PAEDIATRIC LIVER TRANSPLANT ANAESTHESIA

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- This document is a practice guideline and is designed to inform the practice of clinicians while they employ their expertise to provide best patient care.
- In addition to the standard care of a patient requiring general anaesthesia, liver transplantation requires careful attention to fluid and blood product management given the potential for significant fluid shifts and blood losses.
- In those with hepatic disease, blood testing alone does not reveal the full picture relating to the risk of bleeding or tendency to thrombosis as both procogaulant and anticoagulant factors may be altered.
- Guidance on the planned immunosuppression regime will be provided so that the anaesthetics team can commence this at the earliest appropriate moment when there is not too much bleeding.
- Communication through all stages of the procedure remains vital.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
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Team Leader:	Staff Specialist	**Area/Dept**: Anaesthetics

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CHANGE SUMMARY

This document is the 6th edition of the practice guideline, building on the earlier editions initially authored by Dr Victor Harrison, then carried on by Dr Michele O'Brien and Dr Ramanie Jayaweera.

This represents a scheduled revision and changes in this edition include:

- A new checklist section at the start.
- Updated background information, revisions to all other sections, a new section on thromboelastography and a revision of the suggested intraoperative testing routine.
- A link to the perfusion/physiology practice guidelines.

READ ACKNOWLEDGEMENT

This document is available to be read by anyone involved in the liver transplantation service at The Children's Hospital at Westmead.

All consultant anaesthetists involved in liver transplantation and anaesthetics fellows rotating through the department are expected to read this document (Read Only).

Anaesthetics and recovery nursing staff involved in liver transplantation should also read this document (Read Only).

Perfusion and physiology staff, transplant surgeons, transplant medicine staff and intensive care staff may review this document on a Discretionary basis.

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- Do you have a start time confirmed with theatres? ☐
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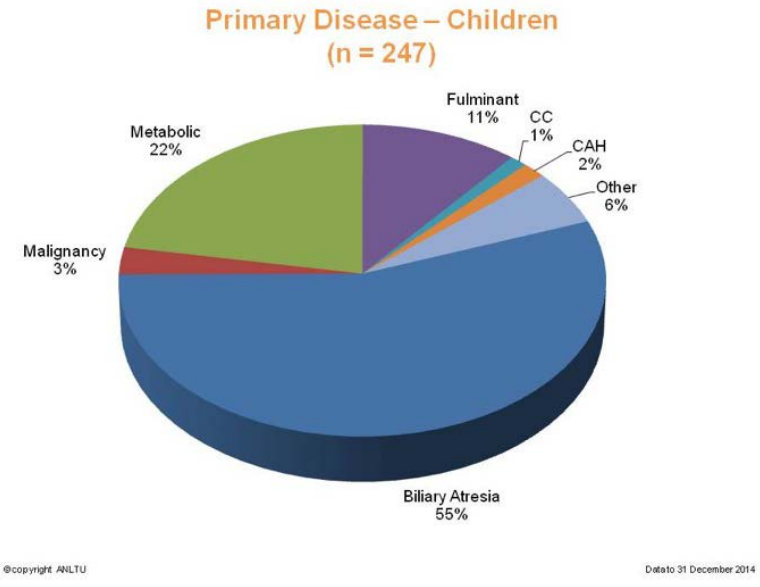
Key Anaesthetic Reminders during the Operation

- Expect blood loss throughout the operation.
- Cardiovascular changes are routine, and frequently related to reversible mechanical vascular obstruction caused by the surgeon – keep communication lines open.
- Potassium is often needed from early in the operation but paused just before revascularization. Potassium often falls again when the new liver starts working.
- Brief hyperkalaemia may occur at revascularization.
- Hypocalcaemia is common with replacement of blood products, especially while anhepatic.
- Hypoglycaemia may occur any time, particularly post-induction and while anhepatic.
- The suggested haematocrit target is 25-28%.
- Immunosuppression:
  - Methylprednisolone is optimal 10-15 minutes before revascularization.
  - Basiliximab is given once the new liver is in place.
  - Do not give immunosuppression when there is lots of bleeding.
- Antithrombin III:
  - After the vascular anastomoses when haemostasis is good.

1 Background

2016 marks the start of the fourth decade of paediatric liver transplantation in Sydney. It started at RPA then transferred to The Children's Hospital at Westmead in 1998. By the end of 2015, 306 transplants had been performed. The patients receiving transplants have become younger. For the 2005-2014 period, the median age at transplant was 1.3 years old. Using figures extending back to 1986, 88% of patients survived 1 year and 83% of patients have survived to 10 years. This has improved recently though: the 2013-2014 review showed 100% survival to 18 months.

The majority of our patients require transplantation to deal with biliary atresia where a Kasai procedure has failed. Our second most common indication is management of an inborn error of metabolism.



This chart is from the 2014 report from the Australian National Liver Transplant Unit. The grouping of "Fulminant" would now be called "Acute Liver Failure". It is mostly secondary to viral non A-G hepatitis but also includes less frequent acute hepatic insults as in the case of drug toxicity or Wilson's disease. "CC" = cryptogenic cirrhosis. "CAH" = chronic autoimmune

hepatitis. "Other" includes a variety of conditions such as α_1-antitrypsin deficiency, Alagille's syndrome and a handful of other rare conditions.

2 Initial Anaesthetic Review During The Work-Up

During transplant work-up patients are reviewed by whichever consultant is covering transplants that week. There are a few simple aims of this review:

- Assess current status; particularly as it relates to liver disease.
- Undertake a general background assessment typical of any anaesthetic assessment.
- Explain the role of the anaesthetics team in the context of the liver transplant operation.

The assessment of current status is obviously very influenced by how acutely the transplant is required. Most patients will not be acutely unwell. A copy of the assessment (or of a summary) should be brought back and placed in the folder in the secretary's office.

3 General Reminders on Anaesthesia and Liver Disease

The liver is an organ with key roles underpinning almost every other organ system. The majority of patients having liver transplant have liver dysfunction, although this is often not the case for patients with metabolic disorders requiring transplant. Some syndromes may be associated with their own associated pathophysiology. Following is a quick refresher on key things to assess when checking on these patients.

3.1 Respiratory Considerations

In addition to a standard review of respiratory status, patients with end-stage liver disease can have particular respiratory issues:

- ***Mechanical:*** Any combination of organomegaly, ascites or pleural effusions can significantly decrease the lung volume and hence functional residual capacity (FRC). This can put patients into the zone where there is closure of small airways in normal respiration and increased work of breathing. That increase in work is further exacerbated by changes in position of the diaphragm, increased abdominal pressures (ascites etc) and the muscle wasting and deconditioning that may be associated with liver disease. Respiratory assessment has to consider these broader issues.
- ***Portopulmonary hypertension:*** This looks histologically like idiopathic pulmonary arterial hypertension but occurs in the setting of portal hypertension. The mechanism is unclear (maybe less removal of vascular mediators, maybe remodelling of pulmonary vessels triggered by increased shear stress) but medications that might be considered at other times may cause splanchnic vasodilation (e.g. calcium channel blockers) and cannot be used. It is possible that patients may therefore be on other agents such as bosentan or sildenafil though no pharmacological agent is presently standard of care.
- ***Hepatopulmonary syndrome (HPS):*** A small percentage of patients with end-stage liver disease get this triad (portal hypertension, widened alveolar-arterial (A-a) gradient and intrapulmonary vascular dilation (IPVDs)). The areas of vascular dilation tend to be more prominent in lower zones of the lungs so these patients, in a seeming paradox, oxygenate better lying flat as blood is more distributed to areas with less IPVDs. An increase from low saturations by > 4% when lying flat is suggestive. IPVDs can be

demonstrated by delayed appearance of agitated fluid in the left atrium on echocardiography, or with nuclear medicine scanning. HPS may be helped a little by oxygen but can only be fixed with a liver transplant.

Note that most patients will be easier to manage from a respiratory point of view sitting up, with the exception of those with hepatopulmonary syndrome, though this pathology is very rare in children.

3.2 Cardiovascular Status

Patients with end-stage liver disease may end up with a high output low resistance systemic circulation. As a result hypovolaemia and/or any co-existing cardiovascular pathology is poorly tolerated. The reason for the lower systemic vascular resistance (SVR) isn't entirely clear but may be a result of enhanced endogenous production or diminished hepatic clearance of vasodilators (like NO, CO, endogenous cannabinoids, TNF-α, adrenomedullin, and hydrogen sulfide) and on some occasions the inflammatory response to bacterial translocation causing splanchnic arterial vasodilation. (1)

Part of the response to low SVR is retention of sodium and water which increases plasma volume. There is also increased venous capacitance where there are any portosystemic shunts.

Another key thing to remember is that some specific diagnoses that cause end-stage liver disease are also associated with cardiovascular dysfunction (things like haemochromatosis, Wilson's disease and amyloidosis).

3.3 Haematological and Bleeding Considerations

While patients with end-stage liver disease have a lack of coagulation factors, low platelet counts (sometimes with platelet dysfunction), dysfibrinogenaemia and elevated tPA levels that might predispose to bleeding, they also have more vWf and fVIII as well as decreased levels of proteins C and S, antithrombin III (ATIII), alpha$_2$-macroglobulin, plasminogen and heparin cofactor II. These latter factors all favour thrombosis. This all means that standard coagulation tests alone don't give the full picture as to whether patients will have a bleeding tendency or not. It is important to consider whether patients have evidence of portal hypertension as this is highly significant in bleeding risk; (around 25-35% of patients with cirrhosis will have bleeding from varices). (2)

3.4 The Kidneys

Acute kidney injury is relatively common in patients with significant liver disease and is most often due to prerenal insults. This underlines how poorly these patients tolerate hypovolaemia. Prerenal insults may include gastrointestinal haemorrhage, diuretic use or diarrhea from infection or use of lactulose. With disease progression and systemic vasodilation there can be activation of the renin-angiotensin system and sympathetic nervous system which contributes to ascites, oedema and renal vasoconstriction. Hepatorenal syndrome is a severe extension of this pathophysiological state but is very rare in kids.(3) Post-transplant kidney dysfunction is increased where there is prior kidney failure, hepatorenal syndrome, intraoperative hypotension or hypovolaemia and in those needing more blood products. (4) Acute kidney injury is a major contributor to bad outcomes post-transplant. (5)

3.5 Neurological Factors

Encephalopathy can be evident in liver disease, particularly with acute decompensation. It is particularly related to hyperammonaemia as the liver's detoxification function fails. Intestinal tract bacteria produce ammonia which, when not cleared, crosses the blood brain barrier and is taken up by astrocytes. In astrocytes this is converted to glutamine and the end result is swollen astrocytes with reduced ability to regulate neurotransmission. [(1)] It's also worth noting that chronic liver disease has its own neurodevelopmental implications. Those with early onset liver disease have a lower IQ than those with later onset of the same disease (as measured 8-11 years after diagnosis) and around 54% will have some form of delay in neurological development. [(6)]

4 Surgical Technique

4.1 The Donor Organ

Following retrieval, the liver is flushed with cold saline and later University of Wisconsin (UW) solution and kept cold. Minimising ischaemia time is always the aim with the maximal ischaemia time allowed 20 hours.

Anatomically, the liver is divided into 8 segments:

- The large right lobe contains segments 5, 6, 7 and 8.
- The caudate lobe comprises segment 1.
- The left lobe consists of segments 2, 3 and 4:
  - Segments 2 and 3 are also referred to as the left lateral segments.
  - Segment 4 is also known as the medial segment.

In paediatric liver transplantation either a whole or reduced liver graft is implanted. The concept of **split** liver grafting refers to transplantation to 2 recipients while **cutdown** implies liver reduction to fit a recipient with the remaining part discarded.

Sizing the graft to the patient is vital. As a rough guide a **whole graft** is suitable if the ratio of donor body weight to recipient body weight ratio (D/R ratio) is $\leq$ 2. This requirement is rarely met in children so reduced grafts are the norm.

In practice, the transplant team will calculate whether the graft will fit by looking at the weight of the graft vs the weight of the patient receiving the graft with a range of 1-5% of recipient body weight being acceptable. As an example:

> If it is known that the donor is an adult weighing 80 kg, the liver weight is generally assumed to be 2% of the total donor weight. This gives a 1.6 kg liver weight. The left lateral segment makes up approximately 30% of the total liver weight and can be reduced further if only a single segment is used. So the graft could be as little as 240 g, making it feasible even for a 5 kg recipient.

4.2 The Operation

It is vital during the operation for the anaesthetists to keep in constant communication with the surgeons and to be aware of the operative phase. This ensures all team members are aware when surgical manoeuvres such as application or release of clamps are about to take place and if there are any new issues arising.

The operative procedure can be considered in 5 stages:

1. Hepatectomy Stage

This is from skin incision until isolation of the native liver from its blood supply. This can be prolonged in patients with prior abdominal surgery. A key consideration for the surgeons during this phase is to avoid any irreversible steps until it is confirmed that there are no issues with the donor organ. Most commonly the biliary system will also be disconnected during this phase both to prepare for the later biliary anastomoses and provide better surgical access to the hepatic vessels.

2. Anhepatic Stage

This starts when both the arterial and portal venous supply are clamped. The inferior vena cava (IVC) is cross-clamped below and above the liver (infra-hepatic IVC and supra-hepatic IVC respectively). A trial cross-clamping of the IVC is done before committing to the anhepatic stage to determine the effect on haemodynamics. Any hypotension can usually be corrected with a fluid bolus. Sometimes titrated vasopressors or inotrope infusions are required.

The donor hepatic vein, usually with a portion of donor IVC, is joined to the recipient's IVC with an end-to-side anastomosis ("the piggy-back technique"). Glycine solution (2 mmol/L) in plasmalyte is used to flush out residual preservative solution. This also has cytoprotective effects on hepatocytes.

The donor liver temperature is raised by running blood from the portal vein into the graft prior to release of the portal vein and hepatic vein clamps. The surgeons will take particular care to avoid air emboli with release of the clamps. Potassium levels of graft flush solution are checked prior to reperfusion to ensure they are below 10 mmol/L. Methylprednisolone 10 mg/kg is generally given in the 15 minutes prior to reperfusion. This timing is not critical and should be delayed if there is significant bleeding.

3. Reperfusion Stage

The first stage of reperfusion is release of the clamps on the portal vein and hepatic vein. The hepatic arterial anastomosis is then performed. It is after this anastomosis that the surgical team will usually take a break to refresh.

When getting on with the next stage of the operation, blood flow through the portal vein and hepatic artery is measured using a Doppler flow probe with the aid of the perfusion and/or physiology teams. An assumption is made that hepatic blood flow is around 25-30% of cardiac output (estimated as 3.0 L/min/m^2) with 75% via the portal vein and 25% via the hepatic artery.

4. Biliary Connection

Once flows are felt to be acceptable and haemostasis is reasonable, the biliary anastomosis is completed. This usually involves a Roux-en-Y biliary-enteric anastomosis. In larger kids a direct bile duct anastomosis may be performed instead. When the new liver starts functioning bile flow will generally commence.

5. Abdominal Closure

In paediatric liver transplants, secondary closure is most common a few days after the initial transplant operation to allow swelling to settle. This is done in preference to risking intra-

abdominal pressure elevation which might compromise graft flow. The intervening temporary closure involves coverage of the defect with a plastic bag. Primary closure may be attempted if the graft function is unlikely to be compromised and there is a strong desire for early weaning off ventilation (e.g. cystic fibrosis patients).

5 The Anaesthetic

5.1 Immediate Pre-Operative Visit

The purpose of the immediate pre-operative visit is to establish current health status and check final preparation steps for the transplant. The key questions of assessment are:

- What is the patient's current health status?
  - Do they have stable liver disease?
  - Do they have worsening chronic disease?
  - Do they have acute end-organ dysfunction on top of the chronic disease?

The development of new pathology since initial transplant work-up (e.g. portal hypertension, respiratory dysfunction, worsened ascites) is important to pick up.

Next you need to check if tests have been updated and preparations made:

- Have preoperative blood tests been done?
- Are blood products available? (Baseline is 3 units PRBCs and check availability of other products.)
- Are there additional medication requirements?
  - Medications for patients with metabolic disorders.
  - Premedication where appropriate and patient not encephalopathic.
  - Are there specific immunosuppression requirements?
  - Are there particular requirements for antibiotic prophylaxis?

5.2 The Preparation

The anaesthetics team generally starts preparation 1 hour before scheduled anaesthetic start time (the perfusionist and the physiologist generally arrive 30 minutes prior to start).

Checks and Equipment

- You need to be prepared for a massive transfusion:
  - 3 units red blood cells in the theatres fridge.
  - Check with blood bank there are no issues with supply of FFP, platelets and cryoprecipitate.
  - Check there is an adequate supply of 4% albumin in the anaesthetic workroom.
- The room checks:
  - Anaesthetic machine in the bay (generally OT 6) and inside the room.

- Temperature management – consider theatre temp, Bair hugger, consider overhead heater, hotline.
- Operating table – brackets, arm supports if needed, anaesthetic screen, patient padding and positioning plan.
- The cardiac induction trolley for induction to allow CXR.

The Draw-Up

- Emergency drugs (agree on a dilution for patient weight as an anaesthetics team):
  - Metaraminol.
  - Calcium chloride.
  - Atropine.
- Drugs to have available on the OT anaesthetics trolley:
  - Lignocaine.
  - Sodium bicarbonate.
  - Adrenaline.
- Consider having an inotrope ready – usually dopamine 15 mg/kg in 50 mL (1 mL/hr = 5 microg/kg/min).
- Infusions (see section 6.4 for further dosing information):
  - Potassium chloride – 25 mmol diluted to 50 mL (in H_2O).
  - Glucose – draw up 50% glucose (if via CVC) or 10% glucose (for peripheral use).
- Other agents:
  - Antibiotics: routine is piperacillin/tazobactam (Tazocin) – 100 mg/12.5 mg per kg IV given 8 hourly (max 4 g/0.5 g plus note dose adjustment in renal dysfunction).
    - Any other antibiotics as discussed with surgical team.
  - Immunosuppression:
    - Methylprednisolone 10 mg/kg available on the anaesthetics trolley.
  - Blood/coagulation management pharmacology:
    - Antithrombin III calculated to order from blood bank.
    - Discuss antifibrinolytics with surgeons.

Items for Other Team Members:

- Perfusion – cell saver, TEG, rapid infusion system, Doppler flow checks (very rarely venovenous bypass).
- Physiology – monitoring, testing routine.

[For more details on perfusion and physiology duties, please see the excellent practice guideline - http://webapps.schn.health.nsw.gov.au/epolicy/policy/3824.]

5.3 The Induction Routine

There is no particular evidence for one induction technique over another specific to liver transplantation. Rapid sequence, intravenous or inhalational induction may be chosen on the basis of patient age, condition and clinician judgment.

Monitors

Pulse oximetry (not with a finger peg), non-invasive blood pressure at the start and ECG once feasible. Patients will need temperature monitoring, IDC, the largest feasible NG and NIRS monitoring to the forehead (severe jaundice may invalidate these readings). Monitoring to minimise awareness is not generally used.

Airway and Breathing

There are no tricks here. A cuffed endotracheal tube, most likely nasally placed and controlled ventilation using an oxygen-air mix. There is no evidence to recommend one inhalational agent over another for maintenance. Isoflurane may maintain more physiological hepatic arterial and portal venous blood flow. There is some evidence patients with end-stage liver disease have lower requirements of volatile agents to avoid awareness. (7)

Circulation and Lines

All lines must be placed with strict precautions to minimise infection risk. Standard lines are:

- 2 x large peripheral cannulae for intravenous volume (preferably upper limb).
- 1 x long saphenous line for pressure monitoring (alternate is a femoral venous cannula).
- 2 x arterial lines (monitoring on right arterial line, blood sampling from left).
- 1 x CVC (5.5F triple lumen unless difficult access/extra infusion requirements).

Once lines are placed and prior to entry of the operating room, chest X-ray is performed to check placement of the ETT/NG and lines (and to help exclude complications).

5.4 Inside the Operating Room

Positioning and Protection Considerations

The surgeons may place a roll under the lower thoracic spine to produce better surgical access. Pad all pressure areas, with gel pads recommended for any slightly older kids. Consider Velband wrapping of limbs as a way of providing padding and managing temperature status. All lines and monitors must be shielded from direct contact with the skin. Standard eye precautions for a longer case are required.

Airway, Breathing and Circulation

Standard ventilation to routine targets of oxygenation and ventilation are appropriate. Nitrous oxide is avoided to avoid gaseous distention of the bowel loops. While there is evidence from adult practice that postoperative pulmonary complications are a significant factor in patient morbidity and mortality, risk factors for development of this seem to be mostly related to excessive fluid and blood product administration, and preoperative presence of severe ascites. (8)

Patients with end-stage liver disease often have a high cardiac output, low systemic vascular resistance system. Excessive fluid administration may be associated with complications in

the postoperative period and maintenance of a high CVP (previously a measure used to prevent air embolus) is no longer standard care. Maintaining CVP in the range of 6-10 mmHg is reasonable to minimise this risk, along with PEEP. Have a high index of suspicion for air embolus if there is sudden cardiovascular collapse.

There is still a difficult balance to maintain in managing fluids. While excessive fluids may not be appropriate, maintenance of CVP as described above may still require large amounts of fluid. Minimum losses to consider per hour would be (maintenance + 10 mL/kg/hour for the open abdomen). Careful attention to fluid responsiveness, which may be aided by monitoring techniques such as measurement of pulse pressure variation (PPV aiming to be < 10), and early utilisation of vasoconstrictor agents (such as metaraminol, noradrenaline or dopamine) seems appropriate, though outcome studies are not available. (1) TOE may be considered in some cases to assess cardiac function.

Maintenance and Analgesia

Maintenance is generally with volatile as mentioned above. Ongoing analgesia is opioid-based, with fentanyl generally preferred. An infusion for ongoing analgesia in PICU should be prepared. In patients having primary closure, consider wound catheters for infusion of local anaesthetic.

Blood Product Management

Rational management of blood products is an area where careful anaesthetic care may meaningfully contribute to patient outcomes. As described earlier, these patients have some deficiencies that predispose to bleeding but others that can potentially promote clotting. Classic coagulation tests do not reliably predict patient bleeding.(2)

Over the last few years the approach to blood product management at The Children's Hospital at Westmead has shifted, aiming to prevent thrombosis through post-revascularisation administration of antithrombin III and early heparinisation. This has been associated with a lower vessel thrombosis rate and fewer biliary complications in the longer term.

There are further reasons to minimise use of blood products. One-year patient and graft survival is associated with the number of RBC and FFP units transfused during surgery. (9) Plasma-containing blood products are associated with development of transfusion-associated lung injury (TRALI) while the RBCs are associated with elevated risk of postoperative infection. (10)

Therefore some basic principles of blood product management are particular to these operations:

- Aim for haematocrit is 25-28%.
- Once the patient has received more than 20 mL/kg of RBCs, consider utilisation of FFP or possibly cryoprecipitate and platelets.
- Thromboelastography may provide useful information but must be interpreted in the context of the amount of bleeding evident clinically.
- Hypothermia and hypocalcaemia may worsen any bleeding noted.

- The metabolic insult of RBC transfusion may be significant, particularly in younger patients. Wash all RBCs utilising the Cell Saver. This reduces the potassium and citrate load and is particularly important in the anhepatic phase.

NB Cytomegalovirus (CMV) infection is a potentially significant post-transplant infectious complication. (11) CMV status of the donor is always noted:

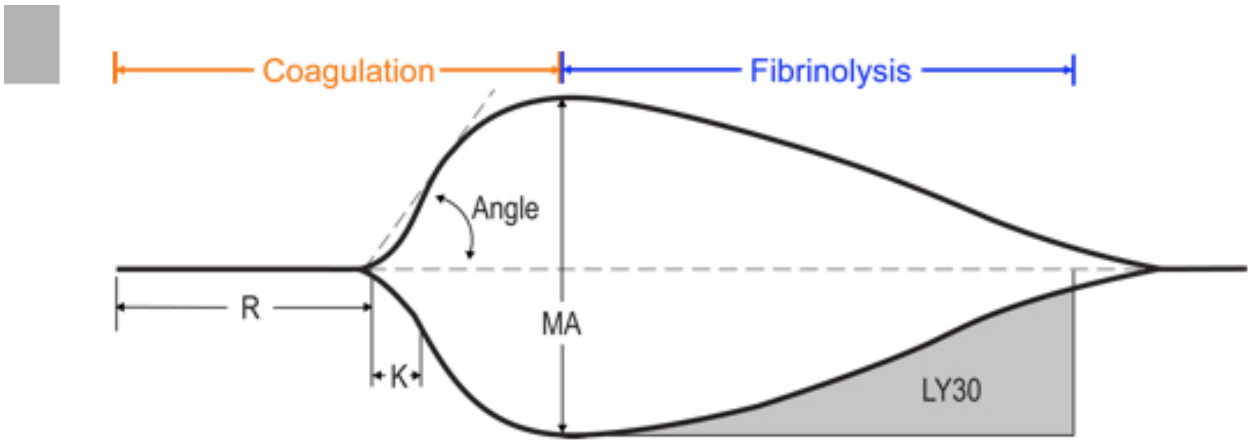
- If donor or recipient are CMV positive, post-operative anti-CMV treatment is given;
- If both the donor and recipient are CMV-negative then it is important that CMV negative blood is utilised for all transfusions.

Thromboelastography (TEG)

Historically blood tests for coagulation were sent regularly throughout the cases. There can be significant delays in these tests returning which makes it hard to use results to guide blood product management. There are some studies suggesting using TEG may be useful and may be associated with transfusion of fewer blood products. (12-16) It should be noted that many of these studies are small and open to issues of bias and there are also studies suggesting no change in blood product use or that results on testing can be equivocal. (17-19)

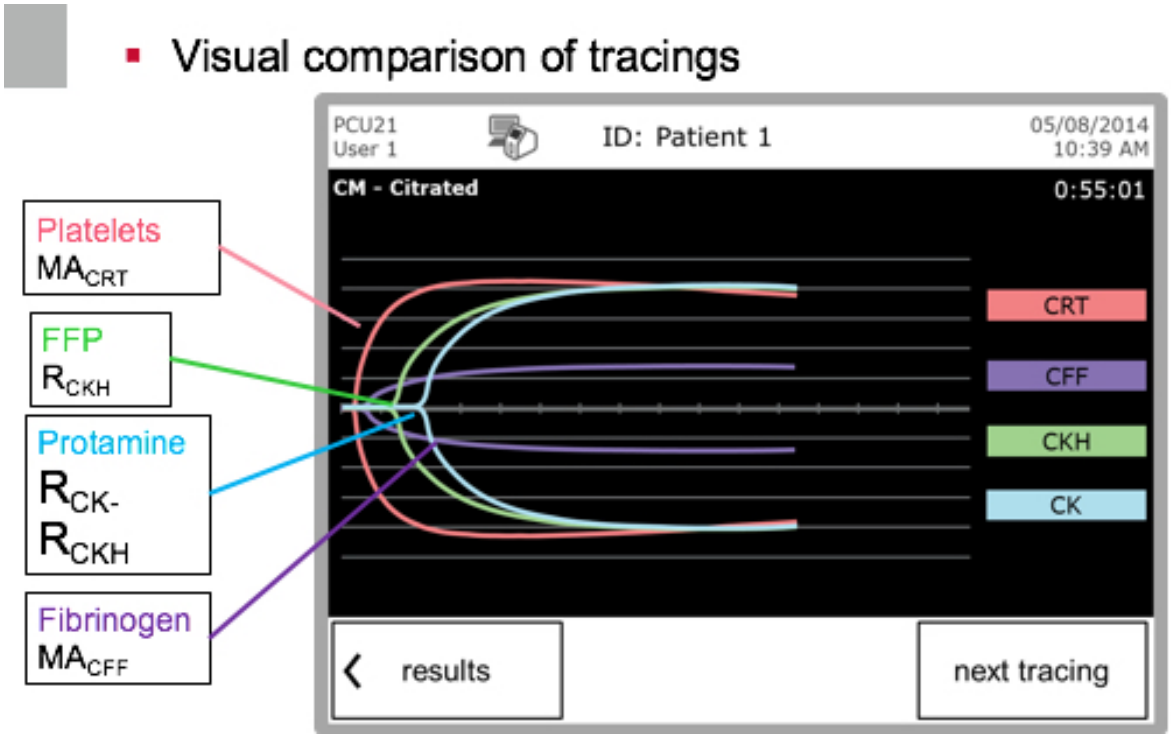
The department, with the particular help of the perfusionists, has a TEG 6S (Haemonetics™) as the primary TEG device available. The information from the company states that this can provide useful information within 10 minutes as you can perform tests relying on Kaolin, Functional Fibrinogen, Heparinase testing and a RapidTEG™ although it's not always as clear as that clinically. It is critical to recall that any result on the TEG is only relevant when interpreted with reference to the degree of bleeding seen clinically.

Below is the general scheme for a TEG tracing and which parameters show particular things (note that these images come from info provided by Haemonetics, so the traces etc will be a little idealised potentially):



R = time to first measurable clot formation
K = fibrin cross-linkage, fibrinogen function
Angle = fibrinogen function
MA (mm) = clot strength, most reflects platelets
LY30 = lysis 30 minutes after MA reached

The TEG 6S provide a number of traces, which can be visualised over the top of each other or viewed separately.



The key question is "how do you interpret these?" This is easiest in table form perhaps:

So basically:

- Look at the functional fibrinogen tracing to see if the fibrinogen seems adequate to make a clot (look at the Maximum Amplitude on this trace).
- Look at the RapidTEG™ Maximum Amplitude when thinking about platelets.
- Look at R time when thinking about FFP.
- Look 30-40 minutes later for LY30 to assess if fibrinolysis is an issue.

It is suggested that the anaesthetics team take a baseline TEG just after induction then repeat once in each phase, or if there is bleeding. The aim is to provide a background understanding of what blood product would be most likely to be appropriate if bleeding became an issue (while starting a new TEG at that time). Your friendly perfusionist or physiologist is very happy to make this testing happen.

Antithrombin III

Antithrombin III concentrate may be given once all anastomoses are complete and clinical evidence of bleeding is not present. Doses are:

- Up to 30 kg: 1 ampoule (1000 units) IV.
- 31-60 kg: 2 ampoules (2000 units) IV.
- > 60 kg: 3 ampoules (3000 units) IV.

Anti-fibrinolytics

These should only be considered in patients with a significantly elevated risk of bleeding. This is likely to be those patients having a repeat liver transplant. Suggested doses of tranexamic acid (TXA) are:

- Loading dose 20 mg/kg IV over 30 minutes.
- Infusion at 10 mg/kg/hr IV.
- Total dose should be limited to 100 mg/kg up to 2 g total dose.

Recombinant Factor VIIa

This would only be considered in a case of life-threatening exsanguination where product replacement and surgical attempts to control bleeding are proving unsuccessful. The dose in this setting is 90 microg/kg IV.

Anti-Rejection Therapy

Optimally anti-rejection medications are given prior to revascularisation. If there is significant bleeding at that time, confirm with the surgeons that therapy should be given. It is best if the anti-rejection medications are not immediately lost due to bleeding.

- 5-10 mins prior to revascularization give methylprednisolone 10 mg/kg intravenously.

On some occasions, the hepatology team may request basiliximab, an IL-2 receptor monoclonal antibody (used when calcineurin inhibitors will be utilised later). It is particularly used when there is pre-transplant renal impairment. This is also given on day 0, but again should not be administered until haemorrhage control is reasonable and is more often given once the patient is in the intensive care unit..

If used, the intraoperative dose of basiliximab (given over 20-30 mins) is:

- 10 mg IV if < 30 kg.
- 20 mg IV if $\geq$ 30 kg.

Metabolic Management

Blood Sugar

Some patients may have minimal liver stores of glucose. Patients requiring glucose pre-operatively should have this continued. During the anhepatic phase, the absence of the liver's glucose stores usually causes a fall in blood sugar. As a separate indication, those with primary metabolic disorders should have glucose maintained at normal levels to ensure minimal protein catabolism.

Therefore if blood glucose falls below 5 mmol/L, commence 10% dextrose at 1 mL/kg/hr (or adjust for concentration used). Aim to keep BSL at 6-10 mmol/L as monitored on regular arterial blood gas testing (see section 7).

Potassium

Serum potassium is often low preoperatively. A pause in any potassium infusion around revascularisation should be considered as there may be a brief spike in potassium when the clamps are released. Once the graft starts working, potassium may fall rapidly and potassium infusion may be required again.

- If K^+ is < 3.5 mmol/L, start an infusion at 0.25 mmol/kg/hour (0.5 mL/kg/hr of the 0.5 mmol/mL solution suggested in this guideline) with titration of the infusion aided by the testing schedule in section 7.

If potassium is being replaced, consider checking serum magnesium and replacing to keep it > 0.7 mmol/L.

In the event of hyperkalaemia with revascularisation (as evidenced by peaked T waves or QRS changes):

- Calcium chloride 10% 0.2 mL/kg IV.
- Consider sodium bicarbonate 1 mmol/Kg IV.
- Consider 0.1 U/kg actrapid insulin with 50% dextrose 0.5 mL/kg IV.

Acid-Base Balance

Metabolic acidosis is common intraoperatively due to the effects of major vessel clamping, reduced renal function and fluid infusion. Patients who have had chemotherapy for hepatoblastoma may sometimes present with metabolic acidosis. The values seen can shock a little but a base deficit up to 15 mEq/L can be well tolerated. These derangements generally recover once the new liver is functioning. Using Hartmann's avoids the additive issue of hyperchloraemic metabolic acidosis with use of 0.9% sodium chloride.

A functioning graft in good haemodynamic conditions will generally allow a rapid normalisation of acid-base status. If this is not the case, sodium bicarbonate up to 1 mmol/kg IV may be considered. If acidosis worsens or stays the same once the graft is in, this may be a sign of dysfunction and should be mentioned to the surgical team.

Renal Protection

This relies on maintenance of good haemodynamics. Note that oliguria is expected during IVC cross clamping and is probably due to back pressure transmitted into the renal veins and an associated fall in glomerular filtration. This should recover once the clamps are removed if all is going well. True hepatorenal syndrome is rare, and intraoperative management still depends on management of haemodynamics and fluid management. There is no evidence supporting the use of diuretic agents to optimise urine output measurements intraoperatively.

6 Intraoperative Testing

Biochemistry and haematology can change quickly over the course of a liver transplant. Regular blood testing can be helpful, but must be interpreted in clinical context and must be available rapidly to usefully guide management. Additionally, some tests can take a reasonable amount of time to come back. For labelling purposes:

1. Pre-induction phase.
2. From induction to the blood supply to the native lung being interrupted.
3. The anhepatic phase.
4. Revascularisation.
5. Start of biliary connection (though to end of all anastomosis).

Simple nomenclature is used to indicate which phase of the operation the bloods were taken in, and in which order. So for phase 2, induction phase to anhepatic, the first tests sent would be test 2.1, the next is 2.2, the next is 2.3 and so on. (See also appendix 1.)

PHASE	TIMING	TESTS REQUIRED
P1	Pre-Induction	Preop bloods on Powerchart.
P2	INDUCTION	
P2.1	While in bay	ABG / BSL and Electrolytes/ Baseline TEG
P2.2, 2.3 etc.	on hour	ABG / BSL and Electrolytes / Coags once during P2) / TEG (minimum once per phase)/ FBC (with 2.2 then as indicated by blood loss)
P2.(last)	10 minutes before P3	ABG / BSL and Electrolytes
P3	ANHEPATIC PHASE	
P3.1	on ½ hour	ABG / BSL and Electrolytes
P3.2, 3.3 etc	on hour	ABG / BSL and Electrolytes / Coags (once in phase 3)/ TEG / FBC with 3.2 then as indicated by blood loss.
P3.x	10 minutes before Revascularisation	ABG / BSL and Electrolytes/ TEG
P4	REVASCULARISATION	
P4.1	5 minute post revascularisation	ABG / BSL and Electrolytes
P4.2	15 minutes post revascularisation	ABG / BSL and Electrolytes/ TEG
P4.3	on ½ hour	ABG / BSL and Electrolytes/ FBC (then as indicated by blood loss)
P4.4&+	on hour	ABG / BSL and Electrolytes / Coags /TEG Consider one set of formal EUCs with LFTs during P4.

- Suggestions for checking coags and TEG are not rigid and should be guided by bleeding state - one TEG should be checked in each phase as a minimum, then repeated as suggested by bleeding or extent of use of blood products.
- While some anaesthetists also perform coagulation tests regularly, results are often delayed more than an hour making it difficult to use them to guide therapy.
- If testing for creatinine clearance is needed, conduct a 2 hour urine sample collection and send that urine for urinary creatinine concentration. Take serum creatinine from blood in the middle of that 2 hour period. Creatinine clearance can then be calculated by the following:
    - Creatinine clearance = urine volume (mL/min) x urinary [creatinine]/serum [creatinine]. {normal value 130 mL/min/1.7m^2}

7 Record Keeping

In addition to the standard anaesthetic record-keeping, the perfusionists record key events during the operative period. Documentation may be aided by annotating key surgical moments, particularly those commencing the anhepatic phase and heralding revascularisation. Standard abbreviations may help:

HA:	hepatic artery.
PV:	portal vein.
SHIVC:	supra-hepatic inferior vena cava.
IHIVC:	infra-hepatic IVC.
Cl:	closed.
Op:	opened.

8 PICU Transfer and Handover

This is a standard PICU transfer requiring:

- A call to PICU around 30 minutes prior to expected departure then again as you are leaving the theatre with the patient.
- Consider a full set of blood tests (FBC, EUC, CMP, LFT, Coags and TEG) at the time of the call so results are available around the time of your arrival.
- Full monitoring for critical care transport (insist on end-tidal carbon dioxide).
- Drugs to take with you during transfer.
- Continue all infusions, including electrolyte replacement and maintenance glucose.
- Continue IV fluid replacement – patients are likely to have significant third space losses and drain output. Continuous replacement is necessary
- Don't forget to take any syringes for analgesic infusions you have arranged, or commence them while still in theatres; this would include wound catheter infusions.

A comprehensive handover is vital. It may be useful to consider the information that needs to be conveyed with a framework like the following:

I	**Intro**	Patient ID, underlying condition, type of donor, CMV.
P	**Preop**	The patient's clinical state before today's operation.
I	**Induction**	What you did at the start of the anaesthetic.
K	**Key events**	Key challenging moments or issues through the case.
S	**Systems**	Each system with issues on the way and current status.
I	**In/Out**	Cover fluids and blood products used plus urine output.
N	**Now/Next**	What's running, analgesia/sedation plan, predicted post-op. issues.

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Appendix 1: Intraoperative Testing Routine

PHASE	TIMING	TESTS REQUIRED
P1	Pre-Induction	Preop bloods on Powerchart.
P2	INDUCTION	
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