Neurological Assessment of the Unresponsive Patient

Raj Dhar, MD, FRCP(C)
Assistant Professor of Neurology
(Division of Neurocritical Care)

Disclosures
• The author has no financial disclosures related to any of the topics covered
• Receives grant support from the American Heart Association for unrelated research
  • Scientist Development Grant: The role of transfusion in optimizing cerebral oxygen delivery and preventing ischemia after subarachnoid hemorrhage

Purpose of the Neuro Exam
• Localize the source of symptoms and deficits
  • "Where is the lesion?"

• Real-time assessment of brain function
  • Detect changes before permanent injury occurs
    • E.g. increasing mass effect / ICP, herniation

• Limited in the comatose ICU patient
  • Sedation also limits ability to monitor patients
  • Need to focus on reflexes and responses to stimuli

Case #1
• Consultation is requested on a 45 year-old woman who is 24-hours post-CABG
• She is not waking up or responding since surgery
  • Head CT has been performed and is ‘negative’
• Possible ‘seizure-like’ movements when stimulated
  • Urgent EEG obtained with generalized slowing
• The cardiac surgeons are perplexed & baffled …
Level of Consciousness

- **Arousal** is mediated by activity of the ascending reticular activating system
  - Projections of neurons from meso-pontine tegmentum to the thalamus and distributed widely into the forebrain
- **Awareness** is separate and encompasses attention, perception, memory and motivation
  - Cannot occur without arousal first
  - Arousal without awareness is hallmark of vegetative state
- **Coma** is a state of “brain failure” where person is unresponsive to stimulation (unarousable and unaware)
  - Does not open eyes or make purposeful movements
  - Failure of arousal due to brainstem or bilateral hemispheric dysfunction (i.e. non-specific)

Arousal Neuro-Anatomy?

- **Reticular Activating System**
  - Cholinergic neurons from tegmental nuclei to relay nuclei of thalamus as well as the midline-intralaminar nuclei
  - Monoamine pathways also project to thalamus (paramedian reticular formation) and hypothalamus
  - Thalamus: projections to basal forebrain are especially important to arousal

Glasgow Coma Scale
Examination of Arousal

- Observe the patient
  - Are eyes open spontaneously?
  - Is there purposeful movement (reaching for tube, crossing legs)?
  - Are there abnormal movements (e.g., myoclonus)?
- Stimulate the patient, first with voice, then with tactile/painful stimuli (graded approach)
  - Is there eye opening to voice or stimulation (what degree?)
  - Open eyes / see if able to follow commands before applying pain
  - Start with midline / central stimuli to assess motor localizing
    - Supraorbital ridge or TMJ => sternum / trapezius => nail beds
  - Are movements symmetric – which is best side?

<table>
<thead>
<tr>
<th>States of Abnormal Responsiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arousal</td>
</tr>
<tr>
<td>Brain death</td>
</tr>
<tr>
<td>Coma</td>
</tr>
<tr>
<td>Vegetative state</td>
</tr>
<tr>
<td>Minimally conscious state</td>
</tr>
<tr>
<td>Akinetic mutism</td>
</tr>
<tr>
<td>Delirium</td>
</tr>
<tr>
<td>Locked-in syndrome</td>
</tr>
</tbody>
</table>

History

- Obtained from friends & relatives, EMS, and past records
- Onset: abrupt vs. gradual
- Recent complaints (headache, vertigo, etc.)
- Medical illnesses, trauma
- Psychiatric history
- Drug use – prescription, illicit, alcohol

Other clues in the examination

- Vital signs
  - Hypertension
  - Fever
- Meningismus
- Optic fundi
- Skin
Neuro Exam in Our Patient

- Does not open eyes to any stimuli
- Pupils 5mm bilaterally and sluggish reaction
- Globes are dysconjugate
- Corneal response present bilaterally
- Oculocephalic response present to both sides
- Intact cough and ventilatory drive

### Brainstem Reflexes

<table>
<thead>
<tr>
<th>Reflex</th>
<th>Examination Technique</th>
<th>Normal response</th>
<th>Afferent Pathway</th>
<th>Brainstem Response</th>
<th>Efferent Pathway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pupils</td>
<td>Response to light</td>
<td>Direct &amp; consensual pupillary constriction</td>
<td>Midbrain (S-W nuclei)</td>
<td>CS III + VI</td>
<td></td>
</tr>
<tr>
<td>Oculocephalic</td>
<td>Turn head side to side</td>
<td>Eyes move conjugately in opposite direction</td>
<td>Semicircular canals = vestibular n.</td>
<td>CS III + VI</td>
<td></td>
</tr>
<tr>
<td>Vestibuloocular (cold calorics)</td>
<td>Irrigate ear canal with cold water</td>
<td>Awake: nystagmus with head extension away; Cerebellar tonic deviation towards</td>
<td>Vestibular nuclei, PPRF</td>
<td>CS III + VI</td>
<td></td>
</tr>
<tr>
<td>Corneal</td>
<td>Stimulation of cornea</td>
<td>Eyelid closure</td>
<td>Trigeminal nerve</td>
<td>CS V</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>Stimulation of carina</td>
<td>Cough</td>
<td>CN IX and X</td>
<td>Medulla</td>
<td>CS IX + X</td>
</tr>
<tr>
<td>Gag</td>
<td>Stimulation of soft palate</td>
<td>Symmetric elevation of palate</td>
<td>CN IX and X</td>
<td>Medulla</td>
<td>CS IX + X</td>
</tr>
</tbody>
</table>

### Anatomy of Pupillary Response

![Diagram of Pupillary Response](image)

### Pupillary Abnormalities

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Localization</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral pupillary dilatation</td>
<td>Oculomotor nerve dysfunction</td>
<td>Unilateral herniation, Aneurysm rupture, mass effect, drug intoxication</td>
</tr>
<tr>
<td>Bilateral dilated (unreactive) pupils</td>
<td>Extensive midbrain injury</td>
<td>Central herniation, Drug intoxication (TCAs, anticholinergics)</td>
</tr>
<tr>
<td>Unilateral miosis* (± ptosis)</td>
<td>Horner’s syndrome (sympathetic injury)</td>
<td>Brainstem injury/fat embolism, Carotid artery dissection</td>
</tr>
<tr>
<td>Bilateral miosis</td>
<td>Pontine tegmentum</td>
<td>Pontine ICH, stroke, Opoid overdose, Cholinergic toxicity (organophosphates, cholinesterase inhibitors)</td>
</tr>
</tbody>
</table>

* More apparent in dark room
Common Pupillary Patterns

Review of Head CT

Where is the light?

Top of the Basilar Syndrome
### What can cause coma?

<table>
<thead>
<tr>
<th>Lesion localization</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Both cerebral hemispheres</td>
<td>Hypoxic-ischemic (e.g. cardiac arrest)</td>
</tr>
<tr>
<td></td>
<td>Trauma (DAI, bilateral contusions)</td>
</tr>
<tr>
<td></td>
<td>Hydrocephalus, encephalitis</td>
</tr>
<tr>
<td></td>
<td>Status Epilepticus</td>
</tr>
<tr>
<td>Unilateral hemispheric lesion (with displacement of midline structures)</td>
<td>Large hemispheric stroke or ICH/SDH</td>
</tr>
<tr>
<td></td>
<td>Abscess or tumor</td>
</tr>
<tr>
<td>Diencephalic</td>
<td>Top of the basilar syndrome</td>
</tr>
<tr>
<td>(e.g. bilateral mesial thalamic)</td>
<td>Deep venous thrombosis</td>
</tr>
<tr>
<td>Brainstem RAS</td>
<td>Rostral brainstem stroke, ICH</td>
</tr>
<tr>
<td></td>
<td>Compression from cerebellar lesion</td>
</tr>
<tr>
<td>Diffuse dysfunction – toxic/metabolic</td>
<td>Drug intoxication / overdose</td>
</tr>
<tr>
<td></td>
<td>Organ failure (sepsis, uremia, hepatic, CO₂)</td>
</tr>
<tr>
<td></td>
<td>Endocrinopathy, hypercalcemia</td>
</tr>
<tr>
<td></td>
<td>Hypothermia, hypoglycemia</td>
</tr>
<tr>
<td></td>
<td>Hyperosmolar coma (e.g. hyperglycemia)</td>
</tr>
<tr>
<td></td>
<td>Wernicke’s encephalopathy</td>
</tr>
<tr>
<td>Non-organic</td>
<td>Psychiatric = “pseudo-coma”</td>
</tr>
</tbody>
</table>

### Intracranial Hypotension
FOUR Score
Full Outline of Unresponsiveness

- Assesses brainstem reflexes and respiratory patterns not covered in GCS
- 4 components:
  1. Eye response
  2. Motor response
  3. Brainstem reflexes
  4. Respiration
- Validated in brain-injured patients

Eye Response

4 = eyelids open or opened, tracking, or blink to command
3 = eyelids open but not tracking
2 = eyelids closed but open to loud voice
1 = eyelids closed but open to pain
0 = eyelids remain closed with pain

Motor Response

4 = thumbs-up, fist, or peace sign
3 = localizing to pain
2 = flexion response to pain
1 = extension response to pain
0 = no responsive to pain or generalized myoclonus status

Brainstem reflexes

4 = pupils and corneal reflexes present
3 = one pupil wide and fixed
2 = pupil or corneal reflexes absent
1 = pupil and corneal reflexes absent
0 = absent pupil, corneal, and cough reflex
Respiration

4 = not intubated, regular breathing
3 = not intubated, Cheynes-Stokes pattern
2 = not intubated, irregular breathing
1 = breathes above ventilator rate
0 = breathes at ventilator rate, or apnea

Airway and Breathing in Brain Injured Patients

• The GCS alone is not a valid indicator of adequate airway protection or ventilation
  • Aphasic patients usually protect airway fine but GCS reduced
  • May serve as a rough marker of risk (posturing is generally bad!)
• Arousal is linked to airway protection mechanisms
  • Although additional factors incl. neuromuscular and brainstem (bulbar) dysfunction can contribute
  • May be important to acutely protect airway if patient is vomiting or has excess secretions
• Hypoventilation can raise ICP and worsen injury so ABG should be checked

Blown Pupil

• Usually an accurate localizing sign of ipsilateral uncal herniation (large hemispheric mass)
• Cases where "false-localizing" and pupil actually dilates CL to side of lesion
  • "Kernohan's notch" phenomenon if ipsilateral hemiplegia also seen
  • Midbrain pushed over and CL CN III (± cerebral peduncle) compressed against tentorium on other side

Herniation
Rostrocaudal Progression

- Patients with large hemispheric lesions go through stereotyped SEQUENCE of stages in neurological deterioration
  - Progressive and orderly brainstem dysfunction

Levels of Herniation

<table>
<thead>
<tr>
<th>Stage</th>
<th>Level of Consciousness</th>
<th>Pupils</th>
<th>Brainstem Reflexes</th>
<th>Motor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early 3rd nerve</td>
<td>Purposeful movements but lethargic</td>
<td>Ipsilateral pupil dilates</td>
<td>Full EOMs on caloric</td>
<td>Contralateral hemiparesis</td>
</tr>
<tr>
<td>Late 3rd nerve</td>
<td>Non-purposeful (reflexive) movements</td>
<td>Ipsilateral pupil fixed and dilated</td>
<td>Calorics: EOMs dysconjugate, III palsy</td>
<td>Bilateral impairment</td>
</tr>
<tr>
<td>Midbrain / upper pons</td>
<td>Posturing bilaterally</td>
<td>Both pupils fixed (dilated / midposition)</td>
<td>EOMs impaired</td>
<td>Posturing</td>
</tr>
<tr>
<td>Pons / medulla</td>
<td>Pain elicits no response or weak posturing only</td>
<td>Both pupils fixed</td>
<td>No EOMS</td>
<td>Flaccid or weak posturing</td>
</tr>
</tbody>
</table>
Ocular Motor Evaluation

• Note the position of the eyes and any movements seen at rest
  • Common to see exophoria (i.e. dysconjugate gaze) in drowsy/comatose patients
  • Latent strabismus may become uncovered
  • Deviation to one side may imply large IL hemispheric lesion (away from weakness), seizure with deviation away from lesion (with fluttering) or CL pontine lesion (eyes on same side as weakness)
• Roving eye movements imply intact ocular motor system and common in metabolic disorders
• Tonic downward deviation (sun-setting) with compression of dorsal midbrain
  • Hydrocephalus, pineal tumor
• Test movements with vestibular stimulation
  • Almost always preserved with metabolic (non-structural) etiologies of coma

Case #2

• A 45-year old man presents to the ED with severe headache, nausea/vomiting, and inability to walk
• His admission BP is 250/126 mm Hg
  • MAP > 160
• Initially he was awake but dysarthric
  • Shortly after arrival to ED becomes lethargic and then unarousable
• As they are preparing to intubate him, you rush to perform a neuro exam!

The Neuro Exam tells the tale …

• He opens eyes to vigorous stimulation but falls asleep immediately
• His pupils are 3mm and equal, reactive
  • He has right gaze deviation
• His corneal reflexes are intact
• Oculocephalic response impaired to left
  • Cold caloriccs performed after intubation (sedated)
    • Eyes deviate tonically to right with right-ear irrigation but no movement to the left with left-ear irrigation
• Cough weak
• Flexor response bilaterally with central stim

Vestibulo-Ocular Response

• Semicircular canals detect head rotation
• Impulses via vestibular n.
• To medial vestibular nucl.
• Cross to CL abducens nucl.
• Stimulate CL abduction
• Cross back to IL CN III nucl.
• Stimulte IL medial rectus muscle for adduction
Testing Eye Movements

- VOR tested by either cephalic or cold water stimulation of semicircular canals
  - Rotating head in one direction = oculocephalic or "Doll's Eye" reflex
  - see eyes move conjugately to opposite side
  - avoid if possible c-spine injury (negated in awake patients)
  - Can also test vertical eye movements
- Caloric response to water irrigation of tympanic membrane
  - HOB at 30°
  - In awake patients, induces brisk response (nystagmus to opposite side, often with nausea/vomiting) = COWS
  - In comatose patients with intact VOR, tonic deviation towards side
  - Wait five minutes before stimulating other side
- VOR will overcome deviation from hemispheric lesion but not brainstem pathology (e.g. pontine stroke)

Doll’s Eye Response

Gaze Palsy

- Supratentorial lesion can lead to imbalance between eye fields in damaged vs. intact hemisphere
  - Eyes deviate toward side of lesion (driven by contralateral hemisphere)
  - Can be overcome by OCR / calorics ("supranuclear")
- Lesion of the pons can damage the lateral gaze nuclei (PPRF – near CN VI and VII nuclei)
  - Impaired eye movements to the side of lesion (eyes will look away from lesion)
  - Cannot be overcome by caloric / cephalic stim

Cerebellar ICH
Saturday morning?

- A 31-year old woman is brought to ED after single-car collision into tree and house (?)
  - Intubated in the field for decreased LOC
- History of seizures, hepatitis C, schizoaffective
- Minimally responsive but localizing bilaterally?
  - Placed on propofol drip because note “agitation” when she is touched or moved ...
- Imaging with only minor “contusions” and a C2-hangman’s fracture

Examination

- Not open eyes to any stimulation
- Eyes midline, occasionally roving
- All cranial nerves intact
  - Left pupil appears slightly smaller (in dark light)
- Extensor posturing with any stimulation
  - Associated with significant autonomic changes
- Concern for raised ICP so EVD placed in NNICU
  - Given mannitol but ICP not elevated

Why is her HR 160?
Motor Response

- Best motor response to stimulation
  - Assess symmetry or asymmetry also
  - Failure to respond may indicate sensory / processing impairment or motor deficit
    - If facial grimace or movement of CL side then motor
    - Failure to move either side but grimace indicates motor impairment below level of pons
- May be purposeful or non-purposeful
- Posturing best differentiated by movement of U/E
  - can be flexor (decorticate) or extensor (decerebrate)

Glasgow Coma Scale

Brain Death

- Irreversible loss of all brain function
- A form of death ... by neurological criteria
- Coma of known cause
  - Exclude confounders (hypothermia, sedation)
- Absence of all brainstem reflexes
- Absence of motor responses
- Absence of respiratory drive
Brain Death Evaluation

Nuclear Brain Perfusion Study

Movements after Brain Death

- A number of both spontaneous and reflexive movements may be seen after brain death
  - May be simple or complex (e.g. Lazarus sign)
- Plantar withdrawal in 35-79%
  - No posturing allowed to central stimulation
- Stereotyped
- Spinal cord generators

Locked-In Syndrome

- Quadriplegia and anarthria
- Preserved awareness and arousal
- May be clinically confused with disorders of consciousness as unable to respond normally
- Acute injury to the ventral pons
  - Spares vertical eye movements and ARAS
- Analogous de-afferented state may occur with severe GBS / neuromuscular failure
A Curious Case

- 44-year old man admitted to ICU with unresponsiveness
  - History of hypertension, depression (off SSRIs)
- Arrested by police for erratic driving
  - Complaining of shoulder pain after cuffed (recent rotator cuff repair) so brought to ED
  - Initially awake, went to make a phone call and became agitated
  - Given toradol for pain and became tremulous and obtunded => intubated
- After few hours in the ICU, became more awake and was successfully extubated
  - One hour later, lapsed into unresponsive state again

Examination

- Afebrile, vitals stable
- Not opening eyes, not responding to pain
- PERL, no blink to threat
- Fast roving eye movements
- OCR appeared absent
- Tone normal, reflexes present
- Underwent 3 sequential tests to confirm dx
The Work-Up

- No improvement after administration of:
  - Narcan
  - Flumazenil
  - Midazolam
- Cold caloric
  - Elicited nystagmus away from side of irrigation
- EEG

Psychogenic Coma

- Often sudden onset ("slump to the floor without injury")
  - In setting of recent stressors and/or psych history
- Actively resists opening of eyelids
- Rapid jerky eye movements rather than roving
- Always looking away from examiner when eyes opened
- Rapid nystagmoid eye movements away from side of cold water irrigation (calorics)
- Hand avoids hitting face when dropped (or falls abnormally slowly ~ catatonia)
- Varying resistance to muscle testing
- May be seen to position self in bed
Brainstem ICH

Brainstem Coma

- Usually sudden onset
- Not typical rostra-caudal pattern of brainstem reflex impairment
- Early EOM abnormality (pontine)
  - Not able to overcome with VOR
- Horner’s syndrome if intrinsic brainstem (IL)
- Facial palsy may be “peripheral” (nuclear)
- May see lower CN palsies early
  - Dysphagia, loss of cough/gag, dysautonomia
- Bizarre breathing patterns