


Coma and Brain Death


MHD – Neuroscience Module

Matthew McCoy, MD
Associate Professor, SSOM
Department of Neurology, LUHS



Goals & Objectives


- Goal: To understand the pathophysiologic basis of coma and brain death
- Objectives
 - 1. Understand the anatomy of states of altered mental status
 - 2. Know the common examination findings for patients with various states of coma and brain death
 - 3. Understand the anatomic underpinning of the vestibulo-ocular reflex



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Terminology

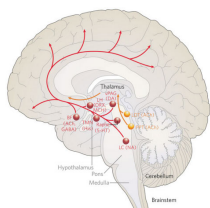
Consciousness	→	Full awareness of self and one's relationship to the environment (the beginning of lecture)
Obtundation	→	"Mental blunting": mild-to-moderate reduction in alertness and lesser interest in the environment (15 min into lecture)
Stupor	→	Deep sleep or similar behavioral unresponsiveness from which one can only be aroused with vigorous stimulation, and is still impaired (30 min into lecture)
Coma	→	Unarousable unconsciousness—cannot be aroused regardless of stimuli (the end of lecture)



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What Makes You...You?

- You need to be awake
 - Intact arousal system, which is a large/diffuse system running from the upper brainstem (pons), through the medial diencephalon (hypothalamus, thalamus), and diffusely spreading out across the cortex
- You need your cerebral hemispheres to be able to process information from the environment and integrate/interpret that information for use



Ascending arousal system (Plum and Posner's *Diagnosis of Stupor and Coma*)



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What Could Alter Mental Status?

- Something big enough, or diffuse enough, to widely and diffusely depress the function of *both* cerebral hemispheres (which in turn can also push down on the brainstem)
- What could do that?
 - Massive stroke that increases intracranial pressure (the skull is a fixed box)
 - Metabolic process, medications, infections, etc that bathe the brain in a bad environment



(Plum and Posner's *Diagnosis of Stupor and Coma*)

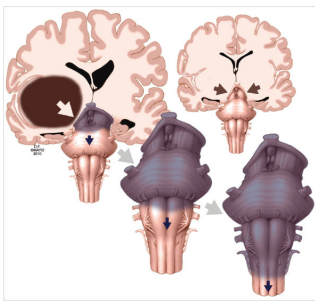


Some of the most challenging cases are patients with aphasia. Are they not speaking because their level of consciousness is impaired or "simply" because they cannot understand or produce language due to a focal lesion? Without delving into philosophy, a patient with aphasia would not be considered to have "altered mental status" but rather a fixed, focal neurologic deficit.

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For Example

- Patient has a large hemispheric stroke
- As the lesion expands (blood, edema) the brain pushes into any space it can
- Compresses the ventricles, crosses the midline, pushes downward onto the brainstem (herniation)

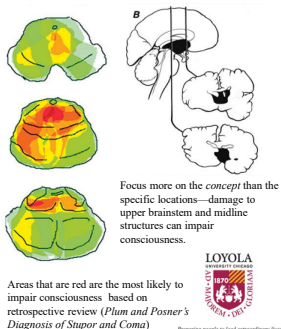


Wijdicks EFM. *Continuum*2015;21(5):1411-1424

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What Could Alter Mental Status

- Abnormalities that depress or destroy the brainstem activating mechanisms near the central core of the diencephalon (thalamus, hypothalamus), midbrain, and rostral pons affect arousal
- What could do that?
 - Cerebellar lesions that cause swelling and push forward into the brainstem
 - Brainstem strokes
 - Some metabolic disorders, inflammatory conditions and infections



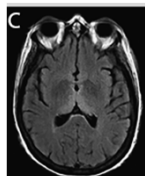
For Example (Dramatic Examples!)

Encephalitis Lethargica
 Described in 1917 by Constantin von Economo: damage to the posterior hypothalamus (a midline structure) produced a profound somnolence (sleeping 20 hours/day) with patients in this sleep-like state for years

Oliver Sacks ("The Man Who Mistook His Wife for a Hat") gave patients L-DOPA with improvement in symptoms in the late 1960s and 1970s

His story was made into the movie *Awakenings* in 1990 with Robert DeNiro and Robin Williams

Midline Thalamic Lesions
 Lesions of the medial thalamus (due to Artery of Percheron strokes or metabolic derangements as can occur due to thiamine deficiency) can lead to alteration in mental status including coma (pictured)



Think Treatable First!

- A thorough history (using any ancillary information you can obtain) and a physical examination are essential
 - Why did this happen?
 - Do not assume "irreversible" as long as the cause remains indeterminate

POTENTIALLY REVERSIBLE/TREATABLE CAUSES OF COMA
 BASILAR ARTERY OCCLUSION
 STATUS EPILEPTICUS
 BACTERIAL MENINGITIS
 HERPES SIMPLEX ENCEPHALITIS
 HYDROCEPHALUS
 SUBARACHNOID HEMORRHAGE
 VENOUS SINUS THROMBOSIS
 INTOXICATION
 HERNIATION (SUBDURAL HEMATOMA/TRAUMA)
 METABOLIC DERANGEMENTS (GLUCOSE, THIAMINE)



Approach to the Altered Patient: Its SIMPLE

- S
- I
- M
- P
- L
- E



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Approach to the Altered Patient: Its SIMPLE

- STRUCTURAL LESION
- INFLAMMATION or INFECTION
- METABOLIC or MEDICATION
- PAROXYSMAL (Seizure, Arrhythmia)
- LATE ONSET DECLINE (Dementia)
- EARLY ONSET (Neurodegenerative condition)



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What do you do with that?

- Structural lesion: Imaging (CT/MRI)
- Infection/inflammation: Imaging/CSF/Labs
- Metabolic/Medications: Labs/history
- Paroxysmal: Electrical studies (EEG/ECG)
- Late Onset: Multiple approaches/good history
- Early Onset: Genetic testing



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Case Example

- A 64 year old male with history of hypertension and diabetes is “found down.” He is brought by EMS to the emergency room. He is intubated. Despite stopping all sedating medications, he is “not waking up.” A non-contrast head CT shows loss of gray-white differentiation and sulcal effacement. Neurology is consulted.
- How do you evaluate the patient?



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Evaluation of the Comatose Patient

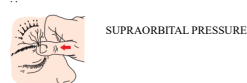
- 1. Do we know what happened and are there any confounding factors?
 - Lingering effects of prior sedation, other medications, illegal drugs or alcohol
 - Major electrolyte, acid-base, or endocrine abnormalities
 - Body temperature: should be normal (or close to normal) (preferably 96.8-98.6°)
 - Blood pressure: Systolic blood pressure should be >90 mm Hg
 - Lower values impair the light reflex



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Evaluation of the Altered Patient

- 2. Is there are a response to stimuli?
 - Response to voice or gentle shaking?
 - If no: Is there a response painful stimuli?
 - Should be done side-to-side, lateralized first and then midline
 - Test all 4 limbs
 - Brain dead patients will not open their eyes or react
 - Reflexes *can persist* in brain dead patients as they are mediated by the spinal cord and *do not* indicate the brain/brainstem are functioning




(Plum and Posner's Diagnosis of Stupor and Coma) Preparing people to lead extraordinary lives



Evaluation of the Altered Patient

- If there is a reaction:
 - Localize to pain (stupor)
 - Posturing responses (coma)
 - Decorticate (both arms flex, legs extend): *usually* more rostral and *usually* less severe
 - Decerebrate (arms and legs extend): *usually* more caudal and *usually* more severe

LOCALIZES TO PAIN





B Upper midbrain damage

DECORTICATE

C Upper pontine damage

DECEREBRATE

(Pham and Posner's Diagnosis of Stupor and Coma)

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"Posturing responses" imply brain or more likely brainstem injury; however, despite ingrained tradition as to localization (which is based on cuts!), both responses can be produced by several different lesions. Both imply injury, but are coordinated movements that require *some* intact brain circuitry (ie, brain dead patients do not posture)

Evaluation of the Altered Patient

- 3A. Is the patient breathing?
 1. NO → BAD
 2. YES
 - ↓
 - WHAT DOES IT LOOK LIKE?
- 3B. If intubated, breathing "above" the ventilator?

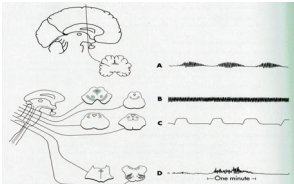
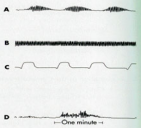


Fig. 16-3 Breathing patterns. A, Cheyne-Stokes respiration. B, Central neurogenic hyperventilation. C, Apneustic. D, Ataxic Breathing. (Modified from Plum F, Posner JB: The Diagnosis of Stupor and Coma, ed 2. Philadelphia, 1980, JB Lippincott)

CHEYNE-STOKES (A): CRESCENDO/DECRESCENDO; CAN OCCUR WITH BILATERAL CORTICAL LESIONS

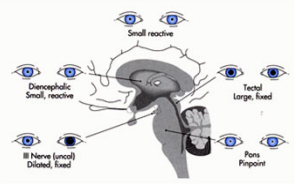
ATAXIC/IRREGULAR (D): IMPENDING RESPIRATORY FAILURE FROM MEDULLARY LESION



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Evaluation of the Altered Patient

- 4. What do the pupils look like?
 - "Normal" pupils are 4-6 mm
 - In a brain dead patient, the pupils are *also* 4-6 mm (there is no sympathetic or parasympathetic innervation!) but *do not* react to light
 - It is essential to have the room darkened and a proper light source



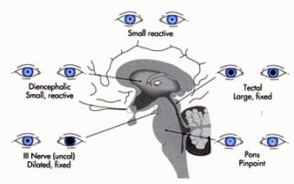
Small reactive
Diencephalic Small, reactive
III Nerve (uncol) Dilated, fixed
Tectal Large, fixed
Pons Pinpoint

ASYMMETRIC PUPILS ARE ALWAYS BAD

SMALL PUPILS CAN BE CAUSED BY NARCOTICS

ATROPINE (FOR CPR) CAUSES LARGE PUPILS

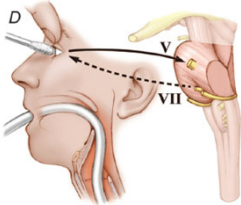
PUPILLARY LIGHT REFLEX IS PRESERVED IN METABOLIC COMA




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Evaluation of the Altered Patient

- 5. Test for the corneal reflex
 - Important to touch the cornea not the sclera
 - Can use a tissue, wisp of cotton or squirting sterile saline from a few inches away
 - Closely observe for *any* movement



Corneal reflex: message is carried from the cornea back to the brainstem (VI), then activates the facial nerve (bilaterally) which causes the blink response

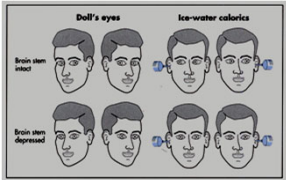


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Evaluation of the Altered Patient

- 6. Evaluate for eye movements (oculocephalics)
 - Rotate the head side-to-side: the eyes should roll counter to the head (“Dolls Eyes”)
 - Cold calorics—injecting cold water into the ear, should induce eye movement
 - Brain dead patients will not move at all (“frozen eyeballs”)



REVIEW MEDICATIONS CAREFULLY:
PHENYTOIN AND TRICYCLIC ANTIDEPRESSANT TOXICITY CAN CAUSE VESTIBULAR FAILURE; AMINOGLYCOSIDES CAN ALSO ALTER VESTIBULAR RESPONSES




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Role of the Vestibulo-Ocular Reflex

- Keep your eyes on the horizon despite head and body movement
- Rapidly orient you to sound (“*is that a bear about to attack me?*”)
- Fun fact: 40% of brain volume is dedicated to eye movements



Motorcycle riding is also a wonderful way to learn about brachial plexus and spinal cord injuries.



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Vestibulo-Ocular Reflex: Normal

- A. Both vestibular apparatus fire at the same rate when the head is facing forward
1. When the head turns to the right, the right vestibular apparatus fires faster
2. A signal is sent to the right vestibular nuclei
3. The right vestibular nuclei "turn off" the neighboring right abducens nucleus (which prevents *either* eye from turning right)
4. The right vestibular nuclei "turn on" the contralateral left abducens nucleus
5. A signal is sent up the MLF from the abducens nucleus to the right oculomotor nucleus
6. Both eyes turn left (opposite the direction of head movement)

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Vestibulo-Ocular Reflex: Cold Calorics

- A. Both vestibular apparatus fire at the same rate when the head is facing forward
1. When cold water is injected into the *left* ear, the firing right is slowed on the *left* making the *right side relatively faster*
2. A signal is sent to the right vestibular nuclei *presuming the head is turning to the right*
3. The right vestibular nuclei "turn off" the neighboring right abducens nucleus (which prevents *either* eye from turning right)
4. The right vestibular nuclei "turn on" the contralateral left abducens nucleus
5. A signal is sent up the MLF from the abducens nucleus to the right oculomotor nucleus
6. Both eyes turn *left* (towards the cold water *presuming the head is going right*)
7. But you're *not going right!* The eyes try to jerk back to the midline (which is *to the right*...the fast motion (nystagmus) is *opposite the cold water*)

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Vestibulo-Ocular Reflex: Cold Calorics

COWS
Cold Opposite Warm Same

Problem with the mnemonic:
refers to the *corrective nystagmus* and NOT the initial eye movement!

COWS

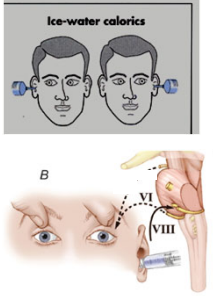
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Evaluation of the Altered Patient

50 mL OF ICE WATER IS INFUSED;
MONITOR FOR 2 MINUTES

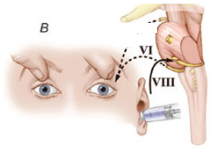
1. COLD CALORICS ON A COMATOSE PATIENT: EYES DEVIATE TOWARDS THE COLD WATER WITH NO CORRECTIVE NYSTAGMUS (BRAIN IS INJURED AND DOES NOT RECOGNIZE THE ERROR)

2. COLD CALORICS IN A BRAIN DEAD PATIENT: THERE IS NO MOVEMENT OF THE EYES (THE BRAINSTEM IS MORTALLY INJURED AND DOES NOT RESPOND)



Ice-water calorics

B

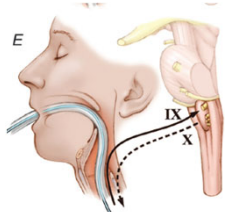


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Evaluation of the Altered Patient

7. Test the gag and cough reflex

- Move the endotracheal tube for the gag reflex and deep bronchial suctioning for the cough
- “Testing is far more reliable when sticking a finger deep in the back of the throat and moving the uvula”



E

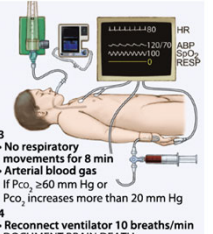
Gag reflex: message is carried from the throat/pharynx by the glossopharyngeal, then activates the vagus nerve (bilaterally) which causes a gag

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Evaluation of the Altered Patient

8. Apnea test

- The patient is pre-oxygenated and blood gas is checked
- Ventilator is stopped for 8 minutes (oxygen continues via catheter)
- Monitor for any spontaneous breaths & monitor vitals
- PaCO₂ will rise (to 60 mm Hg or 20 mm Hg above baseline)



3
• No respiratory movements for 8 min
• Arterial blood gas
If Pco₂ ≥60 mm Hg or Pco₂ increases more than 20 mm Hg

4
• Reconnect ventilator 10 breaths/min
DOCUMENT BRAIN DEATH


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Brain Death

- “Death by neurologic criteria”
 - Patients who are brain dead are dead
 - Systemic circulation is preserved but there is no evidence of any brain or brainstem function
 - The patient is no longer alive; medical interventions should be discontinued as the life of the patient has ended
 - Essential to be clear with communication
 - Discussion about organ donation should occur

In most states, brain death can be declared by a single physician based on a single examination. In 6 states 2 examinations are required: CA, CT, FL, IA, KY, LA.


For pediatrics the rules are more complex and based on the patient's age.



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Other Terms

- Vegetative State (“unresponsive wakefulness syndrome”)
 - Impaired consciousness lasting >28 days
 - Spontaneous eye opening & sleep-wake cycles without any purposeful behavior suggestive of awareness of the environment
- Minimally Conscious State
 - Severe alteration in consciousness but exhibits purposeful behaviors (visual tracking, object manipulation, reactions to external stimuli)
 - Can regain some language function (“minimally conscious state plus”)




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Ancillary Testing in Coma/Brain Death

Ancillary Test	Brain Death	Pitfalls
EEG	Absence of cerebral electrical activity	Electrical artifacts Evaluate the cortex, not brainstem
Somatosensory Evoked Potential (SSEP)	Absence of cortical response (N20)	Evaluates cortex, not brainstem
Cerebral angiogram	Absence of flow	Partial filling of vessels without perfusing branches
Transcranial doppler	Small peaks in systole	Highly operator dependent
Cerebral scintigraphy with nuclear scan	No brain perfusion	Incorrect injection

KEY POINT: ALL *MAY* BE HELPFUL, BUT HAVE LIMITATIONS AND *DO NOT* REPLACE THE CLINICAL EXAMINATION!



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Prognostication

- Patient is not brain dead—what is the chance of meaningful recovery? Clinical Findings

Examination Finding	Prognosis	Challenges
Absent pupillary response at 72 hours	100% specificity for prediction of poor outcome (0% false positive rate)	Poor sensitivity—presence of response <i>does not</i> mean good outcome: only 21% do
Absent corneal reflex	0 patients with good outcome	Only 24% with corneals had a good outcome
Absent motor response or extensor response at 72 hours	Poor outcome with essentially 0 false positives (1 study with a 5% FP; all others 0)	
Myoclonus Status Epilepticus	If present w/in 24 hours, poor outcome in all cases	Rare—4% of post-anoxic cases

"Poor outcome": coma or death at 1 month or severe disability at 6 months



A Tale of Caution in the Modern Era

- A 27 year old female suffered a ventricular fibrillation arrest. Spontaneous cardiac rhythms were restored. She underwent "hypothermia protocol." After cooling was stopped and 72 hours had gone by, pupil responses were absent and SSEPs failed to show an N20 response. Discussion with the family revolved around continuation of care vs terminal extubation. Intensive medical care was continued. She was stabilized enough for transfer to a skilled nursing facility, still ventilated and comatose.



A Tale of Caution in the Modern Era

- Within a few weeks she improved, was extubated, her neurologic examination improved, and she walked into her follow up clinic visit.



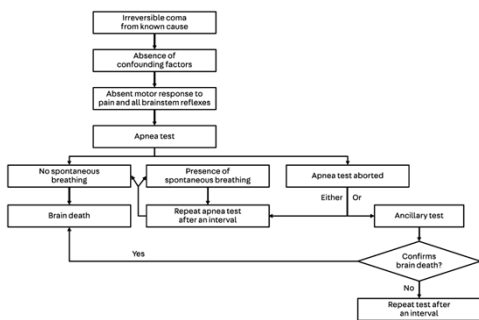
A Tale of Caution in the Modern Era

- Hypothermia makes prior predictive models less predictive
 - May prolong clearance of medications, alter metabolism, physiologic parameters, and cause encephalopathy in-and-of-itself
 - “Fallacy of the self-fulfilling prophecy”: when poor neurologic outcomes are caused by decisions to withdraw or withhold therapy based on the *perception* of a poor neurologic prognosis



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Determining Brain Death



USMLE Content

- Global cerebral dysfunction: altered states of consciousness; delirium; coma/brain death
- Cranial nerve disorders: cranial nerve injury, nystagmus



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