Organ Donor Management

Ali Ashraf

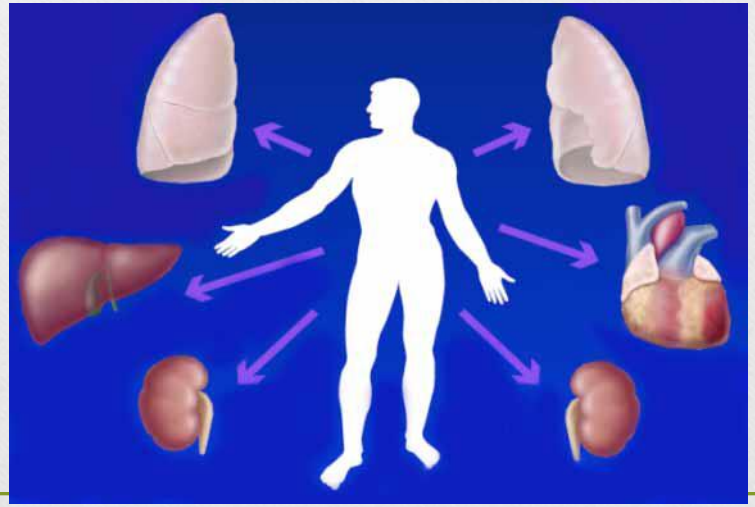
Intensivist AFSA DIU

Brain Death confirmation team

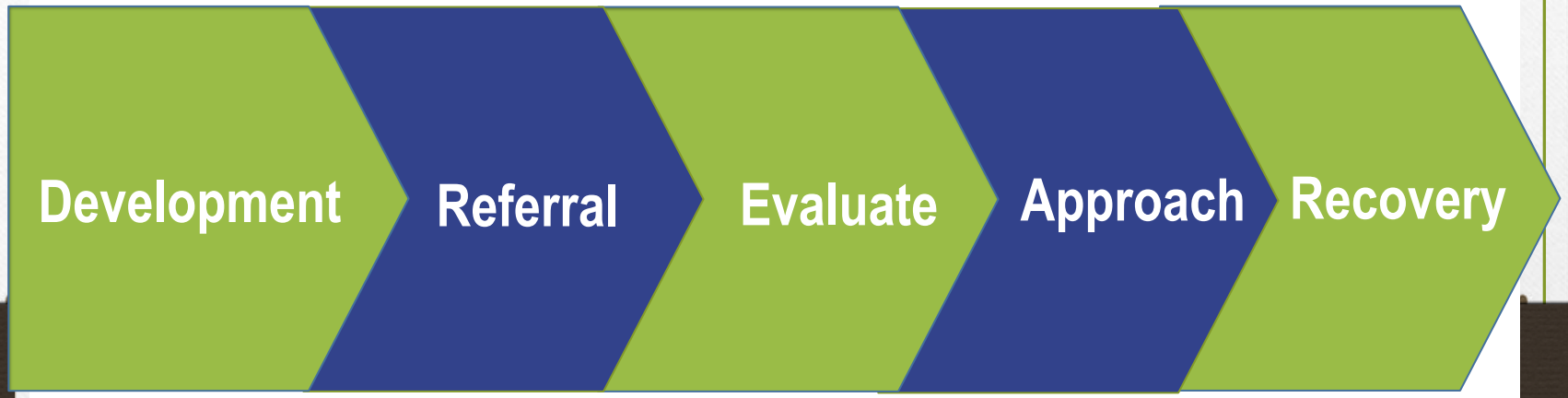
University of Guilan

Organ Donor Management

- Advances in transplant surgical techniques and immunosuppressive therapies have led to increasingly more patients with end-stage organ failure being treated with a transplant.



The Organ Donation Process



Development	Referral	Evaluate	Approach	Recovery
Hospital Services	Identification & Early Referral Based on Clinical Triggers	Suitability	Family Support	Coroner Clearance
Community Outreach		Donor Mgmt.	Huddle	Organ Placement
		Brain Death Declared	Effective Requesting	Organ/Tissue Recovery
		Donation After Cardiac Death	Medical/Soc History	
		Assessment		

Accountability • Quality • Excellence

What is Transplantable for Adults?

NEVADA DONOR NETWORK

ORGANS

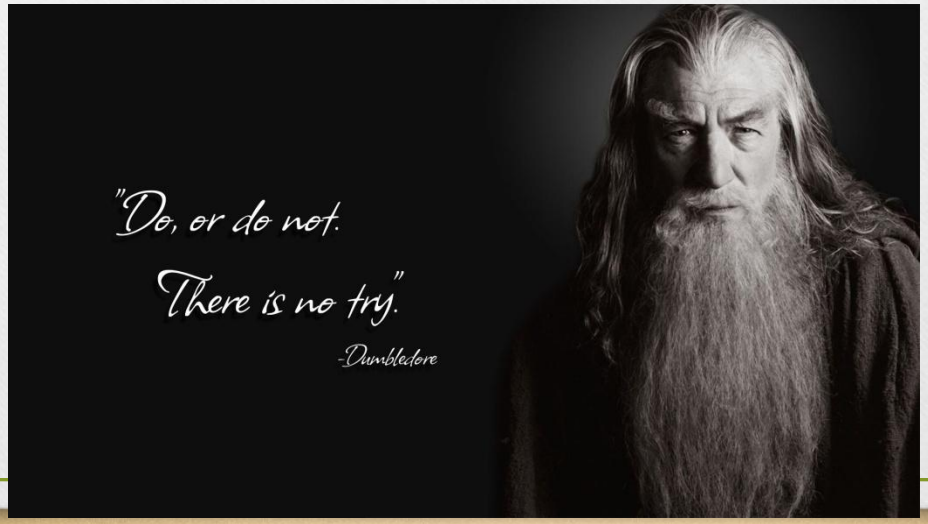
- Kidneys
- Liver
- Heart
- Lungs
- Pancreas
- Sm. Intestine

TISSUES

- Cornea/Eyes
- Heart Valves
- Veins
- Skin
- Bone
- Tendons
- Cartilage

Organ Donor Management

- Donor organs are scarce and the success rate of transplantation depends on appropriate management of the organ donor.



Diagnosing and Declaring Brain Death

Etiology of Brain Death

- Severe head trauma
- Aneurismal subarachnoid hemorrhage
- Cerebrovascular injury
- Hypoxic-ischemic encephalopathy
- Fulminant hepatic necrosis
- Prolonged cardiac resuscitation or asphyxia
- Tumors

R. Erff, D.O., *Walter Reed Army Medical Center*

Prerequisites to the Diagnosis

Evidence of acute CNS catastrophe compatible with brain death:

- **Clinical or Neuroimaging**

Prerequisites to the Diagnosis

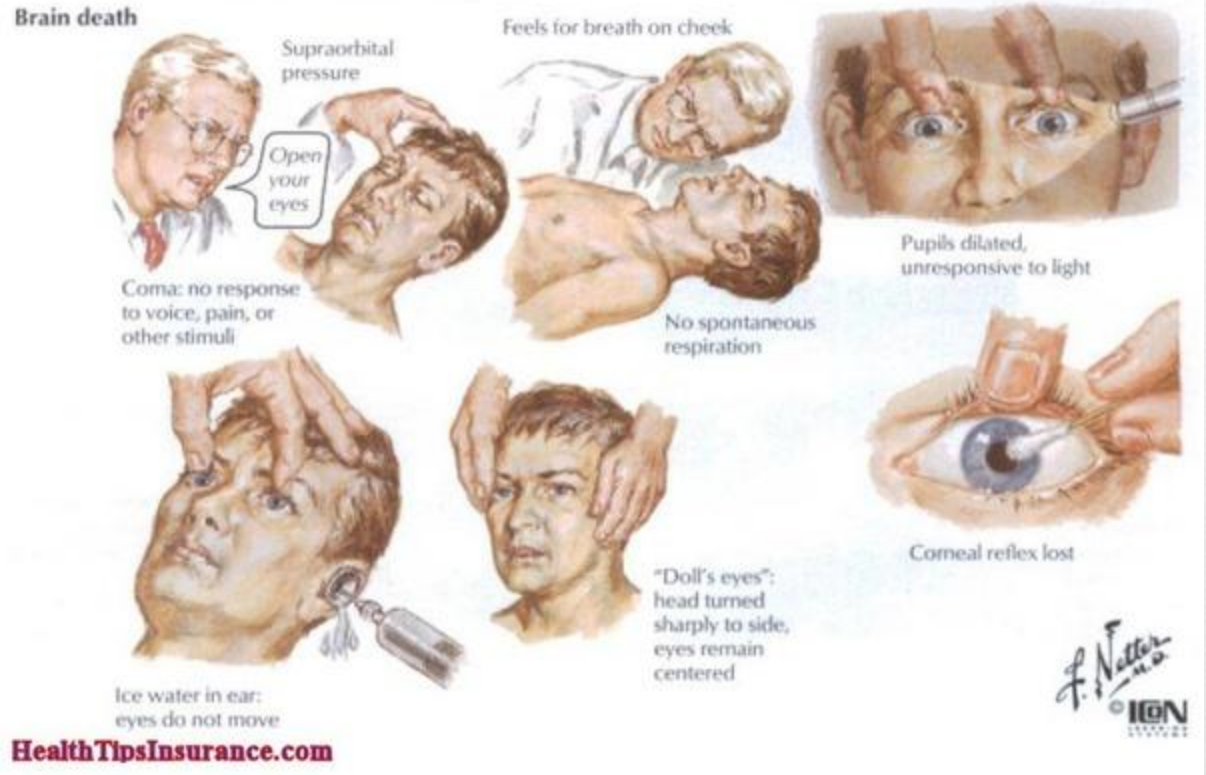
Exclusion of reversible medical conditions

- Severe electrolyte, acid base and endocrine disturbance
- drug intoxication and poisoning
- sedation and neuromuscular blockade
- Hypotension
- severe hypothermia (core temp < 35 C)

Brain Stem Reflexes

- No pupillary response to light.
- Pupils midline and dilated 4-6mm.
- No oculocephalic reflex (Doll's eyes)
- No oculovestibular reflex (tonic deviation of eyes toward cold stimulus) – contraindicated in ear trauma.
- Absence of corneal reflexes
- Absence of gag reflex and cough to tracheal suction.

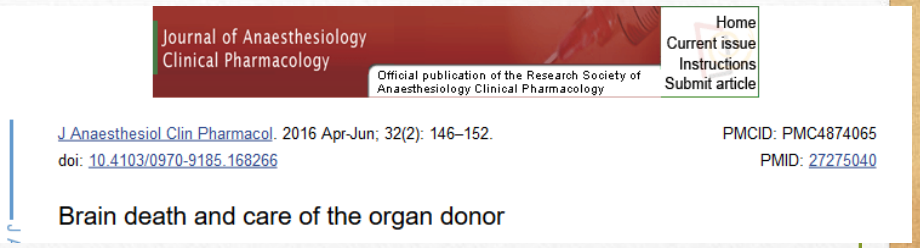
Brain Stem Reflexes



Apnea Testing

- Once coma and absence of brain stem reflexes have been confirmed → **Apnea testing**.
- Verifies loss of most rostral brain stem function
- Confirmed by **PaCO2 > 60mmHg** or **PaCO2 > 20mmHg over baseline value.**
- Testing can cause hypotension, severe cardiac arrhythmias and elevated ICP.
- Therefore, apnea testing is performed last in the clinical assessment of brain death.
- Consider **confirmatory tests** if apnea test inconclusive.

Apnea Testing



- Following conditions **must** be met before apnea test can be performed:

- Core temp > 36.5 C
- Systolic blood pressure > 100mmHg.
- Euvolemia
- Corrected diabetes insipitus
- Normal PaCO2 (PaCO2 35 - 45 mmHg).
- Preoxygenation (PaO2 > 200mmHg).

Confirmatory Testing

- ***Purely optional*** when the clinical criteria are met unambiguously.
- A confirmatory test is needed for patients in whom specific components of clinical testing cannot be reliably evaluated

  - Incomplete brain stem reflex testing
  - Incomplete apnea testing
  - Toxic drug levels
  - Children younger than 1 year old.
  - Required by institutional policy

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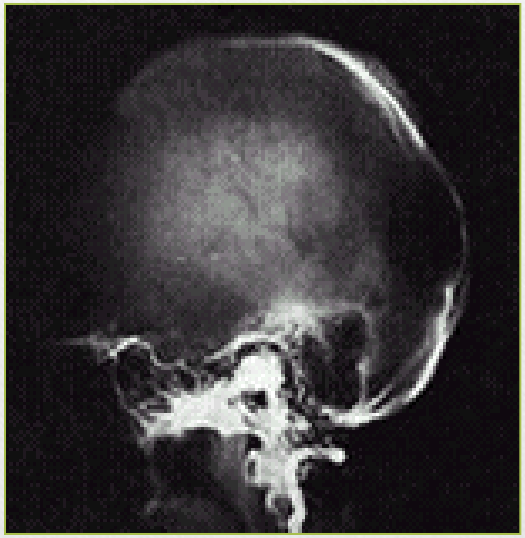
Confirmatory Tests for Brain Death

- Cerebral Blood Flow (CBF) Studies
  - Cerebral Angiography
  - Nuclear Flow Study
- EEG (when brain scan is not utilized)

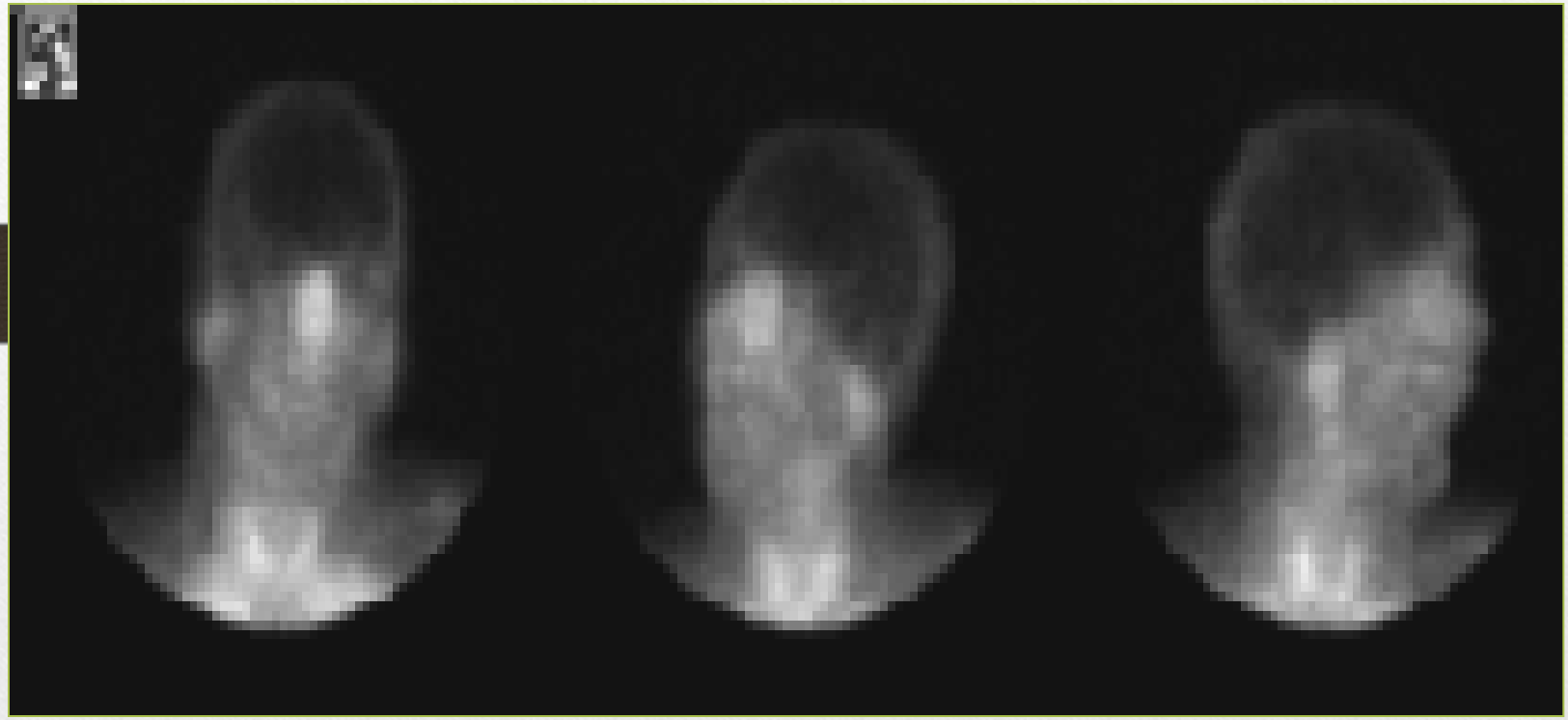
Cerebral Angiography

Normal Blood Flow

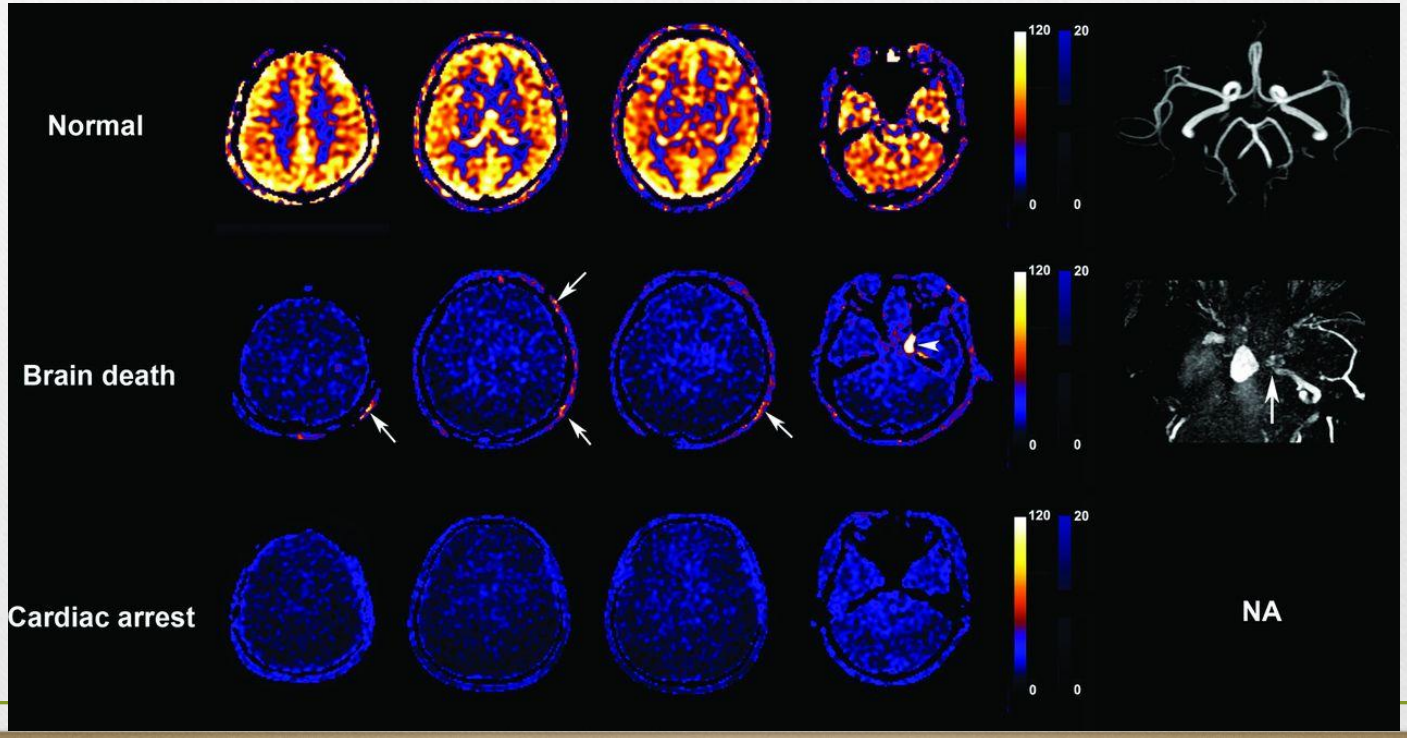


No Blood Flow

Nuclear Flow Study



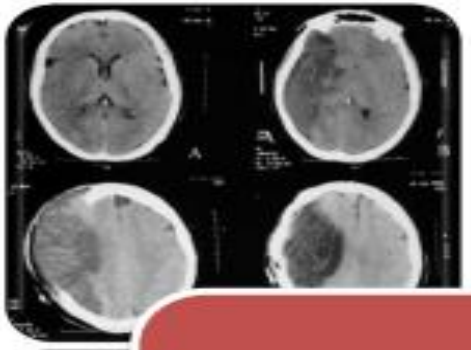
Arterial Spin-Labeling



Elements of brain death declaration

- Date
- Time
- Detailed documentation of Clinical Exam including specifics of Apnea Testing
- Physician signature

↑ ICP
(Cushing Reflex)

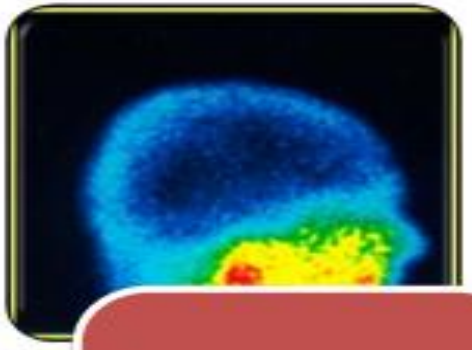


- Hypertension
- Bradicardia
- AVB / S Arrest

"Catecholamine storm"

- Tachycardia / Arytimias
- Coronary ischemia
- Miocardic Lesion
- ATP depletion
- ↑ PW Preasure
- Hypertension

"Brain death"



- Loss of Symp tone
- Periferic VD

What to expect after brain death

Autonomic/Sympathetic Storm

- **Release of catecholamines from adrenals (Epinephrine and Norepinephrine) results in a hyper-dynamic state:**
  - Tachycardia
  - Elevated C.O.
  - Vasoconstriction
  - Hypertension

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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Pathophysiology

- Loss of **brain stem function** results in systemic physiologic instability:

- Loss of vasomotor control → hypotention
- Cardiac arrhythmias → 25% cardiac arrest
- Loss of respiratory function → Apnea
- Loss of temperature regulation → hypothermia
- Hormonal imbalance

Following the diagnosis of Brain Death

- ✓ Therapy shifts in emphasis from cerebral resuscitation to optimizing organ fxn for subsequent transplantation.

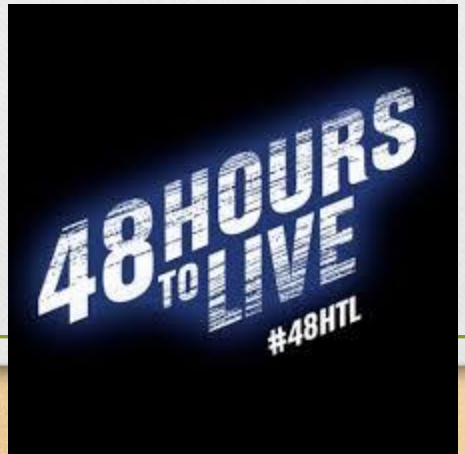
Following the diagnosis of Brain Death

- The normal sequele of brain death results in cardiovascular instability & poor organ perfusion.

Medical staff must focus on:

- Providing hemodynamic stabilization.
- Support of body homeostasis.
- Maintenance of adequate cellular oxygenation and donor organ perfusion.

✓ Circulatory collapse will usually occur within 48hrs.



Basic Standard monitoring:

- Fluid intake and output
- Hourly urine output
- Pulse oximetry
- ECG
- Temperature
- Arterial blood pressure
- Central venous pressure

Laboratory investigations: *12 hrly (+ more often if clinically indicated)*

- Full blood count
- Urea and electrolytes
- Liver enzymes, INR (or PT) and APPT
- Blood glucose, arterial blood gases at least 6 hrly
- Daily blood cultures, cultures of sputum and urine

Effective Donor Management

- Requires clinical expertise, vigilance, flexibility, and the ability to address multiple complex clinical issues simultaneously and effectively.
- Requires collaboration among the OPO, donor hospital critical care staff and consultants, and transplant program staff.

Effective Donor Management

- Donor care is not usually assumed until after consent for donation has been obtained.
- It is appropriate to collaborate prior to brain death, consent, etc, to prevent death and keep the option of organ donation open.

Effective Donor Management

- Revision of existing orders or placement of new medical orders is intended to:
- D/C medications no longer needed or appropriate (e.g., anticonvulsants, mannitol, sedatives, antipyretics)
- Continue needed medications, or therapy (e.g., vasoactive drug infusions, IV fluids and vent settings)
- Create "call orders" that inform bedside personnel of the goals for physiologic parameters and alert OPC of changes in donor status.

Table 1 Incidence of common physiological derangements in brain-dead donors

Derangement	Cause
Hypothermia	Hypothalamic damage; reduced metabolic rate; vasodilation and heat loss
Hypotension	Vasoplegia; hypovolaemia; reduced coronary blood flow; myocardial dysfunction
Diabetes insipidus	Posterior pituitary damage
Disseminated intravascular coagulation	Tissue factor release; coagulopathy
Arrhythmias	'Catecholamine storm'; myocardial damage; reduced coronary blood flow
Pulmonary oedema	Acute blood volume diversion; capillary damage

Hypotension:

- This occurs commonly after brain death. Consider the following causes:
- ***Absolute hypovolaemia***
- ***Effective hypovolaemia***
- ***Myocardial dysfunction***

Absolute hypovolaemia:

- Incomplete resuscitation following trauma
- Osmotic diuresis secondary to mannitol or hyperglycaemia.
- Diabetes insipidus with massive diuresis.

Effective hypovolaemia:

- 'Neurogenic shock' with loss of central vasomotor control and subsequent decrease in systemic vascular resistance.
- Rewarming of a hypothermic patient with resultant vasodilatation.

Myocardial dysfunction:

- Secondary to trauma and myocardial contusion.
- massive catecholamine surge

Hypertension:

- During the period of brain stem 'coning' acute arterial hypertension may occur related to increased intracranial pressure.
- Following brain death, patients may develop hypertension in response to noxious stimuli.

General principles:

- (1) Ensure the patient is adequately volume loaded but not overloaded.
- a combination of crystalloid and colloid
- Avoid nephrotoxic fluids e.g. dextrans (and possibly hydroxyethyl starch).

IV Fluids

۲-۱ لیتر بولوس نرمال سالین یا رینگرحتی در صورت وجود هیپرناترمی در اولین برخورد با مرگ مغزی با افت فشار داده شود

پس از درمان بولوس اولیه، مایعات بیمار بر اساس سدیم بیمار (جهت محاسبه حجم از دست رفته بر اثر دیابت بیمزه ناشی از کمبود هورمون ADH) ، حجم ادرار و Insensible Water Loss محاسبه میشود

اگرحجم مایعاتی که بیمار باید دریافت کند زیاد است لازم است حداقل ۱/۳ آن از مایعات کلوئید باشد

- **وازوپرسورها**

دوپامین داروی انتخابی است. اگر بیمار به بیشتر از ۱۰ میکروگرم به ازای کیلوگرم به دوپامین نیاز داشت داروی بعدی را اضافه می کنیم

IV Fluids

- بعد از بولوس اولیه، مایع نگهدارنده شامل سدیم کلراید ۰.۴۵% یا ۰.۲% می باشد. به دلیل عدم وجود سدیم کلراید ۰.۲% در ایران در موارد هیپرناترمی شدید و مقاوم گاهی می توان با احتیاط از دکستروز ۵% استفاده کرد. بدیهی است هیپوکالمی و هیپرگلیسمی با این سرم تشدید خواهد شد که باید مراقب آن بود
- داخل سرمها بر حسب میزان پتاسیم معمولاً ۲۰ mEq KCL در هر لیتر لازم است.
- در سرم بولوس اولیه نباید پتاسیم اضافه کرد
- معمولاً سرعت انفوزیون مایعات ۲ml/kg/hr می باشد

Most patients need vasopressors

- *Pure vasopressors:*

  Vasopressin, phenylephrine

- *Vasopressors with beta-agonist activity:*
  noradrenaline, adrenaline, dopamine

- *Beta agonists:*

  dobutamine

CARDIOVASCULAR

Vasopressin (AVP, Pitressin)

- Low dose shown to reduce inotrope use
- Plays a critical role in restoring vasomotor tone

Vasopressin Protocol

✓ 4 unit bolus

✓ 1- 4 u/hour – titrate to keep SBP >100 or MAP >60

• Noradrenaline

- is most commonly used, with doses adjusted to maintain mean blood pressure > 70 mmHg.
- If dopamine is used maximum dose should be ≤ 10 microgram/kg/min.

Table 2 Suggested cardiovascular goals for the active management of potential organ donors[38]

Parameter	Target
Heart rate	60–120 beats min^{-1}
Arterial pressure	Systolic pressure >100 mm Hg
	Mean pressure ≥70 mm Hg
Central venous pressure	6–10 mm Hg
Urine output	0.5–3 ml kg^{-1} h^{-1}
Electrolytes	Serum sodium 130–150 mmol $litre^{-1}$
	Normal potassium, calcium, magnesium, phosphate
	Glucose 4–8 mmol $litre^{-1}$
Blood gases	pH: 7.35–7.45
	Pa_{CO_2}: 4.7–6 kPa
	Pa_{O_2}: ≥10.7 kPa
	Sp_{O_2} saturation ≥95%
If pulmonary artery catheter inserted	
Pulmonary capillary wedge pressure	6–10 mm Hg
Cardiac index	2.4 litre min^{-1} m^{-2}
Systemic vascular resistance	800–1200 dyn s cm^{-5}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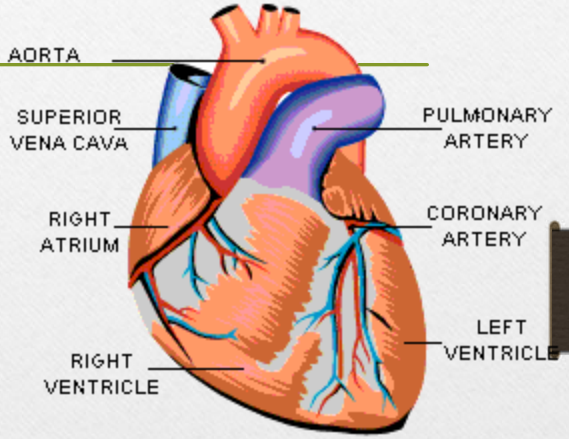
Cardiovascular System

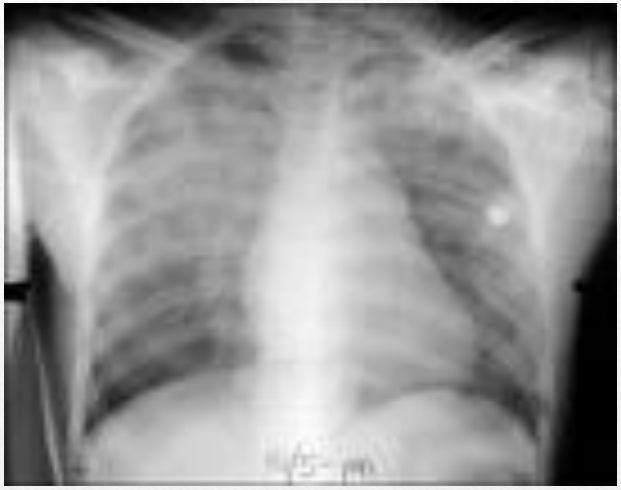
Intensive care management



- "Rules of 100's"
  - Maintain SBP > 100mmHG
  - HR < 100 BPM
  - UOP > 100ml/hr
  - PaO2 > 100mmHg

- Aggressive fluid resuscitative therapy directed at restoring and maintaining intravascular volume. SBP > 90mmHg (MAP > 60mmHg) or CVP ~ 10 mmHg.

Neurogenic Pulmonary Edema



- ✓ Lungs are highly susceptible to injury resulting from the rapid changes that occur during the catecholamine storm
- ✓ Left-sided heart pressures exceed pulmonary pressure,
- ✓ lung tissue is severely injured,
- ✓ interstitial edema and alveolar hemorrhage

Respiratory management

- Pulmonary dysfunction is common in the organ donor due to pneumonia
- aspiration of gastric contents
- neurogenic pulmonary oedema
- pulmonary trauma or ALI / ARDS (which may be secondary to brain injury)

Respiratory management
General prinicples:

- Pulse oximetry
- serial arterial blood gas monitoring
- endotracheal tube suctioning
- physiotherapy
- regular CXRs.

Respiratory management
Nursing care and physiotherapy:

- Routine physiotherapy
- suctioning and mouth toilet
- Strict asepsis during tracheal toilet.
- • PEEP of 5 cmH2O is recommended

Respiratory management

Nursing care and physiotherapy:

- Recruitment may be achieved by periodic increases in PEEP up to 15 cmH2O or by sustained inflations (peak inspiratory pressure of 30 cmH2O for 30 secs.)

Respiratory management

- Diuresis to normovolaemia
- 30° head-up position, cuff pressure ≤ 25cmH2O
- PaCO2: (36-44mmHg)
- pH 7.35-7.45
- FiO2: lowest FiO2 to maintain PaO2 (80mmHg).
- PEEP: 5 cmH2O
- Tidal volume (Vt); 8-10 ml/kg
- Peak inspiratory pressures: ≤ 30cmH2O.

Correct Impaired Gas Exchange and Maximize Oxygenation!

Most organ donors are

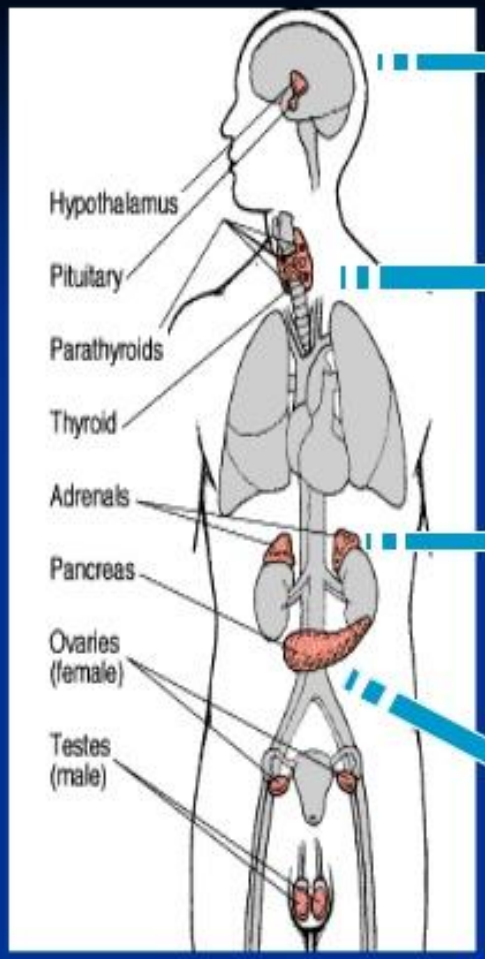
- Chest trauma
- Aspiration
- Long Hospitalization
- Atelectasis or pneumonia
- Impending Neurogenic Pulmonary Edema

Impaired Gas Exchange Goals…

- Goals are to maintain health of lungs for transplant while optimizing oxygen delivery to other transplantable organs
- Avoid over-hydration
- Ventilatory strategies aimed to protect the lung
- Avoid oxygen toxicity by limiting Fi02 to achieve a Pa02 100mmHg & PIP < 30mmHg.

Impaired Gas Exchange Management

- Maintain PaO2 of >100 and a saturation >95%
- Monitor ABG's q2h PEEP 5 cm, HOB up 30^{o}
- Increase ET cuff pressure immediately after BD declaration
- Aggressive pulmonary toilet (Keep suctioning & turning q2h)
- CXR (Radiologist to provide measurements & interpretation)
- CT of chest requested in some cases



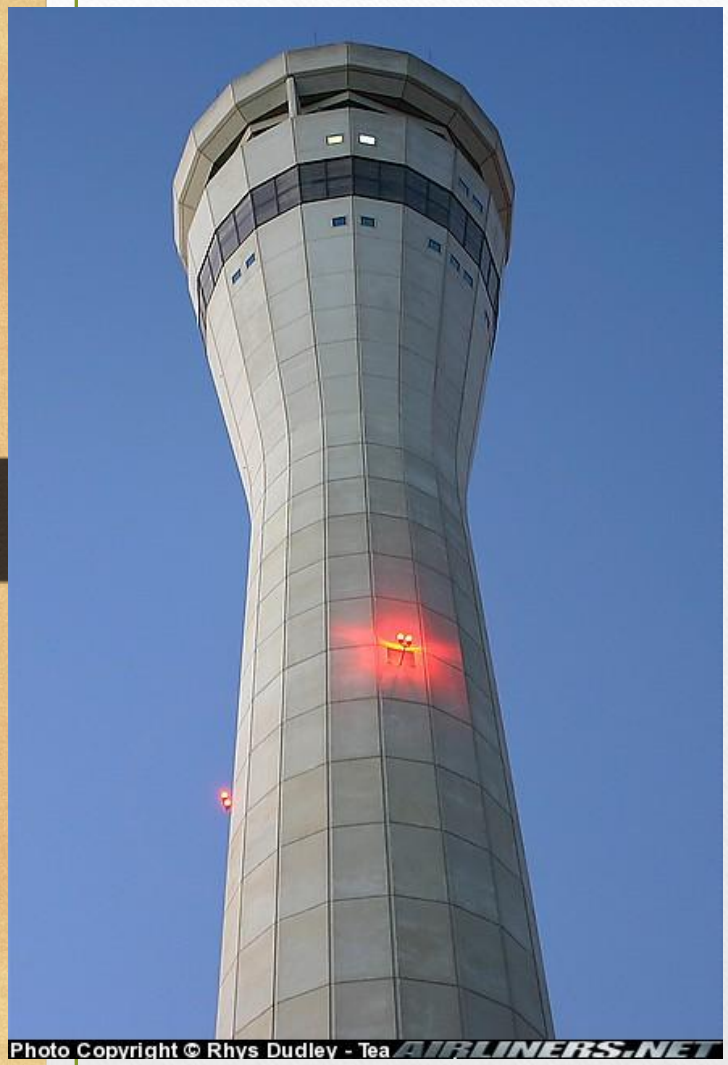
- Failure of hypothalamo-pituitary axis
- Decline in plasma hormone concentration
- ADH, TSH

- Impaired TSH secretion
- Impaired peripheral conversion of T4
- Reduced T3- progressive loss of cardiac contractility
- Increased anaerobic metabolism

- Hypoadrenalism
- Impairs donors stress response
- Cardiovascular collapse

- Decreased insulin secretion
- Hyperglycaemia

Endocrine changes

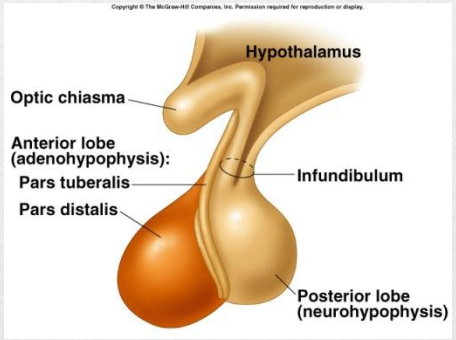


2-24 h after BD

TRH/TSH /GRH/ GH/GnRH/LH/ CRH ❖

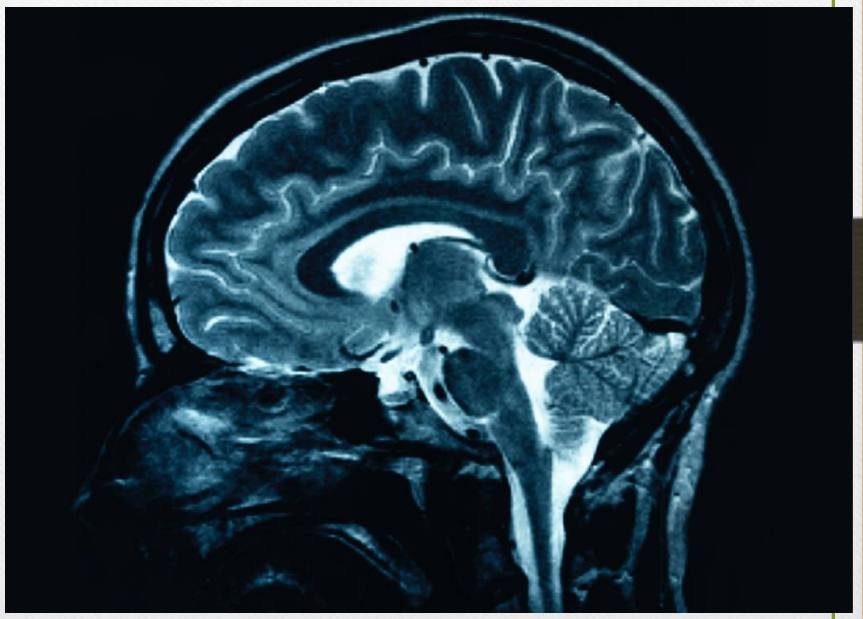
***ADH* ❖**

***BS* ❖**



Normal Pituitary Gland

- Controlled by the hypothalamus
- Releases ADH to conserve water
- Stimulates the release of thyroid hormone



Failure of the Hypothalamus results in:

- Impaired temperature regulation - hypothermia or hyperthermia
- Leads to vasodilation without the ability to vasoconstrict or shiver (loss of vasomotor tone)
- Leads to problems with the pituitary ...

Pituitary Failure results in:

- ADH ceases to be produced = Diabetes Insipidus
- Can lead to hypovolemia and electrolyte imbalances
- Leads to problems with the thyroid gland

Diabetes Insipidus Management

- ✓ Treatment is aimed at correcting hypovolemia
- ✓ Desmopressin (DDAVP) 1 mcg IV, may repeat x 1 after 1 hour.
- ✓ Replace hourly U.O. on a volume per volume basis with MIVF to avoid volume depletion
- ✓ Leads to electrolyte depletion/instability monitor closely to avoid hypernatremia and hypokalemia

Diabetes Insipidus

- Goal is UOP 1-3 ml/kg/hr
- Rule of thumb – 500 ml UOP per hour x 2 hours is DI
- Severe cases – Notify OPC. Assess clinical situation.

Electrolyte Imbalance Management

Hypokalemia

If $K^+ < 3.4$ – Add KCL to MIVF

(anticipate low K^+ with DI & T_4 administration)

Hypernatremia

If $NA^+ > 155$ – Change MIVF to include more free H_20, Free H_20 boluses down NG tube

Calcium, Magnesium, and Phosphorus

Deficiencies here common…often related to polyuria associated with osmotic diuresis, diuretics & DI.

Glycaemic control and nutrition

- Hyperglycaemia is common in organ donors due to large volumes of glucose - containing solutions,
- peripheral insulin resistance
- inotrope infusions.

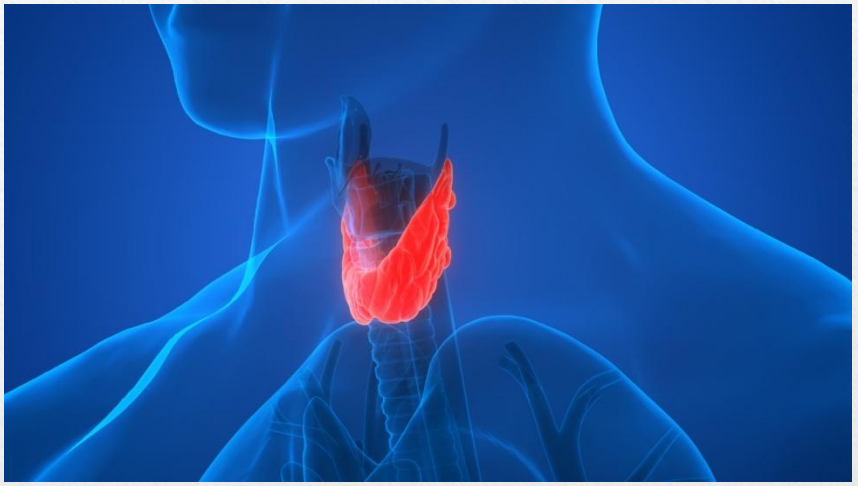
The major consequences

- osmotic diuresis
- ketosis and potential pancreatic graft dysfunction
- • Aim for a blood glucose level 75-150 with an insulin infusion.
- • Routine enteral nutrition should be initiated or continued as tolerated
- • TPN should not be initiated; however when it has been initiated it should be continued.

Thyroid Failure

Leads to:

- ✓ Cardiac instability
- ✓ Labile blood pressure
- ✓ Potential coagulation problems



T4 Protocol

Background

- Brain death leads to sudden reduction in circulating pituitary hormones
- May be responsible for impairment in myocardial cell metabolism and contractility which leads to myocardial dysfunction
- Severe dysfunction may lead to extreme hypotension and loss of organs for transplant

T_4 Protocol

Bolus:

- ✓ 15 mg/kg Methylpred
- ✓ 20 mcg T_4 (Levothyroxine)
- ✓ 20 units of Regular Insulin
- ✓ 1 amp $D_{50}W$

Infusion:

- ✓ 200 mcg T_4 in 500 cc NS
- ✓ Run at 25 cc/hr (10 mcg/hr)
- ✓ Titrate to keep SBP >100

Monitor Potassium levels closely!

hypothermia

Maintaining normothermia

- Hypothermia is common in organ donors due to

- loss of thermoregulatory control
- exposure to cold ambient temperatures
- massive infusions of cold i.v. fluids or blood products.

The consequences of hypothermia

- Arrythmias
- myocardial depression
- Hypotension
- Hypoxia
- Hyperglycaemia
- coagulopathy

Aim for a core temperature > 36°C

- warming blankets
- Fluid warmers
- heated humidifiers in ventilator circuits

Hypothermia Management

- Monitor temperature continuously
- NO tympanic, axillary or oral temperatures. Central only.
- Place patient on hypothermia blanket to maintain normal body temperature

Transfusion thresholds

- **Haemoglobin: A target haemoglobin level of 9-10g/dl is most appropriate to optimize cardiopulmonary function** in the face of haemodynamic instability.
- A level of 7 g/dl is the lowest acceptable limit for management of stable donors in the ICU

Other blood indices

- There are no defined targets for platelet concentration, INR, PT or APPT.

- Platelet, fresh frozen plasma or cryoprecipitate replacement is indicated for clinical bleeding only.

Transfusion

- CMV negative blood products should be used.
- **Antifibrinolytics such as epsilon aminocaproic acid may cause microvascular thrombi in donor organs and** should be avoided.

Anemia

- ✓ Hematocrit < 30% must be treated
- ✓ Transfuse 2 units PRBC's immediately
- ✓ Reassess 1° after completion of 2nd unit and repeat infusion of 2 units if HCT remains below 30%
- ✓ Assess for source of blood loss and treat accordingly

Antimicrobial therapy

- The principles of antimicrobial therapy are similar to those in patients who are not organ donors. Antimicrobial therapy should be based on the results of gram staining or culture or may be empirical
- Nephrotoxic antimicrobials should be avoided when possible.
- Prophylactic antimicrobials are not routinely indicated.

Incidence of pathophysiologic changes following Brain Death:

- Hypotension 81%
- Diabetes Insipidus 65%
- DIC 28%
- Cardiac arrhythmias 25%
- Pulmonary edema 18%
- Metabolic acidosis 11%

Physiologic changes During Brain Stem Death – Lessons for Management of the Organ Donor.

The Journal of Heart & Lung Transplantation Sept 2004 (suppl)

Specific organ care liver

- Na < 150
- Correcting electrolytes imbalances
- Liver enzymes checking
- CT /sonography

Donor Factors Affecting Liver Transplant Outcome

Not Amenable to Change	Amenable to Change
Age	ICU LOS
Sex	Ischemia Times
ABO Blood Type	Hypernatremia
Cause of Death	Nutrition and Liver Glycogen
Macrosteatosis	Hypotension/Vasoactive Drugs
Endotoxins and Cytokines	Preconditioning for I/R

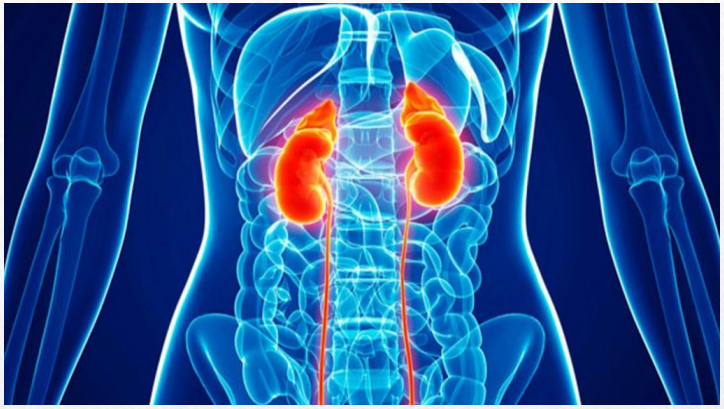
Powner et al: Prog Transplantation 2004;14:241-249

Nutrition and Liver Glycogen

- **Organ donors typically with nutritional depletion**
- **Hepatic glycogen and ATP energy source**
  - Source of energy during warm/cold ischemia
  - Biopsy proven low glycogen stores associated with worse outcome[1,2]
  - Animal experiments support nutritional supplementation to restore liver glycogen[3,4,5,6]
- **Potential benefit of balanced nutritional support[3]**
  - Moderate amounts of carbohydrates
  - Lipids, long-chain triacylglycerols/fish oil
  - Amino-acids

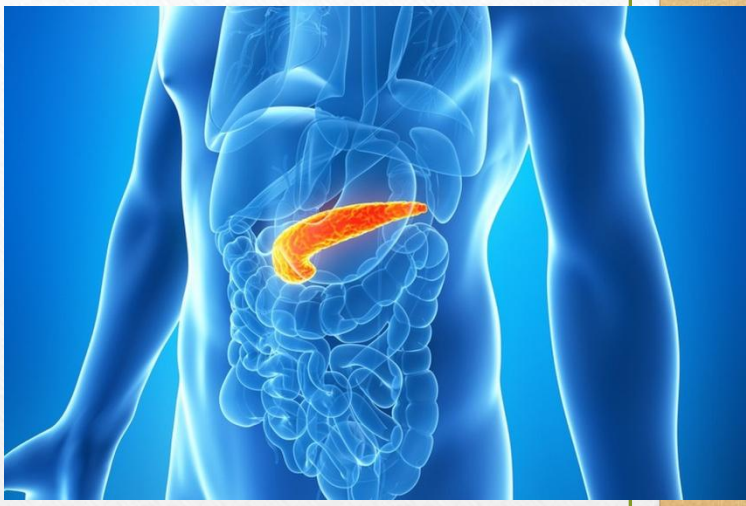
1. Adam Txp Proceed 1993; 25: 1536-1537
2. Lanir Hepatology 1988; 8: 471-475
3. Singer Nutrition 2001; 17: 948-952
4. Boudjema Transplantation 1990; 50: 943-948
5. Palombo Txp Proceed 1989; 21: 1299-1300
6. Cywes Hepatology 1992; 16: 1271-1279

Specific organ care kidney



- Treat Diabetes incipidus
- UA
- BUN/ Creatinine
- dopamine 1-3 mcg/kg/min

Specific organ care pancreas



- Serial Amylase, Lipase
- Blood Glucose = or lesser 150 mg/dl
- Lower glucose containing fluids
- Restricted glucose control

What to be monitored?

- ECG
- CVP
- arterial blood pressure
- urine output
- central body temperature,
- capnography and pulse oximetry.
- PCWP
- Acid-base balance, electrolyte, glycaemia and haemoglobin concentrations

آزمایشات و گرافی های لازم در مرگ مغزی

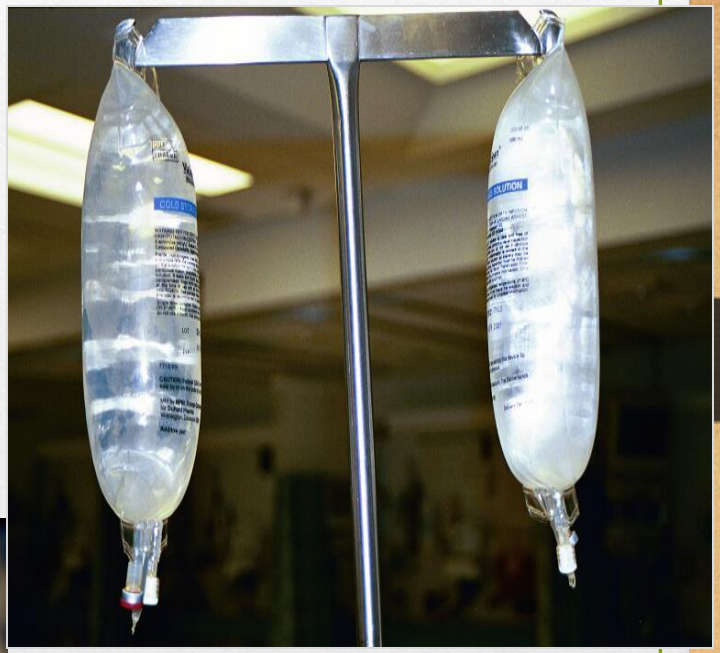
- **ABG**
- **BUN, creatinine, and electrolyte values**
- **Hb, HCT, WBC and platelet counts**
- **Serum Amylase, total Bilirubin, Alkaline Phosphates, SGOT, and SGPT,HBsAg,HBsAb,HBcAb,HCVAb,HIV**
- **Coagulation profile (including PT, PTT ,INR)**
- **U/A & U/C**
- **EKG & CX-RAY**

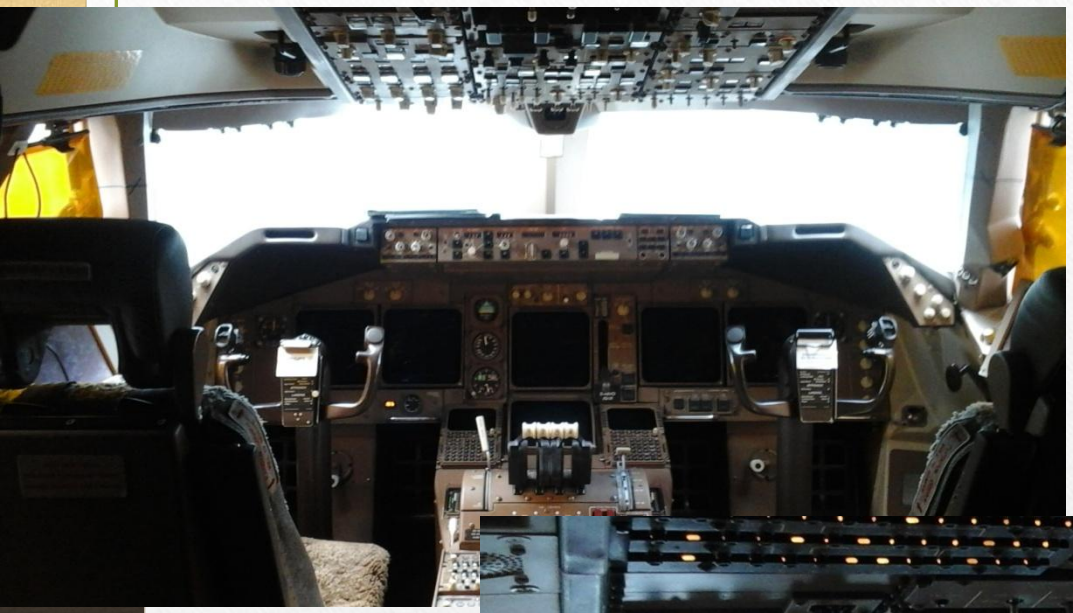
Organ Donation Process

The Teams...

Organ Preservation Time

- Heart: 4-6 hours
- Lungs: 4-6 hours
- Liver: 12 hours
- Pancreas: 12-18 hours
- Kidneys: 72 hours
- Small Intestines: 4-6 hours





Organ donation

Thanks for your attention