

## Care of the Post-Transplant Patient

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## Complications of Liver Transplantation

- Hypertension
- Obesity
- Hyperlipidemia
- Hyperkalemia
- Diabetes mellitus
- Bone disease
- Renal dysfunction

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## Systemic Hypertension

- Develops in 40 to 70% of patients following orthotopic liver transplantation
- Occurs in both adults and children
- Related to underlying renal disease, calcineurin inhibitor and corticosteroid use
  - Prevalence greater in those on cyclosporine than tacrolimus

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## Calcineurin Inhibitors and Hypertension

- Mechanisms
  - Sodium sensitivity greater in those receiving calcineurin inhibitors
    - Causing greater salt and water retention
  - Decreased glomerular filtration with enhanced sodium resorption
  - Increased systemic vascular resistance due to arterial vasoconstriction

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## Systemic Hypertension

- Early therapy
  - Reduce corticosteroids
  - Diuretics as initial therapy to control volume
  - Add calcium channel blockers early
  - Add beta-adrenergic blockers
  - ACE inhibitors of limited value early
- Later therapy
  - Weight loss
  - Diuretics of limited value and increase creatinine
  - Can add ACE inhibitors but watch potassium

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## Obesity

- Common
  - More than 70% of orthotopic liver transplant recipients become obese
  - Effect of corticosteroids on appetite
  - Inactivity
  - Pre-operative obesity equals post-operative obesity
- Those transplanted for NASH may develop NASH in the transplanted organ
- Dietary control and exercise are still the best options

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## Diabetes Mellitus

- 10 to 20% of patients will develop post-OLT diabetes mellitus
  - Severity decreases with calcineurin inhibitor and corticosteroid dose reduction
    - Tacrolimus > cyclosporine in causing diabetes mellitus
  - Hepatitis C associated with greater likelihood of post-OLT diabetes mellitus
  - Obesity increases risk of insulin resistance and clinical diabetes mellitus

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## Diabetes Mellitus

*J Heart Lung Transplant 2004;23:S194*

- Risk factors for new-onset diabetes mellitus post-transplant
  - Family history of diabetes mellitus
  - Pre-transplant glucose intolerance
  - Corticosteroids and CN inhibitors post-OLT
  - Concurrent hepatitis C
  - Obesity
  - Possibly African-American race

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## Diabetes Mellitus

- Post-transplant care
  - At least 20% of recipients will require initial insulin therapy immediately post-OLT
  - Long-term management
    - Dietary control for all
    - Reduce corticosteroids
    - Oral agent with insulin added if control suboptimal?
      - Up to 8% will need long-term insulin therapy
    - Associated hyperlipidemia frequent

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## Hyperlipidemia

- Common
  - Develops in ~ 50%
  - ▣ Associated with risk of cardiovascular complications
- Risk factors
  - ▣ Pre-transplant hyperlipidemia
  - ▣ Hypercholesterolemia with CsA > tacrolimus
  - ▣ Hypertriglyceridemia in > 75% of patients on sirolimus

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## Hyperlipidemia

- Patients should be regularly screened for hyperlipidemia
- Therapy
  - Low fat diet, exercise program, smoking cessation, weight reduction if needed
  - Consider stopping offending medications
  - Utilize statins as needed
    - ▣ Monitor for muscle and liver injury

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## Hyperkalemia

- Common
- Immunosuppressant medications such as cyclosporine or tacrolimus are associated
- Therapy
  - Reduce total potassium intake
  - Utilize binding resins acutely
  - Utilize a mineralocorticoid long-term?
  - Limit ACE inhibitor use?

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## Bone Disease Post-OLT

- Related to underlying liver disease
  - Reduced bone mineral density (BMD) common
    - Especially cholestatic liver disease
  - BMD may worsen during the first year post-op due to corticosteroids -> fracture risk
  - Calcium, vitamin D and bisphosphonates
- Bone pain may develop
  - Symptoms of nocturnal pain
  - Salmon calcitonin may reduce pain
- Avascular necrosis occurs in 5+%

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## Renal Dysfunction

- A serum creatinine > 1.5 mg/dl develops in up to 50-80% of orthotopic liver transplant recipients
  - GFR reduction to 60% early post-OLT
  - Typically occurs as a consequence of immunosuppressant agents
- Renal tubular acidosis may develop from immunosuppressant agents

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## Renal Dysfunction

- Therapy
  - Exclude dehydration
  - Reduce or eliminate diuretics
  - Stop NSAID administration
  - Consider reduction of immunosuppression
  - Consider addition of sirolimus with reduction of cyclosporine or tacrolimus level?
    - Some might argue this is with increased risk

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## Hepatic Dysfunction

- Potential causes
  - Allograft rejection
  - Chronic hepatitis
  - Infections
  - Biliary tract disease
  - Ischemic injury
  - Medications
  - Recurrent disease

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## Acute Allograft Rejection

- Affects up to 30 +% of recipients
  - The majority within the first 3 months
  - Early rejection is more easily controlled
- Early rejection can be associated with a viral infection such as CMV
- Late acute rejection often related to reduction of immunosuppression
  - More difficult to control

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## Chronic Allograft Rejection

- Develops in 6 of 8% of recipients
- Risk accelerated by
  - Late or recurrent acute allograft rejection
  - Inadequate immunosuppression
  - Transplantation for prior chronic rejection
  - CMV infection, PBC, PSC, autoimmune hepatitis, and hepatitis C infection?
- Therapy is continued immunosuppression

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## Chronic Hepatitis

- Histologic evidence of chronic hepatitis
  - Portal inflammation with variable interface hepatitis
- Generally occurs after 1 year post-OLT
- Mild abnormalities of liver tests
  - Anti-nuclear antibody titers may be high
- Can result in progressive liver injury
- Autoimmune hepatitis also reported

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## Infections

- Often related to immunosuppression
- Frequency of infections declines with time
- Bacterial infections account for much of the early mortality following OLTx

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## Prevention of Infections

- Pre-transplant prophylaxis
  - Pneumococcal vaccination
  - HAV vaccination
  - HBV vaccination
- Post-transplant prophylaxis
  - Acyclovir
  - Bactrim or pentamidine (or azithromycin?)

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### Causes of Bile Duct Injury

- Develops in ~20% of patients
- Associations
  - Hepatic artery thrombosis
  - Prolonged cold ischemia time
  - Acute allograft rejection
    - Vasculitis of bile duct arterioles
  - Chronic allograft rejection
  - Viral injury?

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### Causes of Ischemic Hepatic Injury

- Associations
  - Hepatic artery thrombosis
  - Prolonged warm ischemia time
  - Prolonged cold ischemia time?
  - Intraoperative hypotension
  - Severe allograft rejection
  - Cardiopulmonary causes

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### Special Issues following Transplantation

- Malignancies
- Sun exposure
- Ethanol use
- Sexual issues
- Pregnancy
- Travel
- Communication

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## Malignancy

- Types
  - Squamous cell carcinomas
    - ▣ Often multicentric (40%)
    - ▣ Locations include oropharynx, skin, cervix, vagina
  - Basal cell carcinoma
  - Melanoma
  - Lymphomas
    - ▣ B cell lymphomas most common
  - Kaposi's sarcoma

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## Cutaneous Malignancy

- Most common tumors following liver transplantation – incidence of 4.5%
  - Squamous cell and basal cell account for 90%
  - Melanoma and Kaposi's sarcoma occur
  - Overall mortality 1.6%
- Increased risk related to immunosuppression
- Surveillance crucial

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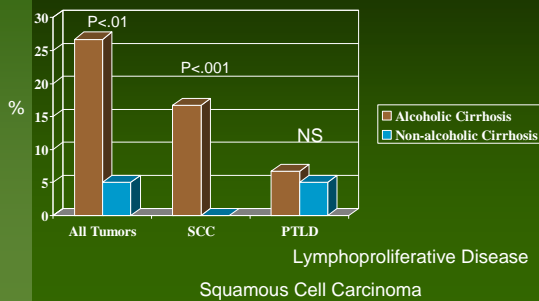
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## Oropharyngeal Carcinomas After Liver Transplantation



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### Post-transplant Lymphoproliferative Disease

- Mostly **polyclonal** B-cell lymphomas
- **EBV**-related
- Frequently **hepatic** infiltration
- Often an **ENT** presentation
  - Sinus, tonsils, neck nodes, Waldeyer's ring, etc.
- Also occurs in the **gastrointestinal tract**, CNS, mediastinum, and mesentery

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### Colon Cancer

- Increased risk in those with **underlying ulcerative colitis transplanted for sclerosing cholangitis**
- **Annual colonoscopy with mucosal biopsy** for dysplasia should be accomplished **in all** those with ulcerative colitis
- Limited de novo risk in others transplanted and lacking UC or Crohn's
  - Colonoscopy every 5 years?

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### Sun Exposure

- Sun exposure should be limited
- Use a **high SPF sun lotion** at all times in prolonged sun
- Good **skin cover-up** essential
  - Hat
  - Long sleeved shirt
  - Slacks
  - Etc.

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### Ethanol Use

- For the alcoholic, never
- For the non-alcoholic
  - Use is discouraged
  - Ethanol use should be limited, especially early after transplantation
- Concerns
  - Abnormal liver tests
  - Drug interactions

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### Sexual Issues Following Orthotopic Liver Transplantation

- Discuss the issues early
- Initial contraception is encouraged
  - Method of choice should depend on the couple and patient
  - An unwanted pregnancy is a problem whether in the patient or the spouse
  - Women pregnant within 6 months of OLTx have an increased risk of acute allograft rejection

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### Pregnancy Following Solid Organ Transplantation

- A normal pregnancy is possible
  - Delay until 1-2 years post-transplantation
- Immunosuppressive medications should be continued throughout the pregnancy
- Potential problems
  - Miscarriage
  - Pre-eclampsia/hypertension
  - Premature labor more common
  - Increased neonatal problems/risk
    - Low birth weight more likely

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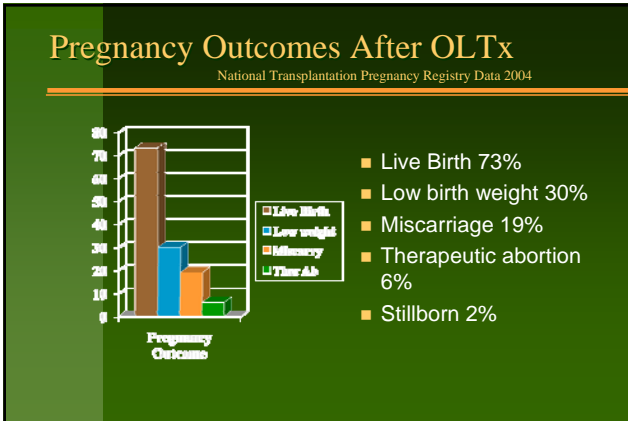
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- ### Travel Following Orthotopic Liver Transplantation
- **Travel is acceptable**
  - The transplant center should be informed
  - The transplant center can assist in arranging:
    - Emergency contacts
    - Laboratory evaluation while traveling
    - Recommendations for vaccination and other travel needs

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- ### Communication
- Good **communication** with the transplant center **is a two-way street**
  - Whenever you have a concern, call
  - The initial contact may be the outpatient nurse coordinator
    - These are highly skilled nurses with an excellent understanding of post-transplantation complications

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### Reasons to Call the Transplant Center

- Uncontrolled hypertension
- Recent onset neurologic problems including headache
- Worsening liver tests
- Worsening azotemia
- Worsening dyspnea/chronic cough
- Any concerns you may have

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