BOOK CHAPTER

Altered Mental Status and Coma

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Key Points

• Because the differential diagnosis of coma is broad, a systematic approach to patient evaluation and diagnostic testing is required.

• Patients with altered mental status may have subtle neurologic dysfunction, so careful neurologic examination is necessary.

• Quickly reversible causes should be sought before the initiation of a more lengthy diagnostic work-up. Naloxone, dextrose, and thiamine administration should be considered initially in patients with undifferentiated coma.

• Structural brain lesions that may require operative intervention dictate immediate consultation with a neurosurgical service.

Perspective

Altered mental status is a spectrum of disease ranging from sleepiness and confusion to frank coma. Approximately 3% of patients arrive at the emergency department (ED) in a altered state.

Epidemiology

Roughly 85% of cases of altered mental status are caused by metabolic or systemic derangements, whereas 15% are caused by structural lesions. Once the ABCs (airway, breathing, and circulation) have been controlled and the patient stabilized, it is the role of the emergency physician (EP) to quickly distinguish structural from metabolic and systemic causes.

Pathophysiology
Consciousness is collectively made up of arousal and cognition. Arousal is defined as the awareness of self and the surroundings. The neuroanatomic structure primarily responsible for arousal is the ascending reticular activating system, which is located in the dorsal part of the brainstem. It controls the input of somatic and sensory stimuli to the cerebral cortex and functions to initiate arousal from sleep. Cognition is the combination of orientation (accurate perception of what is experienced), judgment (the ability to process input data to generate more meaningful information), and memory (the ability to store and retrieve information). The brain's cognition centers are located primarily in the cerebral cortex.

Coma can be caused by damage to the brainstem, the cerebral cortex, or both. These structures are vulnerable to toxins, metabolic derangements, and mechanical injury. Localized, unilateral lesions in the cerebral cortex do not usually induce altered mental status or coma, even with other cognitive functions being impaired. However, if both cerebral hemispheres are affected, altered mental status or coma can occur, depending on the size of the insult and its speed of progression. The ascending reticular activating system can also be vulnerable to small, focal lesions in the brainstem, which can result in coma.

![Fig. 94.1](F0010) Cerebral insults leading to a depressed level of consciousness. A, Ascending reticular activating system; B, bilateral cerebral cortex.

**Presenting Signs and Symptoms**
The chief complaints of patients and their family members are highly variable along the spectrum of altered mental status. Patients may report increased sleepiness or periods of confusion and disorientation. They may have trouble concentrating or maintaining focus on tasks that were previously performed without difficulty. Family members may describe the patient as being less interactive or more difficult to arouse from sleep.

Regardless of the circumstance, the EP will frequently need to use alternative sources of information to answer key historical questions that may alter the breadth and speed of the diagnostic work-up undertaken. Common sources of information include family members, neighbors, prehospital personnel, law enforcement, and nursing home staff. They may know of preceding symptoms such as headache, nausea, vomiting, or fever. It is important to determine the rate of symptom onset and whether the patient had any history of trauma, exposure to drugs or toxins, or new medications or change in dosage. Family members usually have some knowledge regarding the patient's past medical history. Additionally, previous medical records should be reviewed whenever possible to confirm or augment the information provided. If the patient's historical baseline mental status cannot be established, the current findings must be assumed to be an acute change.

The age of the patient can be a key historical tool that may focus the physician on the most probable cause of the patient's symptoms (Box 94.1(a010)).

**Box 94.1**

Common Age-Related Causes of Altered Mental Status and Coma

- **Infant**
  - Infection
  - Trauma, abuse
  - Metabolic
- **Child**
  - Toxic ingestion
- **Adolescent, Young Adult**
  - Toxic ingestion
  - Recreational drug use
  - Trauma
- **Elderly**
  - Medication changes
  - Over-the-counter medications
  - Infection
Alterations in living environment
Stroke
Trauma

In infants, infectious causes of altered mental status are most common; however, nonaccidental trauma and metabolic derangements from inborn errors of metabolism are also possible causes. Toxic ingestions are commonly seen in young children. Adolescents and young adults are often seen in the ED after recreational drug use. The elderly are particularly susceptible to infectious causes and to disorders related to changes in medications or drug doses, use of over-the-counter medications, and alterations in their living environment. Psychiatric illness should be considered in the adolescent through elderly population and must be distinguished from medical illness as a cause of the patient's symptoms.

As with all patients, specific attention should first be paid to assessment of the ABCs and specific vital signs. Alterations in respiratory patterns such as hyperventilation, Kussmaul or Cheyne-Stokes breathing, agonal breathing, or apnea should be noted and may suggest toxic or metabolic derangements or primary central nervous system abnormalities. Marked hypotension or hypertension should be addressed immediately even if the underlying cause is unknown. Bradycardia may be the result of increased intracranial pressure as seen in the Cushing response and suggests a state of hypoperfusion. Tachycardia may also result in hypoperfusion and can be the result of toxic, metabolic, or primary cardiac causes. Assessment of temperature is crucial because both hypothermia and hyperthermia can cause altered mental status from infectious, structural (Box 94.2 (b0015)), environmental exposure, or toxic or metabolic causes (Box 94.3 (b0020)).

Box 94.2
Structural Causes of Altered Mental Status and Coma

<table>
<thead>
<tr>
<th>Trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Subdural hematoma</td>
</tr>
<tr>
<td>• Epidural hematoma</td>
</tr>
<tr>
<td>• Cerebral concussion, contusion</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stroke syndromes</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Embolism</td>
</tr>
<tr>
<td>– Cardiac (atrial fibrillation, endocarditis)</td>
</tr>
<tr>
<td>– Paradoxic (fat embolus)</td>
</tr>
<tr>
<td>• Thrombosis</td>
</tr>
<tr>
<td>– Basilar artery occlusion</td>
</tr>
<tr>
<td>– Cerebral venous sinus thrombosis</td>
</tr>
</tbody>
</table>

Hemorrhage
- Subarachnoid hemorrhage
- Pontine hemorrhage
- Cerebellar hemorrhage
- Intracerebral hemorrhage

Tumor
- Brainstem tumors
- Metastatic disease
- Angiomas

Pituitary apoplexy

Acute hydrocephalus

Infection
  - Subdural empyema, abscess

Box 94.3
Metabolic and Systemic Causes of Altered Mental Status and Coma

Hypoxia, Hypercapnia
  - Severe pulmonary disease (hypoventilation)
  - Severe anemia
  - Environmental, toxic
  - Methemoglobinemia
  - Cyanide
  - Carbon monoxide
  - Decreased atmospheric oxygen (high altitude)
  - Near-drowning

Glucose Disorders
  - Hypoglycemia
    - Chronic alcohol abuse and liver disease
    - Excessive dosage of insulin or other hypoglycemic agents
    - Insulinoma
  - Hyperglycemia
    - Diabetic ketoacidosis
    - Nonketotic hyperosmolar coma

Decreased Cerebral Blood Flow
  - Hypovolemic shock
  - Cardiac
- Vasovagal syncope
- Arrhythmias
- Myocardial infarction
- Valvular disorders
- Congestive heart failure
- Pericardial effusion, tamponade
- Myocarditis

Infectious
- Septic shock
- Bacterial meningitis

Vascular, hematologic
- Hypertensive encephalopathy
- Pseudotumor cerebri
- Hyperviscosity (sickle cell, polycythemia)
- Hyperventilation
- Cerebral vasculitis as a manifestation of systemic lupus erythematosus
- Thrombotic thrombocytopenic purpura
- Disseminated intravascular coagulation

Metabolic Cofactor Deficiency
- Thiamine (Wernicke-Korsakoff syndrome)
- Pyridoxine (isoniazid overdose)
- Folic acid (chronic alcohol abuse)
- Cyanocobalamin
- Niacin

Electrolyte, pH Disturbances
- Acidosis, alkalosis
- Hypernatremia, hyponatremia *(fn0010)*

* Can be associated with dilution of formula in infant feeding.

- Hypercalcemia, hypocalcemia
- Hypophosphatemia
- Hypermagnesemia, hypomagnesemia

Endocrine Disorders
- Myxedema coma, thyrotoxicosis
- Hypopituitarism
- Addison disease (primary or secondary)
Cushing disease
Pheochromocytoma
Hyperparathyroidism, hypoparathyroidism

Endogenous Toxins
Hyperammonemia (liver failure)
Uremia (renal disease)
Carbon dioxide narcosis (pulmonary disease)
Porphyria

Exogenous Toxins
Alcohols
  • Ethanol, isopropyl alcohol, methanol, ethylene glycol

Acid poisons
  • Salicylates
  • Paraldehyde
  • Ammonium chloride

Antidepressant medications
  • Lithium
  • Tricyclic antidepressants
  • Selective serotonin reuptake inhibitors
  • Monoamine oxidase inhibitors

Stimulants
  • Amphetamines, methamphetamines
  • Cocaine
  • Over-the-counter sympathomimetics

Narcotics, opiates
  • Morphine
  • Heroin
  • Codeine, oxycodone, meperidine, hydrocodone
  • Methadone
  • Fentanyl
  • Propoxyphene

Sedative-hypnotics
  • Benzodiazepines
  • Barbiturates
  • Rohypnol
  • Bromide

Hallucinogens
• Lysergic acid diethylamide
• Marijuana
• Mescaline, peyote
• Mushrooms
• Phencyclidine

Herbs, plants
• Aconite
• Jimsonweed
• Morning glory

Volatile substances
• Hydrocarbons (gasoline, butane, toluene, benzene, chloroform)
• Nitrites
• Anesthetic agents (nitrous oxide, ether)

Other
• γ-Hydroxybutyrate
• Ketamine
• Penicillin
• Cardiac glycosides
• Anticonvulsants
• Steroids
• Heavy metals
• Cimetidine
• Organophosphates

Disorders of Temperature Regulation, Environmental

  Hypothermia
  Heat stroke
  Malignant hyperthermia
  Neuroleptic malignant syndrome
  High-altitude cerebral edema
  Dysbarism

Primary Glial or Neuronal Disorders

  Adrenoleukodystrophy
  Creutzfeldt-Jakob disease
  Progressive multifocal leukoencephalopathy
  Marchiafava-Bignami disease
  Gliomatosis cerebri
  Central pontine myelinolysis
Other Disorders with Unknown Etiology

- Seizures
- Postictal states
- Reye syndrome † (fn0015)

† Prominent in the pediatric population.

- Intussusception † (fn0015)

Any signs of trauma should be sought immediately. Scalp lacerations or hematomas, depressed skull fractures, hemotympanum, raccoon eyes, Battle sign, cerebrospinal fluid otorhinorrhea, cervical spine step-offs, and crepitus all suggest a traumatic cause. Other signs of trauma include lesions on the chest, abdomen, or pelvis; long-bone deformities; and gross blood in the rectum or vagina or at the urethral meatus.

In the absence of trauma, breath odors may be helpful, including the smell of alcohol, ketones (diabetic or alcoholic ketoacidosis), and bitter almonds (cyanide toxicity). Abdominal findings include ascites, hepatosplenomegaly, ecchymosis, and striae. Lesions on the skin such as rashes, signs of drug use (needle tracks, medication patches), and embolic phenomena can be telling.

Neurologic Evaluation

A systematic neurologic examination is a key tool in determining whether the cause is structural, systemic, or metabolic. The basic examination includes evaluation of the patient's level of alertness, cranial nerves, strength, sensation, reflexes, gait, and cerebellar function.

The Glasgow Coma Scale (GCS) can be used to assess the patient's level of consciousness. The GCS does not differentiate between causes of altered mental status or coma or assess cognition. However, it is useful in monitoring changes in mental status when serial examinations are performed and serves as an objective reference when communicating with consultants (Table 94.1 (t0010)).

Table 94.1
Glasgow Coma Scale

<table>
<thead>
<tr>
<th>Eye opening</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous</td>
<td>4</td>
</tr>
<tr>
<td>To voice</td>
<td>3</td>
</tr>
<tr>
<td>Motor response</td>
<td>To pain</td>
</tr>
<tr>
<td>----------------</td>
<td>--------</td>
</tr>
<tr>
<td>Verbal response</td>
<td>2</td>
</tr>
</tbody>
</table>

### Verbal response

<table>
<thead>
<tr>
<th>Adult</th>
<th>Oriented</th>
<th>5</th>
<th>Confused</th>
<th>4</th>
<th>Inappropriate words</th>
<th>3</th>
<th>Incomprehensible words</th>
<th>2</th>
<th>None</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pediatric</td>
<td>Appropriate</td>
<td>5</td>
<td>Cries, consolable</td>
<td>4</td>
<td>Persistently irritable</td>
<td>3</td>
<td>Restless, agitated</td>
<td>2</td>
<td>None</td>
<td>1</td>
</tr>
</tbody>
</table>

| Motor response | Obeys commands | 6 | Localizes pain | 5 | Withdrawing to pain | 4 | Flexion to pain | 3 | Extension to pain | 2 | None | 1 |

### Maximum score

| Maximum score | 15 |

A focal neurologic deficit usually suggests a structural cause. Pupillary findings such as unilateral dilation or a “blown pupil” and loss of reactivity indicate uncal herniation, which is a neurosurgical emergency. Funduscopic examination can demonstrate hemorrhage in the setting of trauma or papilledema, which suggests increased intracranial pressure.
Testing of eye movements is a hallmark in the neurologic examination of patients with altered mental status or coma. Eye movements are coordinated by ocular centers in the cerebral cortex and the medial longitudinal fasciculus located in the brainstem. The extraocular muscles are innervated primarily by cranial nerves III, IV, and VI. Disconjugate gaze in the horizontal plane is common and can be associated with sedated or drowsy states or alcohol intoxication. Disconjugate gaze in the vertical plane is more ominous and points to pontine or cerebellar lesions. A persistently adducted eye is caused by cranial nerve VI paresis, whereas a persistently abducted eye is caused by cranial nerve III paresis. These are nonlocalizing lesions; however, elevated intracranial pressure or mass effects from trauma, for example, can compromise cranial nerve functions via extrinsic compression. In the absence of contraindications, oculocephalic (doll's eyes) or oculovestibular reflex testing can be very helpful. If intact, these reflexes demonstrate functional integrity of a significant majority of the brainstem, thus making it exceedingly unlikely as the anatomic location for the cause of the patient's altered mental status. 1 2 5 7

Differential Diagnosis and Medical Decision Making

The differential diagnosis of altered mental status and coma is extensive and can be daunting for the busy EP (see Boxes 94.1 to 94.3). Fortunately, there are many distinguishing features in the physical examination that, when combined with information gleaned from the patient's history of the present illness, past medical history, and response to therapy (i.e., dextrose, naloxone), point to a particular cause and are frequently of greater diagnostic value than imaging, electrocardiograms (ECGs), and laboratory tests. 1 However, a systematic approach is best and reduces the likelihood of missing an important clue. 1 2 8

Diagnostic Testing

Diagnostic testing in patients with altered mental status or coma is based on information gathered from the history and physical examination, which in most cases will point toward a structural versus systemic or metabolic cause. Extensive metabolic work-ups should not precede neuroimaging studies in patients with altered mental status or coma that may be due to structural causes. Similarly, treatment of suspected narcotic overdose or hypoglycemia should not be delayed in favor of imaging studies. However, in undifferentiated patients, diagnostic tests should be performed in parallel whenever possible to avoid unnecessary delays in initiating treatment. A general approach to the diagnostic work-up of patients with altered mental status or coma is shown in Figure 94.2 (f0015).
Fig. 94.2
Diagnostic approach to altered mental status and coma. *BP*, Blood pressure; *CT*, computed tomography; *CVA*, cerebrovascular accident; *ECG*, electrocardiography; *GCS*, Glasgow Coma Scale; *HR*, heart rate; *ICU*, intensive care unit.
care unit; MRI, magnetic resonance imaging; OR, operating room; RR, respiratory rate; RSI, rapid-sequence intubation.

Laboratory Evaluation

Basic laboratory studies are useful in determining the most common metabolic causes of altered mental status. Capillary blood glucose measurement, both prehospital and on arrival at the ED, can often avoid further extensive work-ups, especially in patients with diabetes or alcohol intoxication. Serum electrolytes and renal function studies may demonstrate an anion gap acidosis or significant sodium or potassium imbalance or uremia. Serum calcium may be a marker for metastatic disease, and severe hypercalcemia can be associated with altered mental status.

A complete blood cell count may demonstrate profound anemia from witnessed or occult blood loss. A low white blood cell count raises concern for an immunocompromised state, but an elevated white blood cell count is less helpful in making the diagnosis as a nonspecific marker for infection, inflammation, or stress. Low platelet levels may indicate sepsis, disseminated intravascular coagulation, or intracranial bleeding. Serum coagulation studies may be performed to look for bleeding dyscrasias or supratherapeutic levels of anticoagulants (warfarin) or, when combined with other liver function studies, may provide evidence of liver dysfunction. Blood platelet counts and coagulation studies should be performed before obtaining central venous access and performing lumbar puncture or other invasive procedures if time or the patient's condition allows. Checking the serum ammonia level is controversial; it has not been shown to be a reliable marker for the cause of altered mental status because it can be normal in patients with hepatic encephalopathy but can also be elevated in those with acute hepatic failure from other causes, as well as valproic acid toxicity and inborn errors of metabolism.

Thyroid function studies are useful in patients with suspected myxedema coma secondary to hypothyroidism. Arterial blood gas (ABG) analysis can demonstrate hypercapnia or hypoxia and aid in the classification of acid-base disturbances. Cooximetry can be added to ABG analysis to determine carbon monoxide levels or methemoglobinemia. In the absence of contraindications, cerebrospinal fluid analysis is mandatory when considering a central nervous system infectious cause or to rule out subarachnoid hemorrhage after a negative, non–contrast-enhanced computed tomography (CT) scan of the brain.

Urinalysis is a useful tool that provides information about volume status (specific gravity), spilling of glucose as in hyperosmolar coma, and evidence of infection, which is a common cause of altered mental status in the elderly. Urine drug screening for illicit drug use as a cause of altered mental
status is often less helpful unless other causes are not forthcoming, but it may help confirm a suspected diagnosis. Microscopic analysis of urine can reveal calcium oxalate crystals in the setting of ethylene glycol ingestion.

Imaging

The mainstay of diagnostic imaging in the setting of altered mental status is non–contrast-enhanced CT of the brain. It is fast and readily available in most ED settings and can reveal the vast majority of intracranial hemorrhages large enough to induce coma. Hydrocephalus is also readily detected on non–contrast-enhanced CT. If subarachnoid hemorrhage is suspected, negative CT findings should be followed by lumbar puncture. When tumor or infection is suspected, contrast-enhanced CT may be indicated.

A limitation of brain CT scanning is the potential poor view of the posterior fossa as a result of linear artifacts created by the thick skull base. Magnetic resonance imaging (MRI) of the brain is more helpful in identifying structural lesions in this area; however, its cost and limited availability, as well as the inability to monitor unstable patients, make this imaging modality less feasible in some ED settings. CT angiography or venography may be available for the diagnosis or treatment (or both) of vertebral or basilar artery stenosis or occlusion, intracerebral aneurysms, cerebral venous sinus thrombosis, or arteriovenous malformations. If brain abscess or metastatic lesions are a concern, contrast-enhanced head CT can be useful in making the diagnosis.

Other diagnostic tools include plain radiography, which can reveal serious pneumonia, acute respiratory distress syndrome, ingested illicit substances seen in “body packers,” or specific types of ingestions such as mercury, iron, and lead. This can be particularly helpful in the pediatric population when the history is not reliable. ECGs are useful for diagnosing certain ingestions (e.g., tricyclic antidepressants), electrolyte abnormalities (e.g., potassium, calcium), and hypothermia. Though not commonly used in the ED, electroencephalographic monitoring is mandatory for comatose patients with suspected status epilepticus.

Treatment

Initial stabilization and quick control of the ABCs are paramount in patients with altered mental status. Patients should be placed immediately on telemetry with concomitant administration of oxygen and initiation of intravenous access. Definitive airway control with endotracheal intubation is critical in patients without a gag reflex or with a GCS score lower than 8. Lidocaine premedication should be used for rapid-sequence intubation in patients with suspected elevated intracranial pressure. In the setting of trauma, maintaining spinal precautions with a backboard in addition to initiation of intravenous fluid therapy is mandatory.
Once initial stabilization has been addressed, reversible causes must be sought. A bedside ECG and capillary blood glucose test should be obtained immediately. Blood and urine should be sent to the laboratory for studies early after the patient's arrival, and the patient should be scheduled for emergency head CT. Empiric administration of a “coma cocktail” consisting of dextrose, thiamine, and naloxone is controversial but may bring immediate results and significantly narrow the differential diagnosis.

Physical examination with specific attention to brainstem function dictates further work-up and therapy. Patients whose brainstem function is compromised with evidence of brain herniation require immediate evaluation by neurosurgery. Empiric therapy with mannitol may be indicated in this setting. Elevating the head of bed to 30 degrees (if not contraindicated) and hyperventilation to a \( P_{CO_2} \) of 35 mm Hg are additional temporizing measures. Evidence of brain herniation secondary to a traumatic cause may necessitate the use of burr holes on the side of the dilated pupil as a last resort. Ventriculostomy and monitoring of intracranial pressure are often performed by a neurosurgeon in the ED.

Patients with compromised brainstem function but no evidence of herniation should have immediate consideration for basilar artery or bilateral vertebral artery occlusion and undergo CT or magnetic resonance angiography while receiving supportive care with a concomitant toxic and metabolic work-up. Patients are considered to have unsalvageable brain tissue if they have no brainstem reflexes, have not received neuroactive medications, and are normothermic.

In patients whose brainstem function is intact, supportive care is provided while the work-up proceeds. Lesions discovered on brain CT require immediate evaluation by neurosurgery. In general, patients with operable lesions are transferred immediately to the operating room; patients with inoperable lesions continue to receive supportive care. In cases in which an infectious cause is suspected, empiric antibiotic coverage should not be delayed for lumbar puncture or other diagnostic modalities.

In the setting of suspected toxic ingestion, activated charcoal with or without sorbitol is indicated. Gastric lavage has been used in patients with recent (less than 60 minutes since ingestion), potentially lethal toxic ingestion (e.g., tricyclic antidepressants, beta-blockers); however, this intervention is somewhat controversial and associated with potential complications, including aspiration and esophageal damage. Specific antidotes, if applicable based on the history and physical examination, should be initiated early. Finally, early hemodialysis should be considered in patients who have ingested substances amenable to this therapeutic modality.

Admission and Discharge
The majority of patients who have significant alterations in mental status require admission for further work-up and treatment. The exception is patients with an easily reversible cause, such as opiate overdose or hypoglycemia, who may be discharged after a period of observation during which there is a return to baseline mental status. In addition, patients with alcohol intoxication and no other cause of altered mental status may be discharged once they are deemed clinically sober. Placement in an intensive care unit setting is usually appropriate for patients whose mental status is persistently altered.

Immediate consultation with the neurosurgical service is paramount for patients with potentially operable lesions. After definitive airway control and stabilization of vital signs, rapid transfer to a center with neurosurgical diagnostic and therapeutic capabilities should be sought if the necessary resources are not available locally.

Suggested Readings


References


