

Brain death

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Determination of Death

An individual who has either:

- irreversible cessation of circulatory and respiratory functions (Cardiac death)

or

- irreversible cessation of all functions of the entire brain, including the brain stem (Brain death)

is dead

Definition of brain death

Complete absence of cerebral and brain stem function , but not spinal cord function

- Definition of Brain Death varies by State in USA
- Brain Death Criteria vary by Hospital
- Not uniformly defined between institutions

Identification

- **International medical organization**
1968 Geneva conference (Harvard criteria)
 - a. lose all reactions to environment
 - b. lose physiological reflex and muscles rigidity completely
 - c. no autonomous respiration
 - d. arterial pulse drops swiftly if the life maintain machines canceled
 - e. brain wave keeps no fluctuation

1987 Task force Recommendations

- Presence of coma and apnea
- Absent brainstem function
- Absent oculoccephalic and oculovestibular reflexes
- No cough, gag or corneal reflexes
- Spinal arcs could be present
- Time delay between exams recommended based on patient age
 - 7 d – 2 mo = 48 hr and 2 EEG
 - 2 mo – 1 yr = 24 hr and 2 EEG
 - >1 yr = 12 hr, no EEG

American Academy of Neurology Guidelines (1995)

- **Demonstration of coma**
- **Evidence for the cause of coma**
- **Absence of confounding factors, including hypothermia, drugs, electrolyte, and endocrine disturbances**
- **Absent brainstem reflexes**
- **Absent motor responses**
- **Apnea**

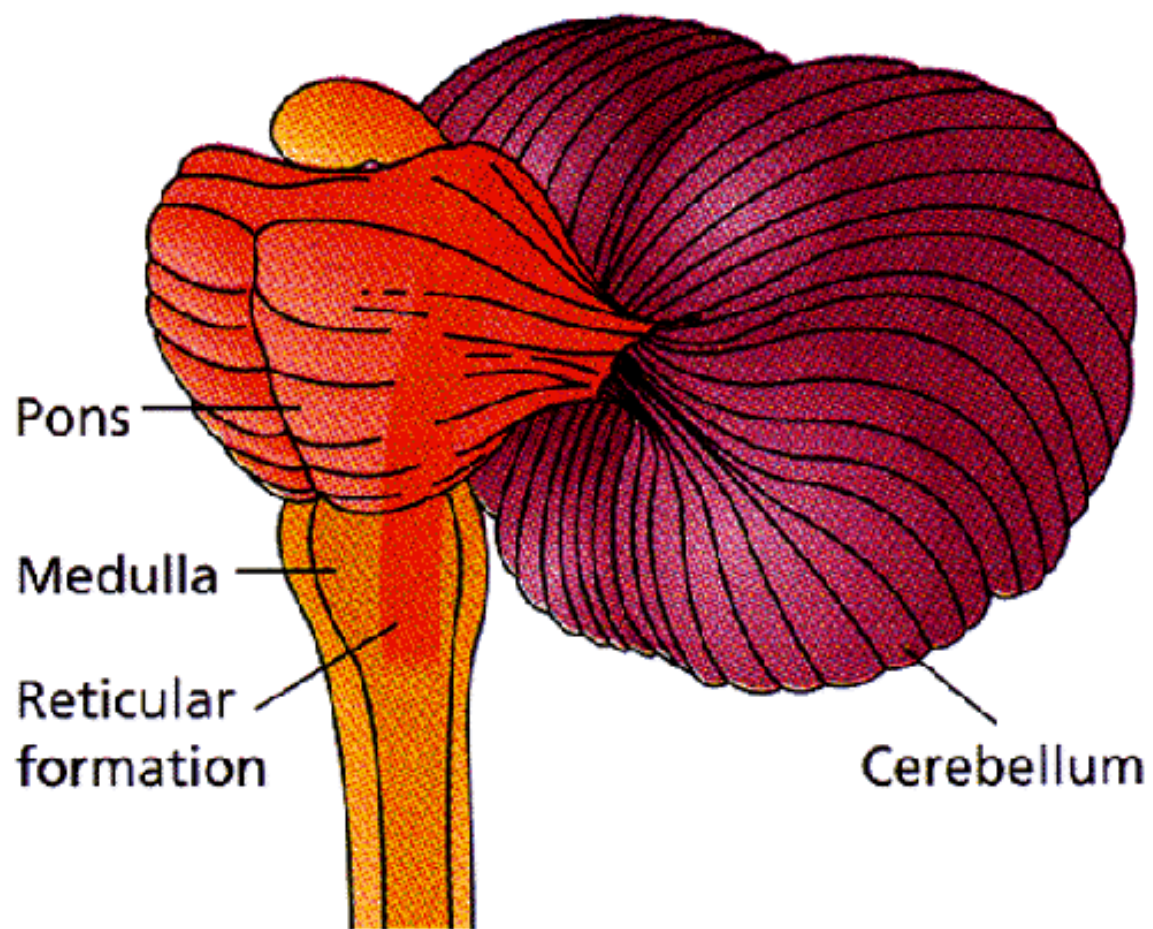
A repeat evaluation in 6 hrs is advised

Confirmatory laboratory tests are only required when specific components of the clinical testing cannot reliably be evaluated.

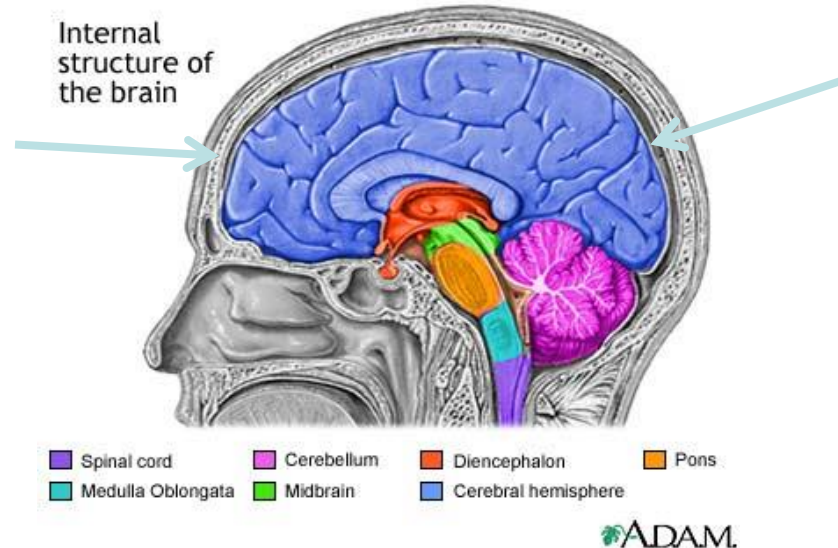
Anatomy of human brain – 3 regions

- Cerebrum
 - Controls memory, consciousness, and higher mental functioning
- Cerebellum
 - Controls various muscle functions
- Brain stem consisting of the midbrain, pons, and medulla, which extends downwards to become the spinal cord
 - Controls respiration and various basic reflexes (e.g., swallow and gag)





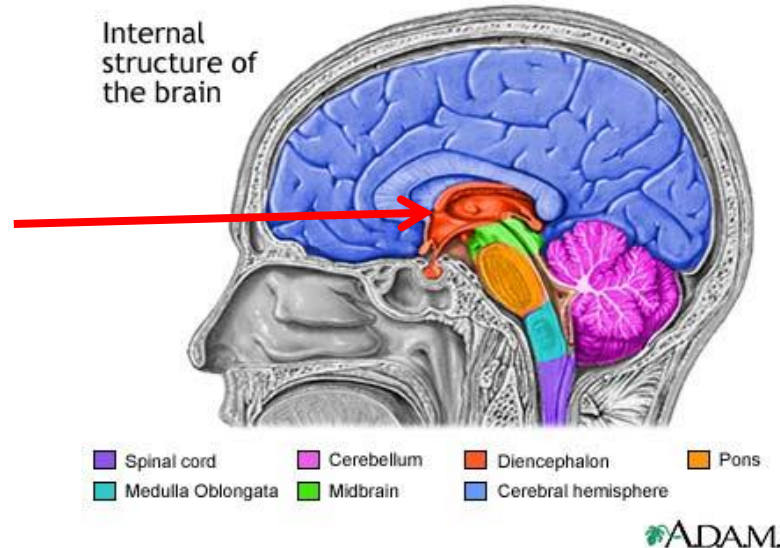
Cerebral hemispheres



Cerebral hemispheres:

- Conscious part of the brain
- Controls thought and memory
- Feels sensations
- Directs conscious movements

Thalamus and hypothalamus



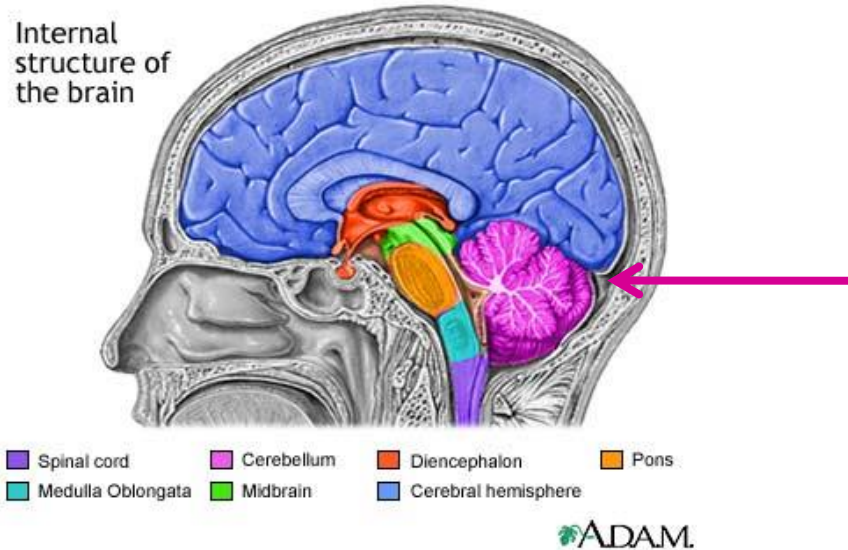
Thalamus

Station for sensory information to go to the brain

Hypothalamus

Temperature control, controls hormone systems, food intake, emotions

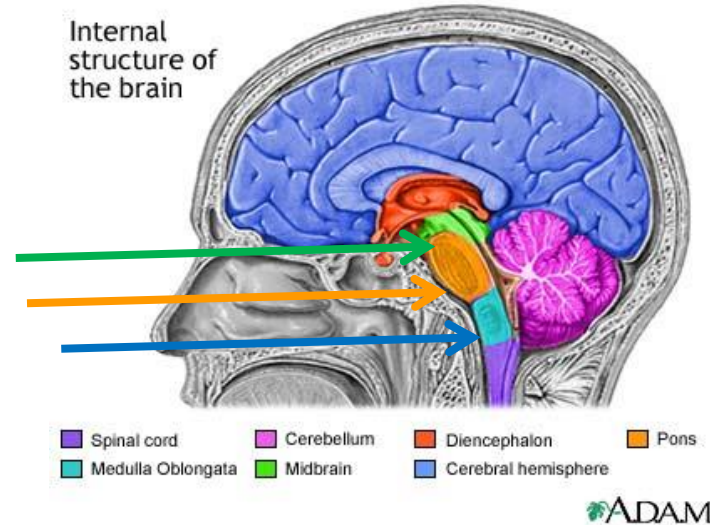
Cerebellum



Cerebellum:

- Balance
- Coordination

Brainstem



Brain stem: Midbrain + Pons + Medulla

Attention & consciousness

Cranial nerve reflexes

Control of breathing

Control of blood pressure, heart function

Brainstem function is vital for preservation of life!

Neurologic states resembling brain death

- Hypothermia
- Acute Poisoning
- Acute Metabolic Encephalopathies
- Akinetic Mutism
- Persistent Vegetative State
- Locked-in-Syndrome

Coma

- Non-responsive to most external stimuli
- At most, such patients may have a dysfunctional cerebrum but, by virtue of the brain stem remaining intact, are capable of spontaneous breathing and heartbeat

Irreversible Coma

- Known etiology and or reversible causes ruled out
- Must have an absence of
 - Hypothermia ($>32^{\circ}\text{C}$)
 - Neuromuscular blockade
 - Shock or significant hemodynamic instability
 - Significant levels of sedatives
 - Severe metabolic disturbance

Conditions Distinct From Brain Death

- Persistent Vegetative State
- Locked-in Syndrome
- Minimally Responsive State

Persistent Vegetative State

- Normal Sleep-Wake Cycles
- No Response to Environmental Stimuli
- Diffuse Brain Injury with Preservation of Brain Stem Function

Persistent permanent vegetative state

Duration: 1 month; if persistent more than 1 year, almost always permanent

Function lost:

- No cognition

- No meaningful sounds or goal-directed movements

Function usually or often preserved:

- Brainstem and autonomically visceral functions Pupillary and oculovestibular reflexes

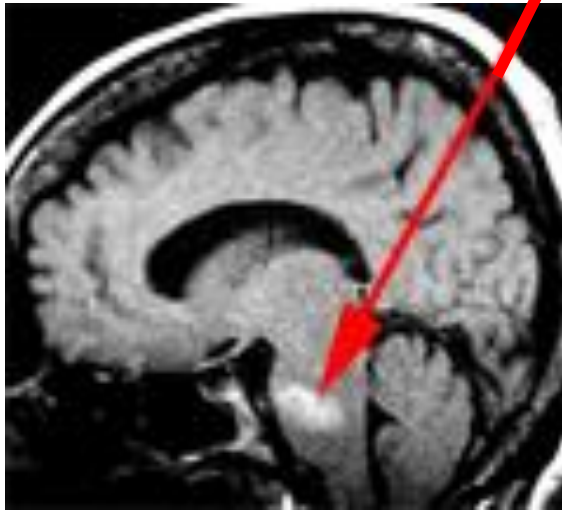
- Brief, inconsistent shifting of head or eyes toward new sounds

- Smiles or tear reactions may occur

- Reflex postural responses to noxious stimuli

Locked-in Syndrome

Ventral Pontine Infarct



- Complete Paralysis
- Preserved Consciousness
- Preserved Eye Movement

Minimally Responsive State

- Diffuse or Multi-Focal Brain Injury
- Preserved Brain Stem Function
- Variable Interaction with Environmental Stimuli

Relationship of organ function

- Heart
 - Needs O_2 to survive and w/o O_2 will stop beating
 - **Not** controlled by the brain but it is autonomous
- Breathing
 - Controlled by vagus nerve, located in the brain stem
 - Main stimulant for vagus nerve is $\uparrow CO_2$ in the blood
 - Causes the diaphragm & chest muscles to expand
 - Spontaneous breathing can not occur after brain stem death
- With artificial ventilation, the heart may continue to beat for a period of time after brain stem death
- Time lag between brain death and circulatory death is ~2-10 days (case report - woman's heart beat for 63 days after a dx of brain death)

Initial requirements for diagnosis of brain death

1. Clinical or radiographic evidence of an acute catastrophic cerebral event
2. Exclusion of conditions that confound clinical evidence (i.e.-metabolic)
3. Confirmation of absence of drug intoxication or poisoning
 - Such as barbiturates
4. Core body temp $>32^{\circ}\text{C}$

Criteria for CNS Determination of Death (Brain Death)

- Irreversible coma
- Absence of cortical function
- Absence of brainstem function
- Apnea
- 2 examinations with interval according to patient's age
- Ancillary tests

Determination of Brain Death

- Determination of Brain Death – 4 Steps
 - 1) Establish irreversible and proximate cause of coma
 - 2) Achieve normal core temperature
 - 3) Achieve normal systolic blood pressure
 - 4) Perform neurologic examination

Step 1

- Establish Irreversible and Proximate Cause of Coma
 - Usually obvious
 - Exclude drugs (including alcohol)
 - No recent or persistent neuromuscular blocking agents
 - No severe electrolyte, acid-base, or endocrine disturbance

Step 2

- Achieve Normal Core Temperature
 - Core body temperature > 32 degrees C (34 degrees is preferable)
 - Important for apnea test
 - Warming blanket and warmed IV fluids may be required

Step 3

- Achieve Normal Systolic Blood Pressure
 - Neurologic examination usually reliable with systolic BP > 100 mmHg
 - May require vasopressors to maintain adequate BP (dopamine often preferred).

Step 4

- Perform Neurologic Examination
 - One examination is sufficient
 - Examiner should be intimately familiar with brain death criteria (a critical care specialist, neurologist, or neurosurgeon)

The Neurologic Examination

- Coma
 - No evidence of responsiveness
 - No eye opening to noxious stimuli
 - No motor response to noxious stimuli other than spinal reflexes

The Neurologic Examination (cont.)

- Absence of Brainstem Reflexes
 - No pupillary response to bright light (typically fixed in 4-9 mm)
 - Absent corneal reflex
 - Absent facial muscle movement to noxious stimulus
 - Absent pharyngeal and tracheal reflexes (gag and deep suction)

The Neurologic Examination (cont.)

- Absent Brainstem Reflexes (cont.)
 - Absent eye movements to oculoccephalic testing (doll's eyes test); integrity of cervical spine must be certain.
 - Oculovestibular testing (cold water calorics) – Head of bed 30 degrees, 50 mL ice water irrigation of each patent ear canal with 5 minutes observation and 5 minutes between tests.

Basic exam 1 - Pain

- Cerebral motor response to pain
 - Supraorbital ridge, the nail beds
 - Motor responses may occur spontaneously during apnea testing (spinal reflexes)
 - Spinal reflex responses occur more often in young

Basic exam 2 - Pupils

- Round, oval, or irregularly shaped
- Midsize (4-6 mm), but may be totally dilated
- Absent pupillary light reflex
 - Although drugs can influence pupillary size, the light reflex remains intact only in the absence of brain death
 - IV atropine does not markedly affect response
 - Paralytics do not affect pupillary size
 - Topical administration of drugs and eye trauma may influence pupillary size and reactivity
 - Pre-existing ocular anatomic abnormalities may also confound pupillary assessment in brain death

Mid position/fixed = MIDBRAIN



Small/reactive = DIENCEPHALIC



Fixed/dilated = III NERVE



Large/fixed = TECTAL



Pin point = PONTINE



Patients with non-structural (metabolic) coma have small reactive pupils

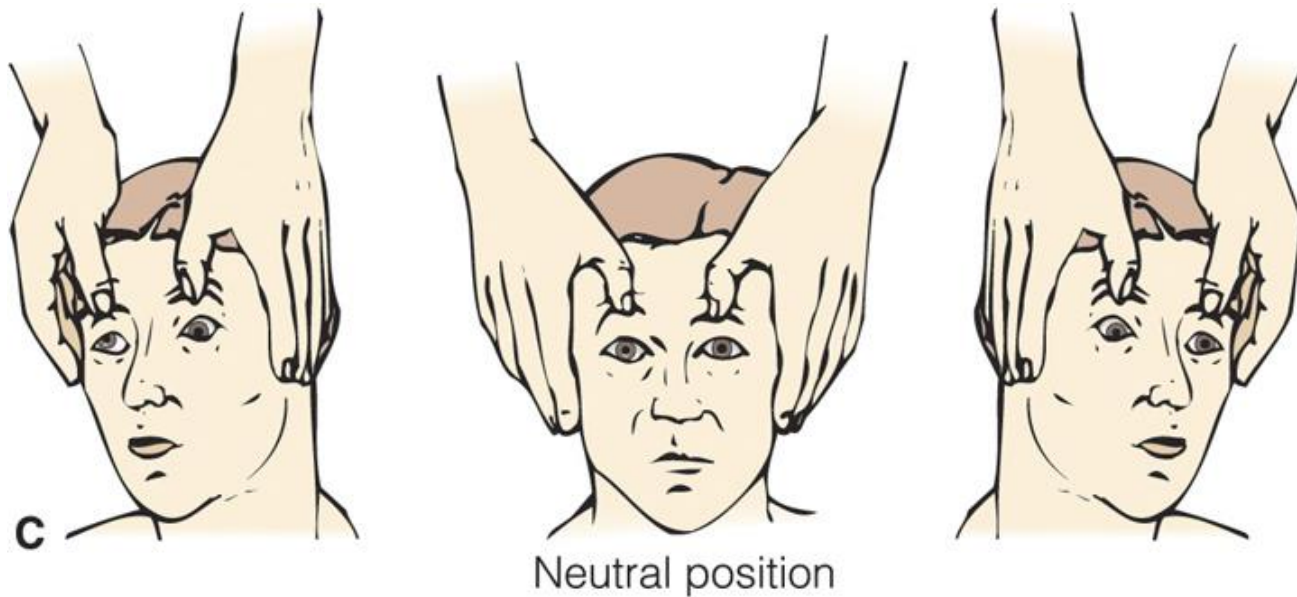
Basic exam 3- Eye movement

- Oculocephalic reflex = doll's eyes
- Oculovestibular reflex = cold caloric test

Oculocephalic reflex

- Rapidly turn the head 90° on both sides
 - Normal response = deviation of the eyes to the opposite side of head turning
 - Brain death = oculocephalic reflexes are absent (no Doll's eyes) = no eye movement in response to head movement

Eye Movements



Occulo-Cephalic Response “Doll’s Eyes Maneuver”

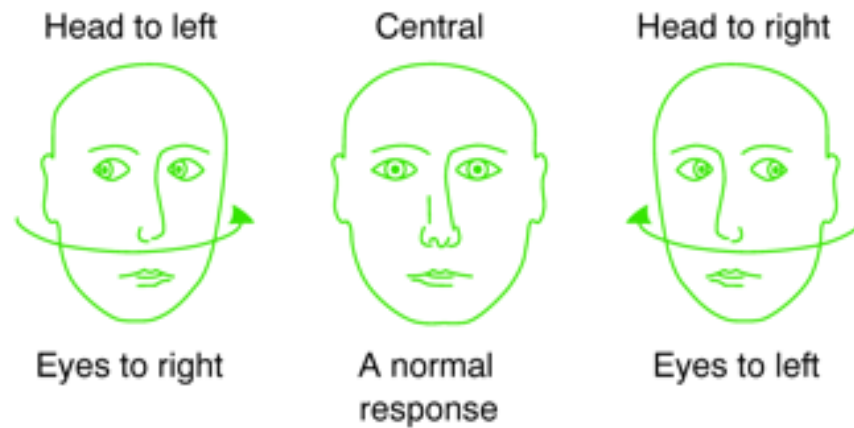
Cold calorics

- Elevate the head for 30°
- Irrigate one tympanic membrane with iced water
 - Observe patient for 1 minute after each ear irrigation, with a 5 minute wait between testing of each ear
 - Facial trauma involving the auditory canal and petrous bone can also inhibit these reflexes

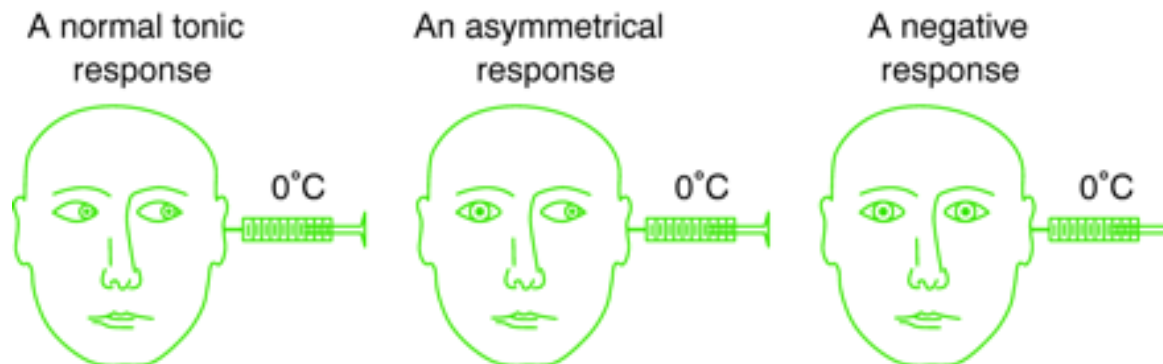
Cold calorics interpretation

- Not comatose
 - Nystagmus; both eyes slow toward cold, fast to midline
- Coma with intact brainstem
 - Both eyes tonically deviate toward cold water
- No eye movement
 - Brainstem injury / death
- Movement only of eye on side of stimulus
 - Internuclear ophthalmoplegia
 - Suggests brainstem structural lesion

Oculocephalic (Doll's eye)



Caloric responses



Basic exam 4- Facial sensory & motor responses

- Corneal reflexes are absent in brain death
 - Corneal reflexes - tested by using a cotton-tipped swab
 - Grimacing in response to pain can be tested by applying deep pressure to the nail beds or supraorbital ridge
 - Severe facial trauma can inhibit interpretation of facial brain stem reflexes

How do we establish brain death?

Corneal reflex



- Cornea touched with cotton swab rolled into ball
- No corneal reflexes in brain death.
- Reflex path: Trigeminal nerve and facial nerve

Basic exam 5- Pharyngeal and tracheal reflexes

- Both gag and cough reflexes are absent in patients with brain death
 - Gag reflex can be evaluated by stimulating the posterior pharynx with a tongue blade, but the results can be difficult to evaluate in orally intubated patients
 - Cough reflex can be tested by using endotracheal tube suctioning

The Apnea Test

- Preconditions
 - Normothermia (core body temp $>32^{\circ}\text{C}$)
 - Most authors are of the opinion that it may be necessary to warm the body to 36°C
 - Systolic BP > 100 mm Hg
 - Euvolemia
 - Eucapnia (PaCO_2 35-45 mmHg)
 - No evidence for CO_2 retention (COPD, severe obesity)

The Apnea Test (cont.)

- Preoxygenate for 10 minutes to PaO₂ >200 mm Hg
- Reduce ventilation frequency to 10 per minute, and PEEP to 5 cm H₂O
- If pulse oximetry remains > 95%, check baseline ABG
- Disconnect ventilator and preserve oxygenation with 100% O₂ in 6-10 L/min via catheter through the endotracheal tube at level of carina

The Apnea Test (cont.)

- Watch closely for respiratory movements (abdominal or chest)
- If no respiratory efforts, perform ABGs at 3-5 minutes and again at 7-10 minutes.
- If arterial PaCO₂ is 60 mm Hg or greater or if >20 mmHg over baseline, the test is positive
- If this is inconclusive, test may extend to 10-15 minutes if patient is clinically stable

The Apnea Test (cont.)

- Abort Apnea Test for:
 - Spontaneous respiratory effort
 - Significant cardiac arrhythmia
 - Pulse oximetry $< 90\%$
 - Systolic blood pressure < 90 mmHg

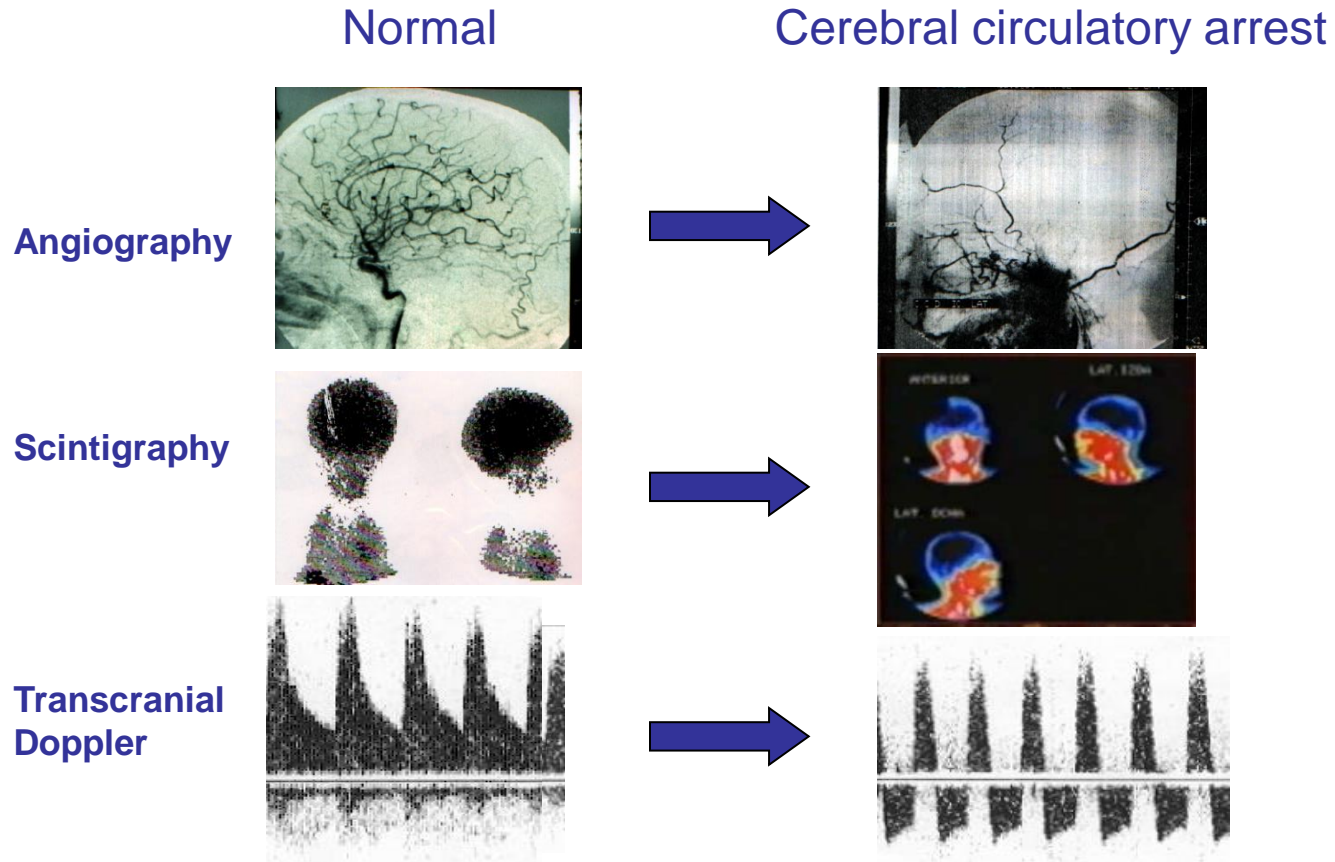
Observations Compatible with Brain Death

- Sweating
- Deep Tendon Reflexes
- Spontaneous Spinal Reflexes- Triple Flexion
- Babinski Sign

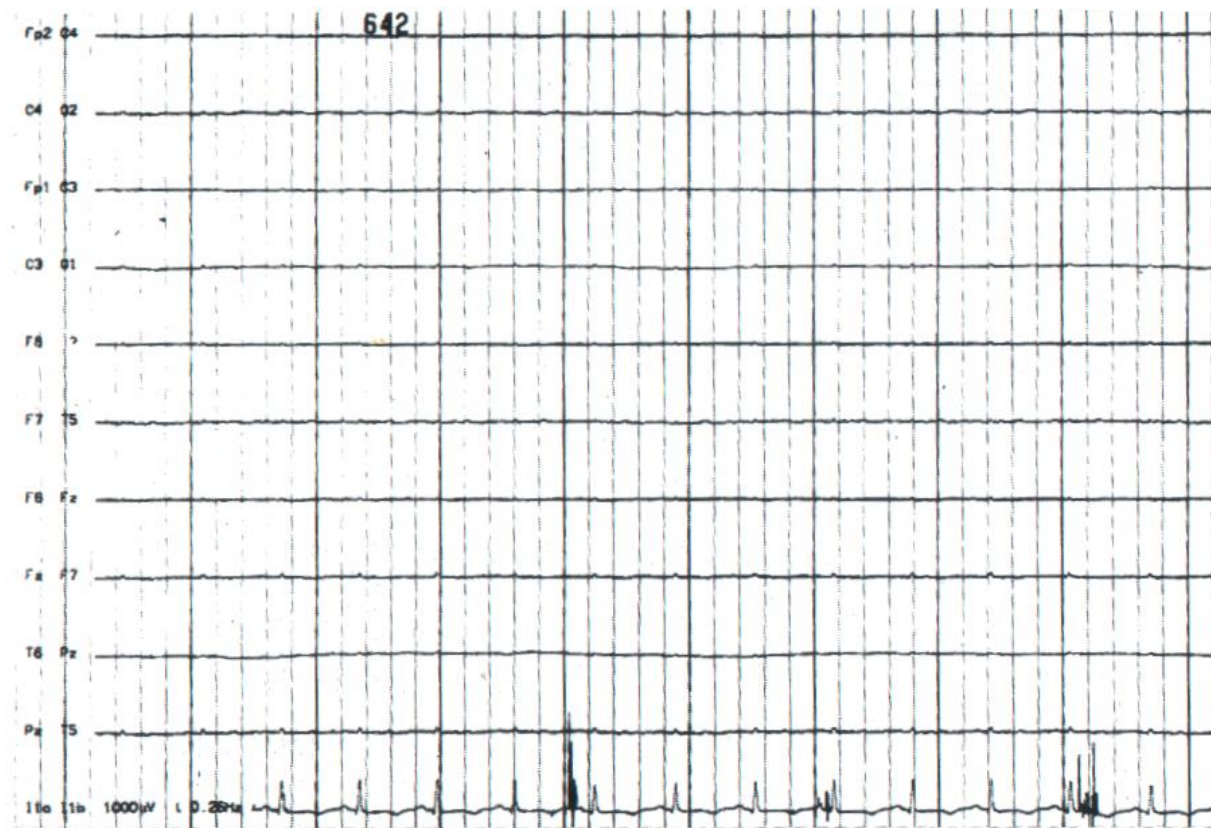
Ancillary Testing

- EEG, TCD, CT angiography, MRI/MRA, cerebral angiography, and nuclear scans have all been used to confirm brain death
- Used when standard testing impossible or inconclusive (i.e. aborted apnea test)
- EEG, cerebral angiography, and nuclear scan are preferred

Cerebral circulatory arrest in brain death



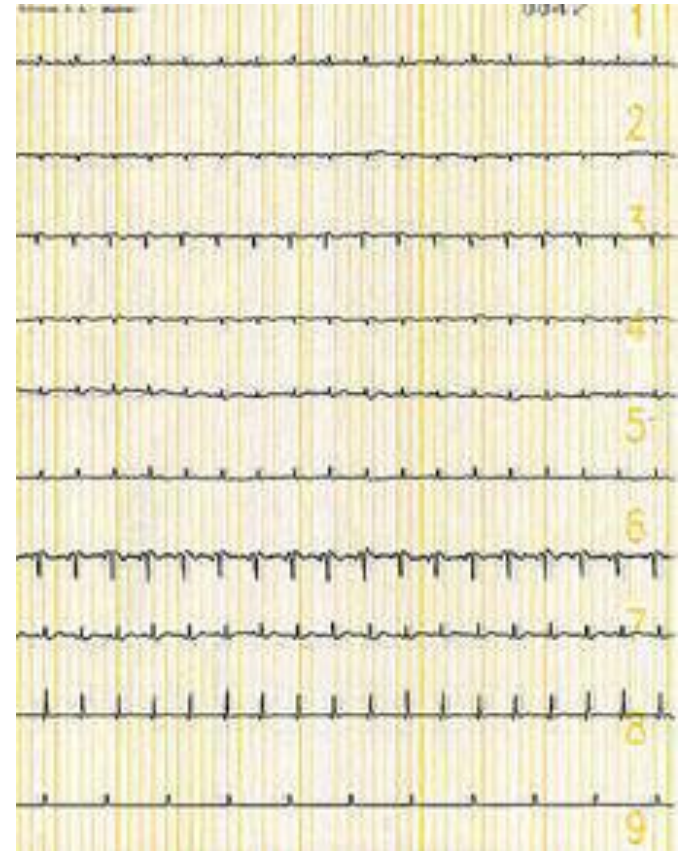
Flat EEG



EEG

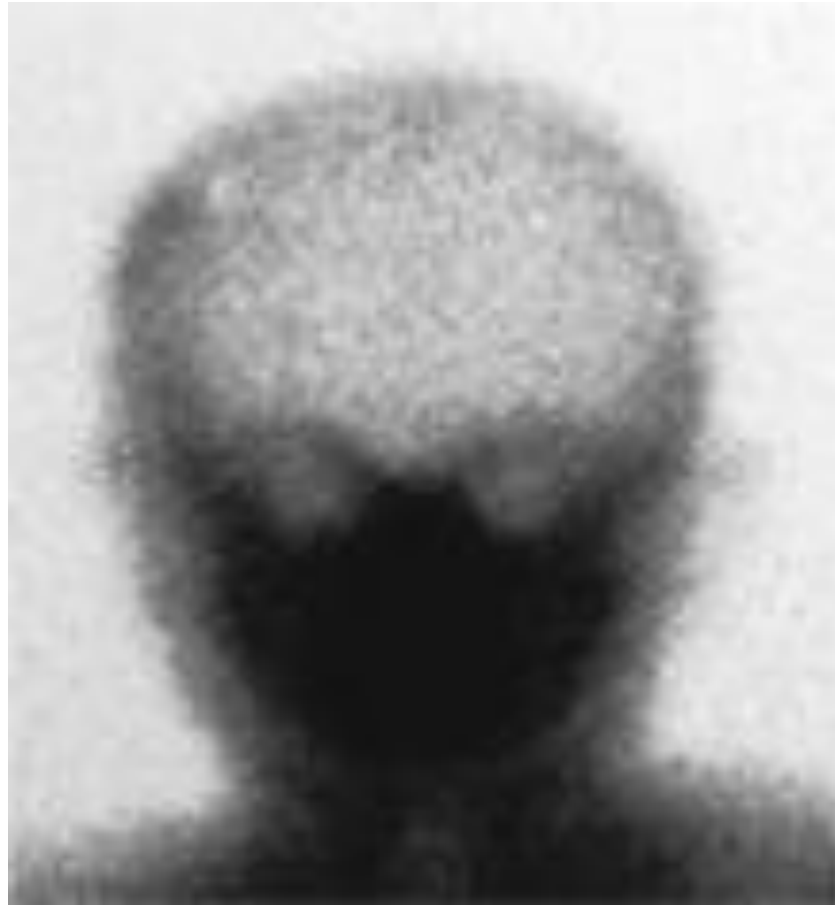


Normal

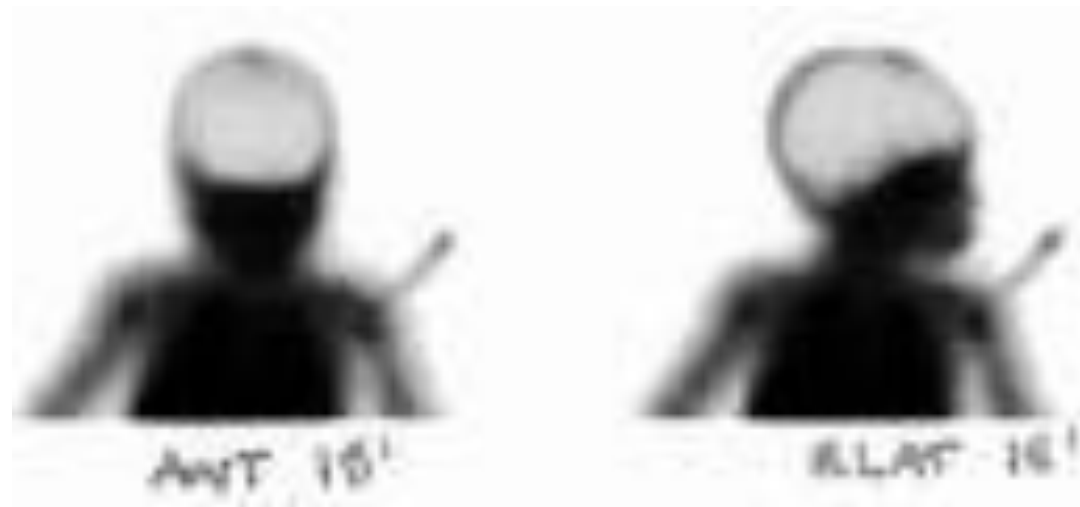


Electrocerebral Silence

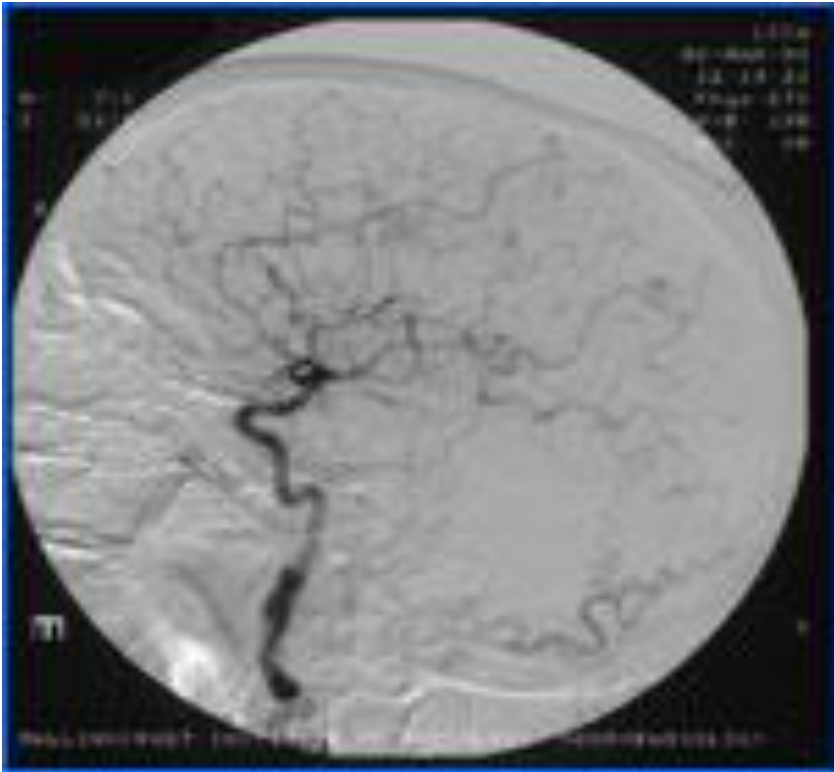
Isotope Brain Scan



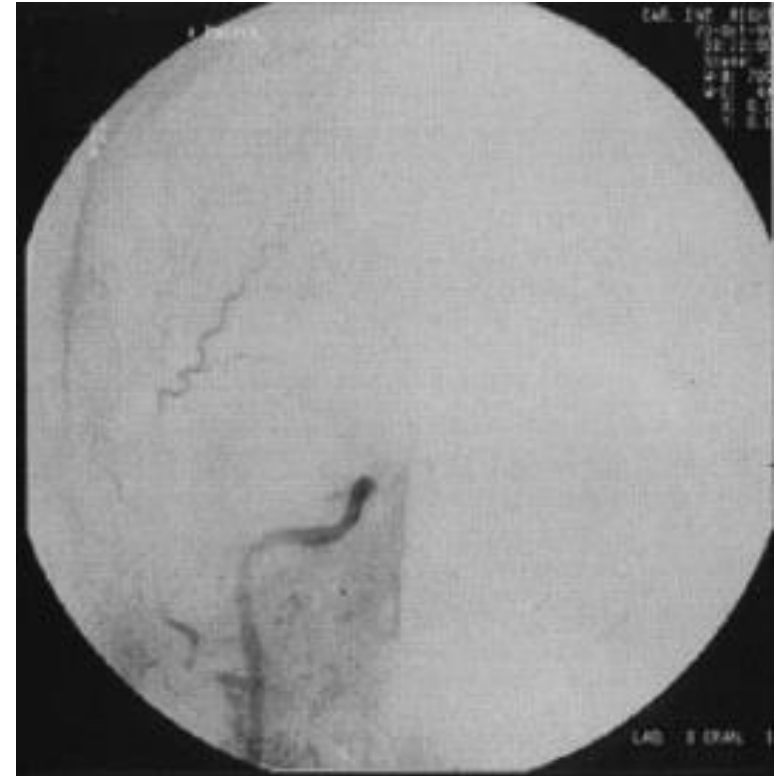
Cerebral perfusion scan in a child with brain death



Cerebral Angiography

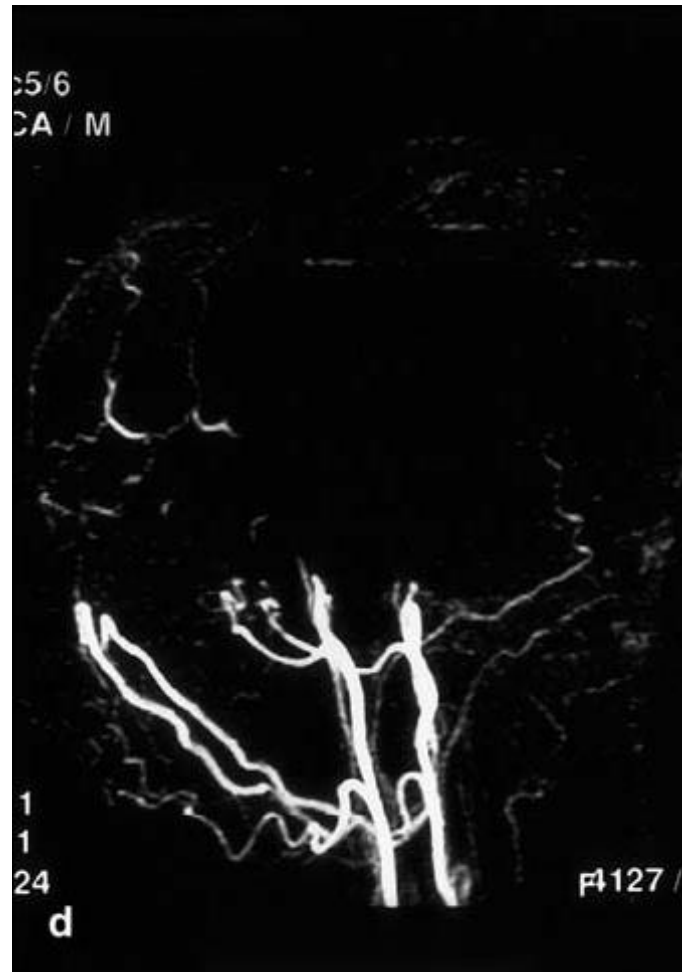


Normal



No Intracranial Flow

MR- Angiography



Brain death determination in children

- No reports of children recovering neurological function who have met adult brain death criteria on clinical examination
- Guidelines for children emphasize **history** and **clinical examination**
- Age-related observation periods and recommended for children:
 - 7 days to 2 months: Two examinations and EEGs 48 hrs apart
 - 2 months to 1 year: Two examinations and EEGs 24 hrs apart, or one examination and an initial EEG combined with a radionuclide angiogram showing no CBF or both
 - More than 1 year: Two examinations 12-24 hrs apart (EEG and isotope angiography are optional)

Kids over 1 year old

- Absence of all brain and brainstem function
 - Comatose: no purposeful response to any stimulus
 - Brainstem function is absent when:
 - Pupils are mid-position and do not react to light
 - Eyes does not blink when touched (corneal reflex)
 - Eyes do not rotate in the socket when the head is moved from side to side (oculocephalic reflex).
 - Eyes do not move when ice water is placed in the ear canal (oculovestibular reflex)
 - Child does not cough or gag when a suction tube is placed deep into the breathing tube
 - Child does not breathe when taken off the ventilator
- Repeat in ~12-24 hours

Children under 1 year

- Necessary to repeat the clinical examination after an 'appropriate' observation period has passed

Age 7 days to 2 months

Two examinations 48 hours apart and one EEG

Age 2 months-1 year

Two examinations 24 hours apart and one EEG or perfusion scan

- Confirmatory EEG is necessary, unless it is determined that there is no blood flow to the brain

Common misconceptions of patient's relatives

- **Since there is a heartbeat, he is alive**
 - Brain dead patients have permanently lost the capacity to think, be aware of self or surroundings, experience, or communicate with others
- **He's in a coma**
 - Reinforce that they are dead
- **With rehabilitation and time he/she will get better**
 - Irreversible, dead brain cells do not regrow

How to make it clear

- Say “**dead**”, not “**brain dead**”
- Say “**artificial or mechanical ventilation**”, not “**life support**”
- **Time of death = neurologic determination of brain death**
 - NOT when ventilator removed
 - NOT when heart beat ceases
- Do not say “**kept alive**” for organ donation