification System for Cranial CT Imaging in Patients with Traumatic Brain Injury

CATEGORY	DEFINITION
Diffuse Injury I	No visible pathology on cranial CT scan
Diffuse Injury II	Cisterns are visible with midline shift 0-5 mm, and/or 1. lesion densities present; 2. high- or mixed-density, lesion present, but < 25 mL in volume; 3. bone fragments or foreign bodies present
Diffuse Injury III	Cisterns compressed or absent with midline shift 0-5 mm, no high- or mixed-density lesions > 25 mL in volume
Diffuse Injury IV	Midline shift > 5 mm, no high- or mixed-density lesions > 25 mL in volume
Evacuated mass lesion	Any lesion surgically evaluated
Nonevacuated mass lesion	High- or mixed-density lesion > 25 mL, not surgically evacuated

Shortened Coma Protocol



Etiologies of Coma

BILATERAL HEMISPHERAL DYSFUNCTION

Neuronal damage caused by deprivation of oxygen, glucose, or metabolic cofactor
Hypoxia of any cause; pulmonary disease, methemoglobinemia
Anemia
Shock state with decreased cerebral flow
Post-cardiac arrest
Cellular toxins: carbon monoxide, cyanide, hydrogen sulfite
Hypoglycemia
Thiamine deficiency (Wernicke's syndrome)

Endogenous CNS toxins

Hyperammonemia, hepatic coma
Postureterosigmoidostomy
Uremia
Hypercarbia, CO_2 narcosis
Hyperglycemia

Exogenous CNS toxins

Alcohols: ethanol, isopropyl alcohol methanol, ethylene glycol
Paraldehyde
Salicylates
Sedatives—hypnotics, narcotics, tranquilizers
Hallucinogens; LSD mescaline, phencyclidine
Anticonvulsants
Psychotropic, lithium, monamine oxidase inhibitors
Isoniazid
Heavy metals
Anti-cholinergics, including cyclic depressants
Bromides
Gamma hydroxy butyrate

Endocrine disorders

Myxedema coma, thyrotoxicosis
Hyperglycemic hyperosmolar state
Addison's disease, Cushing's disease, pheochromocytoma

Abnormalities of ionic environment of CNS

Hyponatremia, hypernatremia
Hypocalcemia, hyperkalemia
Hypomagnesemia, hypermagnesemia
Hypophosphatemia
Acidosis, alkalosis

Environmental disorders and disordered temperature regulation

Hypothermia
Heat stroke
Neuroleptic malignant syndrome, serotonin syndrome
Malignant hyperthermia

Intracranial hypertension

Hypertensive encephalopathy
Pseudotumor cerebri

CNS inflammation or infection

Meningitis
Encephalitis
Encephalopathy
Cereral vasculitis, cerebral malaria
Fat embolism
Disseminated intravascular coagulation
Subarachnoid hemorrhage
Carcinoid meningitis
Overwhelming sepsis

Primary neuronal or glial disorders
Creutzfeldt-Jakob disease
Progressive multifocal leukoencephalopathy
Seizures and postictal state

FOCAL CNS LESIONS

Subtentorial lesions

- Compressive
- Cerebellar hemorrhage
- Posterior fossa subdural or exradural hemorrhage
- Cerebellar infarct
- Cerebellar tumor

Cerebellar Abscess

- Basilar aneurysm
- Destructive
- Pontine hemorrhage
- Basilar migraine
- Brain stem demyelination
- Supratentorial Lesions
- Trauma: Subdural hematoma
  Epidural hematoma

Intracerebral bleed

- Postictal
- Bilateral cerebral disease
- Unilateral cerebral disease withherniation
- Infarction: thrombotic, embolic
- Non-traumatic hemorrhage, including pituitary apoplexy
- Tumor
- Abscess
- Hypertensive encephalopathy
- Subarachnoid hemorrhage
- Encephalitis
- Meningitis
- Trauma with diffuse axonal injury
- Venous occlusion with infarction
- Increased intracaranial pressure

Pertinent Physical Examination in the Comatose Patient

AREA	FINDINGS	COMMENT/INTERPRETATION
Vital signs	Blood pressure—hypotension	Decreased perfusion can result in depressed mental status Suggests hypovolemic, cardiogenic, or septic shock
	Blood pressure—hypertension	Systolic pressures > 200 mmHg, diastolic > 130 mmHg suggests intracranial hemorrhage, thyrotoxicosis, exposure to sympathomimetic agents, hypertensive encephalopathy. Intracranial hemorrhage is the first consideration.
	Respiratory rate—tachypnea	A sign of hypoxemia, brain stem herniation, or metabolic acidosis
	Respiratory rate—bradypnea	Associated with opiate or sedative-hypnotic poisoning
	Respiratory pattern	Look for CSR, CNH, ataxic or Biot's breathing
Airway	Ensure patency and protection; breath odor may suggest cause	Essential examination to anticipate need for airway management Unique breath odors: alcohol, fetor hepaticus, ketones, uremia
Skin	Cyanosis, pallor, jaudice, petechiae/ purpura, surgical scars, needle tracks	Full exposure necessary to look for wide variety of visual clues
Head	Palpation for trauma, previous craniotomy, or ventricular shunt	External injury may reflect acute internal damage or prior hematoma, tumor, or hydrocephalus.
ENT	Signs of infection, hemotympanum, tongue lacerations	May reveal signs of meningitis, basilar skull fracture, or recent seizure
Eyes	Pupillary changes	May be significant in identifying brainsteam dysfunction from structural cause; reactivity usually preserved in metabolic causes
	Eye movement	Conjugate roving eye movement connotes intact brain stem. Oculocephalic testing may assist in locating level of structure damage.
	Funduscopy	Papilledema, subhyaloid hemorrhage, findings of HTN or DM
Neck	Rigidity	Assess after cervical spine clearance (historical or imaging) Nuchal rigidity is meningitis or SAH until proven otherwise.
Lung	Varied	Findings consistent with acute or chronic hypoxia source or acute infection.
Cardiovascular	Varied	Possible murmurs (embolic), dysrhythmias (cerebral perfusion pressure); AI murmur may accompany aortic dissection
Neurologic	Level and content of consciousness	
	Posture	Posture (decorticate, decerebrate) may indicate neurologic level of injury.
	Movement	Movement—specifically looking for purpose (e.g., protective) and asymmetry and spontaneous patterns (e.g., subtle seizure activity)
	Deep tendon reflexes	Reflect spinal cord function; asymmetry may be useful

Key: CSR = Cheyne-Stoke's respiration; CNH = central neurogenic hyperventilation; ENT = ear, nose, and throat; HTN = hypertension; DM = diabetes mellitus ; SAH = subarachnoid hemorrhage

Supplement to *Emergency Medicine Reports*, May 19, 2003: "Coma: A Systematic Approach to Patient Evaluation and Managment."
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From Stingers to Fangs: Evaluating and Managing Bites and Envenomations

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Significant numbers of bites and envenomations occur annually,[1] with bites and stings by arthropods accounting for about one-third of these. Surprisingly, the order Hymenoptera, which includes bees, wasps, and ants, is the source of most deaths from envenomations in the United States. Whether the creature inflicts a bite or sting that results in an anaphylactic reaction, impressive local effects, or a life-threatening systemic reaction, the emergency physician must be able to institute appropriate and effective treatment. Emergency physicians also must be able to recognize clinical envenomation patterns, since some critically ill patients may not be able to convey the details of the "attack." Since all areas of the country are represented in the envenomation statistics, all emergency physicians should be familiar with identification and stabilization of envenomated patients and know what resources are available locally for further management of these often complicated patients.

—The Editor

Snakes

Approximately 8000 bites from poisonous snakes occur each year in the United States, resulting in 5-15 deaths annually.[1-6] Venomous snakes are found in virtually every state. Two snake families, Elapidae (coral snakes) and Viperidae (pit vipers), are found in the United States. Snakes in the Viperidae family, subfamily Crotalidae, include the rattlesnakes, copperheads, and moccasin snakes. This group accounts for about 90-95% of poisonous snakebites, with coral snakes accounting for 2-3% of bites and exotic snakes accounting for 3-5% of bites.[1,2] This report will concentrate on management of the crotalid snakebites.

Pit vipers have a number of characteristic features that distinguish them from other snakes. *(See Figure 1 a-b.)* A pit is located on each side of the head between the eye and nostril and contains heat-sensitive organs that assist in localizing prey. The pupils generally are elliptical and vertical in nature, as opposed to the round pupil of a harmless snake. The head of a pit viper usually is triangular in shape, not round or narrow. A pair of long-hinged fangs are folded against the palate and move forward when the snake strikes.

Epidemiology. Snakes are poikilothermic and are most active during warm weather and in the daylight. Most bites occur between April and October. Males are bitten more frequently than females (9:1).[1,2,5] Bites occur most often on the extremities, with upper extremities more common in adults (85% of bites) and lower extremities affected more frequently

in children (70%).[7-9] More than half of bites occur when a person is purposely handling a known venomous snake.[10]

The venom is a complex mixture of enzymes that function to immobilize, digest, and kill the snake's prey. Proteolytic enzymes, hyaluronidase, phospholipase, and thrombin-like enzymes contribute to the local and systemic effects seen following an envenomation.

Clinical Manifestations. The clinical presentation of envenomation is variable, depending on the type of snake, site of bite, host factors, and amount of venom injected. Up to 20-25% of bites may be described as "dry" with no envenomation taking place.[3] Pit viper envenomation may cause both local and systemic symptoms. Intense, burning pain is seen at the bite site in most cases of envenomation. One or more puncture marks from fangs frequently are noted. *(See Figure 2.)* Edema occurs at the bite site and progresses at various rates, depending on the amount of venom injected. Erythema and ecchymosis often are noted. Over time, fluid-filled or hemorrhagic bullae may form and eventually lead to necrosis. Extremities, especially digits, may become extremely swollen and tense, leading to possible vascular compromise.[3,5,11-14]

Tender regional lymph nodes may be the first systemic sign of envenomation. Other signs include nausea, vomiting, perioral numbness, metallic taste in the mouth, muscle fasciculations, weakness, bleeding, hypotension, and shock. A Snakebite Severity Score has been developed and validated based on symptoms and signs in six areas: local wound, pulmonary, cardiovascular, gastrointestinal, central nervous system, and hematologic system.[15] *(See Table 1.)* Death is an infrequent occurrence, and the patients frequently present with signs of severe massive systemic effects, suggesting direct venous injection of the venom. Anaphylaxis to the venom also may occur, especially in victims of previous bites, because of prior sensitization and development of IgE antibodies to venom.[4,5,11,16,17] Laboratory evaluation frequently reveals a consumptive coagulopathy and thrombocytopenia. Fibrin degradation products often are elevated and PT and PTT are prolonged. Fibrinolysis is caused by snake venom activation of plasminogen and direct fibrinolysis.

Management. *Pre-hospital Care.* Pre-hospital treatment of snakebite victims, whether by medical personnel or lay bystanders, is the subject of much folklore and controversy. Many traditional first-aid measures actually have been proven to be of little benefit or even harmful to the patient.[11,18] Pre-hospital care of snakebite victims should include assessment and maintenance of the "ABCs" (airway, breathing, and circulation); minimization of systemic venom effects without increasing the risk of local tissue damage; and rapid transport to a facility where definitive treatment can take place.

Several first aid measures recommended in the past that no longer are advised include cryotherapy, incision and suction, and electric shock. Cryotherapy involved packing or immersing the bitten extremity in ice or ice water. It was believed that this lowered enzyme activity and slowed absorption. However, no significant benefit has been noted in studies, and harmful effects (such as tissue loss or amputation) have been seen.[18,19]

Incision and suction of the bite is controversial. Incision potentially can damage deeper structures, especially in the hand or neck.[8,20] Oral suction increases the risk of infection. One device made for mechanical suction of snakebites is the Sawyer Extractor. Both animal and human studies have shown a minimal amount of venom recovered using this device with skin necrosis noted in one study.[20-24] This therapy only could be recommended if applied within minutes of envenomation in a victim who is more than 30-40 minutes away from definitive care.

Electric shock therapy use has been reported since 1986, when high-voltage, low-amperage electric shock was used to treat a variety of bites and stings in native South Americans.[25] No animal models support the use of electric shock.[18,24,25] Significant complications, such as burns, seizures, and myocardial infarction, have been reported.[27]

Currently, the most controversial first aid measure is the use of a constricting band to slow systemic absorption of venom. Arterial tourniquets no longer are used because of the potential

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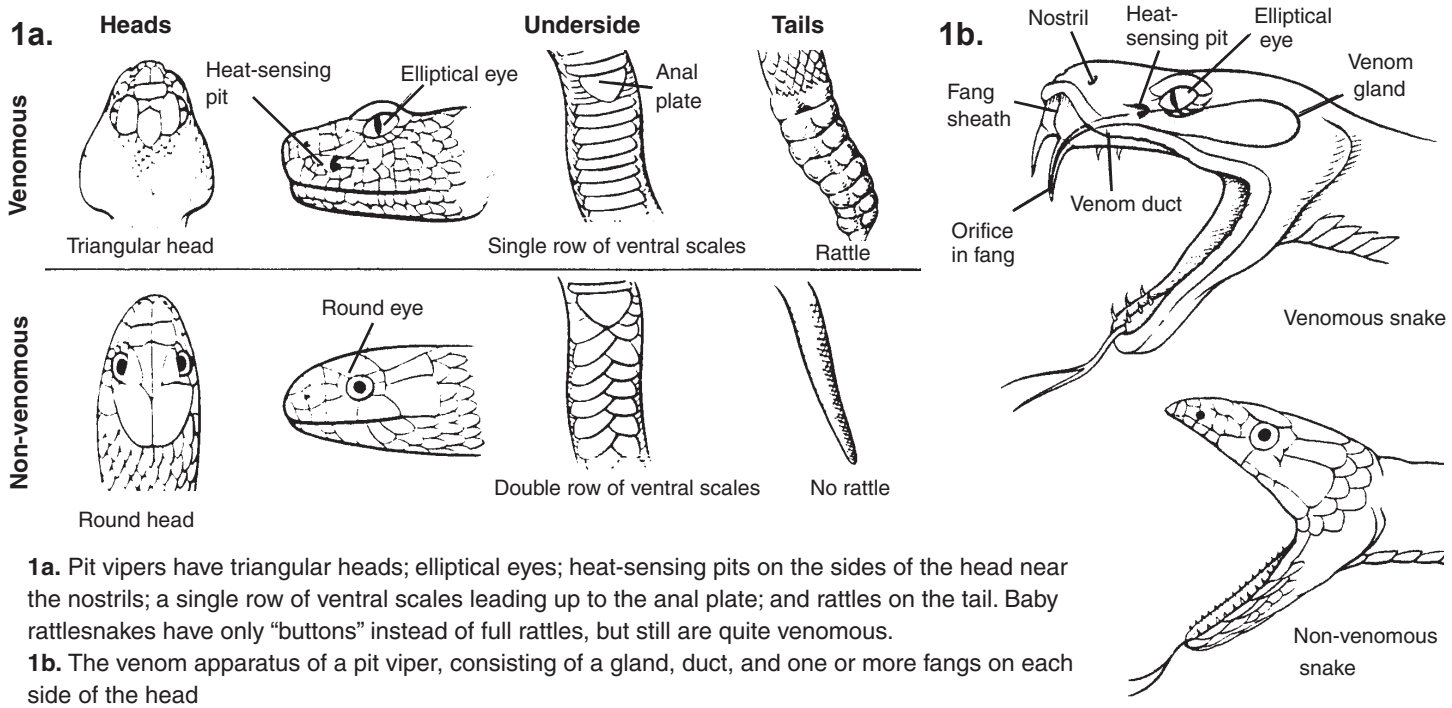
Figure 1a-b. Identification of Poisonous Pit Vipers



1a. Pit vipers have triangular heads; elliptical eyes; heat-sensing pits on the sides of the head near the nostrils; a single row of ventral scales leading up to the anal plate; and rattles on the tail. Baby rattlesnakes have only "buttons" instead of full rattles, but still are quite venomous.
1b. The venom apparatus of a pit viper, consisting of a gland, duct, and one or more fangs on each side of the head

Adapted from: Sullivan JB Jr., Wingert WA, Norris RL Jr. North American venomous reptile bites. *Wilderness Medicine.* 3rd ed. St. Louis:Mosby;1995:684,685.

for limb ischemia.[8] A constricting band is a wide (2-4 cm), flat band that is applied tight enough to occlude superficial veins and lymphatics but loose enough to admit one or two fingers between the band and the extremity to permit deep venous and arterial flow. It has the advantage of delaying the onset of systemic toxicity until antivenin can be given.[28] However, some animal studies have shown that keeping the venom at the bite site may worsen the local necrosis.[28,29] They also show the potential for "bolus effect" of venom into the systemic circulation, leading to rapid deterioration of the patient.[28,30] For now, recommendations for the use of a constricting band would include severe or progressive envenomation in a patient with a prolonged transport time.

While patients are being transported, all nonessential movement should be minimized.[18] The extremity should be splinted in a position of comfort, and constrictive clothing and jewelry should be removed.

Intravenous access should be obtained, vital signs monitored, and parenteral analgesia given if needed. The patient should not be given anything to eat or drink, supplemental oxygen therapy should be administered. Hypotension during transport should be treated vigorously with crystalloid fluid therapy.[11,14,18]

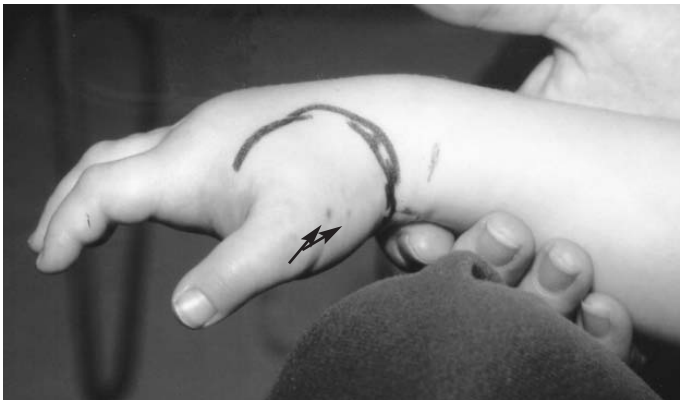
Emergency Department Management. Once again, assessment and maintenance of ABCs should take place on patient arrival in the emergency department (ED). At least one large-bore intravenous line should be started. Recommended laboratory studies are listed in Table 2.[7,12,14] Tetanus status should be determined and updated if needed. Progression of the swelling should be monitored and documented. Antivenin therapy is the mainstay of medical management for moderate to severe envenomations. Surgery may be required in carefully selected patients. Prophylactic antibiotics currently are not recommended.[7,11,31-34] Patients with minimal envenomation may be observed for six hours and sent home if there is no progression of symptoms. All others should be admitted to the hospital, and most should be admitted to an intensive care setting.[11,14,35,36]

Antivenin Therapy. Antivenin administration is the mainstay of medical management of venomous snakebites.[5,8,14] Antivenin (Crotalidae) Polyvalent (ACP) was introduced in 1954 and was the only antivenin available until October 2000. At that time, Crotalidae Polyvalent Immune Fab antivenin (FabAV) was approved for use.[37,38]

ACP is derived from horse serum and carries with it the risk of immediate hypersensitivity reactions, estimated to occur in up to 33% of patients.[8,39,40,41] Doses greater than 10 vials are associated with an almost 100% incidence of serum sickness.[39,40,41] Although ACP has been in use for decades for treating crotalid snakebites, no prospective, randomized trials have been performed.

Indications for administration of antivenin include a progressive venom injury (worsening local injury), coagulation abnormalities, or systemic effects of the envenomation.[11,14,40] Antivenin administration is expected to reverse the coagulopathy and systemic effects and prevent further local injury.[5,7,8,37,42] It currently is recommended that bites from copperheads, the least toxic species of crotalids, not be treated with ACP.[11,43-45] With the increased use and availability of FabAV, this restric-

Figure 2. Copperhead Snakebite



Hand of an 18-month-old child bitten near the thumb *(see arrows)* by a small copperhead snake. Note two fang marks and large amount of swelling.

tion may be reconsidered, as local swelling may be severe.

Dosage of ACP has been based on severity of envenomation. In general, 0-5 vials are used for minimal envenomation, 10-15 vials for moderate envenomation, and 15-20 vials for severe envenomation.[14,46] The patient then is reassessed and additional vials administered when indicated.[14,40,47]

ACP is diluted in a crystalloid solution, depending on the desired amount of volume to be infused. After skin-testing, a small amount of the antivenin is infused slowly, monitoring for anaphylactic reactions. If no adverse reactions occur, the rate of the infusion is increased to deliver the initial antivenin dose during approximately a two-hour period. Anaphylactic reactions are treated in the standard manner.[14,47]

FabAV is produced by immunizing sheep with crotalid snake venom. The serum then is digested, using papain to produce antibody fragments (Fab and Fc). Fc is more immunogenic and is eliminated during the purification process.[37] When initially tested in animals, FabAV was found to be 5.2 times more potent than ACP against crotalid snake venoms.[46] Acute hypersensitivity rates are reported at 20%, with a 23% incidence of serum sickness.[37,40,42,48]

Prospective trials of FabAV have been done and continue to be performed. An initial study of 11 patients who received 4-8 vials of FabAV showed resolution of symptoms with no allergic reactions.[37] However, recurrence of limb swelling and coagulation defects was noted in 27% of these patients. A study done shortly thereafter used a different dosing schedule.[42] Patients initially were treated with six vials of FabAV, and a repeat dose given if needed. They then were randomized to a scheduled group that received two-vial treatments at 6, 12, and 18 hours after initial dose, or to an "as-needed" group. Total dosages were similar in the two groups, with no symptoms recurring in the scheduled group.

Recurrence is described as local or coagulopathy recurrence. Patients with an initial coagulopathy are more likely to experience a recurrence.[49] Recurrence is thought to be due to a number of factors, including failure to neutralize all venom initially and the more rapid clearance of unbound Fab in relation to venom components.[49,50]

Newer recommendations for FabAV administration include an initial dose of 4-6 vials, repeated once for initial control.[11,42,49] Additional two-vial dosages should be scheduled at 6, 12, and 18 hours. All patients should be re-evaluated at least once during the first five days post-treatment. Those with initial coagulation abnormalities should be reassessed approximately every 48 hours until parameters are stable. Retreatment with FabAV may be indicated for recurrence of the coagulopathy.[11,49]

Surgical Management. Several surgical techniques have been used in the management of snakebite victims. The most common ones are incision therapy, excision of the bite site, fasciotomy, and digit dermatomy. Many of these techniques were used in the early management of snakebites to address the issues of tissue necrosis, decreased function, and limb loss,[51-54] in attempts to avoid the risk of antivenin-caused anaphylactic reactions.[39] No randomized, controlled, clinical trials exist comparing surgical procedures to appropriate use of antivenin.[55] A number of studies have shown good functional outcome with minimal or no surgical intervention in patients treated with early, adequate, intravenous antivenin.[5,56-58] With the development and availability of better antivenin products, surgical therapy now is used only in a few carefully selected patients.[55]

Excision of the bite site was used in the hope that significant amounts of venom could be removed.[51] Excisional techniques range from local excision of a subcutaneous "plug" of tissue, to opening an entire extremity and removing all hemorrhagic tissue.[38,51] There is no experimental data to support excision used in this way. It is recommended that debridement of hemorrhagic blebs or frankly necrotic skin take place 3-5 days after the bite occurs.[8,55]

Fasciotomy often has been advocated as primary treatment of crotalid snakebites in the assumption that compartment syndrome is a common complication of the envenomation. The local and systemic toxic effects of crotalid venom mimic the signs and symptoms of compartment syndrome.[55] Massive local edema often is present after a snakebite. This edema, however, generally is confined to the subcutaneous tissue, and rarely is associated with elevated compartment pressures.[59] The only way to determine whether a compartment syndrome exists is to measure intracompartmental pressure.[53,55,56] In cases in which compartment syndrome has developed, use of antivenin has been shown to resolve the majority of them.[11,60,61] It would seem appropriate to proceed to fasciotomy only in those patients with persistently elevated compartment pressure even after antivenin administration.

The finger is an area with limited capacity for edema. Currently, there is no accurate method for measuring compartment pressure in the finger, so a clinical diagnosis is used. A finger that is tense, blue, or pale with absent or poor capillary refill time is a candidate for a digit dermatomy.[53,55] This technique consists of a longitudinal incision through the skin only on the medial or lateral aspect of the digit, extending from the web to the mid-portion of the distal phalanx.[53] This is done using local anesthesia, and

Table 1. Snakebite Severity Score

CRITERION	POINTS
PULMONARY SYSTEM	
No symptoms/signs	0
Dyspnea, minimal chest tightness, mild or vague discomfort, or respirations of 20-25 breaths/min	1
Moderate respiratory distress (tachypnea, 26-40 breaths/min; accessory muscle use)	2
Cyanosis, air hunger, extreme tachypnea, or respiratory insufficiency/failure	3
CARDIOVASCULAR SYSTEM	
No symptoms/signs	0
Tachycardia (100-125 beats/min), palpitations, generalized weakness, benign dysrhythmia, or hypertension	1
Tachycardia (126-175 beats/min), or hypotension, with systolic blood pressure > 100 mmHg	2
Extreme tachycardia (> 175 beats/min), hypotension with systolic blood pressure < 100 mmHg, malignant dysrhythmia, or cardiac arrest	3
LOCAL WOUND	
No symptoms/signs	0
Pain, swelling, or ecchymosis within 5-7.5 cm of bite site	1
Pain, swelling, or ecchymosis involving less than half the extremity (7.5-50 cm from bite site)	2
Pain, swelling, or ecchymosis involving half to all of extremity (50-100 cm from bite site)	3
Pain, swelling, or ecchymosis extending beyond affected extremity (> 100 cm from bite site)	4
GASTROINTESTINAL SYSTEM	
No symptoms/signs	0
Pain, tenesmus, or nausea	1
Vomiting or diarrhea	2
Repeated vomiting, diarrhea, hematemesis, or hematochezia	3
HEMATOLOGIC SYMPTOMS	
No symptoms/signs	0
Coagulation parameters slightly abnormal: PT 20 sec; PTT 50 sec; plts 100-150,000/mL; or fibrinogen 100-150 mcg/mL	1
Coagulation parameters abnormal: PT 20-50 sec; PTT 50-75 sec; plts 50-100,000/mL; or fibrinogen 50-100 mcg/mL	2
Coagulation parameters abnormal: PT 50-100 sec; PTT 75-100 sec; plts 20-50,000/mL; or fibrinogen < 50 mcg/mL	3
Coagulation parameters markedly abnormal, with serious bleeding or the threat of spontaneous bleeding; unmeasurable PT or PTT; plts < 20,000/mL; or undetectable fibrinogen; severe abnormalities of other laboratory values also fall into this category	4
CENTRAL NERVOUS SYSTEM	
No symptoms/signs	0
Minimal apprehension, headache, weakness, dizziness, chills, or paresthesia	1
Moderate apprehension, headache, weakness, dizziness, chills, paresthesia, confusion, or fasciculation in area of bite site	2
Severe confusion, lethargy, seizures, coma, psychosis, or generalized fasciculation	3

Note: Points are assessed on the basis of manifestations caused by the venom itself (antivenin reactions not included). Total score ranges from 1 to 20. A higher score indicates more severe effects.

Key: **PT** = prothrombin time; **PTT** = partial thromboplastin time; **plts** = platelet count

Adapted from Dart RC, Hurlbut KM, Garcia R, et al. Validation of a severity score for the assessment of crotalid snakebite. *Ann Emerg Med* 1996;27:321-326.

the wound heals by secondary intention. This technique should not be used routinely in all finger bites, nor should it be used prophylactically to prevent a digital compartment syndrome.[55]

Spiders

Spiders are in the class Arachnida, part of the phylum Arthropoda. All spiders are carnivores and have fangs that they use to deliver venom to their prey. Most fangs are not strong enough to penetrate human skin. Only two clinically important spiders are found in the United States: the brown recluse and the black widow. These two spiders accounted for about 6% of reported bites and envenomations in 2000.[1]

Brown Recluse. Brown recluse spiders (Loxosceles) are found in most of the United States, but are most common in the

Table 2. Recommended Laboratory Studies in Crotalid Envenomation

Complete blood count
• Platelet count
PT/PTT
• Fibrinogen and fibrin split products
Electrolytes
• Blood urea nitrogen, creatinine
Creatine phosphokinase
• Blood type and crossmatching
Urinalysis

Table 3. Systemic Effects of Brown Recluse Spider Bite

- Fever
- Nausea
- Vomiting
- Arthralgias
- Myalgias
- Rashes
- Hemolysis
- Thrombocytopenia
- Hemorrhage
- Intravascular renal failure

Table 4. Unproven Treatments for Brown Recluse Spider Bites

- Corticosteroids
- Antibiotics
- Dapsone
- Early excision of the bite
- Hyperbaric oxygen therapy
- Cyproheptadine
- Topical nitroglycerin
- Anti-Loxosceles Fab fragments
- Debridement and skin grafting

midwestern and southern states.[62] They are found in woodpiles, sheds, garages, and closets. They also can hide in bedding and piles of clothing. The brown recluse generally is nonaggressive except when threatened or trapped against the skin of a victim.

The spider averages about a centimeter in length and often is light brown to tan in color. There is a distinctive, dark, violin-shaped mark on the dorsal aspect of the cephalothorax. In contrast to most spiders, the brown recluse has six eyes rather than eight.

The venom contains several different enzymes and proteins. Sphingomyelinase D is the enzyme that is most active and the cause for the majority of toxic effects.[62] It is cytotoxic to both endothelial cells and red blood cells.[63] The tissue necrosis is thought to be due to the induction of endothelial disruption, intravascular hemolysis, platelet aggregation, and thrombus formation by sphingomyelinase D. Polymorphonuclear leukocyte-induced vasculitis also contributes to the tissue necrosis.

Clinical Presentation. The bite initially may go unnoticed, but often is accompanied by a mild burning sensation that worsens over several hours.[12,64,65] Pruritus, pain, and erythema occur, as well as a central blister at the bite site. The initial skin lesion then increases in size and develops a purplish discoloration over the next several hours to days.[65] As necrosis continues, the lesion develops into an ulcer of variable size. Extremities are the sites most often affected.[65,66]

Systemic signs and symptoms of envenomation occur in up to 40% of patients, and may include fever, nausea, vomiting, arthralgias, myalgias, and rashes.[62,64,65] Children are more likely to develop hemolysis, thrombocytopenia, hemorrhage, and renal failure.[12,67] Death is rare. *(See Table 3.)*

Management. There currently are no specific tests to diagnose brown recluse spider envenomation, making the definitive diagnosis difficult. Laboratory tests that should be assessed, especially if systemic signs are present, include complete blood count, platelet count, coagulation studies, electrolytes, blood urea nitrogen, creatinine, and urinalysis.[12,64]

All wounds should be cleaned thoroughly and tetanus administered if needed. Other measures should include elevation of the bitten extremity and the judicious use of analgesics.

A variety of treatments have been tried, including corticosteroids, antibiotics, dapsone, early excision of the bite, and hyperbaric oxygen therapy.[68-78] No randomized, controlled studies exist supporting any of these therapies. Animal studies evaluating additional therapies, such as cyproheptadine and topical nitroglycerin, have shown no benefit.[71,79,80] Dapsone, in particular, should be avoided in children as it can lead to methemoglobinemia and hemolysis. *(See Table 4.)*

Animal studies using intradermally administered anti-Loxosceles Fab fragments have shown promise in inhibiting venom-induced inflammation.[81-83] Further research, including human studies, is needed.

If hemolysis occurs, it is important to maintain good urine output. The urine should be alkalinized with the intravenous administration of sodium bicarbonate to keep the urine pH greater than 7. Close monitoring of renal function and hematocrit is important.

Debridement and skin grafting may be necessary if large areas of necrosis are present, but should be delayed until the area clearly has been demarcated.[64,78] In general, skin lesions heal in weeks to months, depending on the size.

Patients with systemic symptoms should be admitted for further monitoring.

Black Widow. Black widow spiders (Latrodectus) are found throughout North America, with the exception of Alaska.[64] They can be found in attics, barns, storage sheds, garages, firewood, hay bales, and outhouses. They also may hide in clothing and shoes, with about 15% of bites occurring while the victim dresses.[84] There are fewer bites from the black widow than the brown recluse.

In the United States, the spider is shiny black, with a red hourglass marking on the abdomen. The female is about 3-4 cm in diameter, and the male is about one-quarter this size. Only the female has fangs large enough to penetrate human skin. The black widow spider has eight eyes and legs.

The venom produced by this spider is one of the most potent venoms known.[85] Although it lacks a tissue toxin, minimizing local effects, it has a potent neurotoxin, alpha-latrotoxin. Its primary site of action is the neuromuscular junction. The venom causes release and inhibits the reuptake of acetylcholine and norepinephrine, resulting in overstimulation of the motor endplate.[86-88]

Clinical Presentation. The bite of the black widow may be painless or present as a pinprick sensation. The majority of bites occur on the extremities.[84] Regional lymph nodes become tender during the next 30 minutes to two hours. Within 1-2 hours, a target lesion may appear at the bite site with some surrounding erythema.[84,89] The hallmark of envenomation is muscle cramping, usually involving the abdomen, chest, and back. This cramping has its onset 30-90 minutes after the bite and peaks in 3-12 hours, with a waxing and waning quality.[84] Autonomic symptoms often include nausea, vomiting, diaphoresis, hypertension, and tachycardia. Death is rare, but hypertension can be life-threatening.[90]

In children, abdominal pain and rigidity are the most common symptoms. There are, however, no peritoneal signs. Marked hypertension is common, as well. Anxiety, agitation, and irritability may be the initial presenting signs, especially in younger children. Grunting and respiratory distress are due to chest and abdominal pain. Weakness, headache, and periorbital edema may be present and persist for days or weeks.[12,84,89-91]

Management. There are no specific tests to diagnose black widow spider envenomation. Laboratory abnormalities rarely occur and are non-specific.[84,89]

As always, the initial priorities should focus on stabilization and maintenance of ABCs, especially in children. All wounds should be cleansed thoroughly and tetanus administered, if indicated. The bitten extremity should be elevated, and a cold compress should be applied.

Treatment is directed at the relief of symptoms. Analgesia is an important component of this treatment. Mild cases may be treated with oral analgesics or narcotics such as codeine or hydrocodone. More severe cases usually require intravenous morphine (0.1-0.2 mg/kg every 2-4 hours). Benzodiazepines such as diazepam, lorazepam, or midazolam can be beneficial in relieving anxiety and providing muscle relaxation through centrally mediated responses. The combination of a narcotic and a benzodiazepine often will alleviate symptoms without further treatment required.[64,89-92]

Calcium gluconate (10%) previously has been used as first-line treatment. Most controlled studies, however, have not shown a benefit to this treatment, and its use has fallen out of favor.[84,90,93]

An antivenin is available for black widow spider envenomations. It generally is indicated only for the severe envenomations that are unresponsive to other treatments.[64,84,89,90,94-96] Indications would include life-threatening hypertension and tachycardia, respiratory difficulty, refractory pain, and high-risk groups such as pediatric patients, pregnant women, and the elderly.[93] One vial of antivenin is diluted in 50-100 mL of normal saline and infused slowly over 30-60 minutes. Rapid, complete resolution of symptoms without relapses is the norm. Administration of the antivenin should be carried out as soon after envenomation as possible, although effective use up to three days after a bite has been reported.[94-96] Immediate hypersensitivity reactions and serum sickness may occur, as the antivenin is derived from horse serum.

Patients with mild symptoms controlled by oral analgesics may be sent home with close follow-up; pain may recur or worsen. Most pediatric patients should be admitted, as well as those patients requiring intravenous analgesics and those exhibiting evidence of hypertension or autonomic symptoms.[64,90,92]

Scorpions

Worldwide, scorpions account for many deaths annually, but in the United States, one death reported in 2000 was the only death reported in the last 30 years.[1] Only one species in the United States, *Centruroides exilicauda*, produces serious toxicity. Otherwise known as the "bark scorpion" because it resides in the bark of trees, this scorpion is found primarily in Arizona and the neighboring southwestern states. It has two pinching claws anteriorly and a tail that ends in a telson. The telson contains a pair of poisonous glands and a stinger. A scorpion grasps its prey with the pincers and stings its victim by arching its tail over its head. Scorpions also may be found in woodpiles, crevices, shoes, and clothing. Most envenomations occur at night.

The venom contains a neurotoxin that is excitatory and affects both autonomic and skeletal neuromuscular systems. Both sympathetic and parasympathetic systems are stimulated.

Clinical Presentation. Most patients will present with only local pain, tenderness, and tingling. Systemic symptoms rarely occur and are more likely to be severe in children.[91,97,98] Sympathetic stimulation may cause tachycardia, hypertension, hyperthermia, diaphoresis, and agitation. Parasympathetic symptoms include hypotension, bradycardia, and SLUDGE (salivation, lacrimation, urination, defecation, and gastric emptying). Young children often present with disconjugate, roving eye movements, jerking of the extremities, and opisthotonus.[64,91,97,99] Complications can include pancreatitis, upper airway obstruction causing respiratory failure, and rhabdomyolysis.[97]

Management. The treatment of scorpion stings is supportive. Cold compresses and over-the-counter analgesics are used for local pain. All wounds should be cleaned thoroughly, and tetanus administered if indicated.[64,91,97]

Assessment and management of ABCs is critical, especially in children. In severe cases, intubation and ventilation may be necessary.[98] Parenteral analgesics and benzodiazepines may be required for severe pain and agitation. Midazolam is preferred by many authors, often as a continuous infusion.[100] Severe tachycardia generally responds to beta-blockers, and hypertension can be treated with intravenous hydralazine.[101]

An antivenin is available for use in Arizona. It is derived from goat serum, and is not approved by the United States Food and Drug Administration. It effectively treats about 70% of cases within 1-3 hours of administration.[98] There is a risk of both immediate hypersensitivity reactions and serum sickness.[102] It is indicated for patients with severe cardiorespiratory or central nervous system dysfunction. The dose is 1 vial mixed in 50 mL of normal saline and infused over 30-60 minutes. Antivenin use may allow discharge from the ED in a select group of patients.[98] Most pediatric patients and others with severe systemic symptoms should be admitted to the hospital.

Hymenoptera

Hymenoptera is an order of arthropods that includes bees, wasps, and ants. They are the leading cause of death from envenomation in the United States, with 40-50 fatalities per year.[1,2] Apids (i.e., honeybees, bumblebees) possess a barbed stinger that remains in the victim after a sting. The vespids (i.e., wasps, hornets, yellow jackets) can sting multiple times and rarely leave the stinger behind.

Yellow jackets cause the majority of allergic reactions from insect stings. They nest in the ground or in walls, and are disturbed by lawn mowing, gardening, and other outdoor activities. Yellow jackets are attracted to food and garbage, as they feed on sugar-containing substances.

Vespids, in general, are more aggressive than bees. The exception would be the Africanized ("killer") honeybee. African bees were brought into Brazil in 1956 to help increase honey production. A few bees escaped and began mating with the established bees. These bees, which have aggressive tendencies, began migrating north, reaching Texas in 1990. They are now found in Texas, Arizona, and southern California.[103] The venom of the Africanized bee is no more toxic than that of other bees.[104,105] However, these bees often attack in swarms, so a large dose of venom is delivered to the victim.

The venom apparatus is located in the posterior end of the abdomen. It consists of the venom glands, a reservoir, and a stinging structure. The venom contains a number of enzymes, including phospholipase A and hyaluronidase. Phospholipase A is thought to be one of the major allergens in the venom.[106] Melittin is a principal component of honeybee venom, which damages cell membranes through detergent-like action.[107]

Clinical Presentation. Hymenoptera stings most often result in swelling, erythema, and pain at the site of the sting. This reaction generally subsides within several hours. Larger local reactions also are common. The swelling extends over a large area, usually peaks within 48 hours, and may last as long as seven days.[108] These probably represent a cell-mediated (type IV) immunologic reaction, although it may be mediated by IgE antibodies. Large local reactions may be confused with cellulitis, although this rarely occurs after a sting.

Serum sickness may occur within 7-10 days after a sting.[109] This is characterized by fever, arthralgias, and urticaria and appears to be immunologically mediated. Other unusual reactions include nephritic syndrome, seizures, Guillain-Barré syndrome, and progressive demyelinating neurologic disease.[110-112]

Anaphylaxis is the most serious complication of a hymenoptera sting. It is estimated that up to 4% of the U.S. population is sensitized to bee stings.[113] Common symptoms include flushing, angioedema, generalized urticaria, pruritus, and nausea. Life-threatening manifestations may include bronchospasm, upper airway edema, hypotension, and shock. Symptoms generally begin within 10-20 minutes after the sting; however, reactions up to 72 hours later have occurred.[108] Most deaths occur within the first hour. This often is due to upper airway obstruction, hypotension, or both.[114] Children suffering anaphylaxis who subsequently are stung tend to have reactions that are similar to or less severe than the initial episode.[115-118]

Management. Mild local reactions can be treated by removing the stinger and cleaning the wound with soap and water. Application of an ice pack or cold compress often provides relief. Oral antihistamines, such as diphenhydramine or hydroxyzine, also are effective.

Traditionally, it has been taught that the stinger should be removed by flicking it or scraping it off, to avoid releasing more venom into the wound. Newer evidence shows that the venom sac continues to contract and inject venom for up to 20 seconds after the sting, so removal of the stinger should be expedited.[119] The method of removal does not seem to affect the amount of venom delivered.

Corticosteroids may be used for the management of large local reactions, as they seem to hasten resolution of the symptoms. Serum sickness should be treated with a course of both oral corticosteroids and oral antihistamines.[64]

Treatment of anaphylaxis starts with the administration of subcutaneous or intramuscular epinephrine. The dose is 0.01 mL/kg of the 1:1000 solution (up to 0.3 mL) and should be administered as quickly as possible.[120] If hypotension or shock is present, an intravenous line should be started and 20 mL/kg boluses of normal saline or lactated Ringer solution given. Intravenous epinephrine (1:10,000 solution) should be given. Multiple doses may be needed.[121]

Attention to airway and breathing occurs simultaneously. Oxygen, intubation, and ventilation may be needed. Inhaled beta-agonists, such as albuterol, may help alleviate bronchospasm. Diphenhydramine (1 mg/kg intravenous) and methylprednisolone (2 mg/kg intravenous) should be given to help block the delayed hypersensitivity reaction. An H_2 blocker such as cimetidine often is used, as well. Patients with life-threatening symptoms should be admitted to the hospital for at least 24 hours.

Patients experiencing allergic symptoms should be discharged with at least two epinephrine autoinjectors (EpiPen, Dey Inc., Napa, CA) and instructions on how to use them. Those patients having anaphylactic reactions should wear a medical alert bracelet and also be referred to an allergist for possible venom immunotherapy.[64]

Conclusion

Envenomations can be frequent occurrences, depending on the area in which you practice. A high index of suspicion is needed to diagnose these conditions, as most do not have specific confirmatory tests. Numerous treatments have been advocated in the past, but supportive care is all that is needed in most instances.

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Physicians and nurses participate in this continuing medical education/continuing education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. **After completing this activity, you must complete the evaluation form provided and return it in the reply envelope provided in order to receive a certificate of completion.** When your evaluation is received, a certificate will be mailed to you.

CE/CME Questions

Please review the text, answer the following questions, check your answers against the key that appears following the questions, and then review the materials again regarding any questions answered incorrectly. ***To receive credit for this activity, you must return the enclosed CE/CME evaluation in the enclosed envelope.*** *For further information, refer to the "CE/CME Instructions" on the previous page.*

This testing procedure has proven to be an effective learning tool for adults. If you have any questions about the new testing method, please contact Customer Service at 1-800-688-2421.

1. Pit vipers have all of the following characteristics *except*:
   A. vertical elliptical pupils.
   B. round head.
   C. heat-sensing pit.
   D. hinged fangs.
   E. single row of ventral scales.

2. Approximately what percentage of snakebites are "dry"?
   A. Less than 5%
   B. 5-10%
   C. Up to 20-25%
   D. 40-50%
   E. 70-75%

3. Cryotherapy is indicated as first-line treatment for victims of snakebites.
   A. True
   B. False

4. Which of the following first-aid measures for snakebites is definitely of value?
   A. Cryotherapy
   B. Incision and suction
   C. Electric shock
   D. Tourniquet
   E. Transport to hospital

5. When should fasciotomy be done on snakebite victims?
   A. As routine treatment
   B. As prophylaxis for extremity bites
   C. When measured intracompartmental pressures remain elevated despite the use of antivenin
   D. When there is massive local edema

6. Which of the following is true?
   A. FabAV appears less potent than ACP.
   B. Recurrence of coagulopathy is more common with FabAV.
   C. Serum sickness is more common with FabAV.
   D. Scheduled does of FabAV are probably not needed for the first 18 hours.
   E. ACP is sheep-serum derived.

7. Which enzyme is thought to be responsible for most of the toxic effects of the brown recluse spider bite?
   A. Sphingomyelinase D
   B. Hyaluronidase
   C. Thrombin-like enzymes
   D. Phospholipase A
   E. Alpha-latrotoxin

8. What is the hallmark of black widow spider envenomation?
   A. Fever
   B. Necrosis at bite site
   C. Tachycardia
   D. Headache
   E. Muscle cramping

9. Which treatment for black widow spider envenomation is no longer recommended as first-line therapy?
   A. Morphine
   B. Valium
   C. Lorazepam
   D. Calcium gluconate
   E. Codeine

10. Which is *not* a sign or symptom of scorpion envenomation?
    A. Tachycardia
    B. Local pain at bite site
    C. Necrotic lesion
    D. Roving eye movements
    E. Hypertension

CE/CME Objectives

Upon completing this program, the participants will be able to:

a.) Quickly recognize or increase index of suspicion for envenomations;

b.) Be educated about how to correctly and quickly stabilize, and then to manage, envenomations;

c.) Understand various diagnostic modalities for envenomations; and

d.) Understand both likely and rare complications that may occur.

Answer Key

1. B	5. C	9. D
2. C	6. B	10. C
3. B	7. A	
4. E	8. E	

In Future Issues: **Pediatric C-Spine**