Donation Process

- Hospital notifies OPO of potential donor
- OPO coordinator assesses potential donor and takes over care after brain death
- Laboratories and ancillary tests performed
- Organ placement
- Arranging OR
- Process may take 12-24 hours
Brain Death

- Clinical diagnosis: loss of cortical and brainstem function
  - coma with established cause in absence of hypothermia and CNS depressants
  - absent spontaneous movements without posturing
  - positive apnea test
    - $p\text{CO}_2 > 55$ after 3 min. without spontaneous respirations (in absence of muscle relaxants)
  - absent cranial nerve reflexes
    - corneal, occulocephalic, dilated pupils, occulovestibular, no response to pain in head, absent gag
Brain Death

• Confirmatory tests
  – EEG
  – cerebral blood flow
Non-Heart Beating Donors

• Terminal injury or disease process without brain death
• Life support discontinued and heart allowed to stop
Donor Management

• Cardiopulmonary resuscitation
• Hemodynamic support
  – volume expansion
    • blood, crystalloids
  – vasopressors
    • dopamine, neosynephrine, levophed
    • vasopressin
• Oxygenation and pH
Donor Management

• Thermoregulation
  – hemodynamic instability
  – cardiac arrhythmia, arrest

• Infection control
  – sterile techniques
  – surveillance cultures
  – CXR
  – antibiotic therapy
Donor Management

• Alpha blockers
  – phentolamine, phenoxybenzamine
    • prevent vasospasm and reduce ischemia

• Calcium channel blockers
  – reduce ischemia

• Free T3
  – Reduce ischemia
Donor Management

• Free radical scavengers
  – steroids
    • also membrane stabilizer
  – allopurinol
  – superoxide dismutase

• Prostaglandin E1
  – vasodilator
  – reduces platelet aggregation
  – cytoprotective
  – counter free radical damage
Donor Assessment

• UNOS mandated information
  – age, gender, race, height/weight
  – ABO blood type
  – cause of death
  – history of hospital treatment, current status
  – indications of sepsis
  – social history
  – hemodynamic status
  – bilirubin, AST/ALT, PT, BUN/Cr, electrolytes, CBC, ABG
  – HIV, hepatitis, CMV, HTLV, VDRL/RPR serologies
Donor Assessment

- Sodium
- Albumin
- Length of hospitalization
- Feeding status
- Urine output
Organ Quality

- Surgical assessment remains best tool
- General exploration
- Physical properties of liver
  - color
  - texture
  - consistency
- Arterial vasculature
- Flush
- ? Biopsy
Donor Operation

• Often involves several teams
  – heart
  – lung
  – liver
  – pancreas
  – kidneys

• May take from 2-4 hours

• Brain death note and consent
Donor Operation

• Midline incision suprasternal notch to pubic symphysis
• General exploration
• Isolation of supraceliac and infrarenal aorta
• Isolation of vena cava
Donor Operation

- Dissection of liver
  - ligamentous attachments
  - bile duct and flushing
  - hepatic artery
  - portal vein
- Exsanguination and flushing
- Topical cooling
Organ Preservation

• Hypothermia
  – slows metabolism
  – inhibits catabolic enzymes
  – inhibits ATP dependent ion pumps
    • cellular edema
University of Wisconsin Solution

- **Lactobionate**
  - impermeant
  - Ca\textsuperscript{++} chelator
    - inhibits Ca\textsuperscript{++} dependent processes
      - phospholipases, proteases, endonucleases
  - iron chelator
    - reduce oxygen free radical production/reperfusion injury
University of Wisconsin Solution

- High K⁺, low Na⁺ concentration
  - helps prevent intracellular K⁺ depletion and Na⁺ accumulation
  - not necessary to prevent cell swelling
- Phosphate
  - H⁺ buffer, ATP precursor
- Hydroxyethyl starch (HES)
  - colloid to suppresses cell swelling
  - not necessary for simple cold storage
University of Wisconsin Solution

- Adenosine
  - precursor for ATP
- Glutathione
  - oxygen free radical scavenger
- Allopurinol
  - xanthine oxidase inhibitor
- Magnesium
  - enzyme cofactor
University of Wisconsin Solution

- Dexamethasone
  - membrane stabilizer
Donor Selection

• Liver
  – ABO
  – HLA
  – size

• Kidney/Pancreas
  – ABO
  – HLA
Arranging the Transplant

• Notification of patient
• Coordinator notifies team members
  – ICU
  – OR
  – blood bank (requires 4-6 hours notice)
  – anesthesia
  – perfusion
• Continual dialogue between donor/recipient teams for timing
Liver Transplant

• General anesthesia
• Hemodynamic monitoring
  – pulmonary artery catheter
  – arterial catheter
• Transfusion therapy
  – PRBC, FFP, platelets, cryoprecipitate
  – hemoglobin
  – prothrombin time, thromboelastogram (TEG)
Hepatectomy

• General exploration
• Incision of ligamentous attachments
• Division of bile duct
• Division of hepatic artery
• Dissection of portal vein
• Dissection of vena cava
Anhepatic Phase

- Venovenous bypass
- Worsening of coagulopathy
- Assure hemostasis of retroperitoneum
Implantation

- Suprahepatic vena cava
- Infrahepatic vena cava
- Portal vein
- Hepatic artery
- “Piggyback”
Reperfusion

- Portal flushing
  - crystalloid
  - blood
- Cardiac arrhythmia
- Hemodynamic instability
- Hemostasis
Biliary Reconstruction

- Choledochocholedochostomy
- Roux-en-y
- ? Biliary drain
- Cholangiogram
Special Considerations

• Portal vein thrombosis
  – SMV graft
  – portocaval anastomosis

• Aortic graft
Postoperative Care

- Intensive care unit
- Anesthesia not reversed
- Hemorrhage
- Vascular patency
- Immunosuppressive therapy
  - CYA, FK 506
  - steroids
  - Azathioprine, Mycophenolate Mofetil
Postoperative Care

• 1-2 days in ICU
• 5-10 days on ward
• Physical therapy
• Nutritional repletion
• Prophylactic antibiotics
• Immunosuppressive adjustment
Kidney Transplant

• Pre-op studies
  – CXR, EKG, CBC, chem.panel
  – ? need for dialysis
  – immunosuppressives
  – antibiotics

• Intra-op management
  – maintain BP
  – volume repletion
Kidney Transplant

- Retroperitoneal approach
- Isolate iliac artery/vein
  - ligation of lymphatics
- Ureteral anastamosis
Postoperative Care

• Early
  – urine output
  – bleeding
  – renal study
  – cardiopulmonary
Immunosuppression

Corticosteroids

- anti-inflammatory
- sequestration of T cells into lymphoid tissue
- inhibits production of T cell promoting cytokines
- doses of 250-1000 mg peri-transplant
- doses of 5-10 mg chronically
Immunosuppression
Corticosteroids

• adverse reactions
  – cataracts, glaucoma
  – Na+/fluid retention
  – HTN
  – muscle weakness
  – PUD
  – Cushing syndrome
  – osteoporosis, avascular necrosis hip, compression Fx
Immunosuppression
Antimetabolites

• Azathioprine (Imuran)
  – interferes with DNA/RNA synthesis
  – inhibits differentiation/proliferation of t & B lymphocytes
  – adverse reactions
    • leukopenia, nausea, neoplasia
  – 100-150 mg qd
  – largely replaced by mycophenolate mofetil
Immunosuppression

Antimetabolites

• Mycophenolate Mofetil (Cellcept)
  – selectively inhibits inosine monophosphate dehydrogenase in de novo pathway of purine synthesis
    • this is uniquely essential for T & B lymphocyte proliferation and function
  – adverse reactions
    • leukopenia, diarrhea, vomiting
  – 500-1000 mg bid
Immunosuppression
Calcineurin Inhibitors

• Cyclosporine (Sandimmune, Neoral)
  – produced by fungus Beuavaria nivea
  – preferential inhibition of T lymphocytes by inhibiting production & release of IL-2
  – adverse reactions
    • renal toxicity, HTN, tremor/neurotoxicity, hirsutism, gum hyperplasia
  – dose 5-10 mg/kg bid
  – trough level 300-350 early, 200-250 late
Immunosuppression
Calcineurin Inhibitors

• FK 506 (Prograf, Tacrolimus)
  – macrolide antibiotic
  – inhibits IL-2 production
  – adverse reactions
    • renal toxicity, tremor/headache/neurotoxicity,
      diarrhea, nausea, HTN, hyperglycemia
  – .05-.1 mg/kg bid
  – trough level 10-15 early, 5-10 late
Immunosuppression

Sirolimus (Rapamune), Everolimus (Certican)

- TOR inhibitors
- TOR is key regulatory kinase in cell division
- No renal toxicity
- Impaired wound healing, hyperlipidemia, mouth ulcers, noninfectious pneumonitis
Immunosuppression
Antibody Preparations

• Polyclonal
  – ATGAM
  – Thymoglobulin

• Monoclonal
  – Muromonab CD3 (OKT3)
  – Basiliximab (Simulect)
  – Daclizumab (Zenapax)
Immunosuppression

Antibody Preparations

- Polyclonals
  - multiple antibody preparations directed against T lymphocyte antigens
  - deplete number of circulating cells
  - inhibit cell function
  - monitor CD2 & CD3 cells for effect
Immunosuppression
Antibody Preparations

- OKT3
  - Murine antibody directed against CD3 antigen
  - inhibits CD3-TCR interaction
  - prevents antigen recognition and activation
  - cytokine release syndrome
  - neurologic effects
  - sensitization
Immunosuppression
Antibody Preparations

• Basiliximab/Daclizumab
  – chimeric/humanized antibody
  – high affinity binding to α chain of IL-2 receptor
  – inhibits IL-2 binding and IL-2 mediated activation of T lymphocytes
  – no cytokine release syndrome