Ascites

Ascites is the accumulation of an excessive amount of fluid in the abdominal cavity. A small amount of fluid is normal and helps to lubricate the surfaces of the peritoneum. For fluid to be detectable by clinical examination there has to be at least 1500ml present, perhaps slightly less in a small, thin person, but significantly more in the obese. Ultrasound can detect much smaller volumes, of 500ml or less.

Aetiology of Ascites

• Around 75% of patients who present with ascites have underlying cirrhosis, and about 50% of patients who have cirrhosis will develop ascites over a 10 year period of follow up. ¹

• There is malignancy in around 15%. The usual causes are:
  o Malignancies of the gastrointestinal tract including carcinoma of stomach, carcinoma of colon, carcinoma of pancreas and both primary hepatocellular carcinoma and metastatic cancer in the liver
  o Carcinoma of ovary. The rare and interesting Meigs' syndrome arises from a carcinoma of ovary and produced ascites out of all proportion to the size of the tumour and it can also produce pleural effusion, often unilateral.
  o Both Hodgkin's lymphoma and non-Hodgkin's lymphoma
  o metastatic carcinoma within the abdominal cavity
• Heart failure in 3%
• Tuberculosis is responsible in 2% and is a disease that is easily overlooked
• Pancreatitis is the cause in 1%
• There are various other rare causes, including myxoedema.

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It can also result from ovarian hyperstimulation, especially when this is iatrogenic as part of IVF.

Pathogenesis of Ascites

Portal Hypertension

Portal hypertension with increased hydrostatic pressure within the hepatic sinusoids encourages the transudation of fluid into the peritoneal cavity. In presinusoidal portal hypertension without cirrhosis, ascites is rare. Ascites does not develop with isolated chronic extrahepatic portal venous occlusion or non-cirrhotic causes of portal hypertension such as congenital hepatic fibrosis, unless liver function is impaired as after gastrointestinal haemorrhage. Acute hepatic vein thrombosis however usually ascites (via postsinusoidal portal hypertension). The old concept that ascites is due to decreased oncotic pressure is false, and plasma albumin concentrations have little influence on the rate of formation of ascites. Portal hypertension with ascites requires a wedged hepatic venous portal gradient of >12 mm Hg. Conversely, insertion of a side to side portacaval shunt to decrease portal pressure often causes resolution of ascites.

Salt and Water Retention

One of the critical events for renal dysfunction and sodium retention in cirrhosis is systemic vasodilatation, which causes a decrease in effective arterial blood volume and a hyperdynamic circulation. However, the haemodynamic changes vary with posture, and there are marked changes in secretion of atrial natriuretic peptide with posture, as well as changes in systemic haemodynamics. When supine, there is an increase in cardiac output and vasodilatation. Renal vasoconstriction in cirrhosis is partly a homeostatic response involving increased renal sympathetic activity and activation of the renin-angiotensin system to maintain blood pressure during systemic vasodilatation. Decreased renal blood flow decreases glomerular filtration rate and excretion of sodium. Cirrhosis is associated with
enhanced reabsorption of sodium both at the proximal and distal tubule. Increased reabsorption of sodium in the distal tubule is due to increased circulating concentrations of aldosterone or possibly increased sensitivity to aldosterone.

**Presentation**

**History**

- The patient usually complains of "getting fat", meaning an expanding waist line. Weight will also rise with water retention. Tense ascites is very uncomfortable but before it reaches this stage there is simply abdominal distension with mild associated discomfort.
- When ascites is tense it pushes on the stomach and gastrointestinal tract, suppressing appetite and possibly causing nausea. It impairs venous return from the lower limbs by pressing on the inferior vena cava and it also pushes up on the diaphragm, impairing expansion of the lungs. This reduction in venous return and impaired ventilation will initially cause shortness of breath on exertion followed by dyspnoea at rest.
- There may be other symptoms related to the cause of the ascites.
- Ask about alcohol consumption, being aware of the difficulties of diagnosis of alcoholism. Also note any history of jaundice or known infection with hepatitis B or hepatitis C.

**Examination**

- Look at the patient, both lying down and standing up. The shape of the abdomen often suggests fluid. On lying down, the flanks are full but on standing the fluid accumulates in the lower abdomen as shown in the illustrations below.
- The high intra-abdominal pressure may push out an umbilical hernia or even an inguinal hernia.
• There may be stigmata of other diseases. Look especially for muscle wasting, gynaecomastia (in men), spider naevi and liver palms as most people who present with ascites have cirrhosis.
• Remember malignancy and the other causes too.
• Perform a full abdominal examination, as described in the article. Only the section specifically related to ascites is repeated here.

Examination for Ascites

• Shifting dullness is used to detect ascites. Fullness of the flanks may be the first indication.
• Percuss from the level of the umbilicus and repeat moving laterally towards one side. When the sound becomes dull, keep your fingers there to mark the spot and ask the patient to move on to the opposite side. Wait briefly for the fluid to sink and percuss again. If it is now resonant that is a positive sign. Percuss down until dullness is reached again. Repeat on the other side. False positives do occur, probably from dilated coils of small intestine reacting to gravity.
• At least 1500ml of fluid must be present for a result. An ultrasound scan will detect much less fluid with greater certainty.
• A succussion splash is much more difficult to demonstrate. It needs a 3rd hand in the examination and probably rather more fluid.
• Occasionally an ovarian cyst is so large as to fill the abdomen invalidating percussion as a distinguishing test. There is a transmitted aortic pulsation if a ruler is laid across the abdomen above the anterior superior iliac spines, and the fingers of both hands press firmly towards the lumbar spine. With an ovarian cyst the pulsations can be felt with the fingers, and seen in the movement of the ruler but this is not present with ascites.
Monitoring

Simple assessment of the progress of ascites may be made by serial measurements of the abdominal girth. The tape measure must be placed in the same position each time. Serial measurement of weight also indicates fluid gain or loss. This tends to be much faster than gain or loss of fat or lean body mass.

Differential Diagnosis

The differential diagnosis of ascites is with other causes of abdominal mass, especially large cysts, although sometimes plain obesity may seem like ascites. The essential feature is the fluidity and shifting of the ascites with position.

Investigations

The cause of the ascites is often apparent after an adequate history and examination. The patient with a high consumption of alcohol and ascites probably has cirrhosis but this must not be assumed and other possible causes should be sought. The aims of investigation for ascites are:

• Confirming the presence of ascites
• Finding the cause for the ascites
• Assessing any complication due to the ascites

Investigation should include a diagnostic paracentesis (see invasive procedures below).

Blood tests

• FBC
• U&E and creatinine
• LFTs including plasma proteins
• Clotting screen, especially if invasive investigations are considered
• TFTs may be included as myxoedema is a rare cause.

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• If cirrhosis is confirmed, further tests will be required to elucidate the cause. This may include antibody tests for hepatitis B.

**Imaging studies**

• Ultrasound examination of the abdomen should include liver, pancreas, spleen and lymph nodes. It is a very sensitive way of assessing ascites and may also show the causative pathology such as carcinoma of ovary or metastatic liver disease.

• Chest x-ray may show pleural effusion, evidence of pulmonary metastases or heart failure.

• If ultrasound has failed to show a cause, then MRI scanning may be used.

**Invasive procedures**

• Tapping of ascites is discussed in its own article. It may be diagnostic, when only about 20ml is required, or therapeutic when a large amount, possibly in excess of 5L may be removed. The caveats and precautions are discussed in the article.

Ascitic fluid should be sent for measurement of albumin or protein, neutrophil count, amylase, culture and sensitivity, ±cytology where malignancy is suspected.¹

• If liver disease is suspected, especially cirrhosis, liver biopsy may be undertaken after appropriate investigations. This is not invariably required.

**Investigation of Ascitic Fluid**¹

After a diagnostic tap the following investigations may be requested:

• **Albumin or protein levels:** Traditionally used to decide whether ascites is an exudate (>25g/l) or a transudate. The serum ascites-albumin gradient (SA-AG) is a better
\[ \text{SA-AG} = (\text{serum albumin concentration}) - (\text{ascitic albumin concentration}) \]

- **SA-AG ≥11g/l**: Likely causes - cirrhosis, cardiac failure, nephrotic syndrome.
- **SA-AG <11g/l**: Likely causes - malignancy, pancreatitis and tuberculosis.

**Microscopy**:
- **Neutrophil Count**: All patients should be screened for *spontaneous bacterial peritonitis* (SBP), which occurs in approximately 15% of patients with cirrhosis and ascites admitted to hospital. An ascitic neutrophil count of >250 cells/mm\(^3\) is diagnostic of SBP in the absence of a known perforated viscus or inflammation of intra-abdominal organs.
- **Red Cell Count**: The concentration of red blood cells in cirrhotic ascites is usually <1000 cells/mm\(^3\) and bloody ascitic fluid (>50,000 cells/mm\(^3\)) occurs in about 2% of cirrhotics. In approximately 30% of cirrhotics with bloody ascites, there is an underlying hepatocellular carcinoma. In 50% of patients with bloody ascites, no cause can be found.

**Amylase**: In pancreatic ascites the amylase in the fluid will be markedly raised.

**Culture and sensitivity**: Preferred method is to inoculate blood culture bottles with ascitic fluid at the bedside.
- Several studies have shown that inoculation of ascitic fluid into blood culture bottles will identify an organism in approximately 70% of cases whereas sending ascitic fluid in a sterile container to the laboratory will only identify an organism in about 40% of cases of SBP.
- Gram stain of ascitic fluid is rarely helpful. The sensitivity of a smear for *mycobacteria* is very poor while fluid culture for mycobacteria has a sensitivity of 50%.
**Cytology:** Only 7% of ascitic fluid cytologies are positive yet cytological examination is 60 to 90% accurate in the diagnosis of malignant ascites, especially when several hundred millilitres of fluid is tested and concentration techniques are used. It is not so valuable for primary hepatocellular carcinoma.

**Grading**

Ascites that is not infected and not associated with hepato-renal syndrome may be graded as follows:

- Grade 1 is mild ascites and is only detectable by ultrasound examination.
- Grade 2 is moderate ascites causing moderate symmetrical distension of the abdomen.
- Grade 3 is large ascites causing marked abdominal distension.

Refractory ascites can be divided into two groups:

- Diuretic resistant ascites is refractory to dietary sodium restriction and intensive diuretic treatment for at least one week.
- Diuretic intractable ascites is refractory to therapy due to the development of diuretic induced complications that preclude the use of an effective dose of diuretic.

**Management**

The first line of management of ascites is medical treatment. Paracentesis may also be required, especially in palliative care of malignancy but it should not be used excessively. Medical treatment of ascites in malignancy should also precede drainage. A working diagnosis of the underlying cause of the ascites is important to give a rationale for treatment. Management depends upon the aetiology. If ovarian hyperstimulation if the cause, no treatment is indicated and it will resolve when the hyperstimulation ceases.
Non-drug Management

• Avoidance of alcohol is important in pancreatitis and cirrhosis of any aetiology, not just alcoholic.
• A no added salt diet, restricted to <90 mmol/day (5.2 g of salt/day) is useful, especially in cirrhosis but is unlikely to be effective in other aetiologies such as malignancy.

Bed rest is not advocated. In patients with cirrhosis and ascites, the upright position activates the renin-angiotensin-aldosterone and sympathetic nervous system, producing a reduction in glomerular filtration rate and sodium excretion, as well as a decreased response to diuretics. This is more marked with moderate physical exercise. However, there have been no clinical studies to demonstrate increased efficacy of diuresis with bed rest or decreased duration in hospital. As bed rest may lead to muscle atrophy, and other complications, as well as promoting extended stays in hospital, it is not generally recommended for the management of uncomplicated ascites.

Drugs

• Diuretics:
  ° Spironolactone is the best initial choice in cirrhosis, it increases sodium excretion and potassium reabsorption in the distal tubules. Initially 100mg/day gradually increased to 400mg as necessary. Monitor serum potassium levels as the development of hyperkalaemia frequently limits the amount of spironolactone. Amiloride can be used but it is generally less effective.
  ° Loop diuretics, e.g. furosemide may be used as an adjunct to spironolactone, generally only when maximum doses of the latter have been reached. Start cautiously with 40mg/day although up to 160mg/day may be used - high doses cause severe electrolyte disturbance, particularly hyponatraemia.
• If the underlying problem is congestive heart failure then treatment needs to be energetic with diuretics, ACE inhibitors and other drugs, in the usual manner.
• Malignancy may respond to appropriate chemotherapy, depending upon the type.
• Myxoedema will resolve with gradual introduction of thyroxine.

**Therapeutic Paracentesis**

• Patients with large or refractory ascites generally benefit from therapeutic paracentesis.¹⁹
• This needs to be a sterile procedure, and it thought to be better done as a single complete procedure rather than serial smaller paracenteses.
  ◦ Paracentesis of <5 litres of uncomplicated ascites should be followed by plasma expansion (with synthetic plasma expander i.e. 150-200ml of gelofusine or haemaccel®).¹
  ◦ Larger volume paracentesis should be done as a single session, but followed by volume expansion using 8g of albumin per litre of ascitic fluid removed (i.e. approximately 250ml of 20% albumin if 6 litres of ascites are removed).

**Surgical**

• **Surgical treatment** may be required for malignancy and some patients may be suitable for liver transplantation.
• **Transjugular intrahepatic portosystemic shunt (TIPS)** can be used in patients with refractory ascites needing frequent paracentesis (>3/month). It is a local anaesthetic procedure (with sedation) and has generally replaced surgically created portocaval shunts. Trial results are conflicting as to whether such a procedure offers improved survival as compared with repeated therapeutic paracentesis. There is a 25% risk of inducing hepatic encephalopathy.¹ A peritoneovenous shunt

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suffers blockage in about a quarter of cases and it may increase mortality.\textsuperscript{10} The TIPS Risk score can be calculated assessing prognosis after the procedure.\textsuperscript{11}

### TIPS Risk Score

\[
\text{TIPS Risk Score} = 0.957 \times \log_e(\text{creatinine mg/dl}) + 0.3789957 \times \log_e(\text{bilirubin mg/dl}) + 1.120 \times \log_e(\text{INR}) + 0.643 \times (\text{cause of cirrhosis})
\]

where (cause of cirrhosis) = 0 for alcohol or cholestasis, 1 for other causes.

- Patients with a risk score > have a median survival of 3 months so TIPS only done as a bridge to liver transplantation.
- Patients with a score of 1.5 have a median survival of 6 months and a score of 1.3 a medial survival of 12 months.

### Complications

**Hyponatraemia on Diuretics\textsuperscript{1}

- Serum sodium 126-135 mmol/l with normal serum creatinine: continue diuretics but watch electrolytes regularly (do not fluid restrict).
- Serum sodium 121-125 mmol/l with normal serum creatinine: stop diuretics\textsuperscript{1} or continue diuretics cautiously at lower dose and watch electrolytes frequently.
- Serum sodium 121-125 mmol/l with elevated serum creatinine: (>150\(\mu\)mmol/l) or >120 \(\mu\)mmol/l and rising: stop diuretics and give volume expansion.
- Serum sodium ≤120 mmol/l: Management is difficult. Guideline suggests stopping diuretics and giving volume

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expansion with colloid or saline, but avoid increasing serum sodium by >12 mmol/24 hours - see hyponatraemia.

Only fluid restrict patients who are not dehydrated and not taking diuretics whose creatinine is normal.¹

**Spontaneous Bacterial Peritonitis (SBP)**

- This occurs in 10-30% of patients with ascites and has mortality rate of 20%.
- Organism is usually *E. coli* streptococci and enterococci.
- Empirical antibiotics (e.g. cefotaxime) should be started if ascitic fluid contains >250 cells/mm³.
- Patients may develop renal impairment - these patients will need also albumin infusions.
- All patients with SBP should be referred for consideration for liver transplantation.

**Prognosis**

- Ascites is a major complication of cirrhosis, occurring in 50% of patients over 10 years of follow up.⁸ The development of ascites is an important landmark in the natural history of cirrhosis as it is associated with a 50% mortality over two years, and signifies the need to consider liver transplantation as a therapeutic option.
- In malignancy it tends to suggest widespread disease and a poor prognosis.