coma
problems of consciousness
in children
definitions

consciousness
state of full awareness of the self and one’s relationship to the environment

consciousness ≠ responsiveness

level of wakefullness / alertness

content or quality: awareness of self/environment, including various and overlapping functions, such as attention, perception, memory
definitions

coma
- a state of deep, unarousable, sustained pathologic unconsciousness with the eyes closed
- persisting for at least 1 hour
- lack of both wakefulness and awareness
- patient cannot be aroused to respond appropriately to painful stimuli

E1M5V2
coma – in general

requires dysfunction of:

**Ascending (Reticular) Arousal (or Activating) System** ([A]RAS)

*upper brain stem*

*diencephalon*

or

**both hemispheres**
coma – in general requires dysfunction of:

**Ascending (Reticular) Arousal (or Activating) System ([A]RAS)**
upper brain stem
diencephalon

or

both hemispheres

causd by:

- structural lesions
  - compressive
  - destructive

- diffuse/metabolic causes
paramedian midbrain
dorsolateral pons
assessing coma – level of consciousness GCS

<table>
<thead>
<tr>
<th>Adult/standard</th>
<th>Score</th>
<th>Pediatric (&lt;4–5 years) [6]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye opening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous</td>
<td>4</td>
<td>Spontaneous</td>
</tr>
<tr>
<td>To speech</td>
<td>3</td>
<td>To speech</td>
</tr>
<tr>
<td>To pain</td>
<td>2</td>
<td>To pain</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Best verbal response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oriented</td>
<td>5</td>
<td>Coos, babbles (age appropriate)</td>
</tr>
<tr>
<td>Confused</td>
<td>4</td>
<td>Irritable, cries</td>
</tr>
<tr>
<td>Inappropriate words</td>
<td>3</td>
<td>Cries to pain</td>
</tr>
<tr>
<td>Incomprehensible sounds</td>
<td>2</td>
<td>Moans to pain</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td>None</td>
</tr>
<tr>
<td>Best motor response</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obey commands</td>
<td>6</td>
<td>Spontaneous movements</td>
</tr>
<tr>
<td>Localizes pain(^a)</td>
<td>5</td>
<td>Withdraws to touch</td>
</tr>
<tr>
<td>Withdraws to pain(^b)</td>
<td>4</td>
<td>Withdraws to pain(^b)</td>
</tr>
<tr>
<td>Abnormal flexion(^a)</td>
<td>3</td>
<td>Abnormal flexion(^a)</td>
</tr>
<tr>
<td>Extensor response(^a)</td>
<td>2</td>
<td>Extensor response(^a)</td>
</tr>
<tr>
<td>None(^a)</td>
<td>1</td>
<td>None(^a)</td>
</tr>
</tbody>
</table>
pitfalls of the GCS

10 year old girl
eyes open
normal pupillary and corneal reflexes
conjugate eye deviation – left
does not obey commands
extends R arm, localizes with L arm
makes sounds to pain

E4M5V2
pitfalls of the GCS

10 year old girl
eyes open
normal pupillary and corneal reflexes
conjugate eye deviation – left
does not obey commands
extends R arm, localizes with L arm
makes sounds to pain

E4M5V2
pitfalls of the GCS

L MCA infarct
pitfalls of the GCS

5 year old boy
after breakfast: “sleepy”
within 2 hours: progressive paresis R, later L, unresponsive

E4 / M5(L) M2(R) / V2
no words, no movements of face/arms/legs at request
eye deviation to R, no roving movements
PR +/+, corneal reflexes -/-
oculocephalic reactions: INO
bilateral Babinski’s sign
pitfalls of the GCS

locked-in syndrome, pontine infarction, basilar artery thrombosis
pitfalls of the GCS

insufficiently examined  too little pain
                   not bilaterally

discrepancy E-M-V scores

aphasia
anarthria
tetraplegia

coma – mimics
## LOC / coma – mimics

<table>
<thead>
<tr>
<th>Severe disorders of consciousness and related conditions</th>
<th>Self awareness</th>
<th>Pain and suffering</th>
<th>Sleep–wake cycles</th>
<th>Motor function</th>
<th>Respiratory function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain death</td>
<td>Absent</td>
<td>No</td>
<td>Absent</td>
<td>None or only reflex spinal movements</td>
<td>Absent</td>
</tr>
<tr>
<td>Coma</td>
<td>Absent</td>
<td>No</td>
<td>Absent</td>
<td>No purposeful movement</td>
<td>Variably depressed</td>
</tr>
<tr>
<td>Vegetative state</td>
<td>Absent</td>
<td>No</td>
<td>Intact</td>
<td>No purposeful movement</td>
<td>Normal</td>
</tr>
<tr>
<td>Minimally conscious state</td>
<td>Very limited</td>
<td>Yes</td>
<td>Intact</td>
<td>Severe limitation of movement</td>
<td>Variably depressed</td>
</tr>
<tr>
<td>Akinetic mutism</td>
<td>Limited</td>
<td>Yes</td>
<td>Intact</td>
<td>Moderate limitation of movement</td>
<td>Normal to variably depressed</td>
</tr>
<tr>
<td>Locked-in syndrome</td>
<td>Present</td>
<td>Yes</td>
<td>Intact</td>
<td>Quadriplegia; pseudobulbar palsy; eye movements preserved</td>
<td>Normal to variably depressed</td>
</tr>
</tbody>
</table>

Ashwal Brain Dev 2003
vegetative state

Criteria
all of the following:
– no evidence of awareness of themselves or their environment; they are incapable of interacting with others
– no evidence of sustained, reproducible, purposeful, or voluntary behavioral responses to visual, auditory, tactile, or noxious stimuli
– no evidence of language comprehension or expression
– intermittent wakefulness manifested by the presence of sleep-wake cycles.
– sufficiently preserved hypothalamic and brain stem autonomic functions to survive if given medical and nursing care
– bowel and bladder incontinence
– variably preserved cranial nerve (pupillary, oculocephalic, corneal, vestibulo-ocular, gag) and spinal reflexes
minimally conscious state

Diagnostic criteria for the MCS

1. Simple command-following
2. Gestural or verbal ‘yes/no’ responses (regardless of accuracy)
3. Intelligible verbalization
4. Purposeful behavior including movements or affective behaviors that occur in contingent relation to relevant environmental stimuli and are not due to reflexive activity. Some behavioral examples of qualifying purposeful behaviors include
   (a) Appropriate smiling or crying in response to the linguistic or visual content of emotional but not to neutral topics or stimuli
   (b) Vocalizations or gestures that occur in direct response to the linguistic content of questions
   (c) Reaching for objects in a manner that demonstrates a clear relationship between object location and direction of reach
   (d) Touching or holding objects in a manner that accommodates the size and shape of the object
   (e) Pursuit eye movement or sustained fixation that occurs in direct response to moving or salient stimuli

Ashwal Brain Dev 2003
**IS PATIENT CONSCIOUS?**

PATIENT HAS SUSTAINED, OR REPRODUCIBLE PURPOSEFUL RESPONSE TO EXTERNAL STIMULI?

- **NO**
  - PT HAS ABSENT BRAINSTEM FUNCTION AND APNEA
    - **YES**
      - PT IS BRAIN DEAD
    - **NO**
      - PT HAS SLEEP WAKE CYCLES AND OPENS EYES SPONTANEOUSLY OR TO STIMULATION
        - **NO**
          - PT IS IN COMA
        - **YES**
          - PT IS IN A VEGETATIVE STATE

- **YES**
  - PT HAS FUNCTIONAL INTERACTIVE COMMUNICATION AND/OR FUNCTIONAL USE OF ONE OR MORE OBJECTS
    - **NO**
      - PT HAS:
        1. SIMPLE COMMAND FOLLOWING AND/OR
        2. GESTURAL OR VERBAL ‘YES/NO’ RESPONSES AND/OR
        3. INTELLIGIBLE VERBALIZATION AND/OR
        4. PURPOSEFUL BEHAVIORS IN RESPONSE TO ENVIRONMENTAL STIMULI, NOT DUE TO REFLExIVE ACTIVITY
          - PT IS NOT ABLE TO EXPRESS PREFERENCES
          - PT IS IN A MINIMALLY CONSCIOUS STATE
          - **NO**
            - PT HAS LOCKED-IN SYNDROME
          - **YES**
            - COMMUNICATION IS LIMITED TO VERTICAL EYE MOVEMENTS AND/OR EYELID BLINKING
              - **YES**
                - PT HAS EMERGED FROM MCS AND MAY HAVE MILD TO SEVERE DISABILITY OR MAY BECOME NORMAL
              - **NO**
psychogenic unresponsiveness

lie with eyes closed

**normal reflexes and ventilatory patterns**

oculocephalic reflexes absent (due to visual fixation)
caloric testing: nystagmus away, no (little) tonic reaction

**passive eye opening: upward deviation, active resistance**

no slow roving eye movements

normal tone, no active resistance to passive movements

**no motor reaction to pain, arm drop: avoids hitting the face**

normal EEG
physical examination

vital signs
   (airway / breathing / circulation / temp / seizures)

evidence of trauma
   (monocle sign / battle sign / hematoma)

evidence of acute or chronic systemic illness?
   (jaundice, anemia, cyanosis, rash, petechiae)

evidence of drug ingestion
   (needle marks, alcohol on breath)
nuchal rigidity
   (once cervical trauma excluded)
neurological examination

GCS – consciousness + laterality

(spontaneous – verbal commands – pain)

start with A, C, or D: M2, M3, M5 (check asymmetry)
if no response: B, bilaterally! M1-5 (check asymmetry)
neurological examination

motor responses – posturing

(+ tone + tendon + plantar reflexes)

B Upper midbrain damage

“decortication”

C Upper pontine damage

“decerebration”
breathing pattern

forebrain
diencephalon
metabolic encephalopathy

midbrain
hepatic coma
sepsis
metabolic acidosis

or Ondine’s curse
brain stem reflexes

**pupillary reflexes**

**metabolic coma:**
- long retained

**after seizures:**
- transiently absent

**hypoxia/ischemia:**
- large + fixed

**opiates:**
- pinpoint (~pons)
- naloxone reverses

**thalamus lesions:**
- complex oculomotor disturbances
neurological examination – brainstem reflexes

eyelids – corneal responses

in coma: closed
after passive opening: slow and gradual closing
during seizures: often opened
alternated opening: vegetative state
unilateral ptosis: Horner syndrome, III nerve palsy
blink reflexes to light/threat: may be present in vegetative state

corneal reflex:
intact afferent (n. V) and efferent paths (n. VII and n. III - Bell’s phenomenon)
contact lenses!
neurological examination – brainstem reflexes

midbrain
pons
frontal eye field
neurological examination – brainstem reflexes

midbrain
pons
frontal eye field
neurological examination – brainstem reflexes

midbrain
pons
frontal eye field
neurological examination – brainstem reflexes

- PPRF
- VI
- III
- midbrain
- pons
- frontal eye field
neurological examination – brainstem reflexes

midbrain
pons
frontal eye field
neurological examination – brainstem reflexes

- **VI**
- **III**
- **PPRF**
- **X**

midbrain
pons
frontal eye field
neurological examination – brainstem reflexes

[Diagram showing connections between brainstem structures, including midbrain, pons, and frontal eye field.]
neurological examination – brainstem reflexes

- **VI**
- **III**
- **MLF**
- **PPRF**

- **midbrain**
- **pons**
- **frontal eye field**
neurological examination – brainstem reflexes

midbrain
pons
frontal eye field
neurological examination – brainstem reflexes

spontaneous eye movements
- often slight exophoria
- metabolic coma: often spontaneous roving movements
- conjugate lateral deviation
  * seizure  (ictally: away from, postictally: towards lesion)
  * gaze paralysis  (hemispheric: towards lesion
                  pons: away from lesion)
- disconjugate: brain stem or III / VI nerve lesions
- skew deviation: brain stem
- *bobbing, dipping, ping/pong*: different localizations
neurological examination – brainstem reflexes

oculocephalic reflex
brainstem intact, metabolic encephalopathy

<table>
<thead>
<tr>
<th>Turn right</th>
<th>Turn left</th>
<th>Tilt back</th>
<th>Tilt forward</th>
</tr>
</thead>
</table>

Oculocephalic responses
R pontine lateral lesion

Oculocephalic responses

Turn right  Turn left  Tilt back  Tilt forward
bilateral INO/MLF lesion

Oculocephalic responses

- Turn right
- Turn left
- Tilt back
- Tilt forward
neurological examination – brainstem reflexes

caloric responses
reserved for the examination of brain death

<table>
<thead>
<tr>
<th>Cool water</th>
<th>5 min 10ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right side</td>
<td></td>
</tr>
<tr>
<td>Left side</td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td></td>
</tr>
</tbody>
</table>

when awake and trying to fixate: + nystagmus to midline
psychogenic unresponsiveness

disoriented to time, space and self, retain new information
lie with eyes closed
normal reflexes and ventilatory patterns

**oculocephalic reflexes absent** (due to visual fixation)

**caloric testing: nystagmus** away, no (little) tonic reaction

**passive eye opening: upward deviation**, active resistance

**no slow roving eye movements**

normal tone, no active resistance to passive movements

no motor reaction to pain, arm drop: avoids hitting the face

normal EEG
causes of coma in children

Infection
- CNS infection: meningitis, encephalitis, abscess
- Systemic infection: sepsis

Inflammation
- Postinfectious/postimmunization: ADEM, AHLE, ANE, HSE, other
- Antibody-related encephalitis: Anti-NMDAR, anti-VGKC, Hashimoto, other
- CNS vasculitis: primary (PACNS) and secondary
- Rheumatic disorder: SLE, HLH, MAS, other

Stroke
- Ischemia
- Hemorrhage
- Sinovenous thrombosis

Hypoxia-ischemia
- Cardiac failure, cardiac arrest, shock
- Respiratory failure
- Near drowning, strangulation, smoke inhalation
causes of coma in children

**Metabolic**
- Diabetic ketoacidosis, hypoglycemia
- Electrolyte and fluid disturbances
- Endocrine disorder
- Hepatic encephalopathy
- Renal encephalopathy
- Inborn errors of metabolism: organic acidemias, amino acidemias, urea cycle defects, mitochondrial disease, fatty acid oxidation and carnitine defects, carbohydrate disorders, other
- Intoxication: accidental, deliberate, Münchhausen by proxy, medication adverse reaction

**Neoplasia**
- Infiltration, edema, mass effect, hydrocephalus, herniation

**Epilepsy**
- Epileptic seizure, status epilepticus, NCSE
- FIRES, other

**Other**
- Hypertensive encephalopathy, PRES, congenital malformation (hydrocephalus), dissociative (conversion) disorder
causes of coma – in general

requires dysfunction of:

**Ascending (Reticular) Arousal (or Activating) System ([A]RAS)**

*upper brain stem*

*diencephalon*

---

**structural lesions**

*compressive*

*destructive*

---

**diffuse/metabolic causes**

or

**both hemispheres**
structural causes of coma

both hemispheres
anox./isch., trauma, hydrocephalus, meningitis, SAH, ICP, central herniation

one hemisphere – secondary brain stem/ARAS involvement
mass lesion, subfalcine or uncal herniation

posterior fossa – brainstem compression
mass lesion, tonsillar herniation

secondary hydrocephalus

intrinsic brainstem lesion
space-occupying

infarct, demyelination

focal signs !

brain stem signs !
herniation syndromes – pressure gradient
herniation syndromes – pressure gradient
herniation syndromes

A. Symmetry
   - Uncal Herniation
   - Central Herniation

B. Asymmetry
   - Falcine Herniation
   - Midline Shift
<table>
<thead>
<tr>
<th>Herniation Syndrome</th>
<th>Physical Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subfalcine</td>
<td>Progressive decrease in level of consciousness, generally in patients with hemispheric deficits (e.g., hemiparesis, ipsilateral forced gaze deviation)</td>
</tr>
<tr>
<td>Central</td>
<td>Fixed midposition pupils and variable motor responses. Pontine reflexes usually remain intact</td>
</tr>
<tr>
<td>Uncal transtentorial</td>
<td>Ipsilateral dilated pupil followed by contralateral paresis. Decreased consciousness due to thalamic pressure. Later, the contralateral pupil is affected</td>
</tr>
<tr>
<td>Brainstem compression from infratentorial lesion</td>
<td>Bilateral miosis and loss of corneal and oculocephalic reflexes</td>
</tr>
<tr>
<td>Tonsillar</td>
<td>Respiratory arrest with loss of medullary function (cough reflex)</td>
</tr>
<tr>
<td>a. Respiratory pattern</td>
<td><img src="image" alt="Cheyne-Stokes" /></td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>b. Pupillary size and reactions</td>
<td><img src="image" alt="Small pupils" /> Small range of contraction</td>
</tr>
<tr>
<td>c. Oculocephalic and oculovestibular responses</td>
<td><img src="image" alt="Doll's Head Maneuver" /> <img src="image" alt="Ice Water Calorics" /></td>
</tr>
<tr>
<td>d. Motor responses at rest and to stimulation</td>
<td><img src="image" alt="Motionless" /> <img src="image" alt="Legs stiffen and arms rigidly flex (decorticate rigidity)" /></td>
</tr>
</tbody>
</table>

**central tentorial herniation**

diencephalic stage
central tentorial herniation

midbrain/pons stage
3 year old boy
E1M3V2, small reactive pupils
CR +/- OCR +/-, posture: flexion arms/hands, extended legs, bilateral Babinski sign

diencephalic stage, central transtentorial herniation
uncal herniation

early III nerve stage
uncal herniation

late III nerve stage
4 months old boy vomited, became drowsy, opisthotonus
E1M4V1
dilated non-reactive R pupil
R: withdraws, L: extends
tonsillar herniation
tonsillar herniation

after 2 days:
diffuse/metabolic causes of coma

II. Systemic derangements causing coma
   Toxic
      Medication overdose/adverse effects (opioids, benzodiazepines, barbiturates, tricyclics, neuroleptics, aspirin, acetaminophen, anticonvulsants)
      Drugs of abuse (opioids, alcohol, methanol, ethylene glycol, amphetamines, cocaine)
      Exposures (carbon monoxide, heavy metals)
   Metabolic
      Systemic inflammatory response syndrome-sepsis
      Hypoxia; hypercapnia
      Hypothermia
      Hypoglycemia; hyperglycemic crises (diabetic ketoacidosis, nonketotic hyperosmolar hyperglycemic state)
      Hyponatremia, hypernatremia
      Hypercalcemia
      Hepatic failure
      Renal failure
      Wernicke’s encephalopathy
   Endocrine
      Panhypopituitarism
      Adrenal insufficiency
      Hypothyroidism; hyperthyroidism
diffuse/metabolic causes of coma

- false localizing signs may occur in metabolic coma
- non-reactive pupils
- focal deficits in hypoglycaemic coma
- bilateral Babinski’s sign
- symmetrical posturing

+ nonconvulsive generalized status epilepticus
+ immune-mediated syndromes (NMDA, Hashimoto)
+ inborn errors of metabolism
+ genetic causes (FHM)
ancillary investigations in coma

blood glucose, electrolytes, urea, ammonia, lactate
arterial blood gases
blood cultures
metabolic screen
tox screen
CT
lumbar puncture
EEG
MRI, CTV, MRV, MRA
specific investigations: endocrine, auto-immune antibodies
DNA, cultures, PCR
glucose, electrolytes, urea, ammonia, lactate, blood gas
urgent CT

lumbar puncture, blood cultures (meningitis suspected: treat!)
toxicology screen

EEG (NCSE? focal / metabolic causes?)
metabolic screen

MRI/MRA (brain stem signs: posterior circulation AIS? pont. myel.? ADEM?)
MRV/CTV (signs of high ICP: sinovenous thrombosis?)

auto-immune antibodies, genes......
diagnostic approach – summary

is the patient in a coma?

  GCS  (exclude aphasia/anarthria/tetraplegia)
  coma mimic  (vegetative or minimally conscious state)
  psychogenic unresponsiveness

structural cause?

  bilateral or focal
  sequence of events – herniation?
  focal signs / brain stem signs

diffuse or metabolic cause?
Does the patient have brainstem signs?

No

CT (or MR) angiography for basilar artery obstruction

Yes

Consult specialist
Treat presumed cause
Further studies (as needed)

Does the patient have a condition that necessitates MRI or vascular imaging?

Does the patient need treatment for poisoning?

Does the patient need a lumbar puncture and intravenous antimicrobials?

Does the patient need an emergency EEG?

Does the patient need hormone or thiamine replacement?
literature

Plum and Posner’s diagnosis of stupor and coma

Sejersen T, Wang CH (eds). Acute pediatric Neurology

Edlow JA et al. Diagnosis of reversible causes of coma
Lancet 2014;384:2064-2076

Kirkham FJ. Non-traumatic coma in children
Arch Dis Child 2001;85:303-312

Ashwal S. Pediatric vegetative state
Neurorehabilitation 2004;19:349-360

Stevens RD et al. Approach to the comatose patient
Crit Care Med 2006;34:31-41