

# Ascites: Tapping into the Problem



By Elaine Yong, BSc, MD; and  
Mary Anne Cooper, MSc, MD, FRCPC

## In this Article:

1. How to investigate.
2. What tests should I order on the ascitic fluid?
3. How should I treat someone with cirrhotic ascites?

## Case Study

A 43-year-old man presented with two weeks of increasing abdominal girth. He had consumed 300 mL of vodka per day for 17 years. He was jaundiced and had multiple spider nevi. The abdomen was markedly distended, with shifting dullness. The liver edge was palpable and hard. Abdominal veins were distended. There was significant peripheral and sacral edema.

He started spironolactone 100 mg/day and furosemide 40 mg/day, began a low-sodium diet with fluid restriction (1.5 L every 24 hours) and was counselled to quit alcohol. He returned three days later with worsening abdominal distension and respiratory distress. He weighed 90 kg. Therapeutic paracentesis alleviated his respiratory complaints. He became compliant with dietary restrictions and abstained from alcohol. Diuretics were increased gradually to spironolactone 400 mg/day and furosemide 60 mg a day. He lost 16.5 kg over a period of eight weeks as his ascites and edema resolved.

## Patient Stats

- Weight 86.4 kg
- Thrombocytopenia (104 x 10<sup>9</sup>/L).
- Hypoalbuminemia (29g/L)
- Hyponatremia (127 mmol/L)
- Elevated INR
- Hyperbilirubinemia
- Transaminitis
- Ultrasound demonstrated hepatosplenomegaly but no liver masses and no hepatic vein thrombosis.
- Straw-coloured ascites with zero white cells and albumin of 5 g/L.

Table 1

## Causes of Ascites

Portal hypertension	Hypoalbuminemia	Miscellaneous
<ul style="list-style-type: none"> <li>• Cirrhosis of the liver</li> <li>• Congestive heart failure</li> <li>• Constrictive pericarditis</li> <li>• Hepatic vein thrombosis (Budd-Chiari syndrome)</li> <li>• Inferior vena cava obstruction</li> </ul>	<ul style="list-style-type: none"> <li>• Nephrotic syndrome</li> <li>• Protein losing enteropathy</li> <li>• Neoplasm</li> <li>• Peritoneal carcinomatosis</li> <li>• Pseudomyxoma</li> </ul>	<ul style="list-style-type: none"> <li>• Tuberculosis</li> <li>• Pancreatic ascites</li> <li>• Nephrogenic ascites</li> <li>• Myxedema</li> <li>• Meigs's syndrome</li> </ul>

Ascites, the accumulation of free fluid in the peritoneal cavity, is most often caused by portal hypertension due to cirrhosis (75% of cases).<sup>1</sup> Other causes include cancer (10%), congestive heart failure (5%), and a variety of other conditions (Table 1). Ascites is the most common complication of cirrhosis. The risk of developing

ascites after the diagnosis of cirrhosis is 50% over 10 years.<sup>2</sup> Two-year survival after onset of ascites is only 50%.<sup>3</sup>

Patients with ascites usually present with

Table 2

## Indications for diagnostic paracentesis

1. New-onset ascites
2. All admission for ascites
3. Clinical deterioration
  - Fever
  - Abdominal pain or tenderness
  - Encephalopathy
  - Ileus
  - Hypotension
  - Sudden increase in amount of fluid
4. Laboratory abnormalities
  - Peripheral leukocytosis
  - Acidosis
  - Worsening renal function
5. Gastrointestinal bleeding



Dr. Yong is a resident and gastroenterology trainee at the University of Toronto, Toronto, Ontario.



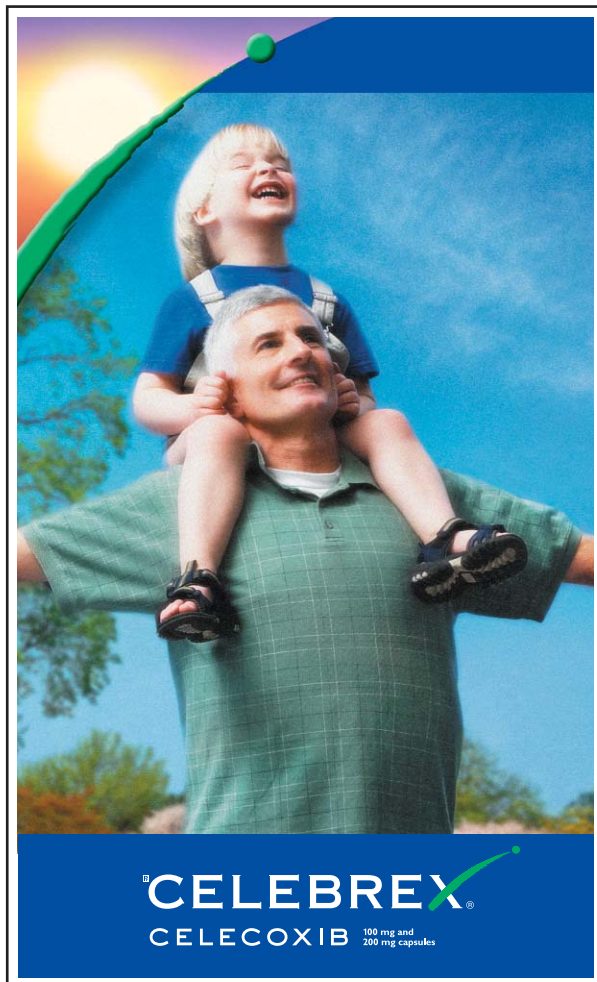
Dr. Cooper is a lecturer at the University of Toronto, and staff of gastroenterology at the Sunnybrook & Women's College Health Sciences Centre, Toronto, Ontario.

increasing abdominal girth, nausea and anorexia. They may have shortness of breath due to elevation of the diaphragm or pleural effusion. Tense ascites can cause pain.

The accuracy of the physical examination for detecting ascites is only 58%, with the most useful finding being flank dullness. Without this, the probability of ascites is below 10%.<sup>4</sup> Other signs of portal hypertension, such as splenomegaly or dilated abdominal wall veins, may be present. Patients may have hyperdynamic circulation with systemic hypotension and tachycardia. Ultrasound is more than 95% sensitive, and 90% specific in detecting ascites. It is useful in obese patients and should be done with Dopplers in all those with new onset ascites or those with a sudden increase in abdominal girth to rule out venous obstruction or hepatocellular carcinoma.<sup>5</sup>

## How to investigate

Diagnostic paracentesis is required in all patients with new onset ascites and those with established cirrhosis and ascites who undergo clinical change (see Table 2).<sup>6</sup> It is safe, despite that 70% of cirrhotics with ascites have an abnormal international normalised ratio (INR) and thrombocytopenia. There are no coagulation parameters beyond which paracentesis should be avoided, unless disseminated intravascular coagulation is present.<sup>6</sup> No data supports routine prophylactic administration of fresh frozen plasma or platelets, as the risk of a large hematoma is only 1% and a hemoperitoneum is 0.1% without these agents.<sup>7</sup>



# Ascites

Table 3

## Classification of ascites by serum-ascites albumin gradient (SAAG)

$$\text{SAAG} = [\text{albumin}]_{\text{serum}} - [\text{albumin}]_{\text{ascites}}$$

### High gradient ( $\geq 11$ g/L)

- Low total protein
- Cirrhosis
- Metastases
- Alcoholic hepatitis
- Fulminant hepatic failure

- Normal total protein
- Congenital hepatic fibroblast
- Hepatic vein thrombosis
- Constrictive pericarditis
- Veno-occlusive disease
- Myxedema

### Low gradient ( $\leq 11$ g/L)

- Peritoneal carcinomatosis
- Tuberculous peritonitis
- Pancreatic ascites
- Biliary ascites
- Nephrotic syndrome
- Serositis or collagen vascular disease

Table 4

## Ascitic fluid tests

### Required

- Macroscopic appearance (straw-coloured, turbid, bloody, chylous)
- Cell count and differential
- Albumin
- Total protein
- Culture in blood culture bottles
- Gram's stain

### Optional

- Glucose (for secondary peritonitis)
- LDH (for secondary peritonitis)
- Amylase (for pancreatic ascites)
- AFB smear and tuberculosis culture
- Adenosine deaminase (for tuberculosis)
- Cytology (for malignant ascites)
- Triglycerides
- Bilirubin
- pH, lactate (for bacterial peritonitis)

## What tests should I order on the ascitic fluid?

**Cell count:** Two main questions to answer with paracentesis are: is there infection? and is there portal hypertension? The most important test is the cell count and differential for the polymorphonuclear (PMN) count. Results are available rapidly, which is essential to reduce mortality from infection. Fluid for culture should be obtained and inoculated directly into blood culture bottles at the bedside, to increase diagnostic yield from 50% to greater than 80%.<sup>8</sup> Culture results, however, may take days.

### What is the serum-ascites albumin gradient?

Albumin should be measured in both serum and ascitic fluid. The presence of portal hypertension is determined by the serum-ascites albumin gradient (SAAG), calculated by subtracting ascitic fluid albumin from serum albumin. A SAAG greater than or equal to 11 g/L predicts portal

hypertension with 97% accuracy.<sup>9</sup>

Total protein concentration of ascitic fluid helps to further characterise the nature and cause of the ascites (Table 3). Other tests are ordered as indicated (Table 4).

## How to treat cirrhotic ascites

Successful management of ascites depends upon accurate diagnosis of the cause.<sup>6,10</sup> The goal of treatment is to improve quality of life, as therapy does not improve prognosis and may cause complications. Small amounts of asymptomatic ascites should not be treated. Etiologic factors should be reversed. Bed rest is not recommended.

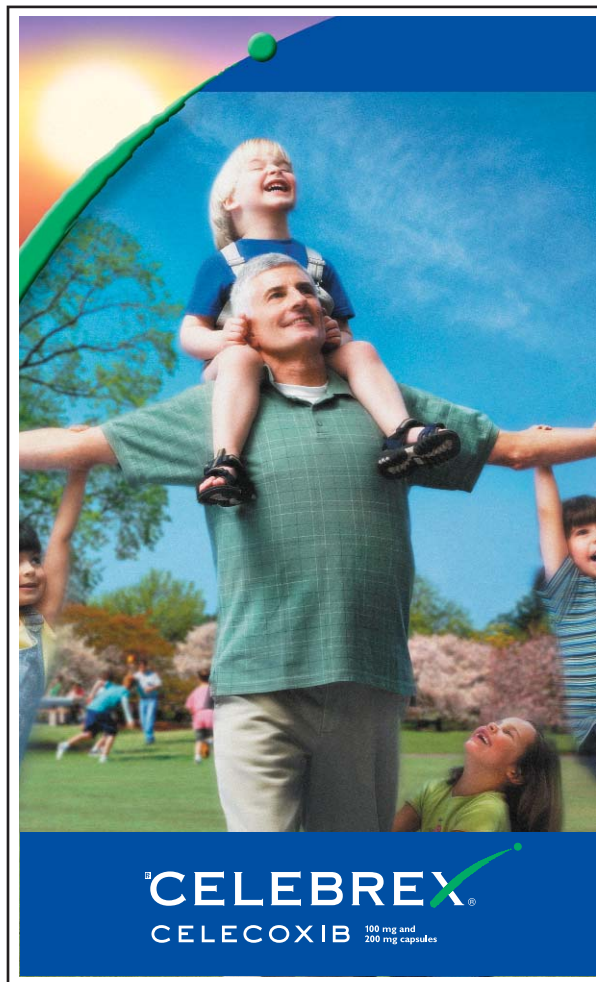
**Dietary sodium restriction:** Dietary sodium restriction is important to achieve negative sodium balance. Two grams (88 mmol) of sodium per day is appropriate for most

patients, however, restriction of 1 g to 1.5 g (44 mmol to 66 mmol) per day may be necessary in patients with significant ascites or very low urine sodium output (less than 10 mEq/L).

Such limitations are unpalatable and professional dietary advice is often necessary to improve compliance. Salt substitutes are contraindicated in patients on potassium-sparing diuretics as they contain potassium chloride. Fluid restriction is not needed unless the patient has hyponatremia.

**Diuretic therapy:** Diuretics are the mainstay of therapy. Spironolactone inhibits aldosterone. It causes greater natriuresis than loop diuretics, such as furosemide, in cirrhotic patients, and

may suffice as monotherapy. Combination therapy of spironolactone and furosemide has a synergistic natriuretic effect and is frequently required. Starting doses are 100 mg spironolactone and 40 mg furosemide once daily.<sup>1</sup> They may be increased to maximum doses of





# Ascites

Table 5

## Patterns of bacterial peritonitis

Type	PMN count (cells/mm <sup>3</sup> )	Bacterial Culture	Management
Spontaneous bacterial peritonitis	≥ 250	Positive (monomicrobial)	Cefotaxime 2 g IV q8h x 5 days
Culture-negative neutrocytic bacterascites	≥ 250	Negative	Cefotaxime 2 g IV q8h x 5 days
Monomicrobial non-neutrocytic bacterascites	< 250	Positive (monomicrobial)	Symptoms: as SBP No symptoms: • repeat paracentesis • as SBP if + tap and another + culture
Polymicrobial bacterascites	< 250	Positive (polymicrobial)	• broaden antibiotics • consider surgery
Secondary bacterial peritonitis	≥ 250	Positive (polymicrobial)	• CT abdomen • broaden antibiotics • consider surgery

Adapted from Garcia N Jr, Sanyal AJ: Minimizing ascites: Complication of cirrhosis signals clinical deterioration. *Postgrad Med* 2001; 109(2):91-103.

## Practice Pointer

**What if the patient does not respond to diuretics?**

**Refractory ascites unresponsive to sodium restriction and high-dose diuretic therapy occurs in 10% of patients.<sup>11</sup> There are two definitions:**

1. Less than 200g daily weight loss occurs despite compliance with sodium restriction and maximum doses of diuretics for two weeks.
2. Ascites cannot be mobilised or recurrence cannot be prevented because of diuretic-related complications.<sup>12</sup>

Refractory ascites has a 50% mortality at six months. Other treatments are required.

400 mg spironolactone and 160 mg furosemide once daily if urine sodium is low or response is inadequate. Spironolactone should be increased only every five to seven days as its half-life is 35 hours. If mastalgia develops, amiloride may be substituted for spironolactone starting at 10 mg a day and increasing to 40 mg a day. Failure to lose weight and urinary sodium excretion greater than reported dietary intake suggests dietary indiscretion.

Diuretic therapy is limited by side effects (encephalopathy, serum sodium below 125 mmol/L, or serum creatinine greater than 130 mmol/L) and slow mobilisation of ascites (Table 5). Twice weekly, renal function and serum electrolytes should be monitored during dose adjustment. Target weight loss should be

1 kg to 2 kg a day if peripheral edema is present but only 0.5 kg a day in patients without edema.<sup>11</sup>

### Other treatments:

Therapeutic paracentesis is the removal of large volumes of fluid. Hemodynamic changes, hyponatremia, and azotemia may occur after removal of 4 L to 15 L of fluid, requiring administration of a plasma expander, usually albumin.<sup>13</sup> Albumin, 6 g to 8 g, should be given per liter of fluid removed for paracenteses greater than 5 L. Paracentesis does not improve survival rate, and ascites frequently recurs requiring repeat procedures.

Transjugular intrahepatic portosystemic shunt (TIPSS) achieves portal decompression, mobilising ascitic fluid in 50% to 90% of patients with refractory ascites. The procedure complication rate is less than 10%, however, 30% develop encephalopathy. Risk factors are previous encephalopathy,

advanced liver failure, and large shunt diameter. If severe and refractory to treatment, the TIPSS may be reversed. The TIPSS may

stenose over time and must be monitored by interval ultrasound with Dopplers. Occlusion is rectified with angiography and stent dilatation.

Peritoneovenous shunts were developed to return ascitic fluid directly back to the systemic circulation. They are rarely used since the development of TIPSS.

Liver transplantation corrects portal hypertension and changes the course of progressive liver failure. Unfortunately, not all patients are candidates and those who are can wait years for a donor

organ.

## What is SBP?

Spontaneous bacterial peritonitis (SBP) is the most common infection in patients with cir-



Anti-inflammatory analgesic agent. Product Monograph available upon request.  
**General warnings for NSAIDs should be borne in mind.**  
 CELEBREX® is a registered trademark of G.D. Searle & Co., used under permission by Pharmacia Canada Inc.

Co-promoted with

**PHARMACIA**  
 Pharmacia Canada Inc.  
 Mississauga, Ontario  
 L5R 4E3

**Pfizer**  
 Pfizer Canada Inc.  
 Kirkland, Quebec  
 H9J 2M5

**CELEBREX**  
 CELECOXIB 100 mg and 200 mg capsules

Member  
 PAB® (R&D)

rhctic ascites and is often fatal. It is present in up to 20% of patients with gastrointestinal bleeding at the time of admission.<sup>14</sup> The annual risk for developing SBP after onset of ascites is 20% to 30%. Predisposing factors include prior SBP, recent variceal hemorrhage, ascitic fluid protein less than 10 g/L, advanced liver failure, urinary tract infection, and intestinal bacterial overgrowth.

The most common symptoms are fever (69%) and abdominal pain (59%). Other features include encephalopathy, diarrhea, ileus, hypothermia, and shock. Importantly, up to one-third are asymptomatic. SBP worsens the hyperdynamic circulatory state and contributes to early rebleeding after variceal hemorrhage and to the development of hepatorenal syndrome. Diagnosis is made by PMN count equal or greater than 250/mm<sup>3</sup> and positive monomicrobial bacterial culture of ascitic fluid.

## How to treat SBP

Despite treatment, SBP prognosis is poor with an in-hospital mortality of 20%. Treatment of choice is cefotaxime, as 70% of cases are due to gram-negative organisms, 25% gram-positive, while anaerobes are uncommon. All patients with ascitic PMN count greater or equal to 250/mm<sup>3</sup> should receive 2 g, cefotaxime, every eight hours for five days.<sup>15</sup> Dosage need not be adjusted for hepatic or renal insufficiency. Aminoglycosides should

not be used because cirrhotic patients are at increased risk of nephrotoxicity. Plasma volume expansion with albumin may reduce the development of renal impairment and death.<sup>16</sup> Repeat paracentesis should be performed if there is no clinical improvement.

Patients may have SBP but demonstrate other patterns of results from their paracenteses and cultures. Because of the high mortality rate, one should have a low threshold for instituting therapy, which can be withdrawn later.

***The annual risk for developing SBP after onset of ascites is 20% to 30%.***

**SBP Prophylaxis:** The one-year probability of recurrence of SBP is 40% to 70%. Prophylactic antibiotic is recommended for patients with cirrhotic ascites admitted for gastrointestinal bleeding.

Ongoing prophylaxis is recommended for patients with a previous episode of SBP. Norfloxacin, 400 mg daily, selectively inhibits gram-negative flora and is the drug of choice. Used indefinitely, it reduces the rate of SBP recurrence from 68% to 20%.<sup>15</sup> Trimethoprim/sulfamethoxazole, 160/800 mg daily, is effective also.<sup>17</sup> Despite decreased SBP recurrence, no change in mortality has been demonstrated. All patients who have had an episode of SBP should be considered for liver transplantation. **Dx**



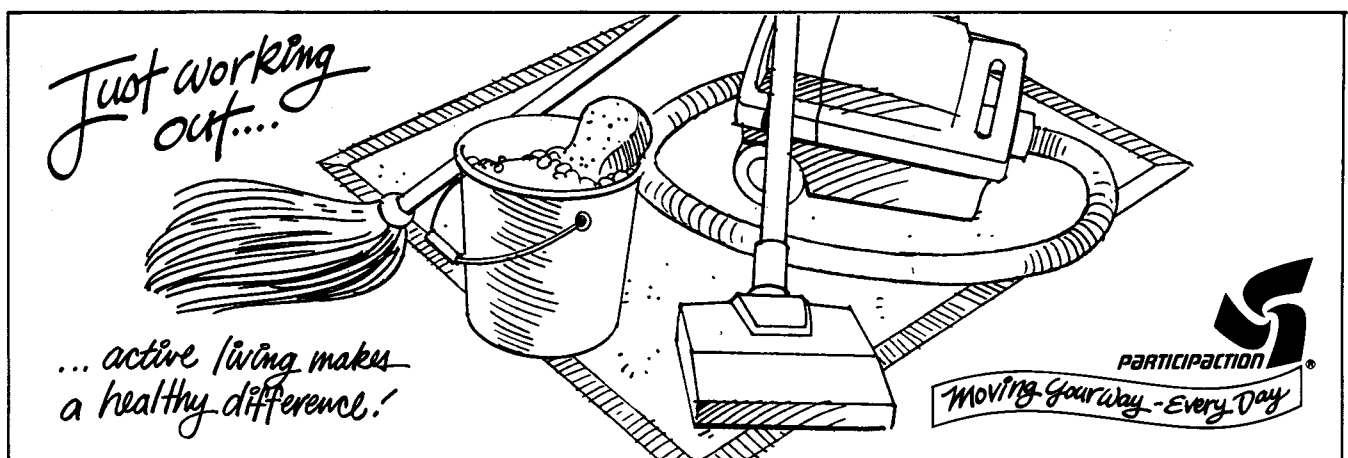
## Take-home message

Ascites is most often due to cirrhosis and is the most common complication of cirrhosis. It heralds a poor prognosis and liver transplantation should be considered. Management requires dietary sodium restriction and diuretics.

Diagnostic paracentesis is essential in the initial assessment of new-onset ascites and when those with established cirrhosis and ascites experience a change in their clinical status. The most important ascitic fluid tests are PMN count and culture to rule out infection, and SAAG to assess for portal hypertension. Patients should be considered for secondary prophylaxis of SBP.

### References

1. Runyon BA: Care of patients with ascites. *N Eng J Med* 1994; 330:337-42.
2. Gines P, Quintero E, Arroyo V, et al: Compensated cirrhosis: natural history and prognostic factors. *Hepatology* 1987; 7:122-8.
3. D'Amico G, Morabito A, Pagliaro L, et al: Survival and prognostic indicators in compensated and decompensated cirrhosis. *Dig Dis Sci* 1986; 31:468-75.
4. Cattau EI, Benjamin SB, Knuff TE, et al: The accuracy of the physical exam in the diagnosis of suspected ascites. *JAMA* 1982; 247:1164-6.
5. Inadomi J, Cello JP, Koch J: Ultrasonographic determination of ascitic volume. *Hepatology* 1996;24:549-51.
6. Runyon BA: Management of adult patients with ascites caused by cirrhosis. *Hepatology* 1998;27:264-272.
7. Runyon BA: Paracentesis of ascitic fluid: a safe procedure. *Arch Intern Med* 1986; 146:2259-61.
8. Runyon, BA, Canawati, HN, Akriviadis, EA: Optimization of ascitic fluid culture technique. *Gastroenterology* 1988;95:1351-55.
9. Runyon, BA, Montano, AA, Akriviadis EA, et al: The serum-ascites albumin gradient is superior to the exudates-transudate concept in the differential diagnosis of ascites. *Ann Intern Med* 1992; 117:215-20.
10. Pockros PJ, Esrason KT, Nguyen C, et al: Mobilization of malignant ascites with diuretics is dependent on ascitic fluid characteristics. *Gastroenterology* 1992; 103:1302-6.
11. Stanley MM, Ochi S, Lee KK, et al: Peritoneovenous shunting as compared with medical treatment in patients with alcoholic cirrhosis and massive ascites. *New Engl J Med* 1989; 321:1632-8.
12. Arroyo V, Gines P, Gerbes AL, et al: Definition and diagnostic criteria of refractory ascites and hepatorenal syndrome in cirrhosis. *Hepatology* 1996; 23(1):164-76.
13. Pozzi M, Osculati G, Boari G, et al: Time course of circulatory and humoral effects of rapid total paracentesis in cirrhotic patients with tense, refractory ascites. *Gastroenterology* 1994; 106:709-19.
14. Bleichner G, Boulanger R, Squara P, et al: Frequency of infections in cirrhotic patients presenting with acute gastrointestinal haemorrhage. *Br J Sug* 1986; 73:724-6.
15. Such J, Runyon BA: Spontaneous bacterial peritonitis. *Clin Infect Dis* 1998;27: 669-74.
16. Sort P, Navasa M, Arroyo V, et al: Effect of intravenous albumin on renal impairment and mortality in patients with cirrhosis and spontaneous bacterial peritonitis. *N Eng J Med* 1999; 341:403-9
17. Singh N, Gayowski T, Yu VL, et al: Trimethoprim-sulfamethoxazole for the prevention of spontaneous bacterial peritonitis in cirrhosis: A randomized trial. *Ann Intern Med* 1995; 122:595-8.



---

# Ascites

# Frequently Asked Questions



## Ascites: Tapping Into the Problem

As presented at the University of Toronto

Elaine Yong, BSc, MD; and Mary Anne Cooper, MSc, MD, FRCPC

### 1. How should I investigate?

Diagnostic paracentesis is required in all patients with new onset ascites and those with established cirrhosis and ascites who undergo clinical change. It is safe despite that 70% of cirrhotics with ascites have an abnormal international normalised ratio and thrombocytopenia.

### 2. What tests should I order on the ascitic fluid?

The most important test is the cell count and differential for the polymorphonuclear count.

### 3. What is SAAG?

The presence of portal hypertension is determined by the serum-ascites albumin gradient (SAAG), calculated by subtracting ascitic fluid albumin from serum albumin. A SAAG greater than or equal to 11 g/L predicts portal hypertension with 97% accuracy.

### 4. What if a patient does not respond to diuretics?

Other treatments include therapeutic paracentesis, trans-jugular intrahepatic portosystemic shunts, and liver transplantation.

### 5. What is SBP?

Spontaneous bacterial peritonitis (SBP) is the most common infection in patients with cirrhotic ascites and is often fatal.

**For an in-depth article on ascites, please go to page 81.**