

Pathophysiology, Diagnosis, and Management of Pediatric Ascites

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ABSTRACT

The pediatric population has a number of unique considerations related to the diagnosis and treatment of ascites. This review summarizes the physiologic mechanisms for cirrhotic and noncirrhotic ascites and provides a comprehensive list of reported etiologies stratified by the patient's age. Characteristic findings on physical examination, diagnostic imaging, and abdominal paracentesis are also reviewed, with particular attention to those aspects that are unique to children. Medical and surgical treatments of ascites are discussed. Both prompt diagnosis and appropriate management of ascites are required to avoid associated morbidity and mortality.

Key Words: diagnosis, etiology, management, pathophysiology, pediatric ascites

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Ascites is the pathologic accumulation of fluid within the peritoneal cavity. The word ascites is derived from the Greek *askites* and *askos*, meaning bag, bladder, or belly. Ascites can occur at any age and *in utero*. In children it is usually the result of liver or renal disease. Detection and appropriate treatment of ascites is important to minimize morbidity from its complications.

PATHOPHYSIOLOGY

Anatomy and Physiology

In the normal liver, blood flow from the hepatic artery and portal vein perfuses the hepatic sinusoids and then leaves the liver through the hepatic veins to the inferior vena cava (Fig. 1). Pressure in the sinusoids is normally low, about 2 mmHg, because resistance to afferent flow is considerably greater than efferent resistance. Hepatic lymph is formed by the filtration of sinusoidal plasma into the space of Disse (bordered by hepatocytes on 1 side and sinusoidal lining cells on the other) (1,2). It drains from the liver via the transdiaphragmatic lymphatic vessels to the thoracic duct, which empties into the left subclavian vein. The sinusoidal endothelium is highly permeable to albumin; therefore, the concentration of protein in hepatic lymph is close to that of plasma, and there is no significant osmotic gradient across the sinusoidal membrane.

In the intestines, blood from the mesenteric capillaries drains via the mesenteric veins into the portal vein (Fig. 1). The mean

pressure of mesenteric capillaries is normally about 20 mmHg. Intestinal lymph drains from regional lymphatics and ultimately combines with hepatic lymph in the thoracic duct. Unlike the sinusoidal endothelium, the mesenteric capillary membrane is relatively impermeable to albumin; the concentration of protein in mesenteric lymph is only about one-fifth that of plasma, so there is a significant osmotic gradient that promotes the return of interstitial fluid into the capillary. In the normal adult, the flow of lymph in the thoracic duct is about 800 to 1000 mL/day (3,4).

Ascites from portal hypertension occurs when hydrostatic and osmotic pressures within hepatic and mesenteric capillaries produce a net transfer of fluid from blood vessels to lymphatic vessels at a rate that exceeds the drainage capacity of the lymphatics. It is not known whether ascitic fluid is formed predominantly in the liver or in the mesentery. The underlying cause of portal hypertension may dictate where the majority of the ascitic fluid is formed. Animal experiments of hepatic vascular outflow restriction show increased hepatic lymph production. When the hepatic vein is ligated in a dog and the liver is placed within the thorax, pleural fluid accumulates instead of ascites; when it is placed within a bag, fluid accumulates in the bag (5,6). In cirrhotic ascites, however, the protein concentration of the ascitic fluid more closely resembles intestinal lymph than hepatic lymph. This suggests that as hepatic fibrosis progresses to cirrhosis, there is decreased capacity for lymph formation by the liver, and that the majority of cirrhotic ascites may be of splanchnic origin (7).

Cirrhotic Ascites

Ascites is a common complication of cirrhosis (8). Alteration of 3 interrelated pathophysiologic processes contribute to the formation of cirrhotic ascites: portal hypertension, vasodilation, and hyperaldosteronism.

In patients with cirrhotic ascites, there is a nitric oxide–mediated systemic vasodilation causing effective hypovolemia, although the trigger for nitric oxide production is not well understood (9). Renal juxtaglomerular apparatuses sense this effective hypovolemia and stimulate the renin-angiotensin-aldosterone system leading to increased sympathetic activity and antidiuretic hormone (ADH) secretion (10). ADH activity promotes free water retention and expansion of plasma volume (11,12). The usual vasoconstrictive effects of angiotensin appear to be blunted in cirrhosis, allowing perpetuation of systemic arteriolar vasodilation (13). Arteriolar vasodilation of the splanchnic bed leads to systemic vascular steal and continued systemic underfilling (14). Thus, compensatory mechanisms are unable to achieve circulatory homeostasis and a hypovolemic response continues.

Portal hypertension also increases the hydrostatic pressure gradient across splanchnic circulation resulting in increased intestinal lymph formation. When lymph formation outpaces lymphatic drainage capacity, it accumulates in the peritoneal cavity. Animal models suggest that there is a 60% increase in hepatic lymph

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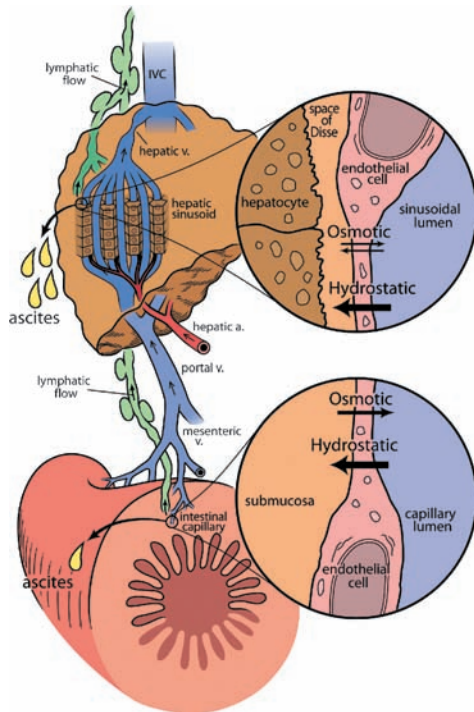


FIGURE 1. Ascites formation. Hepatic lymph is formed by filtration of sinusoidal plasma into the space of Disse. It then drains from the liver via the transdiaphragmatic lymphatic vessels to the thoracic duct. The sinusoidal endothelium is highly permeable to albumin, which results in no significant osmotic gradient across the sinusoid. Hydrostatic forces are the primary driver of hepatic lymph formation and are increased in portal hypertension. Mesenteric capillaries are much less permeable to albumin. The osmotic force of albumin in the capillary promotes the return of interstitial fluid to the capillary lumen and counteracts the intraluminal hydrostatic forces. Ascites occurs when the net transfer of fluid from blood vessels to lymphatic vessels exceeds the drainage capacity of the lymphatics. Reprinted with permission from WB Saunders (2) and Elsevier (3).

production for each millimeter of mercury increase in portal pressure (15).

The patient with decompensated cirrhosis has a hyperdynamic circulatory state with an expanded blood volume, increased cardiac output, tachycardia, a wide pulse pressure, and peripheral vasodilation. The hypoalbuminemia seen with synthetic liver failure exacerbates ascites formation by decreasing the osmotic gradient drawing interstitial fluid into the vascular space.

Noncirrhotic Ascites

Noncirrhotic ascites can develop in multiple ways. Peritoneal carcinomatosis causes ascites by the secretion of proteinaceous material from malignant cells with osmotic forces then favoring movement of fluid into the peritoneum. Tuberculous ascites and other forms of inflammatory ascites develop because of similar fluid shifts in response to proteinaceous secretions (16).

Conditions such as right-sided heart failure, Budd-Chiari syndrome, and portal venous malformations may impair portal

blood flow leading to portal hypertension and ascites. When a noncirrhotic liver is exposed to elevated sinusoidal pressures, there is an increase in hepatic lymph formation (Fig. 1). Hydrostatic forces are also transmitted to the splanchnic circulation resulting in increased intestinal lymph formation as described above.

Heart failure and nephrotic syndrome may cause decreased effective arterial blood volume with secondary activation of the sympathetic nervous system, the renin-angiotensin-aldosterone system and ADH, leading to renal sodium and water retention (17). The hypoalbuminemia of advanced nephrotic syndrome results in decreased intravascular oncotic pressure and subsequent movement of plasma into the interstitium.

Pancreatic and biliary ascites are caused by leakage of pancreatic juice or bile into the peritoneal cavity, and may be complicated by fluid shifts caused by the irritant effect of these secretions on the peritoneum.

ETIOLOGY

The causes of ascites vary according to the age of the patient. Different hepatic and nonhepatic causes of ascites have been reported in the fetus, neonate, infant, child, and adult.

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. It appears that many cases resolve spontaneously before birth, and are not associated with poor outcomes or chronic disease (18,19). A list of described causes of fetal ascites is shown in Table 1.

Cytomegalovirus (CMV) is the most common congenital infection of the fetus and can cause fetal ascites and liver disease (20,21). Ascites is typically detected at a gestational age between

TABLE 1. Causes of fetal ascites (20,21,25,26,99–124)

Gastrointestinal disorders	Chylous ascites
Meconium peritonitis	Cardiac disorders
Intestinal malrotation	Arrhythmia
Small intestinal or	Heart failure
colonic atresia	Chromosomal abnormalities
Intussusception	Trisomy
Volvulus	Turner syndrome
Cystic fibrosis	Neoplasm
Biliary atresia	Hematologic
Portal venous	Hemolytic anemia
malformations	Neonatal hemochromatosis
Infection	Metabolic disease
Parvovirus	Niemann-Pick type C
Syphilis	Congenital disorders of
Cytomegalovirus	glycosylation
Toxoplasmosis	Wolman disease
Acute maternal hepatitis	Lysosomal storage disease
Genitourinary disorders	Other
Hydronephrosis	Maternal/fetal abuse
Polycystic kidney disease	Idiopathic
Urinary obstruction	
Ovarian cyst	
Persistent cloaca	

21 and 30 weeks. The presence of ascites in utero does not necessarily indicate severe infection or a poor prognosis (22), but data are sparse because many fetuses with ultrasound manifestations of CMV infection are electively aborted (23). Histologic examination of severely infected fetal livers has shown hepatocellular degeneration with extensive bridging fibrosis and intrahepatic calcifications (24).

Intrauterine meconium peritonitis, a sterile peritonitis caused by fetal bowel perforation, can cause ascites, and in 1 case was associated with intravascular dissemination of meconium and multiorgan infarction (25). Meconium ileus diagnosed by fetal ultrasound is often milder and has a better prognosis than symptomatic cases diagnosed after birth; however, the presence of ascites in utero indicates a more complicated course (26).

Neonatal Ascites

Neonatal ascites can be caused by many of the same conditions that cause fetal ascites (Table 2), although many congenital diseases do not typically manifest ascites until after birth. There are also multiple iatrogenic causes of ascites in the newborn such as extravasation of parenteral nutrition from femoral or umbilical venous catheters (27–29) and perforation of the bladder or urachal remnant with extravasation of urine into the peritoneal cavity (30,31).

Ascites in Infants and Children

Cirrhosis from chronic liver disease is the most common hepatic cause of ascites in infants and children (Table 3). Inflam-

matory conditions of the bowel that involve the serosal surface, such as eosinophilic enteropathy (32) and Crohn disease (33), may result in ascites. Vitamin A intoxication may also present with ascites, and measurement of retinol-binding protein is important in establishing the diagnosis (34,35).

Pancreatic ascites occurs rarely in children (36). One-third of cases occur in infants younger than 1 year old (37). Serum amylase and lipase levels may be normal and the diagnosis missed unless ascitic fluid is analyzed (38). Ascites appears to be an accurate independent predictor of severity of pancreatitis and pseudocyst formation (39).

Ascites in Adults

The most common cause of ascites in adults is parenchymal liver disease. Cirrhosis (usually from chronic liver disease resulting from hepatitis C infection, alcoholic hepatitis, or nonalcoholic steatohepatitis) accounts for about 85% of cases. Cardiac disease and malignancy are the next most common causes and together account for about 5% of cases (40). Pancreatitis and tuberculosis are responsible in a minority of patients (41).

DIAGNOSIS

Evaluation of the presence, quantity, and etiology of ascites includes the history of the illness, the physical examination, imaging studies, and diagnostic paracentesis.

TABLE 2. Causes of neonatal ascites (27–31,125–147)

Hepatobiliary disorders	Genitourinary disorders
Cirrhosis	Obstructive uropathy
Alpha-1-antitrypsin deficiency	Posterior urethral valves
Congenital hepatic fibrosis	Ureterocele
Viral hepatitis	Lower ureteral stenosis
Budd-Chiari syndrome	Ureteral atresia
Biliary atresia	Imperforate hymen
Bile duct perforation	Bladder rupture
Portal venous malformation	Bladder injury from
Ruptured mesenchymal hamartoma	umbilical artery catheterization
Gastrointestinal disorders	Nephrotic syndrome
Intestinal malrotation	Ruptured corpus luteum cyst
Intestinal perforation	Cardiac
Acute appendicitis	Arrhythmia
Intestinal atresia	Heart failure
Pancreatitis	Hematologic
Chylous ascites	Neonatal hemochromatosis
Parenteral nutrition extravasation	Other
Metabolic disease	Cutis marmorata telangiectatica congenita
	Intravenous vitamin E
	Pseudo-ascites
	Small bowel duplication
	Abdominal trauma
	Idiopathic

TABLE 3. Causes of ascites in infants and children (4,16,32–37,148–179)

Hepatobiliary disorders	Neoplasm
Cirrhosis	Lymphoma
Congenital hepatic fibrosis	Wilm tumor
Acute hepatitis	Clear cell renal sarcoma
Budd-Chiari syndrome	Glioma
Bile duct perforation	Germ cell tumor
Liver transplantation	Ovarian tumor
Gastrointestinal disorders	Mesothelioma
Acute appendicitis	Neuroblastoma
Intestinal atresia	Metabolic disease
Pancreatitis	Genitourinary disorders
Pyloric duplication	Nephrotic syndrome
Serositis	Peritoneal dialysis
Crohn disease	Cardiac
Eosinophilic enteropathy	Heart failure
Henoch-Schonlein purpura	Pseudo-ascites
Chylous ascites	Celiac disease
Intestinal lymphangiectasia	Cystic mesothelioma
Lymphatic duct obstruction	Omental cyst
Lymphatic duct trauma	Ovarian cyst
Parenteral nutrition extravasation	Other
	Systemic lupus erythematosus
	Ventriculoperitoneal shunt
	Vitamin A toxicity
	Chronic granulomatous disease
	Nonaccidental trauma
	Idiopathic

History and Physical Examination

Patients with ascites typically report increased abdominal girth and recent weight gain (42). There may be a history of chronic liver disease or hepatitis. Physical examination may reveal a protuberant abdomen, bulging flanks, or dullness to percussion. Jaundice, spider angiomas, umbilical collateral veins, clubbing, and palmar erythema are other signs suggestive of liver disease.

The presence of bulging flanks can be caused by free fluid in the peritoneum, organomegaly, or obesity. Percussion of the abdomen can be used to distinguish ascites from obesity. In a supine patient with ascites, gas-filled loops of small intestine float to the top of the mid-abdomen. The percussion note of the mid-abdomen will be tympanitic, whereas the ascites-filled flanks will have dullness to percussion. If the patient is then placed in a lateral position, dullness to percussion will shift to the dependent side. The test for shifting dullness has a sensitivity of 60% to 88% and a specificity of 56% to 90%. It has been estimated that the minimum volume of ascitic fluid required to detect shifting dullness in an adult is 1.5 to 3.0 L (43).

A more sensitive test for ascites, which can be easily done in small children, is the “puddle” sign (44). In this test, a supine patient’s abdomen is percussed over the umbilicus. The resonant percussion becomes dull as the patient is moved to a prone position and the ascitic fluid “puddles” in dependent regions. Infants and small children can easily be held prone by a caregiver, whereas the abdomen of older children can be percussed with the patient kneeling on all fours.

The test for a fluid wave requires 2 examiners, 4 hands, and a cooperative supine patient. The sides of the hands of 1 examiner are used to press down the midline of the patient’s abdomen, while the other examiner depresses the flank with 1 hand and senses the resultant fluid wave in the contralateral flank with the other hand. The test for a fluid wave is unreliably sensitive (20% to 80%) but highly specific (82% to 100%) (43).

Body-imaging Studies

Ultrasound is a sensitive imaging technique for the detection of ascites (Fig. 2). Free fluid can be imaged confidently with ultrasound because it layers in the dependent regions, the hepatorenal recess (Morison pouch) and the pelvic cul-de-sac (45). It has been estimated that in supine infants 10 to 20 mL can be detected by ultrasound in the perivesicle area (46). Limitations to ultrasound include obesity and complex, loculated ascites because sound wave transmission to deeper structures can be limited by adipose tissue and intraluminal gas.



FIGURE 2. Ultrasound appearance of ascites with a sizable fluid collection visible in the Morison pouch between the liver and right kidney.



FIGURE 3. The radiographic appearance of ascites is often typified by a fluid density throughout the abdominal compartment and the centralized bowel loops.

Ascites can also be detected by plain radiography, computed tomography (CT), and magnetic resonance imaging (MRI) (Figs. 3–5) (47). CT demonstrates extrapancreatic fluid collections in children with acute pancreatitis (48) and high-density ascites in tuberculous peritonitis (49). Chylous ascitic fluid has been shown by both CT and ultrasound to develop a unique biphasic fat-fluid level when the patient remains recumbent (50). MRI is an excellent modality for detecting intraperitoneal fluid. With the advent of attempts to reduce ionizing radiation exposure, MRI could play a more important role in the detection of free fluid or loculated fluid collections in the abdominal peritoneal cavity. This may become more applicable in children as scanning times in MRI shorten.

Diagnostic Abdominal Paracentesis

In most children, ascites is readily recognizable as caused by hepatitis, portal hypertension, or nephrotic syndrome. When the



FIGURE 4. Diffuse ascites on computed tomography with enteral and intravenous contrast. Note the rim of fluid around a nodular liver, centralized bowel loops, and cephalic displacement of the diaphragm.

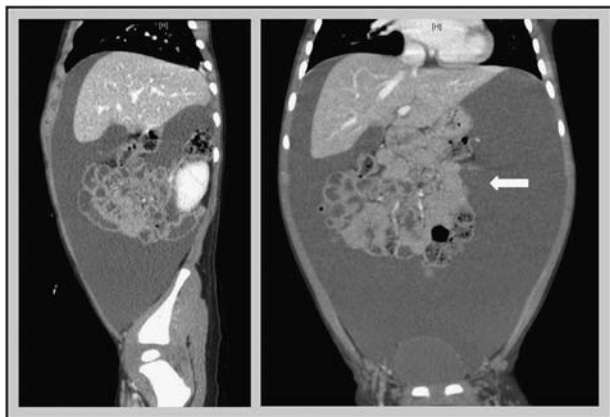


FIGURE 5. Pseudoascites in a 3-year-old boy. Computed tomography images of massive pseudoascites that was found to be secondary to a mesenteric cyst. Note the medially directed mass effect on the intestines (arrow).

cause of ascites is not apparent, however, examination of ascitic fluid can aid in identification of the etiology. Abdominal paracentesis is recommended to detect bacterial peritonitis when ascites accumulates quickly, when patients are hospitalized because of clinical deterioration, or when the patient has fever or abdominal pain (51).

Paracentesis can usually be performed quickly, inexpensively, and, when certain precautions are taken, safely (52). First, the site for needle insertion is selected. With the patient in the semi-recumbent position, the level of dullness is percussed. A site is chosen that is below both the umbilicus and the upper edge of dullness but above the urinary bladder. Scars should be avoided because bowel may be adherent to them. A common needle insertion site is 2 finger breadths medial and cephalad to the anterior superior iliac spine. Ultrasound localization of fluid is typically not necessary but may be warranted if there is difficulty in identifying a safe location.

Following disinfection of the site, a local anesthetic is injected in the skin and subcutaneous tissue. To create a Z-tract (to prevent leakage after the needle is withdrawn) the skin is pushed down about 2 cm over the abdominal musculature and a 22-gauge needle is inserted. The needle is advanced slowly in 5-mm increments, and if blood is seen, the needle is withdrawn. The syringe is aspirated when ascitic fluid is seen in the needle hub. Following aspiration of fluid the needle is withdrawn.

Ascitic fluid collected via paracentesis should be submitted to the laboratory in an anticoagulant tube for a white blood cell count and differential. Bedside inoculation of blood culture bottles with ascitic fluid should be performed (53). In addition, at the time of the first paracentesis, measurement of the albumin concentration is performed. If there is not sufficient fluid to perform all 3 tests, then the white blood cell count and differential is performed first because of its value in deciding whether to treat with antibiotics for possible bacterial peritonitis.

The components of the peritoneal fluid can often help define the etiology of ascites. Amylase elevation indicates pancreatitis or intestinal perforation. Polymicrobial infection is consistent with intestinal perforation, whereas monomicrobial infection suggests spontaneous bacterial peritonitis. Uroascites is present when the concentrations of urea and creatinine are higher in the ascitic fluid than in serum. Elevated ascitic bilirubin indicates perforation of the biliary tree or upper intestine. Chylous ascites is indicated by a milky appearance and a concentration of triglycerides higher in ascitic fluid than in serum.

The concentration of albumin in serum minus the concentration of albumin in ascitic fluid, called the serum-ascites albumin gradient, can reliably separate ascites into 2 categories: high gradient (≥ 1.1 g/dL) and low gradient (< 1.1 g/dL). High-gradient ascites is present when there is portal hypertension, in conditions such as cirrhosis, fulminant hepatic failure, Budd-Chiari syndrome, and portal vein thrombosis. Low-gradient ascites occurs in the absence of portal hypertension in conditions such as peritoneal carcinomatosis, tuberculous peritonitis, pancreatic ascites, biliary leak ascites, nephrotic syndrome, and serositis (54,55).

The exudate-transudate concept, based on the concentration of total protein in ascitic fluid, is unreliable and outmoded (56). In a study of 901 paracenteses, measurement of the ascitic fluid total protein correctly classified the causes of ascites only 56% of the time, whereas the serum-ascites albumin gradient differentiated the causes of ascites resulting from portal hypertension 97% of the time (57).

Complications of paracentesis are uncommon. In a prospective study of 125 adults with 229 paracenteses, there were no deaths attributable to paracentesis (52). Large intraabdominal hemorrhages occurred in 3 patients, 1 of whom required a blood transfusion. Paracentesis can be performed despite prolongation of the prothrombin time, except in cases of frank disseminated intravascular coagulation, and routine administration of fresh frozen plasma or platelets is not necessary.

TREATMENT

The benefits of treatment, primarily patient comfort, must be weighed against the discomfort of treatment and potential complications. Small amounts of ascitic fluid that do not produce symptoms or clinical sequelae may require little or no treatment. Tense ascites causing respiratory compromise, severe pain, or other major clinical problems should be treated promptly.

Mobilization of ascitic fluid is accomplished by creating a negative sodium balance until ascites has diminished or resolved; then sodium balance is maintained so that ascites does not recur. In most patients treatment of ascites consists of restriction of dietary sodium and administration of diuretics. On occasion, fluid restriction is also used. Patients who are resistant to diuretics in the setting of sodium restriction can be treated with large-volume paracentesis or transjugular intrahepatic portosystemic shunting (TIPS). Ultimately, orthotopic liver transplantation may be required.

Restriction of Dietary Sodium

Unrestricted intake of dietary sodium exacerbates ascites because of marked renal sodium retention. Ingestion of < 10 mEq of sodium daily prevents ascites formation; however, such a diet is unpalatable and few patients will adhere to it. It is recommended that dietary sodium be limited to 44 to 88 mEq (1–2 g) per day in adults, or approximately 17 to 35 mEq (0.4–0.8 g) per thousand calories. Most pediatric hepatologists recommend restriction of sodium intake: either a diet with no added sodium or a maximum of 2 mEq/kg of body weight per day. Restriction of dietary sodium by itself will be sufficient for only a minority of patients, and treatment with diuretics is usually required. Restriction of water intake is usually not recommended unless serum sodium falls below 125 mEq/L.

Supine Positioning

Supine positioning causes a decrease in sympathetic adrenergic tone and a reduction in the stimulation of renin, angiotensin, and aldosterone, with subsequent diuresis. Bed rest has a small

effect on natriuresis in most patients with cirrhosis; it is not considered necessary and, particularly for pediatric patients, it is impractical.

Diuretics

Spirolactone is the most effective single diuretic because of its ability to block the marked hyperaldosteronism that is characteristic of cirrhotic ascites. Metabolites of spironolactone act on the cortical and medullary collecting tubules by inhibiting the binding of aldosterone. Because it acts distally, spironolactone can normally inhibit the reabsorption of only 2% of the filtered sodium. In patients with cirrhosis, the bioactive metabolites of spironolactone have prolonged half-lives, ranging from 24 to 58 hours. As a result it often requires >5 days of treatment to achieve steady-state conditions and administration more than once daily is unnecessary (58).

A randomized comparative study demonstrated that 95% of nonazotemic cirrhotic patients with avid sodium retention responded to spironolactone treatment, but only 52% responded to furosemide. Patients who did not respond to furosemide had higher levels of renin and aldosterone, and upon subsequent treatment with spironolactone, 90% responded (59). Cirrhotic patients with ascites who do not respond to spironolactone treatment have a lower fractional sodium delivery to the distal renal tubule because of enhanced sodium reabsorption in the proximal tubule (60).

Furosemide is a loop diuretic that prevents sodium and chloride reabsorption in the thick ascending limb of the loop of Henle; it has no effect on the distal and collecting tubules (Fig. 6). Because 20% to 50% of filtered sodium is reabsorbed in the loop of Henle, furosemide can increase sodium excretion by as much as 30%. It should be used cautiously, however, because it reduces effective circulating volume in patients who are already intravascularly hypovolemic.

Diuretic treatment is begun with spironolactone, either alone or, in more severe cases, in combination with furosemide (61). One approach is to begin treatment with spironolactone 2 to 3 mg/kg of body weight (up to 100 mg) as a single morning dose; if there is no response, the dose is increased by 2 mg/kg (up to 100 mg) every 5 to 7 days until a maximum dose of 4 to 6 mg/kg (up to 400 mg) is reached. The adequacy of spironolactone dosing can be monitored

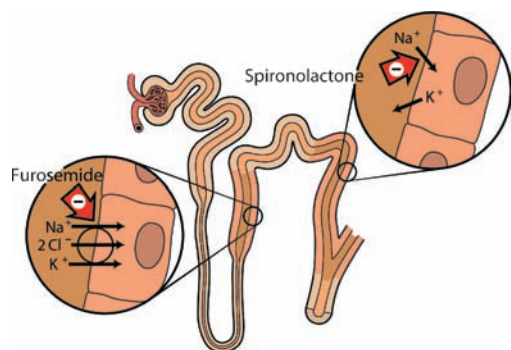


FIGURE 6. Diuretic mechanisms important in ascites treatment. Spirolactone metabolites act on the cortical and medullary collecting tubules by inhibiting binding of aldosterone to its receptor. This results in impairment of sodium absorption and potassium excretion. Furosemide acts on the epithelial cells in the thick ascending loop of Henle by inhibiting the sodium-chloride-potassium cotransporter. Reprinted with permission from WB Saunders (2).

with random urine sodium levels; values >50 mEq/L are desired. If there is still no response, then oral furosemide 1 mg/kg (up to 40 mg) daily is added, increasing the dose by 1 mg/kg (up to 40 mg) every 5 to 7 days if necessary until a maximum dose of 2 to 4 mg/kg (up to 160 mg) is reached. An alternative approach that may hasten the onset of diuresis is to begin treatment with both spironolactone 2 mg/kg (up to 100 mg) and furosemide 1 mg/kg (up to 40 mg) as a single morning dose. If necessary, the dosages of both spironolactone and furosemide are increased every 5 to 7 days until maximum doses of 4 to 6 mg/kg (up to 400 mg) and 2 to 4 mg/kg (up to 160 mg), respectively, are reached, maintaining a spironolactone to furosemide ratio of about 2.5 to 1 (62).

A gradual approach to diuretic therapy is preferred to decrease the likelihood of adverse effects. The goal of therapy is to reduce the body weight by approximately 0.5% to 1% (up to 300 to 500 g) each day until the ascites is gone, and to prevent the reaccumulation of ascites. No more than 900 mL of ascites can be reabsorbed in 1 day in an adult, so weight loss of >900 g will be associated with contraction of plasma volume (63). Spirolactone treatment can lead to hyperkalemic acidosis, and furosemide treatment can lead to hypokalemic alkalosis. When both drugs are used together, disturbances of potassium and pH occur less commonly. Oral potassium salts should not be administered as a sodium salt substitute when spironolactone is used as monotherapy because of the danger of hyperkalemia. Complications of diuretic therapy also include renal failure secondary to intravascular volume depletion, hyponatremia, hepatic encephalopathy, antiandrogenic effects, and muscle cramps. Nonsteroidal anti-inflammatory agents reduce the diuretic effect of furosemide (64). Intravenous furosemide can cause a potentially hazardous sudden decrease in glomerular filtration rate, and hence must be used cautiously (54).

Supplemental Albumin

When ascites results from portal hypertension as a complication of chronic liver disease, hypoalbuminemia is commonly present because of hepatic synthetic dysfunction. As discussed earlier, hypoalbuminemia will exacerbate ascites due to low vascular oncotic pressure. Hence, when serum albumin levels are <2.5 g/dL, supplemental albumin administration may aid ascitic fluid mobilization (65,66). Twenty-five percent albumin may be dosed at 1 g/kg IV up to 3 times per day until serum levels are >2.5 g/dL.

Therapeutic Paracentesis

Therapeutic paracentesis of diuretic-resistant tense ascites has been shown to be a safe, rapid, and effective treatment of ascites (67,68). Large volumes of ascitic fluid can be removed without increasing the risk of adverse alterations of hemodynamics, electrolytes, renal function, or mortality. Repeated removal of 4 to 6 L/day of ascitic fluid has become a standard treatment in adults; however, repeated large-volume paracentesis can lead to protein and complement depletion.

When large-volume paracentesis is performed, there is a significant increase in blood urea nitrogen, elevation of plasma renin activity and plasma aldosterone concentration, and reduction of serum sodium. These changes, which indicate a physiological response to the contraction of blood volume, are not usually manifested clinically by symptoms or signs (69–72).

The need for intravenous albumin after paracentesis is a controversial subject (73). Albumin infusions theoretically can produce an undesirable downregulation of albumin synthesis. Other plasma expanders that have been studied, including dextran 70 and

polygeline, have not been proven to be as effective as albumin in the prevention of postparacentesis circulatory dysfunction. Patients who receive albumin following total paracentesis have a longer time before rehospitalization and longer survival than patients who received other plasma expanders (70). Postparacentesis administration of terlipressin, a vasopressin analogue, was shown in a study to be as effective as albumin in preventing hemodynamic changes following large-volume paracentesis (74).

There is little published about large-volume paracentesis in children. Infants and young children can develop ascites rapidly. Without gradual accommodation of the abdominal wall, they are subject to respiratory distress and other sequelae of rapidly increasing intraabdominal pressure. In such situations paracentesis is performed to provide symptomatic relief (75). Intravenous albumin is often administered after therapeutic paracentesis in children at a dose of 1 g/kg.

Peritoneovenous Shunting

The peritoneovenous shunt was invented to create a conduit for ascites in the peritoneum to return to the vascular space in the superior vena cava (76). The LeVeen and Denver shunts consist of a perforated tube in the abdomen connected with a 1-way pressure-sensitive valve to a catheter that extends subcutaneously into a jugular vein. Peritoneovenous shunting often results in a reduction or elimination of ascites, with restoration of effective blood volume (77,78). Complications are frequent and include coagulopathy, shunt obstruction, superior vena caval thrombosis and obstruction, pulmonary embolism, and sepsis. Technical modifications have not been able to prevent these complications, and pediatric use is generally limited to palliative care (79).

TIPS Shunting

TIPS placement lowers portal pressure and prevents rebleeding from esophageal varices (80). It can also effectively alleviate cirrhotic ascites (81). It induces a delayed natriuresis and improves proximal renal tubular reabsorption of sodium, renin-angiotensin-aldosterone activity, and central blood volume despite continued arterial vasodilation (82). However, it is associated with complications such as hepatic encephalopathy and worsening liver failure, especially in patients with severe liver dysfunction (83). Vascular malformations and patient size may limit application in some pediatric patients (84).

Other Treatments

Attempts to develop techniques to ultrafilter ascites and reinfuse it, either into blood or into the peritoneum, have not been superior to other approaches in either adults (85–87) or children (56,88,89). If a child has symptomatic and intractable ascites because of liver disease, then referral for liver transplantation should be arranged.

SPONTANEOUS BACTERIAL PERITONITIS

Bacterial peritonitis is a complication of ascites with a high mortality rate if treatment is delayed. Spontaneous bacterial peritonitis (SBP) is defined as an infection of ascitic fluid without evidence of an abdominal source. Secondary bacterial peritonitis is defined as an intraabdominal infection caused by a condition that requires surgical treatment, such as intestinal perforation, a perineal abscess, or gallbladder empyema.

The incidence of spontaneous bacterial peritonitis in children is not known (90). In a report of 321 children with chronic liver

disease, there were 12 episodes of SBP in 11 patients; all 11 had ascites (91). Patients presented with rapid-onset abdominal distension, fever, malaise, and abdominal pain; some patients also had vomiting, diarrhea, and worsening jaundice. Diffuse rebound tenderness was present and encephalopathy had developed or worsened in most of the patients. Cultures of ascitic fluid detected a single organism in 11 of the episodes; *Streptococcus pneumoniae* was isolated in 73%, *Klebsiella pneumoniae* in 18%, and *Hemophilus influenzae* in 9%. A more recent report examined 13 culture-positive cases of SBP in 12 pediatric patients. Isolated organisms were *S pneumoniae* (39%), *Escherichia coli* (15%), *S viridans* (15%), *K pneumoniae*, *H influenzae*, *Enterococci*, and nontypable *Streptococcus* (92). The declining prevalence of *Streptococcus* and *Haemophilus* in this pediatric series likely reflects contemporary vaccination protocols. Adult series indicate that 60% of SBP episodes are caused by Gram-negative enteric bacilli (93).

An estimated 10% of SBP cases are not accompanied by symptoms suggestive of peritonitis (94). It is recommended that diagnostic paracentesis be performed when ascites first appears, at the time of a hospitalization, or when there is clinical deterioration, unexplained fever, abdominal pain, or other suspicious symptoms.

The concentration of bacteria in infected ascites is often low. Bedside inoculation of blood culture bottles with ascitic fluid is more sensitive than agar plating in detecting bacterial peritonitis, improving sensitivity from 43% to 93% (53). Gram stains of ascitic fluid are only 10% sensitive; however, they can rapidly identify the polymicrobial infections that are worrisome for intestinal perforation.

Samples of ascitic fluid that contain a leukocyte count >500 cells/mm³ and an absolute polymorphonuclear cell (PMN) count >250 cells/mm³ are assumed to be infected (54). In SBP, the PMN count is elevated and the ascites culture is positive. When the PMN count is elevated but the ascetic fluid culture is negative, it likely indicates a false-negative culture. When the PMN count is normal but the culture is positive, it may represent contamination of the culture, early SBP, or transient bacterascites (a condition that resolves in most cases without antibiotics). A repeat paracentesis is often helpful in interpreting these results.

If SBP is diagnosed by paracentesis or culture, then antibiotic treatment should be initiated. A non-nephrotoxic broad-spectrum antibiotic with Gram-negative coverage, such as a third-generation cephalosporin, is generally recommended. In most cases of SBP, treatment is continued for a total of 5 to 7 days, and the ascitic fluid becomes sterile after 48 hours. Despite advances in supportive care, SBP remains an indicator of poor prognosis. Although pediatric data are not available, adult in-hospital mortality remains between 10% and 30% (95).

Prophylaxis for primary or recurrent SBP has been recommended in certain clinical situations. Ciprofloxacin, norfloxacin, and trimethoprim-sulfamethoxazole have been used in adults (96,97), but not reported in children. A meta-analysis of adults with cirrhosis and ascites indicates that β -blockers may also decrease the risk of SBP (98).

SUMMARY

Understanding of the pathophysiology and possible etiologies of pediatric ascites is critical in making a rapid diagnosis of this condition. Laboratory and radiographic investigations may provide clinically important information because prompt and appropriate treatment of ascites is warranted to prevent related morbidity and mortality.

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