

The Pediatric Transplant
Protocols and Guide to
Management of
Transplant Patients



Stanford
Children's Health

Lucile Packard
Children's Hospital
Stanford

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PREFACE

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1. Liver Transplant

a. Indications for Transplant

i. Acute Liver Failure

1. Severe hepatic dysfunction occurring within 8 weeks of onset of illness, with no known underlying chronic liver disease in patients from birth through 17 years of age with a liver-based coagulopathy (not corrected with vitamin K) with an INR ≥ 1.5 or PT ≥ 15 seconds in patients with encephalopathy or an INR ≥ 2.0 or PT ≥ 20 seconds in patients without encephalopathy.
2. Common Causes Include:
 - a. Indeterminate
 - b. Viral/ Infectious
 - c. Metabolic/ Genetic
 - d. Wilson Disease
 - e. Drug Induced
 - f. Autoimmune
3. Complications of acute liver failure include, but not limited to:
 - a. Hepatic encephalopathy
 - b. Cerebral edema
 - c. Hypercoagulability
 - d. Hypoglycemia
 - e. Multi-Organ Failure
 - f. Acid-Base Disturbances
 - g. Sepsis
4. Poor prognostic indicators in the setting of ALF include:
 - a. Encephalopathy
 - b. Renal failure
 - c. Acidosis
 - d. Rising bilirubin with falling liver enzymes
 - e. Elevated INR
 - f. Hypothermia
 - g. Hypoglycemia
5. Pearls of Management:
 - a. Survival correlates with the stage of coma reached and the extent of renal failure and acidosis.
 - b. Following the progression of liver size is important in patients with ALF-once the liver begins to shrink, the process is irreversible.
 - c. Early intubation with hyperventilation and elevation of the head can help delay the onset of significant cerebral edema.

- d. CVVH may be required to help the body clear toxins as liver failure progresses or if renal failure occurs.
- ii. Chronic Liver Disease
 - 1. Caused by:
 - a. Cholestatic Liver Disease
 - i. Extrahepatic biliary atresia
 - ii. Sclerosing cholangitis
 - iii. Alagille Syndrome
 - iv. Progressive Familial Intrahepatic Cholestasis
 - 1. FIC1 (Byler's Disease)
 - 2. BSEP Disease
 - 3. MDR3 Disease
 - b. Metabolic/Genetic liver disease
 - i. Alpha-1-antitrypsin deficiency
 - ii. Wilson's Disease
 - iii. Tyrosinemia
 - iv. Glycogen storage diseases
 - v. Cystic Fibrosis
 - vi. Hyperoxaluria
 - vii. Defects of Mitochondrial Function
 - viii. Neonatal Iron Storage Disease
 - ix. Protein C Deficiency
 - x. Urea Cycle Defects
 - c. Hepatitis
 - i. Autoimmune
 - ii. Neonatal Hepatitis
 - iii. Hepatitis B and C
 - d. Malignancy
 - i. Hepatoblastoma
 - ii. Hepatocellular Carcinoma
 - iii. Sarcoma
 - iv. Hemangioendothelioma
 - e. Miscellaneous Diseases
 - i. Budd-Chiari Syndrome
 - ii. TPN Associated liver disease
 - iii. Cryptogenic Cirrhosis
 - iv. Caroli's Disease
 - 2. Complications include:
 - a. Failure to thrive
 - b. Splenomegaly

- c. Gastrointestinal bleed from varices
 - d. Hypoalbuminemia
 - e. Ascites
 - f. Coagulopathy
 - g. Pruritus
 - h. Hepatopulmonary syndrome
 - i. Hepatic encephalopathy
- b. Evaluation
- i. Consults:
 1. Hepatologist
 2. Liver Transplant Surgeon
 3. Dietitian
 4. Social Worker
 5. Child Development vs. Child Psychiatry
 6. Other Specialties consulted as indicated based on their underlying diagnosis (i.e. PT/OT, Pulmonology, Cardiology, Genetics, Renal, etc.)
 - ii. Laboratory Evaluation:
 1. Blood Type x 2 (one may be from outside facility if documentation available)
 2. Chem 15, Direct bilirubin, Magnesium, Phosphorus, GGT, Cholesterol and Triglyceride
 3. CBCD
 4. Ammonia
 5. Coagulation Panel
 6. HIV-testing
 - a. If <2 years old send HIV type 1 and 2 antibody and HIV RNA PCR
 - b. If >2 years old send HIV type 1 and 2
 - i. If negative, no further work up
 - ii. If positive obtain HIV RNA PCR and ID consult
 - c. If results needed in <24 hrs send rapid HIV and RNA PCR (must call lab to notify them of sample)
 7. HTLV I/II
 8. CMV/ EBV IgG and IgM
 9. Hepatitis A Antibody IgM
 10. Hepatitis B Surface Antigen, Hepatitis B Surface Antibody, Hepatitis B Core Antibody
 11. Hepatitis C Antibody IgG
 12. Vitamin A, Vitamin E, Vitamin D25 hydroxy for pt with long standing liver disease
 13. Varicella IgG (if greater than 5 years old)

14. PPD (for children <5 years old) or Quantiferon (for children >5 years old)
- iii. Diagnostic Imaging Evaluation:
 1. Abdominal Ultrasound with Doppler (to assess hepatic echotexture and patency of hepatic vessels and portal vein)
 2. Echocardiogram (Assess cardiac anatomy and function.)
 - a. If PFO present must be closed prior to transplant only if shunts right to left
- iv. Liver Biopsy (as requested by team)
 1. For acute liver failure patients- consult IR or transplant surgery on arrival for stat biopsy. Must request:
 - a. Viral culture on liver tissue (EBV, CMV, adeno, parvo)
 - b. EBV, CMV, adeno, and parvo (if PCR positive) staining
 - c. Immunohistochemical staining
- v. Additional work up for FHF
 1. Exposure History: Must be done as part of the evaluation of FHF to identify potential causes. Questioning to include:
 - a. Family history of TB
 - b. Travel history—international travel and within the US during the past 2 years
 - c. Significant time living in another country, and birth in another country and vaccines related to this, i.e. BCG
 - d. Animal exposure—pets, farm animals, petting zoos
 - e. Recent insect bites—ticks, mosquitoes
 - f. Sexual activity
 - g. High risk foods—unpasteurized dairy products
 2. Additional laboratory evaluation (in order of priority)
 - a. Hepatitis E IgM
 - b. EBV nuclear Ag AB, EBV virus early Ag IgG
 - c. Parvovirus IgG, IgM
 - d. Respiratory viral culture of nasopharynx
 - e. Respiratory DFA
 - f. Stool culture if diarrhea
 - g. PPD placement
 - h. Acetaminophen level if exposed
 - i. Urine toxicology screen if concern
 - j. Ceruloplasmin (>1 years old)
 - k. Ferritin level (<3 mo old)
 - l. ANA
 - m. Anti Smooth muscle AB
 - n. Liver kidney microsomes AB

- o. Immunoglobulin levels (IgG, IgM, IgA)
- p. T cell phenotyping/subset 893148 (Mayo)
- q. B cell phenotyping (Mayo)
- r. pANCA
- s. Soluble liver AB
- t. Liver cytosol Auto AB-1
- u. Mitochondrial AB M2, serum
- v. IgG4
- w. Factor 5 level
- x. Alpha 1 Antitrypsin phenotype
- y. Lactate level
- z. Pyruvate level
- aa. AFP
- bb. CRP
- cc. ESR
- dd. Plasma acylcarnitine profile
- ee. Serum amino acids
- ff. Urine organic acids
- gg. Urine reducing substances

c. Listing for Transplant

- i. The United Network for Organ Sharing (UNOS)
 - 1. Maintains a centralized computer network linking all organ procurement organizations and transplant centers
- ii. The Pediatric Model for End Stage Liver Disease (PELD)
 - 1. This is a continuous severity scale that is for candidates under the age of 12. The score incorporates a formula based on Total Bilirubin, INR, Albumin and Growth Failure
 - a. Status 1A:
 - i. Fulminant Hepatic Failure (FHF)- onset of hepatic encephalopathy within 8 weeks of the first symptoms of liver disease, absence of pre-existing liver disease with one of the following:
 - 1. Ventilator dependent
 - 2. Dialysis or CVVH
 - 3. INR>2.0
 - ii. Primary Non-Function (PNF) of a transplanted liver within 7 days. Candidate must meet two of the following conditions to qualify for PNF:
 - 1. ALT \geq 2000
 - 2. INR \geq 2.5

3. Arterial pH \leq 7.3
 4. Total Bilirubin \geq 10
 5. Acidosis defined as having arterial pH \geq 7.3 or venous pH 7.25 and/or lactate \geq 4.0
 6. Qualifying lab values may be drawn as soon as the day following transplant, up to 7 days post-transplant
- iii. Hepatic Artery Thrombosis (HAT) in a transplanted liver within 14 days following implantation
 - iv. Acute Decompensated Wilson's Disease- A clinical narrative is required on the justification form completed in UNet to initially list or extend a candidate with acute decompensated Wilson's disease as a status 1A
 - v. Pearls:
 1. Candidates must be initially listed or extended within 48 hours of the draw date of qualifying lab values.
 2. All lab values used to qualify a candidate for 1A status must be from the same lab draw
- b. Status 1B:
- i. Must have calculated PELD $>$ 25 and meet one of the following criteria:
 1. Ventilator
 2. GI bleed requiring 30ml/kg RBC replacement within previous 24 hours, initial listing on the day of, or the day following transfusion. To extend a candidate using this criterion, the candidate must experience a subsequent GI bleed requiring a transfusion of 30cc/kg during the 7 day period prior to the extension date
 3. Dialysis or CVVH
 4. GCS $<$ 10, candidate must be initially listed or extended within 48 hours of GCS evaluation date
 - ii. Pearls
 1. A user cannot change the criterion for Status 1A or 1B on an extension; the user can only change the supporting data for the same criterion.
 2. If a candidate's criterion for Status 1A or 1B has changed, the user must submit a new, initial Status 1A or 1B justification form
- d. Recertification
- i. The Coordinators recertify the patients listing as follows:
 1. Status 1A/1B weekly
 2. PELD renew based on labs depending on the score

- e. ABO Mismatch
 - i. If A1 donor to O recipient:
 1. Draw antibody (specify Anti-A in order comments) and isohemagglutinin titers
 - ii. If B donor to O recipient:
 1. Draw antibody (specify Anti-B in order comments) and isohemagglutinin titer
 - iii. If AB donor to O send both Anti-A and Anti-B isohemagglutinin titers
 - iv. Pending isohemagglutinin titer copies pt may require admission to PICU for plasmapheresis/line placement prior to transplant
 1. Obtain pediatric Nephrology consult
 - v. Notify Transfusion Services (Attending MD) when patient opened to all blood groups and when donor blood type obtained
- f. Multi-Listing
 - i. Pts have the right to be listed at multiple centers. The information is provided to the parents at the time of the evaluation. Additional costs incurred from being listed at multiple centers may be the responsibility of the parents
- g. Management of ALF Patients
 - i. Any patient admitted for ALF, must have adequate access at all times, at the minimum 2 PIVs. If unable to obtain, consult PICU or the surgical team immediately to insert a central line
 - ii. Treatment will include the following as clinically indicated:
 1. Protonix 1mg/kg IV BID
 2. Octreotide (for portal HTN or GI bleed) 1mcg/kg/hr up to 5mcg/kg/hr
 3. N-acetylcysteine 150mg/kg IV q 24hr (infused continuously)
 4. CVVH (w/o Heparin) is started when:
 - a. Renal insufficiency/failure (as evidenced by oliguria, elevated Cr, volume overload or electrolyte imbalance)
 - b. Hyperammonemia resistant to treatment
 - c. Hepatorenal syndrome
 5. Vitamin K 2.5-10 mg IV QD
 6. Antibiotics according to transplant team
 7. Lasix/ Dopamine/ Epinephrine/ Neosynephrine/ Nipride drips as indicated. Please note that high doses of vasopressor drips may warrant deactivation on the transplant list
 8. Use sedation and pain medications only if absolutely necessary
 - a. Continual assessment of mental status is critical, agents of choice per transplant team

- b. Non-contrast head CT to evaluate for Cerebral Edema or Intracranial Bleed
- 9. Blood Products
 - a. PRBC: Transfuse to keep Hct >23
 - b. Platelets: Transfuse if <20,000 or active bleeding
 - c. FFP: Transfuse if PT/INR >2.5 or active bleeding
 - i. Consider TEG (thrombelastograph clot profile) to further assess bleeding risk
 - d. Cryo: Transfuse if Fibrinogen <100
 - e. Adjust maintenance fluids with transfusions
- 10. Treatment (if suspected autoimmune)
 - a. If no viral inclusions on biopsy and positive for CD3, CD4, or CD8 give 1mg/kg IVIG followed by 2mg/kg solumedrol daily (max dose 60mg daily), transition IV steroids to PO when clinically appropriate
 - b. If liver biopsy only positive for CD20, CD56, CD 138, or CD163 consult Immunology whether to treat
 - c. If improves with treatment consider TPMT enzyme level prior to discharge
- iii. Pearls:
 - 1. Secondary hyperaldosteronism in liver failure is from hyponatremia. Patients are total body sodium overloaded, but due to poor synthetic function of the liver, resulting in low albumin, low intravascular oncotic pressure, low serum sodium, causing sodium and fluid third spacing. There is high extravascular sodium and low intravascular sodium, fooling the adrenals into producing more aldosterone and increase serum sodium.
 - 2. Don't correct hyponatremia rapidly, can cause central pontine myelinosis. Giving sodium for hyponatremia can cause GI bleed by increasing portal pressure. Treat hyponatremia in liver failure patients with fluid restriction.
- h. Pre-Operative Orders
 - i. Laboratory:
 - 1. Type and Screen with Prbc, Plt, FFP and Cryo on-call to OR (include Donor blood type in order for blood products)
 - 2. Chem 15, Magnesium, Phosphorous, GGT, CBCD, Coagulation Studies
 - 3. UA/Urine Culture
 - 4. Blood Culture (if recent history of infection or pre-existing line)
 - 5. If URI/LRI symptoms send respiratory PCR. If no time to wait for results consider IVIG 400mg/kg

- ii. Diet:
 1. Must be NPO a minimum of 6 hours before going to the OR. Please refer to metabolic section for specific details.
- iii. Medications
 1. All preoperative medications are stopped, unless otherwise indicated (i.e. metabolic patients)
 2. Ampicillin (50mg/kg) and Cefotaxime (50mg/kg) are ordered one time unscheduled to be administered in the OR. Confirm antibiotic preference with Fellow or Attending. Zosyn 100mg/kg/dose (max 4g) if pt in house prior to surgery or history of infections
- iv. Radiology:
 1. Abdominal Xray (Chest Xray, as well, if a larger pt to ensure mid-axilla to pelvis obtained on xray) specifying foreign body as the reason and under special instructions be sure to include OR will call for Xray prior to closure, stat wet read called to OR
- v. Consent:
 1. Orthotopic Liver Transplant- be specific if reduced size or split liver; if combined Liver/ Kidney – obtain two separate consents in case unable to do the kidney secondary to patient’s instability; Multi-Visceral (liver/ intestine/ pancreas transplant.) Include feeding gastrostomy vs. jejunostomy, revision of roux-en-Y, possible veno-venous bypass or possible splenectomy, as indicated.
 2. All Attending MDs that may assist in OR must be included on consent
 3. MUST include if applies: CDC high risk, DCD and/or ABO mismatch
- vi. Notify:
 1. OR, Anesthesia, and on-call Perfusionist if veno-venous bypass is indicated
- vii. Living Related Liver Transplant:
 1. Donor
 - a. Consent for evaluation obtained at time of work up
 - b. Work up includes all transplant eval labs with the addition of RPR and urine pregnancy (if female), CXR, EKG, and abdominal MRI
 - c. Consent for surgery should read Living Donor Hepatic Resection, intraoperative ultrasound, intraoperative cholangiogram, gonadal vein removal (if female.)
 - d. Order intraoperative ultrasound and cholangiogram. Order T&S, 2 u prbc, SCDs, and 1g kefzol to be given in OR
 - e. Call SUH radiology department the day before to ensure ultrasound and cholangiogram are ordered
 - f. Check for donor directed blood

2. Recipient
 - a. Consent must have signature of someone other than the donor's
 - b. Consent should read Living Related Liver Transplant, possible roux-en-Y, possible splenectomy, possible veno-venous bypass
 - c. Notify OR, Anesthesia and on-call Perfusionist if veno-venous bypass is required
3. Pearls
 - a. Check LPCH and SUH for compatible vessels and discuss with attending surgeon what is available and consideration of the use of cryo vessels. If additional cryo vessels required, contact the main center at 888-427-9654 and ask for the LPCH representative
 - b. DO NOT give blood products pre-operatively without consulting surgeon
 - c. If Liver-Kidney Transplant, send 10cc red top to Histocompatibility Lab for kidney crossmatch. Notify Histo Lab at 723-6346 and send specimen to Transfusion Services for pick-up
- i. Post-Operative Management
 - i. Basic Principles:
 1. Immunosuppression
 - a. Steroids
 - i. Solumedrol or Solu-Cortef (surgeon will specify form and dose based on clinical status of patient)—generally, Solucortef 10mg/kg administered in OR
 - ii. Taper with Solumedrol started on POD#1, 5/4/3/2/1mg/kg. Surgeon will confirm dosing as indicated by the status of the patient
 - iii. Prednisone started once tolerating po diet and Solumedrol taper complete
 - b. Thymoglobulin (Antithymocyte Globulin- Rabbit) given as indicated (typically used for repeat transplants, ABO incompatible, or autoimmune patients)
 - i. 1-2mg/kg/dose x 2-5 doses (Duration to depend upon clinical response)
 1. Pre-Medicate with:
 - a. Tylenol (15mg/kg; Max 650mg)
 - b. Benadryl (1mg/kg; Max 50mg)
 - c. SoluCortef 5mg/kg(max 100mg) first dose, then 3mg/kg(max 75mg) for subsequent doses
 2. Send transplant monitoring panel after Thymo doses completed to determine if adequate response (CD3<20% and absolute <100).

If concern for infection send after 1st or 2nd dose to help determine number of doses needed

- c. Basiliximab given as indicated
 - i. Dose: <35kg 10mg, >35kg 20mg on POD 0 and 4
 - ii. Pre-Medicate with:
 - 1. Tylenol (10mg/kg; Max 650mg)
 - 2. Benadryl (1mg/kg; Max 50mg)
- d. Prograf (0.1-0.3mg/kg) q 12 hours (8A/8P)—dose initiated by surgeon, NG form while intubated then transition to PO as soon as able
 - i. If inadequate levels achieved at 0.5 mg/kg, consider starting Fluconazole (3mg/kg/day)

Time Post-Op (Months)	Prograf Level	Prograf Level for Hepatoblastoma
0-0.5	12-15	10-12
0.5-1	10-12	8-10
1-3	6-8	6-8
4-6	4-7	4-7
>6	1-7	1-7

- e. Dual or Triple Therapy considered when:
 - i. ABO mismatch
 - ii. Rejection
 - iii. Malignancy
 - iv. Autoimmune Disorder
 - f. CellCept (Mycophenolate Mofetil) 300-450mg/m² BID, max dose 600mg/m² BID (must be 1 hr apart from prograf dose and 2 hrs apart for magnesium supplements)
 - i. Serum levels MTh with target level MPA 1-3.5 and MPA glucuronide 35-100
 - g. Sirolimus
 - i. Generally not started in the 3 week post-operative period secondary to delayed wound healing.
 - 1. Once daily (12N)
 - 2. Serum levels MTh and target level dependent on target FK level
2. Antibiotics/ Antivirals
- a. Perioperative Coverage: 1st dose given intraoperatively
 - i. Cefotaxime 50mg/kg/dose (max 1 gram) q 6hr x 48hr and Ampicillin 50mg/kg/dose (max 1 gram) q 6hr x 48hrs

OR

- ii. Zosyn 100 mg/kg/dose (max 4 grams) q 8 hours x 48 hours (if patient in house prior to surgery and/or history of infection, may decide to give for 1 week)
 - b. Pneumocystis carinii Pneumonia (PCP)
 - i. Pentamidine (IV vs. inhaled form) administered within the first week following transplant as clinically stable, then transition to Septra (5mg/kg, max 80mg) the following month q Mon/Wed/Fri for the first year. Resume if immunosuppression increased for the treatment of rejection
 - c. Candida
 - i. Nystatin: 3ml if < 20 kg and 5 ml if >20 kg swish and swallow QID for as long as pt is on steroids
 - d. Viral Prophylaxis
 - i. Gancyclovir: 5mg/kg IV daily while NPO
 - ii. Valcyte: 15mg/kg daily (max. 450mg) once tolerating po's
 - iii. Consider adjusting dose if pt is neutropenic or creatinine clearance is <50%, reduce dose of Ganciclovir or Valctye by 50%.
- 3. Anticoagulation
 - a. Anti-coagulation is indicated in liver transplant patients to prevent thrombosis of hepatic vessels
 - i. Heparin (10 units/kg/hour) IV drip for 5 days when patient's PTT is less than 50 and INR less than 2 (at discretion of Surgeon)
 - 1. Goal PTT of 50-70
 - 2. DCD donors should be kept on heparin drip 5-7 days
 - 3. Heparin not used when hepatic artery is connected to aorta
 - ii. Dextran (2.4 ml/kg/dose over 8 hours qpm) IV drip for 5 days when patient's INR is less than 2
 - 1. For smaller babies may do up to 10ml/kg/dose x 5 doses w/ first dose given as a bolus in the OR (at discretion of Surgeon)
 - iii. Aspirin (<20kg 40mg po qod and >20kg 81mg po qod) started POD 1 x 1 month (Surgeons may choose to keep on longer if HA concerns)
 - iv. Persantine (<15kg 6.25mg, 15-25kg 12.5mg, >25kg 25mg po bid) started POD 1 x 1month
 - v. Surgeons may defer for older kids (>16 yo) who have larger vessels
- 4. Acid Suppression:
 - a. Pepcid 0.5 mg/kg IV BID (max 20 mg/dose) while NPO
 - b. Zantac 2 mg/kg po BID (max 150 mg/dose) once taking po
 - c. Continue same medication for those patients already on acid suppression, i.e. Prilosec, Prevacid

5. Duct to duct connection
 - a. Actigall 10mg/kg (max 300mg) BID once on PO feeds x 6 months
 - b. Surgeons may defer for older kids (>16 yo) who have large duct
6. Roux En Y prophylaxis
 - a. Cipro 10mg/kg (max 400mg) 30 minutes before and 12 hrs after all invasive procedure to include liver biopsies, bile catheter/T tube removal, PTCs, IR biliary intervention to prevent cholangitis
7. Laboratory Study Standards
 - a. Chem 15/ Mag/ Phos/ GGT/ CBCD/ PT/ PTT/ Fib/ ABG STAT upon arrival to PICU
 - b. PT/PTT/Fib/ABG/Hematocrit/K/Glucose q 6 hours for first 24 hours or as stable
 - c. Chem 15/ Mag/ Phos/ GGT/ CBCD/Prograf Level q a.m. (Chol/TG 1-2x week if on TPN/IL)
 - d. CellCept and Sirolimus levels Monday and Thursday
 - e. EBV and CMV quantitative PCRs
 - i. Once on the Monday following transplant, then
 - ii. q month for a year, then
 - iii. q 3 months for a year, then
 - iv. q 6 months for a year, then
 - v. annually
 - f. EBV/ CMV Serologies
 - i. First and Second year, q 3 months for seronegative pt
 - ii. Third year, q 6 months for sero negative pt
 - g. Transplant Monitoring Panels if pt is on thymoglobulin targeting CD3 < 20% and absolute <100.
 - h. Notify physician of:
 - i. Hct <23 or >30 %
 - ii. Platelets <30,000
 - iii. Electrolytes outside normal ranges
 - iv. Glucose<80 or >200
- j. Postoperative Complications
 - i. Primary Graft Non-function (PNF):
 1. Primary graft non-function results when the graft never begins working, or stops working in the immediate post-operative period in the absence of rejection
 2. Etiology:
 - a. Lengthy cold or warm ischemia time
 - b. Preservation injury
 - c. Infection

- d. Donor hypernatremia
- 3. Signs and Symptoms
 - a. Intra-operatively:
 - i. Poor graft perfusion
 - ii. Minimal bile production
 - iii. Coagulopathy
 - iv. Hard and rubbery liver
 - b. Post-operatively
 - i. Absence of bile output
 - ii. Coagulopathy
 - iii. Lactic acidosis
 - iv. Encephalopathy
 - v. Progression to multi-organ failure
 - vi. Significant rise of transaminases and bilirubin levels that peak in 48 hours then decline
 - c. Diagnostic Evaluation
 - i. Doppler ultrasound (patent HA and PV)
 - ii. Liver Biopsy to differentiate between PNF and preservation injury
 - 1. PNF characterized with parenchymal edema, necrosis of hepatocytes with an acute inflammatory infiltrate
 - d. Treatment
 - i. Relist Status 1A for emergent re-transplantation
- ii. Postoperative Hemorrhage
 - 1. One of the most common complications requiring return to the OR following transplant
 - 2. Etiology:
 - a. Anastamotic leak
 - b. Graft Bleeding
 - c. Cut Surface Bleeding
 - d. Portal Hypertension that persists in the setting of PV/ HV stenosis or reduced size graft
 - e. Coagulopathy
 - 3. Signs and Symptoms
 - a. hypotension
 - b. tachycardia
 - c. irritability
 - d. oliguria
 - e. anemia
 - f. increased abdominal girth
 - g. sanguineous or frank blood JP drainage

4. Diagnostic Evaluation
 - a. Doppler ultrasound
 - b. Laboratory Monitoring (CBCs, coagulation panel)
 - c. Abdominal CT
5. Treatment
 - a. transfuse
 - b. correct coagulopathy
 - c. return to OR as indicated
- iii. Hepatic Artery Thrombosis
 1. Most commonly occurs during first two postoperative weeks and associated with biliary tract complications
 - a. Etiology
 - i. Technical Complication
 - ii. Poor Arterial Flow
 - iii. Hypercoaguable State
 - iv. Overtransfusion
 - v. Acute cellular rejection
 2. Signs and Symptoms
 - a. Sudden high fever
 - b. Abdominal pain and distention
 - c. Acute elevation in liver chemistries
 - d. Bacteremia caused by intra and/or extrahepatic biliary strictures with blood cultures positive for klebsiella, E. coli, pseudomonas, or enterococci
 3. Diagnostic Evaluation
 - a. Doppler abdominal ultrasound of the hepatic artery. If the artery appears pulsatile, the ultrasound is reliable. If arterial patency is questionable, angiogram is indicated (stat CTA vs. MRA)
 4. Treatment
 - a. If liver appears normal on CT/MR without necrosis may attempt urgent Ex-lap to revise artery
 - b. Relist Status 1A, re-transplantation is indicated if liver developing necrosis
 - c. Antibiotics (i.e. zosyn, may also add vancomycin, anidulafungin, and flagyl if concern for abscess formation in necrotic liver)
- iv. Portal Vein Thrombosis
 1. Portal vein thrombosis can often occur without any initial signs or symptoms but is observed on postoperative ultrasounds
 2. Etiology:
 - a. Hypercoaguable

- b. Portal vein sclerosis or stenosis
- c. Overtransfusion
- d. Hepatic vein outflow obstruction
- 3. Signs and Symptoms:
 - a. Asymptomatic
 - b. Fever
 - c. Tachycardia
 - d. Leukocytosis
 - e. Elevation in LFTs
 - f. Ascites
 - g. Abdominal distension
 - h. Splenomegaly
 - i. Portal hypertension, variceal bleeding
- 4. Diagnostic Evaluation
 - a. Doppler abdominal ultrasound
 - b. CT or MR Venogram
- 5. Treatment
 - a. Surgical re-exploration
 - b. Surgical shunt
 - c. Possible re-listing if unable to be revised
- v. Bile Leak
 1. Commonly seen as a result of ischemic injury and in the setting of HAT
 2. Etiology:
 - a. Preservation injury
 - b. Hepatic artery thrombosis with acute bile duct necrosis
 - c. Bile leak from cut surface
 - d. Bile catheter site
 3. Signs and Symptoms:
 - a. JP drains with dark green/yellowish fluid
 - b. Lower quadrant pain
 - c. Mental status changes
 - d. Sepsis
 - e. Increase in liver enzymes
 4. Diagnostic Evaluation:
 - a. Must rule out Hepatic Artery Thrombosis, Doppler US ASAP
 - b. Cholangiogram through bile catheter or MRCP
 5. Treatment
 - a. Based on etiology of the leak, to include
 - i. Return to OR for repair

- ii. IR consultaion for PTC to assess biliary tree and for drain placement.
If T-tube or biliary catheter in place and cholangiogram obtained,
must give antibiotics (i.e. Cipro) prior to study
- vi. Bile Obstruction
 - 1. Etiology:
 - a. Anastamotic stricture
 - b. Technical
 - 2. Signs and Symptoms:
 - a. usually occurs later in postoperative period and manifests as
cholangitis, cholestasis or both
 - b. Fever, jaundice, abdominal pain, bacteremia with GNR, elevated liver
function tests—especially GGT
 - 3. Diagnostic Evaluation:
 - a. Ultrasound not as sensitive for biliary obstruction, consider MRCP
 - b. Liver Biospy will show bile duct proliferation and polys around the
portal tract
 - c. PTC to provide definitive diagnosis of strictures
 - 4. Treatment:
 - a. Broad coverage for GNR organisms, to include zosyn or Cipro
 - b. ERCP or IR consult for PTC for stent placement/ balloon dilation
 - c. Surgical revision of anastamosis
- vii. Reperfusion Injury
 - 1. Usually seen POD 3-5
 - 2. Etiology:
 - a. ongoing portal hypertension
 - 3. Signs and Symptoms:
 - a. Ascites
 - b. Rising bilirubin
 - 4. Treatment:
 - a. Frequent monitoring of liver tests
 - b. Symptomatic treatment of ascites/ coagulopathy/ thrombocytopenia
- viii. Hypertransaminitis
 - 1. A rise in any liver serum marker, to include AST, ALT, Alk Phos, GGT, T-
Bili may be observed for a number of reasons
 - 2. Causes:
 - a. Rejection
 - b. Hepatic Artery Thrombosis
 - c. Portal Vein Thrombosis
 - d. Biliary Obstruction or Leak
 - e. Hepatitis (Drug or Viral Induced)

3. Diagnostic Evaluation:
 - a. Abdominal Ultrasound w/ Doppler (to assess patency of vessels and biliary dilation)
 - b. Recent EBV/ CMV PCR
 - c. Liver Biopsy
 - d. MRI/ MRA/ MRCP
 - e. ERCP
 - f. Cholangiogram (if bile catheter in place to rule out biliary leak)
 - g. IR Consult for PTC, stent placement or balloon dilation
4. Treatment:
 - a. Based on identified cause identified in evaluation process.
- ix. Rejection
 1. Evaluation:
 - a. When an elevation in serum markers are noted, rejection is suspected, and other causes are ruled out a liver biopsy is indicated
 - b. If biopsy is consistent with rejection send DSA
 2. Treatment:
 - a. Based on liver biopsy results and clinical scenario of patient
 - b. Options include:
 - i. Steroids (Solucortef, Solumedrol or Prednisone) administered in: pulse (10mg/kg/dose given 1-3 doses,) bolus (10mg/kg/once), taper (5/4/3/2/1 mg/kg), or as an additional immunosuppressive agent.
 - c. Thymoglobulin
 - i. 1-2mg/kg/dose x 2-5 doses (Duration to depend upon clinical response)
 1. Pre-Medicate with:
 - a. Tylenol (15mg/kg; Max 650mg)
 - b. Benadryl (1mg/kg; Max 50mg)
 - c. SoluCortef (5mg/kg; Max 100mg) first dose then (3mg/kg; Max 75mg) for subsequent doses
 - ii. Transplant Therapy Monitoring Panel drawn at completion of doses to determine response, goal of CD3<20% and ABS <100.
 - iii. Must indicate central or peripheral line when ordering
 - iv. Starting a second immunosuppressive agent like Sirolimus or CellCept
 - v. If DSA positive for antibody mediated rejection (class II):
 1. Request C1Q on HLA sample and C4D staining of biopsy
 2. If DSA C1Q positive (MFI >1000) give patient IVIG 1g/kg x 2 doses, send pre and post IVIG DSA levels to determine treatment

- course. If post DSA C1Q remains positive may repeat IVIG as soon as 3 weeks from last dose.
3. If unsure how to interpret DSA levels consult HLA lab for recommendations
 4. For DSA that does not respond to IVIG therapy x 6 months or if DSA if severe consider bortezomib/pheresis protocol after consultation with the HLA labs (see protocol)
3. Management:
 - a. Given increased level of immunosuppression, ensure patient is taking Valcyte (MD may want ganciclovir), Septra or Pentamidine, Zantac and Nystatin
 - b. Ensure recent EBV and CMV PCRs
 - c. Monitor LFTs and drug levels daily
 - d. Increase Prograf target goal to 10-12
- x. Autoimmune hepatitis after transplant: Consider when patient fails to respond to treatment for rejection or if patient has history of autoimmune disease
 1. Evaluation:
 - a. Liver biopsy- may show increased number of plasma cells
 - b. Send autoimmune markers (ANA, IGG level, anti smooth muscle AB, liver/kidney microsome)
 - c. Send baseline T and B cell phenotyping
 2. Treatment: Consider treatment if IGG level is high/positive autoimmune markers and if plasma cells on biopsy
 - a. Give 375mg/m² rituximab given weekly x 4 doses
 - i. Send T and B cell phenotyping prior to each dose to monitor response and after the 4th dose
 - ii. Monitor IGG levels- consider replacement therapy with IVIG if IGG level becomes low
 - b. Maintenance immunosuppression with prograf, sirolimus, and steroid therapy
 - xi. Graft vs. Host Disease
 1. Occurs in the transplant recipient when the donor T cells react against the recipient tissue antigens. Migration of the donor lymphocytes occurs during the first 5-6 weeks after transplantation, with total replacement of recipient lymphocytes. Epithelial cells of the skin, intestine, and liver are major targets. The incidence of GVHD is 0-14%.
 2. Risk Factors:
 - a. Immunosuppressed prior to transplant
 - b. HLA matched donor

3. Signs and Symptoms:
 - a. Erythematous/maculopapular rash particularly on palms, soles, ears and trunk
 - b. Fever
 - c. Pancytopenia
 - d. Hyperbilirubinemia
 - e. Abdominal cramping, diarrhea
 4. ANY suspicion of GVHD requires urgent Stem Cell Transplant consult
 5. Diagnostic Evaluation
 - a. Biopsy of native skin, GI tract, blood or bone marrow for donor HLA antigens (please ensure SCT is aware to expedite path read)
 - b. Blood chimerism sent to HLA lab (normal result is 0%)
 6. Treatment:
 - a. Increased immunosuppression, to include the use of Thymo and steroids
- xii. Hypercoagulable
1. Evaluation
 - a. Assess for Venous Thrombosis
 - i. Abdominal Ultrasound with Doppler
 - ii. CT or MR-venogram
 - b. Laboratory Evaluation
 - i. PT, PTT, Fibrinogen
 - ii. Factor 8, 9, 11, 12
 - iii. Antithrombin III
 - iv. Protein C
 - v. Protein S
 - vi. Factor 5 Leiden
 - vii. Prothrombin Poort (G20210A)
 - viii. Homocysteine (M, Th, F)
 - ix. If any of the above abnormal, obtain:
 1. Lupus Anticoagulant
 2. Antiphospholipin/ Cardiolipin Antibodies
 3. Lipoprotein A
 4. PA1-I and PNH (CD55/ 59)
 5. Hematology Consult
2. Metabolic/Genetic Liver Disease
- a. Alpha-1-antitrypsin deficiency (AATD)
 - i. Pathophysiology:

1. Patient's with this have a genetic mutation that produces an abnormal form of Alpha-1 antitrypsin which cannot be released from the liver. The role of AAT is to protect the tissues (primarily the lungs) in the body from being attacked by enzymes that are released from inflammatory cells. With AATD the AAT builds up in the liver, thus damaging the tissues.
- ii. Signs and Symptoms:
 1. Typically associated with early onset pulmonary emphysema and various forms of liver disease, to include cirrhosis, neonatal hepatitis, and hepatocellular carcinoma
- iii. Treatment
 1. Symptomatic Treatment
 2. Liver Transplant
 - a. Indications for Transplant
 - i. Liver transplant is generally reserved for patients with end-stage liver disease. It ultimately corrects the deficiency, as the normal donor liver produces and secretes AAT.
- iv. Considerations at time of Transplant and After
 1. There aren't any genetic considerations at the time of transplant or after, as transplant is considered curative
- b. Wilson's Disease
 - i. Pathophysiology:
 1. A rare autosomal recessive disorder of copper metabolism. The patient with Wilson's disease does not release copper into the bile as it should, causing build up and damage to the liver.
 - ii. Signs and Symptoms:
 1. Over time, copper is released into the bloodstream allowing it to be carried throughout the body causing further damage to the brain, eyes and kidneys
 2. Symptoms based on location of buildup of copper, which include:
 - a. Clumsiness
 - b. Depression
 - c. Difficulty speaking, swallowing or walking
 - d. Drooling
 - e. Easy bruising
 - f. Fatigue
 - g. Involuntary shaking
 - h. Joint pain
 - i. Anorexia
 - j. Nausea
 - k. Jaundice

- 1. Edema
 - m. Kaiser-Fleischer rings (brownish or gray-green rings that represent fine pigmented granular deposits of copper in the cornea close to the endothelial surface; copper is primarily deposited in a granular complex with sulfur, which gives the ring its color.)
- iii. Diagnostic Evaluation:
 - 1. 24hr urine for copper (elevated copper)
 - 2. Serum copper and ceruloplasmin (will be low)
 - 3. Liver biopsy (confirms diagnosis with increased quantitative copper levels 250mcg)
 - 4. May have low Hct, hemolytic crisis or low Alk Phos
- iv. Treatment
 - 1. Consult genetic team
 - 2. Consider copper chelating agents (penicillamine or trientine) which are given in two phases. Removing the tissue copper that has accumulated and then preventing reaccumulation
 - 3. Consider high dose oral zinc- interferes with absorption of copper from the GI tract by inducing enterocyte metallothionein, which preferably binds copper from intestinal contents and is lost in feces
 - 4. Vitamin E in conjunction with chelator or zinc to protect tissues from damage, in particular the liver
 - 5. Patients with Wilson's disease should also follow a low copper diet and avoid copper-rich foods such as liver, kidney, shellfish, nuts, dried fruits or beans, peas, unprocessed wheat, chocolate, cocoa, and mushrooms
 - 6. Indications for Transplant
 - a. Liver Transplant is reserved for those who fail to respond to treatment or cannot tolerate the side effects of treatment
- v. Considerations at time of Transplant and After
 - 1. There aren't any genetic considerations at the time of transplant or after, as transplant is considered curative
- c. Maple Syrup Urine Disease
 - i. Pathophysiology:
 - 1. An autosomal recessive disorder of amino acid metabolism. It is caused by a deficiency of the branched chain alpha keto acid dehydrogenase which leads to the accumulation of branched chain amino acids and their derivatives in plasma and tissue
 - ii. Signs and Symptoms:
 - 1. Irritability
 - 2. Lethargy
 - 3. Poor feeding

4. Dystonia
- iii. Treatment
 1. MSUD formula that is low in branched chain amino acids
 2. Liver transplant serves as a safe and effective cure for MSUD
- iv. Preoperative Guidelines:
 1. Consult genetics team immediately upon accepting offer to review plan of care
 2. Continue specialized formula until absolutely necessary for pt to be NPO
 3. Laboratory Evaluation to include serum amino acids, urine osmolality and creatinine and serum osmolality
 4. IVF with D10 1/2 NS run at 1.5xM
 5. If NPO longer than 6 hours, start 20% lipids at 2g/kg continuous infusion
- v. Postoperative Guidelines:
 1. Serum amino acids upon return to the PICU and daily for the first three days
 2. May resume normal management as transplant is considered curative
 3. May require OT therapy as pt frequently exhibit oral aversion given limited variety of foods prior to transplant
- d. Tyrosinemia
 - i. Pathophysiology:
 1. Tyrosine in an amino acid that is important in the synthesis of thyroid hormones, catecholamines, and melanin. Tyrosinemia encompasses four autosomal recessive disorders that result from deficiencies in enzymes in the tyrosine catabolic pathway, to include: hereditary tyrosinemia (HT) types 1, 2, and 3, and alkaptonuria. Impaired catabolism of tyrosine results in elevated plasma tyrosine concentrations. If liver disease is present, additional tests must be done immediately to detect HT type 1, a generally lethal disorder that requires immediate treatment. It is the most severe disorder of tyrosine metabolism. It is characterized by severe progressive liver disease and renal tubular dysfunction.
 - ii. Signs and Symptoms, to include but not limited to as each type has a specific set of symptoms:
 1. Jaundice
 2. Failure to Thrive
 3. Loss of Balance or Coordination
 4. Mental Retardation
 5. Photophobia
 - iii. Treatment
 1. The treatment of choice is nitisinone (Orfadin), which inhibits 4-OH phenylpyruvate dioxygenase (HPD), an early step in the tyrosine

degradation pathway. Nitisinone is generally started as soon as the diagnosis of tyrosinemia. Nitisinone increases the concentration of tyrosine, so controlled intake of phenylalanine and tyrosine should be encouraged upon diagnosis to prevent tyrosine crystals from forming in the cornea. If the blood concentration of phenylalanine becomes too low ($<20 \mu\text{mol/L}$), additional protein should be added to the diet.

2. Indications for Transplant
 - a. Liver transplant is performed in patients with persistent liver failure who do not respond to nitisinone therapy or have hepatic malignancy
3. Considerations at time of Transplant and After
 - a. There aren't any genetic considerations at the time of transplant or after, as transplant is considered curative.
- e. Glycogen storage diseases
 - i. Pathophysiology:
 1. These are a group of inherited disorders where an abnormal amount of glycogen is stored in the liver, thus impairing the liver's ability to regulate glucose metabolism. There are a number of different types of GSDs, the following diseases primarily involve the liver:
 - ii. Liver glycogen synthase deficiency (GSD 0)
 1. Pathophysiology:
 - a. Type 0 Glycogen Storage Disease (GSD 0) is caused by a deficiency in the enzyme glycogen synthase. This enzyme is needed for the body to make glycogen.
 2. Signs and Symptoms:
 - a. Fasting hypoglycemia typically develops in late infancy
 - iii. Glucose-6-phosphatase deficiency (GSD Ia)
 - iv. Glycogen storage disease type I (GSDI)
 1. Pathophysiology:
 - a. characterized by accumulation of glycogen and fat in the liver and kidneys, resulting in hepatomegaly and renomegaly
 2. Signs and Symptoms:
 - a. Doll-like faces with fat cheeks
 - b. Thin extremities
 - c. Short stature
 - d. Protuberant abdomen
 - e. Xanthomas
 - f. Diarrhea
 - g. Thrombocytopenia
 - v. Glucose-6-phosphate transporter deficiency (GSD Ib)
 1. Signs and Symptoms:

- a. Prone to infection because they have an immunodeficiency
- vi. Glycogen debrancher deficiency (GSD III)
 - 1. Pathophysiology:
 - a. GSD type III is caused by a deficiency of glycogen debrancher enzyme (GDE) activity. GDE aids in the glycogenolysis process. Deficiency of GDE results in glycogen with short outer chains in liver, muscle, and heart tissues. The abnormal glycogen is not soluble and causes damage to tissues where it collects (liver and/or muscle) and hypoglycemia. There are two types of GSD III known as type IIIa and type IIIb. Most patients with Type III GSD enzyme deficiency in liver and skeletal muscle. Patients that have enzyme deficiency in liver and muscle (including the heart) have what is known as type GSD IIIa. Some patients (<15%) have debranching enzyme deficiency only in the liver which is type GSD IIIb.
- vii. Signs and Symptoms:
 - 1. During early years of infancy and childhood, the disease may present clinically just like GSD I: small stature, large, hypotonia and hypoglycemia
 - 2. In some patients liver cirrhosis can occur due to accumulation of abnormal glycogen
- f. Glycogen branching enzyme deficiency (GSD IV)
 - i. Pathophysiology:
 - 1. In Type IV GSD there is not an increased amount of glycogen in the tissues, as in other forms of GSD. Instead, the glycogen that does accumulate has very long outer branches, because there is a genetic deficiency of the branching enzyme. This structural abnormality of the glycogen is thought to trigger the body's immune system, causing the body to actually attack the glycogen and the tissues in which it is stored.
 - ii. Signs and Symptoms:
 - 1. Tremendous cirrhosis of the liver as well as muscle
 - 2. Failure to thrive
 - 3. The rate of growth and mental progress of the baby stops at a certain point and does not continue normally
 - 4. The liver and spleen enlarge, there is little weight gain, and muscles develop poor tone
 - 5. The course of the disease is one of progressive cirrhosis and associated problems
 - 6. Death typically occurs by five years of age
- g. Liver phosphorylase deficiency (GSD VI)
 - i. Pathophysiology:

1. Glycogen storage disease type VI (GSD VI), a disorder of glycogenolysis caused by deficiency of hepatic glycogen phosphorylase
- ii. Signs and Symptoms:
 1. Hepatomegaly
 2. Growth retardation
 3. Ketotic hypoglycemia after an overnight fast
 4. Mild hypoglycemia after prolonged fasting (e.g., during an illness)
- h. Phosphorylase b kinase deficiency
 - i. Pathophysiology:
 1. GSD type IX is a disorder in which the body cannot metabolize glycogen. Glycogen is stored in the liver, muscle and rarely heart instead of being used. Patients with type of GSD IX glycogen storage disease have a deficiency of the enzyme called phosphorylase kinase. Phosphorylase Kinase Deficiency, PHK, constitutes the largest subgroup (1:100,000 births) of liver glycogenosis. Phosphorylase kinase is required for glycogen to be broken down completely.
 - ii. Signs and Symptoms:
 1. Hepatomegaly
 2. Growth retardation
 3. Mild delay in motor development
 4. Hyperlipidemia The symptoms usually improve as a child ages, and children usually reach their full potential height and weight by adulthood
 - iii. Treatment
 1. Symptomatic based on deficiency
 - iv. Indications for Transplant
 1. Considered curative following transplant
 - v. Considerations at time of Transplant and After
 1. Consult genetics team immediately upon accepting offer for transplant to discuss plan of care
 2. Start on D10 at 1.5 times maintenance while NPO. Obtain a blood glucose upon pre-op admission then every two hours while NPO
 3. GSD Ib draw preoperative blood and urine cultures, ANC and consult hematology. May consider the use of neupogen post-operatively
 4. GSD III obtain a cardiology consult as part of the transplant evaluation
- i. Cystic Fibrosis
 - i. Pathophysiology:
 1. Mutations in a gene on chromosome 7 that encodes the cystic fibrosis transmembrane conductance regulator (CFTR) protein is the known cause for CF. CFTR protein is found in all exocrine tissues and is a complex chloride channel and regulatory protein Disturbed transport of chloride

and/or other CFTR-affected ions, such as sodium and bicarbonate, leads to thick, viscous secretions in the lungs, pancreas, liver, intestine, and reproductive tract, and increased salt content in sweat gland secretions. CF is a multisystem disease affecting the digestive system, sweat glands, and the reproductive tract. Progressive lung disease continues to be the major cause of morbidity and mortality.

ii. Signs and Symptoms:

1. Bile produced in patients with CF is thick and tenacious, causing blockage of the intrahepatic bile ducts. Impaired secretion of mucins from the submucosal glands and increased glycine-conjugated bile acids. Both of these are thought to contribute to the decreased flow and increased concentration of the bile. Obstruction of the biliary ductules causes the release of pro-inflammatory agents and growth factors that induce the synthesis of collagen in the portal tracts, leading to progressive fibrosis and eventually cirrhosis.

iii. Treatment:

1. One of the most important parts of management of liver disease in CF is optimization of nutrition including the correction of abnormalities of fat-soluble vitamins, essential fatty acids, carnitine, and choline
2. Indications for Transplant
 - a. Patients with liver failure or end-stage liver disease should be referred for liver transplantation
3. Considerations at time of Transplant and After
 - a. Based on each individual patient. If receives an isolated liver transplant, a majority of their care will be driven by the pulmonology team

j. Hyperoxaluria

i. Pathophysiology:

1. A rare metabolic disorder with autosomal recessive inheritance. PHO is triggered by one of two enzymatic defects, which result in enhanced conversion of glyoxalate to oxalate (poorly soluble) which is then excreted in the urine

ii. Signs and Symptoms:

1. In infancy, it is characterized by chronic renal failure with massive parenchymal oxalosis where they do not develop renal calculi
2. In older children, patients will experience symptoms of urolithiasis or complete obstruction with acute renal failure. The calcium oxalate stones are bilateral and radiopaque on x-ray examination

iii. Treatment:

1. How well treatment will work depends on early diagnosis. Modalities found to be effective include:
 - a. Maintenance of a high urine output (above 3 L/day per 1.73 m²) to decrease the tubular fluid oxalate concentration and diminish intratubular oxalate deposition
 - b. Avoid high oxalate foods, which include tea, chocolate, spinach, and rhubarb
2. Indications for Transplant
 - a. Combined liver-kidney transplantation- Combined liver-kidney transplantation is probably the treatment of choice for children with type 1 PHO that demonstrate progressive renal disease. The liver provides the missing enzyme, thereby lowering oxalate production to the normal range. This modality is generally only considered after AGT deficiency has been confirmed by liver biopsy
 - b. Isolated liver transplantation – Isolated liver transplantation has been proposed for patients with rapidly progressive disease who still have a glomerular filtration rate above 30 mL/min
 - c. Isolated renal transplantation – Renal transplantation has been proposed as the treatment of choice for patients who progress to end-stage renal failure, since the rate of oxalate removal with dialysis is inadequate to prevent oxalate accumulation

k. Defects of Mitochondrial Function

i. Pathophysiology:

1. Mitochondrial disorders- Within the mitochondria, organic acids, fatty acids, and amino acids are metabolized to acetyl-CoA, which condenses with oxaloacetate to form citric acid, which is oxidized in the Krebs cycle. Mitochondrial disorders can affect muscle alone, muscle and brain, or multiple systems with variable involvement of the heart, kidney, liver, skeletal muscle, or brain

ii. Treatment:

1. Each patient must be individually evaluated, with the minimum of a cardiology and neurology evaluation to determine the extent of disease. At time of work up consider:
 - a. Brain MRI
 - b. Muscle/skin/liver biopsy
 - c. CSF for lactate
2. If concern for multiorgan involvement, Genetic input and Family meeting to discuss risk/long term prognosis to determine how to proceed

- iii. Considerations at time of Transplant and After
 - 1. In general, outline the plan of care at the time of evaluation as each plan will need to be individualized
 - 2. Consult genetics immediately upon acceptance of offer for transplant to review plan of care
 - 3. Increased risks of hypoglycemia and lactic acidosis. Avoid the use of lactated ringers
- 1. Neonatal Iron Storage Disease
 - i. Pathophysiology:
 - 1. An uncommon form of HH occurs in childhood and is termed juvenile or type II hemochromatosis (JH)
 - 2. Juvenile hemochromatosis is earlier in onset, develops at a greater rate than typical HH, and appears genetically distinct
 - ii. Signs and Symptoms:
 - 1. Cardiomyopathy
 - 2. Reduced glucose tolerance
 - 3. Hypogonadism
 - iii. Treatment:
 - 1. Individualized depending on presentation
 - 2. Indications for Transplant
 - a. End stage liver disease
 - b. Each patient must have a cardiology evaluation at the time of transplant evaluation.
 - 3. Considerations at time of Transplant and After
 - a. Consult genetics immediately upon receipt of offer to discuss plan of care. Generally individualized at the time of evaluation.
- m. Urea Cycle Defects
 - i. Pathophysiology:
 - 1. The urea cycle is the metabolic pathway that transforms nitrogen to urea for excretion from the body. Deficiency of an enzyme in the pathway causes a urea cycle disorder (UCD). The urea cycle disorders are:
 - a. Carbamyl phosphate synthetase I (CPSI) deficiency (supplement with citrulline)
 - b. Ornithine transcarbamylase (OTC) deficiency (supplement with citrulline)
 - c. Argininosuccinate synthetase (ASS) deficiency (also known as classic citrullinemia or type I citrullinemia, CTLN1) (supplement with arginine)

- d. Argininosuccinate lyase deficiency (ASL, also known as argininosuccinic aciduria) (supplement with arginine; well controlled without hyperammonemia, likely wouldn't need ammonul)
 - e. N-acetyl glutamate synthetase (NAGS) deficiency
 - f. Arginase deficiency (no hyperammonemia, so won't require ammonul)
- ii. Treatment
1. The initial approach to treatment consists of the following:
 - a. Rehydrate and maintain good urine output without overhydration
 - b. Remove nitrogen using medications and hemodialysis
 - c. Stop protein intake and minimize catabolism
 - d. Neurologic morbidity is directly correlated with the duration of hyperammonemia. Hence, normalization of blood ammonia levels should be a management priority.
 - e. For chronic management, in addition to serial measurements of growth, we assess the adequacy of protein intake over the course of weeks to months by measuring serum concentrations of total protein, albumin, and prealbumin.
 - f. Indications for Transplant
 - i. Recurrent hyperammonemia
- iii. Considerations at time of Transplant and After
1. Pre-Transplant
 - a. Consult genetics at the time of acceptance of offer for transplant to discuss plan of care. Ammonia stat on admit, then every 6 hours thereafter
 - b. IVF with D10 minimum at 1.5xM
 - c. Arginine and citrulline given up until absolutely NPO, may be given early
 - d. Ammonul initiated once NPO for six hours or more per Genetic recommendations
 2. Post-Transplant
 - a. Unless clinically indicated, no ammonia levels
 - b. May have a full regular diet, once tolerated, check plasma amino acid profile as still at risk for amino acid deficiency
- n. Listing for Transplant
- i. A candidate with a urea cycle disorder or organic academia may be assigned a PELD of 30 if the transplant center submits a PELD exception according to the requirements.
 - ii. If the candidate does not receive a transplant within 30 days of being listed with a PELD of 30, the center may upgrade the candidate to a Status 1B.

- Hospitalization is not a requirement for listing in Status 1B for these candidates.
- o. Recertification
 - i. The coordinators recertify the patients listing every 3 months.
 - p. Follow-Up:
 - i. Generally with the metabolic clinic annually, but will be determined prior to discharge from hospital following transplant
3. Methylmalonic Acidemia (MMA)
- a. Referral:
 - i. Obtain the following data at the time of referral:
 1. Serum/urine MMA levels and trends
 2. Serum Amino acid levels and trends
 3. Current formula and diet
 4. Current medications
 5. Genetics history-course of disease, hospital admissions, etc
 6. Thrombophilia workup-Factor V Leiden, Factor VIII mutations, and homocystine
 7. 24 hour urine for volume, protein and creatinine clearance
 8. Volume of 24 hour fluid intake
 9. B12 responsive or non-responsive
 10. Mutation testing for MMA-MUT 0 or 1 (send to Baylor)
 11. If patient is on dialysis, what is the residual renal function and KT/V
 - b. Evaluation:
 - i. Patient MUST come here for evaluation
 - ii. Consults:
 1. Liver team/transplant
 2. Kidney team/transplant
 3. Genetics consult
 4. Nutrition consult
 5. Developmental assessment
 - iii. Laboratory Evaluation:
 1. Every 3 month serum/urine MMA levels while waiting
 - iv. Selection Committee:
 1. Patient to be presented at a combined liver/kidney selection meeting
 - c. Preoperative Management:
 - i. At the time of admission (Combined Liver/Kidney Transplant):
 1. Admit directly to the PICU
 2. Inform PICU team of admission and that the patient will require a temporary IJ catheter for hemodialysis.

3. Inform the dialysis team of admission and that the patient will require urgent hemodialysis. Plan for 3-4 hours at the maximum tolerated blood flow.
4. Place temporary IJ dialysis catheter for Hemodialysis
5. If patient has a HD catheter, admit to the floor for Hemodialysis
- ii. For all patients at the time of admission (Isolated or Combined):
 1. Draw MMA/ammonia level/serum amino acids/carnitine/Acyl-carnitine
 2. Send urine MMA level (also called: organic acids, urine)
 3. Inform genetics that patient is being admitted
 4. Consult Endocrine if patient diabetic
 5. Once NPO-start [D10-15@1.5-2](#) maintenance + bicarb according to acidosis + lipids 20% @ 2g/kg per Genetic recommendations
 6. Start IV carnitine 1:1 conversion (convert from oral dose)
 7. If required-start Insulin drip to maintain glucose level @100-200
- d. Intra-Operative:
 - i. If not done prior to surgery, initiate or complete hemodialysis treatment at maximum tolerated blood flow rate for 3-4 hours
 - ii. Obtain Pre and Post dialysis serum MMA levels
 - iii. Continue D10-15 and lipids (if access permits) and insulin drip (if necessary)
- e. Post-Operative:
 - i. Obtain a post-transplant serum MMA level then 2x/wk
 - ii. Obtain lactate levels every 6 hours x 24 hrs then daily x 3 days
 - iii. Obtain ammonia levels q am, plasma amino acids 2x/wk, carnitine/aclcarnitine/urine organic acids weekly
 - iv. Resume pre-op fluids
 - v. Genetics to guide nutrition needs including TPN/lipids
 - vi. If patient is on TPN, the protein should be 0.2-0.3 gr/kg, not to exceed 0.5-1gr/kg in the first week
 - vii. Target serum MMA levels during the first 6 months is <150umol/L
 - viii. No planned Hemodialysis post op
- f. Monitoring:
 - i. Post-Operative visits will be coordinated between outpatient kidney and liver coordinators
4. Hepatoblastoma and Hepatocellular Carcinoma
 - a. Evaluation:
 - i. In addition to the standard transplant evaluation these patients should have an AFP, an abdominal CT or MRI to be reviewed by Transplant Surgery and Oncology, chest CT to rule out lung mets, and possible PET scan based on Oncology recommendations

- b. Selection Committee:
 - i. When evaluation is complete, pt will be presented at selection committee with Oncology present (and additional specialties as indicated)
 - a. Determine pre- and post-transplant plan of care to include chemotherapy and/ or chemo-embolization.
 - b. If resectable...decide if needed to list for transplant as back-up. Schedule resection with attending surgeon's secretary, arranging for PICU bed post-operatively
- c. Listing for Transplant:
 - i. A candidate with a non-metastatic hepatoblastoma may be assigned a PELD of 30 if the transplant center submits a PELD exception according to the requirements.
 - ii. If the candidate does not receive a transplant within 30 days of being listed with a PELD of 30, the center may upgrade the candidate to a Status 1B. Hospitalization is not a requirement for listing in Status 1B for these candidates.
- d. Recertification
 - i. The coordinators recertify the patients listing every 3 months
- e. Post-Resection Care
 - i. Check AFP immediately post-operatively, then weekly while in house.
 - ii. Follow-up as an outpatient with transplant surgery as directed by Surgeon, generally two weeks post-operatively
 - iii. Within 3 - 4 weeks of surgery:
 - 1. Labs with AFP
 - 2. UA
 - 3. CT or MRI of abdomen (whichever study patient has been followed with)
 - 4. CT of chest
 - 5. CXR
 - 6. Audiogram/BAER (if CISplatin used)
 - 7. GFR (if CISplatin used)
 - 8. Follow-up with oncology monthly, to include the following exams/ studies.
 - 9. Every month for 6-12 months post-operatively:
 - a. PE
 - b. CBCD
 - c. CXR
 - d. Labs with AFP
 - e. GFR (if initial abnormal)
 - 10. Then every 2 months until 2 years post-resection, then every 3 months until 4 years post-resection, then yearly

- a. CT of chest & CT/MRI of abdomen and pelvis every 3 months until one year post-resection, then every 6 months till 2 years post-resection, then yearly till 4 years post-resection, then PRN
 - b. Audiogram/BAER annually for 4 years post-resection (if CISplatin used)
- f. Post-Transplant Management
 - i. Run immunosuppression lower, please refer to prograf goal chart in post-operative management in previous section
 - ii. Check AFP immediately post-operatively, then weekly while in house
 - iii. Within 3 weeks of surgery:
 - 1. Labs with AFP
 - 2. UA
 - 3. CT or MRI of abdomen (whichever study patient has been followed with)
 - 4. CT of chest
 - 5. CXR
 - 6. Audiogram/BAER (if CISplatin used)
 - 7. GFR (if CISplatin used)
 - iv. Follow-up with oncology monthly, to include the following exams/ studies.
 - v. Every month for 6-12 months post-operatively:
 - 1. PE
 - 2. CBCD
 - 3. CXR
 - 4. Labs with AFP
 - 5. GFR (if initial abnormal)
 - vi. Then every 2 months until 2 years post-transplant, then every 3 months until 4 years post-transplant, then yearly.
 - 1. CT of chest & CT/MRI of abdomen and pelvis every 3 months till one year post-transplant, then every 6 months till 2 years post-transplant, then yearly till 4 years post-transplant, then PRN
 - 2. Audiogram/BAER annually for 4 years post-transplant (if CISplatin used)
- g. HCC Surveillance in patients with cirrhosis:
 - i. Baseline biphasic CT
 - ii. AFP every three months
 - iii. CT every three months
- h. Chemoembolization for HCC
 - i. Return to clinic 1 week post-TACE for CBC, LFTs and INR evaluation.
 - ii. AFP every 3 months.
 - iii. Biphasic CT scan, CBC, LFTs and INR in 10 weeks to reassess need for TACE. Continue biphasic CT scan every 3 months. Follow-up in clinic following repeat imaging.

- i. Surveillance following resection
 - i. AFP every 2 months, notify surgeon if continues to rise.
 - ii. Biphasic CT every 3 months.
 - j. Surveillance following Transplant
 - i. AFP every 2 months for 2 years, then if normal, every 6 months for 5 years.
 - ii. Biphasic CT every 3 months for 2 years if no evidence of recurrence, no further scanning required.
5. Hepatitis B and C
- a. Evaluation:
 - i. Please refer to Liver Transplant Evaluation section.
 - b. Intra-operative Management:
 - i. Hepatitis B
 - 1. If recipient HBV+
 - a. When anhepatic, administer medications as follows:
 - i. For patients weighing >50kg, 20,000u Hepagam given over 1 hour, and NO premeds required.
 - ii. For patients weighing <50kg, 144u/kg HBIG in 100cc NS over 4-6hours. Premedicate with 10mg/kg solumedrol immediately prior to anhepatic phase. Confirm steroid form and dose with surgeon.
 - b. Post-operative
 - i. Continue with same Hepagam dose given intra-operative for 6 days.
 - ii. For pt weighing <50kg and received HBIG, premedicate one hour prior to dose:
 - 1. Steroids per taper
 - 2. Tylenol 15mg/kg
 - 3. Benadryl 1mg/kg
 - iii. Start entecavir 0.5mg daily (>16 y.o.) when pt tolerating po's, taken for life. Be sure to adjust for renal function. Discuss use with attending if pt <16 y.o.
 - iv. Draw HBSab quantitative level on POD#4/ Dose #5, then weekly. Level must be >150, if lower, must redose with hepagam/ HBIG and redraw level the following day.
 - v. If donor HBCAb + and recipient HBV -, recipient gets Entecavir for life, but does not need Hepagam/ HBIG.
 - ii. Hepatitis C
 - 1. Evaluation:
 - a. Please refer to Liver Transplant Evaluation.
 - 2. Intra-operative:
 - a. Decreased dose of steroids administered during induction (Solumedrol 5mg/kg.)

3. Post-Operative:
 - a. Thymoglobulin administered 2mg/kg infused over 8 hours upon return to PICU, pre-medicated with 100mg of solucortef, 15mg/kg Tylenol and 1mg/kg Benadryl. Second and third dose administered at 1.5mg/kg infused over 8 hours, each dose pre-medicated with 100mg of solucortef, 15mg/kg Tylenol and 1mg/kg Benadryl. Target platelet count >25, some patient's may require delaying infusion of thymoglobulin or platelets infused concurrently.
 - b. Steroid form and dosing must be confirmed with surgeon.
6. Intestinal Transplant
 - a. Causes of intestinal failure:
 - i. Short bowel syndrome due to:
 1. Volvulus
 2. Gastroschisis
 3. Necrotizing enterocolitis (NEC)
 4. Hirshsprung disease/Aganglionosis
 5. Trauma
 6. Congenital intestinal atresia
 7. Crohn's disease
 - ii. Poor intestinal absorption due to:
 1. Autoimmune disorders
 2. Brush border element assembly problems
 3. Microvillus inclusion disease
 - iii. Severe disorders of intestinal motility resulting from:
 1. Intestinal pseudo-obstruction (congenital or acquired)
 - iv. Tumors:
 1. Desmoid tumors
 2. Benign tumors (primarily seen in adults)
 - b. Evaluation:
 - i. Laboratory Evaluation
 1. Blood Type x 2 (one may be from outside facility if documentation available)
 2. Chem 15, Magnesium, Phosphorus, GGT, Cholesterol and Triglyceride
 3. CBCD
 4. Ammonia
 5. Coagulation Panel
 6. HIV-testing (see liver evaluation section for tests needed)
 7. HTLV I/II
 8. CMV/ EBV IgG and IgM
 9. Hepatitis A IgM

10. Hepatitis B Surface Antigen, Hepatitis B Surface Antibody, Hepatitis B Core Antibody
 11. Hepatitis C Total Antibody
 12. Vitamin A, alpha-tocopherol, beta-gamma-tocopherol, 25-hydroxy Vitamin D for pt with long standing liver disease
 13. Varicella IgG (if greater than 5 years old)
 14. PPD (pts < 5 years old) or quantiferon (pts > 5 years old)
 15. Amylase
 16. Stool reducing substances, Stool pH, Qualitative fecal fat
 17. Occult blood in stool
 18. Protein S activity, Protein C activity
 19. Factor V Leiden, Antithrombin III
 20. Copper, Zinc, Selenium
 21. Carnitine profile (total carnitine, free carnitine, acyl/free carnitine ratio)
- ii. Diagnostic Imaging Evaluation:
1. Abdominal Ultrasound with Doppler (to assess hepatic echotexture and patency of hepatic vessels and portal vein)
 2. Echocardiogram (Assess cardiac anatomy and function.)
 3. Ultrasound with Doppler of neck vessels (assess patency of jugular and subclavian venous systems)
 4. Upper GI series with small bowel follow through (assess length of residual small bowel)
 5. Gastric emptying study (evaluate gastric motility)
- c. Listing for Transplant
- i. Patients are listed in the following categories:
1. Status 1 (urgent): patients that are being listed for a liver/ intestine. These patients automatically receive an additional 23 points to their calculated PELD.
 2. Status 1B: patients that are being listed for an isolated intestine must be in the PICU and meet the following criteria:
 - a. Ventilator
 - b. GI bleed requiring 10cc/kg RBC replacement within previous 24 hours, initial listing on the day of, or the day following transfusion. To extend a candidate using this criterion, the candidate must experience a subsequent GI bleed requiring a transfusion of 10cc/kg during the 7 day period prior to the extension date.
 - c. Dialysis or CVVH or CVVD
 - d. GCS < 10, candidate must be initially listed or extended within 48 hours of GCS evaluation date.

3. Status 2 (non-urgent): patients that are being listed for an isolated intestine. These patients DO NOT RECEIVE A PELD.
- d. Recertification
 - i. The coordinators recertify the patients weekly.
 - e. Pre-Operative Orders
 - i. Laboratory:
 1. Type and Screen with PRBC, Plt, FFP or Cryoprecipitate on-call to OR as clinically indicated.
 2. Chem 15, Magnesium, Phosphorous, GGT, CBCD, Coagulation Studies
 3. Urine Culture
 4. Blood Culture (from all lumens)
 - ii. Diet:
 1. Must be NPO a minimum of 6 hours before going to the OR. May follow 6.4.2 guidelines. Please refer to metabolic section for specific details.
 - iii. Medications:
 1. All preoperative medications are stopped, unless otherwise indicated (i.e. metabolic patients.)
 2. Immunosuppression- timing to be surgeon's preference based on patient clinical state; either per-transplant once visualization of organs, intra-op or post op once patient stable
 - a. Thymoglobulin 1.5-2mg/kg
 - i. Premedications
 1. Solu-Cortef 5mg/kg (max 100mg) 1st dose then 3mg/kg (max 75mg) for subsequent doses
 2. Tylenol 15mg/kg (max 500 mg)
 3. Benadryl 1mg/kg (max 50 mg)
 3. Antibiotics/Antifungals
 - a. Zosyn 100mg/kg (max 4g) q 8hr
 - i. Start meropenem if previously infected and treated with zosyn
 - b. Anidulafungin 3mg/kg (max 200mg)
 - iv. Radiology:
 1. Order abdominal Xray (Chest Xray, as well, if a larger pt to ensure mid-axilla to pelvis obtained on xray) specifying foreign body as the reason and under special instructions be sure to include OR will call for xray prior to closure, stat wet read called to OR
 - v. Consent:
 1. Isolated Intestinal Transplant, Combined Liver-Intestinal Transplant or Multi-visceral Transplant to include Liver, Intestine and Pancreas. Be sure to include any additional procedures i.e. feeding gastrostomy vs. Jejunostomy, as indicated

f. Post-Operative Management

i. Immunosuppression:

1. Prograf: 0.05 mg/kg IV over 24hrs (MUST order mg/hr)
 - a. Start within 72 hours of transplant at Surgeon's discretion
 - b. Goal level 12-15 mg/ml
 - c. **DESIGNATE 1 LUMEN TO BE USED FOR IV PROGRAF AND REMAIN UNUSED FOR LAB DRAWS THROUGHOUT ADMISSION, ENSURE CLEARLY LABELED FOR NURSING STAFF TO PREVENT FK LEVEL ERRORS**
 - d. When appropriate, start oral/enteral at 0.2-0.4 mg/kg BID
 - e. Adjust to maintain target level 10-12 for 3 month then 8-10 until 1 year post op
2. Steroids (for isolated only):
 - a. Prednisone/Solumedrol: 1mg/kg/day (max 20 mg/day)
3. Consider starting second agent at three weeks post op if isolated or if episode of rejection within first 3 months of transplant.

ii. Antibiotics/Antivirals

1. Zosyn (100mg/kg/dose IV q 8hr) x 1-2 weeks (If previously infected and treated with Zosyn, use Meropenem)
2. Anidulafungin: Peds: 3mg/kg IV one time first dose, then 1.5 mg/kg IV daily. Adults: 200mg IV first dose, then 100mg qdx14d
3. Gancyclovir (DHPG): Peds: 5 mg/kg q12h until diet advanced, then switch to oral Valcyte 15mg/kg po BID. Adult: DHPG 5mg/kg until diet advanced, then switch to Valcyter 900mg daily (monitor WBCs-may need to be decreased to 450mg daily)
4. Cytogam (Peds only): First dose within first week; 150 mg/kg/dose weeks 0/2/4/6/8 then 100mg/kg/dose weeks 12/16
5. PCP Prophylaxis: Peds: Pentamidine monthly x 2-3 months then transition the following month to Septra 5mg/kg daily Mon/Wed/Fri. Adults: Septra 1 SS tablet Mon/Wed/Fri

iii. Anticoagulants

1. Peds: None
2. Adults: Case by case

iv. GI Meds/Enteral Feeds

1. Pediatrics:
 - a. Protonix 1 mg/kg BID IV; follow gastric pH daily (goal 6-8); start Protonix drip if unable to reach within 24hrs
 - b. Feed initiation: Pedialyte start POD 3-evaluate tolerance before advance to formula; Pediatric Vivonex x 4wks. Start with dilute strength (1/2 to start)

- c. ****Continue TPN until enteral/oral feeds provide 50% nutritional goal****
 - d. Imodium 0.5-2 mg/ kg/d (capsules added to feed) started once ostomy output 35-50ml/kg/day AND no rejection
2. Adults:
 - a. Protonix 40 mg/d IV, or PPI PO
 - b. Feed initiation: Tolerex 1/4-1/2 strength x 2 weeks
 - c. Imodium – Start with 4mg TID added to feeds once ostomy output >1L/day AND no rejection
- v. Surveillance
1. Close monitoring of ostomy output-typically 30-50ml/kg/day or 1 liter for adults; increased output concerning for rejection vs infection; if >20ml/kg in 8hrs consider holding feeds, assess fluid status
 2. Enteric biopsies SEND ULTRASTAT
 - a. 2-3x week x 1st month
 - b. 1x week x 2 months
 - c. PRN thereafter
 3. Stool pH and stool reducing substances daily to monitor absorption
 4. EBV/CMV PCR q 2 weeks first month, then q month x 1yr
 5. DSA on POD 1 then every 6 months for isolated pts and every 1 yr for combined pts; or PRN for rejection
- vi. Rejection
1. Grade: Mild: Solumedrol bolus 10mg/kg (max 1 gm) 1-3 boluses
 2. Moderate: Solumedrol bolus 10 mg/kg (max 1 gm)
 3. Steroid recycle: (max 1gm)
 - a. Day 1: 5 mg/kg
 - b. Day 2 4 mg/kg
 - c. Day 3: 3 mg/kg
 - d. Day 4: 2 mg/kg
 - e. Day 5: 1 mg/kg (continue this dose until appropriate to wean)
 4. Severe:
 - a. Campath- dose at surgeon's discretion over 2 hrs (max 30 mg)
 - i. Premedications:
 1. Solu-Cortef 5mg/kg (max 100mg)
 2. Tylenol 15mg/kg (max 500mg)
 3. Benadryl 1mg/kg (max 50mg)
 - b. Thymoglobulin 2mg/kg/dose x 2-5 doses (Duration to depend upon clinical response)
 - i. PreMed with Tylenol/Benadryl and SoluCortef 5mg/kg (max 100mg) first dose then 3mg/kg(max 75mg) for subsequent doses
 5. For all grades of rejection, increase Prograf dose (Target level 10-12)

6. Re-biopsy at 48 hrs to assess treatment efficacy
 7. Consider biopsies of the PROXIMAL graft if clinical picture suggests rejection but ileal biopsies are negative
 8. For Thymo-resistant rejection, consider REMICADE (5mg/kg/wk x 4 wks)
 9. Antibody Mediated Rejection/+DSA
 - a. For a positive DSA (class II MFI>1,000) request C1Q to be performed on the HLA sample and a C4D stain on the biopsy
 - b. If C1Q/C4D positive treat with IVIG 2g/kg (may be given as 1g/kg x2 doses if concerns for reaction/volume overload)
 - i. PreMed with Tylenol/Benadryl and SoluCortef 1mg/kg
 - ii. IVIG can be given monthly, DSA should be sent prior to and after IVIG infusion to monitor response to IVIG therapy
 - iii. If DSA fails to improve with IVIG therapy and pt continues to have ongoing graft dysfunction after 6 months of therapy consider Bortezomib/pheresis protocol after consultation w/ HLA lab (see protocol)
7. Management of Transplant Patient
- a. Respiratory Standards of Care
 - i. Patients arrive intubated to PICU. Patients are to be extubated as soon as possible unless contraindicated surgically or hemodynamically
 - ii. Continuous pulse oximetry is used on all patients
 - iii. CXRs and ABGs q morning or as clinically indicated
 - iv. Endotracheal suctioning is performed as needed
 - v. Chest physiotherapy is provided every 4 hours or less as deemed necessary by the transplant or PICU Attending physician
 - vi. Ventilatory changes are only to be made by a respiratory therapist after consultation with the critical care staff, and only after an order have been written
 - vii. Once extubated, patients are weaned to room air as tolerated
 - viii. Right hemi diaphragm elevation and right lower lobe atelectasis are common and should be treated conservatively; bronchoscopy is indicated if conservative measures fail or the atelectasis is thought to be the cause of delay in extubation
 - ix. Conservative treatment includes:
 1. OOB, ambulation, sitting up
 2. Incentive spirometer or blowing bubbles
 3. Albuterol and Mucomyst treatments

- x. Right pleural effusions are also common and tolerated without thoracentesis unless effusion results in respiratory compromise or the composition of the fluid is in question.
- b. Cardiovascular Standards of Care
 - i. The liver transplant patient must have adequate blood pressure to perfuse the new organ and prevent thrombosis; however the pressure must be controlled to prevent hypertensive sequelae
 - 1. While in PICU, EKG is monitored continuously
 - 2. Heart rate and BP are charted every 15 minutes for first hour, every 30 minutes for second hour, then hourly while in PICU
 - 3. Continuous Cardiac Respiratory Monitoring upon arrival to PICU, may discontinue once stable on acute care status
 - 4. Physician is notified if pt is tachycardic/bradycardic and if MAP is < 50 or > 80 (when <1 y.o.) and <60 or >90 (when >1 y.o.) to ensure organ perfusion and prevention of bleeding
 - a. Hypotension: Significant if below SBP range for age group or MAP less than 60mmHg
 - i. Treat first with a fluid challenge of Albumin 5% or blood products as indicated by fluid management section
 - ii. If intravascular volume is adequate (evident by CVP 8-13mmHg) and patient still hypotensive or not responsive to fluid, use low dose dopamine, norepinephrine, or epinephrine
 - iii. Transfer to IICU/PICU as indicated
 - b. Hypertension: Significant if MAP >90 (in pt >1 y.o.) and >80 (in pt <1 y.o.) or above SBP range for age group
 - i. Identify potential cause: pain, Prograf, steroids, fluid overload, etc
 - ii. TREAT IMMEDIATELY due to risk of PRES; do not assume that it is pain related
 - 1. IV Medications include: Hydralazine, Nipride or Nicardipine
 - 2. Oral Medications include: Dynacirc, Norvasc, Metoprolol
 - 3. Transdermal Medications include: clonidine
 - 4. No ACE Inhibitors
 - 5. Central and peripheral line dressing changes per protocol
 - 6. Any unnecessary lines are removed as soon as possible
 - 7. Consider placement of PICC while in PICU for pt with history of difficult access
- c. Fluids, Electrolytes and Nutrition
 - i. Intravenous Maintenance Fluids while NPO
 - 1. <3 mos old, D5 1/4NS
 - 2. >3 mos old, D5 1/2NS

- ii. INS and OUTS
- iii. Daily weights
- iv. Tubes, UOP, stool, emesis all recorded hourly in PICU and then q 4 on floor
- v. Physician notified if urine output <1 ml/kg/hour (<0.5 ml/kg/hr in adult size patients)
- vi. JP drains are stripped q 2 hours and emptied and recorded q 4 hours
- vii. Biliary bag emptied and recorded q 8 hours; MD notified if no output in 8hrs
- viii. Physician notified for change in drain output color and/or amount
- ix. Fluid Shift Management
 1. If patient is volume depleted and hematocrit <23, give PRBC's (5ml/kg if small HA, otherwise 10 ml/kg)
 2. If patient is volume depleted but normotensive and edematous, give 5-10 ml/kg Albumin 25%
 3. If volume status is unclear, patient normotensive but has low UOP, give fluid challenge of 20 ml/kg Normal Saline, may repeat once. If still oliguric check foley, re-evaluate Prograf level (can decrease urinary output if elevated) serum and urine osmolality and urine electrolytes
- x. Nausea, Vomiting and Diarrhea
 1. Rule out bowel obstruction, biliary complications, and ileus
 2. Zofran (0.1mg/kg IV q 8 hours) and Phenergan (0.25 mg/kg IV q 6 hours) as indicated
 3. Give LR to replace diarrhea, Give D5 1/2NS with 20meq KCl to replace emesis or NG output. Normal output from an ileostomy is <50mL/kg/d
- xi. Nutrition:
 1. All patients will be NPO until passing gas then start clear liquid diet and advance as tolerated
 2. If fresh Roux-en-Y, NPO x 5 days and consider TPN/Lipids
 3. For patients who take formula, start with Pregestimil until no longer cholestatic. When patient is no longer cholestatic, give Pediasure for patients > 1 year old or, Enfamil (or other infant formulas) for patients less than 1 year old
- xii. Bowel Movements:
 1. If no bowel movement by POD #3 or as indicated give glycerin suppository x 1
 2. Miralax (if <25 kg=8.5 g, >25 kg=17 g) as indicated
- xiii. Surgical Drains, Gastric Tubes, and Foley Catheters
 1. Duct to Duct Anastomosis or Roux-en-Y with Biliary Catheter or T-tube
 - a. Biliary bag will be to gravity for a minimum of 5 days, 10 days if cut surface
 - b. Kept in place by silk sutures, benzoin and Kendall Wet Proof tape.

- c. Cap bag on day 5 (full sized) or 10 (cut surface), open for fever/liver numbers rising, or as indicated by surgical attending.
 - d. If biliary bag is clamped on day 5 and no evidence of bile leak after 24 hours of being clamped, remove JP B.
 - e. Remove biliary catheter or T-tube 3 months post op. Give Cipro 10-15 mg/kg dose 1 hour prior to removal and then 12 hours after that dose.
 - f. All duct to duct anastomosis started on Actigall (10mg/kg po bid) for 6 months post op to promote bile drainage due to increased susceptibility for strictures.
2. JP Drains
- a. TYPICALLY JP A placed underneath right lobe of liver to Morrison's Pouch with tip at Vena Cava anastomosis; JP B monitors biliary and portal vein anastomosis, and hepatic artery to hepatic artery anastomosis (if present); JP C placed underneath the left lobe of liver with tip at vena cava anastomosis OR placed at aorta anastomosis
 - b. JPs removed once Heparin and Dextran are stopped and platelet count is greater than 30.
 - c. In the case of hepatic artery to aorta connection, JP C is removed 48 hours post operatively.
3. NG, G-Tube or J-Tube
- a. Flush with 10 ml NS q shift
 - b. Low intermittent suction until bowel sounds and passing gas.
4. Foley Catheter
- a. To gravity and remove as soon as clinically indicated.
- xiv. Pain Control/Sedation
- 1. Will arrive to the PICU intubated, before starting any sedation or pain medications the patient will be allowed to wake up and exhibit consciousness
 - 2. PICU will manage sedation and pain control while patient is intubated. This is usually with Fentanyl and Versed drips and prn.
 - 3. Neuro checks are to be done q hour along with pain scale while in PICU, then per floor protocol
 - 4. Once patient is extubated, prn Fentanyl, Morphine or Dilaudid may be given for pain
 - 5. If indicated patients to have PCA
 - 6. As patient tolerates p.o intake, prn Hycet for severe pain
 - 7. Any change in mental status will result in immediate physician contact and studies ordered as indicated
- xv. Hematologic
- 1. Bleeding and Indication for Transfusion

- a. If evidence of bleeding by visualization in JP drains, drop in hematocrit, or hemodynamic instability- stop anti-coagulation and give blood products as indicated
 - b. Optimal hematocrit of 23-30%. Levels greater may require phlebotomy due to concerns for sludging and risk of HAT/ PVT
 - c. Platelet counts of around 20,000 acceptable unless actively bleeding. OLTxp patients are placed on many drugs that cause thrombocytopenia.
2. CMV Blood Products
- a. Recipients <6 months of age CMV negative, leukoreduced products according to Blood Bank Policy, regardless of the CMV status of the donor and recipient. If pt K+ is elevated, consider washed units.
 - b. Recipients 18 years of age and younger who are CMV negative will receive CMV negative blood, otherwise patient will be given CMV positive products unless specified otherwise by the transplant team.
- xvi. Renal Dysfunction
- 1. Patients transplanted in the standard position are at risk for ATN due to the vena cava being clamped above the renal veins
 - 2. Measure urine sodium to distinguish between hepatorenal syndrome (HRS) and ATN
 - a. Urine sodium will be low in HRS and high in ATN
 - b. HRS is a diagnosis of exclusion; if urine sodium low other causes must first be ruled out. May need a Swan-Ganz catheter to rule out if patient intravascularly dry.
 - c. Urine sodium concentration is about equal to ½ NS; to replace urine output, always use ½ NS.
 - d. Indications for hemodialysis by vowels:
 - i. A-cidosis
 - ii. E-lectrolyte Imbalance
 - iii. I-ntoxicants
 - iv. O-verload (fluid)
 - v. U-remia
 - e. Casts in a urinalysis may represent sloughing of the cortical papillae and indicate ATN
 - f. OLTxp patients with infrarenal Aorta grafts may have renal failure secondary to blood flow being diverted from the kidney to the liver because of the greater blood requirement of the liver. The liver steals blood from the kidney, hence the “steal syndrome.”
- xvii. Metabolic
- 1. Respiratory Acidosis
 - a. Signs and Symptoms:

- i. Respiratory distress
 - ii. Tachypnea
 - iii. Tachycardia
 - iv. Drowsiness, disorientation or headache
 - b. Causes:
 - i. Decrease in alveolar ventilation
 - ii. Oversedation
 - iii. Respiratory muscle weakness
 - c. Evaluation:
 - i. ABG: $PCO_2 > 50$ mmHG, $pH < 7.30$
 - d. Treatment:
 - i. Correct underlying cause
 - ii. Increase O_2 provision
 - iii. Consider bronchodilators if caused by bronchospasm
 - iv. Naloxone if caused by over sedation
 - v. Intubate if not already intubated
- 2. Respiratory Alkalosis
 - a. Signs and Symptoms:
 - i. Tachypnea
 - ii. Respiratory distress
 - iii. Numbness and tingling to extremities
 - iv. Muscle weakness
 - v. Dizziness
 - b. Causes:
 - i. Aggressive mechanical ventilation
 - ii. Anxiety or pain
 - iii. Hypoxemia from anemia or right to left shunts
 - iv. Pneumonia or sepsis
 - c. Evaluation:
 - i. ABG: $PCO_2 < 30$ mmHg, $pH > 7.50$
 - d. Treatment:
 - i. Correct underlying cause
 - ii. IV $NaHCO_3$ 1 mEq/kg IV over 1 hour
- 3. Metabolic Acidosis
 - a. Signs and Symptoms:
 - i. Tachypnea
 - ii. Kussmaul's breathing
 - iii. Pallor, fatigue, lethargy
 - iv. Hypotension
 - v. Nausea, vomiting, abdominal pain

- vi. Coma
 - b. Causes:
 - i. Diarrhea
 - ii. Sepsis
 - iii. Renal tubular acidosis
 - c. Evaluation:
 - i. ABG: PCO_2 nl, $\text{pH} < 7.30$, $\text{HCO}_3^- < 22$ mmHg;
 - ii. Decreased serum bicarbonate level
 - d. Treatment:
 - i. Correct underlying cause
 - ii. IV NaHCO_3 1 mEq/kg IV over 1 hour
 - iii. Potassium supplementation (a decrease in serum pH results in a shift of potassium from the intracellular to extracellular compartment, raising the serum potassium concentration. The serum potassium concentration increases by approximately 0.6 meq/L (range 0.2 to 1.7 meq/L) for every 0.1 unit fall in serum pH. The variability is in part due to the presence of other factors that influence potassium homeostasis (e.g., renal failure with impaired renal excretion)
4. Metabolic Alkalosis
- a. Signs and Symptoms:
 - i. Cardiac arrhythmias
 - ii. Mental confusion, lethargy
 - iii. Muscle weakness or cramping
 - b. Causes:
 - i. Volume depletion
 - ii. Vomiting
 - iii. NG suctioning
 - c. Evaluation:
 - i. ABG: PCO_2 nl, $\text{pH} > 7.50$, $\text{HCO}_3^- > 28$ mEq/L;
 - ii. Serum potassium and chloride are usually both low
 - d. Treatment:
 - i. Correct underlying cause
 - ii. Correct volume depletion
 - iii. Administer KCl IV (0.5 mEq/kg over 1 hour.)
 - iv. Patients with good graft function after OLTxp often develop metabolic alkalosis if they have received a lot of blood products because their liver metabolizes the citrate preservative in blood products and convert it to bicarbonate

- v. In some cases patients need to be given Diamox or started on an HCl Acid Drip
- xviii. Electrolytes
1. Hypercalcemia
 - a. Signs and Symptoms:
 - i. Constipation
 - ii. Weakness or fatigue
 - iii. Nausea or vomiting
 - iv. Bradycardia
 - v. Hypotonicity
 - b. Causes:
 - i. Acidosis
 - ii. Immobilization
 - iii. Hypoproteinemia
 - c. Evaluation:
 - i. Serum Calcium >11
 - ii. Obtain Ph, Alk Ph, total protein, albumin, BUN, Cr, PTH and Vitamin D if elevated
 - iii. EKG: prolonged QRS or PR interval, shortened QT interval
 - d. Treatment:
 - i. Treat underlying cause
 - ii. Obtain serum calcium level every 12-24 hours depending upon severity
 - iii. Keep pt on cardiorespiratory monitoring until normalized
 - iv. Adequate hydration to increase UOP and calcium excretion
 - v. Diurese with Lasix (0.5-1mg/kg/dose),
 - vi. Calcitonin for mod hypercalcemia (11-14 mg/dL), pamidronate for severe hypercalcemia (>14 mg/dL)
 2. Hypocalcemia
 - a. Signs and Symptoms:
 - i. Seizures
 - ii. Positive chvostek's sign
 - iii. Positive trousseau sign
 - iv. Tetany
 - v. Hypotension
 - b. Causes:
 - i. Diuretics
 - ii. Hypoalbuminemia
 - iii. Hypoparathyroidism
 - iv. Alkalosis

- c. Evaluation:
 - i. Calcium <8.8mg/dL; check albumin (if have hypoalbuminemia may be falsely decreased— must correct serum Calcium in this setting), vit D, PTH levels;
 - ii. EKG to check for prolonged QT interval
 - d. Treatment:
 - i. Correct underlying cause
 - ii. IV Calcium Gluconate
 - iii. PO Calcium supplements + Vitamin D
3. Hyperkalemia
- a. Signs and Symptoms:
 - i. EKG changes may include:
 - ii. Peaked T waves
 - iii. Depressed ST segment
 - iv. Lengthened PR interval
 - v. Tingling or paresthesias
 - b. Causes:
 - i. Elevated potassium levels commonly seen in pt receiving Prograf
 - ii. Acidosis
 - iii. Hemolysis
 - iv. Side effect of spironolactone
 - v. Renal failure
 - c. Evaluation:
 - i. K greater than 5 mEq/L
 - ii. Check renal function, urine potassium, cardiac rhythm via continuous monitor, and/or 12-lead EKG
 - d. Treatment:
 - i. Correct underlying cause
 - ii. If CO₂ <20 mHg, give NaHCO₃ 1meQ/kg IV over 1 hour; repeat and bolus as indicated
 - iii. Consider Lasix 0.5-1mg/kg IV
 - iv. Consider Kayexelate 1g/kg/dose p.o
 - v. Consider Florinef 0.05-1mg p.o qd or bid
 - vi. For persistent hyperkalemia, consider insulin and calcium gluconate
4. Hypokalemia
- a. Signs and Symptoms:
 - i. Muscle weakness or cramping
 - ii. Hypotension
 - iii. Tachycardia
 - iv. Ileus

- b. Causes:
 - i. Diuretics
 - ii. Diarrhea or vomiting
 - iii. Alkalosis
 - c. Evaluation:
 - i. $K^+ < 3.5$
 - ii. EKG flat T waves, depressed ST segment, PVCs
 - d. Treatment:
 - i. Correct underlying cause
 - ii. Replete with IV KCl 0.5mEq/kg/dose, monitor serum levels and repeat as indicated
5. Hypomagnesemia
- a. Signs and Symptoms:
 - i. Tremor
 - ii. Spasm
 - iii. Cramps
 - iv. Convulsions
 - b. Causes:
 - i. Side-effect of prograf
 - ii. Renal failure
 - iii. Diuretics
 - iv. GI losses
 - c. Evaluation:
 - i. Serum Magnesium (supplement < 1.4 mg/dL)
 - d. Treatment:
 - i. IV Replacement: Magnesium Sulfate 50mg/kg(max 1 g) every 8 hours(infused over 4 hrs) x 1-3 doses
 - ii. Oral Replacement forms used:
 - 1. Mag carbonate liquid 54mg/5mL = 4.8 meq = 54mg elemental mag
 - 2. Mag oxide 400mg tablet = 20 meq = 240 mg elemental mag
 - 3. Mag plus protein 1 tablet = 11 meq = 133 mg elemental mag
6. Hypernatremia
- a. Signs and Symptoms:
 - i. Thirst
 - ii. Oliguria
 - iii. Nausea and vomiting
 - b. Causes:
 - i. Hyperglycemia
 - ii. Diuretics
 - iii. GI losses

- c. Evaluation:
 - i. $\text{Na} > 150 \text{ mEq/L}$; also check K, Ca, BUN, Cr and glucose
 - ii. IVF, strict I&O and neurological status
 - d. Treatment:
 - i. Correct slowly as rapid correction is associated with myelinolysis of the CNS. Should correct slowly by $1\text{-}2 \text{ mEq/L}$ every 2-4 hours.
7. Hyponatremia
- a. Signs and Symptoms:
 - i. Thirst
 - ii. Tachycardia and tachypnea
 - iii. Decreased urine output
 - iv. Irritability or lethargy
 - b. Causes:
 - i. Fever
 - ii. Vomiting, diarrhea, NG suction
 - iii. Wounds
 - iv. Malnutrition
 - v. Diuretics
 - c. Evaluation:
 - i. $\text{Na} < 130 \text{ mEq/L}$; check Urine sodium level ($< 10 \text{ mEq/L}$ indicative of sodium depletion; $> 50 \text{ mEq/L}$ indicative of expansion of ECF with water and/or renal tubular injury)
 - d. Treatment:
 - i. Correct underlying cause
- xix. Endocrine
- 1. Adrenal Insufficiency
 - a. Signs and Symptoms:
 - i. Hypotension with systolic blood pressure $< 90 \text{ mm/Hg}$ that is resistant to resuscitation
 - ii. Weakness and fatigue
 - iii. Anorexia
 - iv. Nausea and vomiting
 - v. Fever
 - vi. Hyponatremia or hypokalemia
 - vii. Acidosis
 - viii. Hypoglycemia
 - ix. Dehydration from renal sodium wasting
 - b. Causes:
 - i. Acute adrenal crisis is most commonly caused by suppression of the hypothalamic-pituitary-adrenal axis caused by steroid therapy

- ii. Relative adrenal insufficiency results when suboptimal cortisol production during septic shock
- c. Evaluation:
 - i. Adrenal insufficiency due to steroid wean is unlikely until pt reaches doses $<10\text{mg}/\text{m}^2/\text{day}$ hydrocortisone. If suspected once pt has reached this dose hold dose for 1 day and check random cortisol level and ACTH
 - ii. Cortisol Stimulation Test
 1. Obtain cortisol stimulation test when a random cortisol level is $<6\text{mcg}/\text{dL}$ (best to draw between 0600-0800 when endogenous cortisol production is highest)
 2. Draw serum cortisol at 0, 30 and 60 minutes following cosyntropin administration
 3. Administer cosyntropin IV bolus over 2 minutes (<2 y.o. 0.125mg , >2 y.o. 0.25mg)
 4. A maximum increase of cortisol ≤ 9 mcg/dL following intravenous synthetic adrenocorticotrophic hormone (ACTH) stimulation is associated with increased mortality from septic shock.
- d. Treatment:
 - i. Obtain Endocrinology consult
 - ii. If low, administer hydrocortisone. Generally begin steroid therapy (1 to 2 mg/kg per dose of hydrocortisone or its equivalent) after a random cortisol level is drawn
 - iii. A total random serum cortisol level <18 mcg/dL defines absolute adrenal insufficiency and indicates the need for continued glucocorticoid therapy
 - iv. Endocrine will advise a slow hydrocortisone wean if not an absolute insufficiency
 - v. Dexamethasone (0.1 mg/kg, maximum 10 mg) may be preferable for the initial steroid dose if ACTH stimulation testing is planned
- 2. Hypoglycemia:
 - a. Signs and Symptoms:
 - i. Diaphoretic
 - ii. Tachycardia
 - iii. Weakness
 - iv. Headache
 - v. Visual disturbances
 - vi. Confusion

- b. Causes:
 - i. Iatrogenic
 - ii. Liver failure
 - iii. Sepsis
 - iv. Adrenal insufficiency
 - v. Weaning from TPN
 - c. Treatment:
 - i. if conscious and able to swallow safely, provide with 15g carbohydrate (1/2 c juice, regular soda, milk or 3 glucose tablets);
 - ii. if no response within 10 minutes and/or symptomatic/ unable to swallow, D25 bolus 0.25-0.5g/kg over 1-2 minutes; *if no response*, consider glucagon <20kg .5mg, >20kg 1mg—may repeat in 20 minutes prn.
3. Hyperglycemia:
- a. Signs and Symptoms:
 - i. Glucose >200 mg/dL
 - ii. Thirst
 - iii. Polyuria
 - iv. Irritability
 - v. Headache
 - b. Causes:
 - i. Steroids
 - ii. Sepsis
 - c. Treatment:
 - i. For glucose >200 mg/dl, consider insulin gtt, adjusting necessary by checking q 1hr CBG
 - ii. If persists consult Endocrine
- xx. Infectious Disease
1. Infectious complications following transplant tend to be characterized into periods: early, mid or late.
 - a. Early Infection: the month following transplant. Infections that arise during this time are generally bacterial or candidal in origin. They are generally related to pre-existing conditions, intraoperative events or post-surgical risk factors (i.e. indwelling catheters and mechanical issues related to the graft.)
 - b. Mid Infection: months 2-6 following transplant. Characterized by opportunistic infections related to immunosuppression. Specifically, pneumocystis carinii, EBV and CMV.

- c. Late Infection: infections noted greater than 6 months post-transplant. The rate of infections is less as immunosuppression is less. Typically at risk for developing community acquired infections.
2. Febrile Patient
 - a. If patient develops a temperature of or greater than 38°C, the transplant team is to be notified and will order:
 - i. Prior to initiation of antibiotics pan culture patient to include: blood cultures of all central lines (all lumens initially) and peripheral, CXR, urine culture, JP drains (drawn from tubing, not the bulb)
 - ii. Consider additional cultures as indicated to include respiratory swab, stool cultures, wound culture and ET aspirate
 - iii. Obtain an ESR/ CRP for baseline interpretation.
 - iv. Based on pt clinical presentation, may consider KUB, Doppler Ultrasound to evaluate anastomosis and look for fluid collections, or CT Scan
 - v. Start empiric coverage with vancomycin and zosyn, consider broader coverage to include antifungals as directed by the Attending.
 - vi. Give Tylenol 15mg/kg p.o/prn q 6 hours
 - vii. Consider Motrin 10 mg/kg p.o q 8 hours if Tylenol not defervescing and not thrombocytopenic (based on Attending direction)
 - viii. Remove any unneeded or suspicious lines
 3. Bacterial Infections
 - a. Most common in solid organ transplant are staphylococci and enterococci
 - b. Treatment:
 - i. Narrow coverage as soon as indicated by culture results
 - ii. Consider consulting ID service
 4. Fungal Infections
 - a. Predisposing factors include prolonged operation, neutropenia, high level immunosuppression, choledochojejunostomy and prolonged exposure to broad antibiotic coverage
 - b. Aspergillus is the second most common fungal infection in transplant patients. Send serum galactomannan if concerned.
 - c. If documented fungal infection, must obtain yeast dissemination work-up to include Ophthalmology consult, echocardiogram and an ultrasound of the kidney, liver and spleen (as you can get a fungal emboli in all three organs.)

- d. Treatment:
 - i. If suspicious of a systemic yeast infection, consider broadening coverage with fluconazole or anidulafungin. If concerned for aspergillus (yeast or molds) consider broadening coverage with amphotericin or voriconazole as directed by the Attending. Will need to adjust the dose of prograf, as it will be driven up by the addition of fluconazole or voriconazole.
 - ii. Narrow coverage as indicated by sensitivities
- xxi. Pancreatitis
 - 1. Causes:
 - a. Drugs (thiazides, imuran, steroids, pentamidine)
 - b. Viral infection (EBV/ CMV)
 - c. Procedure (revision of bile duct or ERCP)
 - d. Hypercalcemia
 - 2. Evaluation:
 - a. Amylase/ Lipase
 - i. Amylase rises quickly and decreases quickly
 - ii. Lipase rises slowly and decreases slowly
 - b. Ransons Criteria for Pancreatitis Mortality:
 - i. On presentation:
 - 1. WBC >16,000
 - 2. Glucose >200
 - 3. LDH >350
 - 4. AST >250
 - ii. After 48 hrs:
 - 1. Hct drop >10%
 - 2. BUN increase >5mg/dL
 - 3. Calcium <8
 - 4. PaO₂ <60
 - 5. Base deficit >4 mg/dL
 - 6. Fluid needs >6L (adults)
- xxii. Viral Infections
 - 1. Adenovirus: Incidence is as high as 10% in pediatric liver transplant recipients and 50% in intestinal transplant patients. Typically occurs within three months of liver transplant. Source either from reactivation of latent infection or donor-associated transmission.
 - a. Evaluation:
 - i. Adenovirus quantitative PCR of blood
 - ii. If serum PCR +, systemic evaluation needed to include:
 - iii. Urine quantitative PCR

- iv. NP sample adenovirus qualitative
 - v. Stool adenovirus AG and stool viral culture
 - vi. If transaminitis consider liver bx w/ adeno stain
- b. Hand sanitizer is not effective against virus. Ensure “bubbles and bleach” precautions are in place until adenovirus is ruled out
- c. Treatment:
- i. Obtain Infectious Disease consult
 - ii. Lower immunosuppression as able
 - iii. Consider use of cidofovir
 - 1. 1mg/kg three times a week, infused over an hour
 - 2. Pre/post hydration with NS 3xM for 1 hr before and after cidofovir infusion then 2xM for 2 hrs after
 - 3. Initiate Probenecid for renal protection. Dosed at 1.25g/m² 3 hours before, 1 hour after, and 8 hours after treatment
 - 4. Check adenovirus PCR 2x/wk until PCR trends down then weekly
2. Cytomegalovirus (CMV): Most common after organ transplantation, at the rate of 59%. Typically seen 1-3 months following transplant
- a. Evaluation:
- i. CMV PCR. Obtain weekly with active infection
 - ii. If serologically shown with active infection, i.e. CMV IgM + obtain CMV PCR and CMV shell virus of the urine
 - iii. If CMV PCR +qualitative of tissue from liver biopsy, request staining for CMV of the tissue
- b. Treatment:
- i. Switch ganciclovir or valganciclovir administration to twice daily
 - ii. Consider cytogam IV weekly, until clearance of CMV load. Initial dose 150mg/kg, then 100mg/kg/dose thereafter.
 - iii. Discuss decreasing immunosuppression
3. Epstein-Barr Virus (EBV): Most commonly seen within 12 months of transplant
- a. Present as a systemic infection, hepatitis, mononucleosis or PTLD
- b. Evaluation:
- i. EBV PCR. Obtain weekly with active infection.
 - ii. If serologically shown with active infection, i.e. EBV IgM + obtain EBV PCR
 - iii. If EBV PCR +qualitative of tissue from liver biopsy, request staining for EBV of the tissue
- c. Treatment:
- i. Switch ganciclovir or valganciclovir administration to twice daily.

- ii. Consider cytogam IV weekly, until clearance of EBV load. Initial dose 150mg/kg, then 100mg/kg/dose thereafter.
 - iii. Discuss decreasing immunosuppression.
- 4. Herpes Simplex: Uncommon in the early post-operative period, while almost 10% will develop it after transplant.
 - a. Treatment:
 - i. Admit patient to an isolated room
 - ii. Consult ID
 - iii. Start Acyclovir 10mg/kg/dose IV q 8hr (less than 1 year) and 250mg/m²/dose IV q 8hr (greater than or equal to 1 year.)
- 5. Parvovirus
 - a. If suspicious for, check IgG and IgM, CBC, reticulocyte count, haptoglobin, free hemoglobin level, iron studies, serum folate and B12 level. May consider Parvovirus PCR if IgM positive.
 - i. Treatment:
 - 1. Consult ID.
 - 2. PRBC transfusion
 - 3. ferrous sulfate supplementation as indicated
 - 4. Consider decreasing immunosuppression
- 6. Varicella
 - a. Exposure defined as being in an enclosed room with a varicella infection for at least 30 minutes
 - b. If patient is exposed and is <1 year post-transplant or history of recent rejection/ with increased immunosuppression, treat as follows:
 - i. Consult ID
 - ii. Within 96 hours of exposure, administer IVIG (0.4-2g/kg)
 - iii. If pt is exposed and is >1 year post-transplant and has been on stable doses of immunosuppression monitor patient clinically and advise parents to do skin checks multiple times during the day during the incubation periods (10-21 days)
 - iv. If pt is with open lesions:
 - 1. Admit patient to an isolated room
 - 2. Consult ID
 - 3. Start Acyclovir 20mg/kg/dose IV q 8hr (less than 1 year) and 500mg/m²/dose IV q 8hr (greater than or equal to 1 year)
- 7. Post-Transplant Lymphoproliferative Disorder (PTLD): Generally EBV driven. Lesions can be found in the lymph nodes, head, neck, intestine, CNS, lungs or liver. Reported rate of occurrence 10% in pediatric liver transplant recipients with much higher rates in intestine transplant recipients.

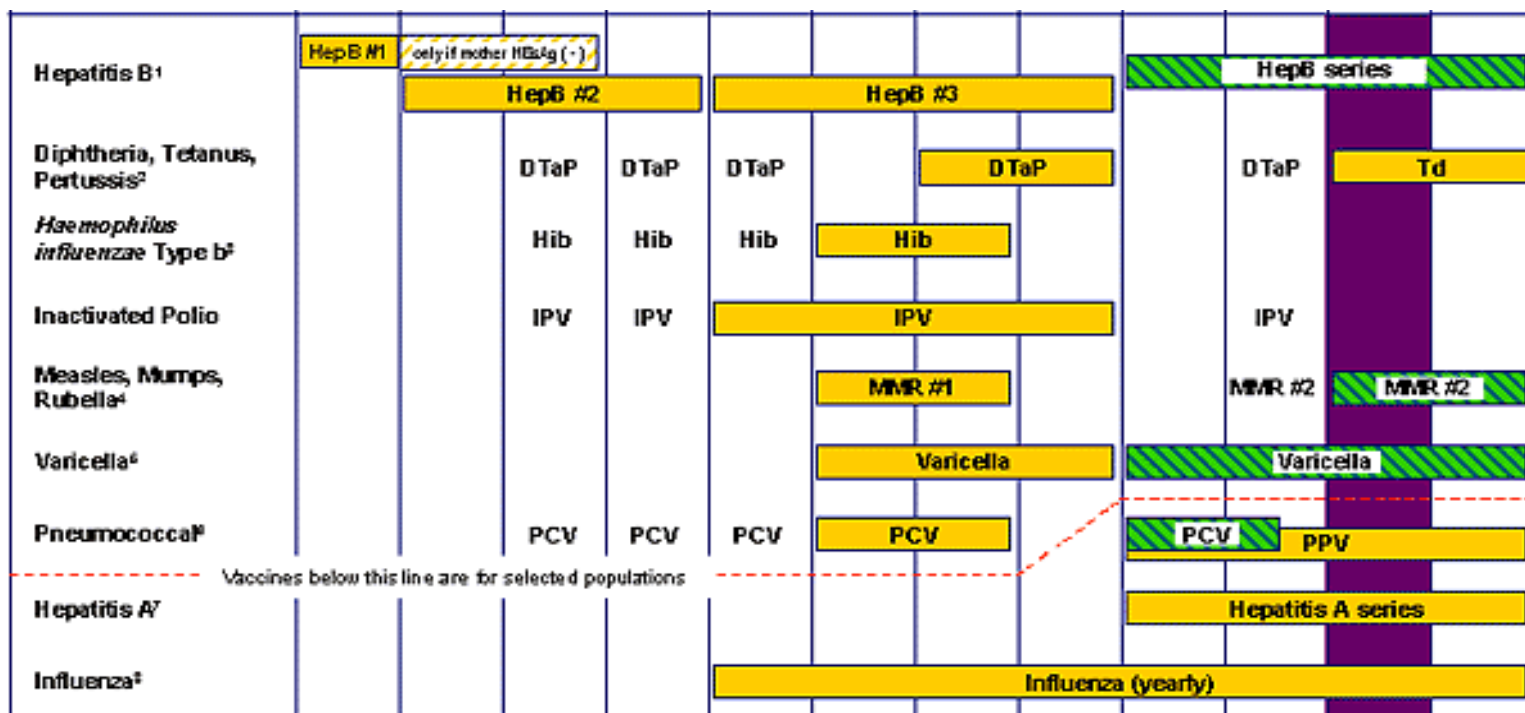
- a. Symptoms: constellation of symptoms varies by patient. If any of the following are noted with unknown etiology be cautious for the occurrence of PTLD
 - i. fever, diarrhea, hepatitis, tonsillar enlargement, lymphadenopathy, transaminitis, fatigue, anorexia, weight loss, abdominal pain, pancytopenia
 - b. Evaluation:
 - i. CT of head, neck and chest (with contrast)
 - ii. MRI of abdomen and pelvis (with and without contrast)
 - iii. Lymph node biopsy of nodes greater than 1cm on imaging or of any lesion concerning on imaging to aid with diagnosis
 - 1. Send biopsy for regular path (formalin), flow cytometry (EDTA medium), cytogenetics (preservation free heparin), and EBV in situ hybridization (formalin)
 - 2. If tissue positive for PTLD, consult Dr. Clare Twist with Oncology immediately and obtain PET and bone scan to complete staging work-up.
 - a. No dextrose may be given prior to PET scans
 - c. Classification as follows:
 - i. Early lesions (reactive plasmacytic hyperplasia & infectious mononucleosis-like)
 - ii. Polymorphic PTLD
 - iii. Monomorphic PTLD (classify according to lymphoma classification)
 - iv. Hodgkin lymphoma and Hodgkin-like PTLD
 - d. Treatment
 - i. Decrease/discontinue immunosuppression
 - ii. Rituximab +/- chemotherapy depending on classification
8. Immunizations
- a. Pre-Transplant:
 - i. Immunizations should be as complete as possible prior to transplant
 - ii. All live vaccinations must be given either on the same day or separated by at least 1 month
 - iii. All vaccines should be given a minimum of 4 weeks prior to transplant
 - iv. Keep patients on regular vaccination schedule if possible
 - v. Routine non-live vaccines: DTaP, IPV, Prevnar, Hib, Hep A, Hep B
 - vi. Routine LIVE: MMR, Varicella
 - vii. Other recommended:
 - 1. Pneumovax (> 2 years) need 2 doses of Prevnar prior to Pneumovax with 2 months separating each dose

- 2. Meningococcal (>11 year; recommended for teenagers and incoming college students)
- viii. If patient has not received pre-kindergarten vaccinations, booster doses should be given prior to transplant for IPV, Hib, DT, and MMRV for patients > 1 year after primary series
- ix. All transplant candidates should receive annual influenza vaccine. Household members should receive annual vaccine as well.
- x. Candidates <2 years should receive Synagis monthly during the determined winter months for RSV prophylaxis
- xi. Re-immunization for negative serology
- b. Infant Transplant:
 - i. Live vaccines could be given a minimum 9 months of age at least 6 weeks pre-transplant
 - ii. Infants should receive 2 doses 4-6 weeks apart prior to transplant for MMR, preferably 3 months apart for varicella if possible.
 - iii. Continue primary series after 3 months post-transplant if not completed before transplant
- c. Post-transplant:
 - i. No live viral vaccinations should be given after transplant (relative contraindications)
 - ii. If stable, refer to PCP to resume immunizations 3 months after transplant.
 - iii. Hep A and Hep B vaccines recommended if off steroids and low dose immunosuppression; titers every 3 months to check immunity
 - 1. Hepatitis B titers every 2 years
 - 2. Hepatitis A in high-risk areas or pre-travel
 - iv. MMR never given, unless there is a local epidemic
 - v. Varicella vaccine never given; if history of Varicella pre-transplant, draw titer 3 months post-op if on low immunosuppression and off steroids
 - 1. After any documented Varicella infection, draw a titer to document immunity status
 - vi. All recipients should receive annual influenza vaccine starting 1 month post-transplant
 - 1. For the first influenza season after transplant, recipients should receive 2 doses one month apart
 - 2. For patients treated with increased immunosuppression (thymo, rituximab, or other monoclonal antibody medications), 2 doses should be given one month apart for that influenza season
 - 3. Transplant patients can NOT receive the nasal spray vaccine

- vii. All recipients <2 years of age should receive monthly Synagis for RSV prophylaxis for 1 year following transplant
- d. Splenectomy Immunizations:
 - i. Prior to splenectomy (at least 2 days, ideally 14d) immunize for pneumococcal/ meningococcal/ HIB.
 1. Tetravalent meningococcal polysaccharide (2-10 y.o.) or Menactra (>2 y.o.)
 2. Prevnar (<2yo) or Pneumovax 23 (>2yo)
 3. HIB
 - ii. CDC recommends booster vaccinations every 5 hrs if asplenic
 - iii. Immediately following splenectomy, initiate antimicrobial prophylaxis with PEN VK <5yo 125mg p.o. bid, >5yo 250mg p.o bid (preferred choice, however, there is increasing resistance noted in the US and Amox tastes better)...alternatively may use amoxicillin 20mg/kg/d.
 - iv. Recommended to stay on prophylaxis up until age 5 and for at least a year post-splenectomy (if >5yo)--unless otherwise indicated.

Pediatric Liver Transplant Lucile Packard Children's Hospital Immunization Protocol

Birth 1mo 2mo 4mo 6mo 12mo 15mo 18mo 24mo 4-6yrs 11-12yrs 14-16yrs



This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines, as of December 1, 2002, for children through age 18 years. Any dose not given at the recommended age should be given at any subsequent visit when indicated and feasible. ■ Indicates age groups that warrant special effort to administer those vaccines not previously given. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and the vaccine's other components are not contraindicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

Approved by the Advisory Committee on Immunizations Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP)

xxiii. Common Procedures

1. Liver Biopsy

a. Pre-Procedure

- i. Make NPO at midnight
- ii. IVF 1xM
- iii. Type and Screen with 1u PRBCs on-hold
- iv. ASA/ Persantine are held for at least 24 hours prior
- v. Cipro (10mg/kg IV q 8hr) if pt has a Roux-En-Y
- vi. Coagulation Panel within 24 hours of procedure

b. Post-Procedure: (if done by Hepatology) Pt MUST stay in PACU until Hct drawn (and resulted) 4 hours post-biopsy. If within range, may be transferred up to acute care floor.

- i. Repeat Hct 8 hours post-biopsy
- ii. If concerns for active bleeding, obtain an abdominal ultrasound STAT

2. Endoscopy (EGD, Colonoscopy, Ileoscopy)

a. Pre-Procedure

- i. If using general anesthesia: Make NPO at midnight
- ii. If scoped via ileostomy, with sedation: NPO 4 hours before procedure
- iii. If scoped via ileostomy without sedation: NPO 1 hour before procedure
- iv. IVF 1xM when NPO
- v. Labs: Plt >50, INR<1.3, Hct>23 - or as otherwise directed. If suspect blood products may be required, type and screen with indicated products on hold
- vi. Medications:
 1. ASA/ Persantine are held for at least 24 hours prior
 2. Bowel Preparation (for colonoscopy): If indicated...
 - a. CL diet following lunch the day before the procedure
 - b. Golytely 10mL/kg/hr via NG, PO, GT up to a maximum rate of 300mL/hr until stools are clear

b. Post-Procedure

- i. Should be able to advance to a regular diet following procedure
- ii. Complications include intestinal perforation, bleeding or ileus. Monitor for nausea, vomiting, abdominal pain, tachycardia or dizziness.

3. Takedown/ Closure of Stoma
 - a. Generally considered 3-6 months following transplant if the patient has been free of complications.
 - b. Pre-Procedure
 - i. Barium Enema to assess anatomy and rule out stenosis or stricture (must obtain at least 2 days before to allow contrast to pass)
 - ii. Consider ileoscopy to assess for infection vs. rejection prior to final closure
 - iii. IVF 1xM when NPO
 - iv. Labs: Plt >50, INR<1.3, Hct>23 - or as otherwise directed. If suspect blood products may be required, type and screen with indicated products on hold
 - c. Medications:
 - i. ASA/ Persantine are held for at least 24 hours prior
 - ii. Bowel Preparation: If indicated...
 1. CL diet the day before the procedure, NPO after midnight
 2. Golytely 10mL/kg/hr via NG, PO, GT up to a maximum rate of 300mL/hr until stools are clear
 3. Be sure sirolimus is off 3 weeks prior
 4. Zosyn (100mg/kg) on call to OR
 - d. Post-Procedure
 - i. Zosyn continued q 8hr for 48 hours post-operatively
 - ii. NPO until motility resumes, advance diet as tolerated
 - iii. Monitor electrolytes daily
4. Percutaneous Transhepatic Cholangiogram (PTC)
 - a. Performed by IR, this study is used to assess pt with biliary complications, either suspected from laboratory results, MRCP or abdominal ultrasound
 - b. Pre-Procedure
 - i. NPO after midnight
 - ii. IVF 1xM
 - iii. Labs: Plt >50, INR<1.3, Hct>23 - or as otherwise directed
 - iv. Medications:
 1. Cipro (10mg/kg) administered during the procedure
 - c. Post-Procedure
 - i. May resume diet once tolerated
 - ii. Cipro continued for 24 hours post-procedure

5. Endoscopic Retrograde Cholangiopancreatography (ERCP)
 - a. Usually performed after an MRCP is performed that reveals pancreatic or biliary stricture with dilation
 - b. Pre-Procedure
 - i. NPO after midnight
 - ii. IVF 1xM
 - iii. Labs: Plt >50, INR<1.3, Hct>23 - or as otherwise directed
 - c. Medications:
 - i. Cipro (10mg/kg) administered during the procedure
 - d. Post-Procedure
 - i. May resume diet once tolerated
 - ii. Cipro continued for 24 hours post-procedure
6. Liver Resection
 - a. Pre-Procedure
 - i. NPO after midnight
 - ii. IVF 1xM
 - iii. Labs: CBCD, Coag Panel, Chem 15, Mag, Phos and GGT. Target Plt >50, INR<1.3, Hct>23 - or as otherwise directed. Type and Screen with products on hold as indicated.
 - iv. Medications:
 1. Ampicillin (50mg/kg) and Cefotaxine (50mg/kg) on call to OR to be administered during the procedure.
 - v. If not on liver transplant list, discuss with surgeon need to list
 - b. Post-Procedure
 - i. Admit to the PICU
 - ii. Place on D10 ½ NS
 - iii. Check Chem 15/Mg/Phos/GGT daily; correct K, Phos, Mg aggressively
 - iv. Once LFTs show a consistent downward trend, may reduce to daily Chem 10's
 - v. Check Hct, PT, INR, K, glucose q 6hrs until stable
 - vi. Discuss/notify fellow/ surgeon prior to giving any blood products
 - vii. Strip J-P drains q 2hr, check for bleeding or bile leaks. If bile leak is present, place drains to LIS and notify fellow/surgeon.
 - viii. Consider removing drains POD #5-7.
7. Choledochojejunostomy with creation of Roux-en-Y
 - a. Pre-Procedure
 - i. NPO after midnight
 - ii. IVF 1xM

- iii. Labs: CBCD, Coag Panel, Chem 15, Mag, Phos and GGT. Target Plt >50, INR<1.3, Hct>23—or as otherwise directed. Type and Screen with products on hold as indicated.
 - b. Medications:
 - i. Ampicillin (50mg/kg) and Cefotaxine (50mg/kg) on call to OR to be administered during the procedure.
 - c. If not on liver transplant list, discuss with surgeon need to list
 - d. Post-Procedure
 - i. Ensure biliary catheter draining properly
 - ii. Check J-P drain for bile. Bile leaks typically occur around POD 5-7
 - iii. Clamp biliary catheter on POD 5-7, per surgeon
 - iv. If no bile leak, DC J-P drain 24 hours after biliary catheter clamped
- 8. Portocaval/ Splenorenal Shunts
 - a. Pre-Procedure
 - i. NPO after midnight
 - ii. IVF 1xM
 - iii. Labs: CBCD, Coag Panel, Chem 15, Mag, Phos and GGT. Target Plt >50, INR<1.3, Hct>23— or as otherwise directed. Type and Screen with products on hold as indicated.
 - iv. Medications:
 - 1. Ampicillin (50mg/kg) and Cefotaxine (50mg/kg) on call to OR to be administered during the procedure.
 - b. Post-Procedure
 - i. Admit to the PICU
 - ii. Check Hct, PT, INR, K+, Glucose, NH₃ q 6hr
 - iii. Start Dextran40 in D5W over 8hr x 5-7 days (2.4mL/kg/dose)
 - iv. NO DEXTRAN if Iron allergy
 - v. US POD#1 and prior to DC to check spleen size and shunt patency
- xxiii. Standard Medications and Immune Suppression
 - 1. Immunosuppressive Agents
 - a. Methylprednisolone (Solu-medrol), Prednisone
 - i. Class: Glucocorticoid (intermediate acting)
 - ii. Actions:
 - 1. Inhibits prostaglandin production and inflammation
 - 2. Impairs T-cell sensitivity to antigens
 - 3. Prevents proliferation of cytotoxic T-cells
 - 4. Impairs interleukin production

- 5. Decreases macrophage mobility
- iii. Administration:
 - 1. IV (methylprednisolone/Solu-medrol)
 - 2. PO (Prednisone)
- iv. Side effects:
 - 1. Decreased resistance to infection, delayed wound healing
 - 2. GI irritation/bleeding
 - 3. Hypertension
 - 4. Hypernatremia, edema
 - 5. Hyperglycemia
- v. Long term:
 - 1. Mood swings, depression
 - 2. Cushingoid appearance
 - 3. Muscle wasting
 - 4. Diabetes mellitus
 - 5. Hirsutism
 - 6. Cataracts
- b. Tacrolimus, FK506 (Prograf)
 - i. Class: Antirejection
 - ii. Actions:
 - 1. Inhibits interleukin 2 production
 - 2. Blocks lymphokines that help activate T-cells
 - iii. Administration:
 - 1. IV-Dose is to be administered over 24 hours - DO NOT BOLUS
 - 2. PO or NG at 08:00 and 20:00
 - iv. Side effects:
 - 1. Nausea, vomiting, abdominal pain, diarrhea
 - 2. Hypertension, headache, flushing
 - 3. Tremors
 - 4. Chest pain
 - 5. Edema
 - 6. Anemia
 - v. Toxicity:
 - 1. Confusion, anxiety, restlessness, insomnia
 - 2. Elevated liver chemistries
 - 3. Nephrotoxicity (elevated BUN and creatinine, decreased urine output)
 - 4. Hyperkalemia, hypomagnesemia

- vi. PEARLS:
 1. Prograf typically is given PO or NG due to risk of seizures associated with IV administration
 2. If IV prograf is used, one lumen must be designated for administration and clearly marked. Please do not use any other lumen and do not draw prograf levels from it. Prograf adheres to the lumen and may cause false elevations in levels.
 3. Oral dose is three to four times the IV dose
- c. Cyclosporine (Neoral, Sandimmune)
 - i. Class: Immunosuppressant
 1. Actions:
 - a. Inhibits macrophage secretion of interleukin 2
 - b. Interferes with production and activity of cytotoxic and helper T-cells
 2. Administration:
 - a. PO (Neoral)
 - b. IV (Sandimmune) over several hours, or as slow continuous drip in designated line
 - c. Use non-PVC tubing
 3. Side effects:
 - a. Decreased resistance to infection
 - b. Nausea, vomiting, diarrhea
 - c. Hypertension
 - d. Headache
 - e. Leg cramps
 - f. Hyperkalemia, hypomagnesemia
 4. Long term:
 - a. Hirsutism
 - b. Gingival hyperplasia
 - c. Lymphocytopenia
 5. Toxicity:
 - a. Nephrotoxicity (elevated BUN and creatinine, decreased urine output, edema)
 - b. Hepatotoxicity (elevated liver chemistries, jaundice)
 - c. Tremors, seizures
 6. PEARLS:
 - a. Bile enhances cyclosporine absorption. If the T-tube/biliary drain is clamped, the cyclosporine dose may be reduced.
 - b. Oral dose is three times the IV dose
 - c. Do not give within 4 hours of sirolimus dose

- d. Rabbit antithymocyte globulin (RATG)
 - i. Actions:
 1. Reduces the number of circulating T-cells
 2. Reduces the proliferative function of T-cells
 - ii. Administration:
 1. IV, over eight hours
 2. Must specify peripheral or central line
 - iii. Premedication:
 1. Acetaminophen (Tylenol), diphenhydramine (Benadryl), and methylprednisolone (Solu-Medrol) 30 minutes before administration
 2. Side effects:
 - a. Decreased resistance to viral infection, especially CMV and HSV
 - b. Thrombocytopenia
 - c. Fever
 - d. Back pain
 3. Allergic reaction:
 - a. Anaphylaxis
 4. PEARLS:
 - a. In spite of premedication, patients may still react with tachycardia, tachypnea, sudden high fever, and anxiety. Reduce the IV rate and call the MD. Breakthrough reaction may be treated with a high dose of short-acting steroid such as hydrocortisone (Solu-Cortef).
- e. Mycophenolate mofetil (CellCept)
 - i. Actions:
 1. Inhibits production and proliferation of T- and B-cells
 2. Inhibits antibody formation
 3. Inhibits production of cytotoxic T-cells
 - ii. Administration:
 1. IV(over two hours), PO (9AM/9PM)
 - iii. Side effects:
 1. Decreased resistance to infection, delayed wound healing
 2. Hypertension
 3. Hyperkalemia
 4. PEARLS:
 - a. Bioavailability may be increased by acyclovir and gancyclovir. Dose may need to be adjusted for patients also receiving acyclovir or gancyclovir.

- b. Food, antacids, magnesium and prograf can inhibit the absorption.
- f. Alemtuzumab (Campath)
 - i. Actions:
 - 1. binds to CD52 surface antigen of multiple cell
 - 2. resulting in lysis (monoclonal antibody)
 - ii. Administration:
 - 1. IV-infused over 2 hours
 - 2. Side Effects:
 - a. Infusion reactions (mild)
 - b. Rigors, fever
 - c. Nausea, vomiting, diarrhea
 - d. Hypertension, Hypotension, dyspnea
 - e. Rash, urticaria, pruritus
 - f. Fatigue
 - 3. Less Common:
 - a. Infusion reactions (severe)
 - b. Anemia, pancytopenia
 - c. SVT, severe hyper/hypotension
 - d. Bronchospasms
 - e. Seizures
 - f. Hepatic failure, pancreatitis
 - g. Infections
 - h. Anaphylaxis
 - 4. PEARLS:
 - a. Must be used within 8 hours of dilution by pharmacy
 - b. Due to possibility of anaphylaxis, ensure reaction medications are ordered prior to administration.
- g. Sirolimus (Rapamune)
 - i. Actions:
 - 1. Inhibits interleukin 2-mediated T-cell activation and proliferation
 - 2. Inhibits cytokine-driven T-cell proliferation
 - 3. Inhibits antibody production
 - ii. Administration:
 - 1. PO, four hours after cyclosporine (Neoral, Sandimmune) administration
 - 2. Doses adjusted to serum level and renal function
 - iii. Side effects:
 - 1. Nausea, vomiting, diarrhea
 - 2. Headache

- 3. Hypokalemia
- 4. Fever, leukopenia
- 5. Anemia, thrombocytopenia
- 6. Hyperlipidemia, hypercholesterolemia
- iv. PEARLS:
 - 1. Sirolimus delays wound healing so is usually not initiated until 3 weeks post op
 - 2. Due to absorption interference, space sirolimus at least 4 hours after prograf or cyclosporine
- h. Basiliximab
 - i. Actions:
 - 1. Immunosuppressant, monoclonal antibody
 - ii. Administration:
 - 1. IV on POD 0 and 4
 - iii. Pre medications:
 - 1. Acetaminophen (Tylenol) and diphenhydramine (Benadryl) 30 minutes prior to each infusion
 - iv. Side effects:
 - 1. Nausea, vomiting, diarrhea
 - 2. Headache
 - 3. Fever
 - 4. Hypertension
 - 5. Anemia
- xxiv. Infection prophylaxis medications
 - 1. Anidulafungin
 - a. Class: Antifungal
 - b. Action:
 - i. Inhibits fungal cell wall synthesis
 - ii. Antifungal prophylaxis for isolated/combined small bowel transplant recipients
 - c. Side effects:
 - i. Diarrhea
 - ii. Hypokalemia
 - iii. Infusion reaction
 - d. Less common:
 - i. Hepatic dysfunction
 - 2. Nystatin
 - a. Class: Antifungal
 - b. Actions:
 - i. Interferes with fungal DNA replication to prevent Candida infection

- c. Administration:
 - i. Oral (swish & spit)
 - ii. Powder
 - iii. Cream
 - iv. Suppository
 - d. Side effects:
 - i. Nausea
 - ii. Vomiting
 - iii. Diarrhea
 - iv. Cramps
 - v. Rash
3. Clotrimazole (Mycelex)
- a. Class: Antifungal
 - b. Actions:
 - i. Provides oral candida prophylaxis
 - c. Administration:
 - i. PO troche
 - ii. Lozenge
 - d. Side effects:
 - i. Nausea
 - ii. Vomiting
4. Pentamidine
- a. Class: Anti-parasitic
 - i. Actions:
 - 1. Interferes with protozoa nuclear metabolism
 - 2. Prophylaxis for pneumonia caused by *Pneumocystis carinii*
 - ii. Administration:
 - 1. IV
 - 2. Inhaled
 - b. Side effects:
 - i. Azotemia
 - ii. Renal impairment
 - iii. Nausea, anorexia
 - iv. Hypo/hyperglycemia
 - c. Less common:
 - i. Cardiac arrhythmias, QT prolongation, VT
 - ii. Bronchospasms
 - iii. Nephrotoxicity, hepatotoxicity
 - iv. Pancreatitis
 - v. Diabetes mellitus

- vi. Anaphylaxis
- 5. Trimethoprim, sulfamethoxazole (Septra, Bactrim)
 - a. Class: Antibacterial
 - b. Actions: Provides prophylaxis for:
 - i. Pneumocystis carinii pneumonia (PCP)
 - ii. E. coli
 - iii. Klebsiella
 - iv. Streptococcus
 - v. Enterobacter
 - c. Administration:
 - i. IV
 - ii. PO/NG
 - d. Side effects:
 - i. Nausea
 - ii. Vomiting
 - iii. Diarrhea
 - iv. Stomach Cramps
 - v. Joint and muscle pain
 - e. Allergic reaction:
 - i. Fever, chills
 - ii. Rash
 - iii. Anaphylaxis
- 6. Cytomegalovirus (CMV) immune globulin (CytoGam)
 - a. Class: Immune globulin
 - i. Used for patients with symptomatic CMV/EBV infection
 - b. Actions:
 - i. Provides high concentration of IgG antibodies against CMV
 - c. Administration:
 - i. IV, in designated line with in-line filter
 - ii. Side effects:
 - 1. Nausea, vomiting
 - 2. Muscle cramps, joint and back pain
 - 3. Fever, chills
 - 4. Flushing
 - 5. Wheezing
 - 6. Neutropenia, thrombocytopenia
 - 7. Hypotension
 - iii. Allergic reaction: Anaphylaxis
- 7. Hepatitis B immune globulin (HBIG)
 - a. Class: Immune globulin

- b. Actions:
 - i. Provides active and passive immunity to hepatitis B
 - ii. Prevents recurrent HBV infection of the liver graft in recipients with HBV
- c. Administration:
 - i. IV, in designated line
- d. Side effects:
 - i. Nausea, vomiting, diarrhea, stomach cramps
 - ii. Headache
 - iii. Fever
 - iv. Muscle and joint pain
 - v. Hypotension
- e. Allergic reaction:
 - i. Anaphylaxis
- xxv. Surgical Prophylaxis
 - 1. Anticoagulants: Anticoagulation is indicated in liver transplant recipients to prevent thrombosis of hepatic vessels. They are typically not used in isolated/combined small bowel recipients.
 - a. Heparin
 - i. Class: Anticoagulant/thrombolytic
 - ii. Actions:
 - 1. acts at multiple sites in coagulation process; binds to antithrombin III catalyzing inactivation of thrombin and other clotting factors
 - iii. Administration:
 - 1. IV continuous infusion
 - iv. Side effects:
 - 1. Prolonged clotting time
 - 2. Fever, chills
 - 3. Urticaria
 - 4. Bleeding
 - v. Less common: hemorrhage
 - 2. Dextran 40
 - a. Class: anti-platelet, volume expander
 - b. Actions:
 - i. enhances endogenous fibrinolysis while reducing platelet adhesion to vWF and platelet activation by thrombin
 - c. Administration:
 - i. IV- may be given as bolus in the OR or infused over 8 hrs (usually overnight)

- d. Side effects:
 - i. Hypotension
 - ii. Nausea/vomiting
 - iii. Fever
 - iv. Nasal congestion, wheezing
 - v. Urticaria
 - e. Less common:
 - i. Pulmonary edema
 - ii. Anaphylaxis
 - f. PEARLS:
 - i. Dosed daily for 5 days; should be timed to 2200-0600 with at least 18 hours between doses
3. Persantine
- a. Class: Anti-platelet
 - b. Actions:
 - i. inhibits platelet adhesion
 - c. Administration:
 - i. PO/NG, twice daily
 - d. Side effects:
 - i. Nausea, vomiting, diarrhea, abdominal pain
 - ii. Dizziness
 - iii. Hypotension
 - iv. Headache
 - v. Flushing
 - e. Less common:
 - i. Hypotension (serious)
- xxvi. Additional medications
1. Lactulose
- a. Class: Ammonia binder, laxative, stool softener
 - b. Actions:
 - i. Prevents reabsorption of ammonia in the colon (binds ammonia for excretion in the stool), stimulates bowel motility, softens stool by drawing fluid into the colon
 - c. Administration:
 - i. PO/NG
 - ii. Enema
 - d. Side effects:
 - i. Diarrhea
 - ii. Nausea
 - iii. Vomiting

- iv. Abdominal cramps
- 2. Octreotide acetate (Sandostatin)
 - a. Class: Synthetic hormone used in patients with acute GI bleeding or risk of GI bleeding
 - b. Actions:
 - i. Decreases splenic circulation, gastric motility, and pancreatic secretions
 - c. Administration:
 - i. IV drip
 - d. Side effects:
 - i. Nausea, vomiting, diarrhea, stomach cramps
 - ii. Dizziness, fatigue
 - iii. URI symptoms
 - e. Less common:
 - i. Bradycardia, arrhythmias
 - ii. Syncope
 - iii. Pancreatitis
 - iv. CHF
- xxvii. Bortezomib/plasmapheresis protocol:
 - 1. Consult pheresis nurses to determine what type of plasmapheresis line patient will require
 - 2. Provide pheresis center with dates patient will be getting pheresis based on protocol
 - 3. Consult Renal to follow patient and write orders for pheresis
 - 4. Contact Pharmacy to notify them of plan to give bortezomib and make sure medication is available
 - 5. Must call pharmacy on bortezomib days to notify them that medication is “okay to give.”
 - 6. If patient’s first time receiving plasmapheresis they will require admission to PICU for monitoring

Treatment Day	1	2	4	5	8	9	11	12	15±1	16±2	17±2	30±7
Plasmapheresis 1.5 volume exchange	X		X		X		X		X	X	X	
Dexamethasone PO 20mg/1.73m ² , to max of 20 mg	X	X	X	X	X	X	X	X				
Bortezomib ^a 1.3mg/m ² IV	X		X		X		X					
Rituximab ^b 500mg/m ²	X										X	
MIG 2 gram/kg IV maximum 140 g/dose											X	
CBC and Fibrinogen Level	X		X		X		X		X	X	X	
Donor Specific Antibody	X											X

Up to 3 cycles have been reported to increase effectiveness. Should be at least 1 month between cycle

^aNo interval between doses of bortezomib less than 3 days due to increased toxicity

^bIf B cells are depleted from previous cycles no need to give further Rituximab

5% albumin. If fibrinogen falls to less than 150, or if bleeding risk, use 100% FFP
To be given the day of and day after Bortezomib. Administer after pheresis is complete on pheresis days
After Oral Dexamethasone and pheresis are complete. Recommend premedicate with Benadryl, solucortef and acetaminophen
May not be needed if previously treated and still has suppressed B cells. Give AFTER pheresis if needed
After last pheresis is complete
Draw PRE pheresis on day 1. For day 26±7 the earliest would be day 19 and the latest day 33. Test closer to day 19 if multiple cycles are anticipated

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