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End of Life in the ED – Brain Death and Organ Transplantation

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ABSTRACT

Every year thousands of Americans die awaiting an organ transplant. While our knowledge and experience with organ transplantation has only improved, organ availability continues to be a major issue due to a lack of suitable donor organs. A large population of organ donors are those who have been clinically diagnosed as brain dead. Brain death is defined as the irreversible loss of all brain and brainstem functions. Despite brainstem functions being lost, mechanical ventilation and perfusion techniques allow for proper organ maintenance. This gives brain-dead individuals a unique opportunity to serve as multiple organ donors. However, due to mistrust of the organ donation process by the families of brain-dead individuals and a lack of physician comfort with making the diagnosis of brain death less than half of all brain-dead individuals end up serving as organ donors. The purpose of this paper is to provide health care professionals with the currently accepted clinical criteria to determine brain death at the bedside. For each set of diagnostic criteria, we include a discussion of the relevant neuroanatomical pathways of brain stem reflexes and spinal tracts examined. We also include discussions on the importance of the brain-dead patient's potential role as an organ donor. We hope that this paper can serve as a tool for providers to help those without medical backgrounds understand brain death. Furthermore, we hope that in doing so we can increase the willingness of brain-dead individuals and their families to act as organ donors.

Keywords: brain death, organ donation, brainstem function, cranial nerve reflexes, apnea testing

INTRODUCTION

The Organ Procurement and Transplantation Network (OPTN) data as of October 26th, 2023, reports that there are 114,056 patients on the organ transplantation wait list. In comparison, in 2023 there were only 17,256 people who served as organ donors. In 2020 alone 21,424 brain deaths were reported. However, only 9,364 brain-dead individuals acted as organ donors (Aboubakr et al., 2022; Ahmad, 2022). While brain dead patients are in fact deceased, their vital organs maintain functionality due to machine operated organ perfusion, making brain dead patients exceptionally suited to act as organ donors. However, despite the practicality of brain-dead organ donation the process remains veiled by uncertainty for both physicians and patient families alike. This contributes to reluctance of both parties to participate in organ donation. The data supports this claim, as only 43% of patients declared brain dead in 2020 acted as organ donors.

Brain death is *legally* defined by the Uniform Determination of Death Act (UDDA) as the irreversible loss of function of the entire brain including the brainstem (American Academy of Neurology, 1995; Wijdicks, Eelco et al., 2010). While this definition of brain death provides legal criteria that has been adopted by *most* US states, it both provokes and fails to answer the question of how medical professionals are to determine *when* the function of the entire brain and brainstem has

been irreversibly lost. The current AAN parameters require the presence of three clinical findings to confirm the irreversible loss of function of the entire brain and brainstem: coma (of a known cause), absence of brainstem reflexes, and apnea (Wijdicks, Eelco et al., 2010). While the criteria for making the diagnosis of brain death are the same for all physicians, there is no agreed upon standard for how the presence or absence of each criterion is assessed. Variations in testing for brain death criteria leads to the potential for variations in results; creating a system where a person can be declared brain dead by one physician and alive by another. Discrepancies in determination of brain-death contributes to the lack of much needed brain-dead organ donors.

With an ever-growing need for organ donors, it is imperative that physicians maintain the trust and respect of the families of brain-dead patients. This can only be accomplished by working towards eliminating discrepancies in the brain death diagnosis so that any physician who identifies a patient in the brain-dead state can confidently diagnose them as such using a uniform standard set of diagnostic criteria. For most families having a loved one declared brain-dead is a new and unfamiliar experience. As such, it is helpful for health care providers to be familiar with the process of evaluating a patient for brain-death. Time taken to prepare family for the brain death exam and explain the implications of its outcome is time well-invested. As in the experience of the senior author, having family members present at the bedside of the patient during the brain death exam proves beneficial for their understanding the exam and the finality of its results.

Brain Death

Over the last 50 years, scientific techniques have developed that can artificially maintain ventilation (airway intubation and respirators), circulation (vasopressor amines), appropriate nutrition (parenteral feeding), and elimination of waste products of metabolism (dialysis) in a body whose brain has irreversibly ceased to function (Brain death). Brain death is declared when brainstem reflexes, motor responses, and respiratory drive are absent in a normothermic, nondrugged comatose patient with a known irreversible massive brain lesion and no contributing metabolic derangements. Prior to the development of life-sustaining technology, determination of death was relatively facile, the patient suffered a circulatory arrest and/or they stopped breathing. The development of the aforementioned advanced life preserving technology has allowed for circulation and respiration to be maintained mechanically, thus eliminating cardiopulmonary death in the presence of brain death and requiring the creation of a new definition of death (American Academy of Neurology, 1995).

The currently accepted *legal* definition of brain death comes from the 1980 Uniform Determination of Death Act which determines brain death as the irreversible loss of function of the *entire brain including the brainstem* (National Conference of Commissioners on Uniform State Laws, 1980). The act placed no legislative burden on the diagnostic criteria, but rather left testing and procedure open to interpretation of the medical profession. Ambiguity of the brain death diagnosis prompted the development of a series of practice parameters for adults and children alike (American Academy of Neurology, 1995; Wijdicks, 1995). For adults, the American Academy of Neurology (AAN) published *Practice Parameters for Determining Brain Death in Adults* in 1995 (Wijdicks, Eelco et al., 2010). These parameters require three clinical findings be present to confirm the irreversible loss of function of the entire brain and brainstem: coma (of a known cause), absence of brainstem reflexes, and apnea (Wijdicks, Eelco et al., 2010).

To confirm that these clinical findings are present intracranial imaging and metabolic panels should be completed upon admission of the patient. Intracranial imaging studies should be consistent with a life-threatening intracranial event and laboratory values should rule out intoxication, metabolic derangements, and hypothermia. In the event of brain death, it is imperative that communication with the patient's family be clear, empathetic, and effective. Many family members do not understand the medical jargon, nor do they appreciate that their loved one has experienced "brain death." Terms, such as fixed and dilated pupils, absence of corneal responses, no dolls eyes etc. have no meaning to those unfamiliar with the lexicon of intensivists and neuro specialists.

Clinical Testing of Brain Death

The clinical diagnosis of brain death is dependent upon three primary findings: coma or unresponsiveness, absent brainstem reflexes, and apnea (American Academy of Neurology, 1995). The clinical depiction of brain death must be differentiated from factors that could mimic brain death, such as severe electrolyte imbalance, acid-base imbalance, endocrine imbalance, drug intoxication, poisoning, or hypothermia (core temperature should be ≥ 32°C) (American Academy of Neurology, 1995). Identifying the causation of brain death symptoms is the most precise and ideal method of differentiating from alternative sources of unresponsiveness. Clinical and/or neuroimaging indications of acute trauma can help identify causation and should be one of the first assessments conducted when considering brain death. The following section details the necessary exams to determine the presence or absence for each of the three criteria required to make the diagnosis of brain death.

1. Coma or Unresponsiveness

Coma or unresponsiveness can be determined by an absence of any cerebral motor response to pain in all extremities. The physician can test for a loss of cerebral motor response by applying nail-bed pressure, temporomandibular joint pressure, and/or supraorbital ridge pressure (Figure 1A) (American Academy of Neurology, 1995; Wijdicks, 1995). Testing for the anatomic response to pain assesses the integrity of the cortex, as well as two major long spinal tract pathways, the corticospinal and spinothalamic tracts (Siegel and Sapru, 2019) (Figure 1B-D).

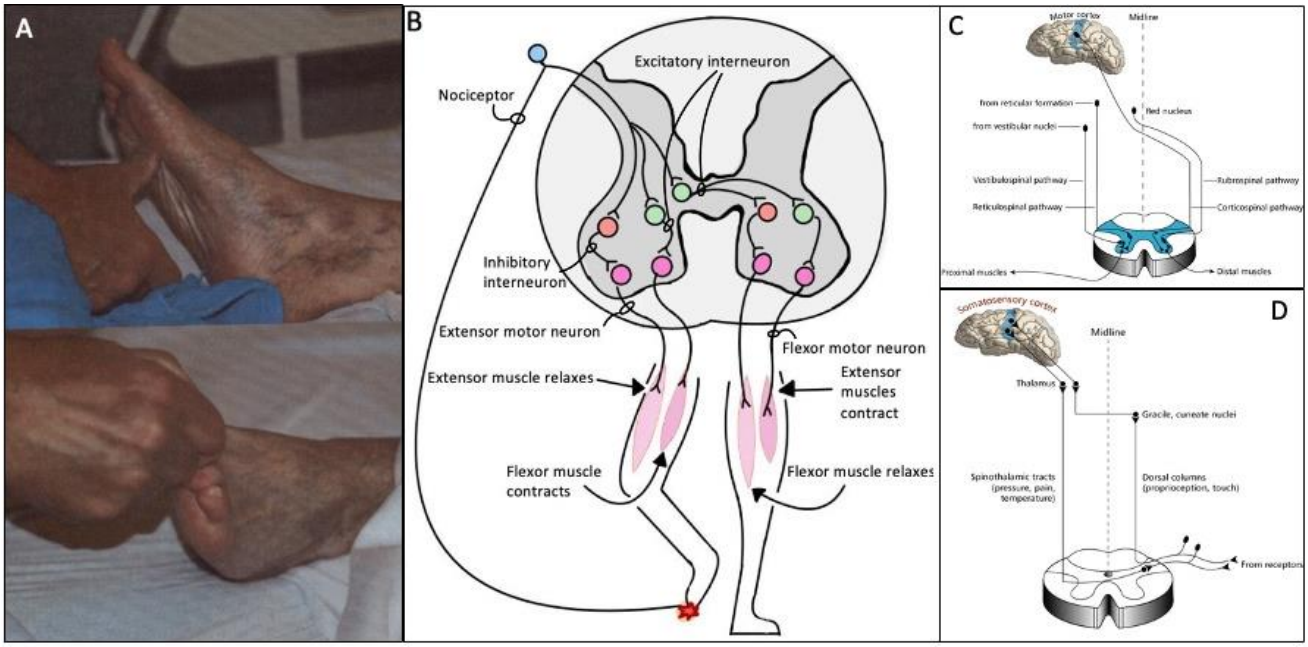

Figure 1: Absent Motor Responses. The physician can test for a loss of cerebral motor response by applying painful, noxious stimuli in the form of nail-bed pressure (seen in 1A), temporomandibular joint pressure, and/or supraorbital ridge pressure. Testing for the anatomic response to pain assesses the integrity of the cortex, as well as two major long spinal tract pathways, the corticospinal (1C) and spinothalamic (1D) tracts. The reflexive response elicited by pain is detailed in Figure 1B. It is important to communicate with family that some motor responses are spinal reflexes and their persistence is still consistent with the diagnosis of brain death (e.g. "Lazarus Sign" and triple flexion). Photos adapted from *'Crossed-Extensor Reflex' by* Casey Henley CC BY-NC-SA *4.0 International License.* "Suprasegmental Motor Pathways (Labeled)" Royal College of Surgeons of Ireland (RCSI) CC BY-NC-SA 1.0 DEED. "Anterolateral and Dorsal Column Systems (Labeled)" by Royal College of Surgeons of Ireland (RCSI) CC BY-NC-SA 1.0 DEED.

The spinothalamic tract takes its origin in the spinal cord where it receives noxious sensory information from nociceptors in the skin relayed by peripheral nerves (first-order neurons). Once in the spinal cord, first-order fibers ascend one or two levels in the lateral funiculus before entering the spinal grey matter and synapsing on second order neurons predominantly in the substantia gelatinosa (lamina two). Second-order neurons then immediately cross in lamina 10 and ascend the cord as the spinothalamic tract, which follows a course to synapse on different thalamic nuclei. The ventral posterolateral nucleus receives sensory stimuli relayed from the body, while the ventral posteromedial nucleus receives sensory stimuli relayed from the head (Siegel and Sapru, 2019). In the thalamus, third-order pain fibers are predominantly directed toward the Primary Somatosensory Cortex, where pain is comprehended. In response to the painful stimulus, a motor movement is initiated in the Pre-Motor Cortex (Siegel and Sapru, 2019). The Pre-Motor Cortex utilizes the basal ganglia nuclei, which relay movement information through the thalamic ventral anterior nucleus and ventrolateral nucleus before reaching the Primary Motor cortex.

Corticospinal Tract

From the Primary Motor Cortex, first-order neurons (pyramidal cells of Betz) of the corticospinal pathway descend through the internal capsule to the brainstem. From the brainstem, fibers are then relayed to the Cerebellum to be processed for fine motor movement. The motor fibers leave the cerebellum and once more access the brainstem, thalamic ventrolateral nucleus, and subsequently the cortex to then be directed toward the spinal cord again by way of the internal capsule. The Corticospinal Tract makes its final descent through the spinal cord to varying sites where it terminates on peripheral motor nerves (Siegel and Sapru, 2019).

Spinal Reflexes vs Cortical Posturing

It is important to explain to the family that there are reflexes that pass solely through the spinal column without entering the brain which can result in movement. Reflexes such as the "Lazarus Sign" phenomenon (spontaneous motor movements that may occur during apnea testing or other hypoxic or hypotensive episodes) and the triple flexion response (dorsiflexion of the foot along with flexion of the thigh and leg upon noxious stimulus of the foot) are commonly seen and compatible with a diagnosis of brain death (American Academy of Neurology, 1995; Van Norman, 1999; Wijdicks, 1995; Wijdicks, 2001). It is also important to note that decorticate or decerebrate posturing are motor movements that are *not* spinal reflexes, and their presence *does not support* the diagnosis of brain death (Van Norman, 1999). Decorticate and decerebrate posturing signify lesions of the brainstem above and below the red nucleus (located in the rostral midbrain) respectively. Decorticate posturing maintains the upper extremity flexor reflex due to sustained function of the intact red nucleus, thus the patient presents clinically with arms hyper-flexed. The opposite is true of decerebrate posturing, as the red nucleus is compromised, and hyperextension of the upper extremity is unopposed (Siegel and Sapru, 2019). *All forms of posturing should be absent in the presence of brain death*. Other than the presence of a possible Lazarus Sign or other spinal reflexes, brain death is heralded by complete loss of motor responses in all four extremities.

2. Absent Brainstem Reflexes

The absence of brainstem reflexes can be elicited by testing the patient's pupillary reflexes, ocular movements, facial sensation, facial motor response, and pharyngeal and tracheal reflexes. Testing these reflexes allows the physician to determine the function of various cranial nerves, which will be discussed in the following sections. Loss of cranial nerve reflexes indicates damage to the brainstem that is incompatible with life.

Pupillary Light Reflex

A test of the Pupillary Light Reflex is performed by shining a bright light in the pupil and observing both the ipsilateral (direct light reflex) and contralateral (consensual light reflex) pupils for normal anatomic constriction in response to the light (Siegel and Sapru, 2019). Testing the Pupillary Light Reflex allows for observance of the integrity of the Optic Nerve (Cn II), Oculomotor Nerve (Cn III), Edinger Westphal Nucleus in the rostral midbrain (parasympathetic component of CN III), and the pretectal area (Siegel and Sapru, 2019). The Optic Nerve (Cn II) serves as the afferent nerve in the pupillary light response and the parasympathetic division of the Oculomotor Nerve (Cn III) serves as the efferent nerve (Siegel and Sapru, 2019). The Pupillary Light Reflex is considered absent when there is no pupillary constriction in response to bright light. An absent response is noted if the size of pupillary enlargement remains fixed anywhere from midposition

(4 mm) to dilated (9 mm) (American Academy of Neurology, 1995; Wijdicks, 1995; Wijdicks, 2001). Pupils may appear dilated due to intact cervical sympathetic pathways that are in control of the dilator pupillary muscle. In the case of brain death, this muscle is unopposed due to a loss of the parasympathetic pathways that normally innervate the constrictor pupillary muscle (Siegel and Sapru, 2019; Wijdicks, 1995). The physician must rule out alternate causes of loss of the pupillary light reflex like corneal or bulbus oculi trauma, and ocular drugs installed topically which are at times capable of causing irregular pupil size or nonreactive pupils. In addition, anatomic anomalies of the iris, and previous surgical effects must be ruled out as causative agents for an abnormal pupillary light reflex (Wijdicks, 1995).

Ocular Movements

Ocular movements can be tested by assessing the presence of the oculocephalic reflex, oculovestibular reflex, and the corneal reflex.

Oculovestibular Reflex

A test of the Oculovestibular Reflex is performed by tilting the head to thirty degrees and irrigating the tympanum with ice water (Figure 2A) (Ahmad, 2022). When uncompromised, the eyes gaze to the side of cold-water irrigation in the external auditory meatus via stimulation of the Abducens N. (Cn VI) on the ipsilateral side and the Oculomotor N. (Cn III) on the contralateral side (Figure 2B) (Siegel and Sapru, 2019). One minute should be allowed for reaction time to the cold-water stimulus, and five minutes should be taken between irrigation of each tympanum (Wijdicks, 1995). Prior to testing the Oculovestibular reflex, the external auditory meatus must be observed otoscopically to ensure that there is no clotted blood or obstruction of any sort which could oppose irrigation of the tympanum, as such an obstruction could compromise the oculovestibular response in a non-brain dead patient and lead to an inaccurate diagnosis. Additionally, there are several drugs that have been shown to reduce or even completely eradicate the Oculovestibular Reflex, including sedatives, aminoglycosides, tricyclic anti-depressants, anticholinergics, anti-epileptic drugs, and chemotherapeutic agents (Jordan et al., 1985; Snavely and Hodges, 1984; Wijdicks, 1995). Finally, the physician should check for any fracture of the petrous part of the temporal bone and eyelid swelling, as those may also diminish the reflex. Temporal bone fracture eliminates the reflex ipsilaterally and can be identified by a "Battle Sign" (ecchymosis around the mastoid process). Eyelid swelling may impair ocular movement, thus preventing the Oculovestibular Reflex from being accurately tested (Wijdicks, 1995).

The Oculocephalic Reflex (Doll's Eye Maneuver)

A test of the oculocephalic reflex is performed by slightly tilting the head forward, and rapidly rotating the head from a middle position to ninety degrees on each side (American Academy of Neurology, 1995). If the reflex is intact, the eyes gaze to the side opposite the direction of rotation of the head under stimulation via Oculomotor N. (Cn III) on the ipsilateral side, and the Abducens N. (Cn IV) on the contralateral side of the head (Figure 2 C-E) (Siegel and Sapru, 2019). Cranial movement is sensed by the proprioceptive properties of the Vestibulocochlear N. (Cn VIII). Testing the Oculocephalic Reflex allows for observation of the integrity of the Oculomotor (Cn III) Motor Nucleus in the rostral midbrain, and the motor nuclei of the Abducens N. (CN VI), the Vestibular N. (Cn VIII), and the medial longitudinal fasciculus (MLF), which are all located in the caudal pons (Siegel and Sapru, 2019). If testing of the Oculocephalic Reflex reveals eyes that move *toward* the direction of cranial rotation, dysfunction of the brainstem between the midbrain and pons (within the MLF) can reasonably be inferred (Siegel and Sapru, 2019). Dysfunction of one pontine gaze center can be assumed when there is intact Oculocephalic Reflex as the head is rotated to one side, while the opposite side generates no gaze response. In this case, the lesion can be isolated to the side of the brainstem contralateral to the direction in which the head is rotated when no Oculocephalic Reflex is elicited (Siegel and Sapru, 2019). Prior to testing the integrity of the Oculocephalic Reflex, cervical imaging must demonstrate no apparent fracture or instability of the cervical spine (Anonymous , 1976; American Academy of Neurology, 1995; Wijdicks, 1995; Wijdicks, 2001).

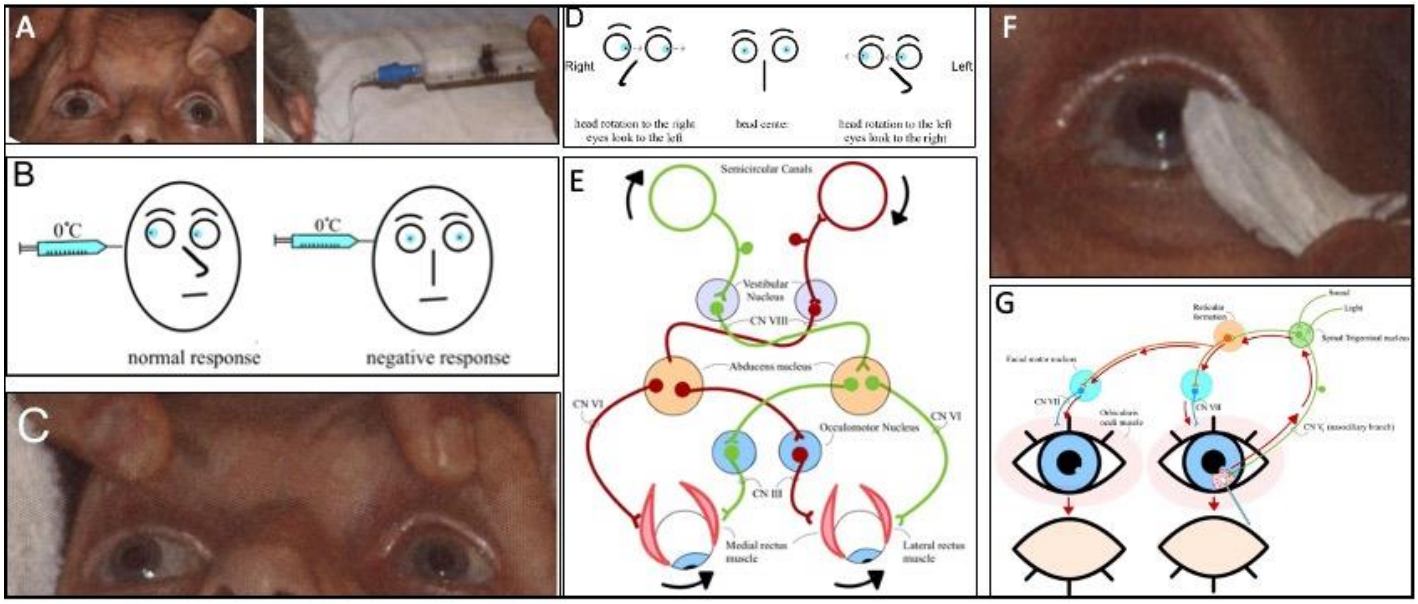

Figure 2: Ocular movements can be tested by assessing the presence of the oculovestibular reflex and the corneal reflex. A test of the Oculovestibular Reflex (2A) is performed by tilting the head to thirty degrees and irrigating the tympanum with ice water. (2B) When uncompromised, the eyes gaze towards the side of cold-water irrigation in the external auditory meatus via stimulation of the Abducens N. (Cn VI) on the ipsilateral side and the Oculomotor N. (Cn III) on the contralateral side. A test of the Oculocephalic Reflex is performed by slightly tilting the head forward, and rapidly rotating the head from a middle position to ninety degrees on each side. If the reflex is intact, the eyes gaze to the side opposite the direction of rotation of the head (2D) under stimulation via Oculomotor N. (Cn III) on the ipsilateral side, and the Abducens N. (Cn IV) on the contralateral side of the head. Testing the Oculocephalic Reflex allows for observation of the integrity of the Oculomotor (Cn III) Motor Nucleus in the rostral midbrain, and the motor nuclei of the Abducens N. (CN VI), the Vestibular N. (Cn VIII), and the medial longitudinal fasciculus (MLF), which are all located in the caudal pons(2E). A test of the Corneal Reflex is performed by opening the patient's eye and lightly stroking the cornea with a cotton swab, as shown in 2F. The normal anatomic response is for the eyelid to blink when the eye is touched with the cotton. For this reflex, the Trigeminal Nerve (Cn V) serves as the afferent nerve and the Facial Nerve (Cn VII) serves as the efferent nerve. The pathways involved in the corneal reflex are detailed in 2G. *Vector eye drawing (Figure 2G) adapted from "Eyes and eyelashes icon eps10 isolated badge vector image" designed by VectorStock (#36449108 at vectorstock.com). Diagram of oculocephalic reflex adapted from "*Vestibulo–ocular reflex*". (2023, November 24). In Wikipedia.* CC BY-SA 3.0

Corneal Reflex

A test of the Corneal Reflex is performed by opening the patient's eye and lightly stroking the cornea with a cotton swab (Figure 2F) (American Academy of Neurology, 1995; Wijdicks, 1995). The normal anatomic response is for the eyelid to blink when the eye is touched with the cotton. For this reflex, the Trigeminal Nerve (Cn V) serves as the afferent nerve and the Facial Nerve (Cn VII) serves as the efferent nerve (Siegel and Sapru, 2019). The Trigeminal Nerve directs fibers to three different nuclei in the brainstem. The fibers elicited in the corneal reflex direct light touch sensation from the sclera to the Principle (Main) Sensory Trigeminal Nucleus located in the rostral pons. The efferent aspect of the Corneal Reflex is induced by the Facial Nerve (Cn VII), the fibers of which are housed in the Facial Motor Nucleus in the caudal pons within the pontine tegmentum (Siegel and Sapru, 2019).

Facial Motor Responses

Jaw Jerk Reflex

A test of the Jaw Jerk Reflex is performed by using a reflex hammer to strike the chin when the mouth is open. In a non-brain-dead patient, this action should elicit a jaw jerk response - a brisk, partial, upward jerk of the jaw (American Academy of Neurology, 1995). To properly elicit the jaw jerk response the patient's mouth is slightly opened and a reflex hammer is used to lightly tap the region below the patient's lower lip on the mandible. This initiates a stretch reflex response from the masseter muscle to the Trigeminal Nerve, which follows a route to the Mesencephalic Nucleus in the rostral pons and caudal midbrain, forming the afferent arm of the Jaw Jerk Reflex (Siegel and Sapru, 2019). The efferent response is also controlled by the Trigeminal

Trigeminal Nerve, only via the Motor Nucleus of the Trigeminal Nerve, located in the rostral pons (Siegel and Sapru, 2019).

Grimacing Response to Pain

The physician should take notice of the presence or absence of the grimacing response. Typically, the grimacing response can be elicited by applying deep pressure or a painful stimulus to the nail bed, supraorbital ridge, and/or the temporomandibular joint; which should force grimacing of the face in response to pain (American Academy of Neurology, 1995). The afferent limb of the grimace response varies depending on the site of the painful stimulus. The afferent limb arises from either the Spinothalamic Tract if the stimulus is initiated in the body or the Trigeminal Nerve utilizing the Principle (Main) Sensory Trigeminal Nucleus in the rostral pons if the stimulus is initiated in the face (Siegel and Sapru, 2019). The efferent limb of the grimace response is under the control of the Facial Motor Nucleus in the caudal pons within the pontine tegmentum, which utilizes the Facial Nerve to innervate the muscles of facial expression (Siegel and Sapru, 2019). Severe facial trauma will make it difficult to assess a facial grimace (Wijdicks, 1995).

Pharyngeal and Tracheal Reflexes

Gag and Cough Reflexes

The pharyngeal reflex can be tested by opening the mouth and slightly stroking the posterior pharynx with a tongue blade (Figure 3A-B). Tracheal reflexes can be tested by inserting a bronchial suction catheter deep into the trachea (American Academy of Neurology, 1995). If functioning properly, a gag reflex will result from stimulating the posterior pharynx with a tongue blade and a cough reflex with the introduction of a bronchial suction catheter deep into the trachea. The afferent limb of these reflexes is the Glossopharyngeal Nerve (Cn IX), which directs light touch sensation from the posterior pharynx to the Solitary Nucleus in the rostral medulla (Siegel and Sapru, 2019). The efferent limb of these reflexes arises from the Dorsal Motor Nucleus of the Vagus Nerve (Cn X) also in the caudal medulla, which directs motor fibers through the vagus nerve to allow pharyngeal muscular contraction needed to perform a gag or cough (Siegel and Sapru, 2019). It should be noted that interpreting the gag reflex in orally intubated patients may prove difficult.

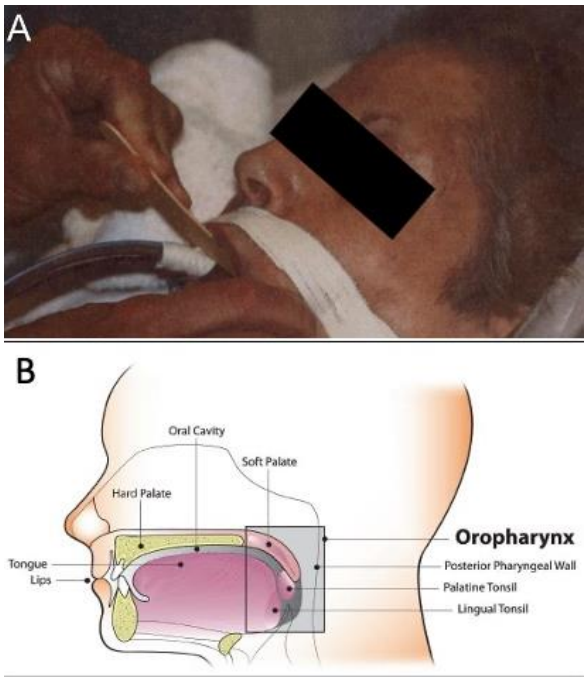

Figure 3: Pharyngeal Reflexes. (3A) The pharyngeal reflex can be tested by opening the mouth and slightly stroking the posterior pharynx with a tongue blade. Tracheal reflexes can be tested by inserting a bronchial suction catheter deep into the trachea. (3B) If functioning properly, a gag reflex will result from stimulating the posterior pharynx with a tongue blade and a cough reflex with the introduction of a bronchial suction catheter deep into the trachea. Testing for the presence of pharyngeal reflexes assesses the integrity of the glossopharyngeal (CN IX) and Vagus (CNX) nerves. Figure 3B from "Source: CDC"; "HPV and Oropharyngeal Cancer".

3. Apnea Testing

As demonstrated previously, testing the cranial nerve reflexes provides important information about the status of brainstem function. If coma or unresponsiveness has been established and the absence of brainstem reflexes has been demonstrated, then clinical apnea testing should be implemented. The absence of brainstem reflexes suggests a severely damaged or dead brainstem, which renders suspicion to the patient's ability to independently respire as the respiratory center resides in the medulla. Because the brainstem reflexes are typically lost in a rostral to caudal fashion, apnea will be amongst the last findings in a brainstem lesion (Wijdicks, 2001). Furthermore, the medullary respiratory center and cardiac center have been shown more resistant to ischemic events than other areas within the

brainstem, which are susceptible to irreversible damage and destruction after 3 to 8 minutes of ischemia (Bhattacharyya and Rai, 2015; Hockaday et al., 1965; Mohandas and Chou, 1971). Because apnea is likely the final symptom to become evident in a brainstem lesion, clinical findings of apnea are very consistent with brain death. Consequently, the apnea test is a vital component of the brain death diagnosis and must be considered greatly significant.

Physiology of Apnea Testing

Central chemoreceptors within the medullary respiratory center detect changes in pCO_2 and pH of the cerebrospinal fluid (Jordan et al., 1985; Wijdicks,, 1995). Typically, when a patient stops breathing CO_2 levels become elevated in the CSF and central chemoreceptors sense the change and trigger respiratory CO_2 blow-off. When brainstem function ceases, the respiratory center can no longer sense the changes in pCO_2 and trigger blow-off, which causes respiration and vasomotor control to be lost (Wijdicks, 1995). Eventually, CO_2 levels become elevated without respiration being initiated leading to apnea and hypotension, which is the premise of the apnea test. It is good practice to confirm the absence of muscle relaxants and respiratory depressant drugs prior to testing for apnea, as these can cause apnea in the absence of brain death (Van Norman, 1999).

Performing the Apnea Test

There are five criteria that must be met prior to conducting an apnea test (Ahmad, 2022).

1. Hypothermia cannot be present (body temp must be greater than 32C)
2. Systolic Blood Pressure should be at least 90 mm Hg
3. Euvolemia (a positive fluid balance) must be established and maintained for approximately 6 hours prior to the test
4. PCO_2 must be normal (arterial PCO_2 40 mm Hg)
5. PO_2 must be normal (PO_2 of 200 mm Hg is recommended).

Prior to performing the apnea test the patient must be pre-oxygenated with 100% O_2 at 6 L/min for 5 minutes (Van Norman, 1999; Wijdicks, 1995). A cannula can be inserted at the tracheal bifurcation to administer the O2. To prevent apnea testing from inducing hypoxic insult, arterial blood gases or a pulse oximeter can be used to monitor blood oxygenation levels (American Academy of Neurology, 1995; Van Norman, 1999). When the ventilator is removed, the chest and abdomen should be monitored for respiratory motions. If the patient is capable of respiration, chest and abdominal expansion typically manifests early in the test. Movements mimicking respiration frequently occur towards the end of the apnea test as oxygenation drops. To differentiate between respiratory movements and respiratory-like movements, a spirometer can be attached to the patient (Wijdicks, 1995). After 8 minutes a final blood gas is taken, and the ventilator is reconnected. The absence of respiratory movements or an arterial PCO_2 of 60 mm Hg or 20 mm Hg above baseline is concomitant with the brain death diagnosis (American Academy of Neurology, 1995; Wijdicks, 1995). If respiratory movements are observed the test is non-confirmatory of brain death and should be repeated. If at any time during the test the systolic blood pressure measures ≤ 90 mm Hg or the pulse oximeter demonstrates considerable oxygen desaturation with cardiac arrhythmias present the test should be aborted and the ventilator reconnected. In case of these findings, an arterial blood gas should be quickly drawn as the ventilator is reconnected. The blood gas is to be assessed as follows:

PCO_2 ≥ 60 mm Hg or ≥ 20 mm Hg above baseline supports the brain death diagnosis.

PCO_2 < 60 mm Hg or < 20 mm Hg above baseline is an intermediate finding and confirmatory testing should be considered at the discretion of the physician (American Academy of Neurology, 1995; Wijdicks, 1995).

A flowchart detailing the procedure for apnea testing is illustrated in Figure 4. Though the original parameters for determining brain death set forth by the Ad Hoc Committee at the Harvard Medical School recommended repeat testing of all clinical findings 24 hours later, the value of re-testing has often been questioned. Wijdicks loosely advises repeat clinical assessment after 6 hours (Wijdicks, 1995). Confirmatory Testing is another area of great dispute. In some circumstances, confirmatory testing has shown relevance. However, in the absence of confounding factors and when a clear cause is evident, brain death is generally declared without a second set of neurologic examinations.

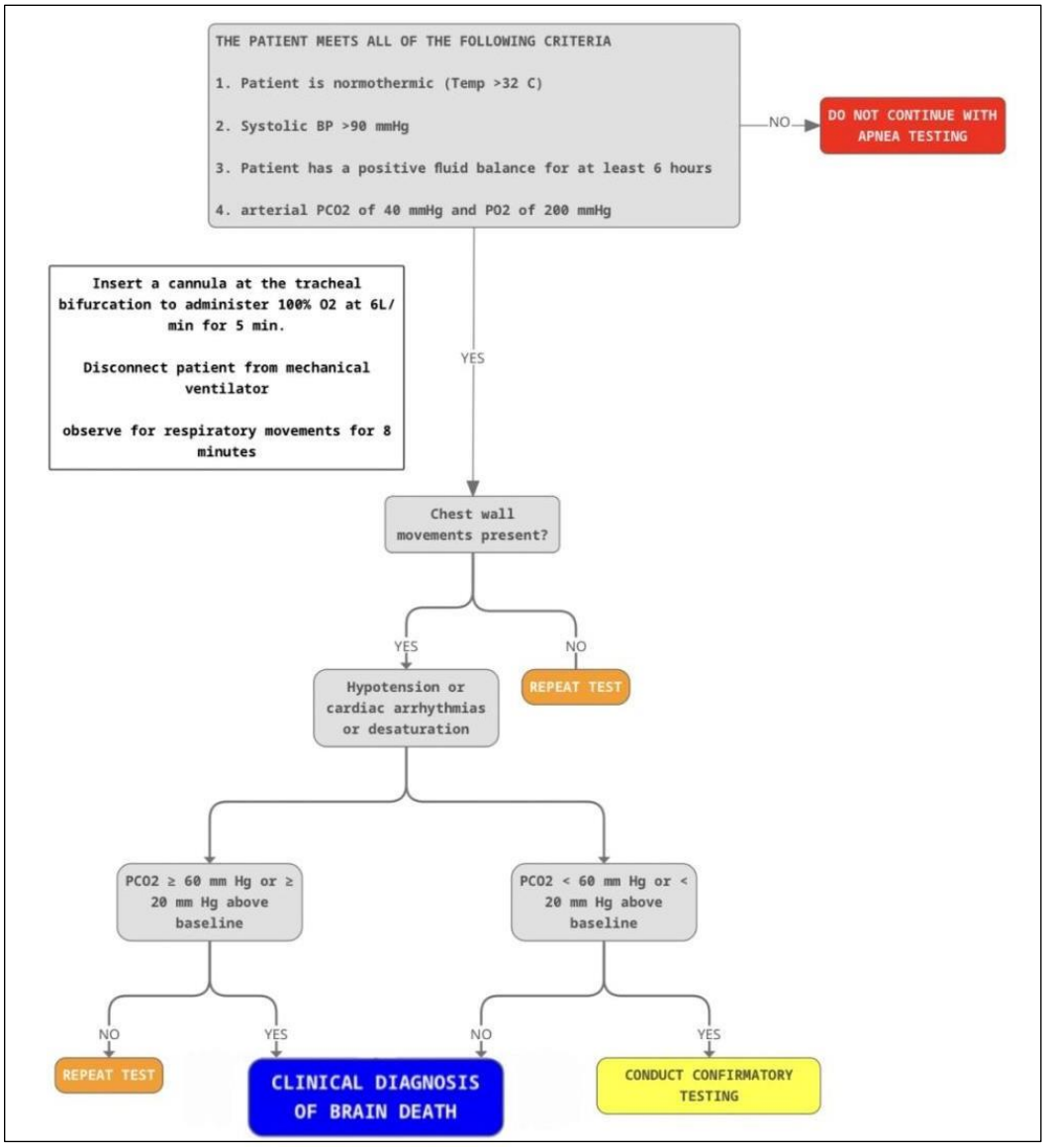

Figure 4. Apnea Testing Procedure. If coma or unresponsiveness has been established and the absence of brainstem reflexes has been demonstrated, then clinical apnea testing should be implemented. Because the brainstem reflexes are typically lost in a rostral to caudal fashion, apnea will be amongst the last findings in a brainstem lesion due to the location of the respiratory centers in the medulla. In circumstances where apnea testing is inconclusive, confirmatory testing has shown relevance. However, in the absence of confounding factors and when a clear cause is evident, brain death is generally declared without a second set of neurologic examinations.

Organ Donation

Although our knowledge and experience with organ donation has dramatically improved over the years, the lack of organ donors remains a significant barrier to transplant success. Brain-dead patients currently account for 74% of deceased organ donors in the US, making them the largest category of deceased organ donors (US Department of Health and Human Services, 2020; Valdes et al., 2002). However, only 43% of eligible brain-dead individuals became organ donors in 2020 (Sheehy et al., 2003). When researchers looked at the reasons why potential organ donors did not become organ donors, they found that the primary reason was a lack of consent to the organ donation request (Sheehy et al., 2003). This lack of consent to organ donation exemplifies that despite the many advancements made in organ donation, some individuals remain wary of the donation process.

Bioethicist Alexander Capron suggests that the mistrust surrounding the brain death diagnosis stems from "many roots" including confusion over terminology used by the Harvard Committee, the life-like appearance of the brain-dead patient, poor language used by hospital personnel and the media, and a lack of statutes which clearly relate brain death to the traditional means of cardiopulmonary death (Capron, 2001). Further research has supported Capron's theories, showing that the three leading reasons why eligible brain-dead patients do not consent to becoming organ donors are loss of patient organ viability, a lack of a supportive and empathetic relationship between the physician and the patient's family, and a lack of effective communication between the organ procurement organizations (OPO) staff and the patient's family (DeJong et al., 1998; Siminoff et al., 2001; Valdes et al., 2002). These reasons demonstrate that both healthcare professionals and OPOs are paramount to increasing the number of organ donors.

There are multiple measures that both healthcare professionals and OPOs could use to promote organ donation and foster a supportive and empathetic relationship with the patient's family. These include: offering the option of organ donation to all families (Williams et al., 2003), improving the level of care of the potential organ donor (DeJong et al., 1998; Valdes et al., 2002; Wood et al., 2004), forming a bond of trust between physician and family (DeJong et al., 1998; Valdes et al., 2002), making the organ request in a private setting (Gortmaker et al., 1998; Williams et al., 2003), decoupling the organ donation request from the brain death diagnosis (de Groot et al., 2010; Garrison et al., 1991; Gortmaker et al., 1998; Shafer, 2009; Simpkin et al., 2009; Valdes et al., 2002; Williams et al., 2003), spending more time with the family (Siminoff et al., 2001; Valdes et al., 2002), utilizing trained personnel in the organ donation request (DeJong et al., 1998; Gortmaker et al., 1998; Valdes et al., 2002; Williams et al., 2003), coordinating organ donation request efforts between the hospital staff and the OPO staff (Gortmaker et al., 1998; Williams et al., 2003), divulging more information to the family regarding brain death and organ donation (de Groot et al., 2010; DeJong et al., 1998; Simpkin et al., 2009; Wood et al., 2004), and allowing sufficient time for the family to form a decision on organ donation (de Groot et al., 2010; Niles and Mattice, 1996; Siminoff et al., 2001; Simpkin et al., 2009; Valdes et al., 2002; Williams et al., 2003).

Furthermore, evidence shows that healthcare professionals who maintain a positive attitude about organ donation and the role they play in the process have more success in leading a family to a decision of consent (Siminoff et al., 1995; Williams et al., 2003). However, while maintaining a positive attitude about the process is essential, in patients that have suffered a traumatically induced brain death physicians only have a short period of time to foster a supportive relationship with families. The physician must keep the patient and their family as the highest priority. In doing so, physicians should separate themselves from OPOs. This can present a challenge because, at many institutions, the physicians performing the brain death exam will inform the family that organ donation is a possibility. In this circumstance, the physician should refrain from any attempt to lead the family to a decision regarding donation. It is important for physicians and OPOs to consider the perceptions of the families of organ donors and the public when organ donation is being considered. As the sole thought that a physician would unintentionally or intentionally kill patients for the purpose of organ procurement could have a detrimental influence on organ donation and the physician patient relationship (Van Norman, 1999; Youngner, 1990). To maintain the separation of the physician and organ donation advice regarding the decision of organ donation should be left to the expertise of the OPOs. With approximately 15,000 to 20,000 deaths by brain death occurring each year, erasing any misconceptions surrounding organ donation and educating patients and their families about brain death is a pivotal step in increasing the number of brain-dead patients that become organ donors.

Care for the Potential Donor

Special care should be given to maintaining the hemodynamic stability of the potential donor, which could "make possible the recovery of organs initially assessed as medically unsuitable, minimize the loss of donors during maintenance, and increase the number of organs that can be procured and transplanted with favorable outcomes" (Wood et al., 2004). The hemodynamic stability of the potential donor can be ensured by preserving normovolemia, optimal blood

pressure, and cardiac output. The physician should aim to use the least amount of vasoactive drug support possible while attaining hemodynamic stability (Wood et al., 2004). If these criteria are preserved, the patient should be monitored until organ procurement. If the criteria are not preserved, a pulmonary artery catheter should be placed for assessment of volume status and adjustment of vasoactive drug support. If following catheter placement, the patient still fails to attain normovolemia, adequate cardiac output, and adequate blood pressure with the use of vasoactive drug support then hormone replacement therapy should be utilized (Dopamine, Dobutamine, Epinephrine, and Norepinephrine) (Wood et al., 2004). Management of respiratory function has also been proposed as a mechanism to improve organ procurement. Mechanical ventilation can be used to improve oxygenation, bronchoscopy can be used for locating and removing aspirated materials, and fluid management can be used to offset pulmonary edema. Additionally, anti-infective therapy and maintenance of pulmonary hygiene also coincide with better organ outcomes (Wood et al., 2004).

Reevaluating Brain Death

Since becoming a necessary capacity, diagnosing brain death has presented difficulty to physicians, not excluding neurologists and neurosurgeons (Wijdicks, 1995). While organizations such as the AAN have laid out criteria for diagnosing brain death there continues to be discrepancies in diagnostic criteria used by physicians. The lack of consistency in diagnosis threatens the trust which is the basis of the physician patient relationship. To combat this, there needs to be a *uniform* standard of diagnostic criteria that must be met to make the diagnosis of brain death. Furthermore, it is imperative that physicians understand these criteria and be competent in explaining their significance to the patient's family. Physicians should reassess their management of brain-dead patients and consider the gravity of their actions and words. Hundreds of thousands of patients are waiting on the organ transplantation list and less than half of eligible brain-dead individuals serve as organ donors. Now is the time to understand the brain death diagnosis and help families to make educated decisions that can save lives; share your heart and encourage organ donation.

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