Spontaneous bacterial peritonitis in adults: Treatment and prophylaxis

AUTHOR: Bruce A Runyon, MD, FAASLD
SECTION EDITOR: Keith D Lindor, MD
DEPUTY EDITOR: Kristen M Robson, MD, MBA, FACG

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Sep 2023.**
This topic last updated: **May 25, 2023.**

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 signs and symptoms such as fever, abdominal pain, or altered mental status (table 1). (See "Spontaneous bacterial peritonitis in adults: Clinical manifestations".)

The diagnosis is established by a positive ascitic fluid bacterial culture and an ascitic fluid absolute polymorphonuclear leukocyte (PMN) count ≥250 cells/microL. Patients with SBP should be started on empiric, broad-spectrum antibiotics immediately after peritoneal fluid is obtained. When culture results are available, antibiotic coverage can be tailored to cover the specific organisms identified. (See "Spontaneous bacterial peritonitis in adults: Diagnosis".)

This topic will review the treatment and prophylaxis of SBP. The performance of paracentesis, the pathogenesis, clinical manifestations, and diagnosis 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 variants" and "Spontaneous bacterial peritonitis in adults: Diagnosis" and "Evaluation of adults with ascites".)

The American Association for the Study of Liver Diseases has updated its guidance on the management of adult patients with ascites due to cirrhosis [2]. The discussion that follows is generally consistent with that guidance.

TREATMENT

In patients with suspected spontaneous bacterial peritonitis (SBP), empiric therapy should be initiated as soon as possible to maximize the patient's chance of survival [3]. However, antibiotics should not be given until ascitic fluid has been obtained for culture. (See 'Timing' below.)

Most cases of SBP are due to gut bacteria such as *Escherichia coli* and *Klebsiella*, though streptococcal and staphylococcal infections can also occur (table 2). As a result, broad-spectrum therapy is warranted until the results of susceptibility testing are available. (See 'Selecting empiric therapy' below.)

In addition to antibiotic therapy, patients with SBP who are taking a nonselective beta blocker should have the medication discontinued.

Discontinue nonselective beta blockers — Among patients with SBP, beta blocker use is associated with worse outcomes compared with those not receiving beta blockers. Because of this, we permanently discontinue beta blockers once SBP has developed [4].

The effect of nonselective beta blocker use on outcomes was examined in a retrospective study of 607 patients with cirrhosis and ascites [4]. Once SBP developed, patients receiving a beta blocker had a 58 percent increase in mortality risk compared with patients who were not receiving a beta blocker (hazard ratio [HR] 1.58, 95% CI 1.10-2.27). In addition, rates of hepatorenal syndrome were higher (24 versus 11 percent) and length of hospital stay was longer (mean 29.6 versus 23.7 days).

Antibiotic therapy

Indications — Empiric antibiotic therapy for SBP is indicated for patients with ascites who have any of the following (table 1):

- Temperature greater than 37.8°C (100°F)
- Abdominal pain and/or tenderness
- Altered mental status
- Ascitic fluid polymorphonuclear leukocyte (PMN) count ≥250 cells/microL

Patients with SBP should be started on empiric, broad-spectrum antibiotics immediately after peritoneal fluid is obtained.

Treatment is also routinely indicated for the following groups:

- **Patients with bacterascites** – In some patients, infection is detected at the bacterascites stage (ie, bacteria are present in the ascitic fluid, but the PMN count is <250 cells/microL) [5]. Patients with bacterascites who progress to SBP commonly have signs or symptoms of infection (usually fever) at the time of the paracentesis [5,6]. Treatment should be started for patients with bacterascites who are symptomatic. For patients who are asymptomatic, a repeat paracentesis should be obtained after 48 hours (or if the patient develops symptoms) and treatment initiated if the PMN count has risen to ≥250 cells/microL. (See "Spontaneous bacterial peritonitis variants".)

- **Patients with alcohol-associated hepatitis** – Patients with alcohol-associated hepatitis regularly develop fever, peripheral leukocytosis, and abdominal pain that can mimic SBP. However, they also can develop SBP. Patients with a peripheral leukocytosis do not have a proportional increase in PMNs in ascitic fluid unless they also have SBP [7]; thus an elevated ascitic fluid PMN count must be presumed to represent SBP and empiric antibiotic therapy started. (See "Spontaneous bacterial peritonitis in adults: Diagnosis", section on 'Distinction from alcoholic hepatitis'.)

  It is also reasonable to give empiric therapy to patients with alcohol-associated hepatitis who have a PMN count <250 cells/microL, but who have fever and/or peripheral leukocytosis. Empiric antibiotic treatment can then be discontinued after 48 hours if ascitic fluid, blood, and urine cultures demonstrate no bacterial growth.

Timing — Patients with suspected SBP (eg, fever, abdominal pain, altered mental status) should receive empiric antimicrobial therapy as soon as possible and after ascitic fluid, blood, and urine samples have been obtained for culture and ascitic fluid has been sent for PMN count (algorithm 1) [2].

For patients without these findings (eg, patients who require diagnostic paracentesis but in whom SBP is not suspected), it is reasonable to wait until the results of the PMN count are available, with initiation of treatment if the ascitic fluid PMN count is ≥250 cells/microL. Collection and processing of the specimen should take no more than one to four hours (hopefully more rapidly) from the time of the paracentesis. (See "Spontaneous bacterial peritonitis in adults: Diagnosis", section on 'Obtaining ascitic fluid'.)

The ascitic fluid PMN count is more rapidly available than the culture and appears to reliably identify patients who need empiric antibiotic coverage [1,8]. Delaying treatment until the ascitic fluid culture grows bacteria may result in death from overwhelming infection. (See "Spontaneous bacterial peritonitis in adults: Diagnosis", section on 'Ascitic fluid cell count'.)

Selecting empiric therapy — Choice of empiric antimicrobial therapy is informed by the following (algorithm 1):

- Microbiology of infection – Most cases of SBP are due to intestinal bacteria such as *E. coli* and *Klebsiella*; however, streptococcal and, infrequently, staphylococcal infections can also occur (table 2). As a result, relatively broad-spectrum therapy is warranted in patients with suspected ascitic fluid infection, until the results of susceptibility testing are available.

- Severity of illness – Severity of illness is determined by the chronic liver failure-sequential organ failure assessment (CLIF-SOFA) score that is similar to the sequential (sepsis-related) organ failure assessment (SOFA) score, a predictive scoring system designed to assess severity of illness in patients with sepsis [9]. (See "Predictive scoring systems in the intensive care unit", section on 'Sequential (sepsis-related) Organ Failure Assessment (SOFA)'.)

  The CLIF-SOFA severity score is based on the following measurements of organ function (calculator 1) [9]:

  - Respiratory system – ratio of arterial oxygen tension to fraction of inspired oxygen (PaO_2/FiO_2).
  - Cardiovascular system – amount of vasoactive medication necessary to prevent hypotension.
  - Hepatic system – bilirubin level.
  - Coagulation system – international normalized ratio.
  - Neurologic system – grade of hepatic encephalopathy (table 3).
  - Renal system – serum creatinine or use of renal replacement therapy.

  The CLIF-SOFA score includes subscores ranging from zero to four for each of these six components. Thus, total score ranges from zero to 24, with higher scores indicating more severe illness.

- Recent antibiotic use and local resistance patterns – Antibiotic resistance is particularly a concern in patients who have received fluoroquinolones for SBP prophylaxis. Resistance to third-generation cephalosporins also appears to be an increasing concern, at least in some

regions, particularly among patients with critical illness, nosocomial infections, or frequent contact with the health care system. (See 'Antibiotic resistance' below.)

- Local drug availability and formularies – Local drug availability and hospital formularies also guide drug selection.

As an example, patients with suspected SBP who are not critically ill (ie, CLIF-SOFA score <7) are typically treated with a third-generation cephalosporin. For such patients, we use cefotaxime 2 g intravenously every eight hours when cefotaxime is available or ceftriaxone 2 g intravenously daily if cefotaxime is not available. Cefotaxime produces excellent blood and ascitic fluid levels throughout the dosing interval, while clinical trials directly comparing different regimens are limited. Adjusting the dose of cefotaxime in patients with azotemia may not be necessary. Alternatives to cefotaxime include other third generation cephalosporins and fluoroquinolones. (See 'Third generation cephalosporins' below and 'Other antibiotics' below.)

Empiric therapy with a carbapenem (eg, ertapenem, imipenem, meropenem) is reserved for patients with severe disease (eg, those who are critically ill with CLIF-SOFA score ≥7) [9].

Antibiotic coverage should be rapidly narrowed when culture and sensitivity data are available. Open-ended use of broad spectrum antibiotics leads to selection of multiple resistant flora, and frequently, infection by those bacteria or even fungi [10].

Regimens

Third generation cephalosporins — Several antibiotic regimens have been shown to be effective for the treatment of SBP, but trials directly comparing different antibiotic regimens are lacking [11-17]. A third generation cephalosporin is a reasonable choice for suspected SBP [1,8,12,18-20]. Our preference is to give cefotaxime 2 g intravenously every eight hours. While ceftriaxone has been shown to prevent SBP in the setting of gastrointestinal hemorrhage in patients with cirrhosis [21], in our experience, cefotaxime is more effective than ceftriaxone for treating SBP. If ceftriaxone is used, patients should be given 2 g per day [20,22].

One randomized trial that examined cefotaxime included 73 patients with cirrhosis and severe infection (either SBP or bacteremia) [18]. The patients were assigned to cefotaxime or the combination of ampicillin and tobramycin. The following benefits were noted with cefotaxime:

- A higher rate of resolution of the infection (85 versus 56 percent), even though almost all of the organisms in both groups were sensitive to the antibiotics given
- No nephrotoxicity versus 5 percent with ampicillin-tobramycin
- No superinfection versus 14 percent with ampicillin-tobramycin

Dosing of cefotaxime 2 g intravenously every eight hours produces excellent ascitic fluid levels [23]. Lower doses or less frequent dosing can be used, especially in patients with impaired renal function. One study, for example, compared two different doses of cefotaxime in 143 patients with SBP: 2 g every six hours and 2 g every 12 hours [13]. The rate of infection resolution was the same in both groups (77 and 79 percent, respectively).

However, adjusting the dose of cefotaxime in patients with azotemia may not be necessary. We have used a dose of 2 g every eight hours in patients with a creatinine level >4 mg/dL (350 micromol/L) without toxicity [23]. Using cefotaxime in patients with azotemia may lead to high blood and ascitic fluid cefotaxime levels throughout the dosing interval, which in theory may result in improved bacterial killing. The main adverse drug reaction of cefotaxime is rash, which occurs in approximately 1 percent of patients.

Carbapenems — Use of a carbapenem for empiric therapy is generally reserved for patients with severe disease (ie, those with critical illness) because carbapenems provide broad antimicrobial coverage and have been associated with lower mortality in such patients [24,25]. Data to guide selecting a specific carbapenem (eg, ertapenem, imipenem, meropenem) are lacking, and carbapenem use is also informed by hospital formularies and local resistance panels. In a study of 865 patients with SBP, there were no significant differences for in-hospital mortality rates for carbapenem therapy compared with third generation cephalosporins (26 versus 25 percent) [25]. However, for critically ill patients with CLIF-SOFA score ≥7, carbapenem therapy was associated with lower risk of in-hospital mortality (23 versus 39 percent; adjusted OR 0.84, 95% CI 0.75-0.94). The pharmacology of carbapenems is presented separately. (See "Combination beta-lactamase inhibitors, carbapenems, and monobactams", section on 'Carbapenems'.)

Other antibiotics — Other antibiotics can be used for the treatment of SBP. Whenever possible, the alternative antibiotic should have been studied for the treatment of SBP. Ciprofloxacin can be used for patients who cannot take a cephalosporin, although it does not penetrate into ascitic fluid to the same extent as cefotaxime [26]. We give ciprofloxacin at a dose of 400 mg intravenously twice daily to patients with normal renal function. (See "Choice of antibiotics in penicillin-allergic hospitalized patients".)

Fluoroquinolones should **not** be used in a patient who had been receiving a fluoroquinolone for SBP prophylaxis because the infecting organism may be resistant to fluoroquinolones. Organisms infecting patients who have been on fluoroquinolone prophylaxis are usually (94 percent) susceptible to cefotaxime [27]. Nephrotoxic antibiotics should be avoided because the underperfused kidneys in cirrhosis tend to be exquisitely sensitive to injury [28]. (See "Manifestations of and risk factors for aminoglycoside nephrotoxicity".)

Certain oral agents may be as effective as parenteral therapy in the treatment of uncomplicated SBP [26,29]. One trial, for example, included 123 patients with SBP (who were not vomiting or in shock) who were randomly assigned to ofloxacin 400 mg twice daily or parenteral cefotaxime [29]. The infection resolution rates were 84 and 85 percent, respectively. Another trial demonstrated comparable outcomes with a short course of intravenous ciprofloxacin (200 mg every 12 hours for two days) followed by oral ciprofloxacin therapy (500 mg every 12 hours for five days) compared with intravenous therapy alone [26]. In our experience, we have successfully used oral therapy in patients with asymptomatic SBP.

Effective oral therapy in the outpatient setting also requires patient compliance.

In addition, confirmatory trials are needed before oral treatment of this life-threatening infection can be routinely recommended.

Antibiotic resistance — A concern related to the choice of antibiotics is the emergence of resistant infections, especially in centers that use fluoroquinolones for SBP prophylaxis. Cefotaxime (or other third generation cephalosporin) is appropriate treatment in patients who have been receiving SBP prophylaxis with a fluoroquinolone.

Resistance to fluoroquinolones was illustrated in a report from a center in Spain where norfloxacin prophylaxis is used routinely [30]. Multiresistant bacteria comprised 18 percent of total bacterial infections. These changes in flora and susceptibility were attributed to use of norfloxacin prophylaxis and invasive procedures (eg, intravascular lines and urinary catheters). Many liver units have avoided the use of urinary catheters for decades. This study provides some data to support the wisdom of this policy. (See 'Antibiotic prophylaxis' below.)

Resistance to third-generation cephalosporins also appears to be an increasing concern, at least in some regions. A report of 246 episodes of SBP in Spain found that 22 percent of cases were caused by strains that were resistant to ceftriaxone (mainly extended-spectrum beta-lactamase-producing Gram-negative bacilli and Enterococci) [31]. The risk of resistance was related to patient characteristics and the clinical context. It was highest in nosocomially acquired cases (41 percent) and in patients with frequent contact with the health care system (22 percent), compared with only 7 percent among community-acquired cases. Additionally, in two large series including a total of over 700 patients with decompensated cirrhosis, the rate of infection with multiple-drug resistant organisms ranged from 23 to 29 percent [32].

In settings where resistance to third-generation cephalosporins has been documented, piperacillin-tazobactam or a carbapenem has been used empirically as an alternative to cefotaxime, although there is less clinical experience [32]. Further study on the efficacy of

alternative antibiotic regimens is needed. (See "Antimicrobial approach to intra-abdominal infections in adults".)

Duration of therapy — Trials have found that short-courses of treatment for SBP are effective. Many patients will respond to a treatment course of five days.

One randomized trial compared 5- and 10-day courses of cefotaxime 2 g intravenously every eight hours in 90 patients with SBP [33]. The two groups had similar rates of bacteriologic cure (93 versus 91 percent), recurrent infection (11.6 versus 12.8 percent), and infection-related mortality (0 versus 4.3 percent). Another randomized trial demonstrated that treating until 48 hours after signs and symptoms of infection have disappeared is also effective [13]. Indirect data from a trial including over 600 patients with gram-negative bacteremia showed that a seven-day course of antibiotic therapy was non-inferior to a 14-day course.

We treat most patients for five days, including patients who are bacteremic (as they did in the 5- versus 10-day trial). Only patients who grow an unusual organism (eg, pseudomonas, Enterobacteriaceae), an organism resistant to standard antibiotic therapy, or an organism routinely associated with endocarditis (eg, *Staphylococcus aureus* or viridans group streptococci) are initially considered for longer treatment [33]. After five days, we reassess the patient. Treatment is discontinued if there has been the usual dramatic improvement. However, if fever or pain persists, paracentesis is repeated, and the decision to continue or discontinue treatment is determined by the PMN response:

- If the PMN count is <250 cells/microL, treatment is stopped.
- If the PMN count is greater than the pretreatment value, a search for a surgical source of infection is undertaken. (See "Spontaneous bacterial peritonitis in adults: Diagnosis", section on 'Distinguishing spontaneous from secondary bacterial peritonitis'.)
- If the PMN count is elevated but less than the pretreatment value, antibiotics are continued for another 48 hours, and paracentesis is repeated.

Special treatment considerations

Albumin administration for patients with renal dysfunction — Renal failure develops in 30 to 40 percent of patients with SBP and is a major cause of death [34]. The risk may be decreased with an infusion of intravenous 25 percent albumin solution that is administered within six hours of diagnosis (1.5 g/kg body weight; maximum dose: 100 g) and on day 3 (1 g/kg body weight; maximum dose:100 g) [35]. Albumin infusion should be given if the creatinine is >1 mg/dL (88 micromol/L), the blood urea nitrogen is >30 mg/dL (10.7 mmol/L), or the total

bilirubin is >4 mg/dL (68 micromol/L) [36]. Once renal failure has developed, treatment with a combination of octreotide and midodrine may be helpful, in addition to infusion of 25 grams of 25 percent albumin solution daily, unless there is massive fluid overload. (See "Hepatorenal syndrome".)

The development of renal failure is associated with activation of the renin-angiotensin system and a decrease in effective arterial volume. Thus, it has been hypothesized that plasma volume expansion could attenuate the hemodynamic changes in patients with SBP, thereby preserving renal function. A meta-analysis of four randomized trials (with a total of 288 patients) evaluated the impact of albumin infusion (in addition to antibiotics) on renal impairment and mortality in patients with SBP [37]. Albumin infusion was associated with a significant decrease in the incidence of renal impairment (8 versus 31 percent) and a significant reduction in mortality (16 versus 35 percent).

Secondary bacterial peritonitis and polymicrobial infections — Patients with suspected secondary bacterial peritonitis should receive broader coverage with cefotaxime and metronidazole. A similar regimen should be used with polymicrobial bacterascites [38]. (See "Spontaneous bacterial peritonitis variants".)

Culture-negative neutrocytic ascites — Patients with an ascitic fluid PMN count ≥250 cells/microL who have negative ascitic fluid cultures have culture-negative neutrocytic ascites. Most patients with culture-negative neutrocytic ascites actually have SBP. Like other patients with a PMN count ≥250 cells/microL, patients with culture-negative neutrocytic ascites should receive empiric broad-spectrum antibiotics. However, because the cultures are negative, the antibiotic regimen cannot subsequently be tailored based on the results of sensitivity testing. (See "Spontaneous bacterial peritonitis variants".)

Repeat paracentesis — A follow-up ascitic fluid analysis to document resolution of the infection (ie, the culture is now sterile) and a marked decrease in PMN count is not needed in most patients treated for SBP. The majority of patients have a typical history including advanced cirrhosis, characteristic symptoms and ascitic fluid analysis (total protein concentration <1 g/dL [10 g/L], glucose concentration >50 mg/dL [2.8 mmol/L], and lactate dehydrogenase less than the upper limit of normal for serum), infection with a single organism, and a dramatic clinical response. Repeat paracentesis is not necessary in such patients. (See "Spontaneous bacterial peritonitis in adults: Diagnosis", section on 'Interpretation of ascitic fluid test results'.)

However, repeat paracentesis should be performed if the setting, symptoms, ascitic fluid analysis, organism(s), or response to treatment are atypical. In settings where resistant organisms are common (ie, recent hospitalizations or recent exposure to antibiotics), repeat

paracentesis can be performed following 48 hours of treatment. If the absolute PMN count is not less than the pretreatment value, we typically substitute an antibiotic with a broader spectrum of coverage while awaiting culture results [20]. Lack of resolution of the infection raises the possibility of secondary peritonitis and should prompt further evaluation and, when appropriate, surgical intervention. (See 'Duration of therapy' above and "Spontaneous bacterial peritonitis in adults: Diagnosis", section on 'Distinguishing spontaneous from secondary bacterial peritonitis'.)

Prognosis — The infection-related mortality from SBP is low with appropriate treatment [1]. Several reports found no infection-related deaths if treatment was started prior to shock or frank renal failure [29,33]. In one systematic review, in-hospital mortality was best predicted by the presence of renal dysfunction (mortality rate 67 versus 11 percent in those with and without renal dysfunction, respectively) and higher Model for End-stage Liver Disease scores [39].

In patients who have developed septic shock, mortality is high, but early initiation of appropriate antimicrobial therapy is associated with improved outcomes. In a retrospective study of 126 patients with cirrhosis and SBP-associated septic shock, the overall in-hospital mortality rate was 82 percent [40]. Patients who survived received antimicrobial therapy earlier than those who died (median delay 1.8 versus 9.5 hours). The adjusted odds ratio for mortality was 1.9 for every hour delay in administering antimicrobial therapy (95% CI 1.1-3.1). This study reinforces the recommendation to obtain ascitic fluid cultures immediately and then initiate empiric antimicrobial therapy in a patient with suspected SBP to maximize the patient's chance of survival, particularly if the patient has developed sepsis. (See 'Treatment' above.)

Regardless of the short-term outcome related to the SBP, patients who have liver disease severe enough to develop SBP have a poor long-term prognosis. In-hospital, non-infection-related mortality may be as high as 20 to 40 percent [29,33], and one- and two-year mortality rates are approximately 70 and 80 percent, respectively [41,42]. In a large, nationwide database study of patients with cirrhosis, the three-year mortality rate for patients following a hospitalization for SBP was 67 percent [43]. Thus, liver transplantation should be seriously considered for survivors of SBP who are otherwise good transplantation candidates. (See "Liver transplantation in adults: Patient selection and pretransplantation evaluation".)

PROPHYLAXIS

Antibiotic prophylaxis for patients with risk factors for spontaneous bacterial peritonitis (SBP) (including ascitic fluid protein concentration <1 g/dL, variceal hemorrhage, or a prior episode of SBP) decreases the risk of bacterial infection and mortality. Prophylactic antibiotics may also

have the beneficial effects of increasing blood pressure and systemic vascular resistance [44]. These hemodynamic improvements, if sustained, may delay development of hepatorenal syndrome. (See 'Antibiotic prophylaxis' below.)

General measures — In addition to antibiotic prophylaxis, there are general measures that should be adopted to prevent SBP. These measures include:

- Diuretic therapy. Diuresis concentrates ascitic fluid, thereby raising ascitic fluid opsonic activity, which may help prevent SBP [45]. (See "Ascites in adults with cirrhosis: Initial therapy", section on 'Diuretic therapy'.)

- Early recognition and aggressive treatment of localized infections (eg, cystitis and cellulitis). This can help to prevent bacteremia and SBP.

- Restricting use of proton pump inhibitors. Proton pump inhibitor use has been associated with an increased risk of SBP in many (but not all) studies [46-48]. As a result, proton pump inhibitors should only be given to patients who have clear indications for their use [10].

Antibiotic prophylaxis

Indications — Antibiotic prophylaxis to prevent SBP is recommended for patients at high risk of developing SBP and is associated with a decreased risk of bacterial infection and mortality [49-56]. However, the use of antibiotic prophylaxis can select for resistant bacteria that may subsequently cause spontaneous infection [51,54,57-60]. It appears that hospitals that were early adopters of antibiotic prophylaxis are reporting multiple-drug resistant flora [32]. As a result, antibiotic prophylaxis should only be used in patients at high risk for SBP. In addition, the early studies examined antibiotic use for one year, but data on longer courses of antibiotics are not available. (See "Pathogenesis of spontaneous bacterial peritonitis", section on 'Risk factors for SBP' and 'Antibiotic resistance' above.)

We give antibiotic prophylaxis to the following patients [2]:

- Patients with cirrhosis and gastrointestinal bleeding. Antibiotic prophylaxis in this setting has been shown to decrease mortality in randomized trials [21,61].

- Patients who have had one or more episodes of SBP. In such patients, recurrence rates of SBP within one year have been reported to be close to 70 percent [41].

- Patients with cirrhosis and ascites if the ascitic fluid protein is <1.5 g/dL (15 g/L) along with either impaired renal function or liver failure. Impaired renal function is defined as a creatinine ≥1.2 mg/dL (106 micromol/L), a blood urea nitrogen level ≥25 mg/dL (8.9

mmol/L), or a serum sodium ≤130 mEq/L (130 mmol/L]). Liver failure is defined as a Child-Pugh score ≥9 and a bilirubin ≥3 mg/dL (51 micromol/L).

In addition, we give antibiotic prophylaxis to patients with cirrhosis who are hospitalized for other reasons and have an ascitic protein concentration of less than 1 g/dL (10 g/L).

There are no published randomized trials of antibiotic treatment for preventing infections in patients awaiting liver transplantation, so we base the decision to give antibiotic prophylaxis on whether the patient is at high risk for SBP.

In the early days of sclerotherapy, the use of long needles and contaminated endoscopic water sources led to bacteremia. Since the recognition of these problems and the use of shorter needles and sterile water, sclerotherapy-related infections have largely disappeared. Thus, parenteral antibiotics to prevent such infections do not appear to be warranted. One study of 97 patients, for example, found a trend toward a lower incidence of bacteremia with imipenem-cilastatin than with placebo (1.1 versus 5.6 percent) [62]. This difference was not statistically significant; furthermore, six of the seven episodes occurred after emergency sclerotherapy. Active bleeding appears to be the risk factor for infection in the current era, not sclerotherapy. In addition, variceal banding is now used much more often than sclerotherapy and is even less likely than sclerotherapy to lead to bacteremia [63].

Choosing a regimen — The antibiotic regimen used for prophylaxis varies with the indication. Our general approach is as follows:

- For patients with a history of SBP and for patients with low protein ascites (<1.5 g/dL [15 g/L]) along with either impaired renal function or liver failure, we use prolonged outpatient trimethoprim-sulfamethoxazole (one double-strength tablet daily) [64,65]. Alternatives include ciprofloxacin 500 mg per day or norfloxacin (400 mg per day; not available in the United States). We do not use weekly or five times per week dosing schedules. For patients on chronic trimethoprim-sulfamethoxazole therapy, renal function should be monitored by checking serum electrolytes, blood urea nitrogen (BUN) and creatinine every one to six months depending on the stability of patient. If there is worsening renal function, trimethoprim-sulfamethoxazole should be discontinued.

- In patients with cirrhosis who are hospitalized for reasons other than SBP or gastrointestinal bleeding and have an ascitic protein concentration of less than 1 g/dL (10 g/L), we use oral trimethoprim-sulfamethoxazole (one double-strength tablet once daily) during hospitalization [66]. We discontinue antibiotic prophylaxis at the time of discharge to minimize the risks of long-term antibiotic use (eg, resistance). Alternatives to

trimethoprim-sulfamethoxazole include ciprofloxacin (500 mg per day) or norfloxacin (400 mg per day) where available.

- In patients with advanced cirrhosis (Child-Pugh class B or C) and gastrointestinal bleeding, we use intravenous ceftriaxone 1 g intravenously daily and switch to oral trimethoprim-sulfamethoxazole (one double-strength tablet twice daily) once bleeding has been controlled and the patient is stable and eating [21]. Alternatives for oral therapy include ciprofloxacin (500 mg orally every 12 hours) or norfloxacin (400 mg twice daily) where available. Seven days of total antibiotic treatment are given. Patients with Child-Pugh class A cirrhosis can be managed with norfloxacin (400 mg orally twice daily), trimethoprim-sulfamethoxazole (one double-strength tablet twice daily), or ciprofloxacin (500 mg orally every 12 hours or 400 mg intravenously every 12 hours).

  The trial that validated ceftriaxone in this setting gave seven days of intravenous therapy [21]. However, patients hospitalized for variceal bleeding are regularly discharged prior to seven days. Switching to an oral regimen to complete the seven-day total antibiotic treatment allows patients to be discharged without having to arrange for outpatient administration of an intravenous antibiotic. (See "Approach to acute upper gastrointestinal bleeding in adults" and "Overview of the management of patients with variceal bleeding".)

While trials have shown efficacy for both continuous (daily) and intermittent administration of antibiotic prophylaxis [55,64,67], intermittent dosing may select resistant flora more rapidly [68].

Preliminary data on alternative antibiotic options are emerging. In a retrospective cohort study including 120 patients with cirrhosis and a history of SBP, rates of SBP recurrence and mortality were not significantly different for patients given doxycycline for prophylaxis compared with trimethoprim-sulfamethoxazole or fluroquinolones [69]. There was a nonsignificant trend toward lower rates of infection with multi-drug resistant organisms for patients on doxycycline (8 versus 26 percent). While these data are promising, randomized controlled trials are needed before doxycycline can be used for SBP prophylaxis in routine clinical practice.

Efficacy — The efficacy of antibiotic prophylaxis to prevent SBP has been demonstrated in several studies and meta-analyses [49-56,70,71]. One meta-analysis included 13 randomized trials in which antibiotic prophylaxis was given to patients with cirrhosis and a variety of risk factors for infection (such as a low ascitic fluid protein concentration, gastrointestinal bleeding, or a history of SBP) [52]. The combined analysis showed an overall mortality benefit (relative risk [RR] 0.70, 95% CI 0.56-0.89) and a decrease in bacterial infections (RR 0.39, 95% CI 0.32-0.48). Similar conclusions were reached in subsequent meta-analyses [70,71].

The most compelling randomized trial compared norfloxacin (not available in the United States) with placebo in 68 patients with cirrhosis and ascitic fluid total protein <1.5 g/dL (15 g/L) who either had impaired renal function (serum creatinine ≥1.2 mg/dL [106 micromol/L], blood urea nitrogen ≥25 mg/dL [8.9 mmol/L], or serum sodium ≤130 mEq/L [130 mmol/L]) or liver failure (Child-Pugh score ≥9 points and serum bilirubin ≥3 mg/dL [51 micromol/L]) [56]. The patients treated with norfloxacin had fewer episodes of SBP (7 versus 61 percent), a lower rate of hepatorenal syndrome (28 versus 41 percent), and improved survival at 3 months (94 versus 62 percent) and at 12 months (60 versus 48 percent). It is unusual to demonstrate a survival advantage in treatment of a complication of advanced cirrhosis.

A subsequent trial demonstrated a mortality benefit from prophylaxis with norfloxacin (not available in the United States) for some patients with advanced cirrhosis. In a trial including 291 patients with Child-Pugh class C cirrhosis, mortality rates at six months were not significantly different for patients given norfloxacin 400 mg daily compared with placebo (15 versus 20 percent; hazard ratio [HR] 0.69 95% CI 0.38-1.23) [72]. However, in a subgroup analysis of patients who had an ascitic fluid total protein concentration <1.5 g/dL (15 g/L), the mortality risk at six months was lower for patients given norfloxacin compared with placebo (HR 0.35, 95% CI 0.13-0.93).

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

- **General principles** – Spontaneous bacterial peritonitis (SBP) should be suspected in a patient with ascites and any of the following (see 'Antibiotic therapy' above):
  - Temperature greater than 37.8°C (100°F)
  - Abdominal pain and/or tenderness
  - A change in mental status
  - Ascitic fluid PMN count ≥250 cells/mm^3

  Most cases of SBP are due to gut bacteria such as *E. coli* and *Klebsiella*, though streptococcal and staphylococcal infections can also occur (table 2). (See 'Selecting empiric therapy' above.)

- **Discontinuing nonselective beta blockers** – In patients receiving a nonselective beta blocker, we permanently discontinue the medication once SBP has developed because nonselective beta blocker use in this setting has been associated with decreased transplant-free survival, increased rates of hepatorenal syndrome, and more days of hospitalization compared with patients not receiving nonselective beta blockers. (See 'Discontinue nonselective beta blockers' above.)

- **Selecting empiric antibiotic therapy** – For most patients with suspected SBP, while awaiting culture results, we suggest treatment with a third-generation cephalosporin (eg, cefotaxime or ceftriaxone) rather than narrower coverage (algorithm 1) (**Grade 2C**). Antibiotics used for the treatment of SBP should provide good coverage for the organisms commonly associated with SBP (eg, *E. coli*, *Klebsiella*) and should achieve good ascitic fluid levels. Cefotaxime (2 g intravenously every eight hours) provides appropriate microbial coverage and attains good ascitic fluid levels. Ciprofloxacin is an alternative for patients who cannot take a cephalosporin. The selection of antibiotics for SBP should include consideration of local resistance patterns and recent antibiotic use (eg, a fluoroquinolone should not be used in a patient who has been receiving SBP prophylaxis with a fluoroquinolone). Antibiotic therapy should be tailored once the results of sensitivity testing are available. (See 'Selecting empiric therapy' above.)

  Empiric therapy with a carbapenem (eg, ertapenem, meropenem, imipenem) is typically reserved for patients with severe SBP (ie, those who are critically ill) (calculator 1).

- **Duration of antibiotic therapy** – We suggest treating most patients with SBP for five days rather than a longer course of therapy (**Grade 2B**). A longer course of therapy is appropriate for patients who grow an unusual organism (eg, pseudomonas, Enterobacteriaceae), an organism resistant to standard antibiotic therapy, or an organism routinely associated with endocarditis (eg, *S. aureus* or viridans group streptococci). In addition, a longer course of therapy is required for patients who fail to respond to therapy appropriately. (See 'Duration of therapy' above.)

  After five days of treatment, we reassess the patient. Treatment is discontinued if there has been the usual dramatic improvement. However, if fever or pain persists, paracentesis is repeated, and the decision to continue or discontinue treatment is determined by the PMN response:

  - If the PMN count is <250 cells/microL, treatment is stopped
  - If the PMN count is greater than the pretreatment value, a search for a surgical source of infection is undertaken

- If the PMN count is elevated but less than the pretreatment value, antibiotics are continued for another 48 hours, and the paracentesis is repeated

- **Albumin administration** – Renal failure develops in 30 to 40 percent of patients with SBP and is a major cause of death. The risk may be decreased with an infusion of intravenous 25 percent albumin solution that is administered within six hours of diagnosis (1.5 g/kg body weight; maximum dose: 100 g) and on day 3 (1 g/kg body weight; maximum dose:100 g). Albumin infusion should be given if the creatinine is >1 mg/dL (88 micromol/L), the blood urea nitrogen is >30 mg/dL (10.7 mmol/L), or the total bilirubin is >4 mg/dL (68 micromol/L). Once renal failure has developed, treatment with a combination of octreotide and midodrine may be helpful. Daily infusion of 25 grams of 25 percent albumin solution should be also given, unless there is massive fluid overload. (See 'Albumin administration for patients with renal dysfunction' above.)

- **Prognosis** – SBP responds well to appropriate antibiotic treatment. However, patients who have liver disease severe enough to develop SBP have a poor long-term prognosis. In-hospital, non-infection-related mortality may be as high as 20 to 40 percent, and one- and two-year mortality rates are approximately 70 and 80 percent, respectively. (See 'Prognosis' above.)

- **Prophylaxis**

  - **Indications** – We recommend antibiotic prophylaxis for patients at high risk for developing SBP, rather than waiting for SBP to develop to initiate antibiotic therapy (**Grade 1A**). In patients at high risk of developing SBP, antibiotic prophylaxis is associated with a decreased risk of bacterial infection and mortality. We give antibiotic prophylaxis continuously (daily) rather than intermittently. Doing so may decrease the risk of bacterial antibiotic resistance. (See 'Prophylaxis' above.)

    Patients at high risk for SBP include:

    - Patients with cirrhosis and gastrointestinal bleeding.

    - Patients who have had one or more episodes of SBP (among whom recurrence of SBP within one year has been reported to be close to 70 percent).

    - Patients with cirrhosis and ascites if the ascitic fluid protein is <1.5 g/dL (15 g/L) along with either impaired renal function or liver failure. Impaired renal function is defined as a creatinine ≥1.2 mg/dL (106 micromol/L), a blood urea nitrogen level ≥25 mg/dL (8.9 mmol/L), or a serum sodium ≤130 mEq/L (130 mmol/L]). Liver

failure is defined as a Child-Pugh score ≥9 and a bilirubin ≥3 mg/dL (51 micromol/L).

- Patients with cirrhosis who are hospitalized for other reasons and have an ascitic protein concentration of less than 1 g/dL (10 g/L).

- **Antibiotic regimens for prophylaxis** – For patients who require prophylaxis, we use antibiotic regimens that have been specifically studied for SBP prophylaxis whenever possible. We use the following regimens (see 'Choosing a regimen' above):

  - For patients with a history of SBP and for patients with low protein ascites (<1.5 g/dL [15 g/L]) along with either impaired renal function or liver failure, we use prolonged outpatient trimethoprim-sulfamethoxazole (one double-strength tablet daily). Alternatives include ciprofloxacin 500 mg per day or norfloxacin (400 mg per day; not available in the United States). We do not use weekly or five times per week dosing schedules.

  - In patients with cirrhosis who are hospitalized for reasons other than SBP or gastrointestinal bleeding and have an ascitic protein concentration of less than 1 g/dL (10 g/L), we use oral trimethoprim-sulfamethoxazole (one double-strength tablet once daily) with discontinuation of the drug at the time of discharge. Alternatives include ciprofloxacin (500 mg per day) or norfloxacin (400 mg per day) where available.

  - In patients with advanced cirrhosis (Child-Pugh class B or C) and gastrointestinal bleeding, we use intravenous ceftriaxone 1 g intravenously daily and switch to oral trimethoprim-sulfamethoxazole (one double-strength tablet twice daily) once bleeding has been controlled and the patient is stable and eating. Alternatives for oral therapy include ciprofloxacin (500 mg orally every 12 hours) or norfloxacin (400 mg twice daily) where available. Patients with Child-Pugh class A cirrhosis can be managed with norfloxacin (400 mg orally twice daily), trimethoprim-sulfamethoxazole (one double-strength tablet twice daily), or ciprofloxacin (500 mg orally every 12 hours or 400 mg IV every 12 hours). Seven days of total antibiotic treatment are given.

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. http://www.aasld.org/practiceguidelines/Documents/ascitesupdate2013.pdf (Accessed on A pril 23, 2013).
4. Mandorfer M, Bota S, Schwabl P, et al. Nonselective β blockers increase risk for hepatorenal syndrome and death in patients with cirrhosis and spontaneous bacterial peritonitis. Gastroenterology 2014; 146:1680.
5. Runyon BA. Monomicrobial nonneutrocytic bacterascites: a variant of spontaneous bacterial peritonitis. Hepatology 1990; 12:710.
6. Pelletier G, Lesur G, Ink O, et al. Asymptomatic bacterascites: is it spontaneous bacterial peritonitis? Hepatology 1991; 14:112.
7. Antillon MR, Runyon BA. Effect of marked peripheral leukocytosis on the leukocyte count in ascites. Arch Intern Med 1991; 151:509.
8. McHutchison JG, Runyon BA. Spontaneous bacterial peritonitis. In: Gastrointestinal and He patic Infections, Surawicz CM, Owen RL (Eds), WB Saunders, Philadelphia 1994. p.455.
9. Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology 2013; 144:1426.
10. Ge PS, Runyon BA. Preventing future infections in cirrhosis: a battle cry for stewardship. Clin Gastroenterol Hepatol 2015; 13:760.
11. Soares-Weiser K, Paul M, Brezis M, Leibovici L. Evidence based case report. Antibiotic treatment for spontaneous bacterial peritonitis. BMJ 2002; 324:100.
12. Chavez-Tapia NC, Soares-Weiser K, Brezis M, Leibovici L. Antibiotics for spontaneous bacterial peritonitis in cirrhotic patients. Cochrane Database Syst Rev 2009; :CD002232.
13. Rimola A, Salmerón JM, Clemente G, et al. Two different dosages of cefotaxime in the treatment of spontaneous bacterial peritonitis in cirrhosis: results of a prospective, randomized, multicenter study. Hepatology 1995; 21:674.
14. Chen TA, Lo GH, Lai KH, Lin WJ. Single daily amikacin versus cefotaxime in the short-course treatment of spontaneous bacterial peritonitis in cirrhotics. World J Gastroenterol 2005; 11:6823.

15. França A, Giordano HM, Sevá-Pereira T, Soares EC. Five days of ceftriaxone to treat spontaneous bacterial peritonitis in cirrhotic patients. J Gastroenterol 2002; 37:119.
16. Dalmau D, Layrargues GP, Fenyves D, et al. Cefotaxime, desacetyl-cefotaxime, and bactericidal activity in spontaneous bacterial peritonitis. J Infect Dis 1999; 180:1597.
17. Rastegar LA, Umrani G, Dehbashi N, Malec F. Evaluation of the therapeutic effect of pefloxacin in comparison with ampicillin and gentamicin in cirrhotic patients with spontaneous bacterial peritonitis. Hepatogastroenterology 1998; 45:783.
18. Felisart J, Rimola A, Arroyo V, et al. Cefotaxime is more effective than is ampicillin-tobramycin in cirrhotics with severe infections. Hepatology 1985; 5:457.
19. Mattos AA, Wiltgen D, Jotz RF, et al. Spontaneous bacterial peritonitis and extraperitoneal infections in patients with cirrhosis. Ann Hepatol 2020; 19:451.
20. Yim HJ, Kim TH, Suh SJ, et al. Response-Guided Therapy With Cefotaxime, Ceftriaxone, or Ciprofloxacin for Spontaneous Bacterial Peritonitis: A Randomized Trial: A Validation Study of 2021 AASLD Practice Guidance for SBP. Am J Gastroenterol 2023; 118:654.
21. Fernández J, Ruiz del Arbol L, Gómez C, et al. Norfloxacin vs ceftriaxone in the prophylaxis of infections in patients with advanced cirrhosis and hemorrhage. Gastroenterology 2006; 131:1049.
22. Mazer L, Tapper EB, Piatkowski G, Lai M. The need for antibiotic stewardship and treatment standardization in the care of cirrhotic patients with spontaneous bacterial peritonitis - a retrospective cohort study examining the effect of ceftriaxone dosing. F1000Res 2014; 3:57.
23. Runyon BA, Akriviadis EA, Sattler FR, Cohen J. Ascitic fluid and serum cefotaxime and desacetyl cefotaxime levels in patients treated for bacterial peritonitis. Dig Dis Sci 1991; 36:1782.
24. Piano S, Fasolato S, Salinas F, et al. The empirical antibiotic treatment of nosocomial spontaneous bacterial peritonitis: Results of a randomized, controlled clinical trial. Hepatology 2016; 63:1299.
25. Kim SW, Yoon JS, Park J, et al. Empirical Treatment With Carbapenem vs Third-generation Cephalosporin for Treatment of Spontaneous Bacterial Peritonitis. Clin Gastroenterol Hepatol 2021; 19:976.
26. Terg R, Cobas S, Fassio E, et al. Oral ciprofloxacin after a short course of intravenous ciprofloxacin in the treatment of spontaneous bacterial peritonitis: results of a multicenter, randomized study. J Hepatol 2000; 33:564.
27. Llovet JM, Rodríguez-Iglesias P, Moitinho E, et al. Spontaneous bacterial peritonitis in patients with cirrhosis undergoing selective intestinal decontamination. A retrospective

study of 229 spontaneous bacterial peritonitis episodes. J Hepatol 1997; 26:88.

28. Cabrera J, Arroyo V, Ballesta AM, et al. Aminoglycoside nephrotoxicity in cirrhosis. Value of urinary beta 2-microglobulin to discriminate functional renal failure from acute tubular damage. Gastroenterology 1982; 82:97.
29. Navasa M, Follo A, Llovet JM, et al. Randomized, comparative study of oral ofloxacin versus intravenous cefotaxime in spontaneous bacterial peritonitis. Gastroenterology 1996; 111:1011.
30. Fernández J, Acevedo J, Castro M, et al. Prevalence and risk factors of infections by multiresistant bacteria in cirrhosis: a prospective study. Hepatology 2012; 55:1551.
31. Ariza X, Castellote J, Lora-Tamayo J, et al. Risk factors for resistance to ceftriaxone and its impact on mortality in community, healthcare and nosocomial spontaneous bacterial peritonitis. J Hepatol 2012; 56:825.
32. Fernández J, Prado V, Trebicka J, et al. Multidrug-resistant bacterial infections in patients with decompensated cirrhosis and with acute-on-chronic liver failure in Europe. J Hepatol 2019; 70:398.
33. Runyon BA, McHutchison JG, Antillon MR, et al. Short-course versus long-course antibiotic treatment of spontaneous bacterial peritonitis. A randomized controlled study of 100 patients. Gastroenterology 1991; 100:1737.
34. Follo A, Llovet JM, Navasa M, et al. Renal impairment after spontaneous bacterial peritonitis in cirrhosis: incidence, clinical course, predictive factors and prognosis. Hepatology 1994; 20:1495.
35. 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 Engl J Med 1999; 341:403.
36. Sigal SH, Stanca CM, Fernandez J, et al. Restricted use of albumin for spontaneous bacterial peritonitis. Gut 2007; 56:597.
37. Salerno F, Navickis RJ, Wilkes MM. Albumin infusion improves outcomes of patients with spontaneous bacterial peritonitis: a meta-analysis of randomized trials. Clin Gastroenterol Hepatol 2013; 11:123.
38. Runyon BA, Hoefs JC, Canawati HN. Polymicrobial bacterascites. A unique entity in the spectrum of infected ascitic fluid. Arch Intern Med 1986; 146:2173.
39. Tandon P, Garcia-Tsao G. Renal dysfunction is the most important independent predictor of mortality in cirrhotic patients with spontaneous bacterial peritonitis. Clin Gastroenterol Hepatol 2011; 9:260.

40. Karvellas CJ, Abraldes JG, Arabi YM, et al. Appropriate and timely antimicrobial therapy in cirrhotic patients with spontaneous bacterial peritonitis-associated septic shock: a retrospective cohort study. Aliment Pharmacol Ther 2015; 41:747.
41. Titó L, Rimola A, Ginès P, et al. Recurrence of spontaneous bacterial peritonitis in cirrhosis: frequency and predictive factors. Hepatology 1988; 8:27.
42. Andreu M, Sola R, Sitges-Serra A, et al. Risk factors for spontaneous bacterial peritonitis in cirrhotic patients with ascites. Gastroenterology 1993; 104:1133.
43. Hung TH, Tsai CC, Hsieh YH, Tsai CC. The long-term mortality of spontaneous bacterial peritonitis in cirrhotic patients: A 3-year nationwide cohort study. Turk J Gastroenterol 2015; 26:159.
44. Rasaratnam B, Kaye D, Jennings G, et al. The effect of selective intestinal decontamination on the hyperdynamic circulatory state in cirrhosis. A randomized trial. Ann Intern Med 2003; 139:186.
45. Runyon BA, Antillon MR, Montano AA. Effect of diuresis versus therapeutic paracentesis on ascitic fluid opsonic activity and serum complement. Gastroenterology 1989; 97:158.
46. Goel GA, Deshpande A, Lopez R, et al. Increased rate of spontaneous bacterial peritonitis among cirrhotic patients receiving pharmacologic acid suppression. Clin Gastroenterol Hepatol 2012; 10:422.
47. Deshpande A, Pasupuleti V, Thota P, et al. Acid-suppressive therapy is associated with spontaneous bacterial peritonitis in cirrhotic patients: a meta-analysis. J Gastroenterol Hepatol 2013; 28:235.
48. Terg R, Casciato P, Garbe C, et al. Proton pump inhibitor therapy does not increase the incidence of spontaneous bacterial peritonitis in cirrhosis: a multicenter prospective study. J Hepatol 2015; 62:1056.
49. Runyon BA. Low-protein-concentration ascitic fluid is predisposed to spontaneous bacterial peritonitis. Gastroenterology 1986; 91:1343.
50. Soriano G, Guarner C, Teixidó M, et al. Selective intestinal decontamination prevents spontaneous bacterial peritonitis. Gastroenterology 1991; 100:477.
51. Ginés P, Rimola A, Planas R, et al. Norfloxacin prevents spontaneous bacterial peritonitis recurrence in cirrhosis: results of a double-blind, placebo-controlled trial. Hepatology 1990; 12:716.
52. Soares-Weiser K, Brezis M, Tur-Kaspa R, et al. Antibiotic prophylaxis of bacterial infections in cirrhotic inpatients: a meta-analysis of randomized controlled trials. Scand J Gastroenterol 2003; 38:193.

53. Grangé JD, Roulot D, Pelletier G, et al. Norfloxacin primary prophylaxis of bacterial infections in cirrhotic patients with ascites: a double-blind randomized trial. J Hepatol 1998; 29:430.
54. Soriano G, Guarner C, Tomás A, et al. Norfloxacin prevents bacterial infection in cirrhotics with gastrointestinal hemorrhage. Gastroenterology 1992; 103:1267.
55. Terg R, Fassio E, Guevara M, et al. Ciprofloxacin in primary prophylaxis of spontaneous bacterial peritonitis: a randomized, placebo-controlled study. J Hepatol 2008; 48:774.
56. Fernández J, Navasa M, Planas R, et al. Primary prophylaxis of spontaneous bacterial peritonitis delays hepatorenal syndrome and improves survival in cirrhosis. Gastroenterology 2007; 133:818.
57. Runyon BA, Borzio M, Young S, et al. Effect of selective bowel decontamination with norfloxacin on spontaneous bacterial peritonitis, translocation, and survival in an animal model of cirrhosis. Hepatology 1995; 21:1719.
58. Ortiz J, Vila MC, Soriano G, et al. Infections caused by Escherichia coli resistant to norfloxacin in hospitalized cirrhotic patients. Hepatology 1999; 29:1064.
59. Wade JJ, Rolando N, Hayllar K, et al. Bacterial and fungal infections after liver transplantation: an analysis of 284 patients. Hepatology 1995; 21:1328.
60. Tandon P, Delisle A, Topal JE, Garcia-Tsao G. High prevalence of antibiotic-resistant bacterial infections among patients with cirrhosis at a US liver center. Clin Gastroenterol Hepatol 2012; 10:1291.
61. Chavez-Tapia NC, Barrientos-Gutierrez T, Tellez-Avila F, et al. Meta-analysis: antibiotic prophylaxis for cirrhotic patients with upper gastrointestinal bleeding - an updated Cochrane review. Aliment Pharmacol Ther 2011; 34:509.
62. Rolando N, Gimson A, Philpott-Howard J, et al. Infectious sequelae after endoscopic sclerotherapy of oesophageal varices: role of antibiotic prophylaxis. J Hepatol 1993; 18:290.
63. Lo GH, Lai KH, Shen MT, Chang CF. A comparison of the incidence of transient bacteremia and infectious sequelae after sclerotherapy and rubber band ligation of bleeding esophageal varices. Gastrointest Endosc 1994; 40:675.
64. Singh N, Gayowski T, Yu VL, Wagener MM. Trimethoprim-sulfamethoxazole for the prevention of spontaneous bacterial peritonitis in cirrhosis: a randomized trial. Ann Intern Med 1995; 122:595.
65. Lontos S, Shelton E, Angus PW, et al. A randomized controlled study of trimethoprim-sulfamethoxazole versus norfloxacin for the prevention of infection in cirrhotic patients. J Dig Dis 2014; 15:260.

66. Novella M, Solà R, Soriano G, et al. Continuous versus inpatient prophylaxis of the first episode of spontaneous bacterial peritonitis with norfloxacin. Hepatology 1997; 25:532.

67. Rolachon A, Cordier L, Bacq Y, et al. Ciprofloxacin and long-term prevention of spontaneous bacterial peritonitis: results of a prospective controlled trial. Hepatology 1995; 22:1171.

68. Terg R, Llano K, Cobas SM, et al. Effects of oral ciprofloxacin on aerobic gram-negative fecal flora in patients with cirrhosis: results of short- and long-term administration, with daily and weekly dosages. J Hepatol 1998; 29:437.

69. Nguyen N, Rago J, Crotty M, et al. Doxycycline for the prevention of spontaneous bacterial peritonitis. Hepatology 2020; 72:1119A.

70. Saab S, Hernandez JC, Chi AC, Tong MJ. Oral antibiotic prophylaxis reduces spontaneous bacterial peritonitis occurrence and improves short-term survival in cirrhosis: a meta-analysis. Am J Gastroenterol 2009; 104:993.

71. Loomba R, Wesley R, Bain A, et al. Role of fluoroquinolones in the primary prophylaxis of spontaneous bacterial peritonitis: meta-analysis. Clin Gastroenterol Hepatol 2009; 7:487.

72. Moreau R, Elkrief L, Bureau C, et al. Effects of Long-term Norfloxacin Therapy in Patients With Advanced Cirrhosis. Gastroenterology 2018; 155:1816.

Topic 1248 Version 50.0

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

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

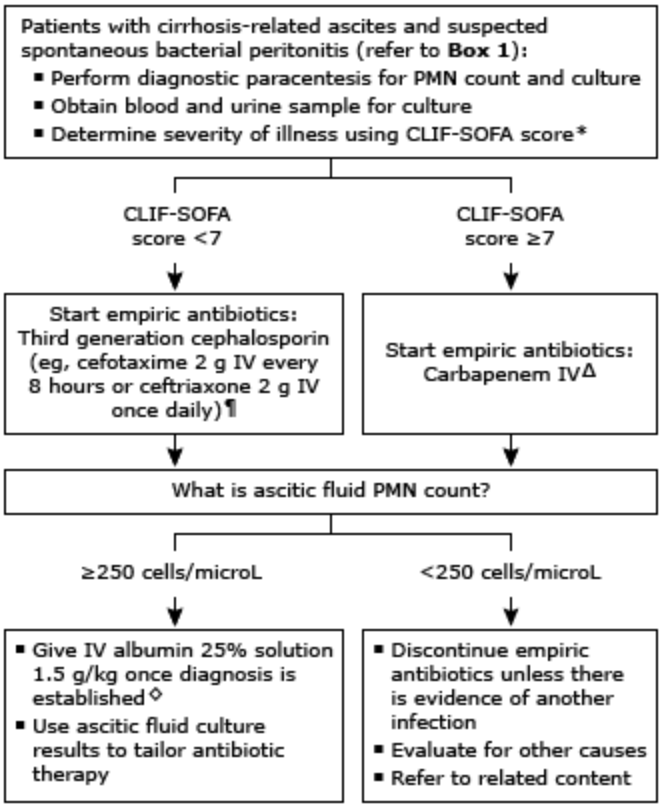
Organism	Percent of isolates
Escherichia coli	43
Klebsiella pneumoniae	11
Streptococcus pneumoniae	9
Other streptococcal species	19
Enterobacteriaceae	4
Staphylococcus	3
Pseudomonas	1
Miscellaneous*	10

*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

Evaluation and initial management for adult patients with suspected spontaneous bacterial peritonitis



Box 1

Spontaneous bacterial peritonitis is suspected in patients with cirrhosis-related ascites and any of the following:

- Abdominal pain
- Abdominal tenderness
- Altered mental status
- Fever
- Hypotension

Refer to content on management of spontaneous bacterial peritonitis.

PMN: polymorphonuclear leukocyte; IV: intravenous; PaO_2: partial pressure of arterial oxygen; FiO_2: fraction of inspired oxygen.

* The chronic liver failure-sequential organ failure assessment (CLIF-SOFA)[1] score includes subscores ranging from 0 to 4 for each of six components (bilirubin, serum creatinine, hepatic encephalopathy grade, international normalized ratio, amount of vasoactive medication necessary to prevent hypotension, and pulmonary status [PaO_2/FiO_2]). Higher scores indicate more severe organ impairment.

¶ Dosing is for adult patients with normal kidney function; refer to individual drug information monographs for more detail, including dosage adjustments (eg, for organ impairment). For patients with an allergy to cephalosporins, a fluoroquinolone such as ciprofloxacin is an alternative option, provided that a fluoroquinolone had not been given as prophylaxis.

Δ For treatment of spontaneous bacterial peritonitis, carbapenems are reserved for patients with severe disease (eg, those who are critically ill). Choice of carbapenem is based on local resistance panels, drug availability, and local formulary options. Examples of carbapenems include ertapenem, imipenem, and meropenem.

◇ Albumin 25% solution is administered at diagnosis (1.5 g/kg IV; maximum dose: 100 g) and on day 3 (1 g/kg IV; maximum dose: 100 g) if creatinine is >1 mg/dL (88 micromol/L), the blood urea nitrogen is >30 mg/dL (10.7 mmol/L), or the total bilirubin is >4 mg/dL (68 micromol/L).

Reference:

1. *Moreau R, Jalan R, Gines P, et al. Acute-on-chronic liver failure is a distinct syndrome that develops in patients with acute decompensation of cirrhosis. Gastroenterology 2013; 144:1426.*

Graphic 59554 Version 4.0

Grading system for hepatic encephalopathy

Grade	Mental status	Asterixis	EEG
I	Euphoria/depression	Yes/no	Usually normal
	Mild confusion		
	Slurred speech		
	Disordered sleep		
II	Lethargy	Yes	Abnormal
	Moderate confusion		
III	Marked confusion	Yes	Abnormal
	Incoherent		
	Sleeping but arousable		
IV	Coma	No	Abnormal

EEG: electroencephalogram.

Graphic 62922 Version 2.0

Contributor Disclosures

Bruce A Runyon, MD, FAASLD No relevant financial relationship(s) with ineligible companies to disclose. **Keith D Lindor, MD** Consultant/Advisory Boards: Pliant [DSMB member]. All of the relevant financial relationships listed have been mitigated. **Kristen M Robson, MD, MBA, FACG** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→