COMA

Consciousness is a state of awareness of the self and the environment (1). Arousal and awareness are the two main interrelated components required for a conscious state (1). Arousal is mediated via input from the ascending reticular activating system (ARAS) located in the pontine and midbrain tegmentum that projects through synaptic relays in the thalamus to the hemispheric cortex (2). A disturbance in arousal leads to diminished alertness. Awareness is dependent on the ability of the aroused cortex to process afferent sensory input and add contextual meaning. A problem with awareness causes a disturbed content of consciousness, which represents cognitive and affective mental functions (1).

Coma is a state of severe disruption in arousal and awareness (1). A comatose patient may be defined as a completely unaware patient, unresponsive to external stimuli with, at best, eye opening to pain (without eye tracking or fixation) and limb withdrawal to noxious stimuli (3). A detailed neurological examination documenting clinical changes over time provides information on changes in the depth of coma (3). Depending on the underlying disease process patients may transition from full consciousness to coma gradually (e.g. hepatic encephalopathy) or abruptly (e.g. cardiac arrest, brainstem hemorrhage). Comatose patients do not remain in coma indefinitely. In most patients there is an evolution over time towards recovery or development of persistent states of impaired consciousness such as a minimally conscious state, vegetative state, or in the most extreme case, brain death (4).

Epidemiology

Coma is common among patients with critical illness. Between 15% and 20% of patients on mechanical ventilation and up to 25% of patients failing to wean off mechanical ventilation are comatose (5). Among elderly (age >65 years) patients admitted to an intensive care unit with critical illness, nearly one-third are comatose on admission (6).

Diagnosis

The causes of coma can be classified as structural and non-structural causes (Table 1) (7). Structural causes are further subdivided according to lesion location: cerebral hemispheric (unilateral or bilateral), brainstem or cerebellum. Findings on the neurological examination may provide clues regarding the underlying etiology. The ARAS is located in the tegmentum of the pons and midbrain; therefore, structural lesions at these sites often also disrupt the function of cranial nerves at these locations.
Compression of the midbrain is often associated with a third nerve palsy (dilated and unreactive pupil), while pontine lesions may be associated with loss of corneal reflexes (5th nerve palsy), loss of lateral rectus function (6th nerve palsy), facial weakness (7th nerve palsy), and absence of the oculocephalic reflex (8th nerve palsy). Hemispheric, unilateral mass lesions typically cause coma by inducing a transtentorial herniation syndrome with compression and distortion of the brainstem. An emergent CT scan of the brain is required in order to determine if there is a structural lesion that is amenable to immediate surgical or medical intervention.

Non-structural causes of coma can be subdivided into acute metabolic-endocrine derangements and diffuse physiological brain dysfunction (e.g. seizures, intoxication, hypothermia, malignant neuroleptic syndrome) (7). These disorders produce coma by diffusely depressing cortical and brainstem function. Non-convulsive status epilepticus may be associated with coma; up to 20% of patients in the ICU with unexplained coma have been shown to be in non-convulsive status epilepticus (8). Therefore, an EEG should be considered as part of the diagnostic work up of comatose patients. Other causes of coma in the ICU that may be challenging to diagnose include cerebral fat embolism (long bone fractures, pelvic/hip surgery), cerebral air embolism (indwelling venous catheters, open heart surgery), Wernicke’s encephalopathy, narcotic overdose, hypothyroidism and Addison’s crisis.

Several disorders may mimic coma. One of them is the locked-in syndrome, in which (the classic form) a patient is completely paralyzed but can open the eyes, blink, and move the eyes vertically. The patient can see, hear, and feel pain but is not able to respond to stimuli, except through blinking and vertical eye movements. This syndrome is caused by a lesion in the ventral pons interrupting the motor tracts but sparing the ARAS. Complete peripheral paralysis may mimic coma and is sometimes seen in extreme cases of Guillan-Barré syndrome, botulism and ethylene glycol poisoning. Other disorders that can be misdiagnosed as coma are psychogenic unresponsiveness and akinetic mutism (see section I psychiatric emergencies), which may be considered after exclusion of other causes (3).

Clinical Examination

The initial evaluation and management of the comatose patient starts with securing an adequate airway, providing ventilation and supporting cardiovascular function. After achieving cardiopulmonary stability, the examination starts with review of the history which may be obtained from relatives, by-standers, or emergency medical services personnel. The onset of coma may provide an important clue. Acute onset is suspicious for a cerebrovascular disorder, a generalized seizure, traumatic brain injury, or intoxication, whereas a gradual onset is more suspect for slowly increasing intracranial pressure, metabolic disorders, or an inflammatory neurologic disorder. General physical examination should include inspection of the skin (e.g. bullae in barbiturate coma, hyperpigmentation in Addison disease, purpura in meningococcal meningitis), looking for evidence of trauma, and review of vital signs such as temperature and blood pressure (7).
The neurological examination of comatose patients can be significantly affected by the presence of sedating agents. Nowadays, sedation and analgesia are frequently used in intensive care units, thus an objective and reliable neurological examination in these patients should be performed in the absence of any sedating agents if possible.

The neurological examination of a comatose patient should include the following:

1. **Level of consciousness**

   Start with assessment of the patient’s response to voice. If a patient does not respond to voice, a noxious stimulus (nail bed, sternal rub or supra-orbital pressure) can be applied. The Glasgow Coma Scale (GCS, Table 2) may be used to assess the eye opening response, the motor response and the verbal response, as an indication of the depth of coma.

2. **Pupils**

   The response to light is assessed separately for both eyes using a strong penlight. Note the size of the pupils and any asymmetry. Ipsilateral dilation of the pupil with loss of pupillary reflex can be the sign of transtentorial herniation, isolated third nerve palsy or midbrain dysfunction.

3. **Eye movements**

   Observe spontaneous eye movements. Note if the eyes are in the midline or deviated and if they are conjugate or disconjugate. Eye movements can be observed by calling the attention of the patient to one side and then the other or by attracting their attention with visual stimulus.

   Elicit the oculocephalic (doll’s eyes) reflex by briskly turning the head side to side (only if cervical spine injury has been ruled out). The eyes should move conjugately in the opposite direction the head is turned. The oculocephalic reflex is absent when the eyes move in the same direction as the head movement (e.g. fixed with the motion) and indicate pontine or midbrain dysfunction.

   Elicit the oculovestibular reflex (cold caloric testing) by irrigating the ear with 30-50 mL cold (33°C) water. Ensure that the tympanic membrane is intact. If the eyes remain fixed this indicates brainstem injury. A normal response to cold water would be a slow tonic deviation of the eyes toward the stimulated ear. In addition, a fast beating nystagmus away from the stimulated ear may be seen in non-comatose patients.

4. **Visual fields**

   Open the patient’s eyes. Bring one finger towards their eye in each of the visual fields. This should elicit a blink reflex.
5. Corneal reflexes

Take a wisp of cotton or tip of sterile gauze. Gently touch the sclera and assess for eyelid closure. The sensory component of the reflex is mediated by the trigeminal nerve and the motor component by the facial nerve. Bilateral loss of corneal reflexes is reflective of a poor level of consciousness. Unilateral loss is seen in lesions involving the trigeminal or facial nerve.

6. Facial movement

Noxious stimulation can be elicited by applying supraorbital pressure. Also observe the face when applying noxious stimuli to extremities. You may see an asymmetry in the face with grimacing.

7. Cough reflex

In intubated patients, a soft suction catheter is advanced through the endotracheal tube. A cough is the normal response which often is lost in deeply comatose patients and patients with a brainstem lesion. The sensory and motor components are mediated through the vagal nerve. The cough reflex is usually the last preserved reflex in patients with deteriorating levels of consciousness.

8. Meningeal signs

Test whether neck stiffness is present (only if cervical spine injury has been ruled out). Discriminate meningeal signs with neck flexion from stiffness of the neck in all directions.

9. Motor system

Apply central noxious stimulus by applying supraorbital pressure or sternal rub. Note muscle tone and bulk in each extremity. If stimulation produces an asymmetric response, limb weakness is usually present. It is important to recognize that the changes in muscle tone and reflexes after upper motor lesions develop over days and it is not unusual to see flaccidity and hyporeflexic extremities in the acute phase.

10. Reflexes

Test all deep tendon reflexes in the arms and legs. Note any asymmetry. Assessment for the presence of extensor plantar responses (Babinski reflex) can be done by scratching the bottom of the foot looking for extension movement of the toes. Extremity weakness with increased muscle tone, hyperreflexia, and an extensor plantar response suggests an upper motor neuron lesion at any level in the corticospinal tract including the motor cortex, brainstem, and spinal cord.
Treatment

Coma is a state of severe brain failure and a medical emergency. It is critical to identify and correct its underlying cause expeditiously to prevent or minimize permanent brain injury. Treatment depends upon the underlying cause. An emergent initial evaluation and treatment algorithm for comatose patients is shown in Figure 1.

VEGETATIVE STATE

The vegetative state is characterized by a global severe impairment in consciousness but retention of arousal. Although these patients may open their eyes spontaneously they do not react in a meaningful way to environmental cues and they are not aware of themselves. The reactions to stimuli are simple, automatic, stereotypic, and predictable. This state usually results from severe cortical injury with brainstem sparing. A duration of greater than one month is required to characterize it as a persistent vegetative state (PVS) (9). The diagnosis of PVS is not based on a laboratory test but rather on the observations of clinicians with expertise in coma and neurological injury. Patients often have roving eye movements. Hypothalamic functions, cranial nerve, and spinal reflexes are usually, but not necessarily, preserved. EEG recordings may show sleep-wake cycles.

Three basic neuropathologic patterns have been recognized in patients who have died of PVS (10): First, the neocortical pattern, which is characterized by cortical laminar-necrosis and usually results from severe anoxic-ischemic insults (11). Second, the thalamic pattern, which is characterized by impaired thalamo-cortical circuits related to cognition and thalamo-efferent fibers directed to the reticular activating system (12). Third, the pattern of diffuse axonal injury, which in most cases is related to trauma, and isolates the cortex from subcortical structures impairing cognitive function (13).

For many years prolonged and repetitive behavioral testing has been the most useful tool in the diagnosis and prognostication of disorders of consciousness like PVS. However, this condition can be misdiagnosed in up to 43% of patients (14). Functional brain MRI holds promise as an adjunct in the diagnosis and evaluation of these patients. A recent study demonstrated neural correlates of speech comprehension using functional brain MRI in two of 41 patients with the diagnosis of PVS (15).

Another persistent altered state of consciousness, distinct from PVS, is a minimally conscious state (MCS). MCS is more common than PVS after severe traumatic brain injury. Patients with a MCS are in an abulic emotionless state; however, they have intact eye tracking movements, can make eye contact and can turn their head to verbal stimuli. Some verbalization may be possible and they may hold or use an object when asked (3).

The vegetative state and the MCS are not necessarily permanent. Patients may show further recovery over time, but there are no good predictors for long-term outcome. The prognosis of comatose patients is strongly dependent on the underlying cause.
Patients in a PVS for more than one month after hypoxic-ischemic brain injury or for more than 6 months after traumatic brain injury rarely demonstrate recovery (3).

DEATH BY NEUROLOGIC CRITERIA, END OF LIFE AND ORGAN DONATION

Brain death is defined as the irreversible loss of function of the brain, including the brainstem. Brain death from primary neurologic disease may be caused by severe traumatic head injury, aneurysmal subarachnoid hemorrhage, and massive hemorrhagic or ischemic strokes, among others. In medical and surgical intensive care units, however, severe hypoxic-ischemic brain insults and fulminant hepatic failure may result in irreversible loss of brain function.

The three cardinal findings in brain death are coma or unresponsiveness, absence of brainstem reflexes, and apnea. The American Academy of Neurology provides guidelines for determination of brain death, which are summarized in table 3 (16). The prerequisites to proceed with a brain death examination are:

A. Establish an irreversible and proximate cause of coma and exclude the presence of CNS-depressant drugs.
B. Exclude recent administration or continued presence of neuromuscular blocking agents (train of 4 twitches testing).
C. Absence of severe electrolyte, acid-base, or endocrine disturbances.
D. Normal core temperature (>36°C).
E. Normal systolic blood pressure (systolic blood pressure $\geq$100 mm Hg).

Generally, a single neurologic examination suffices to pronounce brain death; however, some US states require two examinations by law. In some instances, a clinical determination of brain death may not be possible because some of the neurologic exam findings are deemed unreliable (e.g. because of the presence of severe facial trauma) or because of hemodynamic or respiratory instability preventing the performance of the apnea test. In those instances ancillary tests including EEG, contrast cerebral angiography, nuclear brain scan, transcranial Doppler sonography, computed tomographic angiography, and magnetic resonance angiography may be used. Of these the EEG, nuclear scan, and cerebral angiogram are considered the preferred tests. Ancillary tests cannot replace the neurological examination, and should only be used if parts of the neurological examination cannot be reliably performed. In addition, as ancillary tests may yield false-positive results, their interpretation requires concordance with the proper neurological findings. Most medical institutions have their own brain death protocol shaped in accordance with federal guidelines.

Once brain death has been determined and documented, federal and state law requires the physician to contact an organ procurement organization. Most organ transplants occur in the setting of patients who have progressed to brain death. Unfortunately, the disproportion between the offer and demand of organs grows every day. In 2008, an estimated 17 patients died each day awaiting transplant (17). At most centers, the approach for consent for organ or tissue donation is performed by a member of the organ procurement organization, typically after the patient has been pronounced brain dead.
Maintaining a clear distinction between the patient care team, the organ procurement organization, and the transplant team minimizes any potential (perceived) conflict of interest.

Sometimes intensive medical care is required to optimize organ perfusion and conserve the organs for potential donation until a decision is made by the family to proceed with transplant or an appropriate organ recipient is found (18).

HYDROCEPHALUS

The production, absorption, and flow of cerebrospinal fluid (CSF) play a key role in the dynamics of intracranial pressure. In the average adult there is 90-150 mL of CSF within the ventricular and subarachnoid spaces (19). CSF is produced in the choroid plexus of the ventricles at a rate of approximately 20 mL/h (20), flows through the ventricular system, exits the fourth ventricle into the subarachnoid space, and is reabsorbed by the arachnoid granulations at the cerebral convexity. The flow of CSF can be disrupted in a number of ways resulting in hydrocephalus. Abrupt changes in CSF dynamics may result in life-threatening neurological emergencies, while slow changes over prolonged periods of time may produce minimal or no symptoms. Hydrocephalus may develop when there is CSF overproduction (choroid plexus papilloma), decreased CSF reabsorption, or obstruction of CSF flow. Non-communicating hydrocephalus occurs when there is an obstruction of CSF flow anywhere between the choroid plexus production site and the fourth ventricle outflow whereas communicating hydrocephalus occurs when the arachnoidal reabsorption sites at the cerebral convexity and basal cisterns fail to reabsorb CSF.

Acute obstructive hydrocephalus is common in patients with primary intraventricular hemorrhage and in patients with aneurysmal subarachnoid or intracerebral hemorrhage with ventricular extension. The hydrocephalus in this setting results from blood obstructing the CSF pathways. Other causes of non-communicating hydrocephalus are posterior fossa or third ventricle tumors (21), and posterior fossa hemorrhagic or ischemic strokes causing mass effect with obstruction of the aqueduct or the fourth ventricle. Communicating hydrocephalus may result from any process interfering with CSF reabsorption including dural sinus thrombosis, bacterial meningitis, and subarachnoid hemorrhage. Posterior fossa and intraventricular surgery, the most likely procedures to introduce blood into the subarachnoid space, are occasionally the cause of postoperative hydrocephalus.

The clinical presentation of acute hydrocephalus is often an impairment in consciousness, sometimes associated with a decreased or absent upward gaze and small and poorly reactive pupils due to dilation of the cerebral aqueduct. In extreme cases patients may develop coma over a short period of time due to a rapid increase in intracranial pressure, and eventually a central herniation syndrome may occur. Thus, acute hydrocephalus is a life-threatening condition that requires emergent placement of an external ventricular drain (EVD). If CSF drainage continues to be impaired over prolonged periods of time a permanent indwelling shunt (ventricular-peritoneal shunt) may be required.
In patients with hydrocephalus caused by intraventricular hemorrhage, injections of thrombolytic agents through an EVD may be considered to enhance clot lysis. The presence of unsecured cerebral aneurysms, untreated cerebral arteriovenous malformations, and clotting disorders are contraindications for this intervention. The phase II clot lysis evaluating accelerated resolution of intraventricular hemorrhage (CLEAR-IVH) clinical trial found that low-dose rt-PA can be safely administered to stable IVH clots and increases lysis rates (22). A phase III CLEAR trial is currently under way.

Chronic hydrocephalus may be seen in children with congenital vascular malformations or present in adults as normal-pressure hydrocephalus. These rarely are acute processes and typically do not require emergent interventions.

**INTRACRANIAL HYPOTENSION**

Intracranial hypotension refers to a state of decreased ICP caused by leakage of CSF. Intracranial hypotension may be seen in the setting of spinal interventions, a spontaneous or traumatic dural tear and CSF shunt overdrainage. Iatrogenic intracranial hypotension is often related to neurosurgical procedures using external lumbar CSF drainage intraoperatively to relax the brain and improve surgical access to deep structures (23), or postoperatively to prevent the formation of CSF fistulas (24). Intracranial hypotension is usually characterized by an orthostatic headache present when sitting and standing and improved or resolved while lying flat, sometimes associated with nausea and vomiting (25). Other uncommon symptoms associated with the syndrome are attributed to distortion or compression of the brain and/or spinal cord structures and may require emergent intervention. These include quadriplegia, cerebellar hemorrhage due to rupture of cerebellar bridging veins (26), altered consciousness (27, 28) and meningitis (29).

Although brain MRI can be normal in up to 20% of patients (25) prominent abnormal features include diffuse pachymeningeal enhancement, subdural hematomas or hygromas due to bridging vein rupture (30), tonsillar herniation and descent of the brainstem mimicking a Chiari I malformation, “sagging” of the brain (31), posterior fossa crowding and cerebral venous sinuses engorgement (32). If a CSF leak is suspected, further imaging to identify the leaking site is indicated. Radioisotope cisternography, computed tomographic myelography and magnetic resonance myelography are the preferred methods.

Traumatic CSF leaks with evidence of rhinorrhea and/or otorrhea can be diagnosed obtaining a sample of the nasal or otologic secretions and measuring the β₂-transferrin activity. β₂-Transferrin, a protein highly specific for human CSF, is an immunohistochemical test that is considered the standard for the clinical diagnosis of a CSF leak (33, 34). At least 0.5 mL of fluid is necessary to perform the test. False-positive results have been reported in the setting of chronic liver disease and inborn errors of glycoprotein metabolism (35).
Immediate temporary measures for intracranial hypotension include placing the patient supine or in reverse Trendelenburg, aggressive intravenous hydration, and discontinuation or clamping of CSF drains if present. Iatrogenic or spontaneous leaks in the spinal dural sac may be repaired with an epidural blood patch. Patients with dural leaks who do not respond to an epidural blood patch are potential candidates for surgical exploration and repair.

POSTERIOR REVERSIBLE LEUKOENCEPHALOPATHY SYNDROME (PRES)

A clinical diagnosis of PRES includes the presence of headache, seizures, encephalopathy, and visual disturbances, as well as radiologic findings of focal vasogenic edema, best seen on brain MRI. The syndrome is most commonly encountered in association with acute (relative) hypertension, preeclampsia or eclampsia, renal disease, sepsis, exposure to immunosuppressant agents, autoimmune disease, or a combination of any of these predisposing factors. A typical example would be a patient who develops PRES after cardiac transplant because of immunosuppressant agents and blood pressures that are elevated as compared to pre-transplant measurements.

Despite the syndrome's name, radiographic lesions in PRES are rarely isolated to the “posterior” parieto-occipital white matter and instead often involve the cortex, frontal lobes, basal ganglia, cerebellum, and brainstem (36). It is also a misconception that lesions are always “reversible”: infarction or tissue injury with cytotoxic edema (leading to focal areas of restricted MR diffusion) may occur in areas of severe hypoperfusion (37, 38), and brain hemorrhage (focal hematoma or subarachnoid blood) is seen in about 15% of cases (37).

The exact pathophysiology of the posterior reversible encephalopathy syndrome is unknown (39). Many patients have an associated cerebral vasculopathy (38). The most popular view has been that this is an endothelial “leakage” syndrome resulting from severe arterial hypertension or toxic insults. Immune-mediated mechanisms with T-cell/endothelial cell activation resulting in leukocyte trafficking and cerebral vasoconstriction may also be important (39).

Treatment of PRES is usually supportive and aimed at reversing the offending condition. Adequate blood pressure control is important in all patients with hypertension. Discontinuation or lowering the dose of immunosuppressant agents if often required in transplant patients, and fetal delivery in cases of (pre)eclampsia. Seizures if they occur justify short-term treatment with antiepileptic agents. Such agents can typically be discontinued after a limited period as it is unlikely that these patients develop epilepsy (36).

SPINAL CORD COMPRESSION

Approximately 14,000 patients a year in the United States are affected by injuries of the spinal cord and most involve the cervical spine region. Patients who sustain cervical spinal cord injuries usually have permanent, often devastating, neurological deficits and disability. Acute cord compression is most commonly encountered after traumatic spinal cord injury (TSCI); however, spinal tumors, epidural hematomas or abscesses can also produce acute cord compression.
Underlying spinal disease such as cervical spondylosis, atlantoaxial instability, osteoporosis, and spinal arthropathies like ankylosing spondylitis or rheumatoid arthritis can make some patients more susceptible to TSCI.

In patients with TSCI, the primary injury refers to the immediate effect of trauma, which includes forces of compression, contusion, and shear injury to the spinal cord. Possible mechanisms include ischemia, hypoxia, inflammation, edema, excitotoxicity, disturbances of ion homeostasis, and apoptosis. The phenomenon of secondary injury is sometimes clinically manifest by neurologic deterioration over the first 8 to 12 hours in patients who initially present with an incomplete cord syndrome. Spinal cord edema develops within hours of injury, becomes maximal between the third and sixth day, and begins to recede after the ninth day.

**Diagnosis**

Signs and symptoms of possible TSCI include pain or pressure in the neck, head or back; tingling or loss of sensation in the extremities, trunk, abdomen or pelvis; partial or complete loss of control over any part of the body; urinary or bowel incontinence, urgency or retention; and abnormal band-like sensations in the trunk (Table 4). Traumatic spine injury should always be suspected in trauma patients, even in the absence of symptoms and an expedited radiological evaluation of the spine is mandatory. An initial CT-survey of the whole spine is performed at most centers, primarily looking at the anatomy and alignment of bony structures. For patients with known or suspected spine injuries, MRI is helpful for looking at the actual spinal cord itself, as well as for detecting any blood clots, herniated discs, or other masses that may be compressing the spinal cord.

**Treatment**

The care of patients with TSCI starts at the scene of the inciting event. Proper immobilization and stabilization of the cervical and thoracic spine is now routine management of patients who have sustained trauma. Maintenance of a stable blood pressure, monitoring cardiovascular function, ensuring adequate ventilation and lung function, and preventing and promptly treating infection and other complications, is essential to avoid any superimposed injury and achieve optimal outcome.

The use of methylprednisolone within eight hours of the event remains controversial. The National Acute Spinal Cord Injury Study (NASCIS) II compared methylprednisolone (30 mg/kg IV, followed by 5.4 mg/kg per hour over 23 more hours), naloxone, and placebo in 427 acute TSCI patients (40). The subset of patients treated within eight hours had a modest better motor recovery than the placebo group. A meta-analysis including NASCIS II and two other small trials (one positive and one negative) concluded that methylprednisolone administered within eight hours of spinal cord injury resulted in improved motor recovery (41). These studies have been criticized in part because they did not translate into improved functional outcomes.

In 2002, based upon the available evidence, the American Association of Neurological Surgeons and Congress of Neurological Surgeons concluded that the use of glucocorticoids in acute spinal cord injury should be considered as a treatment option (42). This area remains controversial.
Clinicians might consider methylprednisolone infusion if its potential benefits are felt to outweigh the potential risks of associated complications.

Emergent surgical consultation is required if the spinal cord appears to be compressed by a herniated disc, blood clot, or other lesion. Surgical decompression is most commonly performed in patients with an incomplete TSCI or with progressive neurological deterioration. Even if surgery cannot reverse damage to the spinal cord, it may be indicated to stabilize the spine to prevent further injury, pain or spine deformity.

DYSAUTONOMIA

Autonomic nervous system disturbances are frequent in the neurointensive care unit and may be encountered in patients with traumatic brain injury, spinal cord injury, Guillan-Barré syndrome, aneurysmal subarachnoid hemorrhage, intracerebral hemorrhage, anoxic-ischemic encephalopathy, brain or brainstem tumors, and hydrocephalus. Immediately after any major intracranial catastrophe, there is a massive catecholamine surge that may produce seizures, neurogenic pulmonary edema and myocardial injury. This phenomenon is often seen in patients with severe subarachnoid hemorrhage.

Episodes of paroxysmal sympathetic hyperactivity have most commonly been described in patients with severe traumatic brain injury, but can also be seen after severe hypoxic ischemic brain injury. Various names have been used to describe these events including sympathetic storms, autonomic storms, diencephalic seizures, autonomic dysfunction syndrome, and paroxysmal autonomic instability with dystonia and dysautonomia. Several theories have been postulated in regards to the pathogenesis of paroxysmal sympathetic hyperactivity (43). The initially proposed epileptogenic etiology has been abandoned, because these patients do not exhibit epileptiform activity on EEG, and attempts to treat paroxysmal sympathetic hyperactivity with anti-epileptic agents have been unsuccessful (44). The disconnection theory proposes diffuse or focal cerebral damage affecting cortico-hypothalamic fibers resulting in autonomic hyperactivity (45). A model proposed by Baguley and collaborators proposes paroxysmal sympathetic hyperactivity as a result of lesions to central inhibitory pathways that regulate afferent information leading to hyperautonomic reactions to various stimuli (46).

Clinically, paroxysmal sympathetic hyperactivity is characterized by episodes of autonomic dysregulation manifesting as an increase in heart rate, respiratory rate, body temperature and blood pressure, muscle overactivity, and profuse sweating. The episodes often are misinterpreted or under-recognized by clinicians who are unfamiliar with the syndrome. Paroxysmal sympathetic hyperactivity generally presents during the early recovery phase and can continue for days, weeks, or even months. The reported incidence of this syndrome after TBI varies from 10 to 33% (47-50). A longer duration of the episodes has been associated with worse outcomes. Morphine sulfate (10 mg/4 h), bromocriptine (1.25–2.5 mg three times a day) and non-selective betablockers such as labetalol (100–200 mg twice a day) or propranolol (20–60 mg four times a day) have been successfully used to treat paroxysmal sympathetic hyperactivity (50).
Severe Guillain-Barré syndrome (GBS) is almost always associated with some form of autonomic nervous system dysfunction manifesting as blood pressure fluctuations, sudden cardiac arrhythmias (often bradycardia requiring transient pacemakers), or ileus. Frequent tracheal suctioning may cause “vagal spells” during which the patient even may have brief cardiac pauses. Other patients may have increased bronchial secretions and impaired salivation sometimes responsive to glycopyrrolate. Paralytic ileus is a complication that should be anticipated in GBS patients. Patients will develop an expanding abdomen with diminished bowel sounds. The adynamic ileus is usually treated with oral motility agents and placement of gastric and rectal tubes. If the patient does not have cardiac arrhythmias, patients may respond to neostigmine which increases parasympathetic stimulation and enhances colonic activity.

Spinal cord injury above the T6 segment may cause neurogenic shock, a profound sympathetic loss resulting in hypotension often associated with bradycardia due to unopposed vagal tone. Tracheal suctioning may trigger the episodes of bradycardia in these patients. Autonomic dysreflexia in response to afferent stimuli below the injury level may also occur and typically presents with hypertension, headache, flushing and sweating above the injury level, and vasoconstriction below the injury level. Bladder or gastrointestinal stimuli are often the cause and need to be actively investigated and treated. Thermodynamics, orthostatic hypotension and sweating disturbances are also seen after spinal cord injury and may last for a lifetime.

PSYCHIATRIC EMERGENCIES

Psychiatric conditions such as catatonia, akinetic mutism, and acute psychosis may be encountered by neurocritical care physicians. As catatonia and akinetic mutism can be mistaken for coma or a locked-in stat, a high level of suspicion is required to identify these entities.

Symptoms of catatonia may unveil schizophrenia, although it is important to note that catatonia may also occur in other psychotic mood disorders and in patients with brain injury. Catatonia is defined as a motor behavior with “a marked decrease in reactivity to the environment” (DSM-IV-TR), and appears as if motor execution lacks the input of frontal areas. Certain conditions like neuroleptic malignant syndrome (NMS) share features of malignant catatonia, and deserve to be entertained in the differential diagnosis. Malignant catatonia and NMS can both manifest with hyperthermia and rigidity; however, in the case of catatonia, there is usually a behavioral prodrome characterized by psychosis, agitation, and catatonic excitement.

Akinetic mutism is a state of consciousness with preserved awareness and retention of the ability to move and speak, but failure to do so. Clinically, these patients manifest with profound deficiency of executive function and inability to initiate movement or speech. Typically they are awake, follow with their eyes, but do not exhibit any motor or verbal responses to verbal or noxious stimuli. Muscle tone, reflexes and vital signs remain intact. This condition usually arises from injury to the prefrontal areas responsible for initiating movement.
It is most often seen after trauma, but may also occur in other disease states such as vasospasm affecting the anterior cerebral arteries (ACA), embolic strokes in the ACA territories, brain hemorrhages and cerebral venous thrombosis. It is basically a problem of motor execution, characterized by the patient being able to follow with his eyes but unable to initiate other movements or obey commands.

Psychosis is a disturbance in the perception of reality, evidenced by hallucinations, delusions, or thought disorganization. Psychotic states are periods of high risk for agitation, aggression, impulsivity, and other forms of behavioral dysfunction. Psychotic disorders like schizophrenia, bipolar mania, major depression with psychotic features and schizoaffective disorder are primarily psychogenic entities that may worsen during an ICU hospitalization; although psychosis is often encountered in the intensive care unit (ICU) it is rarely a primary condition in this setting. More frequently, acute psychosis in the ICU is due to alcohol withdrawal (10% of ICU admissions) (51), side effect of medications like sedatives or abuse substances, and medical conditions such as electrolyte abnormalities, hepatic failure and autoimmune disorders. ICU delirium may manifest with psychotic features, and the two conditions overlap given that they share similar etiologies. Common neurological conditions like Alzheimer disease may also present with psychotic symptoms (up to 40%) (52).

Treatment of psychotic events in the ICU is directed towards treating the underlying condition, although sometimes resolution of the medical condition is not sufficient to restore the normal thought process. Antipsychotic medications are a useful aid in the acute management of psychotic events and the main treatment option for psychosis related to primary psychiatric disorders.

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<td>Traumatic contusion</td>
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<td></td>
</tr>
<tr>
<td>Anoxic-ischemic encephalopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple cerebral infarcts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral thalamic infarcts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple cerebral metastasis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningo-encephalitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute disseminated encephalomyelitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral edema</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior reversible encephalopathy syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Air or fat embolism</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Brainstem</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage or infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral pontine myelinolysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cerebellum</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemorrhage or infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tumor</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Glasgow Coma Scale

<table>
<thead>
<tr>
<th>Best eye response</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Does not open eyes</td>
</tr>
<tr>
<td>2.</td>
<td>Opens eyes to painful stimuli</td>
</tr>
<tr>
<td>3.</td>
<td>Opens eyes to verbal command</td>
</tr>
<tr>
<td>4.</td>
<td>Opens eyes spontaneously</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best motor response</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>No motor response</td>
</tr>
<tr>
<td>2.</td>
<td>Extensor response</td>
</tr>
<tr>
<td>3.</td>
<td>Abnormal flexion</td>
</tr>
<tr>
<td>4.</td>
<td>Withdraws purposefully from painful stimuli</td>
</tr>
<tr>
<td>5.</td>
<td>Localizes to painful stimuli</td>
</tr>
<tr>
<td>6.</td>
<td>Follows verbal commands</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Best verbal response</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>No response</td>
</tr>
<tr>
<td>2.</td>
<td>Incomprehensible sounds</td>
</tr>
<tr>
<td>3.</td>
<td>Inappropriate words</td>
</tr>
<tr>
<td>4.</td>
<td>Disoriented and converses</td>
</tr>
<tr>
<td>5.</td>
<td>Fully oriented and converses</td>
</tr>
</tbody>
</table>

SCORE RANGE: 3 – 15
Table 3. Brain death determination criteria

<table>
<thead>
<tr>
<th>Coma</th>
<th>Brainstem Reflexes</th>
<th>Apnea test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack all evidence of responsiveness:</td>
<td>1. Absence of pupillary response to a bright light in both eyes.</td>
<td>Adjust vasopressors to a systolic blood pressure $\geq 100$ mm Hg. Preoxygenate for at least 10 minutes with 100% oxygen to a $P_{aO_2} &gt; 200$ mm Hg. Reduce ventilation frequency to 10 breaths per minute and PEEP to 5 cm H$_2$O. If pulse oximetry oxygen saturation remains $&gt;95%$, obtain a baseline blood gas. Disconnect the patient from the ventilator and preserve oxygenation (e.g., place an insufflation catheter close to the level of the carina and deliver 100% O$_2$ at 6 L/min). Abort if systolic blood pressure decreases to &lt;90 mm Hg. Abort if oxygen saturation measured by pulse oximetry is &lt;85% for &gt;30 seconds.</td>
</tr>
<tr>
<td>1. No eye opening or eye movement to noxious stimuli.</td>
<td>2. Absence of ocular movements using oculocephalic and oculovestibular reflex testing.</td>
<td>1. If no respiratory drive is observed, repeat blood gas ($P_{aO_2}$, $P_{aCO_2}$, pH, bicarbonate, base excess) after approximately 8 minutes.</td>
</tr>
<tr>
<td>2. Noxious stimuli should not produce a motor response other than spinally mediated reflexes.</td>
<td>3. Absence of corneal reflexes.</td>
<td>2. If respiratory movements are absent and arterial $P_{aCO_2}$ is $\geq 60$ mm Hg (or 20 mm Hg increase in arterial $P_{aCO_2}$ over a baseline normal arterial $P_{aCO_2}$), the apnea test result is positive.</td>
</tr>
<tr>
<td></td>
<td>4. Absence of facial muscle movement to a noxious stimulus.</td>
<td>If the test is inconclusive but the patient is hemodynamically stable during the procedure, it may be repeated for a longer period of time (10–15 minutes) after the patient is again adequately preoxygenated.</td>
</tr>
<tr>
<td></td>
<td>5. Absence of the pharyngeal and tracheal reflexes.</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Spinal cord syndromes

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Clinical presentation</th>
<th>Etiology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Central cord</strong></td>
<td>Greater upper motor impairment compared with lower extremities. Bladder dysfunction, and a variable degree of sensory loss below the level of injury. Dissociated sensory loss of pain and temperature in a cape distribution with preservation of light touch, joint position and vibration sense in these regions.</td>
<td>Trauma, syringomyelia, tumors and spinal cord ischemia.</td>
</tr>
<tr>
<td><strong>Anterior cord</strong></td>
<td>All spinal cord functions below the level of lesion are lost: motor, sensory and autonomic. Vibration and position sensation are retained.</td>
<td>Cord ischemia in the distribution of the anterior spinal artery.</td>
</tr>
<tr>
<td><strong>Hemicord or Brown-Sequard</strong></td>
<td>Ipsilateral weakness (corticospinal tract) and loss of joint position and vibratory sensation (posterior column), with contralateral loss of pain and temperature (spinothalamic tract) one or two levels below the lesion.</td>
<td>Trauma.</td>
</tr>
</tbody>
</table>
Figure 1. Emergent evaluation and treatment algorithm for comatose patients

Immediate stabilization of cardiopulmonary status and close monitoring of vital signs → Detailed history if possible

Rule out treatable toxic-metabolic causes

- Hypoglycemia/hyperglycemia
- Electrolyte abnormalities
- Hyperammonemia/renal failure
- Drug screen and blood gas

Use antidotes based on history and examination

- Opioids: Naloxone 0.2 – 4 mg I.V.
- Benzodiazepines: Flumazenil 0.2 – 3 mg I.V.
- Thiamine 100-500 mg with or preceding dextrose

Rule out neurological emergencies with focused neurological examination, a head CT and EEG

- Cerebral venous thrombosis
- Epidural and/or subdural hematomas
- Ischemic and/or hemorrhagic strokes
- Non-convulsive status epilepticus
- Meningitis / encephalitis
- Generalized hypoxia / anoxia

Further evaluation, which may include brain MRI, continuous EEG monitoring, endocrine studies, and lumbar puncture.