Acute Liver Failure

Acute Liver failure presents as encephalopathy, coagulopathy and jaundice. It is rare and is an emergency. The commonest situation is likely to be paracetamol poisoning.

In all cases urgent referral to Liver Unit is needed (telephone to liver medical registrar at QE hospital Birmingham as soon as you are aware of patient).

It is more common to find patients who have chronic liver disease which then deteriorates and presents as liver failure. This is very different from acute liver failure in its prognosis and treatment and is dealt with in another section.

Fulminant Hepatic Failure: This is defined as a potentially reversible condition, the consequence of severe liver injury with the onset of hepatic encephalopathy developing within 8 weeks of the onset of first symptoms in the absence of pre-existing liver disease.

Diagnoses to consider in patients with acute liver failure

- **Note if ALT>1000IU/l consider especially paracetamol overdose and ischaemic hepatitis.**

1. Paracetamol overdose - these patients do not always admit to an overdose
2. Hepatitis A - may present as acute liver failure, especially in the middle aged/elderly. Diagnosis IgM HAV positive.
3. Hepatitis B - may be sAg negative by presentation, IgM core will be positive - first infection can present as acute liver failure as can co-infection or super-infection with delta. Also consider reactivation - relevant in patients on chemotherapy especially if this involves pulsed steroids.
4. Hepatitis C - as a cause of acute liver failure it is very rare, if at all in Europe, usually seen in patients with Chronic Liver Disease. If positive, consider early treatment with interferon.
5. Hepatitis E - travel to endemic areas but occurs in UK. There is a poor maternal and foetal prognosis in pregnant patients. Typical hepatitis, similar to A. Vomiting and nausea are pronounced. Diagnosis on serology.
6. Sero-negative Hepatitis: Presumed non - A, B, C, E hepatitis with a hepatitic picture, may already have ascites, liver large early then small and splenomegaly. Rash is said to be frequent at presentation, symptoms are frequently very non specific in the late onset hepatic failure group, but can also present with a hyperacute picture, usually then marked prolonged INR.
7. Acute presentation of autoimmune hepatitis. The role of steroids is unproven but should be considered.
8. Drug Induced acute liver failure – All drugs should be considered, more common ones include: phenytoin, carbamazepine (rash + lymphadenopathy + hepatitis), NSAID, Rifampicin + isoniazid, halothane, anti-retroviral drugs, flucloxacillin (predominately cholestasis). Always consider vitamins, herbal remedies and illicit drugs such as ecstasy and cocaine.
9. Pregnancy induced liver failure.
    - Acute fatty liver of pregnancy - 3rd trimester of pregnancy, neutrophilia, DIC, hypoglycaemia. Probably always best transferred and always if they are encephalopathic, hypoglycaemic, hypotensive, acidotic or have coagulopathy. Characteristic features include normoblasts and high serum urate. Discuss with obstetricians if the baby has not yet been delivered. Delivery of the baby is the most important initial part of management and bleeding is a major problem in this sub-group.
    - Pre-eclampsia. The liver may be involved in 5 - 10% of patients with pre-eclampsia often as part of the HELLP syndrome (haemolysis, elevated liver function tests and low platelets). Another rare but important sub-group are those with acute liver rupture in association with pre-eclampsia

and fatty liver. Other causes of liver haemorrhage (adenoma etc and trauma may also be referred to the liver services)

10. Wilson's - Fulminant presentation: should always be transferred (encephalopathy, small liver, enlarged spleen, haemolysis, low Alk Phos, K-F rings), as transplantation is the treatment of choice.
11. Lymphoma - Fulminant presentation (hepatosplenomegaly, raised alkaline phosphatase) - need not have any other nodes palpable, may or may not have marrow or peripheral blood film changes. Hepatomegaly is common and there may be a swinging pyrexia.
12. Budd-Chiari - Hepatosplenomegaly, ascites, jaundice, coagulopathy, raised AST and AlkPhos. Should always be transferred, consider procoagulant conditions (see section on Budd-Chiari) note blood for the relevant tests should be taken before the patient is anti-coagulated. Also consider a pre-malignant condition - needs marrow for histology and colony forming factors.
13. Ischaemic Hepatitis - There are two main pictures:
    - Those with predominate right heart failure have cholestasis and an elevated Alk. Phos and some elevation of AST.
    - Those with impaired cardiac function (both R and L ventricles) who then have an acute episode of cardiovascular collapse, (e.g.) VT, AF + hypotension can present with a coagulopathy and significant elevation of AST.

Mangament of Acute Liver failure

(Taken from Birmingham Liver Unit Protocol and is for management whilst awaiting transfer to Liver Unit; at all times seek advice from Liver Unit team)

In all patients with acute liver failure careful attention should be taken to fluid resuscitation. Patients with ALF are often hypotensive. This is caused by a combination of fluid loss (vomiting) and vasodilation. The shock associated with ALF is of a distributive type similar to septic shock. Colloids are required to restore circulating volume. There is a tendency to give large quantities of 5% glucose to patients with ALF because of a worry about hypoglycaemia and in the mistaken belief that a sodium load is bad for the patient. It is not uncommon for patients to become significantly hyponatraemic under these circumstances. This is probably important in the etiology of cerebral oedema in ALF. **It is important to give saline maintenance** and infusions of concentrated glucose (50%) to maintain serum glucose. Avoid administering FFP in all patients unless there is evidence of active bleeding, since the INR is one of the most important prognostic indicators. Platelets can be given if less than 50×10^9/L as bleeding from central lines is not usually a problem.

Baseline tests depend on the history (paracetamol levels following an overdose). All patients regardless of aetiology should have:

- FBC
- U&Es
- INR or PT
- ABG’s
- Lactate
- Phosphate
- Magnesium
- Ammonia

These should be repeated 12 hourly depending of the severity of liver injury**.**

Diagnostic tests to be requested (depends on clinical situation):

- **Viral screen (IgM HAV, IgM anti-HBc, HCV, HEV)**
- **Copper, caeruloplasmin**
- **Auto-antibodies (include LKM)**
- **Immunoglobulins**
- **Pregnancy test (where appropriate)**
- **Clotting studies**

Transfer the patient to a high dependency care area or ICU. The patient must be monitored closely. Insert a central line in patients with acidosis, renal failure or hypotension. It will aid in monitoring and in the administration of infusions.

- Administer N-acetylcysteine in all patients with acute liver failure especially following a paracetamol OD regardless of the time since overdose.
- Insert a urinary catheter and monitor urine output hourly
- Blood glucose should be monitored every 2 hours for hypoglycaemia.
- Avoid all sedating agents, NSAIDs and benzodiazepines and intra-muscular administration of any agents. Vitamin K 1-2 doses of 10mg IV may be given but it is unlikely to significantly affect the INR
- IV PPI
- NG / oral Fluconazole 100mg
- Broad Spectrum antibiotics : eg Tazocin 4.5g TDS if not penicillin allergic
- Treat any low magnesium or low phosphate

Poor Prognostic indicators in acute liver failure

- The INR is greater than 3.0 in non-paracetamol aetiologies or the prothrombin time in seconds is greater than hours since overdose for Paracetamol OverDose (POD).
  (This equates roughly to an INR of 2.0 at 24 hours, 4.0 at 48 hours or 6.0 at 72 hours reflecting poor prognosis in POD)
- If the INR is still rising on between day 3 and 4 following the OD.
- If there is an elevated creatinine (>200) with a significantly raised INR (>3) or acidosis
- Significant hypoglycemia
- Any evidence of encephalopathy
- Anyone who is hypotensive
- Anyone who has evidence of a metabolic acidosis (pH<7.3) following volume resuscitation.

N-acetylcysteine Regime

Should be given in 5% glucose by IVI
Loading dose:
150mg/kg in 200ml over 15 minutes, followed by
50mg/kg in 500ml over 4 hours, followed by
Maintenance regime:
Dose 100mg/kg body weight, diluted in 1000ml 5% Dextrose, given at 62.5ml/hr
(If sodium falling can dilute in 100ml 5% Dextrose and run at 6.25ml/hr **via central line**)

Paracetamol OD (POD)

The significance of the OD will depend on the amount of paracetamol consumed, whether the overdose was staggered, other medication and alcohol use and the time to presentation and the administration of n-acetylcysteine (NAC). The reliance on the use of the treatment normogram is a cause for concern as the timing of OD can be imprecise or if the overdose has been staggered or repeated. Other factors that affect interpretation of drug levels include co-administered drugs and alcohol (either before or with the overdose). In general, NAC should be started at the earliest opportunity. The length of time from OD to NAC administration has great significance to the subsequent outcome and is useful even when started after greater than 24 hours from the OD.

Always refer to Liver Unit as soon as you suspect significant OD, particularly if poor prognostic indicators or delayed treatment. It is better to alert the Liver Unit early rather than late since patients become unstable rapidly and then may not be fit for transfer.

Manage according to section on acute liver failure (above).