Ascites

Definition

Ascites is of Greek derivation (askhos) which refers to a ‘bag’ or ‘sack’. The word describes pathologic fluid accumulation within the peritoneal cavity (Fig. 9.17.1).

Figure 9.17.1 Child with ascites

Background

Inside the abdomen there is a membrane called the peritoneum which has two layers. One layer lines the abdominal wall and the other layer covers the organs inside the abdominal cavity. The peritoneum produces a fluid that acts as a lubricant and allows the abdominal organs to glide smoothly over one another. Sometimes an excess of this fluid can build up between the two layers and this is called ascites.

The accumulation of fluid in the abdominal cavity can be associated with portal hypertension. This means there is an increased blood pressure in the veins draining the liver. The higher pressure can be caused by liver damage. It can also be caused by impaired drainage in the lymph system. This system takes excess fluid and particles away from the liver. Low levels of albumin and other proteins in the blood also contribute to ascites. The force that holds plasma water within the blood vessels is reduced. Plasma water is lost into the abdominal cavity. Albumin in the ascitic fluid pulls yet more fluid across into this cavity. Blood flow to the kidneys might be reduced. This leads to increased secretion of aldosterone. This causes the kidneys to retain salt and water. Urinary output is decreased, and fluid is retained. In some cases, kidney disease contributes to impaired elimination of salt and water. Fluid may leak from capillaries, the pancreas, or the lymph system. Capillary fluid leakage can be caused by inflammation or infection.

Pathophysiology

The accumulation of ascitic fluid represents a state of total-body sodium and water excess, but the event that initiates the unbalance is unclear. Three theories of ascites formation have been proposed.

1. Under filling theory: This suggests that the primary abnormality is inappropriate sequestration of fluid within the splanchnic vascular bed due to portal hypertension and a consequent decrease in effective circulating blood volume. This activates the plasma renin, aldosterone, and sympathetic nervous system, resulting in renal sodium and water retention.

2. Overflow theory: This suggests that the primary abnormality is inappropriate renal retention of sodium and water in the absence of volume depletion. This theory was developed in accordance with the observation that patients with cirrhosis have intravascular hypervolemia rather than hypovolemia.

3. Peripheral arterial vasodilatation hypothesis: This includes components of both of the other theories. It suggests that portal hypertension leads to vasodilatation, which causes decreased effective arterial blood volume. As the natural
history of the disease progresses, neurohumoral excitation increases, more renal sodium is retained, and plasma volume expands. This leads to overflow of fluid into the peritoneal cavity. According to the vasodilatation theory, the under filling theory is proposed to be operative early and the overflow theory is proposed to be operative late in the natural history of cirrhosis (Flow chart 9.17.1).

Although the sequence of events that occurs between the development of portal hypertension and renal sodium retention is not entirely clear, portal hypertension apparently leads to an increase in nitric oxide levels. Nitric oxide mediates splanchnic and peripheral vasodilatation. Patients with ascites have greater hepatic artery nitric oxide synthase activity compared to patients without ascites.

Regardless of the initiating event, a number of factors contribute to the accumulation of fluid in the abdominal cavity. Elevated levels of epinephrine and nor epinephrine are well-documented factors. Hypoalbuminemia and reduced plasma oncotic pressure favor the extravasation of fluid from the plasma to the peritoneal fluid, and, thus, ascites is infrequent in patients with cirrhosis unless both portal hypertension and hypoalbuminemia are present. If the liver is damaged, it may produce less blood protein. This may upset the body’s fluid balance which causes fluid to build up in the body tissues, including the abdomen.

Cancer cells can block the lymphatic system. The lymphatic system is a network of fine channels, which runs throughout the body. One of its functions is to drain off excess fluid, which is eventually got rid of in the urine. If some of these channels are blocked, the system cannot drain efficiently and fluid can build up. The pathophysiologic mechanisms of ascites is shown in Table 9.17.1.

Flow chart 9.17.1 Pathophysiology of ascites

Flow chart 9.17.2 Ascites formation in cirrhosis
Table 9.17.1 Pathogenic mechanisms in ascites formation

- **Increased hydrostatic pressure**
  - Cirrhosis (Flow chart 9.17.2)
  - Hepatic vein occlusion (Budd-Chiari syndrome)
  - Inferior vena cava obstruction
  - Constrictive pericarditis
  - Congestive heart failure
- **Decreased colloid osmotic pressure**
  - End-stage liver disease with poor protein synthesis
  - Nephrotic syndrome with protein loss
  - Malnutrition
  - Protein-losing enteropathy
- **Increased permeability of peritoneal capillaries**
  - Tuberculous peritonitis
  - Bacterial peritonitis
  - Malignant disease of the peritoneum
- **Leakage of fluid into the peritoneal cavity**
  - Bile ascites
  - Pancreatic ascites (secondary to a leaking pseudocyst)
  - Chylous ascites
  - Urine ascites
- **Miscellaneous causes**
  - Myxedema
  - Ovarian disease (Meigs’ syndrome)
  - Chronic hemodialysis

---

**Etiology**

**Neonatal Ascites/Congenital Ascites**

Ascites in the newborn (Fig. 9.17.2) can be grouped as:

I. Associated with hydrops
II. Isolated ascites
III. Ascites due to peritonitis
Associated with Hydrops

- Cardiovascular (20% cases) (failure or poor output)
  a. Rhythm disturbances: Heart block, auricular tachy-cardia
  b. Cardiac malformation: Hypoplastic left heart, Ebstein’s disease
- Hematological disorders (10% cases) (Chronic in utero anemia): Isoimmune hemolytic disease, homozygous alpha thalassemia
- Chromosomal (10% cases): Turner syndrome, trisomy 13, 18 and 21
- Infection (8% cases): TORCH group, syphilis
- Renal (5% cases): Nephrosis, posterior urethral valve
- Pulmonary (5% cases): Diaphragmatic hernia.
- Gastrointestinal (5% cases): Atresia
- Maternal conditions (5% cases): Toxemia, diabetes
- Placenta or cord (rare): Cord compression, chorangioma
- Miscellaneous (10% cases): Wilms’ tumors, neuroblastoma
- Storage disease: Mucopolysaccharidosis VIII
- Skeletal abnormalities: Osteogenesis imperfecta, achondrogenesis
- Cirrhosis: \( \alpha \)-1 antitrypsin deficiency
- Liver failure: Neonatal hemochromatosis
- Unknown (20% cases).

Isolated Ascites

- Chylous: Congenital anomaly of lymphatic channels
- Biliary: Spontaneous perforation of biliary tree
- Pancreatic duct anomaly.

Peritonitis

- Chemical: Bile, meconium
- Bacterial.

Etiology in Children

Associated with Portal Hypertension (Fig. 9.17.3)

1. **Extrahepatic disorders:** Venous obstruction—Splenic vein thrombosis, portal vein thrombosis/cavernous transformation, Budd-Chiari syndrome, inferior vena cava obstruction.
   - **Miscellaneous:** CHF, AV fistulae
2. **Intrahepatic disorders:**
   a. **Biliary tract disease:** EHBA, cystic fibrosis, choledochal cyst, sclerosing cholangitis, intrahepatic cholestasis syndromes.
   c. **Toxins:** Ethanol, methotrexate, 6-mercaptopurine.

![Figure 9.17.3 Ascites with portal hypertension showing dilated veins](image)

---

**Other Causes**

Tuberculosis, heart failure, nephrotic syndrome, pancreatitis, chlamydial infection and rheumatoid arthritis.

---

**Etiology of Acute Ascites**

i. *Venous obstruction*: Budd-Chiari syndrome, portal vein thrombosis, inferior vena cava obstruction, splenic vein thrombosis, veno-occlusive disease of liver.

ii. *Peritonitis*: Spontaneous perforation of bile duct

iii. Fulminant hepatic failure.

---

**Etiology of Ascites in Reference to Normal and/or Diseased Peritoneum**

**Normal Peritoneum**

Portal hypertension (serum-ascites albumin gradient [SAAG] > 1.1 g/dL)

- Hepatic congestion, congestive heart failure, constrictive pericarditis, tricuspid insufficiency, Budd-Chiari syndrome
- Liver disease, cirrhosis, alcoholic hepatitis, fulminant hepatic failure, massive hepatic metastasis

Hypoalbuminemia (SAAG < 1.1 g/dL)

- Nephrotic syndrome
- Protein-losing enteropathy
- Severe malnutrition with anasarca

• Miscellaneous conditions (SAAG < 1.1 g/dL)
  - Chylous ascites
  - Pancreatic ascites
  - Bile ascites
  - Nephrogenic ascites
  - Ovarian disease.

**Diseased Peritoneum (SAAG < 1.1 g/dL)**

Infections

- Bacterial peritonitis
- Tuberculous peritonitis
- Fungal peritonitis
- HIV-associated peritonitis

Malignant conditions

- Peritoneal carcinomatosis
Presentation

History

Most cases of ascites are due to liver disease or due to some precipitating factors deteriorating liver functions, e.g. drugs (NSAIDs). History of abdominal distention, increasing weight, respiratory embarrassment, associated pedal edema.

Risk Factors for Liver Diseases

Chronic viral hepatitis or jaundice
Intravenous drug use
Sexual promiscuity
Transfusions: Hepatitis C has been linked to transfusions
Tattoos
Habitation or origination from an area endemic for hepatitis.

Patients with a history of cancer, especially gastrointestinal cancer, are at risk for malignant ascites. Malignancy-related ascites is frequently painful, whereas cirrhotic ascites is usually painless.

Examination

Ascites needs to be differentiated from abdominal distension due to other causes like gross obesity, gaseous distention, bowel obstruction, abdominal cysts or masses. The clinical manifestations of ascites can vary from an asymptomatic patient to patients complaining of increased abdominal girth, early satiety, and respiratory distress depending on the amount of fluid accumulated in the abdominal cavity. Flank dullness which is present in about 90% of patients, is the most sensitive physical sign.

Per abdomen: Increasing weight and abdominal girth (if previous values are available), shifting dullness (Puddle sign), fluid thrill, peritoneal tap (Table 9.17.2). Elicitation of increased flank dullness to percussion with patient supine and shifting dullness (> 1500 mL free fluid). The physical examination should focus on the signs of portal hypertension and chronic liver disease. Liver is examined to see if it is enlarged or tender. The liver may be difficult to palpate if a large amount of ascites is present (Table 9.17.3).

<table>
<thead>
<tr>
<th>Grade</th>
<th>Severity</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Mild</td>
<td>Puddle sign (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Detected by ultrasound abdomen</td>
</tr>
<tr>
<td>II</td>
<td>Moderate</td>
<td>Shifting dullness (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No fluid thrill</td>
</tr>
<tr>
<td>III</td>
<td>Tense</td>
<td>Fluid thrill (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Respiratory difficulty (+)</td>
</tr>
</tbody>
</table>
Table 9.17.3  Staging of ascites

<table>
<thead>
<tr>
<th>Stage</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1+</td>
<td>Detectable only after careful examination</td>
</tr>
<tr>
<td>2+</td>
<td>Easily detectable but of relatively small volume</td>
</tr>
<tr>
<td>3+</td>
<td>Obvious ascites but not tense ascites</td>
</tr>
<tr>
<td>4+</td>
<td>Tense ascites</td>
</tr>
</tbody>
</table>

**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.

**Neck:** Check for jugular venous distention.

**Heart:** Check for tricuspid murmur or signs of heart disease.

**Lungs:** Examine for signs of fluid (heart failure).

**Skin:** May show cutaneous spider angiomas, palmar erythema, Dupuytren's contracture, or large veins on the abdomen. **Asterixis** may be present, ascitis may be part of generalized edema. Patients with cardiac disease or nephrotic syndrome may have anasarca.

**Lymph nodes:** For enlargement. A pathologic left-sided supraclavicular node (Virchows node) suggests the presence of upper abdominal malignancy.

The puddle sign indicates that as little as 120 mL of fluid is present. When peritoneal fluid exceeds 500 mL, ascites may be demonstrated by the presence of shifting dullness or bulging flanks. A fluid-wave sign is notoriously inaccurate.

**Investigations**

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

**Blood Tests**

- Complete blood counts
- Complete urine examination
- Liver function tests including plasma proteins
- Clotting screen, especially if invasive investigations are considered.

**White cell count:** Normal ascitic fluid contains fewer than 500 leukocytes/mL and fewer than 250 polymorphonuclear leukocytes/mL. Any inflammatory condition can cause an elevated white blood cell count. White cell count when greater than 350/μL is suggestive of infection. A neutrophil count of more than 250 cells/μL is highly suggestive of bacterial peritonitis. In tuberculous peritonitis and peritoneal carcinomatosis, a predominance of lymphocytes usually occurs. If most cells are polymorphonuclear, bacterial infection should be suspected. When mononuclear cells predominated, tuberculosis or fungal infection is likely. This is the single most useful test. Only recent trauma gives false results. To correct this, one polymorphonuclear leukocyte (PMN) is subtracted from absolute ascitic fluid PMN count for every 250 RBC. In old trauma, PMN will have lysed so no correction is needed.

**Red cell count:** When greater than 50,000/μL denotes hemorrhagic ascites, which usually is due to malignancy, tuberculosis or trauma.

**Imaging Studies**
• **Chest and plain abdominal films:** Elevation of the diaphragm, with or without sympathetic pleural effusions (hepatic hydrothorax), is visible in the presence of massive ascites. More than 500 mL of fluid is usually required for ascites to be diagnosed based on findings from abdominal films.

  Many nonspecific signs indicate ascites, such as diffuse abdominal haziness, bulging of the flanks, indistinct psoas margins, poor definition of the intra-abdominal organs, erect position density increase, separation of small bowel loops, and centralization of floating gas containing small bowel.

  The direct signs are more reliable and specific. In 80% of patients with ascites, the lateral liver edge is medially displaced from the thoracoabdominal wall (Hellmer sign). Obliteration of the hepatic angle is visible in 80% of healthy patients. In the pelvis, fluid accumulates in the rectovesical pouch and then spills into the paravesical fossa. The fluid produces symmetric densities on both sides of the bladder, which is termed a “dog’s ear” or “Mickey Mouse” appearance. Medial displacement of the cecum and ascending colon and lateral displacement of the properitoneal fat line are present in more than 90% of patients with significant ascites.

• **Ultrasound:** Abdominal ultrasound can be used to detect ascites in morbidly obese, to indicate appropriate site for paracentesis, in patients with multiple abdominal surgical scars and with serum alphafetoprotein, to detect hepatic malignancy. It can detect as little as 100 mL of fluid in the peritoneal cavity. Uncomplicated ascites appears as a homogenous, freely mobile, anechoic collection in the peritoneal cavity that demonstrates deep acoustic enhancement. Free ascites does not displace organs but typically situates itself between them, contouring to organ margins and demonstrating acute angles at the point at which the fluid borders the organ.

  The smallest amounts of fluid first tend to collect in the Morison pouch and around the liver as a sonolucent band. With massive ascites, the small bowel loops have a characteristic polycyclic, “lollipop,” or arcuate appearance because they are arrayed on either side of the vertically floating mesentery.

  Certain sonographic findings suggest that the ascites may be infected, inflammatory, or malignant. Findings include coarse internal echoes (blood), fine internal echoes (chyle), multiple septa (tuberculous peritonitis, pseudomyxoma peritonei), loculation or atypical fluid distribution, matting or clumping of bowel loops, and thickening of interfaces between fluid and adjacent structures. In malignant ascites, the bowel loops do not float freely but may be tethered along the posterior abdominal wall plastered to the liver or other organs or they may be surrounded by loculated fluid collections.

• **Upper gastrointestinal endoscopy:** To confirm esophageal/fundal varices.

• **CT and MRI:** Ascites is demonstrated well on CT scan images. Small amounts of ascitic fluid localize in the right perihepatic space, the posterior subhepatic space (Morison pouch), and the Douglas pouch. A number of CT features suggest neoplasia. Hepatic, adrenal, splenic, or lymph node lesions associated with masses arising from the gut, ovary, or pancreas are suggestive of malignant ascites. Patients with malignant ascites tend to have proportional fluid collections in the greater and lesser sacs, whereas, in patients with benign ascites, the fluid is observed primarily in the greater sac and not in the lesser omental bursae.

---

**Invasive Procedures**

Ascitic tap (Abdominal paracentesis).

---

**Abdominal Paracentesis**

Abdominal paracentesis is the most rapid and perhaps the most cost-effective method of diagnosing the cause of ascites formation. Therapeutic paracentesis may be performed for refractory or tense ascites.

**Position**

For large volume ascites: Supine with head slightly elevated.

For low volume ascites: Lateral decubitus position.

For small volume ascites: Face down position or hand knee position (Fig. 9.17.4).
Site

1. **Midline site**: Below the umbilicus, this is avascular area.
2. When midline site is inappropriate (presence of scar), then a site two-finger breadth medial to the anterior superior iliac spine is chosen.
3. Ultrasonic guidance is needed only in specific indications.

Technique

Needle is inserted, using a Z tract to prevent leakage of fluid. This is achieved by retracting (with one glove hand) the skin approximately 2 cm caudal in relation to the deep abdominal wall and then slowly inserting the paracentesis needle. The skin is not released until the needle has penetrated the peritoneum or fluid flows. When the needle is finally removed at the end of procedure, the skin resumes its original position and seals the needle pathway (Fig. 9.17.5).

Ascitic Fluid Analysis

- Routine tests
- Optional tests
- Total protein
- Gram’s stain and culture
- Albumin
- AFB smear and culture
- Cell count
- Cytology
- Amylase
- Lactate dehydrogenase (LDH)
- Glucose.

**Lab studies**: Peritoneal fluid should be sent for cell count, albumin level, culture, total protein, Gram stain, and cytology for new-onset ascites of unknown origin.

**Gross appearance**: Most ascitic fluid is transparent and tinged yellow. This may be attributed to either a traumatic tap or malignancy. Bloody fluid from a traumatic tap is heterogeneously bloody, and the fluid will clot. Nontraumatic bloody fluid is homogeneously red and does not clot because it has already clotted and lysed. Neutrophil counts of more than 50,000 cells/mL have a purulent cloudy consistency and indicate infection. It may be red because of presence of red cells more
than 10,000/cumm, milky if it is lipid laden, dark-brown because of bilirubin, black/tea color in pancreatic ascites, cloudy because of absolute neutrophilic count over 5,000/cumm (Table 9.17.4).

**Total protein:** In the past, ascitic fluid has been classified as an exudate if the protein level is greater than or equal to 2.5 g/dL. However, the accuracy is only approximately 56% for detecting exudative causes. The total protein level may provide additional clues when used with the SAAG. An elevated SAAG and a high protein level are observed in most cases of ascites due to hepatic congestion. Those patients with malignant ascites have a low SAAG and a high protein level.

**Gram stain:** Gram stain is only 10% sensitive for helping visualize bacteria in early-detected spontaneous bacterial peritonitis. Approximately 10,000 bacteria/mL are required for detection by Gram stain; the median concentration of bacteria in spontaneous bacterial peritonitis is 1 organism/mL.

**Cytology:** Cytology smear results are reported to be 58–75% sensitive for helping detect malignant ascites. Positive in peritoneal carcinomatosis. Sensitivity increased by centrifuging large volume.

**pH** when less than 7 suggests bacterial infection.

**Serum ascitis albumin gradient (SAAG):** The SAAG is the best single test for classifying ascites into portal hypertensive (SAAG > 1.1 g/dL) and nonportal hypertensive (SAAG < 1.1 g/dL) causes. Calculated by subtracting the albumin concentration of the ascitic fluid from the albumin concentration of a serum specimen obtained on the same day. Serum ascites albumin gradient (SAAG) = serum albumin - ascitic fluid albumin.

It correlates directly with portal pressure. The accuracy of the SAAG results is approximately 97% in classifying ascites. High albumin gradient and low albumin gradient should replace the term transudate and exudate”, in the classification of ascites as accuracy is not good in the latter. The test is accurate despite ascitic fluid infection, diuresis, therapeutic paracentesis, albumin infusion and etiology of liver disease (Tables 9.17.5 and 9.17.6).

**Culture:** The common bacterial infection of ascitic fluid are monomicrobial with a very low bacterial concentration. The sensitivity with bedside inoculation of blood culture bottles with ascites results in 92% detection of bacterial growth in neutrocytic ascites.

**LDH:** LDH estimation is often helpful in distinguishing spontaneous bacterial peritonitis from gut perforation. Lactate dehydrogenase > 225 mU/L, glucose < 50 mg/dL, total protein > 1 g/dL and multiple organisms on Gram stain suggest secondary bacterial peritonitis (ruptured viscus or loculated abscess).

**Triglycerides:** A high level of triglycerides confirms chylous ascites.

**Amylase:** In pancreatitis or gut perforation it is markedly elevated, usually greater than 2000 IU.

**Bilirubin:** An elevated bilirubin level suggest biliary or gut perforation.

**Complications of paracentesis:** Include infection, electrolyte imbalances, bleeding, and bowel perforation. Bowel perforation should be considered in any patient with recent paracentesis who develops a new onset of fever and/or abdominal pain. All patients with long-standing ascites are at risk of developing umbilical hernias. Large-volume paracentesis often results in large intravascular fluid shifts. This can be avoided by administering albumin replacement, if more than 5 liters is removed.

<table>
<thead>
<tr>
<th>Table 9.17.4 Gross appearance of ascites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>Translucent or yellow</td>
</tr>
<tr>
<td>Brown</td>
</tr>
<tr>
<td>Cloudy or tubid</td>
</tr>
<tr>
<td>Pink or blood tinged</td>
</tr>
<tr>
<td>Grossly bloody</td>
</tr>
<tr>
<td>Milky (“chylous”)</td>
</tr>
</tbody>
</table>
### Table 9.17.5 Classification of ascitic fluid infection

<table>
<thead>
<tr>
<th>Type</th>
<th>PMN count (cells/mm&lt;sup&gt;3&lt;/sup&gt;)</th>
<th>Bacterial culture result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>&gt; 250</td>
<td>Positive (one organism)</td>
</tr>
<tr>
<td>Culture-negative neutrocytic bacterascites</td>
<td>&gt; 250</td>
<td>Negative</td>
</tr>
<tr>
<td>Monomicrobial non-neutrocytic bacterascites</td>
<td>&lt; 250</td>
<td>Positive (one organism)</td>
</tr>
<tr>
<td>Polymicrobial bacterascites</td>
<td>&lt; 250</td>
<td>Positive (polymicrobial)</td>
</tr>
<tr>
<td>Secondary bacterial peritonitis</td>
<td>&gt; 250</td>
<td>Positive (polymicrobial)</td>
</tr>
<tr>
<td>PMN, polymorphonuclear neutrophil leukocyte</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

PMN, polymorphonuclear neutrophil leukocyte

### Table 9.17.6 Types of ascites according to the level of the serum-ascites albumin gradient (SAAG)

<table>
<thead>
<tr>
<th>High gradient (&gt; or = 1.1 g/dL)</th>
<th>Low gradient (&lt; 1.1 g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>Tuberculous peritonitis</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>Nephrotic syndrome</td>
</tr>
<tr>
<td>Fulminant hepatic failure</td>
<td>Pancreatic ascites</td>
</tr>
<tr>
<td>Cardiac ascites</td>
<td>Bowel obstruction/infarction</td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>Biliary ascites</td>
</tr>
<tr>
<td>Veno-occlusive disease</td>
<td>Postoperative lymphatic leak</td>
</tr>
<tr>
<td>Myxedema</td>
<td>Serositis in connective tissue diseases</td>
</tr>
<tr>
<td>Massive liver metastases</td>
<td>Nephrotic syndrome</td>
</tr>
</tbody>
</table>
Indications for Admitting Patients of Chronic Liver Disease with Ascites

1. For investigations of the cause of liver disease
2. Child not responsive to appropriate OPD basis therapy
3. For intensive education of the patient in preparing a diet limited to 88 mmol of sodium per day
4. For careful monitoring of serum and urine electrolytes and serum concentration of urea nitrogen and creatinine
5. Grade III ascites with respiratory difficulty/distress
6. Ascites with suspected spontaneous bacterial peritonitis
7. If a child develops diuretic-induced complications
   - Electrolyte imbalances
     - Hyponatremia: Serum sodium < 125 mEq/L
     - Hypokalemia: Serum potassium < 3.0 mEq/L
     - Hyperkalemia: Serum potassium > 6.0 mEq/L
8. Hepatorenal syndrome
   - Increase in baseline serum creatinine by > 100% or an absolute value of 1.5 mg/dL (even if the patient is responding to diuretics)
   - Urinary Na⁺ < 10 mEq/L
   - Creatinine clearance < 0.75 mg/kg/min
9. Hepatic encephalopathy
10. Refractory ascites.

Management

Principles of Treatment

1. Initial evaluation
2. Identify and treat the underlying cause
3. Diagnostic ascitic fluid tap
4. Ascitic fluid analysis
5. Treatment of diuretic-sensitive ascites
6. Indications to stop diuretics
7. Treatment of refractory ascites
8. Spontaneous bacterial peritonitis

Nondrug Management

**Bed rest:** Upright position increases renin-aldosterone activity, increased retention of sodium or water. Bed rest reduces this activity.

**Medical care:** The goals of pharmacotherapy are to reduce morbidity and to prevent complications.

**Diet:** Sodium restriction (20–30 mEq/d) and diuretic therapy constitute the standard medical management for ascites and are effective in approximately 95% of patients. Sodium restriction up to 5 mg per day in child 1–4 years, not greater than 20 mEq per day in child 4–11 years, not greater than 30 mEq per day in child 12–14 years.

**Fluid restriction:** It is the sodium restriction not the fluid restriction, that results in weight loss. Fluid restriction is only indicated when there is persistent hyponatremia, serum sodium < 120 mEq/liter (reduced renal free water clearance). Renal sodium retention is the phenomenon primarily responsible for fluid retention and ascites formation. It occurs months before impairment of renal free water clearance.

Measurements of twenty-four hour urinary sodium excretion (with measurement of creatinine to assess completeness of collection). A major goal of treatment is to increase urinary sodium excretion to > 78 mmol/day.

Drugs

Diuretics

**Spironolactone (Aldactone)**

For management of edema resulting from excessive aldosterone excretion. Competes with aldosterone for receptor sites in distal renal tubules, increasing water excretion while retaining potassium and hydrogen ions. The peak effect of aldactone is approximately 3 days.
Dose: 2–3 mg/kg/day PO in divided doses q6-24h.

**Contraindications:** Documented hypersensitivity; anuria; renal failure; hyperkalemia.

**Precautions:** Caution in renal and hepatic impairment; may cause gynecomastia and impotence in men.

**Furosemide (Lasix)**

Increases excretion of water by interfering with chloride-binding cotransport system, which, in turn, inhibits sodium and chloride reabsorption in ascending loop of Henle and distal renal tubule. Dose must be individualized to patient.

**Dose:** 1–2 mg/kg/dose PO; not to exceed 6 mg/kg/dose; do not administer >q6h 1 mg/kg IV/IM slowly under close supervision; not to exceed 6 mg/kg. When treating infants, titrate in increments of 1 mg/kg/dose until a satisfactory effect is achieved.

**Contraindications:** Documented hypersensitivity; hepatic coma; anuria; state of severe electrolyte depletion.

**Precautions:** Perform frequent serum electrolyte, carbon dioxide, glucose, creatinine, uric acid, calcium, and BUN determinations during first few months of therapy and periodically thereafter.

**Torasemide** is three times more potent and longer acting than furosemide.

**Amiloride (Midamor)**

A pyrazine-carbonyl-guanidine unrelated chemically to other known antikaliuretic or diuretic agents. Potassium-conserving (antikaliuretic) drug which, compared with thiazide diuretics, possesses weak natriuretic, diuretic, and antihypertensive activity.

**Dose:** Not established fully in pediatric practice.

**Contraindications:** Documented hypersensitivity; elevated serum potassium levels (>5.5 mEq/L); impaired renal function, acute or chronic renal insufficiency, and evidence of diabetic nephropathy. Monitor electrolytes closely if evidence of renal functional impairment is present, BUN >30 mg/100 mL, or serum creatinine level >1.5 mg/100 ml.

**Precautions:** Potassium retention associated with use of an antikaliuretic agent accentuated in presence of renal impairment and may result in rapid development of hyperkalemia. Monitor serum potassium level. Mild hyperkalemia usually not associated with abnormal ECG findings.

**Metolazone (Mykrox, Zaroxolyn)**

Helps treat edema in congestive heart failure. Increases excretion of sodium, water, potassium, and hydrogen ions by inhibiting reabsorption of sodium in distal tubules. May be more effective in those with impaired renal function.

**Dose:** 5–20 mg/dose PO q24h.

**Contraindications:** Documented hypersensitivity; hepatic coma or anuria.

**Precautions:** Caution in hepatic or renal disease, diabetes mellitus, gout, or lupus erythematosus.

**Mannitol (Osmitrol)**

Inhibits tubular reabsorption of electrolytes by increasing osmotic pressure of glomerular filtrate. Increases urinary output.

**Dose:** Mannitol (20%) 2 mL/kg every 6 hours for 2 days or 0.5-3.0 g/kg/dose 8th hourly.

**Contraindications:** Documented hypersensitivity, anuria, severe pulmonary congestion, progressive renal damage, severe dehydration, active intracranial bleeding, and progressive heart failure.

**Precautions:** Carefully evaluate cardiovascular status before rapid administration because a sudden increase in extracellular fluid may lead to fulminating CHF. Avoid pseudoagglutination. When blood is given simultaneously, add at least 20 mEq of sodium chloride to each liter of mannitol solution. Do not give electrolyte-free mannitol solutions with blood.

**Which Diuretics in Pediatrics and When to Increase Dose**

Diuretics should be initiated in patients who do not respond to sodium restriction. A useful regimen is to start with spironolactone. The addition of loop diuretics may be necessary in some cases to increase the natriuretic effect. If no response occurs after 4–5 days, the dosage may be increased stepwise.

**Duration of Diuretics Therapy**

**To treat:** Diuretic therapy is continued till ascites.

**To prevent:** In certain conditions like cirrhosis effective doses of diuretics have to continued for months to years, to prevent reaccumulation of fluid.
**Indications to Stop Diuretics**

- Encephalopathy
- Serum sodium < 120 mmol/L despite fluid restriction.
- Serum creatinine > 2.0 mg/dL.
- Clinically significant complications of diuretics.
- Hyperkalemia and metabolic acidosis (spironolactone).

**Diuretic-Resistant Ascites**

For ascites resistant to medical therapy treatment options include:

- Therapeutic paracentesis
- LeVeen or Denver (peritoneovenous) shunt
- Liver transplantation
- Extracorporeal ultrafiltration of ascitic fluid with reinfusion
- Transjugular intrahepatic portosystemic stent shunt.

**β-Blockers (Propranolol)**

Lowers portal pressure and inhibits renin secretion or combination of these effects, results increased natriuresis.

**Surgical**

**Transjugular Intrahepatic Portal-Systemic Stent-Shunt (TIPSS)**

A TIPSS is a side-to-side portal-systemic shunt placed by an interventional radiologist (Figs 9.17.6 and 9.17.7). TIPSS is an efficacious treatment for patients with refractory ascites. Survival may be better than in patients treated with serial large-volume paracentesis. TIPSS is associated with suppression of antinatriuretic systems, and an improvement in renal function and renal response to diuretics. Although the main indication for TIPSS remains variceal bleeding refractory to endoscopic therapy, the procedure reduces the activity of the RAAS and increases natriuresis and GFR. Shunt dysfunction and development of encephalopathy remain the major concerns in this patient group.

![Liver explant showing metal mesh of a TIPS](image)
Peritoneovenous Shunt

Peritoneovenous shunts (e.g. LeVeen [Fig. 9.17.8] or Denver) have been shown to have poor long-term patency. They are associated with excessive complications, including peritoneal fibrosis, and confer no survival advantage relative to standard therapy. It should be reserved for diuretic-resistant patients who are candidates for neither liver transplantation nor serial large-volume paracentesis (because of multiple surgical scars or distance from a physician able to perform paracentesis).

Liver Transplantation

This is the ultimate treatment modality available for refractory ascites in end stage liver disease. By replacing the cirrhotic liver, portal hypertension and its underlying mechanisms of ascites are corrected. Ideally transplantation should be done before hepato-renal syndrome sets in. Scarcity of facility and exorbitant costs are currently the limiting factors in our country. A patient with cirrhosis, the development of ascites refractory to standard medical therapy is associated with an approximately 50% 6-month survival, and an approximately 25% 12-month survival.

Surgical Portosystemic Shunting

Portocaval shunt operation involves the anastomosis of the portal vein and the inferior vena cava, consequently reducing the portal pressure. The shunt also produces a marked diuresis and natriuresis. However, despite reported efficacy, surgical portosystemic shunts are rarely used in the treatment of advanced cirrhotic ascites, because of the high incidence
of post-shunt encephalopathy. In addition, surgical shunts may cause technical difficulties during subsequent orthotopic liver transplantation.

Follow-Up

Further Inpatient Care

• Patients can actually be maintained free of ascites if sodium intake is limited to 10 mmol/dL.
• Twenty-four hours urinary sodium measurements are useful in patients with ascites related to portal hypertension in order to assess the degree of sodium avidity, monitor the response to diuretics, and assess compliance with diet.
• For grade 3 or 4 ascites, therapeutic paracentesis may be necessary intermittently.
• At hospital it is important to monitor body weight and the intake and output of fluids. Fluid restriction is only necessary if the serum sodium concentration drops below 120 mmol per liter. It is also important to determine the sodium balance which can be approximated by monitoring intake (diet, sodium containing medications and intravenous solutions) and urinary excretion because, a negative sodium balance is a predictor of weight loss.
• A reasonable goal for a patient without peripheral edema is a negative sodium balance with a weight loss of 0.5 kg per day.

Response to therapy is indicated by the following parameters:
1. Optimal decrease in body weight is 0.5–1% every 24 hours as compared to the previous day’s weight. Weight loss more than this would be harmful and indicates rapid shift of body fluids and calls for immediate reduction of diuretic dose.
2. Relief of abdominal distention as evidenced by improvement of distress and decreasing abdominal girth.
   • Achieving a negative sodium balance (when the patient is excreting more sodium than the intake) indicates good diuretic response. Inadequate sodium restriction is an important cause of diuretic resistant ascites and can be suspected if the patient does not lose weight and fluid despite an appropriate natriuresis.

Further Outpatient Care

• When a patient is responding to medical treatment, hospitalization is not necessary.
• The best method of assessing the effectiveness of diuretic therapy is by monitoring body weight and urinary sodium levels.
• In general, the goal of diuretic treatment should be to achieve weight loss of 300–500 g/dL in patients without edema and 800–1000 g/dL in patients with edema.
• Once ascites has disappeared, diuretic treatment should be adjusted to maintain the patient free of ascites.
• Body weight, orthostatic symptoms, and serum electrolytes, urea and creatinine are monitored.

Complications of Ascites

Umbilical Hernia

Some patients may develop or may show an increase in the size of already existent umbilical hernia. Most hernias recur after surgical repair unless the ascites is controlled.

Hydrothorax

Pleural effusion, particularly on the right side can develop in some patients with ascites. It occurs due to passage of fluid through small holes in the diaphragm. These effusions may be very large.

Spontaneous Bacterial Peritonitis

Diagnosis

A diagnosis of SBP is made when an ascitic fluid bacterial culture is positive (e.g. *Escherichia coli*, *Klebsiella pneumoniae*, or *Pneumococcus*) with an elevated ascitic fluid absolute polymorphonuclear leukocyte count >250 cells/mm³, and symptoms and/or signs consistent with infection (temperature >100° F, chills, abdominal pain, rebound tenderness, reduced bowel sounds) without an evident intra-abdominal and surgically treatable source of infection. A missed or delayed diagnosis of spontaneous bacterial peritonitis (SBP) could potentially lead to sepsis and significant morbidity and mortality.

Treatment

Patients with a definitive diagnosis or presumptive diagnosis of SBP, should be treated with antibiotics. Treatment should not be delayed in those with a presumptive diagnosis until a positive culture is obtained. Those with positive ascitic fluid
cultures in the absence of a neutrophil response should also be treated with antibiotics, if symptoms and/or signs of infection are present.

When treating empirically a broad spectrum, non-nephrotoxic, antibiotic is administered intravenously, e.g. cefotaxime (third-generation cephalosporin).

In well-characterized patients with SBP a 5-day course is as efficacious as a 10-day course of intravenous antibiotics.

Lack of antibiotic-induced clinical improvement is an indication for repeat diagnostic paracentesis. If the ascitic fluid PMN leukocyte count is lower and the culture negative, a further course of antibiotic is given. If the ascitic fluid PMN leukocyte count is higher and culture yields a new organism, a different antibiotic is chosen. Alternatively, if reculture yields the same organism secondary bacterial peritonitis is suspected.

Co-treatment with intravenous albumin, 1.5 g/kg at the time of diagnosis and 1 g/kg on day 3, reduces the incidence of renal impairment and improves survival.

Oral ofloxacin has been reported to be as efficacious as intravenous cefotaxime in the treatment of patients with SBP, who are not azotemic, vomiting or in shock. However, until more data are available, an intravenous antibiotic regimen is preferred.

Follow-up Paracentesis

Necessary only if there are atypical features (symptoms, clinical setting, ascitic fluid analysis, organism(s), response to therapy) suggestive of secondary peritonitis.

Liver Transplantation

The prognosis in patients who develop SBP is so poor, that liver transplantation should be considered in all survivors of SBP.

Prevention

Cirrhotic patients, with low ascitic fluid total protein levels (< 1 g/dL) or gastrointestinal hemorrhage or those who have recovered from an episode of SBP, are at high risk of developing SBP and are candidates for long-term prophylactic therapy with oral antibiotics.

Oral antibiotic primary prophylaxis, with norfloxacin, ciprofloxacin or cotrimoxazole, appears to be effective in preventing an initial episode of SBP or a recurrence of SBP. The emergence of infections caused by bacteria resistant to specific antibiotics is a potential problem.

Prognosis

Depends on the underlying disorder, the degree of reversibility of a given disease process, and the response to treatment.

Patient Education

The most important aspect of patient education is determining when therapy is failing and recognizing the need to see a physician. Unfortunately, in most cases, liver failure has a dismal prognosis. All patients must be taught which complications are potentially fatal and the signs and symptoms that precede them. Abdominal distention and/or pain despite maximal diuretic therapy are common problems, and patients must realize the importance of seeing a physician immediately.

Monitoring of the Patient

The treatment of ascites depends on it’s cause. In the majority of patients, cirrhosis leading to portal hypertension is the major cause. A particular value of recognizing portal hypertension as a cause of ascites is that medical management using diuretics and salt restriction is often effective in portal hypertensive patients. Conversely, ascites due to peritoneal inflammation or malignancy alone does not respond to salt restriction and diuretics.

Low Albumin Gradient Ascites

These patients usually do not have portal hypertension and do not respond to salt restriction and diuretics. Patients with ‘Tuberculous peritonitis’ are cured by antituberculous therapy. Pancreatic ascites may resolve spontaneously, require endoscopic stenting or operative intervention or need ‘somatostatin’ therapy. Lymph leak usually resolves spontaneously or may require surgical intervention or peritoneovenous shunting: Chlamydial peritonitis requires tetracycline therapy. Nephrotic and lupus ascites may require steroids. Malignant requires surgical debulking and chemotherapy. Ascites may respond to aggressive dialysis.

Urinary Sodium

Twenty-four hours urinary sodium measurement is a helpful parameter. When patient has no urinary sodium excretion despite diuretics, recommend an alternative treatment-paracentesis.
**Refractory Ascites**

**Definition**
Defined as fluid overload that is non-responsive to restriction of dietary sodium to 88 mmol/day and maximal dose diuretic therapy (furosemide + spironolactone), in the absence of ingestion of prostaglandin inhibitors, such as non-steroidal anti-inflammatory drugs. Ascites is also considered to be refractory when there is intolerance of diuretic therapy.

Indications of failure of diuretic therapy include minimal or no weight loss, together with inadequate urinary sodium excretion (< 78 mmol/day).

Less than 10% of patients with ascites complicating cirrhosis meet the criteria of the definition of refractory ascites.

**Management**

**Serial Large-Volume Paracentesis**

Serial large-volume paracentesis (6–10 L) are safe and effective in controlling refractory ascites.

Therapeutic paracentesis volume of fluid to be tapped: Up to 100 mL/kg safely at any time. How frequently one should tap: large volume tap is indicated in one sitting then frequent taps.

**Mechanism of Relief by Paracentesis**
Taking out fluid from peritoneal cavity decreases systemic venous congestion, increases GFR and renal plasma flow which helps in producing diuresis.

Advanced cirrhosis is associated with a hyperdynamic circulation characterized by reduced systemic vascular resistance secondary to splanchnic vasodilatation, which leads to effective hypovolemia. Intense activation of the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system, and nonosmotic release of vasopressin occur, with consequent renal hypoperfusion. This becomes more accentuated as patients progress from decompensated cirrhosis to the hepatorenal syndrome (HRS).

In patients with no urinary sodium excretion and a dietary intake of 88 mmol sodium daily, the required frequency is about every two weeks. The frequency is influenced by the degree of compliance with the low sodium diet. The sodium content of ascitic fluid is about 130 mmol/L. Thus, a 6 L paracentesis removes 780 mmol sodium. Patients, who ingest 88 mmol sodium per day and excrete 10 mmol sodium in non-urinary losses and no sodium in the urine, retain 78 mmol sodium per day. Accordingly, a 6 L paracentesis removes the sodium retained over a period of 10 days, and a 10 L paracentesis removes the sodium retained over approximately 17 days.

Intravenous colloid replacement, e.g. albumin 6 to 8 g/L ascitic fluid removed is recommended immediately following a large-volume paracentesis (>5 L), to minimize intravascular hypovolemia, activation of vasoconstrictor and antinatriuretic systems, and impairment of renal function. Dextran 70 is less efficacious than albumin. If a paracentesis is <5 L, colloid replacement appears to be unnecessary.

**Novel Treatments in Ascites**

**Atrial Natriuretic Peptide**

Atrial natriuretic peptide (ANP) normally increases glomerular filtration rate (GFR) and natriuresis. Patients with advanced cirrhosis and ascites have a reduced natriuretic response to ANP despite elevated levels. Exogenous ANP administration, together with the splanchnic vasoconstrictor terlipressin to counter the hypotensive effect of ANP, increases renal blood flow, GFR and natriuresis in patients with refractory ascites.

**Other Agents**

Although not tested specifically for refractory ascites, a number of agents have been tried in humans which may increase diuresis in cirrhotic patients with ascites. These include the V2 receptor antagonist, OPC-3126, Niravoline, a k-opioid antagonist, and the adenosine-1-receptor antagonist FK352. Future studies using these novel agents may provide further information regarding their efficacy in refractory ascites.

---

**Chylous Ascites**

Turbid, milky or creamy peritoneal fluid due to the presence of thoracic or intestinal lymph having triglyceride (fat) concentration of more than 1000 mg/dL. If patient has nothing by mouth, then milky color will fade and the fluid will look like transudate with predominance of lymphocytes (85%).

**Causes**
Congenital anomaly of lymphatics lymphangiectasis, obstruction of duct within its abdominal portion from trauma, tumor, large lymph nodes, rupture of major lymphatic channel, tuberculosis, filariasis, nephrotic syndrome, cirrhosis, rheumatoid arthritis, other serositis.

**Pseudochylous Ascites**

In chronic peritonitis/persistent ascites fluid have some what similar color, from the degeneration of inflammatory products (leukocytes/tumor cell), and may be confused with chylous fluid (Table 9.17.7).

<table>
<thead>
<tr>
<th>Table 9.17.7</th>
<th>Difference between true and pseudochylous fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>True chylous fluid</td>
<td>Pseudochylous fluid</td>
</tr>
<tr>
<td>Ether test- top thick layers becomes clear fluid</td>
<td>Turbidity is unchanged</td>
</tr>
<tr>
<td>Alkali test- no change in color</td>
<td>Becomes clear (dissolves cellular protein)</td>
</tr>
<tr>
<td>Fat globules stained by Sudan</td>
<td>Not stained</td>
</tr>
</tbody>
</table>

**Management**

a. Dietary:
   i. Low fat diet - containing medium chain triglycerides, because these are absorbed directly into the portal circulation.
   ii. High protein diet, and
   iii. Parenteral nutrition supplementation.

b. Paracentesis: Duration of treatment may require several months for effective medical management. Surgical approach abdominal exploration to detect the site of the leak.

**Monitoring during Diuretic Therapy**

The main concern during diuretic therapy is whether there is too rapid fluid mobilization and diuretic induced complications.

In OPD settings the patient needs to be assessed after one week of starting therapy and thereafter every two weeks. At each visit compliance for low sodium diet, bed rest and diuretic doses should be ascertained. Examination for changes in weight, abdominal girth, pedal edema, ascitic grading and subtle signs of spontaneous bacterial peritonitis should be done. Weight loss of more than 1% per day or 4–6% per week of the previous weight would indicate too rapid fluid mobilization and natriuresis. This cautions us to evaluate renal functions along with reduction in the dose of diuretics.

Evaluation of serum Na, K, blood urea and creatinine and liver function tests would be useful in assessing diuretic response and its attendant complications. Serial measurement of fractional excretion of sodium is an objective measure of the effectiveness of the diuretic response. This requires simultaneous estimation of serum and spot urinary sodium and creatinine concentrations. At the earliest suspicion of spontaneous bacterial peritonitis, an ascitic tap should be performed and antibiotic therapy instituted. Admitted patients are usually those who have resistant ascites or have developed diuretic induced complications. Thus their monitoring is more intense and repeated every 48 hours.

**Summary**

The circulatory disturbances seen in advanced cirrhosis lead to the development of ascites, which can become refractory to diet and medical therapy. These abnormalities may progress and cause a functional renal failure known as the hepatorenal syndrome. Management of refractory ascites and hepatorenal syndrome is a therapeutic challenge, and if appropriate, liver transplantation remains the best treatment. New therapeutic options have recently appeared, including the transjugular intrahepatic portosystemic shunt and selective splanchnic vasoconstrictor agents, which may improve renal function and act as a bridge to transplantation.
ion gradient: A physiologic approach to the differential diagnosis.

Bibliography