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University Hospitals Birmingham NHS
NHS Foundation Trust

# Birmingham Liver Transplant Unit
# Clinical Guidelines Short Version

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# BIRMINGHAM LIVER TRANSPLANT UNIT

## FY1-2/REGISTRAR

## Clinical Guidelines (short version)

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**SHO/REGISTRAR Clinical Care Guidelines**
This is only a short version of the Liver Unit's protocols. A full version is available on the trust intranet

**CONTENTS**

## Section 1
## How to assess a patient for liver transplantation

**•Important points in history**

Full history and systemic inquiry, including full alcohol history

Aetiology and accurate time course of illness and effect on quality of life

Episodes of decompensation (ascites, variceal bleed, encephalopathy and spontaneous bacterial peritonitis)

Details of biopsy and relevant treatments

Full family and social history.

**•BLOOD WORK UP**

**HAEMATOLOGY** Red form (2 purple,1 red, 1 light blue)

FBC AND COAG SCREEN including INR, direct Coombs, blood film and retics

**BIOCHEMISTRY** Green form (1 grey, 3 gold, 1 red and 1 dark blue)

U+E, LFT, GLUCOSE, CALCIUM, PHOSPHATE, TOTAL PROTEIN, ALPHAFOETOPROTEIN, IRON STUDIES, CERULOPLASMIN, THYROID FUNCTION, ALPHA 1 ANTI TRYSPIN

**BLOOD TRANSFUSION** Red form (1 purple)

GROUP AND SAVE x 2 (NHSBT want the blood group to be confirmed on 2 Samples for patient to be registered)

**URINE FOR ACR AND URINARY SODIUM**

**ARTERIAL BLOOD GASES if saturations less than 96%**

**IMMUNOLOGY** Yellow form (2 red tubes)

ANA AMA SMA, Ig subclasses, TTG

**VIROLOGY** Orange form (1 purple, 1 red)

HBsAg AND anti HBc Hep B Surface Antibodies Titres (to determine if patient needs vaccinating), HAV, HCV, CMV IgG (not CMV PCR), VZV, HIV

**•MICROBIOLOGY**

URINE CULTURE, SPUTUM CULTURE, ASCITES CULTURE IF PRESENT + WCC COUNT

**•RADIOLOGY**

CXR AND ABDO ULTRASOUND WITH DOPPLER

**•CARDIAC**

ECG AND ECHO FOR ALL
Please refer to cardiac protocol for guidance can you insert intranet link?

**•UPPER GI ENDOSCOPY**

NOT REQUIRED IF DONE IN PREVIOUS 3 MONTHS

**•PULMONARY FUNCTION TESTS**

Spirometry on ward

**•DIABETES**

HbA1c and urine ACR,

Refer to Surgeon and Anaesthetic team (LRTC will do this)

## Transplant assessment:

- LRTC meets elective patients on day 1 and discusses the assessment week.
- Identify social or psychological issues and refer them on to MDT.
- They will ascertain patients understanding of their liver disease and their expectations.

- Wednesday between11.00-13.00 the LRTC do an education session for the out patient assessments, In patients who are fit and mobile will be taken to this session (Phase 3) (AVOID BOOKING TESTS FOR THIS TIME)

- Naturally plans can change for patients during the assessment week; it is helpful for the LRTC to be kept informed of these changes so they can give accurate information to the patient and MDT (including surgeons and anaesthetists).

- Prior to discharge accepted patients will need prescribing vaccinations for Hepatitis A and/or Hepatitis B (depending on their virology results). Give s/c if clotting deranged or low platelets.

- Prior to discharge inform the LRTC so that they can ensure that all the relevant information for listing (i.e. consent for registration at UK Transplant, their measurements etc) has been obtained.

**Assessment meeting**

•Patient presented to assessment meeting by Liver registrar

•Details of decision to be documented by letter

•Possible outcomes:

1. Patient listed for transplantation (organised by transplant co-ordinator)

2. Patient not listed

3. Decision deferred until further investigations are performed

**LRTC will inform them of the outcome and will call the patient when they have been activated on the list**

**Management on waiting list**

•Patients seen every 6 weeks in outpatient clinic

•If problems occur resulting in the patient becoming unsuitable for transplantation, they need to be suspended from the list (contact transplant coordinator on call).
LRTC Office ext 2422 (Mon – Fri 8-4)
E mail : LRTC
Group Pager : 07699 769075

●USS and Doppler every 3 months
●Group and save on every clinic appointment (this determines if they have developed antibodies and impacts on the decision making process of setting up of the transplant by the LRTC)

**Section 2**
**How to assess a patient with fulminant hepatic failure**

**Important points in history**

Full history and systemic inquiry

If paracetamol, as much information about psychiatric history and precipitating event.

Alcohol and drug abuse should be specifically sought

Full family, travel and social history

Current and previous drug history

**Important points on examination**

Look for stigmata of chronic liver disease

**Urgent psychiatric opinion should be sought in Paracetamol poisoning**

**Blood work up (URGENT)**

HAEMATOLOGY
FBC and COAG screen, PT

BIOCHEMISTRY
U+E'S, LFT'S, GLUCOSE, CALCIUM, MAGNESIUM

**GROUP AND SAVE on admission**

VIROLOGY Phone lab and order as urgent

HIV, HBsAg, HCV, Hep A, Hep E AND CMV.

ARTERIAL BLOOD GASES with lactate
**ECG and CXR (URGENT)**
**Review need for urgent imaging – USS liver**

Note these are all the urgent investigations, they will require the full phase 1 assessment bloods

**Important management points in fulminant hepatic failure**

●Hourly BM stix due to risk of hypoglycaemia

●All patients require close monitoring of there fluid balance.

●If hypoglycaemic less than3.5mmol/l, commence infusion of 50% dextrose at 10ml/hr and adjust depending on blood glucose levels

●Watch for encephalopathy:

Grade 1:Drowsy
Grade 2:Agitated or confused
Grade 3:Unconcious, rousable
Grade 4:Unconcious, unrousable

●ITU should be made aware of any fulminant patient at an early stage

●All fulminants should receive IV PPI Esomeprazole 40mg IV daily

●Any fulminant patient with fever, hypothermia or unexplained clinical deterioration should have blood cultures (remember mycology) and commenced on broad spectrum antibiotics (Tazocin 4.5g tds). Of note, the patients' microbiology results (whether in UHB or from a referring hospital) should be reviewed with regard to resistant organisms.
●Fluconazole 100mg/OD
●Please refer to fulminant protocol once patient is on ITU

**Section 3**
**Kings College criteria (for fulminant liver failure)**

**Note:**

Encephalopathy must be present to fulfill the diagnosis of fulminant hepatic failure

**Paracetamol Overdose**

Arterial blood pHless than7.3 or $H^+$more than50 (irrespective of severity of encephalopathy) after volume loading

OR

Lactate more than3.0mmol/L after fluid resuscitation

OR

Prothrombin time more than100 seconds (INR more than6.5) and serum creatinine more than300umol/l in patients with grade III/IV encephalopathy

**Non-Paracetemol Causes**

Prothrombin time more than 100 seconds (INR more than 6.5) (irrespective of grade of encephalopathy)

OR

Three of the following (irrespective of the grade of encephalopathy):

1) Age less than 10 or more than 40 years
2) Cause being non A non B hepatitis, halothane hepatitis or idiosyncratic drug reaction
3) Duration of Jaundice before encephalopathy more than one week
4) Prothrombin time more than 50 seconds (INR more than 3.5)
5) Serum bilirubin more than300 umol/l

**Selection for Super-Urgent Transplantation**

The current UKT criteria as recently published for registration for a Super-urgent transplant fall into the following 9 categories, the first 4 referring to paracetamol hepatotoxicity;

Category 1: Aetiology: Paracetamol poisoning: pH less than7.25 more than 24 hours after overdose and after fluid resuscitation

Category 2: Aetiology: Paracetamol poisoning: Co-existing prothombin time more than100 seconds or INR more than6.5, and serum creatinine more than300 µmol/l or anuria, and grade 3-4 encephalopathy

Category 3: Aetiology: Paracetamol poisoning: Serum lactate more than 24 hours after overdose more than3.5 mmol/l on admission or more than3.0 mmol/l after fluid resuscitation

Category 4: Aetiology: Paracetamol poisoning: Two of the three criteria from category 2 with clinical evidence of deterioration (eg increased ICP, $FiO_2$ more than50%, increasing inotrope requirements) in the absence of clinical sepsis

Category 5: Aetiology: Seronegative hepatitis, hepatitis A, hepatitis B, or an idiosyncratic drug reaction. Prothrombin time more than100 seconds or INR more than6.5, and any grade of encephalopathy

Category 6: Aetiology: Seronegative hepatitis, hepatitis A or hepatitis B or an idiosyncratic drug reaction. Any grade of encephalopathy, and any three from the following: unfavourable aetiology (idiosyncratic drug reaction, seronegative hepatitis), age more than40 years, jaundice to encephalopathy time more than7 days, serum bilirubin more than300µmol/l, prothrombin time more than50 seconds or INR more than3.5

Category 7: Aetiology: Acute presentation of Wilson's disease, or Budd-Chiari syndrome. A combination of coagulopathy, and any grade of encephalopathy

Category 8: Hepatic artery thrombosis on days 0 to 14 after liver transplantation

Category 9: Early graft dysfunction on days 0 to 7 after liver transplantation with at least two of the following: AST more than10,000 U/L, INR more than3.0, serum lactate more than3 mmol/l, absence of bile production

These are the only indication for entry onto the super-urgent transplant waiting list

Super urgent patients are listed by the LRTC after consultation from the on call surgeon and physician

**Section 4**
**What to do when a patient is admitted for liver transplantation**

When a liver becomes available the registrar and transplant FY1 will be informed by the transplant co-ordinator, they will inform you of theatre times. The recipient will be informed by the LRTC. The hospital notes of the patient should be retrieved from the waiting list shelf in the Dr's office on Ward 726 by the reg.

On arrival to the transplant unit the potential recipient requires the following workup:

**HISTORY AND EXAMINATION:** Concentrating particularly on events since the patient's most recent interview.

**INVESTIGATIONS:**

**BLOOD TESTS**

FULL BLOOD COUNT, COAGULATION SCREEN
U+E'S, LFT's, TOTAL PROTEIN, GLUCOSE
Please phone labs and mark as urgent
If Bloods are dramatically different from the last clinic bloods inform the LRTC

**ASCITIC TAP** (For urgent WCC, absolute neutrophil/lymphocyte count, gram stain and culture unless this has been done in the previous week)

**CHEST X-RAY**

**ECG**

**BLOOD AND BLOOD PRODUCTS** will be ordered by the LRTC (6 units of blood, 2 adult doses of platelets, and 10 units FFP) **They will have discussed with the Consultant Anaesthetists if anything extra is required and will inform you**. The House Officer will need to fill out the request forms and take the blood sample from the patient.

**CONSENT FOR THE OPERATION** (This will be done by the Consultant Surgeon prior to listing). The registrar can confirm the consent.

**CMV STATUS OF PATIENT AND THE DONOR TO BE DOCUMENTED**

**OFTEN REQUIRE FURTHER BLOOD SAMPLING FOR CURRENT TRANSPLANTATION RESEARCH STUDIES.**

**CONSULTANT ANAESTHETIST, THEATRES, ITU, PHYSICIAN AND THE SURGEONS ARE INFORMED BY THE CO-ORDINATORS.**

**It is imperative that the registrar reviews the patient as soon as the results are available. If there are any concerns as to whether the recipient is well enough to undergo transplantation surgery or in cases of ALD had a drink whilst being on the waiting list then the transplant coordinator must be informed. This gives us the opportunity to identify and call in another recipient at the earliest possible opportunity. Delays can cause organs to be wasted.**

**It is important the LRTC are informed if there are any problems as we may need to discuss with the consultant surgeons re swapping patients.**

The organ donation is completely anonymous therefore no donor donation information is given to recipients including where the retrieval team has gone. This information will be given to the patient in an appropriate manner by the LRTC's at a appropriate time.

## 9. ANTIRETROVIRAL ESSENTIALS

1. Stop all antiretrovirals the night before transplant.
2. Start immunosppression after grafting as per **patient specific protocol** and discussion with consultants. Do not restart antiretrovirals until renal function stable and bowels working.
3. On the day antiretrovirals (in practice it's the protease inhibitors that are the problem although Efavrienz induces P450) are re-introduced give 0.5mg of Tacrolimus then **pause** Tacrolimus on PICS. Give further doses according to blood levels (If unsure d/w David Mutimer, Andrew Holt, Geoff Haydon and Ahmed Elsharkaway, and Mandy Smith- liver unit pharmacist as there are difficult drug interactions to consider

A bespoke exposure pack will be prepared for each patient according to their most recent drug sensitivities and will be left with the LRTC by Mandy Smith

**Section 5**
**Post OP management and investigation**

## 1. PATIENT IS TRANSFERRED TO ITU POST OP (SEE FULL PROTOCOL FOR ITU CARE)

## 2. ON RETURN TO ITU

- Read ITU discharge summary
- Summarise history and events post op
- Examine and document findings including CMV status of donor and recipient

## 3.CHECK FBC U+E'S LFTs COAG SCREEN CALCIUM AND PHOSPHATE and TACROLIMUS LEVEL (Must be trough)

## 4.MAINTENANCE FLUIDS

- Hartman's solution or Alternating Nacl 0.9% / 5% Dextrose
- To be titrated to: Blood pressure
  CVP
  Urine output
  Output from abdominal drains and NG tube

## 5.ANALGESIA

- Usually at first provided by morphine / fentanyl PCA.

## 6.MONITORING

- Aim for HRmore than greater than 60/ min and less than less than100/ min
  MAP more than65mmHg
  CENTRAL VENOUS PRESSURE more thangreater than 4 cmH2O andless than less than8 cm H2O
  HAEMOGLOBIN more than greater than 85 g/L and less than less than100 g/L

**7.Immunosupression**

- Triple therapy is standard in most patients

- **TACROLIMUS**: Calcineurin inhibitor

  ORAL

  3mg BD initially, if under 60 kg give 2mg BD and withhold dose if concerns about kidney function

  Aim for 12 hour post dose levels of around 5-8ng/ml

  Monitored daily

  Dose adjustments are based on the clinical picture not only the blood level, and should be discussed with the consultant.

- **AZATHIOPRINE**

  ORAL - Oral dose round to nearest 25mg.

  1.5mg/kg/day

- **PREDNISOLONE**

  20mg /day (22.5mg for AIH) or 100mg Hydrocortisone IV bd until able to take oral drugs

  (Dose reduced in 5mg increments every 3 weeks and discontinued at 3 months post-op.)

**8. Infection prophylaxis**

- **PCP**: Cotrimoxazole 480mg on alternate days for 3 months

- **Anti-Fungal**: Fluconazole 100mg/day, once out of ITU commence nystatin 20,000iu QDS. High risk patients should have Ambisome 50mg od whilst on ITU

- **CMV**: In CMV +ve donors if the recipient is Negative they will commence VALGANCICLOVIR 900mg OD on day 7 (reduce dose in renal dysfunction). Continue treatment for 3 months. Also non-immediate re transplants should receive CMV prophylaxis.

- **TB prophylaxis:** In all at risk patients prescribe Isoniazid 100mg OD with pyridoxine 10mg OD

- **Bacterial:** 3 doses of Tazocin 4.5g IV tds post op if allergic Ciprofloxacin 400mg IV BD and Metronidazole IV 500mg TDS

- **Hepatitis B**

Patients transplanted for hepatitis B will normally have undetectable viral load, as indicated by undetectable HBV-DNA in serum, either as a result of

previous seroconversion or as a result of recent administration of lamivudine 100mg daily. In both these circumstances, patients transplanted for HBV disease will receive hepatitis B immunoglobulin (HBig) during the anhepatic phase (10 000 units) and then for 3 consecutive days post-operatively (5 000 units/day). It is then given according to Hepatitis B surface antibody titres.

Blood should be sent to microbiology to check hepatitis B surface antibody titres and hepatitis B surface antigen twice weekly while the patient is in hospital. The aim of HBIg administration is to maintain titres above 100 IU/L.

When the patient is discharged from hospital, HBIg is administered in the Liver Unit Out-patient Department. Longer term, HBIg is given every 3 months

If a donor liver is Hep B core Ab +ve the recipient will require lamuvidine 100mg OD.

**9.PEPTIC ULCER PROPHYLAXIS**

- lansoprazole 30mg OD (esomeprazole 40mg IV whilst on ITU)

**10.BLOOD MONITORING**

- Daily FBC, COAG, U+E'S, LFTs, Tacrolimus, Ca2+ Po4+ and Mg2+. daily

**11. CONSIDER ASPIRIN 75MG OD PO IF AT RISK OF HEPATIC ARTERY THROMBOSIS**

**Section 6**
**Common post-op problems**

- **Fever**
- **Abnormal LFT's post transplant**
- **Poor urine output**
- **Graft rejection**

**Fever**
Fever may be due to
- sepsis
- Rejection
- Resolving haematoma
- Thrombosis
- Graft infarction

**Remember:**
- Not every fever will be sepsis
- Sepsis will not always be accompanied by fever

All patients are at risk of infection in liver transplantation

1. Examine patient looking for sites of infection (chest, urinary tract, abdomen and lines)
2. Carry out a full sepsis screen

- Bacteriology: blood cultures, MSU, sputum, ascitic tap, and skin and wound swabs.
- Mycology: as above
- Virology: consider CMV (if suspected send CMV-PCR)

3. Consider U/S and liver biopsy

4. Aim to remove CVP line, A-line, urinary catheter as early as possible(culture line tips). Under guidance of Hepatology registrar.

5. If sepsis suspected i.e.
- Temp more than38°C
- Unexplained ↓ in BP and ↑ in HR
- WCC more than10 less than2
- Unexplained deterioration especially conscious level
- Unexplained deterioration of hepatic function
- Unexplained oliguria

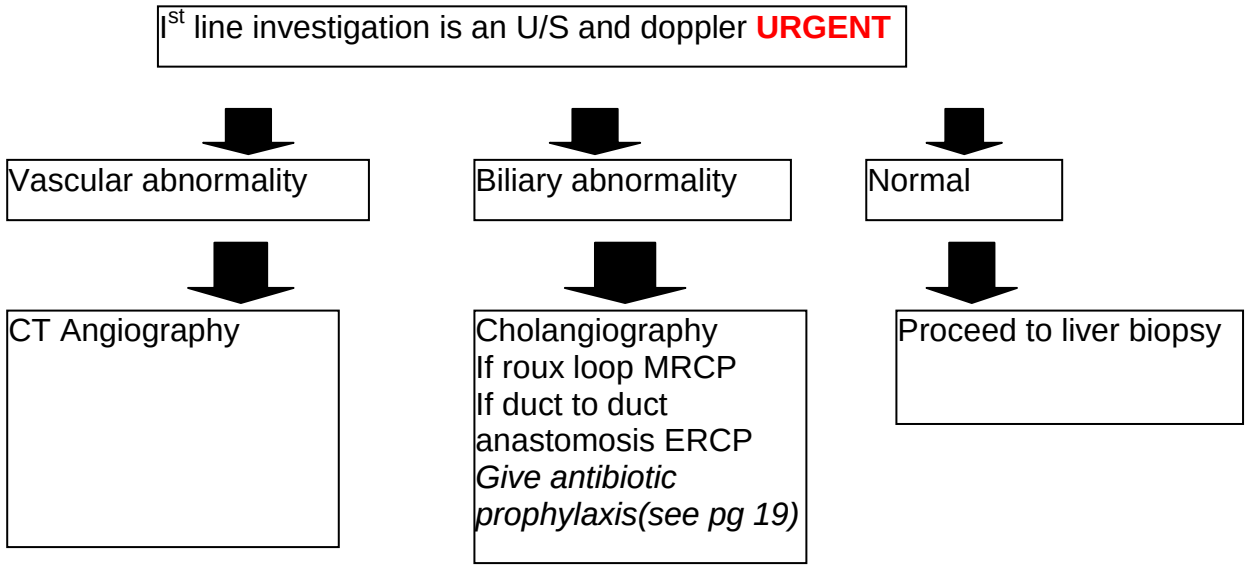
Review recent microbiology reports and commence the following antibiotics

Tazocin 4.5g tds IV, if previous MRSA add in vancomycin.
After 5 days of Tazocin consider changing to meropenem.
After 5 days on ITU change fluconazole to Ambisome

**Abnormal LFT's post-transplant**

An increase in liver function tests post-transplant can be for a number of reasons:

- Rejection
- Re-perfusion injury
- Ischaemia / vascular abnormality
- Infection
- Biliary problem
- Drug toxicity



**Graft rejection**

Graft rejection is detected by both clinical and biochemical suspicion

Clinically: Often asymptomatic but may have fever and jaundice

Biochemically: Elevated transaminases

Generally an ultrasound should be performed prior to the liver biopsy

Consideration on whether a biopsy is required should be made on **DAY 7**

**Liver biopsy (see BSG guidelines)**

- Check if reduced size graft transplanted if so do under U/S guidance

- Check PT and Plt count prior to Bx
(If Plt less than60 PT more than4 may require FFP, Plt or Trans-jugular biopsy)

- Consent patient

- Aseptic technique

- Post biopsy observe for 6 hours 1° BP + HR

- If history of cholangitis or Roux loop cover with prophylactic antibiotics

- Inform on-call transplant pathologist.

**Treatment of rejection**

**Decision to treat or not decided by consultant**

**Mild rejection No** treatment

**Moderate rejection** Varies according to clinical circumstances

**Severe rejection** Prednisolone 200 mg/day orally for three days (or Methyl Prednisolone 1 g iv x 3). The prednisolone is given as a single daily dose.
Subsequently, resume maintenance prednisolone at 20mg/day and taper by 5mg/day after 3 weeks etc
Check Tacrolimus trough blood level more than 10 ng/ml

**Poor urine output**

It is common for the FY1-2 to be called to assess a post- operative patient with oliguria, defined as urine output less than 40 mls/hr

**Aetiologies to consider**

- Hypovolaemia (including bleeding)
- Sepsis
- Drug toxicity — Excess diuretics; Tacrolimus/ Ciclosporin toxicity
- Graft dysfunction/marginal graft
- Previous renal dysfunction

**Management**

- Assess patient particularly fluid status — Pulse and Blood Pressure; JVP; Ankle and sacral oedema; Chest for pulmonary oedema; CVP; Previous fluid input /output
- Check most recent bloods
- If clinically hypovolaemic THINK WHY? — Inadequate fluids; Bleeding; Excess diuretics

Then give fluid challenge Normal saline 500mls STAT

- If no response post fluid challenge or oliguria occurring without hypovolaemia

Consider — Sepsis; Graft dysfunction; Nephrotoxic medication

- If no improvement discuss with senior colleagues and consider informing renal team as they may require renal support.

**Section 7**
**Microbiological considerations**

- **CMV infection**
- **Fungal infection**
- **Prophylaxis for procedures post-transplant**

## CMV infection

- Pre-transplant:
  All patients' CMV status is checked prior to transplant

- Post transplant:

1. Prophylaxis:
   CMV-ve recipients of a CMV +ve graft receive valganciclovir 900mg OD for 3 months (reduce in renal impairment – see full protocol)

2. Post transplant infection:
   Those at highest risk are
   a) CMV –ve recipient of CMV +ve graft
   b) Re transplants
   c) Patients on high dose immunosupression

If infection is suspected i.e. swinging pyrexia, leucopenia, dyspnoea, graft dysfunction and diarrhoea, a blood sample should be sent for the following

- CMV-PCR Inform virology consultant.
- Of note liver Bx and rectal Bx can be examined for CMV

Treatment of CMV infection GANCICLOVIR 10mg/kg/day IV in 2 divided doses for 14 days (reduce dose in renal dysfunction).

## FUNGAL INFECTION

1. If candida cultured from 3 or more sites or local candidiasis, increase fluconazole dose to 200mg /day and check sensitivities.

2. If systemic candidiasis phone consultant.

3. If aspergillosis prescribe Ambisome 3mg/kg/day or Abelcet 5mg/kg/day IV

## PROPHYLAXIS FOR PROCEDURES POST TRANSPLANT

For cholangiography and invasive angiography:
Tazocin 4.5g IV (2 doses)
PLUS Metronidazole 500mg IV if roux loop
At 1hr pre and 6hrs post procedure.

**Section 8**
**What to check prior to discharge**

- Check Patient has been seen by the transplant coordinator and the pharmacist (this is organised by the transplant coordinators)
- Inform transplant co-ordinators of discharge
- The ward clark will book the OPA according to the information on the discharge summery. (Please state the date of the OPA so that they can be booked on the correct clinic. Follow up weekly for 6 weeks then fortnightly up until 3 months), requires detailed discharge letter (do not put the operation notes in as this contains donor information).

**Section 9**
**Common problems post discharge**

•**Immunisation:** No vaccines in first 3 months. After this liver transplant recipients may receive dead or inactivated vaccines but should never receive live or attenuated vaccines

•**Contraception:** Females should be advised not to become pregnant in their first year post transplant. The oral contraceptive pill is contraindicated in the first 6 months due to the risk of thrombosis but thereafter well tolerated.

•**Travel:** Foreign travel is discouraged for the first 6 months post-transplant. Thereafter**,** if the patient is well there is no reason why they cannot travel abroad. They should be advised to take out adequate insurance cover and inform the company of their transplant.

**Unit meetings**

**Tuesday** Liver pathology/ HPB MDT 1pm Education centre

**Wednesday** Audit meeting 8am first Wednesday of every month

**Thursday** MDT Liver meeting Education centre 2pm
Liver educational meeting 3.30pm

**Friday** Transplant assessment meeting 12.30 pm Education centre

Auditable outcomes

1. Percentage of CMV negative recipients of a CMV positive graft receiving Valganciclovir prophylaxis
2. Incidence of post operative acute kidney injury