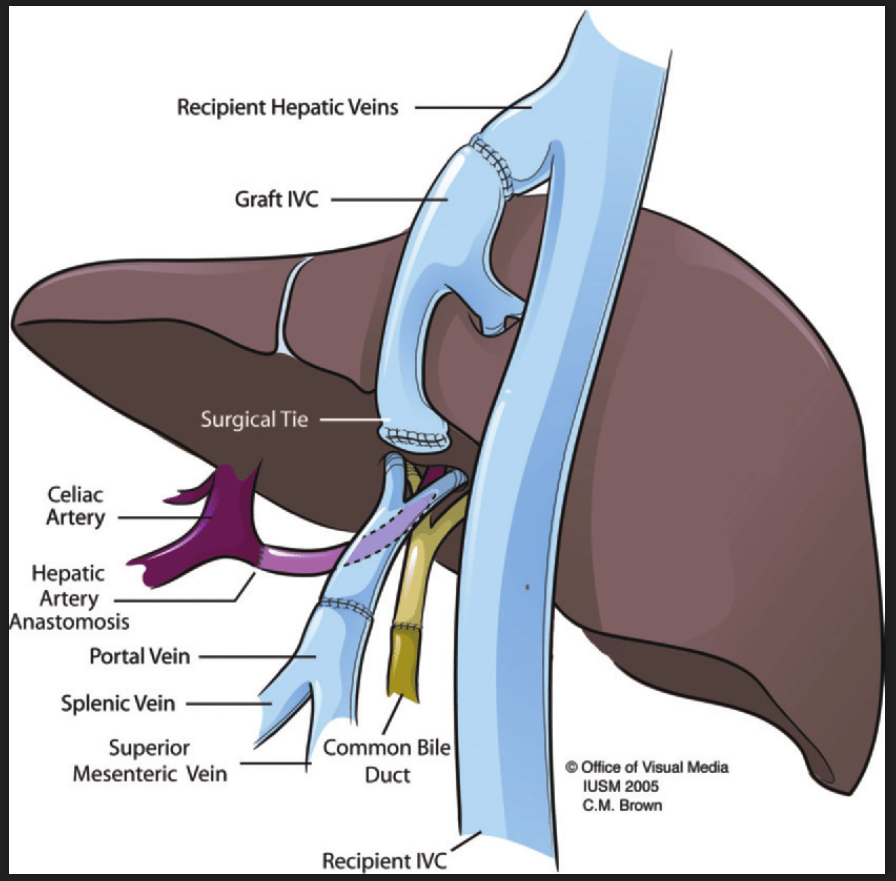
Post Operative Complications and Infections in Liver Transplants

What the heck is going on in there?

What is actually involved in an “OLTx”

- You need to understand the basics for you to understand why these complications and infections occur.
  - So firstly, what all occurs during a liver transplant?



Common Post OLTx Complications

- Acute Cellular Rejection
- Vascular Thrombosis
- Biliary Leak or Stricture
- Bleeding
- Primary Non-function
- **Infections**

Acute Cellular Rejection

- Acute cellular rejection (ACR) occurs in 15–25% of liver transplant recipients on Tacrolimus based immunosuppression regimens and generally improves with steroids in majority
- ACR does not affect long term graft or patient survival in most of cases
- High dose steroids are standard of care for ACR and doses vary depending on the program. Usually 500–1000 mg pulse of methylprednisolone is given for 1–3 days followed by taper
- Steroid resistant ACR may happen in approximately 10% of ACRs
  - Treatment typically at this center is Thymoglobulin

Vascular Thrombosis

- Portal Vein Thrombosis and/or Hepatic Arterial Thrombosis
- Although vascular complications following OLTx seldom occur (7%). They are the most feared complications with a high incidence of both graft loss and mortality, as they compromise the blood flow of the fresh transplant.
- Hence why we get doppler ultrasounds ~12 hours after transplant

What happens if an acute thrombosis occurs?

- A hepatic artery thrombosis (HAT) usually occurs in the very early stages after liver transplantation.
- Because the liver depends on the hepatic artery for most of its oxygenated blood and perfusion of bile ducts, HAT can lead to acute massive hepatocyte necrosis, formation of a central biloma secondary to intrahepatic duct necrosis, multiple biliary structures, or intermittent bacteremia.
- Venous complications are less frequent
- However, they can be potentially devastating and lead to graft failure if they occur early post operatively.
- If developed later, manifestation of portal hypertension can be seen
- Surgical thrombectomy is traditionally required in the early post-operative period (for both), but for venous percutaneous radiological intervention has progressively become the best therapeutic option with good outcomes and safety.

Biliary Stricture

- Most common complication post transplant (~15% to 30%)
- Anastomotic stricture vs NAS
- Causes for AS typically due to: improper surgical techniques, small caliber of the bile ducts, a mismatch in size between the donor and recipient bile ducts, tension at the anastomosis, excessive use of electrocauterization for control of bile duct bleeding, and infection
- Causes for NAS include preservation injury, prolonged cold and warm ischemia times, donation after cardiac death, and prolonged use of vasopressors in the donor) and immunogenicity (chronic rejection, autoimmune hepatitis, and primary sclerosing cholangitis)
- ERCP with stent placement is the most common treatment for anastomotic stricture

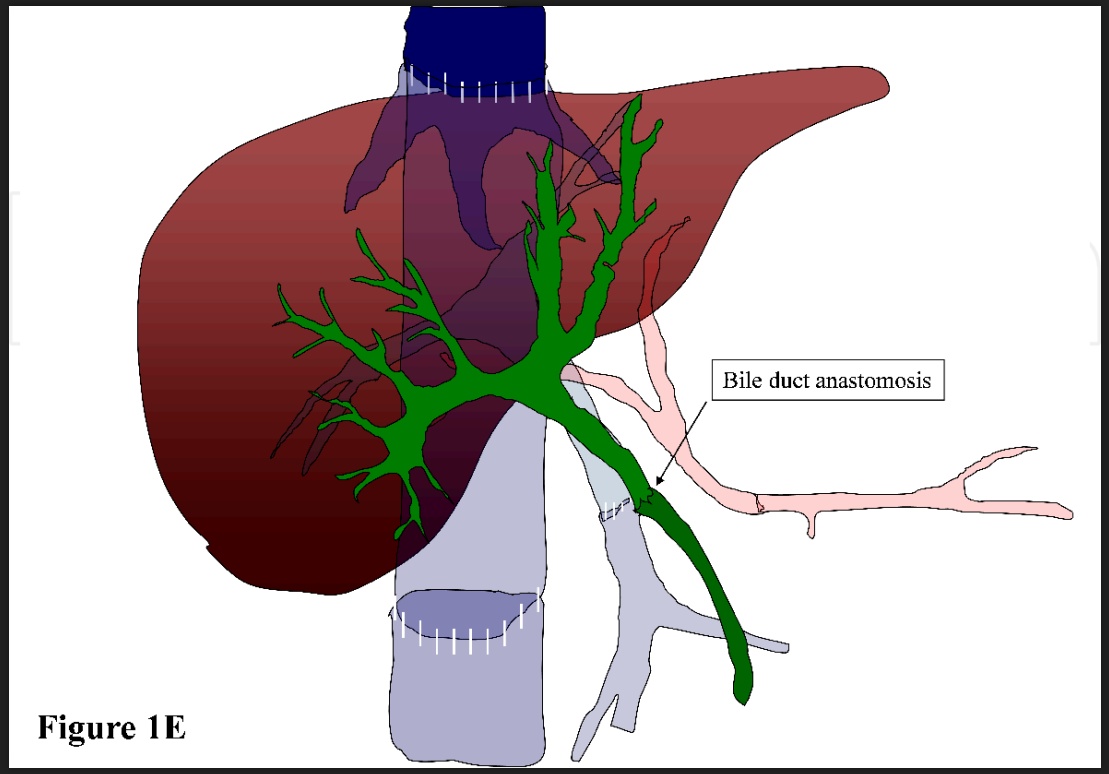


Figure 1E

Bleeding

- Delayed graft function, coagulopathy, imperfect hemostasis, or slippage of a tie can result in postoperative bleeding that requires re-exploration or post operative resuscitation.
- Postoperative bleeding occurs 15 to 30%% of patients and requires re-exploration in approximately 25% of those that bleed.

Primary Non-Function

- Super Rare
- PNF is characterized by post-transplantation encephalopathy, coagulopathy, minimal bile output, and progressive renal and multisystem failure.
- Typically you will notice increasing lactate and rapidly rising liver enzyme levels and histologic evidence of hepatocyte necrosis in the absence of any vascular compromise.
- Reducing cold ischemia times, and newer preservative solutions, the risk of primary nonfunction has decreased.
- Patients with initial dysfunction, also known as primary graft dysfunction, might recover with support, but those who progress to show evidence of extrahepatic complications, such as hemodynamic instability, renal failure, or other organ system dysfunction, can require urgent retransplantation.

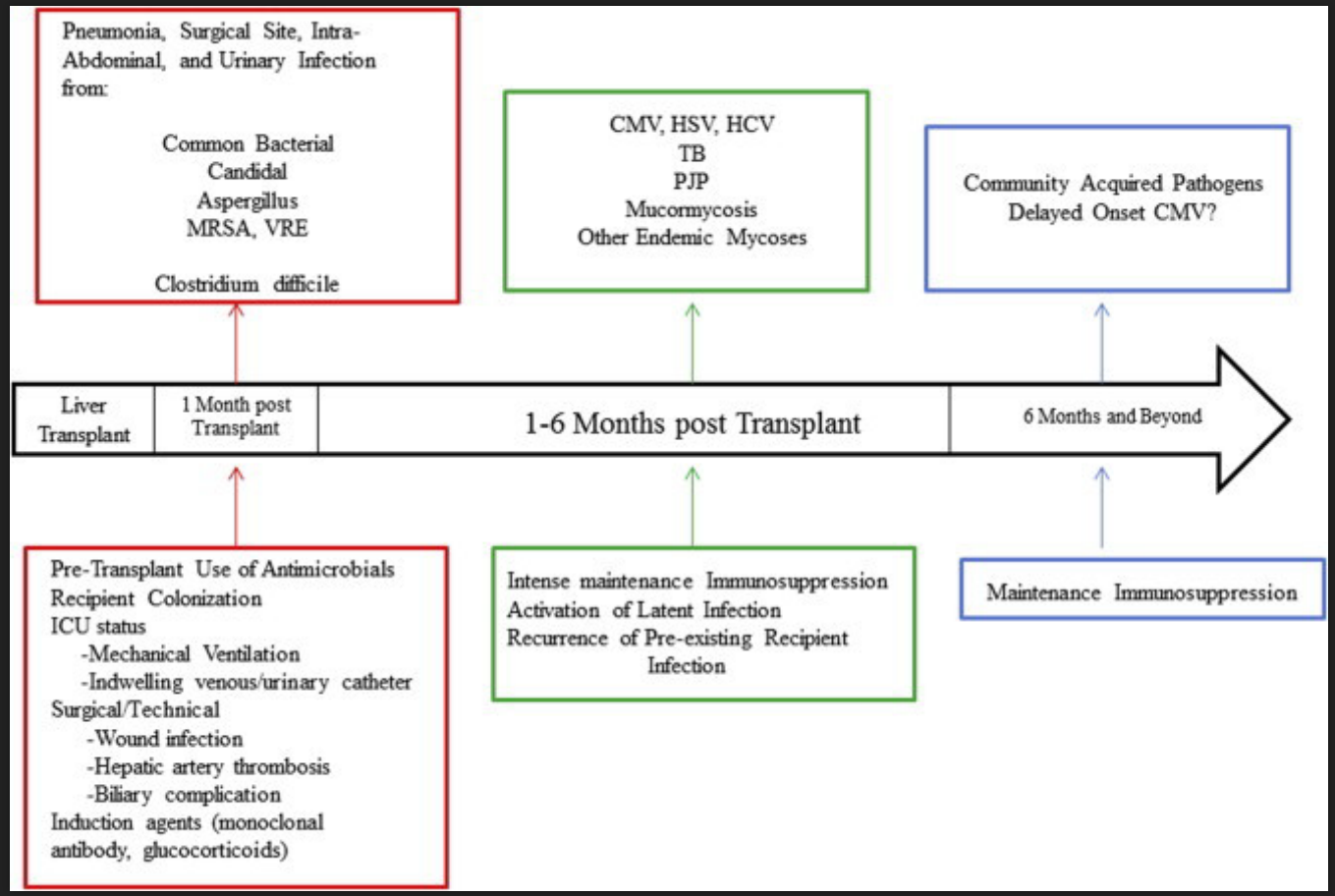
Infections

- High patient and graft survival rates have been achieved due to the efficacy of potent immunosuppressive agents. (60-70% 5-10 year survival rate post Transplant)
- Systemic immunosuppression has made the transplant patients susceptible to de novo infections as well as reactivation of preexisting latent infections.
- The risk of infection after OLT is strongly influenced by the net state of immunosuppression
- Post OLTx infections are estimated to occur in more than **60% of OLT patients!**
- **Leading Cause of death for transplant recipients within their first year**
- Infections occurring during the first month post-OLTx are usually nosocomial, donor-derived, or the result of a perioperative complication.

Factors that cause increased rate of infections

- Pretransplant MELD score greater than 30
- Need for a second operation after OLTx
- Post transplant RRT
- ICU longer than 48 hours (eek!)
- Invasive devices
- Protein-calorie malnutrition
- Immunosuppression

Time Line


Pneumonia, Surgical Site, Intra-Abdominal, and Urinary Infection from:
Common Bacterial
Candidal
Aspergillus
MRSA, VRE
Clostridium difficile
CMV, HSV, HCV
TB
PJP
Mucormycosis
Other Endemic Mycoses
Community Acquired Pathogens
Delayed Onset CMV?
Liver Transplant
1 Month post Transplant
1-6 Months post Transplant
6 Months and Beyond
Pre-Transplant Use of Antimicrobials
Recipient Colonization
ICU status
-Mechanical Ventilation
-Indwelling venous/urinary catheter
Surgical/Technical
-Wound infection
-Hepatic artery thrombosis
-Biliary complication
Induction agents (monoclonal antibody, glucocorticoids)
Intense maintenance Immunosuppression
Activation of Latent Infection
Recurrence of Pre-existing Recipient Infection
Maintenance Immunosuppression

Most common infections post transplant

- Bacteria
  - Bacterial infections account for most posttransplant infections (up to 70%), followed by viral and fungal infection
  - Bacterial infections can occur anywhere in the recipient but most frequently occur in the abdomen, blood stream, lung, and urine
  - Most common bacteria include *MRSA, VRE, ESBL Klebsiella Pneumonia, ESBL E. Coli, and C. Diff*
    - *Unfortunately mostly MDROs*
    - Frequent use of antibiotics prior to surgery for varying indications (e.g. infection and SBP prophylaxis) render liver transplant recipients vulnerable to multi-drug resistant strains of bacteria

Viral

- CMV! Most common viral infection that influences outcomes after transplant
  - Donor/Recipient status matter
  - CMV syndrome accounts for over 60% of CMV diseases after OLT, and it is usually presents with fever, malaise, and bone marrow suppression.
  - Less frequently, CMV may manifest as a tissue-invasive disease (all the "itits" ie colitis, enteritis, esophagitis, gastritis, hepatitis, pneumonitis, encephalitis, retinitis)
  - CMV has immunomodulatory effects, which can make patients more susceptible to developing opportunistic infection
- EBV
  - Not as common
  - EBV infection can lead to posttransplant lymphoproliferative disease (PTLD) in SOT recipients
- Varicella Zoster
- HSV
- HHV
- Adenovirus
- Parvovirus

Fungal

- Candidiasis is the most frequent fungal infection encountered after orthotopic liver transplantation and the leading cause of invasive fungal infection.
  - The gastrointestinal tract is often colonized with candidal species and those with advanced liver disease/cirrhosis may be predisposed to super-colonization
  - CMV infection is a big risk factor for all types of candidal infections, and CMV prophylaxis among high-risk patients has been shown to significantly decrease the incidence of invasive *Candida* infection
- *Aspergillus* is the second most common fungal infection after orthotopic liver transplantation and account for approximately one quarter of invasive fungal infections after transplant

So what do we do to combat this?

- Prophylactic Antibiotics/Antivirals/Antifungals
  - PCP
  - Candida (Thrush vs systemic)
  - CMV
- Good steward of antibiotics
- Attention to and constant assessment of the need for invasive catheters and drains
- Incentive spirometry and early mobilization may potentially combat atelectasis and pneumonia or aspiration pneumonitis