SNACC Quiz No. 38 – BRAIN DEATH

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SNACC EDUCATION QUIZ TEAM
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START
LEARNING OBJECTIVES!

- A REVIEW OF BRAIN ISCHEMIA AT THE CELLULAR LEVEL
- REQUIRED CRITERIA FOR DETERMINING BRAIN DEATH IN ADULTS AND CHILDREN
- CONDUCTING THE APNEA TEST
- BRAIN STEM REFLEXES USEFUL IN THE DIAGNOSIS OF BRAIN DEATH
- PATHOLOGIC CONDITIONS WHICH MAY MIMIC BRAIN DEATH
1. All of the following are true regarding ischemia in the brain except:

A. Neuronal cell death may occur after intracranial hemorrhage, head trauma, or generalized hypoxia
B. Neurons require energy in the form of ATP to maintain their structure and function.
C. Once cerebral blood flow reaches between 6 and 10ml/100g/min, neurons die.
D. Cushing’s phenomenon manifested by hypertension and tachycardia is the last event before infarction of the brain.
A. Neuronal cell death may occur after intracranial hemorrhage, head trauma, or generalized hypoxia

**This is true.** Brain death occurs commonly after intracranial hemorrhage, head trauma, and/or generalized hypoxia. In children abuse is also a common factor. Damage in the brain from hypoxia or ischemia is due to reduced oxidative phosphorylation and consequent decreased ATP with subsequent increased intracellular calcium and sodium. Neuronal depolarization follows together with the release of glutamate causing further cell depolarization and increased calcium. Free radical formation from increased calcium leads to cell membrane damage and irreversible cell death.

*Kass, Cottrell, Ch 1 in Cottrell and Young’s Neuroanesthesia, 2010, Elsevier, PA*
B. Neurons require energy in the form of ATP to maintain their structure and function.

This is true. Neurons require energy in the form of ATP to maintain their structure and function. Carbohydrates, lipids and proteins necessary components of neurons together with ion channels and enzymes use about 40% of the cell’s energy for synthesis with the other 60% of the brain’s energy used for its functional activity.

Kass, Cottrell, Ch 1 in Cottrell and Young’s Neuroanesthesia, 2010, Elsevier, PA
C. Once cerebral blood flow reaches between 6 and 10ml/100g/min, neurons die.

This is true. Normal CBF is 50ml/100g/min. At CBF of 10-15 ml/100g/min, the EEG is suppressed and the brain will gradually lose it’s energy supply with membrane failure and neuronal death occurring in hours unless blood flow is restored. Once CBF is decreases to between 6 and10ml/100g/min, neurons are depolarized with increased intracellular calcium and potassium efflux resulting in potentially irreversible neuronal cell death.

Kass, Cottrell, Ch 1 in Cottrell and Young’s Neuroanesthesia, 2010, Elsevier, PA

Patel, Ch 6 in Essentials of Neuroanesthesia and Neurointensive Care, 2008, eds Gupta and Gelb, Elsevier, PA
D. Cushing’s phenomenon manifested by hypertension and tachycardia is the last event before infarction of the brain.

This is false. Cushing’s phenomenon refers to the hemodynamic effect of brainstem compression from progressive increases in intracranial pressure. Hypertension and Bradycardia (not tachycardia) define Cushing’s phenomenon, the last effort the brain may make to compensate for a major ischemic event. Once the entire brainstem becomes ischemic, unopposed sympathetic stimulation with tachycardia and hypertension are notable due to ischemia in the vagal cardiomotor nucleus. Attempts to reduce the blood pressure at this point may not be necessary nor recommended.

*Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier saunders, PA*
2. All of the following are true regarding criteria for brain death except:

A. Apnea testing is mandatory.
B. In the United States, confirmatory tests like EEG and Cerebral angiography are mandatory for determining brain death in adults.
C. Criteria for brain death include loss of consciousness, absent brainstem responses and apnea.
D. They are necessary for fulfilling the requirements of the “dead donor rule” which should be established before organ transplantation.
A. Apnea testing is mandatory.

This is True. After ensuring that the patient is normotensive (SBP > 100mmHg), normothermic (core temp >36), and eucapnic (PaCO₂ 35-45 mmHg), the patient is pre-oxygenated with 100% Fio₂ for 10 min (goal of PaO₂>200). With 100% O₂ delivery, a positive test is defined by absence of spontaneous respiratory efforts in response to hypercapnic stimulation (PaCO₂ >60mmHg)

Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier saunders, PA
B. In the United States, confirmatory tests like EEG and Cerebral angiography are mandatory for determining brain death in adults.

This is false. While confirmatory tests like EEG and angiography are mandatory in some European, Central, South American and Asian countries, they are not required in the United States. These confirmatory tests are helpful when clinical tests for brain death are unclear. EEG testing recorded for at least 30 minutes will reveal absent electrical activity or isoelectric EEG. Cerebral angiography, a widely recommended test to confirm brain death in adults reveals no intracerebral filling at the level of the carotid bifurcation or circle of Willis.

Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier saunders, PA
Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21
C. Criteria for brain death include loss of consciousness, absent brainstem responses and apnea.

**This is true.** After ruling out reversible syndromes which may produce signs similar to brain death, clinical diagnosis (two examinations separated by 6 hours) demonstrating loss of consciousness (absent motor response to painful stimulus like pressing on the supraorbital nerve, temporomandibular joint or nail bed of a finger), loss of brainstem responses and positive apnea test establishes the diagnosis of brain death. Most hospitals require that the diagnosis be confirmed by 2 or 3 physicians and that at least one of the physicians be a Neurologist, Neurosurgeon or Anesthesiologist. Confirmatory tests in determination of brain death are not always mandatory but they may be helpful when the clinical picture is not clear.

Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier saunders, PA

Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21
D. They are necessary for fulfilling the requirements of the “dead donor rule” which should be established before organ transplantation

This is true. The “dead donor rule” (DDR) states that vital organs should be taken from persons who are as deceased. The concept of brain death (over traditional focus on cardiac and respiratory systems to determine death) was developed in part to allow patients with severe neurologic injury to be declared dead before official cardiopulmonary arrest, potentially avoiding ischemic injury to the other organs. Criteria for brain death established in 1968 by a Harvard ad hoc committee continues to be widely used prior to organ procurement.

Truog et al, 2003, CCM; 31(9):2391-96
Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier Saunders, PA
Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM;344(16):1215-21
3. Which of the following is true regarding the evaluation of brainstem reflexes for determining brain death?

A. In brain dead patients, pupillary constriction in response to bright light is absent.
B. In brain death, the Oculocephalic reflex is elicited by irrigating the tympanum with ice water.
C. The Brain dead patient responds with nystagmus as part of the Cold Caloric vestibular-ocular reflex.
D. The brainstem dead patient will respond by blinking when his/her cornea is touched with a tissue or swab.
A. In brain dead patients, pupillary constriction in response to bright light is absent.

**This is true.** The pupillary light reflex functions to allow the size of the pupil to decrease or constrict in response to bright light. In brain dead patients, pupils do not react to light but their size remains fixed. The afferent limb consists of the optic nerve (CN II) which projects through the optic chiasma and optic tract to the pretectal nucleus and parasympathetic preganglionic fibers from the Edinger-Westphal nucleus. The efferent limb consists of the parasympathetic preganglionic fibers from the Edinger-Westphal nucleus which accompany the oculomotor nerve (CN III) and synapse in the ciliary ganglion.


B. In brain death, the Oculocephalic reflex is elicited by irrigating the tympanum with ice water.

This is false. The Oculocephalic reflex or doll’s eye reflex is one of the reflexes used to help in the determination of brain death. This reflex is elicited by turning the head to one side (while keeping the eyes open) and observe contralateral movement of the eye. Keeping the head in that position, the eyes should slowly return to midline. In the brain dead patient there is persistent fixed gaze or no eye movement. This reflex requires intact function of CN III, IV, and VI.

Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21
C. The Brain dead patient responds with nystagmus as part of the Cold Caloric vestibular-ocular reflex.  

This is false. In the brain dead patient, the cold Caloric vestibular-ocular reflex elicited after infusion of 50 ml of iced water into the ear canal reveals eyes which remain midline. This test is performed in both ear canals with the patient’s head of the bed at 30 degrees after confirmation that the ear drum is intact. In the conscious patient, movement of the eyes toward the cold stimulus followed by nystagmus beating away (from the stimulus) of the eyes is observed. This brainstem reflex is often tested if the oculocephalic reflex response is not clear.

Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21
D. The brainstem dead patient will respond by blinking when his/her cornea is touched with a tissue or swab.

This is false. In the brain dead patient, no eyelid movement is seen in response to touching of the cornea. The afferent fibers of this stimulus is from CN V and the efferent limb is from CN VII.

Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21
4. All of the following problems can mimic brain death except:

A. Locked in syndrome
B. Hypothermia
C. Guillian Barre Syndrome
D. Malignant Hyperthermia
A. Locked in syndrome

This is true. Locked in syndrome maybe a consequence of the destruction of the base of the pons. Patients can't move their limbs, grimace or swallow, but upper rostral mesencephalic structures involved in voluntary blinking and vertical eye movements remain intact. These patients have their consciousness intact because the tegmentum (with it's reticular formation) is not affected. A common cause of this syndrome is acute embolus to the basilar artery.

Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21

Patterson, Grabois. Locked-in syndrome: a review of 139 cases. 1986; 17(4):758-64
B. Hypothermia

This is true. Accidental hypothermia from prolonged environmental exposure may mimic loss of brain function. Hypothermia causes loss of brain-stem reflexes and pupillary dilatation: the pupillary response to light is lost at temperatures between 28°-32°C and brainstem reflexes disappear when core temperature drops below 28°C. But unlike brain death, neurological function may return after rewarming. Patients must be normothermic or mildly hypothermic (temp >36 °C) before beginning the clinical examination for brain death.

Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21
C. Guillian Barre Syndrome

This is true. This acute inflammatory polyneuritis is caused by an immunologic reaction. There appears to be an association with a viral or bacterial infection. Guillian Barre Syndrome (GBS) is characterized by symmetric peripheral flaccid muscle weakness and sensory loss develops in the lower extremities first and then symptoms may progress to involve the upper extremities and cranial nerve innervated muscles. GBS may also involve the autonomic nervous system leading to fatal cardiac and circulatory collapse. Cerebrospinal fluid analysis reveals increased protein and normal cell count. Conversely, post-mortem CSF cell counts are high. Treatment GBS is supportive and includes plasmapheresis.

Wijdicks, The Diagnosis of brain death, Current concepts, 2001, NEJM; 344(16):1215-21
Zhou et al, Malignant Hyperthermia and muscle related disorders (Ch. 43) in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier saunders, PA
D. Malignant Hyperthermia

This is false. This anesthetic related disorder of increased skeletal muscle metabolism is characterized by muscle rigidity, increased temperature, tachycardia, hypercapnia, metabolic acidosis, and hyperkalemia. While mortality is likely if left untreated, these acidotic patients with intact brainstem reflexes in addition to tachycardia and fever do not appear brain dead.

Zhou et al, Malignant Hyperthermia and muscle related disorders (Ch. 43) in Miller’s Anesthesia, 2015, 8th ed.,Ch76, Elsevier saunders, PA
5. Regarding guidelines for brain death in children, which of the following is true?

A. Preterm infants <37 weeks gestational age are excluded from the guidelines.
B. Apnea testing is not required in children for diagnosing brain death.
C. EEG is mandatory in determining brain death in children.
D. One examination will suffice for determining brain death in children.
A. Preterm infants <37 weeks gestational age are excluded from the guidelines.

This is true. In the United States, the Guidelines for the determination of brain death in children exclude preterm infants less than 37 weeks because some of the brainstem reflexes are not completely developed in this group. Furthermore, the assessment of loss of consciousness in critically ill sedated and intubated neonates is difficult.

Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier Saunders, PA
B. Apnea testing is not required in children for diagnosing brain death.

This is false. Apnea testing is required for diagnosing brain death in children in the United States as well as in most countries worldwide. The arterial PaCO$_2$ should increase ≥20 mm Hg above baseline and reach at least 60 mm Hg, with the patient demonstrating no respiratory effort.

Koh et al, in Miller’s Anesthesia, 2015, 8$^{th}$ ed., Ch 76, Elsevier Saunders, PA
C. EEG is mandatory in determining brain death in children.

This is false. Ancillary studies like EEG used to be mandatory in infants less than 1 year of age in the 1987 guidelines for brain death. However, in the revised guidelines, these tests were made optional. These tests may be helpful in determining brain death in children if the practitioner is unable to complete apnea testing (hemodynamic instability), uncertainty regarding the neurological exam, or a medication effect interferes with neurologic testing.

Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier Saunders, PA
D. One examination will suffice for determining brain death in children.

This is false. The neurologic exam together with apnea testing must be repeated at specific intervals: Apnea testing together with a clinical exam is repeated after 24 hours in term newborns to 30 days of age and after 12 hours in children from 31 days to 18 years of age.

Koh et al, in Miller’s Anesthesia, 2015, 8th ed., Ch 76, Elsevier saunders, PA

End of Quiz