Supplementary Online Content

Greer DM, Shemie SD, Lewis A, et al. Determination of brain death/death by neurologic criteria: The World Brain Death Project. *JAMA*. doi:10.1001/jama.2020.11586

Supplement 11. Somatic Support After Brain Death/Death by Neurologic Criteria for Organ Donation and Other Special Circumstances

This supplementary material has been provided by the authors to give readers additional information about their work.

Somatic Support After Brain Death/Death by Neurologic Criteria for Organ Donation and Other Special Circumstances

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Key words: brain death, somatic support, organ donation, pregnancy

Abstract

Introduction Somatic support may be continued after brain death/death by neurologic criteria (BD/DNC) if 1) organ donation is planned, 2) the decedent is pregnant, or 3) the family objects to the use of neurologic criteria to declare death, and the hospital agrees to continue support for legal or social reasons.

Methods We conducted a review of the literature and formulated recommendations with an expert panel on prevention and management of systemic complications after BD/DNC.

Results and Conclusions Provision of somatic support after brain death can be medically complex, but it is feasible to maintain systemic organ function for months or, rarely, years after BD/DNC. There is debate over the optimal strategies to provide somatic support after BD/DNC. We provide recommendations and suggestions for management strategies to avoid and respond to systemic complications after BD/DNC.

Introduction

After declaration of brain death/death by neurologic criteria (BD/DNC), somatic support is discontinued unless 1) organ donation is planned, 2) the decedent is pregnant and the decision is made to continue support for the sake of the fetus, or 3) the family requests continuation of somatic support after BD/DNC due to religious or moral beliefs or other concerns about the use of neurologic criteria to declare death, and the hospital complies with this request for legal or social reasons.[1-3] In order to decrease practice variability, we sought to establish international consensus on somatic support after brain death amongst experts on this topic.

Methods

Authors conducted the initial literature searches of the Cochrane, Embase and MEDLINE databases for the time period between January 1, 1992 and July 2017. Subsequent searches were performed to capture relevant articles between July 2017 and April 2020. Because of the significant lack of data from randomized controlled trials or large studies, GRADE evaluation of the evidence was not performed. However, evidence was reviewed by a multidisciplinary group of clinicians (see supplementary material) and recommendations were generated according to the following criteria. Strong recommendations ("It is recommended that") were based on expert consensus that clinicians should follow the recommendation unless a clear and

compelling rationale for an alternative approach was present, and where actions could be adopted as policy. Even though most evidence in this area is limited and of low-quality, strong recommendations were made as a precautionary, conservative approach, to prevent premature or erroneous determinations of death (false positives). Conditional or weak recommendations ("It is suggested that") were generated when there were potentially different options and the best action may differ depending on circumstances, patients, resources or societal values, or where there is a need for further evidence or discussion among clinicians and stakeholders. In cases where there was insufficient evidence and the balance of benefits versus harms was neutral, no recommendations were made.

Organ Dysfunction After Brain Death

Provision of somatic support after BD/DNC requires substantial time and resources and is fraught with multiorgan complications due to an inflammatory storm, marked by increased cytokines and free radicals, and severe catecholamine derangements (a massive surge for 20-30 minutes immediately prior to and following BD/DNC, when the body is attempting to improve cerebral perfusion, followed quickly by exhaustion of catecholamine stores).[4-10] Complications seen after BD/DNC and their frequencies are listed in Table 1 and discussed extensively below. Instability often worsens with time, but there have been reports that aggressive medical management can lead to organ function stabilization and even improvement.[9, 11-20] For example, Casartelli et al. described recovery of ejection fraction and cardiac index in the 48 hours after BD/DNC in decedents who received insulin, methylprednisolone, vasopressin, and thyroid hormone.[20] Additionally, in a retrospective study of 12 brain dead decedents with a mean of 16 ± 8 hours between BD/DNC declaration and organ procurement (range 6-32 hours), Grigoras et al. found that there was a significant decrease ($p < 0.05$) in vasopressor requirements (75% to 0%), oxygenation disturbances (8% to 0%), renal dysfunction (75% to 17%), liver dysfunction (58% to 8%) and metabolic acidosis (75% to 8%).[19]

Although organ dysfunction and cardiopulmonary arrest ultimately occur after BD/DNC, provision of aggressive support can delay arrest by months or even years.[11-16, 21-24] In a 2010 systematic review of 30 brain dead pregnant women, somatic support was continued for the sake of the fetus and there was a delay between declaration of BD/DNC and cardiopulmonary arrest of 2-107 days.[14] Although the validity of the determinations of BD/DNC in a 1998 meta-analysis of 56 reports of delays longer than one week between BD/DNC and cardiopulmonary arrest has been questioned, this series showed an inverse relationship between age and the length of time between BD/DNC and cardiopulmonary arrest, with the longest reported delay being 14 years.[23, 25] However, a lengthy delay between BD/DNC and cardiopulmonary arrest is atypical: in a 1200 decedent series, 100% had cardiopulmonary arrest after two weeks; in a prospective study of 73 brain dead decedents, 97% had cardiopulmonary arrest by the end of one week; and in a 63 decedent series, 100% had cardiopulmonary arrest within nine days.[26]

Herein, we address the management strategies to avoid and respond to systemic complications after BD/DNC. The breadth of options that are available to living persons can be utilized when managing brain dead decedents, but when somatic support is provided after BD/DNC, it is important to consider the ethical and social implications of doing so. These are discussed in the chapter on Religion and Brain Death: Managing Requests to Forego a Brain Death Evaluation or Continue Somatic Support after Brain Death.

Table 1. Complications after BD/DNC

Complication	Frequency
Arrhythmias	25-65% [10, 15, 20, 27-30]
Coagulopathy	5-83% [27-29, 31-33]
Diabetes Insipidus	9-90% [4, 12, 27-29, 34]
Hyperglycemia	70% [4, 35-37]
Hypotension	65-97% [4, 27-29, 31, 32, 38, 39]
Hypothermia	41-100% [27, 28, 30, 40, 41]
Pulmonary edema	13-52% [7, 27, 29, 31, 42]

Cardiac Instability after BD/DNC

Cardiac arrhythmias occur in 25-65% of brain dead decedents due to atrial and ventricular conduction disturbances, subendocardial myocyte necrosis secondary to the catecholamine storm during herniation, hypovolemia or as a byproduct of inotrope administration.[10, 12, 15, 20, 27-30] Bradycardia is the most common arrhythmia after BD/DNC.[43]

Although bradyarrhythmias can be the terminal rhythm before cardiopulmonary arrest in decedents who are brain dead, ventricular fibrillation is the most common terminal rhythm in adult donors and asystole is the most common terminal rhythm in pediatric donors.[4, 5, 12, 27, 37, 43-45] Cardiopulmonary arrest has been reported to occur in 1-25% of decedents awaiting organ donation, but with aggressive management, the frequency is minimal.[4, 5, 27, 37, 44, 45] Management of cardiopulmonary arrest in brain dead organ donors varies: some recommend that cardiopulmonary resuscitation (CPR) be performed because if cardiac function is recovered, organs can still be procured; some note that chest compressions are not recommended, but defibrillation can be performed at the discretion of the clinician; some caution that performing CPR on a brain dead decedent can cause physical harm to their body and psychological harm to the healthcare team and family and recommend that informed consent for performance of CPR be obtained from families of consented organ donors; and some neither recommend nor discourage performance of CPR.[44, 46]

Perfusion Derangements in BD/DNC

Hypotension and circulatory shock develop in 65-97% of brain dead decedents due to a multitude of reasons including 1) loss of hypothalamic function; 2) loss of central vasomotor regulation of sympathetic tone leading to unopposed peripheral vasodilatory influences from local accumulation of carbon dioxide, hydrogen ions, and lactic acid; 3) decreased contractility due to cardiac dysfunction; 4) hypovolemia due to osmotic agents administered to treat elevated intracranial pressure before BD/DNC, diabetes insipidus, or traumatic blood loss; and 5) preexisting conditions leading to cardiogenic, hemorrhagic, distributive or obstructive shock.[4, 27-29, 31, 32, 38, 39]

Although there is agreement that hypotension should be treated aggressively with fluids before adding vasopressors due to concern that premature use of vasopressors in the setting of hypovolemia could lead

to circulatory deterioration, there is some debate as to whether crystalloids or colloids should be used first.[27, 32, 38, 47] In a study comparing the effects of administering colloids (500 mL of fresh frozen plasma, albumin, hydroxyethyl starch), crystalloids (one liter of lactated Ringer's or saline) and one unit of packed red blood cells, only colloids were found to have a significant effect on mean arterial pressure (increase from 77 ± 21 mmHg to 85 ± 24 mmHg, $p < 0.01$).[38] Additionally, some authors note concern that crystalloid administration is more likely to lead to pulmonary edema.[47] Others, however, worry that colloids, particularly hydroxyethyl starch, can lead to renal injury, coagulopathy or anaphylactic reactions.[36, 48, 49]

Vasoactive support is required by 80-90% of organ donors.[4, 36] However, the selection of agents is debated. While some authors recommend starting with dopamine then adding vasopressin if needed, others favor early use of vasopressin due to its catecholamine-sparing effects.[4, 27, 38, 42] On the other hand, some advocate for dopamine because it 1) has both inotropic and vasopressor effects, 2) can potentially improve renal and splanchnic perfusion, and 3) has immunomodulatory effects that favorably reduce the systemic inflammatory response to BD/DNC. It is important to note, though, that dopamine can suppress the function of the anterior pituitary hormones or cause dysrhythmias.[34, 40, 42, 47, 50, 51] The maximum dose of dopamine described in the literature ranges from 4-20 ug/kg/min, but some authors believe these limits are arbitrary, and go so far as proposing that it is impossible to define a maximum dose because of variability in residual level of vascular tone, vascular reactivity, and pharmacokinetics.[35, 36, 48, 52, 53] In a randomized controlled trial, Pennefather et al. found that in comparison to administration of a placebo, administration of vasopressin to brain dead decedents led to a significant increase in systolic blood pressure ($p < 0.01$) and a decrease in inotrope requirement ($p < 0.01$).[54] Some favor early administration of norepinephrine and phenylephrine, but it has been suggested that these agents can cause myocardial damage and severe vasoconstriction leading to end-organ ischemia. This view is not universally held though, and some authors believe BD/DNC itself, rather than vasopressors, should be blamed for these phenomena, and that these drugs can actually have favorable immunomodulatory effects.[40, 50, 51, 55]

In addition to fluid support and use of vasopressors and inotropes, other therapies are sometimes utilized to maintain hemodynamic stability. In some cases, extracorporeal membrane oxygenation (ECMO) or placement of an intra-aortic balloon pump (IABP) can be considered.[9, 28, 56, 57] Fu et al. found that use of ECMO in this population led to improved oxygenation and decreased vasoactive medication requirement.[57] Smith et al. also conducted research on use of direct peritoneal lavage as a non-pharmacologic local vasodilator to improve visceral microcirculatory flow in shock.[58]

Hypertension occurs frequently during the evolution of BD/DNC, but rarely after BD/DNC.[32] It is generally only noted briefly during the catecholamine surge that immediately follows BD/DNC, so while some recommend not treating it because it is transitory, others recommend using short-acting agents such as esmolol, labetalol, nicardipine, sodium nitroprusside or urapidil in anticipation of pending hypotension.[5, 9, 14, 27, 32, 40, 47, 59]

Thermoregulation after BD/DNC

Hypothalamic failure can lead to inability to thermoregulate, resulting in poikilothermia and wide variations in temperature after BD/DNC.[14, 27, 31, 40] Hypothermia (temperature < 35˚C) is far more common than hyperthermia after BD/DNC and is seen in 41-100% of brain dead decedents due to altered

sympathetic regulation and catecholamine levels.[27, 28, 30, 40, 41, 60] Hypothermia can lead to hypotension, impaired oxygen delivery, platelet dysfunction, coagulopathy and arrhythmias.

Respiratory Complications after BD/DNC

The most common etiology for pulmonary instability after BD/DNC is neurogenic pulmonary edema, which is seen in 13-52% of brain dead decedents. It can present within minutes of BD/DNC when autonomic storming leads to systemic vasoconstriction and increased vascular resistance, which causes decreased left ventricular output and increased retrograde pulmonary venous pressure resulting in increased hydrostatic pressure across pulmonary capillary membranes.[7, 27, 29, 31, 42] Neurogenic pulmonary edema usually resolves with time.[27] Although experimental models suggested naloxone might reverse hypoxemia due to neurogenic pulmonary edema after BD/DNC, a randomized trial comparing administration of naloxone to placebo showed naloxone did not improve oxygenation.[61] While large tidal volumes of 10-15ml/kg were previously targeted in brain dead decedents, most contemporary authors recommend use of lung protective ventilation strategies targeting tidal volumes of 6-8 ml/kg.[5, 17, 40, 53, 62]

Endocrine Complications after BD/DNC

Although the hypothalamic-hypophyseal axis may remain intact after BD/DNC due to perfusion from subsidiaries of the external carotid arteries, this is often not the case.[5, 48] The posterior pituitary gland is more frequently and more intensely affected than the anterior pituitary gland.[52] The extent to which hormonal derangements impact hemodynamics is unclear, and the need and dosing strategy for replacement therapy is debated.[4, 39, 42, 47]

Diabetes insipidus in brain dead decedents can lead to hemodynamic instability due to hypovolemia and hypernatremia. Occurrence varies markedly from 9-90% in adults and 38-41% in children.[4, 12, 27-29, 34] Diabetes insipidus management varies. Some authors recommend use of a vasopressin infusion in all instances where a brain dead decedent develops diabetes insipidus, but others believe this is only indicated in the setting of hypotension. While there are no studies in brain dead decedents, a meta-analysis of the effect of vasopressin in adult vasodilatory shock did demonstrate a reduction in norepinephrine dose.[63] Of those who support use of a vasopressin infusion, some describe doses ranging from 0.04-0.3 units/min, but others note concern that doses >0.04 units/min can cause coronary/renal/splanchnic vasoconstriction leading to ischemia. In lieu of a vasopressin infusion, some authors recommend use of desmopressin, but dosing recommendations are highly variable and range from 2mcg q12hrs to 4mcg q2hrs, and route of administration is also inconsistent (intravenous/intranasal/intramuscular).[4, 12, 27, 35, 44, 47, 50, 64]

Although thyroid hormone derangements can be seen in BD/DNC (60-81% of brain dead organ donors have low levels of triiodothyronine (T3), 15% have very low T3 levels and 29% have low levels of thyroxine (T4)), the issue of whether this is due to “sick euthyroid syndrome,” which does not warrant therapy, or true hypothyroidism, which can lead to hemodynamic instability, is contested.[14, 31, 39, 52] As a result, routine versus as-needed replacement therapy for refractory hypotension or cardiac instability is debated.[65] If replacement therapy is given, the object is to improve cardiac output, cellular energy production, and tissue perfusion.[40] Agent selection and route of administration vary. T4 can be administered intravenously, as a bolus or an infusion, or enterally.[40, 59] However, it has been argued that intravenous T3, the active form of thyroid hormone, may be more effective than T4 at treating hypothyroidism.[40] While some studies demonstrate that thyroid replacement therapy can improve

myocardial dysfunction and hemodynamic stability and decrease inotrope requirements, others have not demonstrated these effects, prompting some authors to argue that thyroid hormone replacement is unnecessary unless somatic support is being continued longer than 24-48 hours.[48, 55, 66] In a randomized controlled study, Goarin et al. found that, in comparison to placebo administration, administration of T3 did not improve hemodynamic status or myocardial function.[67] Despite that, use of thyroid replacement therapy in brain dead organ donors increased from 25% to 75% from 2001 to 2012.[68]

Hypocortisolism and adrenal insufficiency may develop after BD/DNC, leading to impaired ability to respond to stress, but adrenal function is reported to be normal or increased in this population.[5, 69] The clinical implications of these values are unsettled.[52] Administration of steroids (usually methylprednisolone (1-5 grams or 15-60mg/kg), but less commonly hydrocortisone) in an attempt to counteract the inflammatory cascade of cytokine release and improve hemodynamics and oxygenation has been described.[6, 40, 69] In a prospective observational study, Dhar et al. found that switching from high-dose steroids (15mg/kg of methylprednisolone) to low-dose steroids (300mg hydrocortisone) did not affect cardiopulmonary function.[70] In fact, in a review of 11 randomized controlled trials and 14 observational studies, Dupuis et al. found no evidence that steroid administration improved stability of brain dead decedents.[69] Similarly, a meta-analysis by D'Aragon et al. found that corticosteroid use did not impact the rate of vasopressor use (pooled RR of 0.96, 95% CI 0.89 to 1.05, moderate quality).[71] The benefit of steroids was best shown in a retrospective observational study looking at hydrocortisone, insulin and T3 administration to unstable brain dead decedents with elevated dopamine, dobutamine, or noradrenaline dependency. A significant increase in mean systolic blood pressure (106 ± 24 to 128 ± 26mmHg, p = 0.032) from the time of BD/DNC determination to the time of organ retrieval was seen.[72]

Hypo- or hyperglycemia may also develop after BD/DNC.[32] Hyperglycemia is more common and can be seen in 70% of decedents due to catecholamine surges and infusion of dextrose-containing fluid. High doses of insulin (up to 20 units/hour) may be required to treat hyperglycemia in this setting as a result of peripheral insulin resistance.[4, 35-37]

Hematologic Complications after BD/DNC

Coagulopathy, thrombocytopenia and anemia can develop after BD/DNC. Coagulopathy has been reported in 5-83% of brain dead decedents due to 1) systemic release of plasminogen activator from necrotic brain, 2) hypothermia or 3) disseminated intravascular coagulation secondary to trauma or resuscitation requiring transfusion of fresh frozen plasma or cryoprecipitate.[27-29, 31-33] Platelet and INR goals are both debated: some authors recommend targeting platelets > 50,000mm^3 and some recommend targeting > 80,000mm^3; some authors favor an INR goal < 2 and some prefer < 1.5.[18, 34, 35, 73] The threshold for blood transfusion is also not uniformly agreed upon, though it is generally felt that it is appropriate to target Hct > 25-30%, keeping in mind that transfusions are still associated with risks after brain death, just as they are in living patients. [27, 32, 44, 50, 59]

Pregnancy Considerations

Provision of support to pregnant brain dead women can sometimes lead to delivery of a viable fetus, but because the intended duration of support is often significantly longer in this setting than it is when organ donation is planned, and normal pregnancy is associated with numerous physiologic changes, this process is increasingly complex and volatile.[24, 74] The greatest risk to maternal somatic function and fetal

health in this setting is sepsis, which is often caused by growth of highly resistant bacteria leading to pneumonia, urinary tract infections, or bloodstream infections.[11]

The earliest report of provision of somatic support to a pregnant woman after brain death identified in a meta-analysis on ten pregnant brain dead women and a systematic review of 30 pregnant brain dead women is from 1982. The longest duration of support in these series was 107 days.[14, 24] In the systematic review, the mean gestational age at the time of BD/DNC was 22 weeks (range 1-40 weeks) and the mean gestational age at the time of delivery was 29.5 weeks (range 26-33 weeks). Delivery was prompted by maternal or fetal instability in the majority of cases. There were two cases of spontaneous abortion at weeks 13 and 19 and four cases of intrauterine death, but 63% of cases led to delivery of a viable infant, all by cesarean section. The mean Apgar scores were 7 and 8, at 1 and 5 minutes, and the mean birthweight was 1,384 grams (range 815-2,083 grams). Only one infant had congenital defects (due to hydantoin syndrome related to prior maternal phenytoin use).[14] Of 8 infants who had postnatal outcome data available, 4 required only routine care and 4 required mechanical ventilation. All of the 6 infants who had available outcome data at the age of 18 months met their developmental milestones and were physically and mentally normal. However, it is important to keep in mind that publication bias impacts our understanding of the rate of good outcomes when somatic support is provided to pregnant women after BD/DNC because it is less likely that one would publish a report on a case with a bad outcome.[24]

Recommendations and Suggestions

1. It is recommended that the decision of whether or not to continue somatic support after BD/DNC for the purposes of organ donation be made based on discussion between a local organ procurement representative and the family of the decedent, taking into consideration the decedent's known or presumed wishes about donation.
2. It is recommended that the decision of whether or not to continue somatic support after brain death in a pregnant decedent be made after a multidisciplinary discussion with the decedent's family about potential fetal outcome, taking into consideration the decedent's advanced medical directives or expressed wishes and local laws on continuation/discontinuation of support in this setting.
3. It is recommended that the decision of whether or not to continue somatic support to accommodate an objection to the use of neurologic criteria to declare death or discontinuation of somatic support be made in accordance with local guidelines, as discussed in the chapter on Religion and Brain Death: Managing Requests to Forego a Brain Death Evaluation or Continue Somatic Support after Brain Death.
4. If organ support is being continued after BD/DNC for the purposes of organ donation, if a decedent is pregnant, or to accommodate an objection to the use of neurologic criteria to declare death or discontinuation of somatic support:

    a. In an effort to prevent and manage arrhythmias after BD/DNC, it is suggested that:
        i. Hypokalemia and hypomagnesemia be avoided/corrected,
        ii. Amiodarone or lidocaine be used to treat ventricular arrhythmias,
        iii. Amiodarone be used to treat supraventricular arrhythmias,

iv. Atropine not be used to treat bradyarrhythmias because the vagus nerve is nonfunctional after BD/DNC,
v. Dopamine, dobutamine, epinephrine or isoproterenol be used to treat bradyarrhythmias in the setting of decreased cardiac output,
vi. Pacing be considered to manage bradyarrhythmias in the setting of organ donor management or pregnancy, but not in the setting of requests to provide somatic support due to objection to the declaration of BD/DNC,
vii. The healthcare team and decedent's family discuss the potential for cardiopulmonary arrest and the use of cardiopulmonary resuscitation if/when arrest occurs.

b. In an effort to prevent and manage perfusion derangements after BD/DNC, it is suggested that:
   i. Traditional measures of hemodynamic function and cardiac output be monitored,
   ii. Blood pressure be targeted based on individual patient characteristics to maintain organ perfusion,
   iii. Boluses of fluid and maintenance fluid be started immediately after BD/DNC to target euvolemia,
   iv. Crystalloids and/or colloids be used to achieve volume goals, but hydroxyethyl starch be avoided,
   v. Vasopressin be used to treat hypotension in the setting of diabetes insipidus,
   vi. Dopamine, norepinephrine or phenylephrine be started at the lowest dose necessary to maintain hemodynamic stability if a decedent remains hypotensive despite fluids,
   vii. If cardiopulmonary instability is refractory to the above interventions, initiation of ECMO or placement of an IABP be considered in the setting of donor management or pregnancy, but not in the setting of requests to provide somatic support due to objection to the declaration of BD/DNC,
   viii. Short-acting medications such as nicardipine, labetalol or esmolol be used to treat hypertension.

c. In an effort to maintain normothermia after BD/DNC, it is suggested that:
   i. Room temperature be kept ≥ 24˚C,
   ii. Warming blankets, automated temperature regulation devices, thermal mattresses, warmed fluids and/or warmed oxygen be used, but heat lamps, immersion in hot water or infusion of warm fluids into the bladder, stomach, pleural or peritoneal cavity not be used to treat hypothermia,
   iii. Cooling blankets or automated temperature regulation devices be used to treat hyperthermia.

d. In an effort to prevent and manage respiratory complications after BD/DNC, it is suggested that:
   i. Ventilator settings be adjusted as needed to provide the minimum ventilator support to achieve normal pH, eucapnia, and normoxemia,
   ii. A tidal volume of 6-8 ml/kg be targeted,

iii. Aggressive suctioning, corticosteroids, positive end-expiratory pressure, nebulizers, prone positioning, recruitment maneuvers or high frequency oscillation be considered to improve oxygenation,
iv. Diuretics may be considered to treat pulmonary edema if hemodynamically stable.

e. In an effort to prevent and manage endocrine complications after BD/DNC, it is suggested that:
   i. Urine output, serum sodium and urine specific gravity be closely monitored for evidence of diabetes insipidus,
   ii. Vasopressin be used if a decedent with diabetes insipidus is hypotensive, or desmopressin be used to treat diabetes insipidus in the absence of hypotension,
   iii. Thyroid hormone replacement and/or steroids be considered in the setting of hemodynamic instability,
   iv. Insulin and dextrose be given as needed to target euglycemia.

f. In an effort to prevent and manage hematologic complications after BD/DNC, it is suggested that:
   i. An INR and platelet goal be established based on the clinical situation,
   ii. Red blood cells be transfused as needed in the setting of active bleeding or symptomatic anemia, such as in the setting of hypotension.

5. When the decision is made to continue somatic support for a brain dead pregnant decedent, it is recommended that:
   a. A multidisciplinary team of intensivists, obstetricians and neonatologists be involved,
   b. Medications be selected based on their safety profile in pregnancy,
   c. The fetus be monitored routinely with at least daily heart rate checks and non-stress testing, weekly ultrasounds and monthly biophysical profiles, as well as performance of amniocentesis on an as-needed basis, given that fetal health may affect decision-making regarding continuation of somatic support,
   d. Antenatal corticosteroids be administered to facilitate lung maturation,
   e. Tocolytics (preference for calcium channel blockers and prostaglandin inhibitors over ß-mimetic agents) be utilized as needed to prevent preterm uterine contractions,
   f. Preparations be made for delivery by caesarean section between 26 and 33 weeks when fetal lung maturity is reached, with the understanding that it may be necessary to perform a delivery earlier in the setting of maternal somatic instability or fetal distress,
   g. Nutritional requirements be calculated based on maternal serum alimentary values, maternal weight and growth of the fetus and nutrition be provided enterally if the decedent is able to tolerate tube feeds, or parenterally if they are not,
   h. A tracheostomy be placed if long term ventilation is anticipated,
   i. Maternal carbon dioxide levels of 25-35 mmHg be targeted to facilitate elimination of carbon dioxide from the fetus,
   j. Infection prevention practices be rigorous, and infections be treated aggressively,

k. Precautions be taken to prevent catheter-associated urinary tract infections, corneal abrasions, deep vein thrombosis, line infections, skin ulceration, and ventilator-associated pneumonia.

Questions to Inform Research Agendas

1. How often is somatic support continued in the setting of organ donation, pregnancy and requests to provide somatic support due to objection to the declaration of BD/DNC?
2. How long can the body continue to function after BD/DNC with provision of aggressive somatic support?
3. How does prolonged somatic support influence the degree, intensity and characteristics of spinal motor reflexes?
4. Does fluid, inotrope and/or vasopressor selection impact the length of time before cardiopulmonary arrest after BD/DNC?
5. Does timing to initiate vasopressin impact the length of time before cardiopulmonary arrest after BD/DNC?
6. Does thyroid hormone replacement impact the length of time before cardiopulmonary arrest after BD/DNC?
7. Does steroid replacement impact the length of time before cardiopulmonary arrest after BD/DNC?
8. What is the incidence of CPR use after BD/DNC?
9. What are the indications and optimal duration of CPR after BD/DNC?
10. What is the incidence of recovery of spontaneous circulation after CPR for circulatory arrest in brain dead decedents?
11. How often are pregnant brain dead decedents carried to gestation, and what are fetal outcomes?

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