ORGAN DONATION

As of May 2012, there were over 114,000 patients on the Organ Procurement and Transplantation Network (OPTN)/ United Network for Organ Sharing (UNOS) waiting list. In 2011, however, only 28,535 organ transplantations were performed from 14,145 donors, while over 6,600 patients died while waiting for an available organ. This disparity between need and supply of transplantable organs is growing steadily in the United States, with the waiting list far surpassing the number of available donors and organs. The majority of transplanted organs come from donors after neurologic determination of death (DNDD, previously termed “brain death”). Being that all of these donors enter the intensive care unit (ICU) at some point during their treatment, intensivists are often involved in the diagnosis, referral, and initial stabilization of patients with severe brain injuries. When these injuries would not benefit from neurosurgical or neurologic intervention and are deemed to be non-survivable, they are “catastrophic brain injuries”. The intensivist’s goals shifts from optimizing cerebral perfusion pressure to maintaining hemodynamic stability and diagnosing neurologic death, should it occur. This is often challenging as dramatic and severe physiologic changes accompany the transition to neurologic death, and require specialized knowledge on the part of the treating physician.

**Determination of Death by Neurologic Criteria**

In general, neurologic death is the irreversible loss of all brain function. To establish a diagnosis of neurologic death, the clinician must first identify the underlying causes and determine that they are irreversible. Trauma, stroke, cerebral hypoxia, intracranial hemorrhage, tumors, meningitis, and encephalitis are all well-known causes. All confounding factors must be eliminated, such as hypothermia (< 35° C), hypoxia, intoxication by legal or illegal drugs,
shock/hypotension, and severe electrolyte disturbances. The clinical brain death assessment is usually made in the ICU. This evaluation involves three steps: verifying unconsciousness, documenting absent brainstem reflexes, and the apnea test. To verify unconsciousness, a score of 3 on the Glasgow Coma Scale is required. Documenting absent brainstem reflexes include: the absence of pupillary response to bright light; absence of ocular movements using oculocephalic testing; absence of corneal reflex; absence of facial muscle movement to noxious stimuli; and absence of pharyngeal and tracheal (cough) reflexes. If all brainstem reflexes are absent, an apnea test is performed. The patient should have a pCO₂ within the normal range and be pre-oxygenated with 100% FiO₂. The apnea test ensures the patient has lost the drive to breathe, and confirms the diagnosis of neurologic death. Criteria for a positive apnea test are: no attempt to breathe while disconnected from the ventilator (as oxygen is still delivered to the airway), a pCO₂ greater than 60mmHg or a rise greater than 20mmHg above baseline, and an arterial pH less than 7.3. It usually takes 5-10 minutes of apnea for the pCO₂ to meet criteria and we recommend drawing blood gasses every 3 minutes until either brain death is confirmed or the patient becomes hemodynamically unstable, at which point the patient should be reconnected to the ventilator. Some institutions recommend that the clinical exam, including the apnea test, be performed twice, six hours apart for adults and as much as 48 hours apart for neonates, but the need for a second assessment remains controversial.

If the patient is hemodynamically unstable and would not tolerate even a few minutes off the ventilator for fear of causing cardiopulmonary arrest, other confirmatory tests may be used. Historically, the most common confirmatory test in the United States is cerebral angiography. If the carotid arteries cut off at the base of the skull and there is no blood flow within the calvarium, the patient is brain dead. Recently, clinicians have used magnetic resonance or
computed tomography angiograms in lieu of more invasive traditional angiography. 

Electroencephalography (EEG) is a well-validated modality and is frequently utilized to confirm brain death with absence of electrical activity. The disadvantage of EEG is that devices in the ICU may cause artifacts, leading to spurious results. Other tests include transcranial Doppler ultrasound to assess cerebral blood flow and nuclear imaging to assess uptake of tracer in the brain. This last method is preferred for secondary confirmation in many institutions. However, none of these confirmatory tests replace the clinical exam.

Deciding who is qualified to determine death by neurologic criteria is another difference. Some centers advocate that at least two clinicians concur on the diagnosis and that at least one of those clinicians is a neurologist or neurosurgeon.

**Pathophysiology of Neurologic Death**

Neurologic death occurs when the elevation in ICP forces the brainstem to herniate through the foramen magnum, causing additional ischemic injury and ultimately brain stem infarction. Early pontine ischemia results in a catecholamine surge with hypertension, known commonly as first stage of the Cushing’s reflex. As ischemia progresses caudally to the vagal nucleus in the medulla oblongata, the loss of baroreflexor reflexes and unopposed sympathetic activity results in a profound hyperdynamic state – or the “sympathetic storm”. Systemically, sympathetic vasoconstriction causes compromise of end organ perfusion.

As the brain continues to herniate, a sudden cardiovascular collapse can develop, in part due to direct catecholamine-induced myocardial injury and subsequent cardiac dysfunction, as well as destruction of pontine and medullary vasomotor centers. The effects of this hemodynamic instability can cause marked damage to potentially donatable end-organs.
Profound hypotension develops due to loss of sympathetic tone, amplified by the development of diabetes insipidus due to infarcted posterior pituitary. This diabetes insipidus, which has been reported in up to 80% of patients with neurologic death, is a result of a reduction in vasopressin in the posterior pituitary. Major swings in hormone levels are seen. The hypothalamic-pituitary axis is particularly vulnerable to ischemic injury. Anterior pituitary hormone deficits resulting in hypothyroidism and hypocortisolism have also been described. A number of pre-clinical and clinical studies have indicated that pharmacologic replacement of these hormones may promote hemodynamic stability, improve organ function and increase the likelihood of multi-organ retrieval.

The physiologic changes that manifest as different portions of the brain become injured during the herniation process present a multifaceted challenge to the treating intensivist. These physiologic alterations result in diffuse vascular regulatory disturbances and widespread cellular injury. Severe alterations also occur in metabolism, immunology, and coagulopathy. In sum, these disturbances frequently lead to the development of multiorgan system failure, and cardiovascular collapse.

**Approach for Donation**

Once declared dead by neurologic criteria, the patient may become an organ donor with family authorization and/or an advanced directive. It is highly recommended that healthcare providers not approach family members about organ donation without first consulting with their local organ procurement organization (OPO). In general, representatives from the OPO who are formally trained to talk with families about organ donation make the first, formal approach after end-of-life discussions have taken place and the family understands the concept of neurologic death. Healthcare providers with a close relationship to the family may be involved in the
process as well. After a family or advanced directive authorizes the donation of organs, the OPO assumes care of the donor, both medically and financially, but physician involvement is still important to perform procedures and provide expert critical care advice.

**Donation after Circulatory Determination of Death (DCDD)**

In the last two decades, the scarcity of organs available for transplantation has renewed the interest in “Non-heart beating donors”, Donation after Cardiac Death (DCD) or Donation after Circulatory Determination of Death (DCDD). Potential DCDD donors are patients who either do not have a neurological injury or otherwise do not meet the criteria for brain death, yet have no meaningful chance of survival due to their injuries/illness and are likely to suffer a cardiac arrest if life support is withdrawn. Examples of such patients include ventilator-dependent amyotrophic lateral sclerosis (ALS) patients, high spinal cord injuries, or severe strokes/anoxic brain injury patients who do not regress to neurologic death. Organ donation in such patients may occur after the withdrawal of life support and the declaration of circulatory death. This planned process can occur in the operating room, the pre-op area, or the intensive care unit. In general, a DCDD must experience asystole within 60 minutes of planned withdrawal of life-sustaining treatments in order for their organs to be suitable for transplantation. Once asystole occurs, the recovering transplant surgery team cannot make their incision until a 3-5 minute observation period occurs, during which the potential for autoresuscitation is ruled out. After this waiting period, an incision is made and the organs are preserved with ice and cold fluids.
REFERENCES