Pediatric Ascites Revisited

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ABSTRACT

Ascites is the pathologic fluid accumulation within the peritoneal cavity. Ascitic fluid represents a state of total-body sodium and water excess. Its Etiology includes gastrointestinal, genitourinary, cardiac and metabolic disorders, infections, haematologic and chromosomal abnormalities. Causes neonatal ascites are different from infants and children group. Most cases of ascites are due to liver disease or due to some precipitating factors deteriorating liver functions. History of abdominal distension, increasing weight, respiratory embarrassment, and associated pedal edema associated with it. Ascites needs to be differentiated from abdominal distension due to other causes like gross obesity, gaseous distension, bowel obstruction, abdominal cysts or masses. Investigations should be directed to rule out the cause of ascites. Ascitic fluid drainage is a useful procedure to made a diagnosis and decide the line of treatment accordingly. Umbilical Hernia, Hydrothorax, Spontaneous Bacterial Peritonitis are some dreadful complications of Ascites and its underlying etiology. Its management includes non pharmacological and medical treatment. Various advanced medication and surgeries like TIPSS, Peritoneovenous Shunt, Portosystemic Shunting and Liver Transplantation will promise a better outcome.

Key words: Ascites, TIPSS, Paracentesis, Peritonitis

INTRODUCTION

Ascites is of Greek derivation (askites/askhos) which refers to a “bag”, “bladder” or “sack”. The word describes pathologic fluid accumulation within the peritoneal cavity (Figure 1). Ascites can occur at any age and in utero. In children it is usually the result of liver or renal disease.

Background

The peritoneum produces a fluid that acts as a lubricant and allows the abdominal organs to glide smoothly over one another. An excess of this fluid which can build up between visceral and parietal layers is called ascites.

Ascites can be associated with portal hypertension. The higher portal pressure can be caused by liver damage. It can also be caused by impaired drainage in the lymph system which 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 imbalance 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 (Figure 2A).

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 (Figure 2B).

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 (Figure 2C). 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 favour the extravasation of fluid from the plasma to the peritoneal fluid, and, thus, ascites is infrequent in patients with cirrhosis unless both portal hypertension (Figure 3) 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 mechanism of ascites is shown in Table I.

![Figure 2: Pathophysiology of ascites](image)

![Figure 3: Ascites formation in cirrhosis](image)

Etiology

**Fetal ascites:**

Isolated ascites in the absence of hydrops-fetalis is uncommon. Although examination of the fetus by ultrasound has become common even in a normal pregnancy, there have been only a small number of reported cases of isolated fetal ascites (Table II).

Table II: Causes of Fetal Ascites

- **Gastrointestinal disorders:**
  - Meconium peritonitis
  - Intestinal malrotation
  - Small intestinal or colonic atresia
  - Intussusception
  - Volvulous
Cystic fibrosis
- Biliary atresia
- Portal venous malformations

**Genitourinary disorders:**
- Hydronephrosis
- Polycystic kidney
- Urinary obstruction
- Ovarian cyst

**Cardiac disorders:**
- Arrhythmia
- Heart failure

**Metabolic disease:**
- Niemann pick type C
- Congenital disorder of glycosylation
- Lysosomal storage disease

**Chylous ascites**

**Infections:**
- Parvovirus
- Syphilis
- Cytomegalovirus
- Toxoplasmosis
- Acute maternal hepatitis

**Haematologic:**
- Haemolytic anaemia
- Neonatal haemochromatosis
- Homozygous alpha thalassemia

**Chromosomal abnormalities:**
- Trisomy 13,18 and 21
- Turner’s syndrome

**Neoplasm**

**Others:**
- Maternal/fetal abuse
- Idiopathic

Cytomegalovirus (CMV) is the most common congenital infection of the fetus and can cause fetal ascites and liver disease. Ascites is typically detected at the gestational age between 21 and 30 weeks. The presence of ascites in utero does not necessarily indicate severe infection or a poor prognosis. Histologic examination of severely infected fetal liver has shown hepatocellular degeneration with extensive bridging fibrosis and intrahepatic calcifications.

**Neonatal ascites:**

There are multiple iatrogenic causes of ascites in the newborn such as “extravasations of parenteral nutrition from femoral or umbilical venous catheters” and “perforation of the bladder or urachal remnant with extravasation of urine into the peritoneal cavity” (Figure 4).

Table III: Causes of neonatal ascites

1. **Hepatobiliary disorders:**
   - Cirrhosis
   - Alpha-1-antitrypsin deficiency
   - Congenital hepatic fibrosis
   - Viral hepatitis

2. **Genitourinary disorders:**
   - Obstructive uropathy-
     - Posterior urethral valves
     - Ureteroceles
     - Lower ureteral stenosis
     - Ureteral atresia
     - Imperforate hymen
     - Bladder rupture
   - Bladder injury from umbilical artery catheterization
   - Nephrotic syndrome

3. **Gastrointestinal disorders:**
   - Intestinal malrotation
   - Intestinal perforation
   - Acute appendicitis
   - Intestinal atresia
   - Pancreatitis

4. **Cardiac:**
   - Arrhythmia
   - Heart failure

5. **Hematologic:**
   - Neonatal hemochromatosis

6. **Parenteral nutrition extravasation**

7. **Metabolic disease:**
   - Mucopolysaccharidosis VIII

8. **Others:**
   - Cutis marmorata telangiectasia congenital
   - Intravenous vitamin E
   - Pseudo-ascites: small bowel duplication
   - Abdominal trauma
   - Idiopathic

Ascites in infants and children:

Cirrhosis from chronic liver disease is the most common hepatic cause of ascites in infants and children. Inflammatory conditions of the bowel that involve the serosal surface, such as eosinophilic enteropathy and Crohn’s disease, may result in...
ascites. Vitamin A intoxication may also present with ascites, and measurement of retinol-binding protein is important in establishing the diagnosis.

Pancreatic ascites occurs rarely in children. One-third of cases occur in infants younger than 1 year old. Serum amylase and lipase levels may be normal and the diagnosis missed unless ascitic fluid is analyzed. Ascites appears to be an accurate independent predictor of severity of pancreatitis and pseudocyst formation.

Table IV: Causes of ascites in infants and children

<table>
<thead>
<tr>
<th>Hepatobiliary disorder (Associated with portal hypertension, Figure 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Cirrhosis</td>
</tr>
<tr>
<td>• Congenital hepatic fibrosis</td>
</tr>
<tr>
<td>• Acute hepatitis B,C</td>
</tr>
<tr>
<td>• Budd-chiari syndrome</td>
</tr>
<tr>
<td>• Bile duct perforation</td>
</tr>
<tr>
<td>Serositis:</td>
</tr>
<tr>
<td>• Crohn’s disease</td>
</tr>
<tr>
<td>• Eosinophilic enteropathy</td>
</tr>
<tr>
<td>• Henoch-Schonlein purpura</td>
</tr>
<tr>
<td>Neoplasm:</td>
</tr>
<tr>
<td>• Lymphoma</td>
</tr>
<tr>
<td>• Wilm’s tumor</td>
</tr>
<tr>
<td>• Clear cell renal sarcoma</td>
</tr>
<tr>
<td>• Glioma</td>
</tr>
<tr>
<td>• Germ cell tumor</td>
</tr>
<tr>
<td>• Ovarian tumor</td>
</tr>
<tr>
<td>• Mesothelioma</td>
</tr>
<tr>
<td>• Neuroblastoma</td>
</tr>
<tr>
<td>Cardiac</td>
</tr>
<tr>
<td>• Heart failure</td>
</tr>
<tr>
<td>Parenteral nutrition extravasation</td>
</tr>
<tr>
<td>• Metabolic disease</td>
</tr>
<tr>
<td>Gastrointestinal disorders:</td>
</tr>
<tr>
<td>• Acute appendicitis</td>
</tr>
<tr>
<td>• Intestinal atresia</td>
</tr>
<tr>
<td>• Pancreatitis</td>
</tr>
<tr>
<td>• Pyloric duplication</td>
</tr>
<tr>
<td>Pseudo-ascites</td>
</tr>
<tr>
<td>• Celiac disease</td>
</tr>
<tr>
<td>• Cystic mesothelioma</td>
</tr>
<tr>
<td>• Omental cyst</td>
</tr>
<tr>
<td>• Ovarian cyst</td>
</tr>
<tr>
<td>Genitourinary disorders</td>
</tr>
<tr>
<td>• Nephrotic syndrome</td>
</tr>
<tr>
<td>• Peritoneal dialysis</td>
</tr>
<tr>
<td>Chylous ascites</td>
</tr>
<tr>
<td>• Intestinal lymphangiectasia</td>
</tr>
<tr>
<td>• Lymphatic duct obstruction</td>
</tr>
<tr>
<td>• Lymphatic duct trauma</td>
</tr>
<tr>
<td>Other:</td>
</tr>
<tr>
<td>• Systemic lupus erythematosus</td>
</tr>
<tr>
<td>• Ventriculoperitoneal shunt</td>
</tr>
</tbody>
</table>

- Vitamin A toxicity
- Chronic granulomatous disease
- Non-accidental trauma
- Toxins: Ethanol, Methotrexate, 6-Mercaptopurine
- Histiocytosis X, Schistosomiasis

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 distension, 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.

Figure 5: Ascites with portal hypertension showing dilated veins

Examination

Ascites needs to be differentiated from abdominal distension due to other causes like gross obesity, gaseous distension, 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. Jaundice, spider angiomias, umbilical collateral veins, clubbing, and palmar erythema are other signs suggestive of liver disease.
Per abdomen: Increasing weight and abdominal girth (if previous values are available), shifting dullness (Puddle sign), fluid thrill, peritoneal tap (Table V). Elicitation of increased flank dullness is present on percussion when patient is in supine position and shifting dullness if >1500 ml free fluid is present. 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 VI).

Table V: Grading of ascites

<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>II</td>
<td>Moderate</td>
<td>Shifting dullness (+) No fluid thrill</td>
</tr>
<tr>
<td>III</td>
<td>Severe</td>
<td>Fluid thrill (+)</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 distension.

**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 oedema. Patients with cardiac disease or nephrotic syndrome may have anasarca.

**Lymph nodes:** For enlargement. A pathologic left-sided supra-clavicular node (Virchow’s 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
- Renal Function tests
- Clotting screen, especially if invasive investigations are considered.

**White cell count:** Normal ascitic fluid contains less than 500 leukocytes/ml and less 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/ml is highly suggestive of bacterial peritonitis. In tuberculous peritonitis and peritoneal carcinomatosis, a predominance of lymphocytes usually occurs. If most of the cells are polymorphonuclear, bacterial infection should be suspected. When mononuclear cells predominated, tuberculosis or fungal infection is likely to be present. This is the single most useful test. Only recent trauma gives false results. To correct this, one PMN is subtracted from absolute ascitic fluid PMN count for every 250 RBC. In old trauma, PMN would already have been lysed, so no correction is needed.

**Red blood count:** When RBC Count is greater than 50,000/µl, it 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 thoraco-abdominal wall (Hellmer’s sign). Obliteration of the hepatic angle is visible in 80 percent of healthy patients. In the pelvis, fluid accumulates in the rectovesical pouch and then spreads 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 percent 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 α-fetoprotein, 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 (Table VII) suggest that the ascites may be infected, inflammatory, or malignant.

Table VII: USG findings in ascites

<table>
<thead>
<tr>
<th>Condition</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tuberculous</td>
<td>Multiple Septa, Matting or Clumping of Bowel loops, Thickening of interfaces between fluid and adjacent structures</td>
</tr>
<tr>
<td>Blood</td>
<td>Coarse internal echoes</td>
</tr>
<tr>
<td>Chyle</td>
<td>Fine internal echoes</td>
</tr>
<tr>
<td>Malignant</td>
<td>Bowel loops do not float freely but may be tethered along the posterior abdominal wall plastered to the liver or other organs or surrounded by loculated fluid collection.</td>
</tr>
<tr>
<td>Pseudomyxoma peritonie</td>
<td>Multiple septa</td>
</tr>
</tbody>
</table>

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’s 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

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 position with head slightly elevated.

For low volume ascites: Lateral decubitus position.

For small volume ascites: Face down position or hand knee position (Figure 6).

Site

a. Midline site: Below the umbilicus, this is avascular area.

b. When midline site is inappropriate (presence of scar), then a site two-finger breadth medial to the anterior superior iliac spine is chosen.

c. 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 to procedure, the skin resumes its original position and seals the needle pathway (Figure 7).

Gross Appearance:

a. Most ascitic fluids are transparent and tinged yellow. This may be attributed to either a traumatic tap or malignancy.

b. 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.
c. Purulent cloudy: 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.
d. Milky if it is lipid laden
e. Dark-brown because of bilirubin,
f. Black/tea color in pancreatic ascites,
g. Cloudy because of absolute neutrophilic count over 5,000/cumm. (Table VIII).

**Ascitic Fluid Analysis**

Ascitic fluid thus aspirated is subjected to:

a. Cell count / Cytology  
b. Gram’s stain and culture

c. AFB smear and culture  
d. Total protein (albumin/globulin ratio)  
e. Glucose  
f. Amylase  
g. Lactate dehydrogenase (LDH)  
h. Estimation of ADA (adenosine deaminase)

**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 percent for detecting exudative causes. The total protein level may provide additional clues when used with the serum ascites albumin gradient (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.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Gross Appearance</th>
<th>Protein, g/dl</th>
<th>SAAG g/dl</th>
<th>Cell Count</th>
<th>Other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tuberculous peritonitis</strong></td>
<td>Clear, turbid, haemorrhagic, chylous</td>
<td>&gt;2.5(50%)</td>
<td>&lt;1.1</td>
<td>7%</td>
<td>Peritoneal biopsy, stain and culture for acid fast bacilli, Ascitic fluid ADA is raised</td>
</tr>
<tr>
<td><strong>Neoplasm</strong></td>
<td>Straw-colored, hemorrhagic, mucinous, or chylous</td>
<td>&gt;2.5(75%)</td>
<td>&lt;1.1</td>
<td>20%</td>
<td>Cytology, cell block, peritoneal biopsy</td>
</tr>
<tr>
<td><strong>Cirrhosis</strong></td>
<td>Chylous, Straw-colored or bile-stained</td>
<td>&lt;2.5(95%)</td>
<td>&gt;1.1</td>
<td>1%</td>
<td>Peritoneal biopsy, stain and culture for acid fast bacilli</td>
</tr>
<tr>
<td><strong>Nephrosis</strong></td>
<td>Straw colored or chylous</td>
<td>&lt;2.5(100%)</td>
<td>&lt;1.1</td>
<td>unusual</td>
<td>If chylous, ether extraction , sudan staining</td>
</tr>
<tr>
<td><strong>Congestive heart failure</strong></td>
<td>Straw colored</td>
<td>Variable</td>
<td>&gt;1.1</td>
<td>10%</td>
<td>&lt;1000(90%); usually mesothelial , mononuclear</td>
</tr>
<tr>
<td><strong>Pyogenic peritonitis</strong></td>
<td>Turbid or purulent</td>
<td>If purulent &gt;2.5</td>
<td>&lt;1.1</td>
<td>unusual</td>
<td>Predominantly polymorphonuclear leukocytes</td>
</tr>
</tbody>
</table>
| **Pancreatic ascitis (pancreatitis pseudo cyst)** | Turbid, haemorrhagic or chylous | Variable, often >2.5 | <1.1      | Variable, may be blood stained Variable | Increased amylase in ascitic fluid and serum

**Gram’s stain:** It 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’s stain; the median concentration of bacteria in spontaneous bacterial peritonitis is 1 organism/ml.

**Cytology:** Cytology smear results are reported to be 58% Positive in peritoneal carcinomatosis. Sensitivity increased by centrifuging large volume, pH when less than 7 suggests bacterial infection.

**Serum Ascites Albumin Gradient:** The SAAG is the best single test for classifying ascites into portal hypertensive (SAAG > 1.1 g/dl) and non-portal 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 percent 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 (Table IX).

**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 ascitic fluid results in 92 percent detection of bacterial growth in neutrocytic ascites.

### Table IX: Classification of ascitic fluid infection

<table>
<thead>
<tr>
<th>Type</th>
<th>PMN count (cells/mm³)</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 nonneutrocytic 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 Count</td>
<td>--</td>
<td>--</td>
</tr>
</tbody>
</table>

**LDH:** LDH estimation is often helpful in distinguishing spontaneous bacterial peritonitis from gut perforation. Lactate dehydrogenase >225mU/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.

**Figure 8:** Types of Ascites according to level of serum ascites albumin gradient (SAAG)
Figure 9: Differential Diagnosis of Ascites (Approach by Abdominal Paracentesis).

**Abdominal Paracentesis**
- **Transparent yellow or Crystal clear or cloudy yellow**
  - Subtract 1 WBC/750 RBC, Subtract 1 PMN/250 RBC
- **Bloody**
- **Milky**
- **Dark Brown**
  - Quantitative Bilirubin Concentration

**WBC Count cells/mm^3**
- < 500
- ≥ 500

**PMN Count cells/mm^3**
- < 250
- ≥ 250

**SAAG g/dl**
- ≥ 1.1
- < 1.1

**Other testing**
- **Total Protein < 2.5 g/dl**
- **Total Protein ≥ 2.5 g/dl**

- **Cardiac Ascites**
- **Nephrotic Ascites**
- **SBP**
- **Secondary Bacterial Peritonitis**
- **Pancreatic Ascites**
- **Peritoneal Carcinomatosis with portal HTN**
- **TB Peritonitis with underline Cirrhosis**
- **Peritoneal Carcinomatosis**
- **TB Peritonitis**

- **Uncomplicated Cirrhotic Ascites**
- **USG and/or Liver Biopsy**
- **Chest X-ray and Echo**
- **24 hour Urinary Protein Excretion**
- **Clinical Response to antibiotics**
- **Upright abd. Film, water soluble gut contrast studies**
- **Pancreatic protocol, abd. CT**
- **Search for Primary tumor**
- **Mycobacterial growth on culture of laparoscopic biopsy of peritoneum**

**Consideration of surgical intervention if gut rupture is documented**

**Antituberculous therapy**
**Table X: Interpretation of Ascitic Fluid in SBP**

<table>
<thead>
<tr>
<th>PMN count</th>
<th>Ascitic culture</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;250 cells/mm³</td>
<td>Positive</td>
<td>SBP</td>
</tr>
<tr>
<td>&gt;250 cells/mm³</td>
<td>Negative</td>
<td>False negative culture</td>
</tr>
<tr>
<td>Normal</td>
<td>Positive</td>
<td>Contamination of culture/early SBP*</td>
</tr>
</tbody>
</table>

* When PMN count normal and ascitic culture positive it represent early SBP or transient bacterascites. A repeat paracentesis is helpful in interpreting results.

**Contraindications of paracentesis:**
- Disseminated intravascular coagulation
- Primary fibrinolysis
- Massive ileus with bowel distension
- Surgical scar at proposed site

**Indications for Admitting Patients of Chronic Liver Disease with ascites**
1. For investigating the cause of liver disease
2. Child not responsive to appropriate OPD basis therapy
3. For careful monitoring of the patient in preparing a diet limited to 88 mmol of sodium per day
4. For care of ascites with respiratory difficulty / distress
5. Ascites with suspected spontaneous bacterial peritonitis
6. If a child develops diuretic induced complications

**Management**

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

**Non-Drug 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 medial management for ascites and are effective in approximately 95 percent of patients.

**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.

**Treatment with Drugs**

**Diuretics**

**Spiironolactone (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 to 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.

**Frusemide (Lasix)**

Increases excretion of water by interfering with chloride binding co-transport 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 to 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 to 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 to 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).
- Painful gynaecomastia
- Muscle cramps

**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.

**Updated Guidelines for Management of Ascites**
- Drugs that lower arterial pressure, including angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, and even beta-blockers, should be avoided or, if used, should be accompanied by careful monitoring of blood pressure and renal function.
- Vaptans, which inhibit the action of vasopressin on its receptors, should be avoided in patients with cirrhosis.
- The use of intravenous albumin infusion after large-volume paracentesis has been controversial. Albumin infusion should be given at a rate of 6 to 8 grams per liter of fluid removed when >5 liters of ascites are drained.
- Terlipressin plus albumin was shown to reduce mortality compared with albumin alone in patients with type 1 hepatorenal syndrome. Until then, octreotide plus midodrine should be considered.
- The common use of quinolones to prevent spontaneous bacterial peritonitis in high-risk patients with cirrhosis has led to an increase in multidrug-resistant organisms. To reduce the risk for resistance, prophylactic antibiotics should be used only when indicated and for a limited duration when possible. The spectrum should be narrowed once susceptibility results are available.

**Drugs contraindicated in Ascites:**
- NSAIDS are contraindicated in patients with ascites because of risk of developing further sodium retention, hyponatremia, renal failure and diuretic resistance
- Drugs that decrease arterial pressure or renal blood flow such as ACE inhibitors, angiotensin II antagonist or alpha-1-adrenergic receptor blocker are contraindicated because of increased risk of renal impairment
- Amioglycosides are associated with an increase risk of renal failure.

**Surgical**

**Transjugular Intrahepatic Portal-Systemic Stent-Shunt:**
A TIPSS is a side-to-side portal-systemic shunt placed by an interventional radiologist (Figures 11 & 12). 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.

**Peritoneovenous Shunt:**
Peritoneovenous shunts [e.g. LeVeen (Figure 13) 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 percent 6-month survival, and an approximately 25 percent 12-month survival.

Figure 11: Liver explant showing metal mesh of a TIPS

Figure 12: TIPS shunt from hepatic vein to portal vein

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’s 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.

Further Outpatient Care

- Daily weight recording.
- The dose of diuretics depends upon the degree of ascites and the severity of the liver disease. A usual regime is 2-3

Response to therapy is indicated by the following parameters:

1. Optimal decrease in body weight is 0.5 to 1 percent 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 distension 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.
mg/kg spironolactone (or 10 – 20 mg amiloride) daily with frusenide 2-6 mg/kg/day daily for the patient with more marked ascites initially, or with a poor response to spironolactone alone.

- Serum electrolytes, creatinine, urea and liver function tests are monitored every 4 weeks for the stable out-patient. In the patient who has been treated initially as an in - patient, an earlier check at 1 week after discharge allows an adjustment to the management plan before electrolyte or clinical imbalance has occurred.
- As liver function improves and the oedema and ascites resolve, it may be possible to stop the frusenide first and then the spironolactone.
- The ‘no added salt’ (1-2 meq/kg/day for infant and children, and 1 – 2 g/day adolescent) is maintained in the majority of patients.

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

Spontaneous bacterial peritonitis is an infection of ascitic fluid in patients with cirrhosis and is defined by an ascitic polymorphonuclear leucocyte (PMN) count of >250 cells/mm³. SBP is thought to develop as a result of delayed intestinal transit and increased permeability of the intestinal wall. In this setting bacteria migrate from the intestinal lumen to the mesenteric lymph nodes, a process known as bacterial translocation.

Most patients present with fever, abdominal pain, chills, general malaise, loss of appetite, nausea or vomiting. A diagnostic paracentesis should be carried out in all patients with cirrhosis and ascites at hospital admission to rule out SBP. A diagnostic paracentesis should also be performed in patients with gastrointestinal bleeding, shock, fever, or other signs of systemic inflammation, gastrointestinal symptoms, as well as in patients with worsening liver and/or renal function, and hepatic encephalopathy. The diagnosis of SBP is based on neutrophil count in ascitic fluid of >250/mm³ as determined by microscopy (Level A1). At present there are insufficient data to recommend the use of automated cell counters or reagent strips for the rapid diagnosis of SBP. Ascitic fluid culture is frequently negative even if performed in blood culture bottles and is not necessary for the diagnosis of SBP, but it is important to guide antibiotic therapy (Level A1). Blood cultures should be performed in all patients with suspected SBP before starting antibiotic treatment (Level A1).

The most common isolated microorganisms are Gram-negative bacteria, most often *Escherichia coli* or *Klebsiella* species. Usually, only a single bacterial species is found. Recent studies suggest that diagnosis of SBP may be improved by using reagent strips. The principle of these strips is based on the detection of leucocyte esterase. The esterase in the fluid reacts with an ester on the test strip and in combination with a dye it corresponds to the amount of leucocytes present. The main advantages of reagent strips are the fact that the results are immediately available and the costs are low.

**Treatment:** Antibiotic treatment should be started as soon as the diagnosis, based on the PMN count in ascites, is made. Empirical antibiotics should be started immediately following the diagnosis of SBP (Level A1).

Since the most common causative organisms of SBP are Gram-negative aerobic bacteria, such as *E. coli*, the first line antibiotic treatment are third-generation cephalosporins (Level A1). Alternative options include amoxyccillin/ clavulanic acid and quinolones such as ciprofloxacin or ofloxacin. However, the use of quinolones should not be considered in patients who are taking these drugs for prophylaxis against SBP, in areas where there is a high prevalence of quinolone-resistant bacteria or in nosocomial SBP (Level B1). SBP resolves with antibiotic therapy in approximately 90% of patients. Resolution of SBP should be proven by demonstrating a decrease of ascitic neutrophil count to <250/mm³ and sterile cultures of ascitic fluid, if positive at diagnosis (Level A1). A second paracentesis after 48 h of start of treatment may help guide the effect of antibiotic therapy. Failure of antibiotic therapy should be suspected if there is worsening of clinical signs and symptoms and/or no marked reduction or increase in ascitic fluid neutrophil count compared to levels at diagnosis. Failure of antibiotic therapy is usually due to resistant bacteria or secondary bacterial peritonitis. Once secondary bacterial peritonitis has been excluded, antibiotics should be changed according to in vitro susceptibility of isolated organisms, or modified to alternative empiric broad spectrum agents (Level A1).

HRS occurs in approximately 30% of patients with SBP treated with antibiotics alone, and is associated with a poor survival. The administration of albumin (1.5 g/kg at diagnosis and 1g/kg on day 3) decreases the frequency of HRS and improves survival (Level A1). It is unclear whether albumin is useful in the subgroup of patients with baseline serum bilirubin <68 μmol/L and creatinine <88 μmol/L (Level B2). Until more information is available, we recommend that all patients who develop SBP should be treated with broad spectrum antibiotics and intravenous albumin (Level A2).

**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.

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 (<1g/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 distension 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 its 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.

Figure 14: Approach to the diagnosis and treatment of spontaneous bacterial peritonitis

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**

It is defined as ascites that cannot be mobilized or prevented from recurring by medical therapy. It is divided into diuretic resistant (ascites is not mobilized despite maximum diuretic dosage) and diuretic intractable ascites (development of diuretic induced complications that preclude use of an effective diuretic dosage). Dietary history, use of NSAID or angiotensin converting enzyme or angiotensin 2 receptor blockers and patient compliance with treatment regimen must be reviewed before confirming diagnosis.

**Criteria:**

- Lack of response to maximal doses of diuretic for at least one week
- Diuretic induced complications in absence of other precipitating factors
- Early recurrence of ascites within four weeks of fluid mobilization
- Persistent ascites despite sodium restriction
- Mean weight loss <0.8kg over 4 days
- Urinary sodium excretion < sodium intake

**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 hypertrophy. 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 removal 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.
Chylous Ascites:

<table>
<thead>
<tr>
<th>Color</th>
<th>Milky and cloudy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglyceride</td>
<td>Above 200 mg/dL</td>
</tr>
<tr>
<td>level</td>
<td></td>
</tr>
<tr>
<td>Cell count</td>
<td>Above 500 (lymphocytic predominance)</td>
</tr>
<tr>
<td>Total protein</td>
<td>Between 2.5 and 7.0 g/dL</td>
</tr>
<tr>
<td>SAAG</td>
<td>Below 1.1 g/dL*</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Low (ascites/serum ratio &lt; 1)</td>
</tr>
<tr>
<td>Lactate</td>
<td>Between 110 and 200 IU/L</td>
</tr>
<tr>
<td>dehydrogenase</td>
<td></td>
</tr>
<tr>
<td>Culture</td>
<td>Positive in selected cases of tuberculosis</td>
</tr>
<tr>
<td>Cytology</td>
<td>Positive in malignancy</td>
</tr>
<tr>
<td>Amylase</td>
<td>Elevated in cases of pancreatitis</td>
</tr>
<tr>
<td>Glucose</td>
<td>Below 100 mg/dL</td>
</tr>
</tbody>
</table>

Table XI: Difference between true and pseudochylous fluid

<table>
<thead>
<tr>
<th>True chylous fluid</th>
<th>Pseudochylous fluid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ether test- top thick layers</td>
<td>Turbidity is unchanged</td>
</tr>
<tr>
<td>becomes clear fluid</td>
<td></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>

Pseudochylous Ascites

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

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 1 week of starting therapy and thereafter every 2 weeks. At each visit compliance for low sodium diet, bed rest and diuretic doses should be ascertained. Examination for changes in weight, abdominal girth, and pedal edema, ascitic grading and subtle signs of spontaneous bacterial peritonitis should be done. Weight loss of more than 1 percent per day or 4 to 6 percent 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 splanchic vasoconstrictor agents which may improve renal function and act as a bridge to transplantation.

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