Spontaneous bacterial peritonitis

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PERITONITIS MAY BE DEFINED as infectious or chemical irritation of the peritoneal membrane, and spontaneous peritonitis as bacterial peritonitis arising in the absence of intra-abdominal findings, such as intestinal perforation. The reported incidence of spontaneous peritonitis has increased over the past two decades, which may be related to an increased awareness of populations at risk, especially patients with ascites. Several diagnostic tests that may facilitate early diagnosis and allow prompt initiation of antimicrobial therapy have been advocated recently. Spontaneous peritonitis continues to be a life-threatening illness and must be considered in the evaluation of acute abdominal complaints.

DEFINITION AND HISTORICAL PERSPECTIVE

Harken and Shochat cited what may be the first report of spontaneous peritonitis, observed in 1581 in a 7-year-old girl who developed fatal peritonitis after an episode of painless diarrhea. Annand and Bowen, in 1906 published a review of gram-positive bacterial peritonitis, and McCartney and Fraser, 16 years later, reported 56 patients with pneumococcal peritonitis and no detectable extraperitoneal infective focus. The association of pneumococcal peritonitis with the nephrotic syndrome was established in 1940, and the first report of pneumococcal peritonitis in cirrhotic patients was published by Epstein et al. in 1968. Spontaneous peritonitis caused by gram-positive organisms has also been described with systemic lupus erythematosus and lymphedema. A uniform definition of spontaneous peritonitis has not been evident. Several authors include patients with upper respiratory tract and urinary tract infections, but others adhere to the strict definition of McCartney and Fraser. Preexisting ascites is a disposing factor in most series.

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INCIDENCE AND EPIDEMIOLOGY

The incidence of spontaneous peritonitis in the pediatric age range is unknown. It presently accounts for 1% to 2% of abdominal emergencies requiring surgical intervention, compared with 8% to 10% earlier in this century. The apparent decline in the operative incidence is misleading, because spontaneous peritonitis is now usually diagnosed nonoperatively. The age of peak incidence continues to be 5 to 9 years, although 75% of the large series of patients reported by Gross in 1953 were younger than 5 years of age. The sex incidence is nearly equal despite an earlier opinion that girls were more frequently affected. Early investigators reported the incidence in patients with nephrotic syndrome to be 28% to 33% more recently, it appears to be nearer 2%. The incidence in adults with cirrhosis is 6%, but the incidence in children with cirrhosis is unknown.

Earlier reports reviewing the preantibiotic era incriminated Streptococcus pneumoniae and other streptococci exclusively, whereas series published since 1960 indicate an apparent increase in the proportion of cases caused by gram-negative enteric organisms. Haemophilus influenzae and Neisseria meningitidis (Figure). Fowler reported that S. pneumoniae was isolated from peritoneal fluid obtained from 50 of 72 patients with spontaneous peritonitis seen between 1925 and 1955, but from only six of 33 patients between 1956 and 1970. Speck et al. reviewed the records of 37 children with nephrosis who developed spontaneous peritonitis between 1946 and 1972. Gram-positive cocci were isolated from 22 of 26 patients diagnosed prior to 1960, and from six of 11 between 1960 and 1972. This epidemiologic shift has been attributed to the advent of antimicrobial therapy, as well as to increased use of systemic corticosteroid therapy, without proof exists to verify these hypotheses. Anaerobic organisms do not appear to play an important etiologic role in spontaneous peritonitis, although many of the published reports preceded modern techniques for isolation and cultivation of anaerobic bacteria. Isolated cases of primary anaerobic peritonitis have been reported in adults. Fowler, in 1957, reported that 20% of peritoneal fluid cultures were sterile despite evidence of bacteria on Gram-
stained smears of peritoneal fluid. This may reflect earlier difficulties in isolating anaerobic organisms, or perhaps there is free oxygen exchange between the systemic circulation and intraperitoneal fluid that creates an inhospitable environment for anaerobes. Gram-positive bacteria isolated from children with spontaneous peritonitis include *S. pneumoniae*, *Streptococcus pyogenes*, and *Staphylococcus aureus*; gram-negative organisms include *Escherichia coli*, *H. influenzae*, *Proteus*, *Pseudomonas*, *Aerobacter*, *Klebsiella*, *Paracolon*, and *Citrobacter*.

Cultures of other body fluids have been examined, seeking correlation with the peritoneal cultures. Blood is the most reliable alternative source, yielding the same organism in up to 75% of patients. Isolates from urine, sputum, and the vagina do not appear to correlate closely with isolates from peritoneal cultures.

**PATHOGENESIS**

An understanding of peritoneal defense mechanisms is necessary before speculation as to the pathogenesis of spontaneous peritonitis can begin. First-line defense appears to be the absorption of bacteria and particulate matter <10 μm in diameter. Peritoneal fluid is drawn upward into transdiaphragmatic lymphatics, and eventually into the thoracic duct by diaphragmatic motion. Bacteria can be recovered from the thoracic duct within minutes of an intraperitoneal injection.

Peritoneal contamination results in an immediate inflammatory response. Mast cell degranulation leads to vasodilation, with exudation of plasma rich in antibodies and fibrinogen. Fibrinogen is converted to fibrin, which traps bacteria, resulting in decreased absorption of bacteria, and probably endotoxins as well. Peritoneal cellular defenses respond to increased vascular permeability and complement activation. Neutrophils phagocytize bacteria within hours of contamination, and mononuclear cells scavenge cellular debris within 24 hours.

Isolated components of the peritoneal defense system are being examined for possible manifestations of dysfunction. Transdiaphragmatic removal of bacteria could be impaired when intestinal motility and respiratory effort are decreased. Fluid within the peritoneal cavity may alter neutrophil function by impairing locomotion directly, or it may inhibit phagocytosis by lowering the redox potential. Fibrin formation could release extracellular phagocytic enzymes, which might promote abscess formation. Some foreign substances (hemoglobin, bile, barium, gastric mucus) act as adjuvants and increase bacterial lethality. Some bacterial species (*E. coli* and *Bacteroides fragilis*) act synergistically, enhancing their virulence. Thus, peritoneal contamination may resolve spontaneously, lead to abscess formation, or spread diffusely over the entire peritoneum.

The route by which bacteria gain access to the peritoneal cavity is difficult to establish; four principal mechanisms have been considered: ascent through the female genital tract, spread via transdiaphragmatic lymphatics, direct extension through the intestinal wall, and inoculation by hematogenous dissemination.

Vaginal infection was postulated as a cause of spontaneous peritonitis earlier in this century because of an apparent greater incidence in females and the frequent operative observation of inflammatory changes in fallopian tubes. It has been unclear whether those changes represented cause or effect. Organisms isolated from the vagina correlate poorly with organisms isolated from the peritoneum. Vaginal discharge is an infrequent complaint in patients with spontaneous peritonitis. The alkaline vaginal secretions of prepubertal girls could be less inhibitory to bacterial growth than those of postpubertal females. McDougal et al. found a concomitant urinary tract infection in 10 of 26 cases of spontaneous peritonitis. In nine of these, the isolates from the urine and peritoneal cultures were the same. Colony counts, methods of specimen collection, Gram stain, and specific organisms were not reported. Reflux of urine into the uterus has been documented, although further spread to the peritoneal cavity has not.

Transmural migration of bacteria across the intestinal wall has been considered in patients with spontaneous peritonitis. Gastrointestinal symptoms, particularly diarrhea, are frequently present, but direct examination of the intestinal tract and mesenteric lymphatics at laparotomy has failed to yield consistent abnormalities. Patients
with cirrhosis have congested splanchnic veins and lymphatics along with chronic diarrhea. These factors could result in compromised mucosal integrity and alterations of the intestinal microflora, which might contribute to direct bacterial extension across the intestinal wall. Although an earlier study in rabbits failed to demonstrate transmural migration of fed \textit{S. pneumoniae},^7 a more recent experiment in dogs did identify intraperitoneal to intestinal lumen migration of radiolabeled \textit{E. coli}.^9 It is unfortunate, from our perspective, that migration of intraluminal bacteria to the peritoneal cavity was not evaluated in the latter study.

Transdiaphragmatic migration of bacteria through lymphatic channels is commonly mentioned as a cause of spontaneous peritonitis, although no direct evidence exists to support this route of spread.

Rischbeith^10 was the first to suggest that spontaneous peritonitis may result from hematogenous seeding of the peritoneum. The same organism has been recovered from both blood and peritoneal cultures in up to 75% of patients with spontaneous peritonitis, although a cause-and-effect relationship has not been established.\footnote{\textsuperscript{5, 7, 11, 12}} Transient bacteremia is not rare, and bacteria bypass the hepatic reticuloendothelial system in patients with advanced cirrhosis as well as those with portosystemic shunts. Among 28 patients with complete portosystemic shunting, reviewed by Conn and Fessel,\footnote{\textsuperscript{39}} spontaneous peritonitis developed in three, all of whom had preexisting ascites. They concluded that preexisting ascites was a predisposing factor more important than the shunt. The total number of patients developing ascites postoperatively was not stated. It is unclear whether the ascites serves as a culture medium or, by its existence, indicates altered host defenses. Serum immunoglobulin concentrations have been found to be reduced at the time of infection in patients with nephrotic syndrome.\footnote{\textsuperscript{5, 20, 23}} The role of complement and cell-mediated immunity in spontaneous peritonitis has not been evaluated. Previous paracentesis as well as vasopressin therapy are mentioned as causes of spontaneous peritonitis in adults.\footnote{\textsuperscript{19, 39, 49}}

We believe that spontaneous bacterial contamination of the peritoneal cavity most likely occurs by hematogenous seeding. This opinion is based on the greater than chance correlation of blood and peritoneal cultures and the frequent identification of extra-abdominal pathogens such as \textit{S. pneumoniae}. Peritoneal contamination by transmural migration of bacteria seems to be preceded by hematogenous dissemination.

**Clinical Presentation**

The presenting signs and symptoms of spontaneous peritonitis differ in infants and children. The infant frequently has poor feeding, lethargy, fever, and a distended, doughy abdomen.\footnote{\textsuperscript{13}} Acute scrotal swelling may be noted in infant boys.\footnote{\textsuperscript{40}} Symptoms in older children include nausea, vomiting, diarrhea, and diffuse abdominal pain.

Physical examination reveals fever, abdominal distention and rigidity, diffuse rebound tenderness, and diffuse rectal tenderness. Pigmentation of the abdominal wall may be seen.\footnote{\textsuperscript{42}} Although the clinical features of spontaneous peritonitis overlap considerably with secondary peritonitis, some authors\footnote{\textsuperscript{16, 12}} have emphasized a more rapid onset of the symptom complex with the former.

**Diagnostic Evaluation**

A patient with a clinical assessment suggesting peritonitis should be evaluated with flat and upright abdominal radiographs, chest radiographs, complete blood count, serum amylase determination, urinalysis, and blood and urine cultures. Abdominal paracentesis must be performed in all patients with ascites and signs of peritonitis, because patients with preexistent ascites can also suffer intestinal perforation.\footnote{\textsuperscript{43}} The presence of extraluminal air on abdominal films precludes further evaluation and dictates surgical intervention.

We have described our paracentesis technique previously.\footnote{\textsuperscript{44}} Laboratory determinations that should be performed with the fluid, because of the variety of conditions that may simulate spontaneous peritonitis, include WBC count with differential; specific gravity; glucose, total protein, amylase, and triglyceride levels; pH and lactic acid and LDH determinations; Gram stain and smear test for fungi and acid-fast bacilli; aerobic and anaerobic cultures, fungal and mycobacterial cultures; and cytology.

The specific gravity and protein content classify the fluid as a transudate (specific gravity <1.015 and total protein value <2.5 mg/dl) or exudate (specific gravity >1.015 and total protein value >2.5 gm/dl). Exudative peritoneal fluid is commonly associated with infection, malignancies, and pancreatitis. Elevated ascitic fluid levels of LDH, leucine aminopeptidase, and glycoprotein are seen with intraperitoneal malignancies. Elevated levels of amylase, lipase, and LDH strongly support pancreatic disease, whereas tuberculous peritonitis is often accompanied by an ascitic fluid glucose level <30 mg/dl. Chylous peritonitis results from the sudden release of chyle into the peritoneal cavity, as with a ruptured mesenteric cyst. The ascitic triglyceride level exceeds that of plasma and is frequently >400 mg/dl.

The presence of gram-positive bacteria in peritoneal fluid strongly suggests spontaneous peritonitis. If the smear reveals both gram-negative and gram-positive bacteria, the likelihood of intestinal perforation is increased and laparotomy may be necessary. A Gram stain revealing...
only gram-negative bacteria could be consistent with either spontaneous peritonitis or secondary peritonitis; the patient can be managed nonoperatively with very close observation.

When no organisms are identified on stained smears of the peritoneal fluid, physicians have traditionally relied on the peritoneal fluid cell count and differential in their therapeutic decision making. Unfortunately, an occasional patient with spontaneous peritonitis will not have ascitic fluid leukocytosis. It has been suggested recently that depression of the peritoneal fluid pH is more sensitive than the cell count. Gitlin et al.\(^4\) found an ascitic fluid pH <7.31 in six patients with spontaneous peritonitis, whereas 50 patients with sterile ascites had ascitic fluid pH determinations >7.37. \(E.\) \(c\)ol\(i\) was responsible for five of the six infections; \Streptococcus\ fecalis accounted for the remaining case. No patient had systemic acidosis. An accompanying editorial cautioned against substitution of pH determinations for cell counts until more experience is gained with a variety of intraperitoneal infections.\(^5\) Several investigators have found elevated peritoneal fluid lactate levels in patients with spontaneous peritonitis.\(^4\)\(^6\) Elevated levels were also found, however, in 38% of patients with ascites related to intra-abdominal malignancies.\(^4\) The origins of the elevated lactate level and the reduction in pH in spontaneous peritonitis are unknown. We recently encountered a patient with long-standing cirrhosis and ascites who developed fever, abdominal distention, and abdominal tenderness. Her peritoneal fluid was cloudy and contained 28,800 polymorphonuclear leukocytes/\(\mu\)l. The ascitic fluid pH was 7.41, and the lactate level was 4.7 mEq/L (normal <3.7 mEq/L). Blood pH and lactate values were normal. Ascitic fluid Gram stain and bacterial culture were negative, although \(E.\) \(c\)ol\(i\) was cultured from her bloodstream. Defervescence occurred within 12 hours of the initiation of antibiotic therapy. Failure to culture an organism from the ascitic fluid precluded the diagnosis of spontaneous peritonitis. It does appear, however, that pronounced ascitic leukocytosis does not alter the pH of sterile peritoneal fluid, although it may account for mild lactate elevation. All three determinations (cell count with differential, pH, and lactate) should be performed on ascitic fluid until further information is available. Simultaneous blood pH and lactate determinations should also be performed.

Counterimmunoelectrophoresis of peritoneal fluid may provide a rapid diagnosis of pneumococcal peritonitis.\(^6\) This technique could be an important adjunct to the Gram stain. Unfortunately, the recent epidemiologic shift to enteric organisms limits its usefulness.

Antibiotic therapy should be initiated in all patients with polymorphonuclear leukocytes >500/\(\mu\)l of peritoneal fluid and in any patient with signs of peritonitis and >250 polymorphonuclear leukocytes/\(\mu\)l.\(^9\) Further experience with ascitic fluid pH and lactate levels is necessary before specific treatment criteria can be offered, although ascitic fluid pH <7.35 and lactate levels >3.7 mEq/L have been found in patients with spontaneous peritonitis.\(^4\)\(^7\)

**TREATMENT**

Therapeutic efforts should be directed toward (1) treatment of abnormalities of vascular perfusion resulting from rapid shifts of fluid and electrolytes; (2) minimizing the accompanying paralytic ileus; (3) managing the effects of bacterial toxins, such as coagulation defects, increased vascular permeability and shock; and (4) eradication of extra-abdominal sites of infection.

Antimicrobial therapy should be started promptly when the ascitic fluid examination is consistent with spontaneous peritonitis. The Gram stain and rapid diagnostic tests such as counterimmunoelectrophoresis and latex particle agglutination assays for specific bacterial antigens aid in the initial selection of antibiotics. Should bacteria not be seen on Gram stain, a combination of ampicillin (200 to 300 mg/kg/24 hr administered intravenously in six doses) and gentamicin (7.5 mg/kg/24 hr administered intravenously every 8 hours) should adequately eradicate the majority of pathogens associated with spontaneous peritonitis. Specific antibiotic therapy may be initiated when the sensitivity tests are known. Aqueous penicillin G (300,000 U/kg/24 hr administered intravenously in six doses) is quite effective in streptococcal and pneumococcal peritonitis. A 10-day course is usually adequate.

Infection with enteric organisms is more difficult to eradicate, and longer periods of intravenous therapy are often required. Treatment must be individualized, and may take from 10 days to 3 weeks. Antibiotic blood levels must be monitored to assure effective and nontoxic concentrations. There are no available studies that define the optimum duration of antibiotic therapy. Patients who respond to antibiotic therapy promptly and have negative cultures initially may be treated for 10 days and carefully observed for a recrudescence after antibiotic therapy is terminated. Surgical exploration must be considered if improvement is not evident after 48 hours.

Intraperitoneal administration of antimicrobial agents is considered heroic therapy.

**SUMMARY**

Spontaneous bacterial peritonitis should be considered in the evaluation of any patient with acute abdominal complaints, especially in the presence of preexistent ascites. Paracentesis is indicated in all suspected cases of spontaneous peritonitis in order to obtain necessary
studies, including microbial cultures. Broad-spectrum antibi
otic coverage has become necessary because of the in
creasing incidence of gram-negative isolates. Ascitic pH
and lactate may provide accurate information in the
evaluation of spontaneous peritonitis, although increased
clinical awareness remains the key to proper diagnosis.

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