ENLS Version 4.0

The ENLS Course presents a stepwise approach to clinical care in the “golden hour(s)” of a neurocritical care emergency. The 14 ENLS topics span the broad range of neurologic emergencies and cover aspects of general emergency medicine and critical care that need to be specifically tailored to the patient with acute nervous system illness or injury. Each module contains an initial algorithm, a checklist of important clinical points, a list of information needed for communication to improve transitions across care settings, clinical pearls, and more. ENLS is relevant for a wide array of care providers, from prehospital to specialist. Content is research-based and is updated every two years.

Changes in ENLS Version 4.0

- Updated diagnostic and management algorithms and checklists of “to-do” items in the first few hours
- Expanded sections for prehospital providers, nursing and pediatrics
- Revised pharmacotherapy manuscript with relevant medications as well as the addition of alternative medications to reflect global variability
- Updated/new figures and neuroimaging
- New management protocol and clinical pearls sections
- Detailed communication tables with sample scenarios to use when transitioning care from prehospital to emergency department (ED) and from ED to neurocritical care unit.
- Starred references in the bibliography section highlighting key papers along with a short description of their importance
- Attention to both internal consistency amongst manuscripts and external consistency with published guidelines from the Neurocritical Care Society as well as sister societies involved in emergency and critical care of these patients

NEUROCRITICAL CARE SOCIETY

ENLS Version 4.0

Neurocritical Care Society

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Neurocrit Care
https://doi.org/10.1007/s12028-019-00813-5

NEUROCRITICAL CARE SOCIETY

COMA

Emergency Neurological Life Support: Approach to the Patient with Coma

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Abstract

Coma is an acute failure of neuronal systems governing arousal and awareness and represents a medical emergency. When encountering a comatose patient, the clinician must have an organized approach to detect remediable causes, prevent neurological injury, and determine a hierarchical approach for diagnostic testing, treatments, and neuromonitoring. Coma was chosen as an Emergency Neurological Life Support protocol because timely medical and surgical interventions can be lifesaving and need implementation in a rapid manner. The initial workup of such patients is critical to establish a correct diagnosis.

Keywords: Coma, Consciousness, Critical care, Neurocritical care, Encephalopathy

Introduction

Coma is characterized by the absence of arousal (wakefulness, vigilance) and awareness of self and environment, lasting for more than 1 h [1]. Comatose patients have closed eyes, do not communicate, and do not arouse to verbal, tactile, or noxious stimuli. Certain causes of coma are readily identified, while others may require extensive testing to discover an etiology. Diagnostic and therapeutic steps should occur simultaneously. An organized and sequential plan can form the basis for discovering common causes of unresponsiveness and for selecting studies for less common causes of coma [2].

The Emergency Neurological Life Support (ENLS)-suggested algorithm for the initial management of coma is shown in Fig. 1. The initial step is to assess for common and reversible conditions while incorporating available history and physical examination findings to best diagnose and concurrently treat patients with acute coma. Suggested items to complete within the first hour of evaluating a patient with coma are shown in Table 1. These suggestions are meant to give a broad framework for the principles of diagnosis and emergent management of coma, which can be adapted to reflect global and regional variations based on the local availability of diagnostic tools and treatments.

Prehospital Considerations

If coma is identified in the prehospital setting, initial evaluation and management steps as outlined in this protocol should be implemented as soon as possible to maximize chances of neurological recovery. Emergency medical services (EMS) teams will assess airway, breathing, and circulation (ABCs), check Glasgow Coma Scale [3] (GCS), pupils, and vital signs, including blood glucose, and obtain intravenous (IV) or intraosseous (IO) access. Based on assessment findings, EMS teams will establish an airway, ventilate if needed, check for and correct hypoglycemia, administer naloxone, and treat for shock with fluids and pressors if indicated. In addition, prehospital personnel should collect pertinent information from witnesses and from contextual or environmental observations. Witnesses may be able to provide information on the time course of the neurological decline as well as any prodromal symptoms. Family or friends may have information regarding the patient's past medical history, prescribed medications, drug or alcohol use, any history of recent illness that might suggest an infectious cause,

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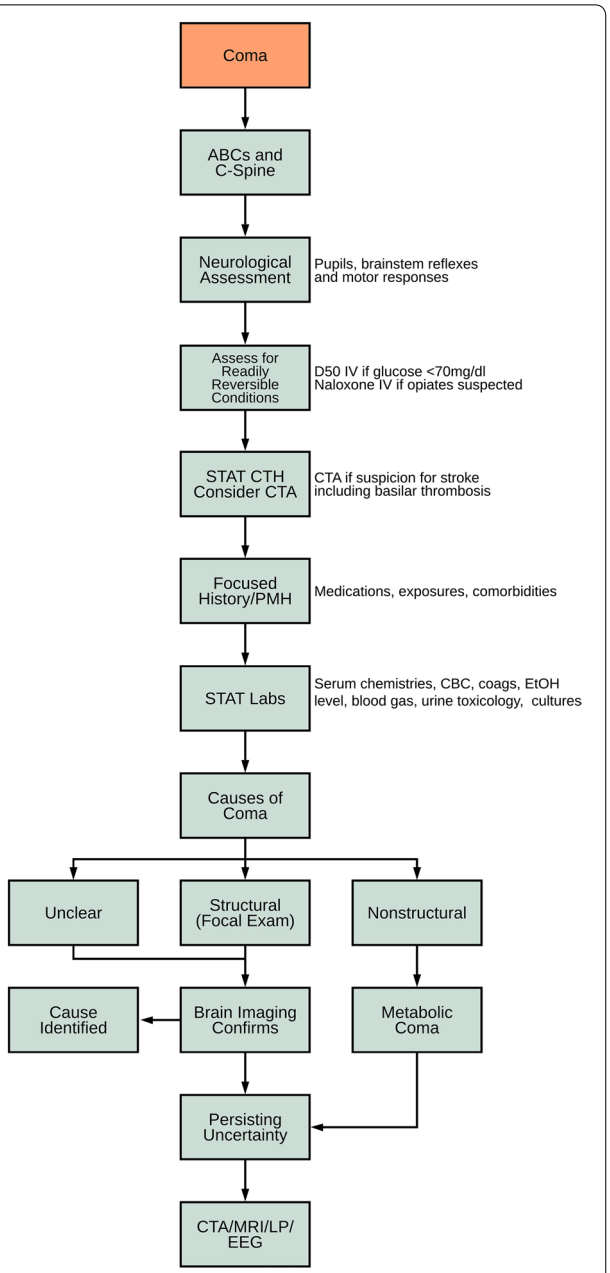


Fig. 1 ENLS approach to the patient with coma protocol

Table 1 Coma checklist for the first hour

Checklist
☐ Evaluate/treat circulation, airway, breathing, and cervical spine
☐ Exclude/treat hypoglycemia or opioid/benzodiazepine [13] overdose
☐ Serum chemistries, arterial blood gas, urine toxicology screen
☐ Emergent cranial CT (CT angio brain if appropriate) to determine if coma etiology is structural or vascular

signs that might suggest a drug or medication overdose, seizure activity, or recent trauma. A quick look around the site in which the patient was found can yield valuable information including signs of trauma or environmental exposures, current prescription bottles, empty pill bottles, drugs, or alcohol that might suggest overdose or intoxication (Table 2).

ABCs and Cervical Spine Precautions

The unconscious patient's ABCs should be quickly assessed and concurrently treated (see the *ENLS Airway, Ventilation, and Sedation* protocol). Verifying patency of the airway is an overriding initial priority to ensure adequate oxygenation and ventilation. The patient's cervical spine should be immobilized if the possibility of injury cannot be ruled out. A rapid initial survey should follow to evaluate for notable physical findings of the head, neck, chest, abdomen, and extremities.

IV or IO access should be established during the initial evaluation. Prompt blood glucose testing should be performed in all unconscious patients. If the blood glucose is < 70 mg/dL, dextrose should be administered IV. Thiamine should be given intravenously prior to dextrose in patients at risk for nutritional deficiency (e.g., chronic ethanol users, bariatric surgery patients, patients with malabsorption states) or if relevant history is unknown. If there is suspicion of opioid toxicity (e.g., history of illicit drug use, apnea/bradypnea, or small pupils), naloxone can be administered IV or intranasally and repeated as needed. Use of flumazenil in benzodiazepine overdose or poly-drug/alcohol abuse [4] is controversial [5]. Physostigmine may be administered if anticholinergic toxicity is a consideration, and have atropine ready in case of bradycardia or other signs of cholinergic toxicity. See Table 3 for doses, routes of administration, and pharmacological consideration for common reversal agents.

General and Neurological Assessment

A general physical examination should be performed including assessment of vital signs/respiratory patterns, facial and motor symmetry, and cranial and peripheral reflexes [6]. If hypotension is present, the cause should be pursued while fluid repletion and/or vasopressors are started. Blood pressure elevation in the comatose patient may be a sign of an underlying life-threatening process, such as elevated intracranial pressure (ICP) or acute stroke, which must be identified and treated promptly. Extremely high blood pressure should be treated if intracranial hemorrhage is suspected as a cause of coma (history of anticoagulation, fall) [7]. A search for signs of trauma and other conditions that might require emergent surgical or medical management are central goals of the initial survey.

Table 2 Prehospital checklist and handoff

Prehospital checklist and handoff
☐ Airway, breathing, ventilation issues
☐ GCS, pupils, and vital signs on presentation
☐ IV or IO access, site, and patency
☐ Ruled out hypoglycemia
☐ History from bystanders, witnesses, contextual, or environmental observations (pill bottles, signs of trauma, or seizure activity)
☐ Naloxone, dose administered and response
☐ Medications administered, dose and response (naloxone, benzodiazepine, dextrose, etc.)
☐ Time when patient was last seen normal
☐ Prodromal symptoms when last seen

Table 3 Pharmacology

Cause of coma	Pharmacological therapy
Hypoglycemia	Dextrose 50% 20–50 ml IV 10% Dextrose 50–100 ml IV can be given if D50 unavailable
Opioid overdose	Naloxone 0.04–0.4 mg IV/IM or 1–2 mg per nare into both nares can be repeated every 2–3 min for desired degree of counteraction. If initial use intranasal, switch to IV/IM when possible.
Anticholinergic toxicity	Physostigmine 0.5–2 mg slow IV push with rate not to exceed 1 mg/min. Dose can be repeated in 30–60 min if clinically effective to ameliorate symptoms. Atropine 1–2 mg IV must be kept ready nearby for immediate use if bradycardia or other signs and symptoms of cholinergic excess. Dose can be repeated every 3–5 min if previous dose did not induce a response
Elevated ICP	Hypertonic saline 3% 5 mL/kg over 5–20 min (range 2.5–5 mL/kg) can be given through peripheral IV as 250-ml bolus over 30 min or 500-ml bolus over 60 min.
	Mannitol 20–25% dose 0.5–1 gm/kg over 5–15 min can be redosed every 4–6 h. Caution must be exercised in heart and renal failure due to the high osmotic load infused, and lower doses (0.25–0.5 g/kg) may be used. Requires in-line filter (precipitates–crystal formation); may require warming to dissolve crystals before administration.

The emergency neurological assessment of the unconscious patient has four parts [1]: level of consciousness (LOC), brainstem assessment, evaluation of motor responses, and appraisal of breathing patterns. Arousal is assessed by looking for spontaneous opening of the eyes, visual fixation or pursuit (tracking), and spontaneous and purposeful movements of the extremities. Altered motor strength can also be tested via resistance to movement. The examination of a comatose patient should involve increasing intensity of stimulation until a response is evoked or it is deemed that the patient is unable to respond. Start with a simple verbal cue (e.g., "Are you ok?") and progress to louder voice, physical stimuli, and noxious stimuli. Noxious stimuli could include a sternal rub, nailbed pressure, or trapezius muscle squeeze.

The LOC can be expressed quantitatively by the GCS (see Tables 4 and 5) [3]. The GCS is most valuable for trending sequential LOC examination responses of a particular patient. However, the GCS is limited by its inability to account for alterations in brainstem function, hemiparesis, or aphasia or help differentiate between different etiologies of coma. Patients with identical total GCS scores may have very different clinical presentations

Table 4 Glasgow Coma Scale (GCS) for use in adult patients [9]

Glasgow Coma Scale (GCS)	
Eye opening	
Spontaneous	4
To speech	3
To pain	2
No response	1
Best motor response	
Obeys	6
Localizes	5
Withdraws	4
Abnormal flexion	3
Abnormal extension	2
No response	1
Best verbal response	
Oriented	5
Confused conversation	4
Inappropriate words	3
Incomprehensible sounds	2
No response	1
GCS range 3–15	

Table 5 Pediatric Glasgow Coma Scale (PGCS) [17] Adapted with permission

Pediatric Glasgow Coma Scale (PGCS)				
	> 1 year		< 1 year	Score
Eye opening	Spontaneously		Spontaneously	4
	To verbal command		To shout	3
	To pain		To pain	2
	No response		No response	1
Motor response	Obeys		Spontaneous	6
	Localizes pain		Withdraw to touch	5
	Flexion—withdrawal		Flexion—withdrawal	4
	Flexion—abnormal (decorticate rigidity)		Flexion—abnormal (decorticate rigidity)	3
	Extension (decerebrate rigidity)		Extension (decerebrate rigidity)	2
	No response		No response	1
	> 5 years	**2–5 years**	**0–23 months**	
Verbal response	Oriented	Appropriate words/phrases	Smiles/coos appropriately	5
	Disoriented/confused	Inappropriate words	Cries and is consolable	4
	Inappropriate words	Persistent cries and screams	Persistent inappropriate crying and/or screaming	3
	Incomprehensible sounds	Grunts	Grunts, agitated and restless	2
	No response	No response	No response	1
Total Pediatric Glasgow Coma Score (3–15)				

due to different combinations in the motor, verbal, and eye subscores. The Full Outline of UnResponsiveness (FOUR) score incorporates more detailed information on brainstem responses and has been validated in a variety of clinical settings (Fig. 2) [7–9]. Use of the FOUR tool can assist the clinician in determining the presence of a locked-in state versus a true vegetative state [10]. Similar to the GCS, each section is scored separately and allows for a trending of LOC.

Cranial Nerve Testing

Testing of the cranial nerves is focused on assessing the integrity of the afferent limb of the brainstem reflex being tested, brainstem nuclei involved, and the efferent tracts [11]. Brainstem reflexes are key to the initial coma evaluation and include pupillary assessment (size, reactivity, and symmetry), corneal reflex, response to visual threat, oculocephalic reflex (performed only if cervical trauma or instability is not a consideration), gag, and cough reflex. Pinpoint pupils are suggestive of pontine damage, usually from hemorrhage or ischemic infarction. Enlarged and unreactive pupils suggest damage to the midbrain or compression of the third cranial nerve. Pupillary changes can also be suggestive of drug overdose (see Table 6). Spontaneous roving eye movements suggest bilateral cortical dysfunction and an intact brainstem. Dysconjugate resting gaze may occur with structural or metabolic processes or extraocular movement impairment from cranial third, fourth, or sixth palsies. Psychoactive and anti-epileptic drugs have been associated with depressed vestibulo-ocular responses. Jerky, nystagmoid movement may indicate non-convulsive status epilepticus or brainstem or cerebellar ischemia. Fundoscopy may reveal retinal hemorrhages or papilledema if there has been prolonged increased ICP; more acutely, high ICP may manifest as optic disk blurring or lack of spontaneous venous pulsations in the optic disk. A thorough brainstem examination can uncover early signs of basilar stroke and allow early therapies capable of minimizing long-term disability. Brain stem reflexes may be absent in hypothermic patients, up to a few hours after cardiac arrest, or in patients who have received neuromuscular paralysis.

Motor function is assessed by observing spontaneous movements, responses to verbal command, or noxious stimulation or for posturing. Symmetric posturing, either extensor ("decerebrate") or flexor ("decorticate"), may occur in either structural or metabolic coma. Generalized or symmetric findings raise the possibility of a toxic or metabolic process that involves brainstem or thalamic and brainstem arousal centers. Muscle tone of the extremities may be assessed by passive movement of the limbs mainly elbow and knee flexion. The examiner should distinguish purposeful movements from reflex activity. Examples of purposeful activity include following commands: axial (sticking out tongue) or acral (showing

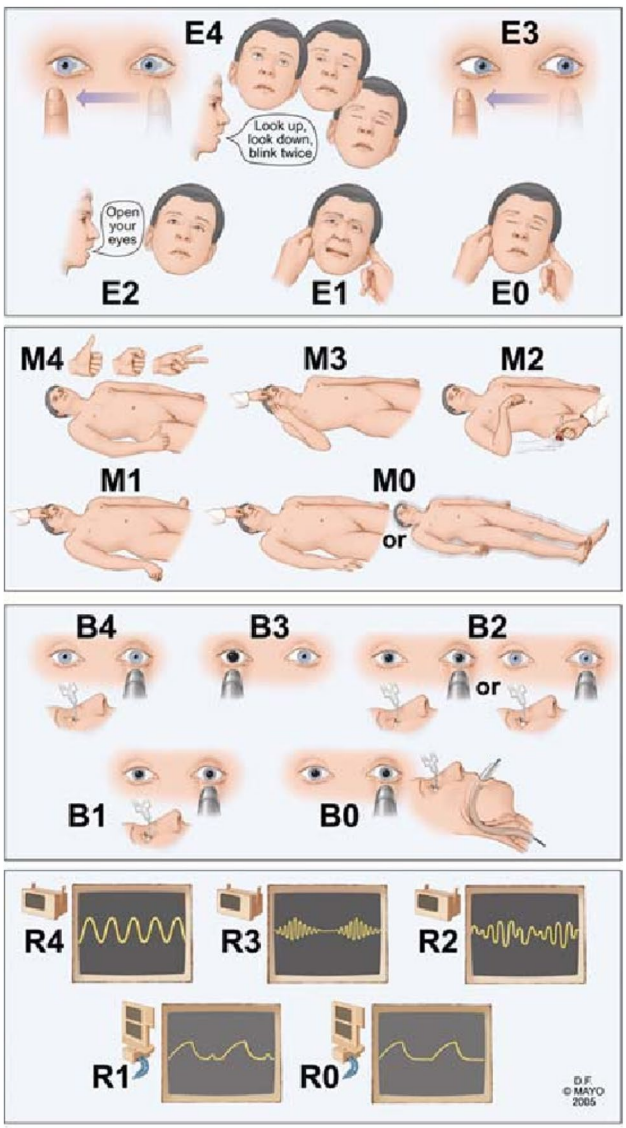


Fig. 2 Full Outline of UnResponsiveness (FOUR) score [10] Reprinted with permission

two fingers or thumbs up), pushing the examiner away, reaching for the endotracheal tube, or localizing to noxious stimulation. Examples of reflexive activity include withdrawal, flexion, or extensor posturing to noxious stimulation. Ability to grasp should not be considered following commands without the ability to reproducibly let go on command, as this too can be a reflex rather than a conscious movement. Deep tendon reflexes should be performed with particular attention to briskness and symmetry of findings.

Observed breathing patterns may also have localizing value in evaluation of coma. Lesions of the pons or midbrain can result in neurogenic hyperventilation. Central hyperventilation may also be a sign of underlying acidosis and compensatory respiratory alkalosis. Cluster (Biot's) breathing may be seen resulting from pontine lesion. Ataxic or absence of spontaneous breathing (apnea) may be seen in medullary injury (Table 7) [1].

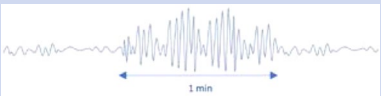
Focused Presenting and Past Medical History

Historical information elicited from witnesses, friends, family, co-workers, or EMS personnel may suggest the cause of coma. EMS personnel may have valuable details about the circumstances in which the patient was found.

Table 6 Pupillary changes reflecting underlying etiology [1]

Pupillary change	Possible etiologies/localization
Pinpoint pupil	Opioids Cholinergic intoxication Pontine damage (interrupts descending sympathetic pathways)
Dilated, non-reactive pupils	Cerebral anoxia, global Barbiturates Atropine Hypothermia Brain death
Dilated, reactive pupils	Pretectal lesions Stimulants (cocaine, methamphetamine), hallucinogens including PCP/LSD
Anisocoria (pupillary asymmetry)	Third nerve compression from uncal herniation Localized drug effect (e.g., ipratropium, tropicamide)
Mid-position, fixed or irregular	Midbrain lesion

Table 7 Respiratory patterns reflecting underlying etiology [1]

Respiratory pattern	Pattern	Localization
Cheyne–Stokes		Global/metabolic encephalopathy Impaired forebrain or diencephalon
Central neurogenic hyperventilation		Metabolic encephalopathy High brainstem tumors (rare)
Apneusis		Bilateral pontine lesions
Cluster breathing/ataxic breathing		Pontomedullary junction lesions
Apnea		Lesions affecting ventrolateral medulla bilaterally (ventral respiratory group)

The time course of the alteration of consciousness may be helpful in suggesting an etiology. An abrupt or acute onset of symptoms suggests a stroke, seizure, or a cardiac event with impaired cerebral perfusion. A more subacute onset of encephalopathy evolving into coma could suggest a metabolic or possibly infectious process. Past medical, surgical, or psychiatric history; alcohol or illicit drug use history; and any environmental toxic exposures should be included in the information gathering. Medication history is paramount in identifying a possibility of overdose and may also provide valuable clues to the medical history in the absence of other sources [12]. The electronic medical record may provide rapid access to the patient's past medical history if the patient can be reliably identified [13].

Recommended Laboratory Testing

Unless a readily reversible cause of unresponsiveness, such as hypoglycemia, has been discovered and corrected, additional laboratory testing should be obtained. Serum chemistries, a basic hematological panel, and blood gas analysis should be considered. Point of care (POC) testing should be utilized where available. Co-oximetry may be beneficial in selected patents suspected of carbon monoxide poisoning. Toxicology testing such as ethanol level and urine toxicology screen should be obtained, though variability and availability of exhaustive toxicology screens are limited in emergent settings. Microbiologic studies, including cultures of blood and urine, are helpful in many cases.

Initial Formulation: Structural, Non-structural, or Unclear Causes of Coma

Information obtained during initial stabilization, physical assessment, neurological assessment, focused history, and stat laboratory results will typically help in classifying patients into likely structural or non-structural causes of coma and direct further investigations and emergent therapies. This is a critical early distinction, since structural coma may require emergent medical or surgical

Table 8 Primary neurological etiologies of coma

Cause	Examination/history findings
Trauma	
Subdural hematoma	Focal weakness, seizure, altered level of consciousness, aphasia
Epidural hematoma	Lucid period with rapid decline
Parenchymal hemorrhage	Focal neurological findings
Diffuse axonal injury	Non-focal examination, dense coma
Neurovascular	
Intracerebral hemorrhage	Focal neurological findings
Subarachnoid hemorrhage	Coma with/without focal findings,
Ischemic stroke	Focal findings consistent with vascular distribution
CNS infections	
Meningitis	Coma or stupor, meningismus, seizures
Encephalitis	Coma or stupor, seizures
Abscess	Focal neurological deficits, exposure history, seizures
Neuroinflammatory disorders	
Acute disseminated encephalomyelitis	History of preceding illness, HA, fever, N/V, acute coma, focal motor deficits, brainstem findings
Autoimmune encephalitis	Subacute progression, seizures, psychiatric symptoms
Neoplasms	
Metastatic	History of primary cancer, focal findings, slow progressive symptoms
Primary CNS	Focal neurological deficits, neuropsychiatric symptoms, seizures, ocular symptoms
Carcinomatous meningitis	HA, meningismus, encephalitis/stupor, seizures, cranial neuropathies, cerebellar symptoms
Seizures	
Non-convulsive seizures or status epilepticus	Epilepsy/recent seizure, unexplained coma
Postictal state	Recent seizure, focal neurological deficits (Todd's paralysis), EEG without ongoing seizure
Other	
Reversible posterior leukoencephalopathy syndrome	Severe hypertension, history of immunosuppressant use. Pregnancy
Osmotic demyelination syndrome	History of polydipsia, excessive alcohol use or prior low sodium levels
Anoxic-ischemic encephalopathy	History of cardiac arrest or asphyxiation

intervention and/or advanced neuromonitoring (see Tables 8 and 9). If there is concern for a structural etiology of coma, or if the cause of coma cannot be identified after initial assessment, brain imaging should be obtained immediately.

Brain Imaging

Non-contrast cranial computed tomography (CT) imaging should be obtained emergently in unconscious patients with a presumed structural cause of coma and in patients with an unclear cause of coma after initial assessment of the ABCs and stabilization of the cervical spine. CT identifies structural etiologies of coma such as cerebral infarction, intracranial hemorrhage, brain masses, cerebral edema, and acute hydrocephalus. Rapid sequence magnetic resonance imaging (MRI) may be helpful if brainstem involvement is suspected [14].

If acute ischemic stroke is suspected, CT angiography and CT perfusion can provide valuable information on vascular patency and regional perfusion. Non-contrast CT imaging in the hyperacute phase of ischemic stroke is often normal; this can be another reason to consider rapid sequence MRI if patient can be cleared from metal risks swiftly. In this setting, clinical diagnosis of stroke rests on a reliable history and focal findings on examination. Ischemic stroke does not typically cause coma acutely unless the ischemia involves the arousal systems located in the pontomesencephalic tegmentum (e.g., basilar artery thrombosis). Subacutely, coma may develop due to progression of a hemispheric infarct with transtentorial herniation or non-communicating hydrocephalus. If there is any suspicion for basilar artery thrombosis, a CTA should be obtained emergently. When a central nervous system (CNS) infection is being considered, cranial CT with and without contrast should be ordered to