

Brain-dead Donor Management Protocol

Outline

- Rational for protocols
- The evidence
- ICU Protocol

The Rational

Donor Management - Goals

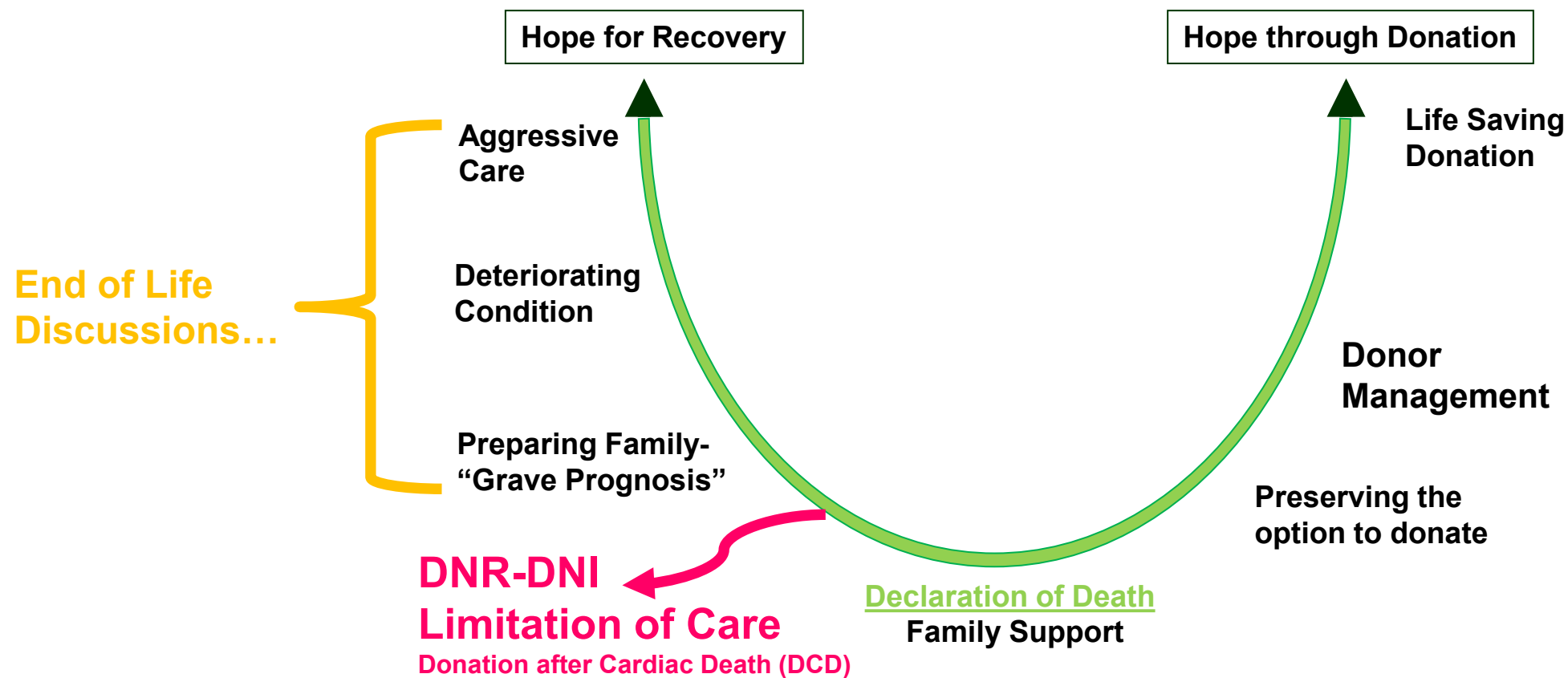
Optimize Organ
Viability

Proper
Assessment of
Organ Quality

Maximize
Organ
Utilization

Optimize
Outcomes of
Transplantation

Changing Paradigm in Critical Care



If the patient has the ability to donate and is thought to be dead by neurological criteria then brain death testing should be pursued

ICU Support

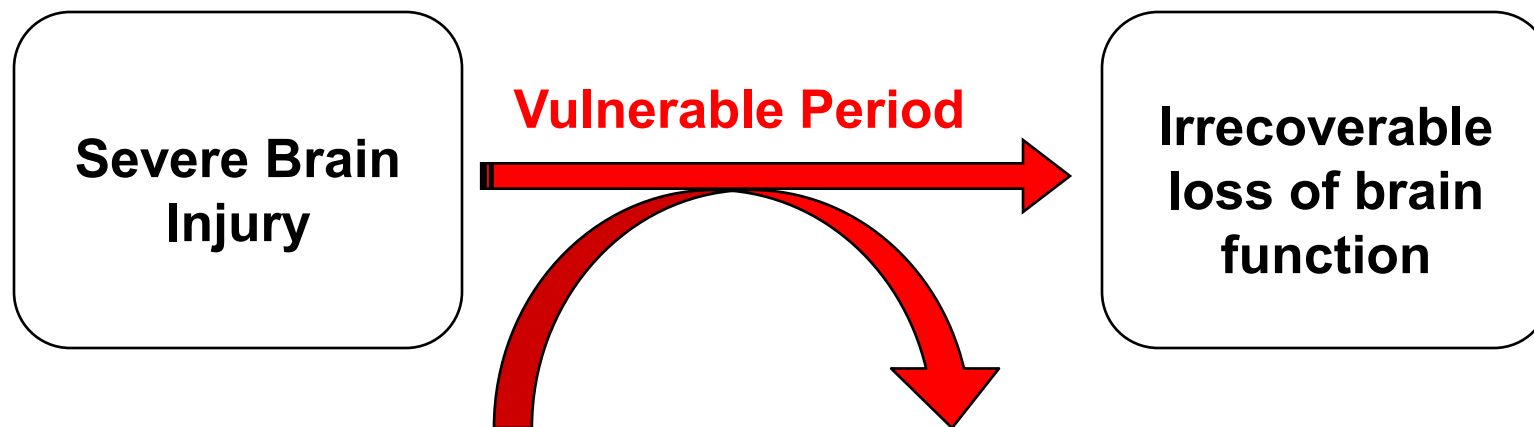
- Invasive arterial monitoring
- Central venous access allows administration of potent vasoactive drugs.
- Cardiac output measurement is helpful to guide therapy, particularly if cardiothoracic organ donation is contemplated.
- However, despite active standard support, the incidence of donor loss before retrieval may be up to 25%.
- Alternative goals may be useful and ‘Aggressive Donor Management’ in one center (including full support and pulmonary artery catheterization) reduced cardiovascular collapse in donors from 18% to 2%, and in another center from 13% to 0.

Pre-Donor Management

- “Just Good Critical Care”
 - Catastrophic Brain Injury Guidelines
 - Maintain MAP > 65 (IVF resuscitation vasopressor support)
 - Maintain oxygenation (Sat > 90%)
 - Monitor and correct electrolyte abnormalities

- “What is good for the patient is good for the donor”

The Pathway to Organ Donation

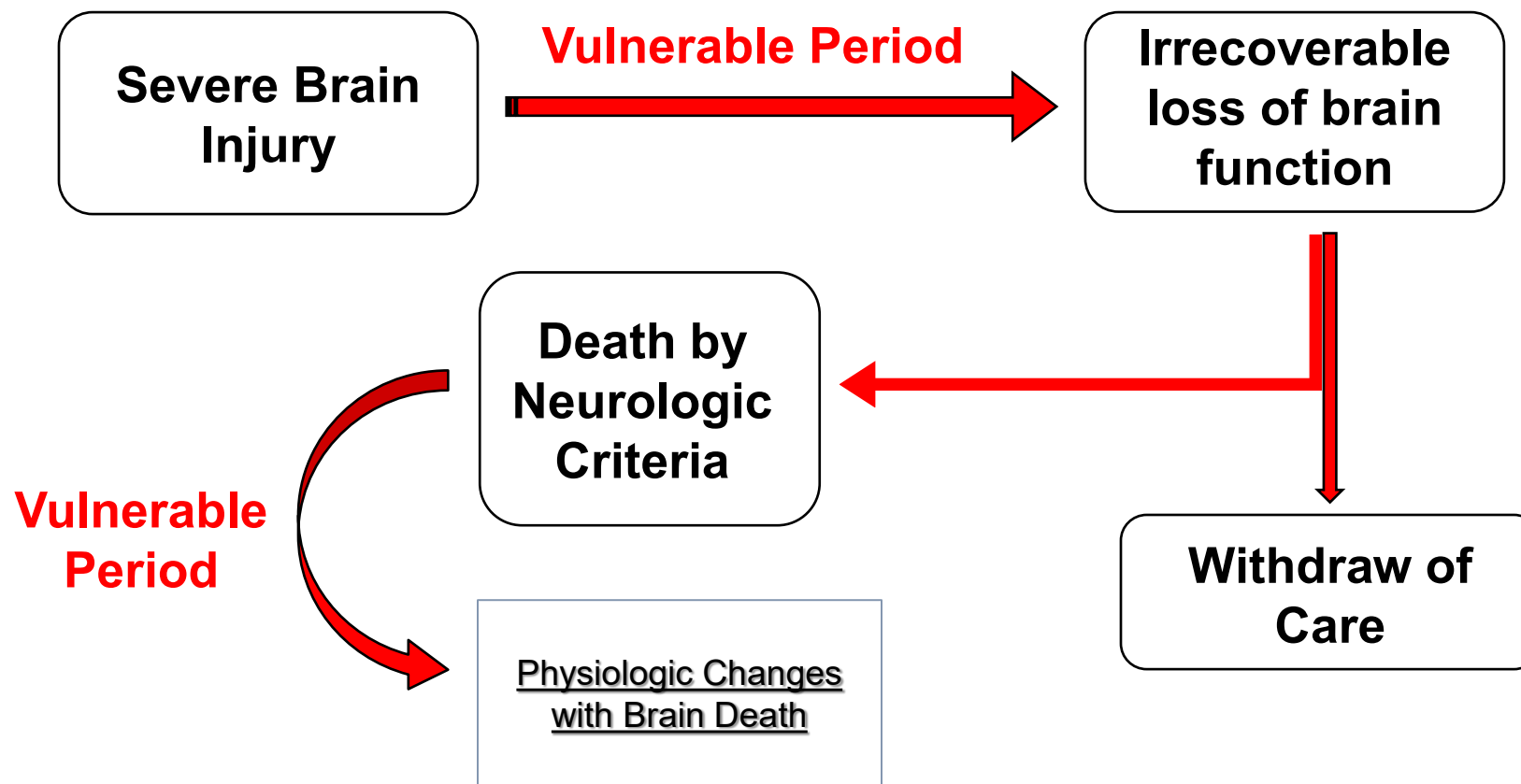


Healthcare providers often recognize poor outcome early on....

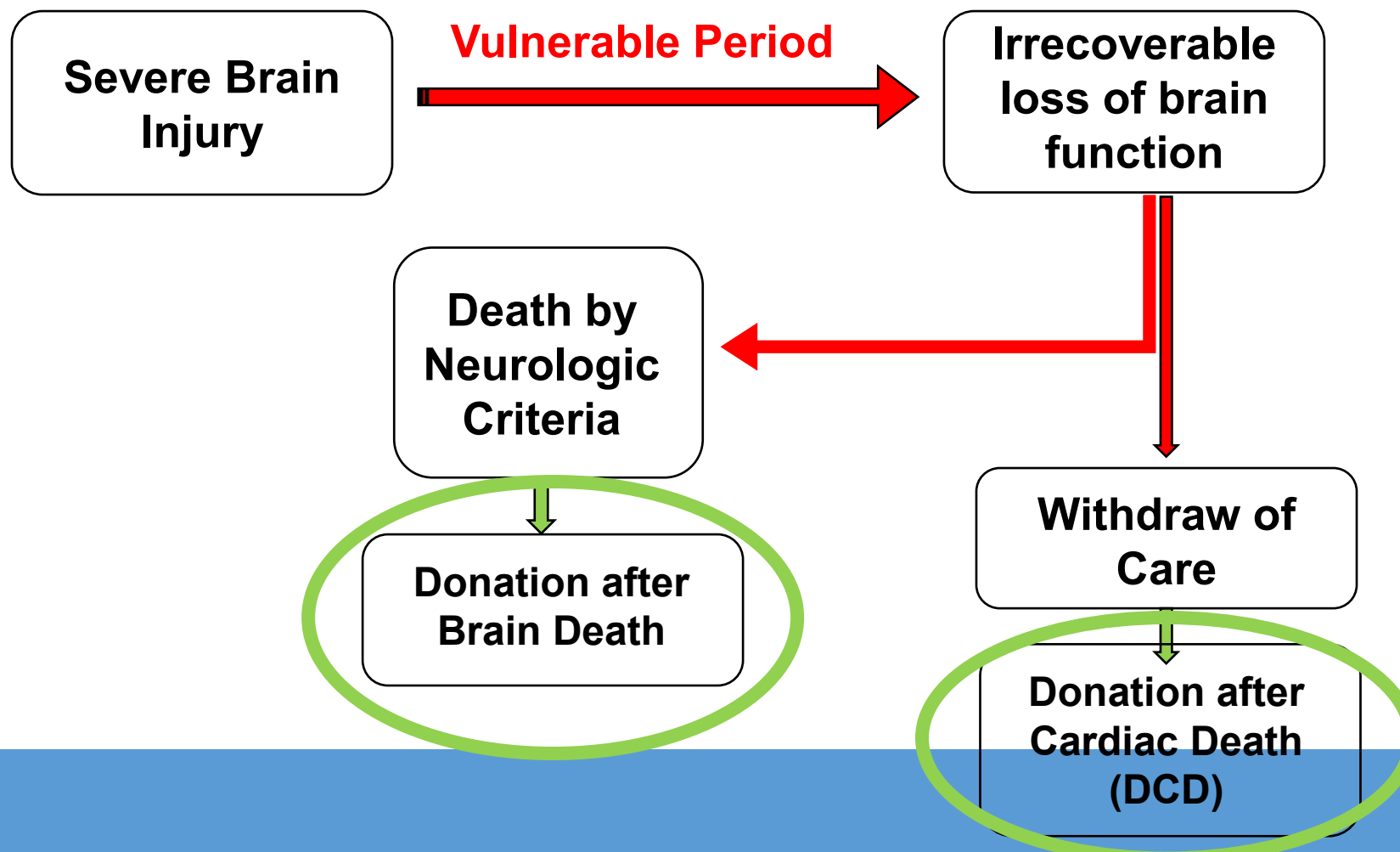
Healthcare providers can feel conflicted.....

Ongoing Support vs. DNR-DNI or Limitation of Care

The Pathway to Organ Donation



The Pathway to Organ Donation



Decline in Organ Function after Brain Death

Physiologic Changes

Hemodynamic Instability
Inflammatory response

- Capillary leak
- Coagulopathy

Volume depletion
Hypothermia
Hormonal Abnormalities

Pre-existing Co-morbidities
&
Associated Injury (trauma)

**Organ Dysfunction
(Loss of Opportunity to Donate)**

Treatments

- Mannitol
- Steroids
- Volume Resuscitation

Outcomes are better with organs obtained from live donors compared to organs from brain-dead donors as these physiologic insults are avoided

Aggressive Donor Management

- Donor management remains one of the most neglected areas of transplantation
- Failure to provide adequate physiological support to potential donors accounts for 25% of lost donors

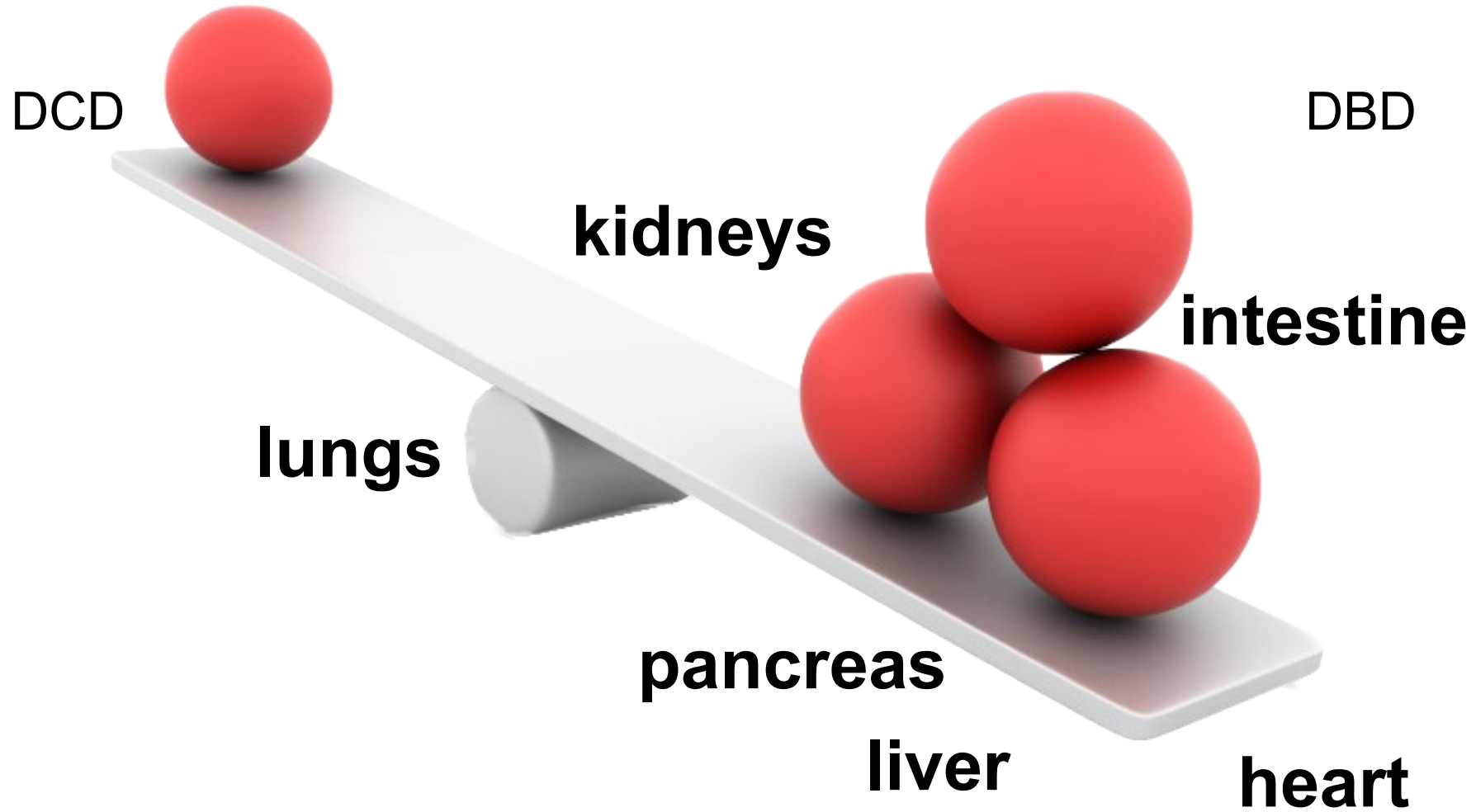
Aggressive Donor Management

Success of transplantation depends on the quality of organs and quality of organs depends on the quality of management

Possible recovery of organs that were initially assessed as unsuitable

Minimize the loss of donors during maintenance

Increase number of organs per donor



Donor Optimization

- Ameliorate 'systemic' effects of brain stem death
- Why?
 - Increase number of donors
 - Increase number of organs per donor
 - Increase quality of organs
- Who takes responsibility?
 - ICU staff: medical and nursing
 - SN-ODs
 - Retrieval teams



"My brain is dead but they have the rest of my body on a life-support system!"

The Evidence

Evidence

- **Totsuka** *Transplant Proc.* 2000; 32:322-326
 - High sodium in liver donor doubles graft loss
- **Rosendale** *Transplantation* 2003. 75 (4): 482-487
 - Protocol increased organs per donor 3.1 to 3.8. Increased probability of transplant.
- **SnellJ** *Heart Lung Transplant* 2008;27:662-7
 - 54% of Australian lung donations used for transplant vs. 13% in UK

Why bother with a protocol?

- We know that:
 - Recipient needs continually outnumber organs available
 - Many organs both procured and evaluated are not transplanted — organs are ‘unacceptable’

- Questions:
 - Can an ‘unacceptable donor’ be changed to an ‘appropriate donor’?
 - Can a standardized protocol help in this transformation?

‘unacceptable donor’ → Acceptable donor?

- 150 donors — 52 were inappropriate for txp:
 - Hypotension / high inotrope requirements
 - High CVP / PCWP
- **DONOR MANAGEMENT TEAM**
- After ‘appropriate management’ 44 of 52 donors yielded transplantable organs (29 hearts, 15 heart and lung blocks).

The Origins of donor management Guidelines

- **2001 Crystal City Consensus Conference**
 - Developed consensus guidelines to improve organ recovery and txp

Does a standardized protocol increase organ procurement?

- 10 US OPOs; 88 ICUs; 4 month prospective study; 130 donors vs 140 historical controls

10.3% increase in number of organs recovered (p<0.01)

Organ	Pre-Critical Pathway		Critical Pathway	
	N	Per 100 donors	N	Per 100 donors
Kidney	255	182.1	235	180.8
Liver	119	85.0	116	89.2
Pancreas	33	23.6	53	40.8
Heart	77	55.0	78	60.0
Lung	45	32.1	59	45.4
Intestine	5	3.6	6	4.6
Total	534	381.4	547	420.8

Does a standardized protocol increase organ procurement?

- Prospective study
- 8 OPOs in UNOS 5 — CA, AZ, NV, NM, UT
- If 7/9 parameters were achieved, pt was considered to have 'met' DMGs

Donor Management Goals	Parameters
Mean arterial pressure	60–100 mm Hg
Central venous pressure	4–10 mm Hg
Ejection fraction	>50%
Vasopressors	≤1 and low dose ^a
Arterial blood gas pH	7.3–7.45
Pao ₂ :Fio ₂	>300
Serum sodium	135–155 mEq/L
Blood glucose	<150 mg/dL
Urine output	0.5–3 mL/kg/hr over 4 hrs

^aLow dose of vasopressors was defined as dopamine ≤10 µg/kg/min, neosynephrine ≤60 µg/kg/min, and norepinephrine ≤10 µg/kg/min.

Can a standardized protocol help in this transformation?

- Independent predictors of ≥ 4 organs transplanted per donor were:
 - Age (OR = 0.95 per year),
 - Final creatinine (OR = 0.75 per 1-unit increase)
 - Donor management goals “met” at:
 - consent (OR=2.03),
 - prior to organ recovery (OR= 2.34), and
 - change in the number of donor management goals achieved from consent to 12–18 hrs later (OR = 1.13 per additional donor management goal).

Intensivist-Led Management of Brain-Dead Donors Is Associated with an Increase in Organ Recovery for Transplantation

K. Singbartl^{a,*}, R. Murugan^a, A. M. Kaynar^a,
D. W. Crippen^a, S. A. Tisherman^a, K. Shutterly^b,
S. A. Stuart^b, R. Simmons^c and J. M. Darby^a

^aDepartment of Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA

^bCenter for Organ Recovery and Education, University of Pittsburgh School of Medicine, Pittsburgh, PA

^cDepartment of Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA

*Corresponding author: Kai Singbartl, kas148@pitt.edu

The disparity between the number of patients in need of organ transplantation and the number of available organs is steadily rising. We hypothesized that intensivist-led management of brain dead donors would increase the number of organs recovered for transplantation. We retrospectively analyzed data from all consented adult brain dead patients in the year before (n = 35) and after (n = 43) implementation of an intensivist-led donor management program. Donor characteristics before and after implementation were similar. After implementation of the organ donor support team, the overall number of organs recovered for transplantation increased significantly (66 out of 210 potentially available organs vs. 113 out of 258 potentially available organs, p = 0.008). This was largely due to an increase in the number of lungs (8 out of 70 potentially available lungs vs. 21 out of 86 potentially available lungs; p = 0.039) and kidneys (31 out of 70 potentially available kidneys vs. 52 out of 86 potentially available kidneys; p = 0.044) recovered for transplantation. The number of hearts and livers recovered for transplantation did not change significantly. Institution of an intensivist-led organ donor support team may be a new and viable strategy to increase the number of organs available for transplantations.

Received 31 August 2010, revised 17 December 2010
and accepted for publication 6 January 2011

Introduction

Solid organ transplantation is the only definitive treatment option for patients with end-stage organ failure, and brain-dead donors are the most common source of organs. Despite advances in recipient selection and transplant allocation, there still remains a drastic shortage of transplantable organs, causing many patients to die while awaiting transplantation. According to the United Network for Organ Sharing (UNOS), there are currently more than 109 000 patients in the US awaiting more than 119 000 solid organs, but less than 22 000 organs have been transplanted in 2010 so far, resulting in the death of almost 7% of candidates on the waiting list (1).

As the shortage in transplantable organs steadily rises, a public health crisis in the United States and the world ensues. The use of marginal, high-risk donors and the extension of donor criteria have provided some alleviation of the shortage (2). Administrative and clinical programs have also been developed to address this problem. In-house transplant coordinator programs have increased identification, consent and conversion rates of potential donors (3). Goal-directed donor management protocols have raised the organ yield from individual donors by up to 80% (4). These measures by themselves, however, are insufficient to reduce the shortage of transplantable organs; additional measures are required to improve the supply of transplantable organs.

Transplantation International 2011, 22(1): 24-31

ICU Protocol

Cardiovascular management

- MAP: 60 – 80 mm Hg
- CVP: 4 – 10 mm Hg
- Heart rate: 60 – 100/min SR
- CI: > 2.1 l/min/m² (can be higher, be aware of myocardial stunning)
- Filling targets: no good evidence for any specific targets, depends on device
- SvO₂ $> 60\%$
- SVRI target
 - Secondary target
 - Dehydration → temptation to maintain MAP with vasopressors rather than filling

Respiratory management

- **Recruitment manoeuvre**
 - Post BSD testing: apnoea test resulting in atelectasis
 - After suctioning / disconnection
 - When SpO₂ drops / FiO₂ increases
- Lung protective ventilation: 4 – 8 ml/kg ideal body weight
- Permissive hypercapnia with pH > 7.25
- Optimum PEEP (5 – 10 cm H₂O) and FiO₂ (aim for < 0.4 as able)
- Head—up positioning (30 - 45°)
- Suctioning, physiotherapy as required
- Antibiotics for purulent secretions: local microbiology surveillance
- Avoid over-hydration

Hormonal treatment

- **Vasopressin**
 - Reduction in other vaso-active drugs
 - Dose: 1 – 4 units/h (can start with boluses of 1 unit at a time)
- **Liothyronine (T3)**
 - No clear evidence yet for either use or not
 - May add haemodynamic stability in very unstable donor
 - Dose: 3 units/h, sometimes bolus of 4 units asked for by retrieval team
- **Methylprednisolone in all cases**
 - Dose: 15 mg/kg up to 1g
- **Insulin**
 - At least 1 unit/h (Occasionally may need to add glucose infusion)
 - ‘Tight’ glycaemic control (4 - 10 mmol/l)

Managing Diabetes insipidus

- Very common occurrence
- Pathophysiology
 - Posterior pituitary failure
 - Polyuria: output $> 4\text{ml/kg/h}$
 - Dehydration with $\uparrow \text{Na}^+$
- Usually at least partially addressed with stabilization for BSD testing
- Treatment:
 - Fluids
 - Vasopressin
 - DDAVP
- Aim for u-output $0.5 - 2.0 \text{ ml / kg / h}$

Haematological management

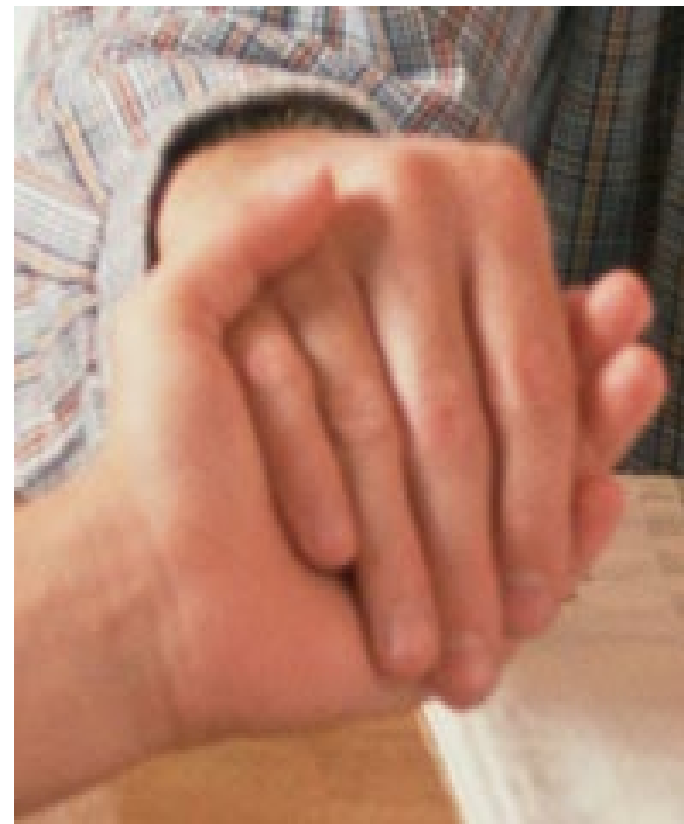
- DIC seen occasionally as direct consequence of BSD
 - May require correcting prior to BSD testing if bleeding
- Hb > 8 g/dl (~ 10 g/dl traditionally advocated) (even > 7g/dl ?)
 - No evidence on harm with lower Hb, but some evidence of harm with blood transfusions and organ function post transplant
 - Where Hb borderline, ensure blood available for retrieval procedure: local protocols and antibodies will determine whether T&S only, or units to be cross matched
- Use of clotting factors
 - Only where bleeding is an issue
 - Monitor clotting status
 - Use local hospital protocol
 - Retrieval procedure may require additional products

General measures

- **Maintain normothermia (active warming may be required)**
- **Thrombo-embolism prophylaxis**
 - Stockings
 - Sequential compression devices
 - LMWH
- **Positioning**
 - Head-up
 - Side to side
 - Attention to cuff pressures and leaks to prevent aspiration
- **Continue NG feeding (may be reduced/ stopped for bowel transplant)**
- **Antibiotics according to sensitivities or empirical according to Trust guidelines**

GENERAL CARE

- PROPER NURSING CARE.
- SUPPORT FOR RELATIVES.



Monitoring optimisation

- **Implementation: use of care bundle**
 - Adherence easy to monitor
 - Audit first 5 priorities
- **Results of optimisation evaluated**
 - Number of organs retrieved
 - Increase in cardiothoracic organs retrieved
- **Quality of organs: organ function in recipients**
 - Delayed graft function
 - Quality: biomarkers
 - Duration of graft function: long term project

Devastating Brain Injury Order Set

- Appropriate fluid resuscitation to euvolemia
- Correction of coagulopathy
- Maintain oxygen delivery
 - Transfuse to Hb 10
 - Use of inotropes
 - Hormone replacement
- Optimize oxygenation and ventilation
- Management of DI

HARBOR-UCLA MEDICAL CENTER ADULT DEVASTATING BRAIN INJURY ORDERS	
COUNTY OF LOS ANGELES DEPARTMENT OF HEALTH SERVICES This order set is a general guideline and does not represent a professional care standard governing provider obligations to patients. Care is revised to meet individual patient needs. This order set is intended as orders for the patient in the intensive care unit who has a devastating brain injury; i.e., a patient who has incurred massive head trauma, intracranial hemorrhage, or hypoxic ischemic damage. The patient should be evaluated by Neurology or Neurosurgery and anticipated to have a poor neurological prognosis and not an operative candidate.	
Instructions	ALLERGIES:
1. If an order is desired, please "X" the box; leave blank if not desired. Orders with checked boxes are strongly recommended. If a checked box is not desired, cancel the order by drawing a line through it followed by your initials.	WEIGHT: _____ lb / kg
I. GOAL: Early identification of and initial therapy for a patient with a devastating brain injury.	
<input checked="" type="checkbox"/> Admit to / maintain in _____ (ICU), _____ (Service), _____ (Physician). <input checked="" type="checkbox"/> Diagnosis: Devastating Brain Injury <input checked="" type="checkbox"/> Draw on arrival: CBC, PT/PTT, Chem-8, magnesium, phosphorous, liver function tests, type and cross 4 units PRBC, ABG, arterial lactate, troponin, blood alcohol level. <input checked="" type="checkbox"/> Send on arrival: Urine toxicology screen <input checked="" type="checkbox"/> Send on arrival: Sputum gram stain and culture. <input checked="" type="checkbox"/> Obtain CXR on arrival and every morning. <input checked="" type="checkbox"/> Draw labs every 4 hours for the first 24 hours: CBC, PT/PTT, Chem-8, magnesium, phosphorus, ABG, and arterial lactate. (May discontinue serial PT/PTT when INR less than 1.2.) Confirm frequency of serial labs after 24 hours. <input checked="" type="checkbox"/> Daily labs: CBC, PT/PTT, Chem 8, magnesium, phosphorous, ABG, arterial lactate, liver function tests. <input checked="" type="checkbox"/> Place Foley catheter and monitor strict Ins and Outs. <input checked="" type="checkbox"/> Place orogastric tube (OGT) to low continuous wall suction. <input checked="" type="checkbox"/> Place peripheral IV (unless patient has central venous line). <input checked="" type="checkbox"/> Bair Hugger / cooling blanket to maintain normal core temperature (36.5-37.5°C). <input checked="" type="checkbox"/> Bilateral lower extremity sequential compression devices. <input checked="" type="checkbox"/> Set up for arterial and central line placement to monitor continuous arterial pressure and central venous pressure. <input checked="" type="checkbox"/> Tylenol 650 mg down OGT (preferentially) or PR every 4 hours as needed for temperature greater than or equal to 38.0 °C (100.4 °F). Not to exceed 4 grams in 24 hours. <input checked="" type="checkbox"/> If patient not already receiving stress ulcer prophylaxis, begin Pepcid 20 mg IV every 12 hours.	
II. GOAL: Hemodynamic stabilization by fluid resuscitation (targeting central venous pressure to 8-12 mmHg with transfusion or IV fluids) prior to initiating a vasopressor.	
<input checked="" type="checkbox"/> Administer Normal Saline (0.9% NaCl) 1 liter IV bolus on arrival in ICU. <input checked="" type="checkbox"/> Notify practitioner if mean arterial pressure (MAP) is less than 65 mmHg or systolic blood pressure (SBP) is less than 90 mmHg after 1 liter IV fluid bolus is given. <input checked="" type="checkbox"/> Measure CVP every 30 minutes via subclavian or internal jugular line; notify practitioner if CVP less than 8 mmHg. <input checked="" type="checkbox"/> If hemoglobin less than 10 (hematocrit less than 30), notify practitioner of plan for transfusion: (Practitioner to complete separate transfusion order form) <ul style="list-style-type: none"> <input checked="" type="checkbox"/> Hb 9.0-9.9 gm/dL (Hct 27-29.9%): transfuse 1 unit of packed red blood cells IV bolus. <input checked="" type="checkbox"/> Hb 8.0-8.9 gm/dL (Hct 24-26.9%): transfuse 2 units of packed red blood cells IV bolus. <input checked="" type="checkbox"/> Hb less than or equal to 8 gm/dL (Hct less than or equal to 24%): transfuse 3 units of packed red blood cells IV bolus. <input checked="" type="checkbox"/> If INR greater than 1.4 or PTT greater than 40, notify practitioner for orders for plan of transfusion with goal of correcting coagulopathy: <ul style="list-style-type: none"> <input checked="" type="checkbox"/> INR greater than 1.4: transfuse 2 units of fresh frozen plasma IV bolus. <input checked="" type="checkbox"/> INR greater than 1.6: transfuse 3 units of fresh frozen plasma IV bolus. <input checked="" type="checkbox"/> INR greater than 1.8: transfuse 4 units of fresh frozen plasma IV bolus. <input checked="" type="checkbox"/> If CVP less than 8 mmHg, give 1000 cc IV every 30 minutes until CVP greater than or equal to 8 mmHg. <input checked="" type="checkbox"/> If CVP 8 – 12 mmHg, give Normal Saline (0.9% NaCl) IV at 150 ml/hr and measure CVP every hour. <input checked="" type="checkbox"/> If CVP 12-18 mmHg, maintain Normal Saline at 120 ml/hr and measure CVP every hour. <input type="checkbox"/> Other IV fluid (consider hypertonic saline if serum Na less than 135): _____	
ADULT DEVASTATING BRAIN INJURY PROTOCOL ORDERS <small>File in Medical Record Page 1 of 3</small>	

Order Set for Potential Brain-dead Donor

- Transfer care to [Name of OPO]
- Discontinue all prior orders
- Blood pressure, heart rate, temperature, urine output, central venous pressure (CVP) [if central venous catheter present], pulmonary artery occlusion pressure (PAOP) [if pulmonary artery (PA) catheter is present] q 1 hour
- Reorder mechanical ventilator parameters as previously set
- Maintain head of bed at 30-40 degrees elevation
- Continue routine pulmonary suctioning and side-to-side body positioning.
- Warming blanket to maintain body temp above 36.5°C
- Maintain sequential compression devices (SCDs)
- [If present] Continue chest tube suction or water seal as previously ordered 1
- [If present] Nasogastric (orogastric) tube to low intermittent suction.
- Intravenous fluid - D5 0.45% saline plus 20 meq KCl per liter at 75cc/hour

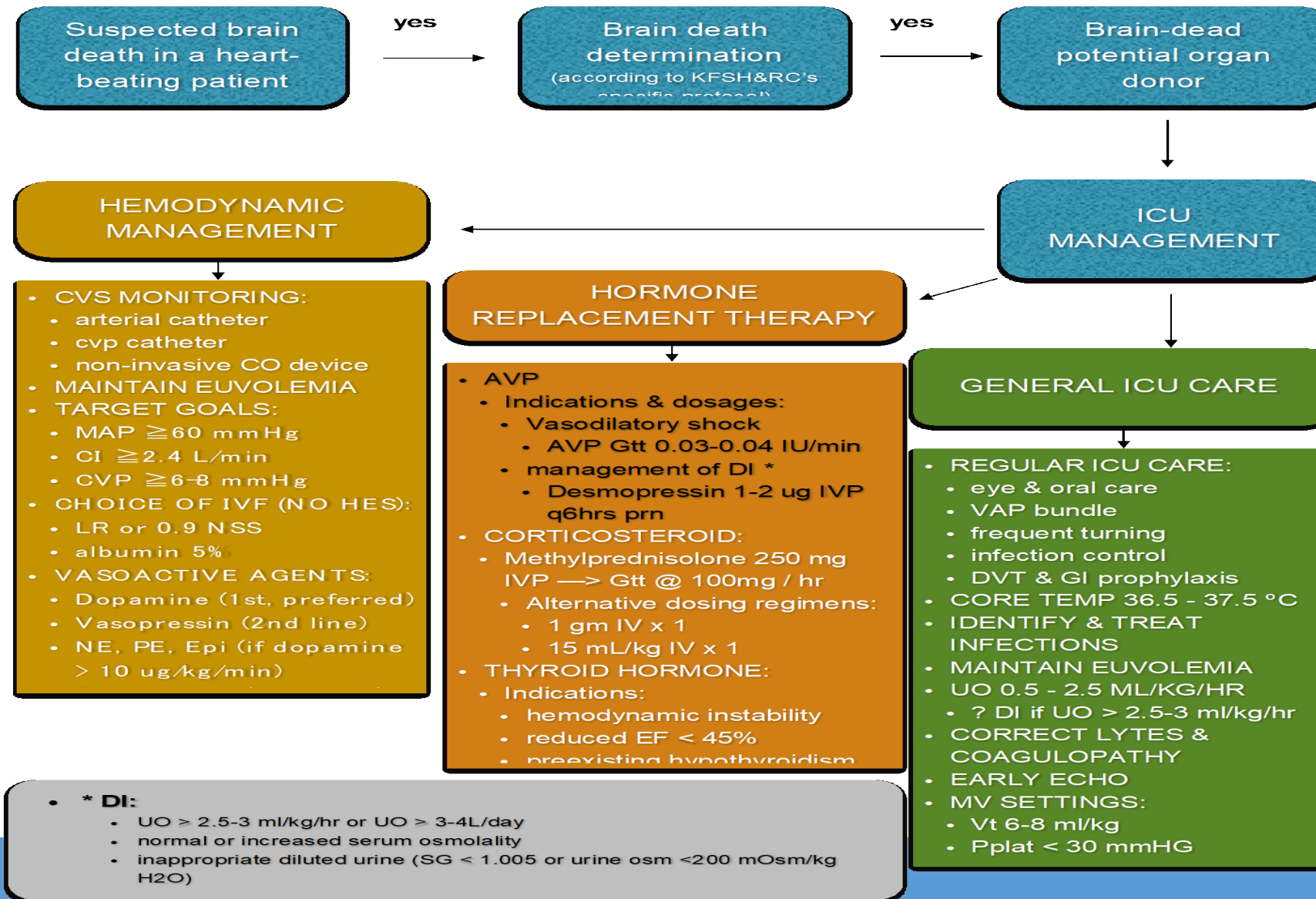
Order Set for Potential Brain-dead Donor

- Call OPO coordinator if:
 - MAP < 70 mm Hg
 - Systolic pressure > 170 mm Hg
 - Heart rate > 130 bpm
 - Temp > 37.8°C
 - Urine output < 250 cc/hr;
 - CVP or PAOP > 18 mm Hg
- Send electrolytes, magnesium, ionized calcium, CBC, platelets, glucose, blood urea nitrogen, creatinine, phosphorous, arterial blood gas, prothrombin time (PT), partial thromboplastin time (PTT), STAT and repeat q 4 hours.
- [If not previously done] Send blood for type and screen
- Finger stick glucose q 2 hours — call glucose > 180 mgm/dL
- Electrocardiogram STAT
- Chest X-ray STAT- Indication: initial donor evaluation.

Order Set for Potential Brain-dead Donor

- **Medications:**
 - Pantoprazole 40 mg IV q 24 hours, first dose now
 - Artificial tears q 1 hour and prn to prevent corneal drying
 - Albuteral and Atrovent unit dose per aerosol q 4 hours
 - Continue antibiotics previously ordered at same dose and frequency
 - Continue vasoactive drug infusions (dopamine, norepinephrine, etc) at previously ordered concentrations and infusion rates
 - [Review all medications previously ordered.
 - Most (anticonvulsants, pain medications, laxatives, gastrointestinal motility agents, eye drops, antihypertensives, anti-nausea agents, subcutaneous heparin, osmotic agents (mannitol), and diuretics) are unnecessary during donor care and will be discontinued automatically with order #1 above.
 - Review any other medications in question with MD]

ICU management of the potential brain-dead heart-beating organ donor



Conclusion

- **Intensivist-Led Management of Brain-Dead Donors**
 - Ameliorate ‘systemic’ effects of brain stem death
 - Increase number of donors
 - Increase number of organs per donor
 - Increase quality of organs

Thank You