Clinical Management of the Organ Donor

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There is a critical mismatch between available organs for transplant and acutely or critically ill patients with end-stage organ disease. Patients who may benefit from organ transplantation far outnumber available organs. The causes for this imbalance are multiple. One cause is family refusal to donate. A second cause is nonrecognition or delay in determination of brain death. A third cause is donor loss due to profound cardiopulmonary and metabolic instability consequent to brain-stem herniation and brain death. Family refusal may be addressed by education, public awareness, as well as close attention to social, cultural and ethical issues, and optimal communication with donor families. Brain death may be consequent to traumatic brain injury, ischemic versus hemorrhagic stroke, as well as massive cerebral anoxia/ischemic following cardiac arrest. Nonrecognition or delay in brain death determination may be addressed by clinician education and frequent clinical assessment to detect early stages of brain-stem herniation refractory to aggressive measures for control of intracranial pressure. Donor loss due to profound cardiopulmonary and metabolic instability may be addressed by aggressive, mechanism-based treatment for clinical instability based on affected body system, as well as measures to support metabolic activity at the cellular and tissue level in the brain-dead organ donor. This article explores cerebral physiology related to impending brain death and catastrophic intracranial pressure elevations. In addition, physiologic consequences of brain death are correlated with affected body systems and mechanism-based therapies to support organ function pending transplantation. Ethical/legal issues are explored as related to patient autonomy and optimal family outcomes. Effective family communication, astute clinical assessment, and optimal clinical management of the organ donor are illustrated using a case study approach, highlighting the role of the advanced practice nurse in donor management.

(KEYWORDS: advance directive, brain death, brain-stem herniation, cardiogenic ventilator triggering, clinical stress, family communication at end-of-life, metabolic resuscitation, physiologic consequences of brain death)
Organ transplantation is currently considered an optimal treatment option for patients suffering from end-organ failure who are medically suitable, clinically stable, and able to survive organ transplantation. As of July 14, 2005, there were 88,927 patients on transplant waiting lists. Patient waiting lists for organs include kidney, liver, pancreas alone, pancreas with kidney, intestines, heart, lung, and combined heart/lung transplants. It has long been recognized that the amount of patients who potentially may benefit from solid organ transplantation dramatically outnumber the available donor organs. There are multiple causes for the imbalance between available donor organs and patients who are appropriate transplant candidates. One cause is family refusal to donate. A second cause is nonrecognition of evolving brain death and subsequently not recognizing a potential organ donor. A third cause is potential donor loss due to cardiac arrest or dramatic and refractory physiological instability during and following development of brain death. Even following restoration of a stable cardiac rhythm and organ perfusion, the potential donor organs may be unusable owing to periods of severe tissue ischemia, hemodynamic stress, and hypoxia. Specifically, up to 17% to 25% of potential donors are lost due to clinical failure during this period. Family refusal to donate may be addressed in part by increased public awareness and education, as well as use of appropriate language, approach, personnel, and surroundings with families during updates about severity of injury and the concept of “brain death.” Such an approach would include involvement of the hospital chaplain and consistent communication and messages from the interdisciplinary team. Donor loss due to nonrecognition of evolving brain death can be minimized by appropriate education on the part of healthcare professionals toward rapid recognition of clinical assessment and cardiopulmonary findings consistent with impending and completed brain death. Potential donor loss due to profound hemodynamic/cardiovascular failure can be minimized by healthcare professionals improved understanding of the physiologic consequences of brain death with appropriate support measures for cardiopulmonary, hemodynamic, endocrine, fluid/electrolyte, and coagulation alterations. In the potential organ donor, all control of the brain over physiologic stability is lost. Physiologic stability needs to be supported aggressively by the team. The benefits of optimal physiologic support are not limited to relative stability of vital signs and cardiopulmonary parameters, but extend to the organ recipient as well. Aggressive management of physiologic changes following brain death contributes to improved outcomes such as larger numbers of organs transplanted, longer recipient survival times, and improved organ function following transplantation.

One purpose of this article is to review cerebral physiology as related to the evolving process ending in brain death, as well as highlighting the multiple global physiological changes seen in all body systems following progression to brain death. A second purpose is to address in detail the clinical interventions utilized to optimize physiologic support for the brain-dead, heart-beating organ donor. The role of the bedside clinician and advanced practice nurse will be highlighted as integral to successful and therapeutic interaction with bereaved family members. In addition, the advanced practice nurse will be highlighted as integral to coordinating care among all disciplines, in recognizing of the potential organ donor, maintaining physiologic stability in the organ donor, and addressing end-of-life issues with bedside clinicians and donor families.

**Cerebral Physiology and Impending Brain Death**

Catastrophic intracranial pressure (ICP) elevations and brain death may occur from a variety of causes including craniocerebral trauma, cerebral ischemia/infarction, cerebral hemorrhage, prolonged cardiopulmonary arrest, subarachnoid hemorrhage, intracranial tumors, meningitis, encephalitis, as well as intoxication with agents such as cocaine, lead, organophosphates, and ecstasy. Between June 1, 2004 through May 31, 2005, there were a total of 374 organ donors within the tri-state area as reported by the local Gift of Life Donor program. Of this total,
185 patients progressed to brain death due to stroke, 119 due to brain trauma, and 70 due to massive brain anoxia (J. Abrams; oral communication; Director, Transplant Information Center, Gift of Life Donor Program, June 21, 2005). With statistics such as these, clinicians should remain vigilant for the possibility of catastrophic progression of brain injury whether due to trauma, stroke, anoxia, or postcardiac arrest. Cardiac arrest may be an initiating event to begin the cycle of neuronal death that may occur over time. For this reason, patients following cardiac arrest may retain some short-term neurological function or brain-stem reflexes. As the cycle of neuronal death progresses, following the initial insult, residual neurological function may be lost, and the patient progress to brain death. What may be considered a final common pathway in the progression of many patients to brain death is the development and evolution of deadly ICP elevations, leading to brain-stem ischemia, infarction, hemorrhage, or herniation.

The initial brain injury may not be fatal outright, but, even despite aggressive therapy, may begin the cycle of secondary brain injury. Secondary brain injury could occur as an evolving process over hours to days. The end result could be progressive and catastrophic ICP elevations, leading to supratentorial herniation syndromes and concluding with catastrophic brainstem injury or herniation.13 With the brain having a significant role in blood pressure management, progressive brain injury will cause severe blood pressure alterations14,15 that reflect activation of the baroreceptor reflex, physiologic stress response, and changes in vasomotor tone.16 In the setting of a rapidly expanding supratentorial lesion or swiftly progressive brain edema, a proposed sequence for evolution to brain death may proceed as follows. The upper brain may typically lose function as evidenced by decreased level of consciousness. Further progression of severe intracranial hypertension and brain injury may lead to pathologic posturing or seizure activity. Continued increases in pressure may cause transtentorial herniation, distorting the posterior fossa and infratentorial compartment with pressure on the pons. Cushing’s response may then occur as evidenced by hypertension, bradycardia, and wide pulse pressure.14 Further pressure increases cause mass effect and impinges on the medulla oblongata/brain stem, resulting in brainstem ischemia, infarction, compression, hemorrhage, and distortion.17 At this stage, dramatic cardiopulmonary instability may occur. This cardiopulmonary instability includes alterations in respiratory rate, depth, and pattern, as well as marked changes in vascular tone, cardiac output, and blood pressure following mobilization of catecholamine stores. Mobilization of catecholamine stores may be evidenced by profound tachycardia and hypertension of varying duration.2,14,15,17 Following depletion of catecholamine stores, heart rate and blood pressure may decline correspondingly with decreased myocardial contractility and vascular tone.2,14,15 Typically at this stage, the neurological assessment shows loss of protective reflexes, loss of consciousness, and loss of all cranial nerve function as and temperature regulation.4,11,17–19 For these reasons, close patient surveillance post-cardiac arrest or other brain insult will remain vital. Illustration of brain anatomy as related to contents of supratentorial and infratentorial compartments is found in Figure 1.

Determining Brain Death

Appropriate testing to confirm a diagnosis of brain death includes serial neurological examinations to document irreversible loss of total brain and brain-stem function.6,17 Within the context of serial neurological examinations, it is vital to realize that catastrophic brain injury may be the result of an evolving process, occurring in any number of settings such as a medical critical care or cardiac unit. It may also potentially begin in a nonmonitored setting and necessitate transfer to a critical care unit. For this reason, incorporation of frequent neurological assessments into daily routines is paramount. Changes in the level of consciousness are the single most important measure of stability of brain function. Any change in level of consciousness, further deterioration of the examination, and critical ICP elevations may be caused by brain hemorrhage/hematoma formation, compression, edema, and stroke, as well as expanding solid tumors and brain trauma among other causes.13 Normal computed tomography
Figure 1. MRI of normal brain anatomy as related to contents of supratentorial and infratentorial compartments. Note the relative size of supratentorial versus infratentorial compartments. Expanding mass lesions within the posterior fossa can more rapidly progress to brain stem pressure, distortion, and herniation/brain death.

Monitoring of consciousness and arousal by using the Glasgow Coma Scale (GCS) is vital. The GCS is easily integrated into existing unit flow sheets for ongoing documentation. Determination of brain death is based primarily on clinical evaluation and includes total loss of consciousness, no evidence of seizure activity, and no response to stimulation. Brain death means total loss of function in the cerebral hemispheres and the brain stem. Loss of brain and brainstem function is assessed by total loss of any responses and reflex activities mediated by both the brain and the brain stem. Many excellent references exist, including practice
Figure 2. Normal computed tomography of the head as a basis for comparison. Points of reference in this normal study are a symmetrical ventricular system, no midline shift, and no abnormality of the skull or the cerebral cortex.
Figure 3. Neuroimaging of intracerebral hemorrhage. Of significance are effacement of the sulci on the affected side, brain edema adjacent to the expanding hemorrhage, and distortion of the ventricle on the affected side.

0.1 or 0.3 sec, and 70 Hz.\textsuperscript{19} Electroencephalogram findings are affected by high barbiturate dosing.\textsuperscript{22} A third neurodiagnostic test includes a technetium nuclear medicine scan. In this instance, brain death is demonstrated by absence of cerebral blood flow as indicated by no uptake of the radioisotope.\textsuperscript{18,20,21} A nuclear medicine scan indicating normal brain perfusion is illustrated in Figure 8. A nuclear medicine scan consistent with brain death is illustrated in Figure 9.

\section*{Physiological Consequences of Brain Death}

In the evolution of catastrophic neurological injury to a diagnosis of brain death, a
multitude of global physiological changes in virtually all body systems occur in response to total, irrevocable loss of brain and brain-stem function. Most significantly, brain death is associated with profound and complex derangements in hemodynamic stability, fluid and electrolyte balance, metabolic stability, and challenges with oxygenation. These complex physiologic changes and instability are responsible for the loss of up to 25% of potential organ donors. Additional organs may potentially be lost due to uncorrected metabolic derangements or excessive vasopressor
Effects on Cardiovascular System

One consequence of brain death is dramatic hemodynamic instability. Hemodynamic instability occurs in 2 phases. The initial phase consists of a massive outflow from the sympathetic nervous system related to a large mobilization of catecholamine stores. Clinical findings of this stage include severe tachycardia, hypertension, increased systemic vascular resistance, and dramatic increases in cardiac workload, myocardial oxygen consumption, and increased calcium levels within myocardial cells.\textsuperscript{1,2,5,14,17,25–27} This initial high sympathetic outflow is followed by...
Figure 6. Neuroimaging of subdural hematoma. The expanding lesion has produced midline shift, massive displacement of the ventricles, and effacement of the sulci on the affected side.

autonomic collapse due to exhaustion of available catecholamine stores.\textsuperscript{2,14,17} The second phase of hemodynamic instability is characterized by reduced sympathetic outflow, loss of vascular tone, decreased peripheral resistance in arterial and venous systems, and reduced cardiac output and end-organ perfusion.\textsuperscript{1,5,25–28} This second phase results in significant relative hypovolemia due to tremendous increase in vessel capacitance in addition to any actual fluid volume deficit. Additional causes of hemodynamic instability beyond cessation of brain and brainstem function include further volume depletion due to use of diuretics, such as mannitol and furosemide, to manage ICP elevations. Continued blood loss from concurrent injuries, volume deficits related to insensible fluid losses, and diabetes insipidus contribute to dramatic hemodynamic instability.\textsuperscript{28} Volume losses related to diabetes insipidus may exceed 1–2 liters per hour. Close monitoring of urine output is vital as an indicator of development of diabetes
insipidus, end-organ perfusion, cardiac output, fluid balance, and response to therapy. Hemodynamic instability also may be caused by residual effects of barbiturate therapy, which may reduce cardiac contractility and cause vasodilation in a dose-related manner. Residual effects of previously administered sedative and analgesic agents may also contribute to hemodynamic instability. In addition to fluid balance, previous drug therapy, and profound changes in vascular tone and sympathetic outflow, cardiovascular stability may be compromised by the systemic inflammatory response associated with brain death. This systemic inflammatory response has 2-fold consequences. First, circulating inflammatory mediators produce further vasodilation and increased vessel capacitance, making relative hemodynamic stability more difficult to achieve. Second, it may further development of lung injury and increased immune sensitivity for the organs following transplant.

Interventions for Cardiovascular Stability

Given the massive hemodynamic shifts seen following brain death, hemodynamic management proceeds in 2 phases. The first phase would entail efforts to modulate the
Figure 8. Nuclear medicine scan indicating normal brain perfusion (non-brain dead). In this image, brain metabolism and blood flow is indicated by uptake of the radioisotope tracer as shown by white color within outlines of the skull.

dramatic surges in perfusion pressure and heart rate and to mediate excessive systemic vascular resistance. The second phase entails correction of both absolute and relative fluid volume deficits. In the first phase, duration of hemodynamic surges consequent to catecholamine mobilization may be unpredictable. Because of this, some clinicians may choose to monitor closely without aggressive treatment in the short term. If hemodynamic surges are treated, short-acting agents, such as nitroprusside or esmolol, may be appropriate for 2 reasons. First, they are effective and easily titrated. Second, these agents have a short duration of action that is significant in anticipating the dramatic fall in blood pressure after depletion of catecholamine stores. In the second hypotensive phase, an initial intervention is rapid replacement of circulating blood volume with crystalloid or colloid intravenous fluids. This fluid resuscitation must replace actual fluid volume deficits as determined by calculation of intake/output and insensible fluid losses that may approximate 1 to 1.5 liters per day. Insensible fluid losses may be markedly increased in a febrile patient. Aggressive fluid resuscitation in this stage also must account for the relative fluid volume deficit produced by a profound vasodilated state from catecholamine depletion as well as the systemic inflammatory response. Use of multiple, large-bore intravenous (IV) catheters or central IV access, if available, is appropriate for aggressive volume resuscitation. To rapidly deliver large fluid volumes, large-bore peripheral IV catheters may be very effective, due to flow dynamics. The volume infused through a 16-gauge peripheral IV catheter may exceed 200 mL/min. Initial volume resuscitation is generally titrated to an initial central venous pressure (CVP) of 8 to 10 mm Hg. With aggressive fluid resuscitation producing a dilutional anemia as well as possible pre-existing anemia, blood products may be titrated to a hemoglobin of 10.0 g/dL. The goal for blood pressure management should be at least 100 mm Hg systolic or a mean arterial pressure (MAP) of 60 to 70 mm Hg. Recommended pharmacological therapy for vasopressor support includes dopamine with a target dose of <10 mcg/kg/min or dobutamine with a target dose of <10 mcg/kg/min if the focus is toward cardiac donation. In other instances, norepinephrine may be used, with a target dose of 0.5 to 5 mcg/min. Catecholamines, in addition to providing cardiovascular

Figure 9. Nuclear medicine indicating absent cerebral perfusion, consistent with brain death. Absence of brain metabolism and blood flow is indicated by much darker color within skull outline, showing on uptake of radioisotope tracer. Cerebellum and brain stem are not evaluated, so correlation with neurological examination is required.
support for the organ donor, also promote lower incidence of kidney rejection and better long-term graft survival with optimal dosing.\textsuperscript{24} In addition to blood pressure changes in this stage, the brain-dead patient is at risk for bradyarrhythmias. In clinical circumstances other than brain death including high vagal tone, bradyarrhythmias, such as symptomatic sinus bradycardia, may be treated with atropine sulfate. The clinical effects of atropine are mediated by its effects as a vagolytic agent, attenuating cardiac slowing caused by elevated vagal tone. In the brain-dead patient, the heart is effectively denervated and resistant to atropine.\textsuperscript{2,4,20,33,34} Some clinicians incorporate this lack of response in the determination of brain death. In the absence of brain death, a 2 mg IV bolus dose of atropine should cause an increase in heart rate. If the vagus nerve in unresponsive, there should be no significant increase in heart rate.\textsuperscript{20,34} Treatment options for symptomatic sinus bradycardia with hypotension, such as titration of dopamine or small bolus doses of IV epinephrine (0.05 to 0.1 mg) for catecholamine support and titrated to effect, have been utilized.

\section*{Effects on Pulmonary Stability}

The catastrophic physiological changes seen following brain death have profound consequences on lung function and gas exchange. There are multiple mechanisms by which pulmonary dysfunction occurs in this setting. One mechanism is neurogenic pulmonary edema.\textsuperscript{2,35} Intense vasoconstriction and elevated systemic vascular resistance related to severe catecholamine surges causes shifting of large fluid volumes from the periphery to the central circulation. Dramatic shifting of blood volume, in turn, causes an acute increase in left atrial pressure, and increased pulmonary capillary pressure with resulting pulmonary edema. Ultimately, this state is related to elevated hydrostatic pressure as well as probable damage to the pulmonary capillary bed.\textsuperscript{1,27,30,31,33,36} Another possible related cause of neurogenic pulmonary edema is direct alteration of pulmonary capillary permeability due to the intense alpha-adrenergic stimulation.\textsuperscript{30} Lung function also may deteriorate due to aspiration, pulmonary contusions,\textsuperscript{35} as well as pneumonia,\textsuperscript{35} pulmonary emboli, mucous plugging,\textsuperscript{2} low tidal volumes, and lack of positive end-expiratory pressure (PEEP).\textsuperscript{3,27,31,33} The inflammatory process also plays a role in compromised lung function in the brain-dead patient.\textsuperscript{5,30} Mobilization of inflammatory cells, proteases, cytokines, leukotrienes, and chemoattractants contributes to donor lung injury. Inflammatory mediators also may directly damage lung tissue in the brain-dead patient.\textsuperscript{4} Other possible causes of lung dysfunction include volutrauma and barotrauma. Pulmonary microemboli may also occur in response to alterations in coagulation status. Additionally, in a marked vasodilated state, there may be lung areas that are not effectively perfused, with resulting ventilation/perfusion mismatch. Mechanism of lung injury in the potential donor may also be related to volutrauma secondary to alveolar overdistention from excessive tidal volumes. It may additionally be related to biotrauma in which cytokines released in response to physical distortion cause inflammation of the alveolus.\textsuperscript{37}

\section*{Interventions for Pulmonary Stability}

Given that pulmonary dysfunction following brain death has multiple components, it follows that optimal pulmonary management would pursue a multimodal approach. One approach to optimize lung ventilation is aggressive pulmonary care and secretion removal by repositioning, chest physiotherapy as clinically appropriate, and frequent suctioning for airway clearance.\textsuperscript{1,4,28,30,35} In-line suctioning and frequent oral hygiene with pharyngeal suctioning are appropriate to minimize risk of hypoxemia and infection, particularly ventilator-associated pneumonia. A second approach is by careful fluid management in attenuating fluid shifts into the lung.\textsuperscript{35} Judicious use of crystalloid and an aggressive approach to managing the potential organ donor, including close titration of intravascular volume to minimize risk of pulmonary edema, is appropriate.\textsuperscript{1,30,33,35} A third approach is to carefully titrate ventilator flow rate and tidal volume, as well as careful application of PEEP. PEEP should be less than 7.5 cm H\textsubscript{2}O and peak inspiratory
pressures should be maintained less than 30 cm H$_2$O if possible. Lung protective ventilation with tidal volumes of 6 to 8 mL/kg may maintain minute ventilation and attenuate risk of volutrauma or barotrauma.\(^1\) In addition, avoidance of high plateau pressures and auto-PEEP may minimize the risks of additional hemodynamic compromise in a patient who is already hemodynamically unstable. A fourth approach is intervention in the inflammatory process contributing to lung injury. In one retrospective study, steroid administration to the organ donors resulted in improved lung function and more organs available for transplant.\(^{1,8,30}\) Methylprednisolone at 14.5 mg/kg has been utilized in a small sampling of patients and resulted in better oxygenation. It may be appropriate to consider high-dose methylprednisolone therapy for potential lung donors for this reason, as well as to potentially attenuate risk of rejection following transplantation.\(^{1,8,30}\) Ventilation options include use of pressure-control inverse ratio ventilation for hypoxemia refractory to standard volume control ventilation.\(^{38}\) The importance of careful ventilator management cannot be overstated. Significant hemodynamic compromise may occur in addition to direct lung injury, with excessive tidal volumes or inadequate expiratory times. This may be of particular concern in actual or potential donors with histories of reactive airway diseases such as chronic obstructive pulmonary disease (COPD) and asthma. In these settings, pulmonary hyperinflation is a risk in which seemingly “standard” minute ventilation may not allow sufficient expiration times and lead to air-trapping in the alveoli. This may result in decreased venous return, increased pulmonary vascular resistance, and interference with blood flow between the right and left sides of the heart. Ultimately, decreased blood pressure and cardiac output may result.\(^{39}\) Closely titrating minute ventilation and prolonging expiratory times may facilitate hemodynamic stability\(^{39,40}\) in this subset of potential organ donors.

□ Effects on Endocrine/Metabolic Stability

Brain death is associated in most patients with a multitude of physiological changes far beyond cardiopulmonary complications related to catecholamine surges and a pronounced inflammatory state. With the onset of brain death, multiple endocrine derangements occur that are intimately tied to overall metabolic and hemodynamic stability.\(^{2,14}\) Dramatic dysfunction of hypothalamic and pituitary function\(^{2,14}\) following brain death causes loss of thermoregulation in which hyperthermia might occur following intense vasoconstriction and might be followed by hypothermia, further placing physiologic stability at risk.\(^{26,35}\) Hypothermia could also be caused by factors independent of brain death, such as heat loss by radiation and convection.\(^{1}\) Risks associated with hypothermia are multiple. One risk of hypothermia is decreased ability of the kidneys to concentrate urine (cold diuresis). A second risk is a left shift of the oxyhemoglobin dissociation curve, impairing tissue oxygen delivery. Additional risks include further decrease in cardiac output, coagulopathies, and, potentially, cardiac arrest.\(^{1}\)

There are also marked decreases in circulating adrenocorticotropic hormone (ACTH), cortisol, triiodothyronine, thyroxine, insulin, and vasopressin.\(^{1,5,23,25–28,33,41–43}\) In a subset of brain-dead patients, residual hypothalamic/pituitary function may exist, due to collateral perfusion maintaining some blood flow to the hypothalamic/pituitary axis.\(^{32,42}\) Initiated by brain death, this dramatic decrease in hormone levels has far-reaching effects on metabolic and hemodynamic function. Low levels of circulating triiodothyronine (T-3) causes a change from aerobic to anaerobic metabolism and mitochondrial/cellular dysfunction.\(^{1,23,24,27,31,33,44}\) Resulting anaerobic metabolism generates elevated serum lactate and pyruvate levels and may further contribute to hemodynamic instability. Myocardial energy stores are also depleted.\(^{53}\) Decreased cortisol levels are associated with higher dose requirements for vasopressor and inotropic agents.\(^{53,42}\) Decreased insulin levels and insulin resistance following brain death and associated catecholamine surges cause hyperglycemia.\(^{1,5}\) Associated risks of hyperglycemia are multiple. One risk is osmotic diuresis, exacerbating volume loss through the kidneys. A second risk is potential islet-cell exhaustion in the pancreas.\(^{1,5}\) Decreased vasopressin
(ADH) levels are associated with diabetes insipidus, in which the kidney tubules lose ability to reabsorb water and copious amounts of urine are produced, causing dramatic volume losses and further compromising hemodynamic stability.1,5,26,31,33 This, in turn, can also lead to multiple electrolyte imbalances such as hypernatremia,5 hypokalemia, hypomagnesemia, hypocalcemia, and hypophosphatemia.1

**Management of Endocrine/Metabolic Instability**

Ultimately, the ICU and organ procurement personnel have to stabilize the multitude of physiologic changes following brain death and reverse harmful metabolic, pulmonary, cardiovascular, and endocrine derangements in the potential organ donor. The best results in controlling physiologic instability involve aggressive support for all metabolic and endocrine consequences of brain death.

Management of lost temperature regulation leading to hypothermia is accomplished ideally by prevention and frequent monitoring. Close and frequent monitoring of body temperature can identify emerging trends and provide opportunity for the team to institute measures, such as aggressive surface warming with heat lamps, warming blankets, warmed IV fluids, and heated humidified ventilator systems.1

Decreased levels of circulating T-3 are effectively treated by IV supplementation with T-3. An initial bolus dose of 4 mcg T-3 is administered followed by a T-3 infusion at 3 mcg/hr.8,9,27 This approach is effective in reversing myocardial compromise as indicated by lower vasopressor and inotropic dosing requirements, improved blood pressure, and decreased central venous pressure (CVP). Cardiac output is improved, which reverses hypoperfusion-related metabolic (lactic) acidosis. Tissue and organ perfusion is improved with conversion from anaerobic to aerobic metabolism.9,43

Hyperglycemia is treated by IV administration of insulin by infusion at least 1 unit/hr and may be titrated to a serum glucose level of 120 to 180 mg/dL.31 This prevents additional fluid loss due to osmotic diuresis. Decreased serum cortisol levels are associated with impaired ability of the brain-dead patient to respond to physiologic stress. It is also well-established that the intense mobilization of inflammatory mediators following brain death contributes to up-regulation of cytokines in organs to be transplanted, risking additional immune response to the transplanted organs in the organ recipient.1,8,9,43 In practice, methylprednisolone is recommended in dosages of 15 mg/kg and may be repeated at intervals of 24 hours.1,8,9,43 High-dose steroid therapy is also associated with improved oxygenation during ICU management, as well as improved lung function and survival in organ recipients due to attenuation of recipient immune response and attenuation of proinflammatory cytokines released following brain death.8,9,43

Diabetes insipidus (DI) is a consequence of decline in circulating ADH due to loss of function within the hypothalamic/hypophyseal tract, ultimately dramatically limiting posterior pituitary function and ADH production.42 This consequence of brain death results in dramatic increases in urine output and may be managed 2 ways. One way is by replacing volume losses from excessive urine output, which will correct circulating fluid volume deficit.1,2,5 This is most effective when done concurrently with hormonal replacement therapy. With this approach, one option is desmopressin (DDAVP).1,5 A loading dose of 8 ng/kg may be administered followed by an infusion of 4 ng/kg/hour with titration as indicated for controlling urine output.1,5 Desmopressin also has only very minimal vasopressor activity and a longer half-life than vasopressin.1,5,43

A second option for hormonal replacement therapy is administration of arginine vasopressin.1,2,5,43 This agent has vasoconstrictive properties and may effectively lower vasopressor requirements in the donor. It may augment the clinical effects of concurrent treatment with catecholamines.40 Dosing begins with bolus administration of arginine vasopressin 1 unit, followed by an infusion of the agent at doses ranging from 0.5 to 4.0 units/hr and titrated to clinical effect.8,9,27,32 Given the pronounced vasodilated states encountered following brain death, vasopressin may be very effective for cardiovascular support. If Swan-Ganz monitoring is utilized, arginine vasopressin is titrated to a systemic vascular resistance of 800 to 1200 dynes/sec-cm.9,32
Coagulopathy in the Organ Donor

Coagulation abnormalities in the organ donor are common. One cause is release of thromboplastin, fibrinogen, and tissue plasminogen from injured and necrotic brain tissue.1,2,5,33 This results ultimately in a consumptive coagulopathy where circulating clotting factors are rapidly utilized.32 A second, concurrent cause of coagulopathy in the organ donor is dilution of platelets and circulating clotting factors with large volumes of colloid and crystalloid used during fluid resuscitation.1,5 Hypothermia, often seen in the organ donor may also contribute to coagulopathy, due to its effects on platelet aggregation, clotting times, and increased risk of disseminated intravascular coagulation.2 Aggressive management of coagulopathies encountered in the organ donor consists of administration of cryoprecipitate,1 fresh frozen plasma, and pooled platelets.1,5,33

Nutrition Issues

Due to catastrophic physiologic instability in the organ donor, basal metabolic rate after resuscitation may be dramatically elevated owing to profound mobilization of the stress response. Liver glycogen stores are also depleted within 12 hours following brain death. This is further complicated by the fact that brain death may potentially occur many hours prior to formal declaration of brain death. One direction in research is potentially providing nutrition to organ donors in an attempt to maintain end-organ function, restore liver glycogen stores, and potentially optimize graft function following transplantation.1 With intact function of the gastrointestinal (GI) tract, enteral feedings may be appropriate and present less risk of infection than that associated with parental nutrition.

Specialized Issues: Movements in Brain Death

Apparent movements in the brain-dead patient may take 1 of 2 general forms. The first type is generated by complex spinal reflexes and may take the form of complex movements following stimulation.45 These movements may include adduction of the arms with flexion of the elbows. They may resemble the brain-dead patient attempting to grasp the airway. These movements may possibly be concurrent with body flexion (Lazarus sign).5,21 Other movements observed include shivering, piloerection (gooseflesh), and extensor movements of the upper extremities.21 A small number of patients in one case series raised all extremities off the bed in response to passive neck flexion. In these patients, evoked potential testing showed residual function in the cervical spinal cord with no function in the brain or brainstem.21 A wide variety of movements in the brain-dead patient may be seen, including stepping motions, persistent Babinski reflexes, and tendon and abdominal reflexes. In all cases cited, these movements were consistent with spinal cord-generated reflexes and did not preclude a diagnosis of brain death.5,21,45 If unprepared, nursing and medical staff may be concerned about the brain-death diagnosis. If witnessed by family members, movements may be cause for concern if organ donation is under consideration.5,21 Education for staff and especially family members of potential organ donors is clearly indicated in an effort to allay concerns regarding brain death determination and organ donation.5,21,45 As indicated, if doubt exists about a brain-death diagnosis, confirmatory testing should be performed.5,21

The second type of apparent movement in the brain-dead patient occurs with ventilator management in which the brain-dead patient appears to trigger a ventilator breath. During controlled ventilation, a variable such as either flow or airway pressure triggering may be utilized. Pressure triggering of ventilation is patient-initiated when the patient generates a negative pressure within the airway, typically <2 cm H2O.46 Flow triggering is when a baseline flow is maintained and when a threshold is reached with patient effort, volume is delivered from the ventilator.46 In a patient who initiates a ventilator breath, a flow or airway pressure threshold must be reached in order to initiate an assisted breath from a mechanical ventilator.47,48 Potential problems occur when the sensitivity to trigger a controlled ventilation is too sensitive so that spurious ventilation may occur46 and be initiated by factors other than intrinsic respiratory drive.
Intrathoracic pressure dynamics and airway pressures may change in phase with the cardiac cycle. Even in patients receiving neuromuscular blocking agents following cardiothoracic surgery, this pressure change in phase with cardiac oscillation has been noted to initiate a ventilator-assisted breath. Variables contributing to these spurious ventilator-assisted breaths independent of inspiratory efforts include higher cardiac output and filling pressures, as well as a more dynamic cardiovascular system. In addition, patients who have lower systemic vascular resistance may be more likely to experience autotriggering during controlled ventilation. In one study, it was found that cardiogenic oscillations produced an airway pressure change of 1.37 ± 0.28 cm H₂O. This becomes significant in ventilator management because the pressure sensitivity during ventilator management may be set at a threshold of 0.5 to 1.5 cm H₂O. In these cases, cardiac motion may be sufficient to trigger an assisted ventilator breath. Physiologically, as the heart ejects blood during systole intrathoracic volume decreases, creating a negative intrathoracic pressure. Lung tissue, being compliant, may respond and fill the space created, generating a slight negative intrathoracic pressure and, potentially, airway pressure. In addition, during systole, blood leaves the thorax more rapidly than blood returns via the venous system. As such, there is a net volume loss from the chest. This may be an additional factor producing a net decrease in airway pressure. Depending on trigger thresholds set on the ventilator, this may be sufficient to trigger an assisted ventilation. Potential issues with spurious, autotriggering of ventilation are multiple: increased minute ventilation, decreased expiratory time, increased plateau pressures, and auto-PEEP as well as potential delay in brain death determination. This may increase risk of volutrauma and barotrauma, as well as hemodynamic compromise from altered intrathoracic pressure dynamics.

Intrathoracic and airway pressure dynamics may change during the cardiac cycle and be sufficient to trigger an assisted ventilation. Clinicians must be aware of this possibility while managing the brain-dead patient awaiting organ donation. One of the hallmarks of the clinical evaluation of brain death is apnea. Apparent assisted ventilation may be interpreted as inconsistent with brain death. It is worthwhile noting that physiological changes associated with increased risk of autotriggering cited previously are common in the brain-dead patient (dynamic cardiovascular system, higher cardiac output/stroke volume, and lower systemic vascular resistance). There exist multiple reports of apparent triggering of ventilation by the brain-dead patient. In all cases, brain death was confirmed by additional clinical evaluation and/or neurodiagnostic testing as indicated. Seeing apparent patient-triggered breaths from a brain-dead individual may be misinterpreted as patient effort rather than cardiogenic oscillation. Critical care clinicians should be aware of the physiologic basis for these spurious triggered breaths for two reasons. First, to avoid delay in diagnosis of brain death with possible negative impact on number or quality of organs transplanted. Second, as appropriate, to educate the patient’s families should this occur and avoid undue stress during an already difficult time.

To potentially avoid spurious ventilator triggering in the brain-dead patient, the pressure sensitivity may be set at 2 cm H₂O or higher. If flow triggering is utilized, the sensitivity may be set to 3 to 5 L/min. A third option is assessment of the graphics display of airway pressure or flow. Pressure or flow oscillations in phase with the cardiac cycle may indicate potential for cardiac triggering of the ventilator. Additionally, direct assessment of the patient’s chest should be done. Chest wall or precordial movement in phase with the cardiac cycle may indicate a patient is at risk for autotriggering. Ventilator triggering consequent to cardiogenic oscillation being mistaken for intrinsic inspiratory effort can occur even to experienced clinicians. It is appropriate to closely examine any potentially brain-dead patient, such as one who has lost cough, gag, and corneal reflexes and who appears to be triggering ventilator breaths for the possibility of spurious triggering related to cardiogenic oscillation. Preventing this phenomenon from clouding or delaying a determination of brain death may be easily done by increasing awareness of the possibility through clinical examination and education of clinicians. This is important so that families can have closure, and it
expedites brain death determination and possible organ donation. The importance of this cannot be overstated, given implications for the family, donor management, and potential recipients who may benefit. Assessing for cardiogenic ventilator triggering should also be done in deeply sedated or pharmacologically paralyzed patients. In these cases, ventilator triggering may not require upward drug titration, but they will need close assessment and adjustment of ventilator trigger sensitivities as appropriate. An example of the cardiac cycle producing significant deflection in the airway pressure waveform is found in Figure 10.

Role of the Advanced Practice Nurse

The roles and contributions of the advanced practice nurse (APN) in management of physiologic instability related to brain death are multiple. Role of the APN may begin with making unit rounds and identifying patients who may be at high risk of brainstem herniation from progression of neurologic injury. Prior to evolution to brain death, the APN may expedite aggressive care to control ICP elevations, and coordinate and facilitate additional neurodiagnostic studies as indicated. The APN also may use such patient situations as “teaching moments” as appropriate to illustrate clinical and physical assessment findings associated with dramatic ICP elevations. In addition, the APN may use these situations to illustrate aggressive measures utilized in controlling potentially lethal ICP elevations. Measures, such as aggressive, short-term hyperventilation, drug-induced coma, and ventricular drainage may be illustrated as modulating the relative volume of one or more components contained within the skull. The APN may also rapidly help determine relative effectiveness of these therapies. The APN is also well-positioned to educate bedside clinicians and nursing assistants regarding optimal positioning, such as degree of head elevation and maintenance of neutral head and neck positioning, to maximize venous return and facilitate ICP control prior to progression to brain death. Other aspects of care that may be addressed include eye care to prevent corneal lesions and dehydration. This may be accomplished by saline moistened pads or irrigations. Given the emergent nature of evolving patient care situations such as these, the APN is well suited to look at the “larger picture,” and to assess needs for resource utilization and coordinate delivery of care and resources with the goal of optimal patient outcome. The APN in this setting may facilitate communication between and among bedside clinicians, specialty care and other physician providers, and, as indicated, patient family members. In managing the

Figure 10. Example of the cardiac cycle producing significant deflection in the airway pressure waveform. The pressure deflections produced by cardiogenic oscillation in these images range between 1.5 to 2.5 mm Hg. In a ventilator with overly sensitive trigger settings, this may be sufficient to trigger a controlled ventilation. This may occur in patients receiving deep sedation/analgesia or neuromuscular blockade. It also may occur in the brain-dead patient.
patient with severe neurologic injury prior to evolution to brain death, the APN has multiple roles including expert clinician, educator, and system-wide roles in coordinating delivery of resources to a critically ill patient in an emergent, evolving situation.

Given the high potential of severe brain injury and refractory ICP elevations to progress to brainstem herniation and brain death, the APN is well-positioned as an expert clinician to recognize signs of impending brain death. These signs include dramatic vital sign changes and rapid progression of the neurological examination to loss of brainstem reflexes. During these moments, a tremendous physiological instability affects virtually all body systems. The APN can be proactive in insertion of additional large-bore IV accesses for the patient, as well as obtaining involvement of all appropriate physician healthcare team members. In addition, consultation with the appropriate organ procurement agency can be initiated at an early stage as indicated. Moreover, with the well-documented physiological instability of the brain-dead patient, the APN can facilitate neurological examinations and/or confirmatory testing as appropriate to determine a diagnosis of brain death. Astute cardiopulmonary assessment by the APN may also identify cardiogenic triggering of controlled ventilation and differentiate it from intrinsic respiratory drive, thus facilitating brain death determination. This is potentially vital for a number of reasons. One reason is to provide closure to a patient’s family and determine the outcome of a severe neurological injury in a timely manner. A second reason is to optimally manage the physiological changes seen during and following brain death, many of which are inconsistent with aggressive care to preserve neurological function. Third, more rapid determination of brain death and appropriate involvement of organ procurement personnel can reduce the time interval between occurrence of brain death and organ transplantation. Longer management times have been associated with adverse outcomes in transplant recipients.54

The multiple roles in which the APN can effectively facilitate within a dynamic and evolving situation, such as organ donor management, also illustrate the value of critical thinking in decision making. In addition, the APN can, in real time, model and teach critical thinking skills within “teaching moments” as they occur.

**Bedside Clinicians and the Brain-dead Patient**

It is worth noting that the consequences of brain death and management of the organ donor are not limited to those associated with the physiologic consequences of brain death. In many cases, brain death and the option of organ donation are the end result of a process that may have begun with the initial brain injury that may have been traumatic, ischemic, or hemorrhagic in origin. During this time of aggressive curative care, the team members may develop rapport with patient family members and be directing all of their efforts toward recovery of the patient and ICU discharge. When patients progress to brain death, bedside clinicians experience change as well.55 Feelings experienced by critical care nurses have been reported as sadness and hurting for the family, as well as a sense of confusion regarding how the body should be treated.53 Support for critical care nursing colleagues is important due to the nature of ICU care, exposure to family distress, and patient suffering.56–58 Stress may also arise from clinicians avoiding or repressing feelings of loss.59 Stress experienced during these situations also arises from inadequate resources56 and the need to rapidly change focus from aggressive care undertaken to preserve brain tissue to another type of aggressive care meant solely to preserve organs for transplant.55,60 A significant change occurs when the focus shifts from the “person” to the potentially transplantable organs.55 The APN role may be effective in this situation in providing support to nursing colleagues and offering opportunities to “debrief” regarding feelings experienced during these situations. The APN may also be instrumental in providing timely support with families, as appropriate.

**Family Considerations and Brain Death**

Consequences of brain death are not limited to physiological changes within the
brain-dead patient or stressors experienced by bedside clinicians in dealing with an emergent and rapidly evolving situation. The consequences of brain death, by their very nature, also affect the patient’s family. During this time, a patient’s family is exposed to a multitude of stressors. These include seeing a loved one, who may have been at home and interactive the previous day and currently is nearly hidden underneath a maze of tubes and monitoring devices. Stress also arises from having to address the myriad of new personnel and healthcare team members in attendance. Early visiting with the patient and early and effective realistic communication with the family about prognosis and consistency in approach during ICU management are important interventions that assist the family in coming to terms with potentially catastrophic injury. In addition, having to interpret and assimilate a multitude of new terms and make many decisions that may not have been anticipated previously can be overwhelming to families. Such situations provoke anxiety, even before a determination of brain death has been made. Once a brain death determination has been made or is imminent, the patient’s family may experience confusion because they may only associate death with no heartbeat and no respirations. Having their brain dead family member in the ICU will mean having all these functions supported artificially. Family members may be more vulnerable because death occurs in an environment with potential sensory overload, and the family may have difficulty differentiating brain death from a coma state.

Under these circumstances, families need utmost support and communication from healthcare team members. Before proceeding with any discussions regarding end-of-life-issues or organ donation, families must be assessed very carefully due to the tremendous stress they are experiencing. In the critical care setting in the midst of discussions regarding brain death and organ donation, family members are suffering more than the patient. Also in this setting, these may very well be the most difficult decisions they’ve ever had to make. A recent study identified that more than two thirds of visiting family members experienced symptoms of anxiety or depression. Given the importance of informed consent in healthcare decisions, families should be assessed carefully regarding decision-making capacity. Effective interventions by the healthcare team at this time may include effective communication and attempting to anticipate family needs for information and resources. Also, taking additional time to ensure that the family understands that brain death means the patient is dead; some individuals interpret “brain dead” as different from “dead.” When the patient, after the diagnosis of brain death was confirmed, the rate of consent for organ donation increased. Allowing more time for family members to speak and ask questions and less time spent talking by healthcare providers during a family conference on prognosis and brain death is associated with better family satisfaction. Respect, compassion, empathy, understanding, and effective communication have been identified as enhancing family satisfaction during end-of-life situations. Decoupling the discussion of brain death from any discussion of organ donation is also key and is associated with increased consent rates for organ donation. This approach may also facilitate ventilation of feelings for family members. Ultimately in many cases, the family of the brain-dead organ donor needs a great deal of support, attention, and caring during this period in which they may start their grieving process.

In virtually every successful instance of organ donation, effective nursing for the patient and their family is the foundation. Nursing is the most effective link among the multiple healthcare providers involved in managing the brain-dead patient, family members, and the organ procurement coordinator. Given the central role of nursing, the role of the APN is critical as well. The APN may effectively educate, mentor, and model behaviors and facilitate communication among family members as decisions are being made. Moreover, the APN role is well suited to establish an effective relationship with the family and to serve as liaison between family and other team members, as well as be a consistent “face” providing information and support. The APN role in education for bedside clinicians is key in that additional barriers to nursing involvement in organ donation can be removed. Comfort on the part of the nurse participating in the process is
important. If a family perceives uncertainty from nursing or other team members, they may be hesitant about a diagnosis of brain death and organ donation.70

Compassionate, caring, and empathetic communication with families; involvement of clergy; and aggressive clinical management all are integral to successful organ donation. For some families, cultural and psychosocial factors may still exist that provide barriers to organ donation. A comprehensive discussion of all these factors is beyond the scope of this article, but for additional information, the reader is referred to any of the excellent references on this subject.71–75

Ethical and Communication Issues/Advanced Directives

The APN may be pivotal in coordinating interdisciplinary care, in particular, a coordinated approach to end-of-life issues such as brain death. Managing the dying patient and family issues is clearly best done by an interdisciplinary approach in which the nurse is integral.76 Few other situations are more challenging than those encountered in clinical management of the organ donor. The clinical management of the organ donor does not occur in isolation but within a much larger context of complex family dynamics and other end-of-life issues. The challenging issues raised in managing the potential organ donor are multiple. One issue is ascertaining whether a patient has an advanced directive and, if so, ensuring to it that it is honored. A second issue is that of giving bad news. It is increasingly well documented that families rate communication on the part of healthcare team members as key to their satisfaction with how end-of-life issues are resolved. A third issue is involvement of institutional ethical consultation, which is particularly important if the potential donor has no family members that can be contacted.

The role of APN in pursuing an advanced directive may be pivotal. Many patients die with their advanced directives either unknown or not honored.77 In the presence of an advanced directive indicating a preference for organ donation, such as indications on a state driver’s license, there are opportunities for APN involvement. One way is to advocate for the patients wishes and to coordinate this message with all team members. One approach that may be utilized with a potentially grieving family is putting it in terms of “the patient has already told us what his wishes are.” In the absence of another type of written directive, the key ethical principle here is that of autonomy, where the outcome is a reflection of the patient’s wishes.78–81 This can make the donation process easier because ultimately the patient has made their decision. The family does not need to make a decision, and the APN as well as other team members may put it in terms to them of not having the burden to do so.78,82

The role of APN in giving bad news and facilitating end-of-life discussions may also be pivotal. Discussions should begin as early in the ICU course as feasible, occurring first between and among all team members to ensure a consistent message is being given to the patient’s family. Components of discussions in which bad news is given to a family should contain multiple components. One is assessing the level of understanding the family possesses about the situation. A second component is informing the family of the topic of discussion and who will be present. A third component is introducing all team members involved. A fourth component is honest and open discussion about prognosis without confusing the family with excessive technical detail or medical terminology while demonstrating caring on the part of the team. A fifth component is active listening and reflection to encourage questions and to facilitate families expressing strong emotions.77,79,83–85

Nurses, particularly advanced practitioners, should be involved actively on institutional ethics committees. In having close proximity to the patient, other team members, and the family, as appropriate, the APN is well-positioned to facilitate earlier ethical consultation as indicated for end-of-life issues including organ donation. For a more comprehensive discussion of ethical and communication issues encountered during end-of-life care the reader is referred to any of the excellent references available on the subject.77,79–86
Case Study

MG is a 71-year-old woman initially presented to the emergency department following transport by a local emergency medical services (EMS) unit. Her family had reported that she had gone to bed earlier than usual the previous evening and was difficult to arouse the following morning at approximately 10:00 AM. At this point, the EMS system was activated and she was transported to an acute care facility. Her past medical history was significant for chronic obstructive pulmonary disease (COPD) and insulin-dependent diabetes mellitus.

Upon admission, MG’s Glasgow Coma Score (GCS) was 8. She opened her eyes to painful stimulation (eye-opening: 2); she was localizing to painful stimulation such as peripheral venipuncture (motor response: 4); and she was only producing incomprehensible sounds in response to stimulation (verbal: 2). With decreased level of consciousness (LOC) and significant risk of further decline in neurological status, irregular rate, depth and pattern of respirations, MG was tracheally intubated for airway protection and to control lung ventilation. She received sodium thiopental immediately prior to intubation for rapid sequence induction (RSI). Her cardiopulmonary status was stabilized, including treatment of hypotension following barbiturate administration and alterations in intrathoracic pressure from controlled ventilation. This was accomplished by administration of 1 L NSS over 30 minutes and titration of inspiratory flow rates/tidal volume to minimize auto-PEEP and plateau pressures. Maintenance of systemic blood pressure also preserved cerebral perfusion. After stabilization, MG was transported to the radiology department for a stat computed tomography (CT) of the head and brain. Normal head CT is shown in Figure 2. MG’s initial head CT was positive for ischemic changes within the left cerebral hemisphere, including early onset of cerebral edema and beginning compression of the ventricular system and is shown in Figure 11.

Immediately following arrival in the ICU, she received 70 gm mannitol IV bolus (1 gm/kg based on an estimated weight of 70 kg). In addition, she was hyperventilated in the short term for a PaCO₂ of 30 to 32 mm Hg. Pending bloodwork included Pt/Ptt/INR, which were within normal limits. Since aggressive care was still being pursued, informed consent was obtained from her son and an intraparenchymal sensor was placed in her right frontal area for ICP monitoring. Initial ICP readings of 30 to 32 mm Hg indicated intracranial hypertension. Elevation in the P-2 ICP waveform component indicated poor intracranial compliance. With aggressive management, ICP stabilized between 17–20 mm Hg. Mean arterial pressure (MAP) was 90, giving MG a cerebral perfusion pressure (CPP) approximately 70 mm Hg. During and after endotracheal suctioning, ICP surges were noted with pressure elevations to 40 to 44 mm Hg that required 20 to 30 minutes to return to baseline. In addition to ventilator dys-synchrony, poor tolerance of endotracheal suctioning contributed to further ICP elevations that increased risk of further injury and herniation. To control ventilation and ICP elevations associated with airway suctioning, aggressive sedation/analgesia was administered using a combination technique of short-acting agents: fentanyl and midazolam for aggressive analgesia and sedation. These measures were effective for controlling ventilator synchrony including ICP elevations associated with airway suctioning. These agents were titrated to achieve desired clinical endpoints and maintain ability to assess neurological status.

Following stabilization, rapport was developed with her family including regular updates on her condition. It was explained that given her age, her condition was considered very critical. MG remained hemodynamically stable, with a stable neurological examination for the next 24 hours. During ICU day 2, 36 hours following admission, she had a pronounced decline in her neurological examination with markedly decreased protective reflexes (cough, gag, and corneal). This was accompanied by ICP elevations to 30 to 35 mm Hg with even minimal stimulation, less frequent assisting of ventilation, and transient tachycardia and hypertension. When her cardiopulmonary status was stabilized, she was transported to the radiology department for a follow-up stat head CT scan. The second head CT study showed markedly increased cerebral edema with dramatic midline shift and near total obliteration.
of the ventricular system and is shown in Figure 12.

Within one hour following her return to the ICU, MG’s blood pressure and heart rate became markedly unstable; HR was 100–230/min, and MAP was 115–135 mm Hg. Graphics illustrating trends in heart rate, ICP, and MAP are found in Figure 13. ICP became markedly elevated (90–95 mm Hg) and was refractory to therapy. After 3 hours, her protective (brain stem) reflexes were lost, no spontaneous movement was evident, and her systemic blood pressure and heart rate declined significantly, requiring hemodynamic support. Sedative and analgesic agents were discontinued with no change in her neurological examination or responsiveness. Neurology consultation was obtained.
immediately to begin determination of brain death.

At this stage, family was notified of the changes and was asked to come to the hospital for a conference. Upon arrival, they sat with the patient and all activities were explained. Opportunity was available for them to ask questions and the meeting was continued in a conference room. It was explained that MG’s condition significantly worsened and no hope of recovery was possible. The family asked questions about her care and was as comfortable as circumstances allowed. The APN was effective as a liaison between the family and other healthcare providers and initiated contact with the local organ procurement agency to assess suitability of the patient as a potential organ donor.

Figure 12. The case study’s second head computed tomography study showing markedly increased cerebral edema with dramatic midline shift and near total obliteration of the ventricular system.
Figure 13. Heart rate/mean arterial pressure (MAP) and MAP/intracranial pressure (ICP) over time. A, Graphic illustrating trends in heart rate and MAP in response to catastrophic ICP elevation. Initial hemodynamic consequences of brain death related to catecholamine surges are depicted; B, Graphic illustrating catastrophic ICP elevation and lethal cerebral perfusion pressure (CPP) during brain stem herniation. CPP range is between 10 to 32 mm Hg during this time frame.

The initial clinical neurological examination was consistent with no activity in the brain or brain stem. Following institutional protocol, a second clinical neurological examination was completed after an interval of 12 hours. In addition to the clinical evaluation, an apnea test was performed. Following normalization of PaCO₂ to 38 mm Hg, the apnea test was completed, and at the 10-minute endpoint, MG’s PaCO₂ was 68 mm Hg, indicative of no intrinsic respiratory drive. There was no clinical evidence of respiratory drive on visual assessment, and the patient received appropriate oxygen delivery through the artificial airway as well as hemodynamic support throughout. These findings were shared separately with the organ procurement coordinator (OPC), other team members, and the patient’s family. Continued hemodynamic instability and declining urine output in the setting of brain death was a concern. Given fluid deficits associated with insensible fluid losses and osmotic diuresis as well as a significant relative hypovolemia related to the pronounced vasodilated state associated with brain death, aggressive volume resuscitation was initiated. Over 2 hours, MG received 5 liters of crystalloid for volume support with recovery of urine output. Catecholamine support of blood pressure and cardiac output was provided with dopamine at 12 to 18 mcg/kg/min. Dopamine was effective to support blood pressure as well as heart rate due to denervation of the heart at this stage. One somewhat surprising development at this stage was apparent ventilator triggering by the patient. The patient’s PaCO₂ was normalized with the following
ventilator settings: assist/control at 12/min; tidal volume at 550 mL; PEEP at 5 cm H₂O and FiO₂ of 0.5. At intervals, MG’s respiratory rate was 14 to 16/min. Further assessment was done and revealed multiple findings. One finding was that after short-term disconnection from ventilation (while receiving 100% oxygen), inspiratory efforts were absent on close visual inspection as noted by multiple clinicians. A second finding was a hyperdynamic precordium with each cardiac cycle. A third finding was elimination of apparent patient triggering with increase of the sensitivity threshold to 2 cm H₂O. These findings were strongly suggestive of cardiogenic triggering of controlled ventilation. To confirm this assessment, close examination of the airway pressure waveform was done. The airway pressure was transduced to the bedside monitor and printed 2-channel tracings were obtained. Airway pressure and ECG tracings were closely compared and indicated deflections in the airway pressure waveform in phase with the cardiac cycle only. This, in addition to thorough clinical evaluation, confirmed that additional ventilator breaths were triggered by the cardiac cycle. Thus, any confusion or question regarding brain death determination was eliminated. It was important to quickly assess and establish this in order to avoid confusion or concern on the part of MG’s family or other clinicians as to the reliability of brain death determination. Pressure tracings illustrating deflections in airway pressure in direct correlation with the cardiac cycle can be found in Figure 14.

Pastoral care was arranged and was immediately available for which the family was grateful. At this stage, MG’s family was notified of the findings and ample time was allowed to answer all questions and encourage ventilation of feelings related to the patient’s death. Pastoral care was particularly instrumental in this setting. Following the pronouncement of death and allowing ventilation of feelings as well as answering all questions, the organ procurement coordinator then spoke at length with MG’s family. The family ultimately gave informed consent for organ donation and viewed it as an opportunity to give a gift. Given the patient’s age and past medical history (PMH), she was not an optimal candidate for heart and lung donation. As such, kidney and liver function and hemodynamic support were priorities. Moist saline pads were utilized to prevent corneal drying and ulceration. Aggressive volume resuscitation was effective for support of circulating blood volume and urine output was appropriately responsive. A graphic illustrating fluid management and response of urine output is illustrated in Figure 15A.

Additional concerns related to hemodynamic support included high catecholamine doses required to maintain blood pressure and cardiac output. In addition, profound metabolic changes following brain death risked further compromising organ function. The OPC recommended hormonal resuscitation. To that end, T-3, arginine vasopressin, methylprednisolone, and insulin were administered intravenously. Hormonal resuscitation protocol is shown in Table 1. Within hours, dopamine dosing requirements were markedly reduced, with improved stability of blood pressure and overall hemodynamic status. A graphic illustrating effectiveness of hormonal resuscitation protocol is shown in Figure 15B.

During that evening, MG was transported to the operating room (OR) for organ harvesting. Ultimately, what can only be described as great loss for a family is tempered somewhat because the experience of organ donation was handled in a sensitive, kind, and very professional manner by the team. Appropriate attention to the interpersonal and the spiritual needs of the family was a priority. Aggressive management of ICP elevations was pursued as appropriate until MG experienced brain and brainstem death. Rapid recognition of significant changes in the neurological assessment and rapid coordination of diagnostic testing and formal determination of brain death facilitated closure for the family and minimized duration of hemodynamic instability associated with brain death. This ultimately served both the family and the organ recipient well.

□ Summary

Among the most challenging patients in critical care practice are those with significant brain injury who ultimately progress to brain death. Requisite understanding to most
Figure 14. Pressure tracings illustrating deflections in airway pressure and in direct correlation with the cardiac cycle. In top tracing, the only deflections in airway pressure are those caused by cardiogenic oscillation. No indication of intrinsic respiratory drive is evident. In the bottom two strips, cardiogenic oscillation is sufficient to trigger ventilator breaths. On the pressure scale used in these tracings, the pressure deflection generated by the cardiac cycle ranges between 1 to 2.5 mm Hg, sufficient to trigger a controlled ventilation depending on ventilator sensitivity.
effectively manage these patients is not limited to intracranial physiology, but includes virtually every body system. Following brain death, a multitude of dramatic physiological changes occurs throughout the body. For successful donation, these changes must be recognized and quickly treated. The most effective clinical management of the organ donor is not limited to aggressive cardiopulmonary support. Given the multiple changes at the cellular level, including compromise of mitochondrial function and anaerobic metabolism, it may also be helpful to think of optimal organ donor management as entailing aggressive metabolic resuscitation as well as cardiopulmonary support.

One must consider the devastating effect death of a loved one has on family members. In addition, there may be caregiver stress affecting bedside clinicians repeatedly exposed to death and dying. Working together, the APN, bedside clinicians, and other team members can support and care for each other when dealing with their own stress and sense of loss in the clinical setting. As such, the bedside clinician, the APN, and all other team members work in concert to effectively manage all aspects of care for both the patient and his or her family. The APN and bedside clinicians benefit the patient and family by application of critical thinking skills, facilitating optimal decision making and improving
TABLE 1  □  Hormonal Resuscitation Protocol for Aggressive Hemodynamic and Metabolic Support of Organ Donor8,9,23,32,43

1. Triiodothyronine (T-3): Initial bolus done-4 mcg
   a. Triiodothyronine (T-3): Infusion at 3 mcg per hr
2. Arginine vasopressin: 1 unit IV bolus
   B. Arginine vasopressin: Infusion at 0.5 to 4 units per hr. If invasive hemodynamic monitoring available, titrate to SVR 800–1200.
3. Methylprednisolone: 15 mg/kg IV bolus (may repeat every 24 hours)
4. Insulin infusion as indicated: Infusion dosing 1 unit per hr and titrate to serum glucose level: 120 to 180 mg/dL

outcomes for colleagues, families, and ultimately organ transplant recipients.

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