CIRRHOSIS OF THE LIVER

Cirrhosis of the liver consists of diffuse fibrosis and nodule formation. The normal zonal architecture of the liver is lost. These features result from hepatocyte necrosis, collapse of the supporting reticulin network with subsequent connective tissue deposition, distortion of the vascular bed and nodular regeneration of the remaining liver parenchyma. This pathologic process should be viewed as a final common pathway of many types of chronic liver injury, irrespective of its aetiology.

Classification of cirrhosis

Cirrhosis can be classified by morphology or aetiology. The aetiological classification is more useful clinically. The major causes of cirrhosis are listed in Table 1.

Clinical features of cirrhosis

Clinically, cirrhosis may be either, latent and well compensated or active and decompensated.

Latent and well compensated cirrhosis

This condition is usually incidentally discovered on a routine examination, on biochemical screening or at operation. Mild fever, vascular spiders, palmar erythema, unexplained epistaxis or oedema of the ankles, a firmly enlarged liver and splenomegaly are helpful diagnostic signs. Biochemical tests may be normal. The most frequent biochemical changes are a slight increase in serum transaminases and a constant excess of urobilinogen in the urine. The diagnosis is confirmed by needle liver biopsy.

Table 1: Common causes of cirrhosis

1. Viral Hepatitis - Type B; Non - A, Non - B
2. Alcohol
3. Metabolic
   - Wilson’s disease
   - Haemochromatosis
   - others
4. Autoimmune
   - Chronic active hepatitis
   - primary biliary cirrhosis
5. Hepatic venous outflow obstruction
   - constrictive pericarditis
   - chronic right heart failure
6. Budd - Chiari syndrome
7. Veno - occlusive disease
8. Prolonged cholestasis
9. Toxins and therapeutic agents
   eg : methotrexate, methyldopa
   Isoniazid
10. Miscellaneous
    - Indian childhood cirrhosis
    - Intestinal bypass
11. Cryptogenic cirrhosis

Active and decompensated cirrhosis

These patients usually present with features of hepatocellular failure and portal hypertension.

A. Hepatocellular failure

This comprises some or all of the following features:

1. Weakness and easy fatiguability
2. Jaundice - in acute liver failure, eg. viral hepatitis, jaundice parallels the extent of liver cell damage. In cirrhosis this is not so, for jaundice may be mild or absent with severe disease, but if jaundice occurs, the liver is failing.
3. Circulatory and pulmonary changes.
   a. Hyperkinetic circulation - flushed extremities, bounding pulses, capillary pulsation, tachycardia, active precordial impulse and an ejection systolic murmur. This is due to a decrease in the vasomotor tone and possible opening up of a large number of arteriovenous anastomoses under the influence of a vasodilator substance.
   b. Pulmonary changes - Pulmonary vasodilatation with arteriovenous shunting combined with ventilation perfusion inequality results in cyanosis in a small proportion of patients with decompensated cirrhosis.
4. Fever - about a third of patients with active advanced cirrhosis show a continuous low-grade fever. This is frequent in alcoholics.
5. Skin changes - Vascular spiders, palmar erythema and white nails.

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6. Endocrine changes - Males tend to become feminized and develop gynaecomastia, diminished libido and potency, small soft testes, and loss of secondary sexual characteristics. Females either masculinize or develop gonadal atrophy. Young women lose libido and become infertile with irregular periods. The breasts and uterus usually atrophy.

7. Neurological changes - hepatic encephalopathy.

8. Ascites.

B. Portal Hypertension

1. Most commonly presents with hematemesis and/or melena

2. Abdominal wall veins drain away from the umbilicus

3. Splenomegaly.

Investigations in cirrhosis

1. Liver function tests: Bilirubin total/direct, SGOT, SGPT, alkaline phosphatase, serum proteins, albumin/globulin ratio, prothrombin time and BSP retention tests. Derangement of LFT are found in almost all patients, but the degree of abnormality is quite variable. A low serum albumin, and BSP retention of more than 15% in 45 minutes are the most sensitive diagnostic parameters.

2. Oesophageal varices are better demonstrated by endoscopy than by barium swallow.

3. Ultrasonography is a simple non-invasive investigation which can determine the liver size and texture, the size of spleen, the anatomy of collateral vessels and the patency of the extrahepatic portal system.

4. Needle biopsy of the liver confirms the diagnosis. This procedure must always be carried out except in cases who have ascites and clotting abnormalities in whom it may be dangerous.

Prognosis of cirrhosis

Prognosis is determined by the extent of the hepatocellular failure. Patients with well compensated cirrhosis may remain so until they die from another cause. Some proceed within months to years to hepatocellular failure. Decompensation carries a poor prognosis unless decompensation follows a correctable precipitating factor. Clinical findings such as jaundice, ascites and encephalopathy are poor prognostic factors. Persistent hypotension is serious. The greater the number of abnormal laboratory findings like serum bilirubin, albumin, prothrombin time, the worse the prognosis. Serum transaminases and globulin levels are no guide to prognosis. Histologically necrosis, inflammation, Mallory bodies and eosinophilic parenchymal infiltrates are all poor prognostic factors.

Five year survival rates vary from 90% in five years if the patient has alcoholic cirrhosis without ascites, jaundice, haematemesis or continued alcoholism to as low as 0% in those presenting with encephalopathy. 5 Year survivals of 7% 10% and 19% are reported for patients presenting with ascites, jaundice and haematemesis respectively, however the course in individual patients is difficult to predict.

Treatment of cirrhosis

1. Withdraw toxic substances eg. alcohol, drugs

2. Prescribe a nutritious, well-balanced diet with Ig protein/Kg body weight. Butter, fats, fried foods need not be avoided.

3. Vitamin supplements.

4. Correct anaemia with iron or folic acid if deficiencies are found. Blood transfusion may be needed.

5. Correct fluid and electrolyte imbalances

6. Complications should be treated promptly

7. Antifibrotic drugs like colchicine, penicillamine, and corticosteroids have been used as they suppress collagen synthesis. They are not generally accepted yet and more controlled trials are needed.

Surgery in cirrhotics

All operations in cirrhotic patients carry a high mortality. Surgery in nonbleeding cirrhotic patients has an operative mortality of 30%. Operations on the biliary tract, for peptic ulcer disease or colon
resection have a particularly bad prognosis. Surgery should therefore be undertaken in cirrhotic patients only for clear indications which are life saving.

Major complications of cirrhosis and their management

The major complications are

1. Bleeding varices
2. Hepatic encephalopathy
3. Ascites
4. Hepato-renal syndrome
5. Spontaneous bacterial peritonitis
6. Hepatocellular carcinoma - this is especially seen in cirrhotics who have a positive hepatitis B surface antigen in the serum or in the liver tissue

Hepatic encephalopathy

Porto-systemic encephalopathy (PSE) is a complex neuropsychiatric syndrome, characterised by disturbed consciousness, impaired intellectual function, personality changes and neuromuscular abnormalities.

Severe hepatocellular dysfunction and shunting of portal blood into the systemic circulation leads to excessive systemic concentrations of unknown substances toxic to the central nervous system. Ammonia is the substance most often incriminated, but other nitrogenous substances also seem to be involved.

In the patient with otherwise stable cirrhosis, hepatic encephalopathy often follows a clearly identifiable precipitating event listed in Table 2.

Table 2: Common precipitants of hepatic encephalopathy (PSE)

<table>
<thead>
<tr>
<th>No.</th>
<th>Precipitant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Increased nitrogen load</td>
</tr>
<tr>
<td>a.</td>
<td>Gastrointestinal bleeding</td>
</tr>
<tr>
<td>b.</td>
<td>Excessive dietary protein</td>
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<tr>
<td>c.</td>
<td>Renal failure</td>
</tr>
<tr>
<td>d.</td>
<td>Constipation</td>
</tr>
<tr>
<td>2.</td>
<td>Electrolyte imbalance</td>
</tr>
<tr>
<td></td>
<td>Hypokalaemia and alkalosis induced by diuretics, para-centesis and vomiting.</td>
</tr>
<tr>
<td>3.</td>
<td>Drugs: Narcotics, tranquilisers, sedatives</td>
</tr>
<tr>
<td>4.</td>
<td>Miscellaneous</td>
</tr>
<tr>
<td>a.</td>
<td>Infection</td>
</tr>
<tr>
<td>b.</td>
<td>Surgery</td>
</tr>
<tr>
<td>c.</td>
<td>Hypoxia</td>
</tr>
<tr>
<td>d.</td>
<td>Hypovolaemia</td>
</tr>
<tr>
<td>e.</td>
<td>Superimposed acute liver disease</td>
</tr>
<tr>
<td>f.</td>
<td>Progressive liver disease</td>
</tr>
</tbody>
</table>

Clinical features and diagnosis of encephalopathy

Any neurologic abnormality, including focal deficits, may be encountered in hepatic encephalopathy. In acute encephalopathy, neurologic deficits can be completely reversed by correcting the underlying precipitating factors and/or improving liver function, but in patients with chronic encephalopathy the deficits may be irreversible and progressive. Grading or classifying the stages of hepatic encephalopathy is often helpful in following the course of the illness and assessing response to therapy. One useful classification is shown in Table 3.
Hepatic encephalopathy is usually diagnosed by exclusion. There are no diagnostic liver function abnormalities, although an elevated serum ammonia level in the appropriate clinical setting is highly suggestive of the diagnosis.

**Treatment of encephalopathy**

Early recognition and prompt treatment of hepatic encephalopathy is essential. (i) Eliminate or treat the precipitating factors (ii) lower the levels of toxins by decreasing the absorption of protein and nitrogenous products from the intestine.

1. **General measures:**
   a. Stop diuretics - correct electrolyte abnormalities especially hypokalaemia.
   b. Stop all sedatives, tranquilisers, analgesics.
   c. Control haemorrhage and clean the bowel of blood.
   d. Treat infections with appropriate antibiotics.
   e. Correct hypoglycemia.
   f. Administer oxygen to patients with arterial desaturation, a common finding in cirrhosis.

2. **Diet**

All dietary protein is stopped. At least 1500 calories are supplied daily as glucose drinks or as 20% glucose through a gastric drip or parenterally.

With recovery, protein can be added in 20g increments on alternate days. The protein is divided between 4 meals. In patients with an acute episode of coma, a normal protein intake can be soon achieved. In chronic encephalopathy, permanent protein restriction is needed to control mental symptoms. Different sources of proteins have different coma producing potential. Meat protein is more comatogenic than dairy protein which is worse than vegetable protein. A vegetarian diet is therefore preferred.

3. **Empty bowel of nitrogen containing materials**
   a. Magnesium sulphate purge: 30ml of 50% MgSO4 twice daily.
   b. Enemas - Tap water, or lactulose enemas. All enemas must be neutral or acid to reduce ammonia absorption. Alkaline enemas like soap and water enemas favour ammonia absorption and should not be used.

**Table 3 : Clinical Stages of Hepatic Encephalopathy.**

<table>
<thead>
<tr>
<th>Grade of encephalopathy</th>
<th>State of consciousness</th>
<th>Intellectual function</th>
<th>Personality behaviour</th>
<th>Neuromuscular abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Hypersomnia</td>
<td>Subtly</td>
<td>Euphoria</td>
<td>Tremor</td>
</tr>
<tr>
<td></td>
<td>Insomnia</td>
<td>Impaired</td>
<td>Depression</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inversion of</td>
<td>Computation</td>
<td>Irritability</td>
<td></td>
</tr>
<tr>
<td></td>
<td>sleep pattern</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>Lethargy</td>
<td>Grossly</td>
<td>Inappropriate</td>
<td>Slurred</td>
</tr>
<tr>
<td></td>
<td>Confusion</td>
<td>Impaired</td>
<td>behaviour</td>
<td>speech</td>
</tr>
<tr>
<td></td>
<td></td>
<td>computation</td>
<td></td>
<td>Hypoactive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gross dyspraxia</td>
<td></td>
<td>reflexes</td>
</tr>
<tr>
<td>III</td>
<td>Marked</td>
<td>Inability to</td>
<td>Paranoia</td>
<td>Hyperactive</td>
</tr>
<tr>
<td></td>
<td>Confusion</td>
<td>compute</td>
<td>Anger</td>
<td>reflexes</td>
</tr>
<tr>
<td></td>
<td>Semi-stupor</td>
<td>Apraxic</td>
<td></td>
<td>Rigidly</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Nystagmus</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Clonus</td>
</tr>
<tr>
<td>IV</td>
<td>Coma</td>
<td>No intellect</td>
<td>None</td>
<td>Coma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pupils dilated</td>
</tr>
</tbody>
</table>

..29..
Asterixis may be present in grade I, occur in grades II and III, and is absent in grade IV. The EEG is usually normal in grade I but abnormal in grades II - IV.

4. Others

a. Lactulose: This is a synthetic disaccharide which is neither absorbed nor metabolised in the upper intestinal tract, but is degraded by bacteria in the lower intestine causing acidification of the lumen. The acid produced acts as a stimulus to catharsis, as an inhibitor of coliform organisms and an inhibitor of ammonia metabolism and as a trap for ammonia. Lactulose also stimulates the incorporation of ammonia into bacterial protein. In double blind, controlled clinical trials lactulose is as effective as neomycin in the treatment of acute episodes of PSE. Since lactulose induces fewer side effects, it is the preferred drug, if the patient can afford it. The dose is 10.30ml three times/day and is adjusted to produce 2-4 semisolid stools daily. Lactulose requires intestinal bacteria to be activated, while antibacterial agents like neomycin inhibit bacterial growth. Despite this antagonism, the two agents have additive or synergistic effects. The combination of lactulose and antibiotics should be used only when each of these agents alone has not given optimal results.

b. Lactitol: (β-galactoside sorbitol) is a disaccharide with activity similar to lactulose. It is more palatable than lactulose and can be dispensed in powder form.

c. Branched chain amino acids (BCAA)

The use of BCAA whether IV, in acute encephalopathy, or orally, for chronic coma is controversial. Controlled trials have shown little effect in encephalopathy compared with placebo treated controls.

d. L-Dopa

If PSE is related to a defect in dopaminergic neurotransmission, then replenishment of cerebral dopamines should be beneficial. L-Dopa does cause temporary arousal in acute hepatic encephalopathy, however, few patients benefit.

Ascites

The two most important factors in the development of ascites are

Portal hypertension and a failure of the liver to synthesise albumin, causing a lowered plasma oncotic pressure. Other factors include renal sodium and water retention, and hepatic lymph weeping freely from the surface of the cirrhotic liver due to obstruction of hepatic sinusoids and lymphatics. Although ascites is commonly due to cirrhosis, it can also be caused by intraperitoneal seeding of carcinoma, intra-abdominal tuberculosis, and pancreatitis. Spontaneous bacterial peritonitis may complicate simple cirrhotic ascites.

Diagnosing the different causes of ascites

Paracentesis (about 50ml) is always performed even if the cause of the ascites is obvious.

There are no reliable cut off points to diagnose the varying causes of ascites but the following generalisations can be made.

1. The higher the white cell count (especially the neutrophil count) the more likely the patient has a spontaneous bacterial peritonitis.
2. A high lymphocyte count suggest tuberculosis or carcinoma.
3. Spontaneous bacterial peritonitis usually has low ascitic protein levels
4. Ascitic protein levels are usually low in cirrhosis and cardiac failure and high in neoplasms, tuberculosis and pancreatitis. However, even with correction for serum protein levels, there is considerable overlap between these diagnoses.
5. Spontaneous bacterial peritonitis usually has a positive ascitic culture, but treatment must start before cultures are back.
6. Cytology for neoplasm is only positive in 30% of cases.
7. Ascitic amylase is positive in 80% of cases with pancreatitis.
8. Peritoneal biopsy is positive in 50% of cases with neoplasm and 65% of patients with tuberculous peritonitis.

Management of ascites

Overzealous attempts to reduce ascites may precipitate renal failure. Therapy should be gentle and incremental.
1. **Bed rest**

   Although bed rest per se has never been proven effective, it is used because the supine position improves the renal clearance of fluid.

2. **Salt restriction**

   This is the keystone to the conservative treatment of ascites. The cirrhotic patient usually excretes less than 10mEq (0.2 g) sodium daily in the urine. Daily extrarenal loss is about 0.5 g therefore an intake of more than 0.75g of sodium daily will cause ascites, every gram retaining 200 ml fluid. With effective diuretics it is no longer necessary to restrict sodium so severely. In fact less frequent and less severe hyponatraemia and azotemia may occur if excessive salt restriction is avoided. A patient with massive ascites may therefore be given a palatable diet and thus provide the nutrition that strict salt restriction may prevent. The patient needs to be clearly educated about the amount of salt to take, and his salt balance needs to be carefully monitored. Many patients stop salt altogether and develop hyponatraemia and encephalopathy as a result.

3. **Fluid restriction**

   It is often recommended that fluid restriction to about 1-1.5 l/day be instituted along with sodium restriction in the management of massive ascites. In cirrhotic patients, fluid restriction to levels less than the urine output can guarantee progressively decreasing urine output, hepatorenal syndrome and death. So, in the absence of hyponatraemia caused by excessive water administration or inappropriate water retention, there is no place for water restriction. Fluids should be given as the patient desires, unless the patient exhibits excessive water retention.

4. **Diuretics**

   Diuretic therapy seeks to block all renal sodium conserving mechanisms. Diuretics can be divided into two main groups. The first group comprises thiazides, frusemide, bumetamide and ethacrynic acid. These are powerful natriuretic agents, but also powerful kaliuretics. The second group comprises spironolactone (an aldosterone antagonist), amiloride and triamterene. These are weakly natriuretic, but conserve potassium. In India, amiloride and triamterene are only available as combinations with thiazides. This limits their usefulness in cirrhotics.

   Start with spironolactone 100 mg daily, which may be given as a single daily dose or in divided doses. If by the fourth day, there has been no weight loss or the urinary sodium concentration remains low (< 10mEq/L), the doses of spironolactone may be doubled or a diuretic from group one like frusemide (40-80 mg) may be added. Spironolactone alone in response determined dosage up to 400 mg per day is an effective diuretic agent and superior to frusemide or hydrochlorothiazide, but this therapy is costly. The combination of triamterene and benzthiazide can be used for poorer patients, but patients may develop hyponatraemia and need careful monitoring.

   Whatever diuretic agents are used, a safe and sane rate of diuresis should be maintained. The maximal absorption rate of ascitic fluid from the peritoneum is approximately 900 ml/day equivalent to a weight loss of just under 600 gm daily. A faster rate of diuresis can only be achieved by loss of oedema or by reducing the plasma volume with impairment of renal function. The dosage of diuretics should be adjusted to maintain the diuresis at a weight loss of less than half a kg per day. Abdominal girth measurements frequently used as an index of fluid loss are unreliable.

   The following are complications of diuretic therapy:

   i. **Encephalopathy** which is often associated with hypokalaemia and electrolyte imbalance.

   ii. **Electrolyte disturbances**:

      a. **Hypokalaemia** Levels of less than 3.1 mEq/ indicate severe potassium depletion, which necessitates stopping the diuretic and giving potassium chloride supplements.

      b. **Hyponatraemia** reflects urinary excretion of sodium in excess of water. When combined with other electrolyte abnormalities it indicates a particularly bad prognosis.

      c. **Hypochloraemic alkalosis** complicates treatment with diuretics like frusemide and ethacrynic acid. It is due to urinary sodium and chloride loss with normal tubular reabsorption of bicarbonate.

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d. Hypochloraemic acidosis complicate spironolactone therapy.

iii. Azotemia reflects an altered renal circulation.
A brisk diuresis results in contraction of the extracellular fluid volume and accentuates this tendency. Many of these patients will progress to the hepatorenal syndrome.

Follow up advice
1. Patient should adhere to salt restriction
2. Diuretics should be continued. Serum electrolytes, blood urea and LFT should be monitored every 4 weeks. As liver function improves, it may be possible to stop first the frusmid and then the potassium conserving diuretic. Finally, the low sodium diet is relaxed, first to 'no added salt' and then to a normal diet.

Refractory ascites
Most patients respond to diet and diuretics. Failures indicate either a failure to comply or terminal liver failure. In some patients with gross ascites only high doses of diuretics produce any diuresis. In them, there is a real danger of depleting the intravascular compartment and developing the hepatorenal syndrome. Alternative therapy consists of

1. Repeated paracenteses with infusion of albumin Each day 4-6 L ascites are removed over a period of 3-4 hours by a fine catheter while 40g salt poor albumin is infused IV over the same period.
2. Ascites ultrafiltration and reinfusion
An automated ultrafiltration apparatus (Rhodlasit) removes ascitic fluid via a peritoneal dialysis catheter and passes it over an ultrafilter which selects molecules less than 50000 molecular weight. The concentrate, which contains 2-4 times as much protein as the ascitic fluid is returned to the patient intravenously.
3. Peritoneo-venous shunt (LeVeen Shunt)
This system consists of a silastic pressure sensitive one way valve allowing ascitic fluid to flow from the abdominal cavity to the superior vena cava.

Its precise place in the treatment of ascites is not known. Ascites may be mobilised but the failure rate is very high and complications such as infection and disseminated intravascular coagulation are common, severe and frequently lethal. Clinical trials are still assessing whether the gains outweigh the losses.

HEPATO-RENAL SYNDROME (FUNCTIONAL RENAL FAILURE)
This syndrome is characterised by renal failure with normal tubular function in patients with chronic liver disease. The exact basis for this syndrome is not clear, but altered renal hemodynamics appear to be involved. The histology of the kidney is virtually normal and renal failure is functional. Kidneys from patients who have died of HRS can be transplanted into patients with chronic uremia. Virtually all have ascites, which is often tense. It frequently follows diuretic therapy, paracentesis, gastrointestinal tract haemorrhage, worsening azotemia, and progressive oliguria. Hyponatraemia, hypokalaemia, and mild hypotension are the hallmarks of the hepatorenal syndrome. A modest decrease in systemic blood pressure is often present and common terminally but profound hypotension is not part of the syndrome. This disorder stubbornly resists attempts to improve renal function and usually ends in death.

Diagnosis of hepatorenal syndrome
Chronic liver disease with ascites
Slow onset of azotemia (plasma Creatinine > 1.5 mg/ 100 ml)
Tubular function good
Urine to plasma osmolality ratio > 1.0
Urine to plasma creatinine ratio > 30
Urine sodium concentration < 10mEq/100 ml
No sustained benefit by expanding the intravascular space

Treatment
This is usually unsuccessful.

1. Treat reversible factors
Treat dehydration, hyponatraemia, hypokalaemia urinary tract infection or obstruction.

2. General supportive therapy
a. Nutritional support appropriate fluids and electrolytes
b. Treat/prevent porto-systemic encephalopathy

3. Specific therapeutic measures

a. Increase effective plasma volume-administer albumin/dextran

b. Paracentesis - may help by relieving compression of the IVC or decreasing intra abdominal and renal venous pressures. Some observations suggest small paracenteses of 500 ml provide optimal responses.

c. A combination of paracentesis and plasma volume expansion seems logical as they work similarly and plasma volume constriction which sometimes follows paracentesis.

d. Peritoneal or renal dialysis should be considered for a reversible precipitating cause or HRS, but it has not been shown to improve survival and may precipitate gastro intestinal haemorrhage and shock.

The following agents have been reported to be of transient or no benefit: dibenzylene, dopamine, papaverine, aminophylline, mannitol, isoproterenol and adrenal steroids.

Spontaneous Bacterial Peritonitis (SBP)

Spontaneous bacterial peritonitis is defined as infection of ascitic fluid in the absence of recognizable secondary causes of peritonitis. It develops in about 8% of cirrhotic patients with ascites. It should be suspected if a patient with known cirrhosis deteriorates, particularly with encephalopathy. Classic SBP is characterised by an abrupt onset of fever, with chills, abdominal pain with rebound tenderness, absent bowel sounds and leucocytosis. The fullblown syndrome need not be present, and any one or all or its components may be missing. Always suspect and treat on the basis of a slight suspicion. It is better to have given the patient two or three days of unnecessary antibiotics than to have a patient die of a treatable cause.

Diagnosis of SBP:

Ascitic fluid polymorphonuclear leukocytes > 250/mm3. Ascitic fluid pH < 7.34.

Arterial - Ascitic fluid pH gradient > 0.1

Gross appearance, specific gravity and protein concentration of ascitic fluid are not able to discriminate between infected and uninfected fluid. The number of PMN leukocytes is the most reliable parameter but there is considerable overlap between SBP, intra abdominal neoplasm and cirrhosis. If we make a cut off > 1000 neutrophils/mm3 we will more surely diagnose SBP, (increase the specificity of the test) but decrease the sensitivity (increase the number of false negatives). If we make a cut off > 250 neutrophils/mm3, we will pick up more cases of SBP (increase the sensitivity, decrease the false negative rate) but at the expense of specificity (we increase the false positive rate). We recommend antibiotics if (I) the clinical picture of SBP is present regardless of the number of leukocytes (II) ascitic fluid is greater than 250/mm3 and clinical picture is compatible with SBP and (III) whenever the number of PMN leukocytes in ascitic fluid is greater than 1000/mm3 even in the absence of any clinical evidence of SBP.

In about 20% of cases of SBP, ascitic fluid cultures are negative. Approximately, 75% of organisms isolated are enteric. E. Coli is the most common. Pneumococcus is the most common nonenteric organism. Anaerobic bacteria are conspicuous by their near absence. In 90% of patients a single type of organism is isolated.

Prompt and vigorous treatment with antibiotics directed against gram negative bacteria is essential, usually with a combination of cephalosporins or ampicillin and gentamicin. With sensitivity testing the regime can be made more specific. Continue therapy for 10-14 days. In addition, treat the shock and encephalopathy, and search for and treat any primary focus of infection.

The prognosis depends on the severity of the underlying liver disease and of the superimposed acute liver injury resulting from the infection. The overall outlook is grave, unless the patient is treated early.