Liver Failure in the setting of Chronic Liver Disease.

This is far more common than Acute Liver Failure (see separate guideline on acute liver failure). May present as deteriorating liver function, generalised deterioration or progressive jaundice or encephalopthy in patient with known or suspected liver disease.

The commonest cause is alcoholic liver disease and if you suspect that patient is still drinking then Pabrinex should be commenced and need to be aware of withdrawl (Give benzodiazepines, but beware of precipitating encephalopathy and therefore use small doses and titrate effects : see guidelines on Alcohol Withdrawal).

The deterioration or decompensation in a cirrhotic patient is often precipitated by an identifiable cause and this should be sought and remedied. These include :-

- **GI bleed**
- **Sepsis**
- **Metabolic disturbance**
- **Further Alcohol abuse**
- **Drugs**

Management

Basics : Admit, review notes to determine underlying diagnosis, History of alcohol, drugs, GI bleed and source / focus of sepsis. Examine for signs of chronic liver disease.

Investigations :
-FBC, INR, GpSave, U/E, LFT's, Phosphate, Magnesium
In all ascitic patients urgent Ascitic tap needed : send for White Cell Count (red topped EDTA blood tube), protein / albumin Content (universal container) and for culture (universal container and blood culture bottles.
-Blood Culture
-CXR
-PR examination for melaena
-OGD if signs of bleeding

Initial Treatment : Broad Spectrum Antibiotics (Tazocin unless allergic) if any suspicion of sepsis
PPI
Fluconazole 50-100mg PO
Terlipressin 2mg QDS if suspicion of GI bleed

Fluid management : Monitor fluid balance, catheterize if necessary.
Avoid Saline
Use 5% dextrose unless low sodium (<125) (if IV needed in hyponatraemic patients consider colloid (albumin 20% 100mls; 1-3 x100mls /24 hrs to maintain oncotic pressure))

If ascites or hyponatraemic then fluid restrict to 1.5L day i**f renal function permits**, but may have to accept deteriorating ascites as a price of rehydration in severe decompensation. **Beware of inducing hypovoleamia.**

Specific Situations needing consideration are outlined below including : Hepatorenal Syndrome, Role of ITU, Managmenent of Ascites, Spontaneous Bacterial Peritonitis, Encephalopathy.

Hepatorenal Syndrome

Defined as Low GFR (creatinine clearance <40ml/min) or serum creatinine >132umol/l in advanced hepatic failure and portal hypertension.

Exclude other aetiologies :-
Shock, ongoing bacterial infection, recent nephrotoxic drug administration, Proteinuria, ultrasound evidence of renal tract disease

Discuss with the GI team regarding further management : The prognosis is usually poor and it is important to consider both the acute and long-term management issues. Temporary treatment of Hepatorenal syndrome is sometimes possible / successful (with albumin and terlipressin), particularly if there is a reversible factor and a long-term plan such as transplantation. Dialysis is usually not indicated.

Role of ITU The following outlines how mortality varies with the number of organs systems involved based on observations on ITU patients with chronic liver disease:

0 organs	: 6% mortality
1 organ	: 33% mortality
2 organs	: 73% mortality
3 organs	: 97% mortality

If renal failure, then approx 90% mortality in critically ill patients irrespective of number of other systems involved.

Therefore ITU needs to be considered carefully : if there is multi-organ failure then the outcome is poor despite ITU and therefore ITU may be inappropriate. This decision should ideally be made early and ‘in hours’. Ask seniors.

Ascites

Where possible follow the guidelines below. However be aware that in the setting of severe decompensation other problems such as hypovolaemia may need addressing first, in this case fluid restriction and other treatments of ascites are inappropriate. Once over acute phase then re-consider the management of ascites :-

All Patients with Ascites need a diagnostic ascitic tap :
(this is a clean procedure ie gloves, alcohol to skin, sterile green needle with fluid being sent for culture in blood culture bottles, an EDTA tube and a universal container, also for biochemistry for albumin levels and if appropriate for cytology).

All Patients need daily weights.

Review Results to look for SBP (see below) and to confirm diagnosis of ascites secondary to portal hypertension.

Use Serum Ascites-Albumin gradient. (SAAG) gradient to confirm diagnosis :
ie serum albumin – ascites albumin

>11 = Cirrhosis, Cardiac failure, Nephrotic
<11 = Malignancy, TB, Pancreatitis

If <11 consider pancreatitis and measure the ascites amylase content and check cytology.

Treatment of Ascites

Patients with ascites have secondary hyperaldosteronism and a potent sodium retaining state. Any salt given to such patients results in further accumulation of ascites,.

Treatment :

(1) Low Salt Diet (no salt added diet)
(2) Diuretics : spironolactone is an aldosterone antagonist and is first line diuretic.
    a. 100 mg spironolactone working up to 400mg daily.
    b. There is a lag of 3-5 days, therefore no point in increasing every day.
    c. Frusemide 40-160mg may be added
    d. Ideally look for a weight loss of 0.5kg per day : over diuresis is associated with renal failure (1 kg per day is OK if peripheral oedema).
    e. Monitor sodium and renal function
(3) If hyponatraemic : (taken from BSG guidelines)
    126-135 , normal serum creatinine: continue diuretics
    121-125, normal serum creatinine : Stop diuretic
    121-125, creatinine rising: stop diuretic + give volume expansion
    <120 : Difficult. Stop diuretics. Involve registrar/ consultant.

4) The role of water / fluid restriction is controversial. Most authorities recommend fluid restriction if hyponatraemic (Na < 130). Usually the restriction is 1.5L per day, occasionally this is more stringent but **beware of inducing hypovoleamia and renal failure.** Review fluid balance in all patients : even if not hyponatraemic ensure they are not drinking excess fluids (>2.5L day).

5) Patients with ascites should not normally be given the following:
(1) Normal saline (including drug infusions)
(2) Dextrose- Saline
(3) NSAIDS

Crystalloid should be given as 5% Dextrose (although this will exacerbate any tendency to hyponatraemia)

6) Large Volume Paracentesis (see below) : this may be required for those patients presenting with tense ascites or in those patients in whom are diuretic resistant (fail to respond to maximal dose diuretics) or those who are intolerant of diuretics (renal failure or hyponatraemia).

ASCITES IS ASSOCIATED WITH A 50% MORTALITY WITHIN 2 YEARS.
The development of ascites is therefore one of the indications to consider the long term options for the patient including referral for transplantation.

Large Volume Paracentsis

1) Theoretical considerations

-Large volume paracentesis (LVP) is the removal of 5000mls or more of ascitic fluid during a single session.
-Cardiac output increases immediately after removal of 4 to 15 Litres of ascitic fluid.
-Within 6 to 12 hours, decreases in central venous pressure , pulmonary capillary wedge pressure and cardiac output occur. Therefore a plasma expander is used at the time of LVP to maintain effective circulating volume.
-Albumin is the plasma expander of choice and failure to use a plasma expander has been associated with an increased risk of hyponatremia and renal impairment after LVP.
- Ascites should be drained rapidly - there is no advantage of slow or interrupted drainage, this merely increases the risk of infection.
-Paracentesis may precipitate Hepatorenal failure in high risk groups, including those with Spontaenous Bacterial Peritonitis (SBP :see below) and those with a degree of renal impairment.

Therefore if SBP or renal impairment is present then discuss with GI consultant / SpR : alternative options are to treat SBP first or to consider small volume (5 or 6 litre only) paracentesis.

-Patients who are admitted simply for elective paracentesis have low rates of SBP (0.5 3%) whilst those who have been admitted as emergenices with decompensated liver

disease who go onto need paracentesis have high rates (15-50%). Therefore routine diagnostic taps is not needed prior to paracentesis in those being admitted for elective LVP but is essential in those who are inpatients with decompensated liver disease.

2) Timing of LVP

-In order to facilitate the albumin infusion, patient monitoring and safe removal of the paracentesis drain it is sensible to insert the drain at the beginning of the working day with the aim to remove it after approximately 6-8 hours.
This should be the standard practice with only exceptional circumstances permitting the insertion of paracentesis drains late in the working day/weekends.

Patients admitted for elective paracentesis are often admitted late in the afternoon early evening (as beds become available) for drainage the following day. It is imperative that they are reviewed on the evening of admission and FBC, U/E and clotting are checked. Ensure that albumin is requested from blood bank at this point (100mls of 20% Human albumin solution for every 3 litres of fluid removed; request 5 x100mls) to enable drainage the following morning.

3) Practicalities of LVP (see "Tapping Ascites & Paracentesis for technical guidance)"

-Review blood results. Paracentesis is not contraindicated in patients with an abnormal coagulation profile & there are no data to support the use of fresh frozen plasma before paracentesis. If thrombocytopenia is severe (<40,000) give 1 unit of platelets.

-Discuss with seniors if SBP or Renal failure or profound coagulopathy (INR>3).
-Ensure weight is recorded.
-Ensure that albumin is available and prescribed (100mls of 20% HAS for every 3 litres ascites removed).
-Once drain inserted do not clamp the drain.
-Send a specimen for cell count (in red topped EDTA blood tube) if not recently done. If this indicates SBP (WCC > 0.4) then it may be appropriate to limit the volume of paracentesis to 5 Litres. The patient will need treatment with 5 days of antibiotics.
-If the patient has attended for elective paracentesis they will usually be discharged later that day, therefore write TTO's.
-The drain should be assessed by nursing staff at **6 hours** post insertion. If it is still draining and has drained 1000mls or more in the last hour continue draining for another 1 hour. Assess hourly as above up to a **maximum of 12 hours.**

All drains should be removed by 12 hours.

-For elective paracentesis patients can go home if the drain has been removed, there is no significant leakage and the blood pressure has been stable throughout the procedure, and there is no sign of SBP. There is no need to routinely check U/E's.

SBP

Spontaneous Bacterial Peritonitis is associated with 50% reduction in survival

Diagnosed by a raised ascitic White Cell Count **(>0.4 if done in EDTA tube)** or >500/mm^3 WCC or >250/ mm^3 neutrophils if assessed by microbiology manual count.

Treat with : Tazocin 4.5g TDS unless allergic for 5 days

If renal failure develops then give albumin at 1.5 g albumin/ kg in the first six hours followed by 1 g/kg on day 3.

Patients with ascites and previous episodes of SBP should be considered for long-term antibiotic therapy to prevent further episodes of SBP Additionally patients with low levels of ascitic protein (<15g/L) should also be considered.

Cotrimoxazole 960mg OD is recommended for prophylaxis against recurrent SBP.

All patients receiving Cotrimoxazole treatment should be informed before commencing it that there are risks (and benefits) associated with Cotrimoxazole. All patients should have the potential side effects explained (especially rash, and blood dyscrasias) together with the need for treatment. After this, the patient should give verbal consent and this should be documented in the notes, including

1) The need to stop treatment immediately and refer to the prescriber should be emphasised if the patient develops a rash, or unexplained fever / sore throat.
2) All this should be documented in the patient's notes.
3) A letter should be sent to the GP to continue the prescribing after discharge.

[A simple sticker documenting the consent is available on D18]

Encephalopathy

This represents severe liver failure, either acute or chronic. Avoid all sedative agents. Need to plan if ITU appropriate since endotracheal intubation may be needed if progresses and it is best practice to have such decisions made in advance, not out of hours.

Aim to treat underlying cause of liver disease or precipitant of decompensation.
Supportive measures include Phosphate enema and lactulose to keep bowels open 2x day.

<u>Grading of Encephalopathy</u>

1: Drowsy
2: Confused
3: Agitated / incoherent
4a) Responds to pain
4b) Unresponsive