Spontaneous bacterial peritonitis in adults: Diagnosis

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INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is defined as an ascitic fluid infection without an evident intra-abdominal surgically treatable source [1]. The presence of SBP, which almost always occurs in patients with cirrhosis and ascites, is suspected because of suggestive signs and symptoms, such as fever, abdominal pain, or altered mental status (table 1), though some patients are asymptomatic and are detected when they undergo paracentesis after being admitted to the hospital for another reason. (See "Spontaneous bacterial peritonitis in adults: Clinical manifestations".)

This topic will review the diagnosis of SBP, as well as distinguishing SBP from secondary bacterial peritonitis or alcoholic hepatitis with ascites. The performance of paracentesis, the pathogenesis, clinical manifestations, and treatment of SBP, and the general evaluation of adults with ascites are discussed elsewhere. (See "Diagnostic and therapeutic abdominal paracentesis" and "Pathogenesis of spontaneous bacterial peritonitis" and "Spontaneous bacterial peritonitis in adults: Clinical manifestations" and "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis" and "Spontaneous bacterial peritonitis variants" and "Evaluation of adults with ascites".)

The American Association for the Study of Liver Diseases (AASLD) and other professional societies have updated their guidance on the management of adult patients with ascites due to cirrhosis [2,3]. The discussion that follows is generally consistent with society guidance.

OVERVIEW OF DIAGNOSTIC APPROACH

Spontaneous bacterial peritonitis (SBP) should be suspected in patients with cirrhosis who develop signs or symptoms such as fever, abdominal pain, altered mental status, abdominal tenderness, or hypotension (table 1). In addition, patients with ascites admitted to the hospital for other reasons should also undergo paracentesis to look for evidence of SBP. A low clinical suspicion for SBP does **not** obviate the need for testing [4]. Paracentesis can be performed in the interventional radiology suite or at the bedside. It is important that trained personnel be available to perform the procedure at off hours (such as at night or on weekends). Paracentesis should be carried out promptly in patients with suspected SBP, as delays in performing paracentesis have been associated with increased mortality. (See 'Paracentesis' below and "Spontaneous bacterial peritonitis in adults: Clinical manifestations", section on 'Clinical manifestations' and "Diagnostic and therapeutic abdominal paracentesis".)

The importance of paracentesis was demonstrated in a review of a database of 17,711 patients with cirrhosis and ascites who were admitted to the hospital with a primary diagnosis of ascites or encephalopathy [5]. Paracentesis was performed in 61 percent. Patients who underwent paracentesis had a lower in-hospital mortality rate than those who did not undergo paracentesis (6.5 versus 8.5 percent; adjusted odds ratio 0.55, 95% CI 0.41-0.74).

If SBP is suspected, a paracentesis should be performed with analysis of the ascitic fluid (algorithm 1). It is important that the paracentesis be performed **prior** to the administration of any antibiotics. Appropriate handling of the ascitic fluid is crucial to ensure the proper tests are obtained, to minimize the risk of skin flora contaminating the cultures, and to avoid obtaining a falsely negative culture. Tests obtained on the fluid include aerobic and anaerobic cultures, cell count and differential, and fluid chemistries (albumin, protein, glucose, lactate dehydrogenase, amylase, and in some cases bilirubin). (See 'Handling the ascitic fluid' below.)

A diagnosis of SBP is made if the polymorphonuclear cell (PMN, also referred to as neutrophils) count in the ascitic fluid is ≥250 cells/mm^3, culture results are positive, and secondary causes of peritonitis are excluded. However, in selected cases, fluid chemistries may be needed to support the diagnosis. While awaiting the results of the fluid cultures, patients with a PMN count ≥250 cells/mm^3 should be started on empiric antibiotic treatment. Some publications recommend treatment when the PMN count is >250 cells/mm^3 and no treatment if the PMN count is <250 cells/mm^3. However, some patients will have a PMN count equal to 250 cells/mm^3, and such patients should be treated. (See 'Interpretation of ascitic fluid test results' below and "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis", section on 'Treatment'.)

OBTAINING ASCITIC FLUID

Diagnosing spontaneous bacterial peritonitis (SBP) depends on analysis of the ascitic fluid, which is typically obtained by performing a paracentesis. Prior to performing a paracentesis in a patient suspected of having SBP, it is important to have the equipment necessary not only to obtain the fluid, but also to send it for analysis (eg, blood culture bottles, purple- and red-top blood-drawing tubes).

Paracentesis — It is vital that patients suspected of having SBP undergo abdominal paracentesis **before** receiving any antibiotics (a single dose of a broad-spectrum antibiotic can lead to no growth in 86 percent of patients after six hours) [6]. In the vast majority of patients, a paracentesis can be safely carried out despite an elevated international normalized ratio (INR). Giving fresh frozen plasma to attempt to correct the international normalized ratio (INR) may be futile and even harmful in one-third of patients [7]. Paracentesis should not be delayed in patients suspected of having SBP. In a retrospective study of 239 hospitalized patients with SBP, mortality rates were higher for those who underwent paracentesis 12 to 72 hours after hospitalization compared with those who underwent paracentesis within 12 hours of hospitalization (27 versus 13 percent; adjusted odds ratio 2.7, 95% CI 1.3-4.8) [8]. Each hour of delay in paracentesis was associated with a 3.3 percent increase in mortality. (See "Diagnostic and therapeutic abdominal paracentesis", section on 'Abnormal coagulation studies and thrombocytopenia'.)

The performance of paracentesis and the complications that may occur during and after paracentesis are discussed in detail elsewhere. (See "Diagnostic and therapeutic abdominal paracentesis".)

Handling the ascitic fluid — Appropriate handling of the ascitic fluid is crucial to minimize the risk of skin flora contaminating the cultures. Appropriate handling of the ascitic fluid is also required to minimize the risk of obtaining a falsely negative culture, possibly leading to the diagnosis of culture-negative neutrocytic ascites (ie, ascites with a PMN count ≥250 cells/mm^3, but with negative cultures of the ascitic fluid) [9]. Most patients with culture-negative neutrocytic ascites actually have SBP. (See "Spontaneous bacterial peritonitis variants".)

The ascitic fluid should be tested for the following:

- Aerobic and anaerobic culture
- Cell count and differential
- Gram stain
- Albumin

- Protein
- Glucose
- Lactate dehydrogenase
- Amylase
- Bilirubin (if the fluid is dark orange or brown)

Typically, two 20 mL syringes of ascitic fluid will be needed for the above tests.

If tuberculous peritonitis is suspected, additional fluid should be obtained and sent for an acid-fast bacteria smear and mycobacterial culture. However, these tests will frequently fail to detect tuberculous peritonitis, so if there is high suspicion, peritoneoscopy with mycobacterial culture and histology of a biopsied tubercle are the most rapid route to the diagnosis. (See "Abdominal tuberculosis".)

Culture — Cultures should be sent in blood culture bottles. At least two bottles (one for aerobic and one for anaerobic culture) should be inoculated immediately at the bedside using a new, sterile needle. A needle that has passed through the skin should **not** be used to inoculate the bottles because it may lead to contamination of the sample with skin flora. Ideally, at least 10 mL of fluid should be introduced into each bottle. The volume of fluid introduced is ideally coordinated with the local pathology laboratory.

We use the following approach when obtaining ascitic fluid cultures:

- Immediately prior to the paracentesis, we wipe the top of each blood culture bottle with an alcohol wipe and leave the wipe on the bottle top in an attempt to maintain sterility while the paracentesis is being performed.

- During the paracentesis, a 20 mL syringe is connected to the needle that is in the abdominal wall and filled with ascitic fluid. Additional syringes are filled to obtain fluid for additional testing (eg, cell count and chemistries), and if needed, to increase the volume of fluid obtained for culture.

- Immediately after the paracentesis, a new, sterile needle should be placed on the 20 mL syringe. The new needle can be used to inoculate multiple bottles. However, each syringe should have its own new needle. This is to decrease the risk of a needle-stick injury that could occur if the needle is transferred among syringes.

- The alcohol wipes are removed and the blood culture bottles are inoculated, preferably with at least 10 mL of ascitic fluid each. However, some bottles will not permit more than the recommended amount of fluid to be instilled without infringing upon the "head space"

in the bottle, in which case the upper end of the recommended amount of fluid should be instilled.

- If tuberculous peritonitis is suspected, ascitic fluid should be sent to the lab as per local procedure.

- The blood culture bottles are sent to the microbiology laboratory immediately for both aerobic and anaerobic culture.

It is important to use blood culture bottles because SBP is a low-colony-count monomicrobial infection similar to bacteremia. If a syringe or tube of fluid is sent to the laboratory for culture, the sensitivity for detecting SBP is dramatically decreased [9-11]. Culturing ascitic fluid as if it were blood (with immediate bedside inoculation of ascitic fluid into blood culture bottles) has been shown to increase the culture-positivity of the ascitic fluid. In a study of patients with an ascitic fluid PMN count ≥250 cells/mm^3 (in the absence of prior antibiotic treatment, pancreatitis, tuberculous peritonitis, or malignancy-related ascites), immediate inoculation increased the sensitivity of cultures from about 50 to 77 percent (with delayed inoculation) to 80 to 100 percent [1,10,11].

The volume of fluid cultured also has a dramatic impact on the sensitivity of ascitic fluid cultures. In one report, for example, inoculation of 10 or 20 mL of fluid into 100 mL blood culture bottles led to a much higher culture-positivity rate than a 1 mL inoculum (93 versus 53 percent) [9].

Gram stain — A few milliliters of ascitic fluid should be sent for Gram stain in a sterile urine container or red-top tube. Centrifugation of the fluid prior to performing a Gram stain is not necessary since it does not increase the yield and may actually decrease the likelihood of obtaining a positive result [9].

Fluid from the blood culture bottles can only be used for Gram stain after they have incubated for 12 to 24 hours, so sending a separate sample immediately after the paracentesis permits receiving the Gram stain results much more rapidly.

Cell count — Approximately 1 mL of fluid should be injected into a purple-top EDTA blood-drawing tube for cell count. An accurate cell count cannot be obtained if the fluid is allowed to clot or is submitted in a non-anticoagulated tube. The cell count and differential should be ordered "stat," otherwise many laboratories will prioritize the cell count below routine peripheral blood counts.

Chemistries — Several milliliters of fluid should be injected into a red-top blood-drawing tube for chemistries. Chemistries obtained should include albumin (so the serum-ascites albumin gradient can be determined), total protein concentration, glucose, lactate dehydrogenase, and amylase. If the fluid is dark orange or brown, a bilirubin concentration should be obtained.

INTERPRETATION OF ASCITIC FLUID TEST RESULTS

Spontaneous bacterial peritonitis (SBP) is typically diagnosed if there is an elevated ascitic fluid absolute polymorphonuclear cell (PMN, also referred to as neutrophils) count (≥250 cells/mm^3), a positive ascitic fluid bacterial culture, and absence of secondary causes of peritonitis, such as bowel perforation. However, in some cases, additional tests may be needed to support the diagnosis or to differentiate SBP from secondary bacterial peritonitis.

Culture and Gram stain results — In the setting of an elevated PMN count (≥250 cells/mm^3), positive culture results from ascitic fluid not only confirm a diagnosis of SBP, but also allow for tailored antibiotic therapy. However, antibiotic therapy should not be delayed while awaiting culture results in patients with a PMN count ≥250 cells/mm^3. Instead, patients should be started on broad-spectrum antibiotics, with narrowing of the antibiotic coverage once a pathogen has been identified. Pathogens commonly associated with SBP included *Escherichia coli*, streptococcal species, and *Klebsiella pneumoniae* (table 2). (See "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis", section on 'Treatment' and "Pathogenesis of spontaneous bacterial peritonitis", section on 'Microbiology and bacterial entry into ascitic fluid'.)

Gram stain is notoriously insensitive for detecting SBP and is associated with a high false-positive rate [9]. One study found that 16 of 31 positive Gram stains were false positives, and that only 1 Gram stain out of 796 led to a change in antibiotic treatment [12]. However, a Gram stain can help differentiate SBP from secondary bacterial peritonitis due to gut perforation. In the latter, the Gram stain may show multiple different bacterial forms. (See 'Ascitic fluid analysis' below.)

Ascitic fluid cell count — The absolute PMN count in the ascitic fluid is calculated by multiplying the total white blood cell count (or total "nucleated cell" count) by the percentage of PMNs in the differential. The diagnosis of SBP is established by a positive ascitic fluid bacterial culture and an elevated ascitic fluid absolute PMN count (≥250 cells/mm^3).

If the laboratory provides an "expanded differential" including bands or even earlier forms of PMNs, these should be added to the count of PMNs. The cell count and differential are

performed manually, so the accuracy of the differential is dependent upon the skill of the medical technologist. Some investigators have found that automated cell counts can be accurate [13]. However, this has not been our experience; we have found that their accuracy is poor when the PMN count is low. Nevertheless, the automated approach has the potential to improve the speed with which results are obtained if it can be validated [14].

One potential source of error in the PMN count is that hemorrhage into the ascitic fluid, as in a traumatic paracentesis, leads to red cell and white cell entry into the fluid. A corrected PMN count should be calculated if there is bloody fluid:

- One PMN is subtracted from the absolute PMN count for every 250 red cells/mm^3 [15].

PMNs lyse rapidly, much more so than red cells. Thus, if the bleeding episode occurred prior to (rather than during) paracentesis, the PMNs that entered the fluid may have lysed, and the corrected PMN count may be a negative number.

The results of the cell count should be reviewed and a decision made about treatment within a few hours of the paracentesis. Delaying empiric antibiotic treatment could result in the death of the patient from infection. It is prudent to write the initial antibiotic order to be given "stat" to prevent an inadvertent delay in administration of the first dose. (See "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis".)

Use of dipsticks to detect PMNs could provide presumptive evidence of SBP in 90 to 120 seconds and is being studied. Use of dipsticks could lead to initiation of treatment within minutes rather than hours. (See 'Investigational tests' below.)

Ascitic fluid chemistries — Occasionally, a diagnosis of SBP cannot be made based on the results of cell count, differential and culture, particularly if there is also concern for secondary bacterial peritonitis. In those cases, examination of the fluid chemistries may help confirm the diagnosis or suggest an alternative diagnosis. (See 'Distinguishing spontaneous from secondary bacterial peritonitis' below.)

Serum-ascites albumin gradient — The vast majority of patients with SBP have advanced cirrhosis with portal hypertension. The serum-ascites albumin gradient indirectly measures portal pressure [16,17]. It is helpful in the diagnosis of SBP because, with the exception of patients with nephrotic syndrome, SBP rarely develops in patients who do not have portal hypertension [18]. (See "Pathogenesis of spontaneous bacterial peritonitis".)

The albumin concentration of ascitic fluid and serum must be obtained on the same day. The ascitic fluid value is subtracted from the serum value to obtain the gradient (table 3):

- If the difference (**not a ratio**) is >1.1 g/dL, the patient has portal hypertension, with 97 percent accuracy [17]
- If the difference is <1.1 g/dL, portal hypertension is not present [17], and SBP is unlikely

Ascitic fluid total protein concentration — Measurement of the ascitic fluid total protein concentration assists in separating SBP from secondary bacterial peritonitis. It correlates inversely with the risk of developing SBP [19]. Patients with the most dilute ascites (ie, protein concentration less than 1 g/dL) have the lowest concentration of opsonins in the ascitic fluid and are at the highest risk for SBP [19,20]. The total protein concentration does not change during an episode of SBP [21]. (See 'Distinguishing spontaneous from secondary bacterial peritonitis' below.)

Ascitic fluid glucose concentration — Neutrophils can consume large quantities of glucose. Thus, the concentration of PMNs in ascitic fluid and their degree of stimulation have a rough inverse correlation with the glucose concentration [21]. The glucose concentration generally remains above 50 mg/dL (2.8 mmol/L) in SBP but frequently falls below this level in secondary bacterial peritonitis. This difference may be related to the fact that patients with SBP typically have lower ascitic fluid PMN counts than patients with secondary bacterial peritonitis [22]. In the setting of gut perforation, the ascitic fluid glucose concentration may fall to near zero [6].

Ascitic fluid lactate dehydrogenase — Lactate dehydrogenase (LDH) in ascitic fluid is released from PMNs that have lysed. The concentration is increased in SBP [21] and is even further elevated in secondary bacterial peritonitis [6]. One study, for example, analyzed 22 patients whose ascitic fluid was examined before and then during an episode of SBP. The LDH concentration increased significantly during infection [21]. The upper limit of normal for LDH varies by laboratory. In sterile ascitic fluid in the setting of cirrhosis, the LDH is generally in the range of 43 +/-20 units/L [21].

Ascitic fluid amylase — The amylase concentration is increased in ascitic fluid in patients with pancreatitis or gut perforation [6,23]. Every segment of the gut, with the exception of the gallbladder, leaks amylase into the fluid when it perforates. In one report, two patients with pancreatic ascites had a mean ascitic fluid amylase concentration of 1957 international unit/L, a value more than five times that in the plasma. By contrast, the mean amylase concentration in patients with nonpancreatic ascites was 42 international unit/L, a value just under one-half of the plasma value [23].

Ascitic fluid bilirubin concentration — An elevated bilirubin concentration in the ascitic fluid suggests perforation of the gallbladder into the peritoneum (choleperitoneum) [24]. The bilirubin concentration should only be measured if the ascitic fluid is dark orange or brown.

Gallbladder perforation is likely if the ascitic fluid bilirubin concentration is higher than that of serum, is greater than 6 mg/dL, and is not associated with an elevated ascitic fluid amylase (which would suggest upper intestinal perforation rather than gallbladder perforation). In patients with causes of ascites other than gallbladder perforation, the ascitic fluid bilirubin concentration is typically low. In one report of patients with ascites not due to gallbladder perforation, the ascitic fluid bilirubin concentration averaged 0.7 mg/dL, a value that was approximately one-third of the plasma value [24].

Investigational tests — Testing for leukocyte esterase (and thus PMNs) in ascitic fluid using a dipstick as a rapid bedside test for SBP is being developed but is not yet available.

Initial tests used a reagent strip designed for testing urine [25-28]. Reported sensitivities range from 31 to 100 percent, with specificities of 81 to 100 percent [29]. A large study that looked at 2123 samples demonstrated a sensitivity of only 45 percent, with a specificity of 99 percent [26].

A dipstick specifically designed to be used in ascitic fluid is in development and will likely provide much better sensitivity [27]. Ongoing studies will help to clarify the role of this approach, which is potentially attractive since it may reduce the time before initiating appropriate treatment. One practical issue in the United States and other countries is the requirement that bedside laboratory testing comply with hospital accreditation standards.

Measurement of ascitic fluid lactoferrin has also been proposed as a marker for SBP. Lactoferrin is an iron-binding protein that is believed to help protect humans from enteric pathogens and contributes to the antimicrobial effects of PMNs. Higher levels in ascitic fluid have been correlated with the presence of SBP. A study involving 148 patients with ascites (with 218 ascitic fluid samples) found a sensitivity and specificity of 96 and 97 percent, respectively, using a cutoff level of 242 ng/mL [30]. Additional validation studies are needed.

Unhelpful tests — In the late 1980s and early 1990s, numerous papers were published that purported to show the utility of ascitic fluid pH, lactate, and other difficult-to-measure indirect markers of infection. Subsequent larger studies that used available culture methods and appropriate grouping of patients failed to confirm the utility of these tests [31,32].

DISTINGUISHING SPONTANEOUS FROM SECONDARY BACTERIAL PERITONITIS

Spontaneous bacterial peritonitis (SBP) must be differentiated from secondary bacterial peritonitis. Secondary bacterial peritonitis is an ascitic fluid infection in which there is a positive ascitic fluid bacterial culture and an ascitic fluid PMN count ≥250 cells/mm^3 in the setting of a

surgically treatable intra-abdominal source of infection [6,22]. The distinction of SBP from secondary bacterial peritonitis is based largely upon ascitic fluid analysis, imaging studies, and the response to treatment (algorithm 1) [6].

Two varieties of secondary bacterial peritonitis have been reported: perforation peritonitis (eg, perforated peptic ulcer into ascites) and nonperforation peritonitis (eg, perinephric abscess) [6,33,34].

The distinction of secondary bacterial peritonitis from SBP is crucial because of the importance of appropriate therapy:

- The mortality of secondary bacterial peritonitis approaches 100 percent if treatment consists only of antibiotics with no surgical intervention [6].
- The mortality of SBP is approximately 80 percent if a patient receives an unnecessary exploratory laparotomy [35].

A scoring system for distinguishing SBP from secondary peritonitis has been developed, although differentiating the two conditions may be challenging [36]. Fortunately, secondary bacterial peritonitis is unusual; approximately one episode will be encountered for every 20 episodes of SBP [37].

Clinical signs and symptoms — The signs and symptoms of both SBP and surgical peritonitis in the presence of ascites can be surprisingly subtle. Ascites prevents the development of a rigid abdomen by separating the visceral from the parietal peritoneal surfaces [6]. Thus, even with frank perforation of the colon and leakage of tens of grams of fecal material into the peritoneal cavity, a classic surgical abdomen does not develop.

Ascitic fluid analysis — The initial (pretreatment) ascitic fluid analysis can be extremely helpful in determining the degree of suspicion of secondary bacterial peritonitis. Proposed laboratory criteria for diagnosis of secondary bacterial peritonitis (sometimes referred to as Runyon's criteria) include at least two of the following ascitic fluid findings [6]:

- Total protein >1 g/dL (10 g/L)
- Glucose <50 mg/dL (2.8 mmol/L)
- LDH >the upper limit of normal for serum

In addition, cultures showing a polymicrobial infection or a Gram stain demonstrating large numbers of different bacterial forms suggest gut perforation (picture 1) [33].

Studies have found that these criteria are specific for secondary bacterial peritonitis. A study that evaluated these criteria compared 24 patients with secondary bacterial peritonitis with a

control population of 106 patients with SBP [22]. The estimated sensitivity and specificity of the criteria for predicting secondary bacterial peritonitis were 67 and 96 percent, respectively. Fulfillment of the two of the criteria and/or the presence of a polymicrobial ascitic fluid culture was present in 96 percent of patients. In a second study, these criteria were met in 67 percent of patients with secondary bacterial peritonitis versus only 4 percent of those with SBP [6].

The ascitic fluid carcinoembryonic antigen level and alkaline phosphatase levels may also suggest secondary bacterial peritonitis due to gut perforation. In one study, an ascitic fluid carcinoembryonic antigen >5 ng/mL and/or an alkaline phosphatase >240 international units/L was 92 percent sensitive and 88 percent specific for detecting gut perforation into ascitic fluid [38].

Imaging studies — Patients who meet the criteria for secondary bacterial peritonitis should undergo emergency plain and upright abdominal films and a computed tomographic scan of the abdomen. Emergency laparotomy should be performed if free air or a surgically treatable source of infection is documented [6]. Even with surgery, mortality rates among patients with cirrhosis and secondary bacterial peritonitis are high (54 percent in one study) [22,33].

Response to treatment — If neither free air nor a surgically treatable source of infection is documented, emergency laparotomy is not justified, even if the suspicion for secondary bacterial peritonitis persists. Repeat paracentesis after 48 hours of treatment (with coverage of aerobic and anaerobic flora) can be helpful in this setting:

- If the follow-up PMN count is lower than the pretreatment value, and the initial culture grows only one organism, the patient likely has SBP; in that case, the second culture will usually be sterile.

- If the PMN count rises and the initial culture grows multiple organisms (especially if enterococcus or fungi are among the flora), the patient probably has nonperforation secondary peritonitis and warrants additional imaging to look for an intra-abdominal abscesses. Many of these patients will require laparotomy [6].

This differential response to therapy assumes that an appropriate antibiotic has been administered. If an empiric antibiotic is chosen that does not penetrate ascitic fluid well or does not cover the flora fully, the response of a patient with SBP can mimic that of secondary bacterial peritonitis. (See "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis", section on 'Selecting empiric therapy'.)

Peritonitis developing during antibiotic treatment — A patient who is receiving broad-spectrum parenteral antibiotics and develops peritonitis likely has secondary bacterial

peritonitis. This is because SBP is exquisitely sensitive to appropriate treatment and is thus unlikely to develop in a patient already on broad-spectrum antibiotics. If such a patient develops bacterial peritonitis, a surgical source should be sought.

Other conditions masquerading as secondary bacterial peritonitis — Occasionally, peritoneal carcinomatosis or tuberculous peritonitis can be associated with a PMN count ≥250 cells/mm^3 and an initial ascitic fluid analysis that meets criteria for secondary bacterial peritonitis. (See 'Ascitic fluid analysis' above.)

There are two clues that the diagnosis may not be secondary bacterial peritonitis:

- A predominance of non-PMNs on the differential white cell count
- The absence of fever

In addition, SBP that is detected late may also meet criteria for secondary bacterial peritonitis and may have a slow PMN response to therapy. The monomicrobial nature of the infection and the sterility of the second culture help provide evidence that SBP is the correct diagnosis.

DISTINCTION FROM ALCOHOLIC HEPATITIS

The patient with alcoholic hepatitis warrants specific comment. These patients regularly develop fever, peripheral leukocytosis, and abdominal pain, which can masquerade as SBP. Furthermore, they also can develop SBP.

An important distinguishing point is that peripheral leukocytosis does not lead to an elevated ascitic fluid PMN count [39]. Thus, an elevated ascitic fluid PMN count must be presumed to represent SBP. If the patient has already been started on empiric antibiotic treatment because of a fever and/or peripheral leukocytosis, the antibiotics can be discontinued after 48 hours if ascitic fluid, blood, and urine cultures demonstrate no bacterial growth and the ascitic fluid PMN count is <250/mm^3. (See "Alcoholic hepatitis: Clinical manifestations and diagnosis", section on 'Clinical manifestations'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Portal hypertension and ascites".)

SUMMARY AND RECOMMENDATIONS

- **Clinical features –** Spontaneous bacterial peritonitis (SBP) should be suspected in patients with cirrhosis who develop suggestive signs or symptoms, such as fever, abdominal pain, altered mental status, abdominal tenderness, or hypotension (table 1). (See "Spontaneous bacterial peritonitis in adults: Clinical manifestations", section on 'Clinical manifestations'.)

- **Obtaining ascitic fluid –** If SBP is suspected, a paracentesis should be performed with analysis of the ascitic fluid. It is important that the paracentesis be performed **prior** to the administration of any antibiotics. There are no data to support prophylactic transfusion of blood products prior to paracentesis. Transfusion of fresh frozen plasma may actually be harmful. (See "Diagnostic and therapeutic abdominal paracentesis".)

  Appropriate handling of the ascitic fluid is crucial to ensure the proper tests are obtained, to minimize the risk of skin flora contaminating the cultures, and to avoid obtaining a falsely negative culture. (See 'Handling the ascitic fluid' above.)

- **Analysis of ascitic fluid –** The ascitic fluid should be tested for the following (table 4):

  - Aerobic and anaerobic culture (using bedside inoculation of blood culture bottles)
  - Cell count and differential
  - Gram stain
  - Albumin
  - Protein
  - Glucose
  - Lactate dehydrogenase
  - Amylase
  - Bilirubin (if the fluid is dark orange or brown)

- **Establishing the diagnosis –** A diagnosis of SBP is made if the polymorphonuclear cell (PMN, also referred to as neutrophils) count in the ascitic fluid is ≥250 cells/mm^3, culture results are positive, and secondary causes of peritonitis are excluded. However, in selected cases, fluid chemistries may be needed to support the diagnosis or to differentiate SBP from secondary bacterial peritonitis (algorithm 1).

  The distinction of secondary bacterial peritonitis from SBP is crucial because the former usually requires antibiotics and surgical treatment, whereas the latter only requires antibiotics. (See 'Distinguishing spontaneous from secondary bacterial peritonitis' above.)

- **Initial management –** While awaiting the results of the fluid cultures, patients with a PMN count ≥250 cells/mm^3 should be started on empiric treatment. (See "Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis", section on 'Treatment'.)

REFERENCES

1. Such J, Runyon BA. Spontaneous bacterial peritonitis. Clin Infect Dis 1998; 27:669.
2. Biggins SW, Angeli P, Garcia-Tsao G, et al. Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatology 2021; 74:1014.
3. Aithal GP, Palaniyappan N, China L, et al. Guidelines on the management of ascites in cirrhosis. Gut 2021; 70:9.
4. Chinnock B, Hendey GW, Minnigan H, et al. Clinical impression and ascites appearance do not rule out bacterial peritonitis. J Emerg Med 2013; 44:903.
5. Orman ES, Hayashi PH, Bataller R, Barritt AS 4th. Paracentesis is associated with reduced mortality in patients hospitalized with cirrhosis and ascites. Clin Gastroenterol Hepatol 2014; 12:496.
6. Akriviadis EA, Runyon BA. Utility of an algorithm in differentiating spontaneous from secondary bacterial peritonitis. Gastroenterology 1990; 98:127.
7. Rassi AB, d'Amico EA, Tripodi A, et al. Fresh frozen plasma transfusion in patients with cirrhosis and coagulopathy: Effect on conventional coagulation tests and thrombomodulin-modified thrombin generation. J Hepatol 2020; 72:85.
8. Kim JJ, Tsukamoto MM, Mathur AK, et al. Delayed paracentesis is associated with increased in-hospital mortality in patients with spontaneous bacterial peritonitis. Am J Gastroenterol 2014; 109:1436.
9. Runyon BA, Canawati HN, Akriviadis EA. Optimization of ascitic fluid culture technique. Gastroenterology 1988; 95:1351.
10. Runyon BA, Antillon MR, Akriviadis EA, McHutchison JG. Bedside inoculation of blood culture bottles with ascitic fluid is superior to delayed inoculation in the detection of spontaneous bacterial peritonitis. J Clin Microbiol 1990; 28:2811.
11. Wong CL, Holroyd-Leduc J, Thorpe KE, Straus SE. Does this patient have bacterial peritonitis or portal hypertension? How do I perform a paracentesis and analyze the results? JAMA

2008; 299:1166.

12. Chinnock B, Fox C, Hendey GW. Gram's stain of peritoneal fluid is rarely helpful in the evaluation of the ascites patient. Ann Emerg Med 2009; 54:78.
13. Angeloni S, Nicolini G, Merli M, et al. Validation of automated blood cell counter for the determination of polymorphonuclear cell count in the ascitic fluid of cirrhotic patients with or without spontaneous bacterial peritonitis. Am J Gastroenterol 2003; 98:1844.
14. Runyon BA. The evolution of ascitic fluid analysis in the diagnosis of spontaneous bacterial peritonitis. Am J Gastroenterol 2003; 98:1675.
15. Hoefs JC. Increase in ascites white blood cell and protein concentrations during diuresis in patients with chronic liver disease. Hepatology 1981; 1:249.
16. Hoefs JC. Serum protein concentration and portal pressure determine the ascitic fluid protein concentration in patients with chronic liver disease. J Lab Clin Med 1983; 102:260.
17. Runyon BA, Montano AA, Akriviadis EA, et al. The serum-ascites albumin gradient is superior to the exudate-transudate concept in the differential diagnosis of ascites. Ann Intern Med 1992; 117:215.
18. Ackerman Z. Ascites in Nephrotic syndrome. Incidence, patients' characteristics, and complications. J Clin Gastroenterol 1996; 22:31.
19. Runyon BA. Low-protein-concentration ascitic fluid is predisposed to spontaneous bacterial peritonitis. Gastroenterology 1986; 91:1343.
20. Runyon BA. Patients with deficient ascitic fluid opsonic activity are predisposed to spontaneous bacterial peritonitis. Hepatology 1988; 8:632.
21. Runyon BA, Hoefs JC. Ascitic fluid chemical analysis before, during and after spontaneous bacterial peritonitis. Hepatology 1985; 5:257.
22. Soriano G, Castellote J, Alvarez C, et al. Secondary bacterial peritonitis in cirrhosis: a retrospective study of clinical and analytical characteristics, diagnosis and management. J Hepatol 2010; 52:39.
23. Runyon BA. Amylase levels in ascitic fluid. J Clin Gastroenterol 1987; 9:172.
24. Runyon BA. Ascitic fluid bilirubin concentration as a key to choleperitoneum. J Clin Gastroenterol 1987; 9:543.
25. Castellote J, López C, Gornals J, et al. Rapid diagnosis of spontaneous bacterial peritonitis by use of reagent strips. Hepatology 2003; 37:893.
26. Nousbaum JB, Cadranel JF, Nahon P, et al. Diagnostic accuracy of the Multistix 8 SG reagent strip in diagnosis of spontaneous bacterial peritonitis. Hepatology 2007; 45:1275.

27. Mendler MH, Agarwal A, Trimzi M, et al. A new highly sensitive point of care screen for spontaneous bacterial peritonitis using the leukocyte esterase method. J Hepatol 2010; 53:477.
28. Sapey T, Mena E, Fort E, et al. Rapid diagnosis of spontaneous bacterial peritonitis with leukocyte esterase reagent strips in a European and in an American center. J Gastroenterol Hepatol 2005; 20:187.
29. Koulaouzidis A. Diagnosis of spontaneous bacterial peritonitis: an update on leucocyte esterase reagent strips. World J Gastroenterol 2011; 17:1091.
30. Parsi MA, Saadeh SN, Zein NN, et al. Ascitic fluid lactoferrin for diagnosis of spontaneous bacterial peritonitis. Gastroenterology 2008; 135:803.
31. Runyon BA, Antillon MR. Ascitic fluid pH and lactate: insensitive and nonspecific tests in detecting ascitic fluid infection. Hepatology 1991; 13:929.
32. Albillos A, Cuervas-Mons V, Millán I, et al. Ascitic fluid polymorphonuclear cell count and serum to ascites albumin gradient in the diagnosis of bacterial peritonitis. Gastroenterology 1990; 98:134.
33. Runyon BA, Hoefs JC. Ascitic fluid analysis in the differentiation of spontaneous bacterial peritonitis from gastrointestinal tract perforation into ascitic fluid. Hepatology 1984; 4:447.
34. Runyon BA. Bacterial peritonitis secondary to a perinephric abscess. Case report and differentiation from spontaneous bacterial peritonitis. Am J Med 1986; 80:997.
35. Garrison RN, Cryer HM, Howard DA, Polk HC Jr. Clarification of risk factors for abdominal operations in patients with hepatic cirrhosis. Ann Surg 1984; 199:648.
36. Würstle S, Hapfelmeier A, Karapetyan S, et al. Differentiation of Spontaneous Bacterial Peritonitis from Secondary Peritonitis in Patients with Liver Cirrhosis: Retrospective Multicentre Study. Diagnostics (Basel) 2023; 13.
37. Pinzello G, Simonetti RG, Craxì A, et al. Spontaneous bacterial peritonitis: a prospective investigation in predominantly nonalcoholic cirrhotic patients. Hepatology 1983; 3:545.
38. Wu SS, Lin OS, Chen YY, et al. Ascitic fluid carcinoembryonic antigen and alkaline phosphatase levels for the differentiation of primary from secondary bacterial peritonitis with intestinal perforation. J Hepatol 2001; 34:215.
39. Antillon MR, Runyon BA. Effect of marked peripheral leukocytosis on the leukocyte count in ascites. Arch Intern Med 1991; 151:509.

Topic 1249 Version 28.0

GRAPHICS

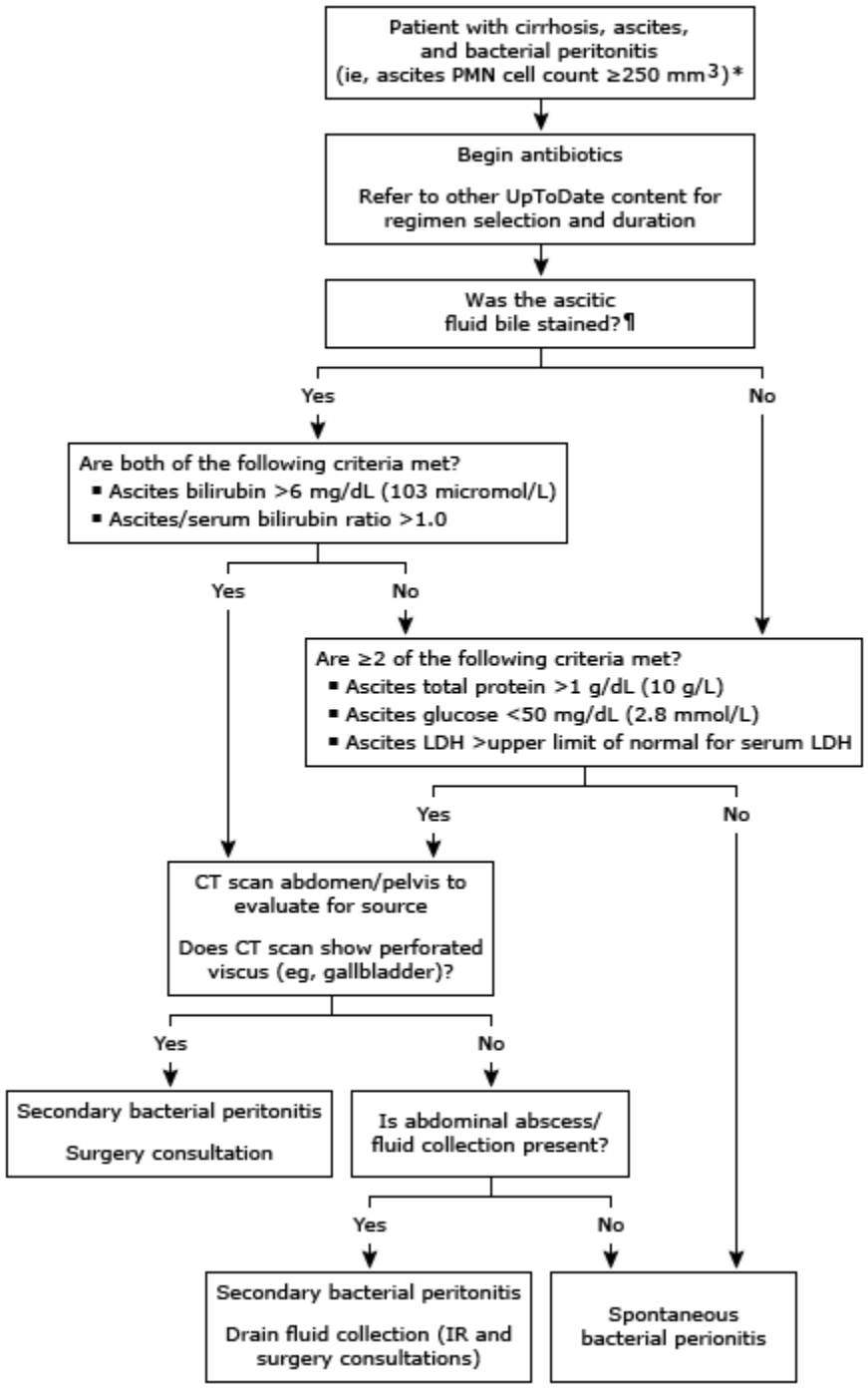
Signs and symptoms at the time of diagnosis in 489 patients with spontaneous bacterial peritonitis

Clinical feature	Percent with sign or symptom
Fever	69
Abdominal pain	59
Altered mental status	54
Abdominal tenderness	49
Diarrhea	32
Paralytic ileus	30
Hypotension	21
Hypothermia	17

Data from McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders Company, Philadelphia 1994. p.455.

Graphic 71038 Version 2.0

Distinguishing spontaneous from secondary bacterial peritonitis



Secondary bacterial peritonitis is infected ascites in the setting of an underlying intra-abdominal source of infection. The distinction of spontaneous from secondary bacterial peritonitis is based upon ascitic fluid analysis, imaging studies, and response to treatment. Refer to UpToDate content on the management of spontaneous bacterial peritonitis and secondary bacterial peritonitis.

PMN: polymorphonuclear; LDH: lactate dehydrogenase; CT: computed tomography; IR: interventional radiology.

* The following tests are routinely performed on ascitic fluid when peritonitis is suspected: Gram stain, aerobic and anaerobic culture (ie, in blood culture bottles at the bedside), cell count and differential, albumin, total protein, glucose, LDH, amylase, bilirubin (if the fluid is dark orange or brown).

¶ Bile-stained ascites typically appears dark orange or brown.

Graphic 122552 Version 2.0

Bacteria isolated from ascitic fluid in 519 patients with spontaneous bacterial peritonitis

Organism	Percent of isolates
Escherichia coli	43
Klebsiella pneumoniae	11
Streptococcus pneumoniae	9
Other streptococcal species	19
Enterobacteriaceae	4
Staphylococcus	3
Pseudomonas	1
Miscellaneous*	10

*In some regions of the world, such as Korea, Aeromonas hydrophila infection is an important cause of SBP, particularly in warm weather months. Affected patients commonly also have diarrhea. [Choi JP, et al. Clin Infect Dis 2008; 47:67.]

Data from McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and Hepatic Infections, Surawicz CM, Owen RL (Eds), WB Saunders, Philadelphia 1995. p.455.

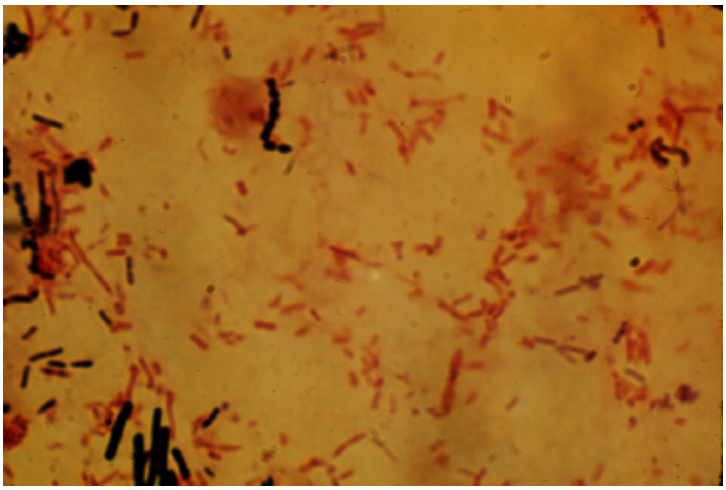
Graphic 80188 Version 3.0

Classification of ascites by the serum-to-ascites albumin gradient

High albumin gradient (SAAG ≥1.1 g/dL)
Cirrhosis
Alcoholic hepatitis
Heart failure
Massive hepatic metastases
Heart failure/constrictive pericarditis
Budd-Chiari syndrome
Portal vein thrombosis
Idiopathic portal fibrosis
Low albumin gradient (SAAG <1.1 g/dL)
Peritoneal carcinomatosis
Peritoneal tuberculosis
Pancreatitis
Serositis
Nephrotic syndrome

Graphic 81696 Version 5.0

Mixed flora in peritoneal fluid from a ruptured viscus



Gram stain of peritoneal fluid (x1000) shows several different organisms, including gram-positive cocci in chains, gram-positive rods, plump enteric gram-negative bacilli, and thinner gram-negative rods. Mixed fecal flora grew from this specimen.

Courtesy of Harriet Provine.

Graphic 77736 Version 3.0

Tests performed on ascitic fluid

Routine tests
Cell count and differential
Albumin concentration
Total protein concentration
Optional tests
Culture in blood culture bottles
Glucose concentration
Lactate dehydrogenase concentration
Gram stain
Amylase concentration
Unusual tests
Tuberculosis smear and culture
Adenosine deaminase activity
Cytology
Triglyceride concentration
Bilirubin concentration
Serum pro-brain natriuretic peptide
Carcinoembryonic antigen (CEA) concentration
Alkaline phosphatase concentration

Graphic 62032 Version 5.0

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