PROTOCOL FOR ASSESSMENT AND MANAGEMENT
OF PATIENTS WITH ACUTE LIVER FAILURE

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# Acute Liver Failure Protocol Sept 2014

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1. **INTRODUCTION**

Acute (fulminant) hepatic failure (AHF) is defined as the onset of hepatic encephalopathy within eight weeks of the onset of symptoms attributable to severe hepatocellular dysfunction in patients without previously known liver disease. Subacute hepatic failure (SHF) is the development of encephalopathy between 2 and 6 months after the onset of symptoms.

2. **CAUSES**

The commonest cause in the U.K. is paracetamol overdose, with less common causes being acute viral hepatitis (hepatitis A, hepatitis B and non-A, non-B hepatitis or seronegative hepatitis) and toxicity from drugs such as rifampicin and ecstasy. Wilson’s disease may present with AHF, although cirrhosis is present. Similarly autoimmune chronic active hepatitis may present as AHF. Other rare causes are detailed in Appendix 1.

3. **REFERRAL**

The decision to accept or refuse a referral must always be made by the consultant hepatologist of the week. Before patients are accepted to the Liver Transplant Unit as much information as possible should be obtained from the referring centre (see e.g. Appendix 2). Patients can deteriorate quickly, particularly during transfer and deterioration in patients with AHF can be unpredictable. However, particularly for paracetamol overdose, the natural history of the condition can be derived with some accuracy from early observations. For example, 50% of patients with a prothrombin time longer than 36 seconds, 36 hours after the overdose will develop AHF.

Referring hospitals are encouraged to discuss at an early stage any patient that they may be concerned about. No hard and fast guidelines exist for which patients should be transferred to liver transplant units with non-paracetamol AHF. King’s College Hospital has suggested that transfer criteria for patients with non-paracetamol induced AHF should include pH < 7.3 (H+ concentration > 50), INR > 1.8 (prothrombin time > 20 seconds), oliguria, renal failure, encephalopathy, hypoglycaemia, shrinking liver size, sodium < 130 mmol/L and bilirubin > 300 umol/L. General consensus would suggest that those with AHF following paracetamol overdose should be transferred to a liver transplant unit regardless of whether or not they would be transplant candidates if; the prothrombin time is greater than the number of hours after the overdose, any prothrombin time is greater than 50 seconds, or if a metabolic acidosis persists after initial fluid resuscitation, or the patients have been hypoglycaemic or have established encephalopathy.
4. TRANSFER

The condition of the patient is important in deciding both the time and means of transfer. The distance the patient has to travel may also influence the timing of transfer. If the patient is well, not encephalopathic and clearly not in need of assisted ventilation, transfer by ambulance with an accompanying nurse will generally be appropriate. Patients with hepatic encephalopathy often deteriorate by one grade of encephalopathy during transfer i.e. grade 1 deteriorates to grade 2. However, if the patient is unstable, may soon require, or is already ventilated the consultant anaesthetist on call for ITU should be contacted, they will liaise with the referring hospital and the Anaesthetist on call for SLTU if necessary regarding accepting the patient and arranging patient transfer by an experienced anaesthetist/intensivist or in the case of the West of Scotland by the Shock Transfer Team. The administration of FFP at the referring hospital should be discouraged. Central venous access may well be considered necessary, but encourage an experienced practitioner to site the line with the coagulation uncorrected.

5. INFORMATION REQUIRED FROM REFERRAL CENTRE (SEE APPENDIX 2)

1. As much information as possible about the underlying cause and, if paracetamol poisoning is the likely cause, as much information as possible about the psychiatric history and precipitating event. Alcohol and drug abuse should be specifically sought. Discussion with the patients GP may be useful even before the patient arrives at the Royal.
2. Conscious level, encephalopathy grade, Glasgow Coma Scale.
3. Arterial blood gases.
4. Present haemodynamic status including urine output.
5. Previous and current liver function tests.
6. Previous and current clotting studies.
7. Blood glucose level.
8. All patients should have intravenous access and infusion of 5% dextrose.
9. Hepatitis A and B status.
10. Past medical history.
11. Referring consultant and patient's general practitioner.
6. MANAGEMENT OF ACUTE HEPATIC FAILURE

6.1. Liver Transplantation

Many patients with AHF will not require or are unsuitable for liver transplantation. Patients deemed unsuitable for transplantation will not be admitted under the liver transplant programme but may be admitted for treatment on an UNPAC basis. Early transfer is desirable rather than waiting for the criteria for liver transplantation to be met. In some patients with AHF, the prognosis is so grave that liver transplantation should be considered. The following guidelines indicate patients for whom liver transplantation should be considered, although each case requires individual decisions. Early consultant psychiatrist involvement in selected cases should be sought, preferably before encephalopathy develops.

6.1.1 Criteria for liver transplantation in acute hepatic failure

The criteria for considering transplantation in patients with AHF are stated below. It is important that serial measurements of prothrombin time, creatinine, pH, bilirubin and lactate are recorded in all patients admitted.

The indications for transplantation are detailed on the following page:
6.1.1.6 Category 1

Paracetamol: pH <7.25 (H⁺>50) more than 24 hours after overdose and after fluid resuscitation.

6.1.1.7 Category 2

Paracetamol: Co-existing prothrombin time >100 seconds or INR >6.5, and serum creatinine >300 umol/l or anuria, and grade 3-4 encephalopathy.

6.1.1.8 Category 3

Paracetamol: Serum lactate more than 24 hours post-overdose >3.5 mmol/l on admission or >3.0 mmol/l after overdose and after fluid resuscitation.

6.1.1.9 Category 4

Paracetamol: Two of three criteria from category 2 with evidence of deterioration (e.g. increased ICP, FiO₂>50%, increasing inotrope requirements) in the absence of clinical sepsis.

6.1.1.5 Category 5

Aetiology: Hepatitis A or hepatitis B or an idiosyncratic drug reaction or seronegative hepatitis, and prothrombin time >100 seconds or INR >6.5, and any grade of encephalopathy.

6.1.1.6 Category 6

Aetiology: Hepatitis A or hepatitis B or an idiosyncratic drug reaction or seronegative hepatitis, and any grade of encephalopathy, and any three of the following: unfavourable aetiology (idiosyncratic drug reaction, seronegative hepatitis), age >40 years, jaundice to encephalopathy time >7 days, serum bilirubin >300 umol/l, prothrombin time >50 seconds or INR >3.5.

6.1.1.7 Category 7
Aetiology: Acute presentation of Wilson’s disease or Budd-Chiari syndrome, and a combination of coagulopathy, and any grade of encephalopathy

6.1.2 **Contraindications**

6.1.2.1 MEDICAL:

- Untreated or progressive infection
- Clinically apparent extrahepatic or metastatic malignancy
- Progressive hypotension resistant to vasopressor support
- Clinically significant ARDS, FiO2 > 0.8
- Fixed and dilated pupils > 1 hour, in the absence of thiopentone therapy
- Severe coexistent cardiopulmonary disease
- AIDS.

6.1.2.2 PSYCHIATRIC/ PSYCHOLOGICAL:

- Multiple episodes of self harm (>5) within an established pattern of behaviour (especially if non drug methods used)
- Consistently stated wish to die, in the absence of established mental illness (especially depression)
- Chronic refractory schizophrenia or other mental illness, resistant to therapy
- Incapacitating dementia or mental retardation
- Active intravenous drug abuse
- Active poly-drug use, in a severe chaotic fashion
- Alcohol dependence or use of alcohol in a severe and chaotic fashion

6.1.3 **Listing for liver transplantation**

If the patient’s prognosis is so grave and there are no contraindications to transplantation, then patients will be considered for liver transplantation after discussion with the consultant hepatologist on-call, consultant transplant surgeon and consultant anaesthetist in discussion with other colleagues as considered appropriate by this core group of personnel. It is absolutely essential that the information detailed in Appendix 3 is available before the patients reach transplant criteria as in such situations, time is of the essence. In addition, dynamic variables such as the prothrombin time, bilirubin and creatinine may be measured more than twice daily if this is considered appropriate. Once the decision is made to list the patient for a super-urgent
liver transplant the weight and blood group restrictions will be discussed and agreed between the hepatologist on-call for the week, the liver transplant surgeon and consultant anaesthetist. The details will then be faxed to NHS Blood and Transplantation (NHSBT) and the transplant co-ordinator on-call contacted to provide NHSBT with further information.

6.2 **Metabolic and haematological**

Some patients with AHF will develop severe hypoglycaemia. All patients require IV administration of 5 or 10% dextrose. Higher concentration and lower volume of dextrose (50%) via a central line should be used if the serum sodium is < 135mmol/l. Capillary blood glucose is monitored by hourly BM stix. If blood glucose falls below 3.5mmol/L, an infusion of 50% dextrose is administered via a central venous line, commencing at 10 ml/hour and adjusted according to subsequent blood glucose levels. Blood sugar should be maintained between 5 and 8mmol/L. Because of the speed patients with AHF can deteriorate, repeated measurements of plasma electrolytes are important particularly serum potassium, sodium and creatinine as well as the FBC and prothrombin which should be measured at least twice daily. The Hb should be kept > 80g/L. Serum phosphate, calcium and magnesium should be measured daily and replaced as necessary. There is some evidence that supernormal plasma sodium reduces the incidence of raised ICP. It is not our routine practice to increase the plasma sodium >145mmol/l but consideration should be given to hypertonic saline administration in any patient with plasma sodium < 135mmol/l or acutely decreasing below 140mmol/l. Consideration should be given to making up N acetyl cysteine in normal saline rather than 5% dextrose. The use of hypertonic saline should be discussed with the Consultant Hepatologist or Anaesthetist first before administration. Blood ammonia will be measured in the biochemistry lab at RIE. A level>100Umol/L suggests patients with a greater risk of clinical deterioration.

6.3 **Respiratory system**

Appropriate concentrations of oxygen should be administered as necessary by pulse oximetry and/or arterial blood gas analysis to maintain arterial saturation > 95% or PaO2 > 10 kPa. If the patient is hypoxic or requiring increasing concentrations of inspired oxygen, consider infection, bronchospasm, pneumothorax, fluid overload or developing ARDS. Intubation and ventilation are indicated if the conscious level is sufficiently depressed and the patients' airway and/or ventilation are compromised. Generally this occurs when grade III coma is present. (see below).
6.4. Conscious level

Encephalopathy may develop rapidly in AHF. Coma in these patients is not always due to encephalopathy; hypoglycaemia and a post ictal state must be excluded. Agitation or confusion may also be attributed to alcohol withdrawal in some patients.

The use of sedation in patients nursed in Ward 117 with AHF should be discussed with the consultant hepatologist on-call but is generally not recommended. Haloperidol or Diazepam should not be administered unless a clear plan has been documented. Sedating agitated encephalopathic patients with AHF should be avoided, ventilation is the preferred and safer option given the risk of cerebral oedema.

Grade of coma in encephalopathy is classically divided into -

- Grade 1 Drowsy.
- Grade 2 Agitated or confused.
- Grade 3 Unconscious, rousable.
- Grade 4 Unconscious, unrousable.

The Glasgow Coma Scale (E,M,V) (see Appendix 4) is less prone to inter-observer variability and should be employed, especially when assessing the needs for transfer of a patient with AHF.

The most important decision in patients with AHF with deteriorating conscious level is when to initiate mechanical ventilation; usually Grade III coma or Grade II (if agitation is compromising their care). Patients with a GCS of 8 will normally require ventilation. Ventilation should be considered for any person with a GCS of 10 or less. If there are concerns about the ability of the patient to protect their airway, intubation and ventilation are indicated particularly before transfer. Within the RIE, patients requiring mechanical ventilation will generally be transferred to ITU before this is commenced. If no beds are available in ITU, it will be undertaken in the HDU of SLTU.

All patients with encephalopathy should be nursed in a quiet environment, should not be turned routinely (Nimbus mattress), and any interference should be kept to a minimum to reduce the risk of raised ICP. Lactulose and neomycin are not indicated.

6.5. Management of elevated ICP

A common cause of death is cerebral oedema and although this usually occurs in patients with Grade IV coma, it may occur rapidly in patients with lesser degrees of encephalopathy.
Increased ammonia on admission (especially if >200Umol/L) may identify patient with increased risk of developing HE or elevated ICP. Cerebral oedema may develop even when the prothrombin time is falling and liver function improving. ICP may increase rapidly and waiting for clinical signs of cerebral oedema such as pupillary abnormalities, bradycardia, systemic hypertension and opisthotonos may result in irreversible brain damage before treatment can be initiated.

In non ventilated patients who develop clinical signs of raised ICP or when ICP monitoring is not available, patients should be treated as detailed below. Subsequently, the consultant anaesthetist on call should be contacted, arrangements made for ventilation and consideration of intracranial pressure monitoring when patient stabilised.

Ventilated patients listed for transplantation should be considered for ICP monitoring. The greatest rise in ICP commonly occurs on reperfusion and rises in ICP in the immediate postoperative period (first 24 hrs) are common. For this reason the ICP monitor will generally be left in place for at least 24 hours post-operatively and removal guided by response of ICP to a gradually rising PaCO₂. Ventilated patients meeting criteria but not listed for transplantation may also be considered for intracranial pressure monitoring. The aims are to keep ICP below 20 mmHg and cerebral perfusion pressure (MAP-ICP) > 60 mmHg.

A CPP < 40 mmHg is critical, and ICP > 40 mmHg is associated with poor prognosis and indicates that ICP is on a very steep part of the intracranial volume pressure curve i.e., there is very low compliance. Sudden and extreme rises in ICP may then occur.

Detailed management of intracranial hypertension can be found in the critical care guidelines.

6.5.2 Management

Mannitol: When clinical signs of raised ICP (pupil dilatation, hypertension, and bradycardia) occur before ICP monitoring can be instituted, mannitol 200 ml 20% solution should be administered over 20 minutes. Intensive care should be contacted immediately in this situation.

6.5.2.1 Ensure adequate venous drainage from the head at all times. (no neck restrictions and maintaining 30° head up tilt) This is standard practice for all ICU patients to reduce the incidence of ventilator associated pneumonia.

6.5.2.2 Titrate sedation and analgesia to optimise synchrony with mechanical ventilation in order to achieve target blood gases. Ensure PaCO₂ in range 4.5 – 5 kPa
6.5.2.3. Optimise intravascular volume using CVP or PCWP as appropriate. Bear in mind that many of these patients are young and will have a PCWP or CVP that is appropriately less than 8 cm H$_2$O especially when vasodilated. Norepinepherine is appropriate at this stage if peripheral perfusion is good to maintain CPP > 60 mmHg. MAP should not normally be allowed to exceed 120 mmHg or SAP 180 mmHg. Dobutamine probably has least effect on cerebral vasculature. However norepinepherine is most commonly used to maintain blood pressure in the face of a low SVR. (see haemodynamic cardiovascular monitoring).

6.5.2.4 Hypertonic therapy - first line sodium chloride 5% 100ml iv over 15 mins to maintain serum sodium levels of 140-145mmol/l

Hypertonic therapy second line mannitol 20% 200ml iv over 15 mins. If on CVVH remove 400ml over next hour. Careful review of volume status.

The serum sodium and osmolality must be measured after 3 treatments and following each treatment thereafter. Repeated treatments may be ineffective if the patient is in renal failure unless haemofiltration has been commenced due to the risk of volume overload. Management of raised ICP may be an indication to institute CVVH earlier than otherwise indicated and this should be discussed with the renal physicians. If CVVH is instituted, 400 mls may be removed in the hour following a mannitol treatment.

Alternatives to osmotherapy should be used if the plasma osmolality exceeds 320mOsm/L.

6.5.2.4 Moderate hypothermia (core temperature ≤ 34°C) should be considered in patients with raised ICP unresponsive to 2 osmolar treatments and should be instituted promptly in the patient with high jugular bulb saturation and refractory ICP.

6.5.2.5 Thiopentone is third line therapy and is indicated when ICP is raised and jugular bulb oxygen saturation is high (> 75%). This indicates hyperaemia or brain death, which should be considered in these circumstances. Thiopentone reduces cerebral blood flow by cerebral vasoconstriction and reduction of cerebral metabolic rate. Thiopentone should be administered by infusion otherwise sudden decreases in CPP are likely. 40ml/hr for 20 minutes, 25 ml/hr for 1 hour and then 5-15 ml/hr continuous infusion. Thiopentone is not without hazard and may lead to circulatory impairment (hypotension and reduced CPP) and an increased likelihood of infection.
6.5.2.6 Hyperventilation may have a place in the management of raised ICP secondary to hyperaemia, but this is usually only to deal with an acute crisis secondary to rapid rise in ICP. Routine hyperventilation has been shown to be ineffective and hyperventilation from an early stage of management may lead to greater difficulty controlling ICP later if chest problems ensue. An arterial PaCO$_2$ of 4.5-5 kPa should be the initial goal.

6.5.2.7 In extreme situations when there is difficulty controlling a patient's intracranial pressure or systemic blood pressure, total hepatectomy may be considered appropriate after discussion with consultant hepatologist on-call, the liver transplant surgeon and consultant anaesthetist. Consideration should also be given to Indomethacin IV.

6.6 Renal Function

At least 50% of patients with paracetamol induced AHF will develop acute renal failure due to a combination of renal toxicity, acute tubular necrosis and functional renal failure. Urine output requires close monitoring with hourly urine volumes, requiring bladder catheterisation in the majority of cases. All patients with oliguria should have a central venous pressure line inserted and colloid/crystalloid administered to maintain the CVP 5-10 cm H$_2$O. The plasma creatinine, not the urea, and potassium must be measured at least twice daily. The renal team should be contacted early in the clinical course. In the majority of cases renal support will be by use of continuous veno-venous haemofiltration which allows correction of hyperkalaemia, acidosis and volume overload. Hyponatraemia must be avoided.

6.7 Haemodynamic Cardiovascular Monitoring

Hypotension (systolic blood pressure < 80 mmHg) occurs in many patients with AHF. In some cases, the hypotension can be explained by sepsis, gastrointestinal haemorrhage, or cardiac dysrhythmias and these should be excluded. Fungal infection should be particularly considered if hypotension occurs after day 4 in paracetamol poisoning cases, especially if they have received antibiotics. In other cases it results from the haemodynamic disturbance associated with AHF itself, namely vasodilatation and reduced systemic resistance associated with reduced CVP and PCWP.

Initial management of patients will require insertion of a central venous pressure line and a urinary catheter to ensure that the patient has been adequately fluid resuscitated. This will be undertaken with synthetic colloid/crystalloid solution to achieve a central venous pressure of 5 -
10 mmHg. If there is no response to volume loading (MAP ≤60mmHg) an arterial line should be placed in the radial artery to allow continuous blood pressure monitoring, and a PA flotation catheter should be considered, preferably via the internal jugular vein, to allow measurement of PACWP, cardiac output and systemic vascular resistance. PACWP should be kept above 8 mmHg by volume expansion. Low systemic vascular resistance should be corrected by the pressor agent norepinephrine (8mg %), commencing at 1 ml/h and increasing as necessary. The consultant anaesthetist on call should be consulted before insertion of a PA flotation catheter. It should be remembered that CVP and PCWP are usually low in the severely vasodilated patient. Caution should be exercised with IV volume administration in these circumstances and early consideration given to norepinephrine administration, if CVP/BP shows little improvement to volume loading.

6.8 Sepsis and Antibiotics

(Please see updated antibiotic protocols on RIE Intranet )

Bacterial and fungal infections are common in patients with AHF; a high index of suspicion should be maintained. Strict adherence to the hospital infection control measures is essential. Most patients are admitted directly to HDU or ITU. Use of alcohol gel, plastic aprons and gloves are required and the bedside stethoscopes should be used in these areas. Aseptic techniques are required for insertion of invasive lines.

On admission, each patient should have an MRSA screen performed (nose, throat, groin or wound). Other cultures should be performed on admission as clinically indicated. In addition, any patient with fever, hypothermia, or unexplained clinical deterioration should have further cultures taken.

All active infection should be treated with appropriate antimicrobials, guided by microbiology results. If bacterial infection is suspected, empirical antibiotic treatment with co-amoxiclav (Augmentin) 1.2g TDS I.V. should be commenced. In penicillin allergic patients, confirmation of the nature of the allergy is necessary; if mild penicillin allergy is confirmed then empirical therapy with ceftriaxone 1g/day and metronidazole , in cases of severe penicillin allergy the combination of vancomycin/ciprofloxacin/metronidazole should be substituted as empirical therapy (this could be modified in the light of the admission MRSA screen).

All patients transferred to ITU AND ventilated will be administered the above broad spectrum antibiotics routinely on a prophylactic basis and should start and continue prophylactic fluconazole 400mg daily.
Fungal infection is common in patients with ALF. If yeast infection is suspected and patient already treated with fluconazole then treatment with anidulafungin should be commenced (200mg loading dose in 250ml 0.9% saline over 1h; maintenance 50mg in 100ml 0.9% saline over 1h daily. Suspicion of cryptococcal infection requires liposomal amphotericin B (Ambisome) 3mg/kg/day I.V. in single dose with flucytosine, while mould (e.g. aspergillus) infection generally requires use of voriconazole. Seek expert advice and consult Critical Care antifungal policy on intranet.

6.9 Gastrointestinal Bleeding
All patients with AHF should receive intravenous ranitidine 50 mg IV 8 hourly (bd in renal failure) If there is evidence of gastrointestinal bleeding an upper GI endoscopy should be performed to assess the site and degree of bleeding. Bleeding from varices is unusual in AHF, especially paracetamol poisoning, but adrenaline injection of bleeding peptic ulcers may be necessary.

6.10 Coagulopathy
Coagulopathy is almost universal in AHF. The prothrombin time should be monitored at least twice daily. This measurement provides the best indication for changing liver function, and prophylactic correction is therefore undesirable, but may be undertaken at the discretion of the consultant hepatologist or the consultant anaesthetist on-call. However, before surgery or insertion of an intracranial pressure monitor coagulopathy may be corrected. A combination of fresh frozen plasma, cryoprecipitate and specific factor concentrates may be required to partially correct the prothrombin time. The prothrombin time may be influenced for at least 24 hours following the administration of FFP. Therefore if this is undertaken the PT can no longer be used as a criterion for transplant assessment. This is important if correction is undertaken when the PT has not reached those defining “transplant criteria”. Therefore where important decisions are dependent upon changes in coagulation, measurement of factor V and/or VII will be undertaken. Patients with thrombocytopenia (platelet count < 100 x 10^9/l) should be considered for prophylactic platelet transfusions if surgery or ICP monitor insertion is to be undertaken. Platelet transfusions may also affect the PT and hence should be used with caution when the issue of transplantation is unresolved.

6.11 N-acetylcysteine
N-acetylcysteine will be administered by infusion using the standard regime of 150 mg/kg over 15 minutes, 50 mg/kg over 4 hours and 100 mg/kg over 16 hours. This will be administered only to patients who have AHF following paracetamol overdose who have not previously received N-acetylcysteine in the referring hospital. The 100mg/kg over 16 hours regime will be continued until the prothrombin time is improving or at the discretion of the hepatologist on call for the week.
Infrequently N-acetylcysteine may induce allergic reactions. This is treated by discontinuing the infusion, administering intravenous hydrocortisone and chlorpheniramine and recommencing the infusion at a slower rate. Any severe allergic reaction should be treated with IV epinephrine (1-2ml increments of 1:100 000 solution). Electrolytes must be monitored as can be made up in normal saline where indicated.

6.12 Feeding
Patients with AHF who require nutritional assessment need to be referred to the SLTU dietician. Enteral nutrition is the method of choice.

6.13 Psychiatric Treatment
All patients admitted with a paracetamol overdose to the unit must have a psychiatric referral either to the Royal Infirmary psychiatric team (if from Lothian) or to the local psychiatric service if from outside Lothian. If no psychiatric evaluation has been performed in the referring hospital, the patient should be reviewed or discussed with the Royal Infirmary psychiatric team. Prior to transfer back to the referring hospital patients should be reviewed by the Royal Infirmary psychiatric team to determine the suicide risk and allow planning for the level of supervision required during transfer. If the patient is transferred back to the referring hospital the state of psychiatric intervention must be communicated by telephone at the time of transfer.

6.14 Transjugular Liver Biopsy
This may be undertaken in the Department of Radiology if the aetiology of acute liver failure is unclear. Patients should have an attempt at correcting the coagulation prior to transjugular biopsy, unless it is considered by the consultant hepatologist on for the week that the issue of transplantation remains unresolved.
Stepwise Management

Conscious level

1. Monitor conscious level hourly using the Glasgow Coma Scale.
2. If evidence of encephalopathy monitor continuous pulse oximetry
3. Nurse, semi-recumbent or in recovery position
4. Nil orally
5. Intubate and ventilate early

Biochemistry

1. Check BM stix hourly
2. Continuous infusion of 5-10% dextrose, 50% dextrose (via central vein) if hypoglycaemic
3. Monitor pH, lactate, U & E’s, creatinine and liver function tests at least once daily (usually twice)

Gastrointestinal Bleeding

1. Intravenous H2 antagonists
2. Endoscope if evidence of upper GI bleeding
3. Consider platelet and clotting factor infusion.

Cerebral Oedema

1. Neurological observation, especially pupillary reactions, should be carried out hourly in all patients with encephalopathy.
2. Intracranial pressure monitor and cerebral perfusion pressure may be monitored in patients requiring mechanical ventilation.
3. Hypertonic saline and mannitol should be used as the agent of first choice and moderate hypothermia, thiopentone, or hepatectomy as second line treatments to reduce ICP. Cerebral perfusion pressure should be maintained > 60 mmHg by volume expansion and use of inotropes as required.
Renal Function

1. The creatinine, not urea should be monitored.
2. Urinary catheter should be inserted and urine output monitored hourly.
3. If there is oliguria despite adequate central filling, or the creatinine is raising a renal specialist should be contacted. Haemofiltration via a central or femoral vein will be undertaken if necessary and should be instituted early to attenuate problems with intracranial pressure.

Sepsis

1. Strict adherence to infection control measures is essential. Hand-washing and plastic aprons are required. Use of the bedside stethoscopes not your own. Aseptic techniques are required for insertion of invasive lines.
2. Close scrutiny for sepsis must be undertaken. Daily cultures of urine and blood should be sent.
3. If infection is suspected administer antibiotics early.
4. Prophylactic antibiotics and antifungals will be administered to patients in the intensive care unit.

Cardiovascular

1. Hypotension unresponsive to volume loading is an indication for more invasive monitoring.
2. Adequate central filling pressures should be maintained.
3. Norepinepherine will be used to support the systemic vascular resistance.
   (aim for MAP > 80mm.Hg)
APPENDIX 1

Causes of AHF.

- paracetamol poisoning

- viral hepatitis; A, B, B and D, E, non-A-E (or seronegative) hepatitis, herpes simplex, EBV, adenovirus.

- drugs including halothane, isoniazid, ketoconazole, tetracyclines, MAOI, ecstasy and non-prescribed drugs, herbal remedies.

- pregnancy associated: pre-eclampsia, acute fatty liver, HELLP

- Reye's syndrome.

- poisons; carbon tetrachloride, Amanita phalloides.

- Budd-Chiari.

- cardiac failure.

- miscellaneous: metastatic cancer, lymphoma, liver abscess.

- autoimmune hepatitis

- Wilson's Disease
APPENDIX 2

LIVER FAILURE - URGENT TELEPHONE REFERRALS

Please seek the following information:

Date:                            Time:

Name:

Date of birth:

Referring Hospital/Ward:          Tel No:
Referring Doctor:                 Bleep/Ext No:
Referring Consultant:             Bleep/Ext No:
General Practitioner             Address:
                                 Tele No:

Suspected Diagnosis:

Time and date of ingestion paracetamol OD suspected
NAC     Y/N
Previous self poisoning          Y/N
Previous psychiatric history     Y/N
Arterial blood gases            pH
Bilirubin                        FBC
Prothrombin time/INR
Urea                             Creatinine
Blood glucose                    HBs Ag
Conscious level                  HR       BP
GCS
Ventilatory status
Urine output
Therapy given (inc drugs, IV fluids, FFP, etc)
Other relevant details of history especially recent drug history. If paracetamol is not the cause, all information about the possible cause must be sought.

Next of kin
**APPENDIX 3**

**Information necessary before transplantation in ALF.**

- Full blood count, coagulation, urea and electrolytes, creatinine and liver function tests.

- HBs Ag and HIV status (IgM anti HBc, and HBsAg negative, recent HBV infection)

- HCV, HEV and CMV status.

- Blood group.

- CXR, ECG.

- details of social/family/occupational background.

- results of liver histology (if biopsy has been undertaken).

- presence/absence of cerebral oedema.

- details of previous surgery.

- details of past medical history, including psychiatric.

- current drug therapy.

- family consent.

- BTS must be contacted early for provision of adequate blood, FFP and platelets).

- Psychiatric opinion should be sought in paracetamol poisoning.

- Tell transplant co-ordinator

These data should be collected before the patient is listed for transplantation. If it seems likely, using the criteria for transplantation described earlier, that the patient will be a candidate; this information should be urgently collected, not waiting for the criteria to be met.
## APPENDIX 4

### Glasgow coma scale

<table>
<thead>
<tr>
<th>Score</th>
<th>Motor response</th>
<th>Verbal response</th>
<th>Eye opening</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Obeys simple commands</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Attempts to remove source of painful stimuli to head or trunk</td>
<td>Orientated</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Attempts to withdraw from source of pain, Normal flexion</td>
<td>Disorientated</td>
<td>Eyes open spontaneously</td>
</tr>
<tr>
<td>3</td>
<td>Flexes arm at elbow and wrist in response to nail bed pressure, Abnormal flexion</td>
<td>Random speech</td>
<td>Open to speech</td>
</tr>
<tr>
<td>2</td>
<td>Extends arms at elbow and wrist in response to nail bed pressure</td>
<td>Mumbling, Incoherent Sounds</td>
<td>Open to pain</td>
</tr>
<tr>
<td>1</td>
<td>No motor response to painful stimuli</td>
<td>No speech</td>
<td>No opening</td>
</tr>
</tbody>
</table>

Add the individual scores: best = 15, worse = 3