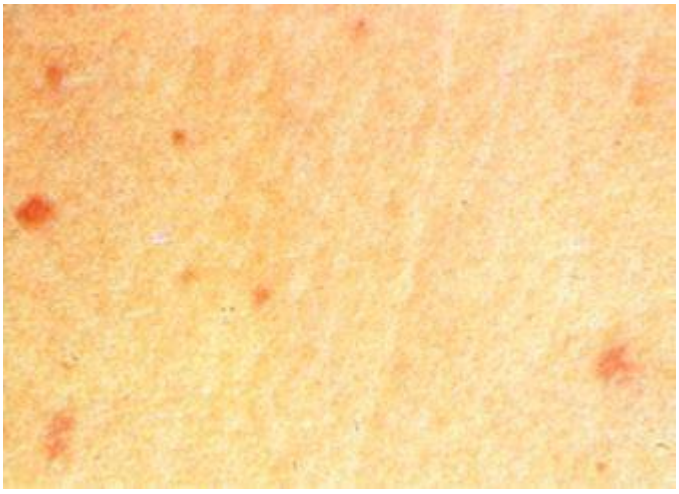

FIGURE 190-2 **"Rose spots,"** the rash of enteric fever due to *Salmonella typhi* or *Salmonella paratyphi*.

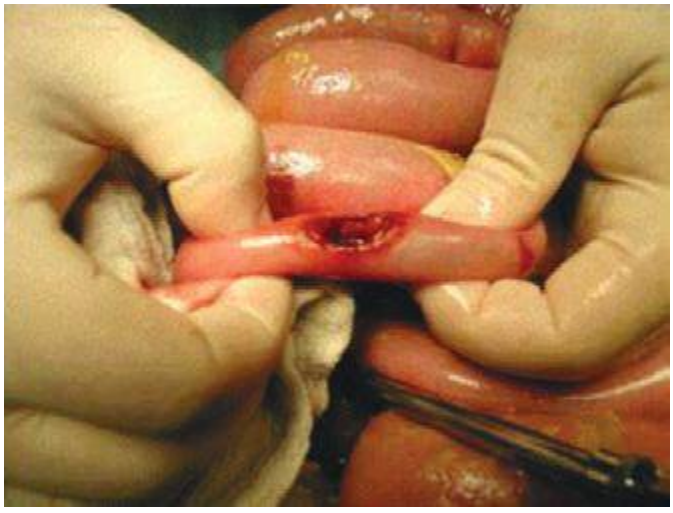

FIGURE 190-3 **Typical ileal perforation associated with *Salmonella typhi* infection.** *(From JM Saxe, R Cropsey: Is operative management effective in treatment of perforated typhoid? Am J Surg 189:342, 2005.)*

up to 4 weeks if untreated. *S. paratyphi* A is thought to cause milder disease than *S. typhi*, with predominantly gastrointestinal symptoms. However, a prospective study of 669 consecutive cases of enteric fever in Kathmandu, Nepal, found that the infections caused by these organisms were clinically indistinguishable. In this series, symptoms reported on initial medical evaluation included headache (80%), chills (35–45%), cough (30%), sweating (20–25%), myalgias (20%), malaise (10%), and arthralgia (2–4%). Gastrointestinal manifestations included anorexia (55%), abdominal pain (30–40%), nausea (18–24%), vomiting (18%), and diarrhea (22–28%) more commonly than constipation (13–16%). Physical findings included coated tongue (51–56%), splenomegaly (5–6%), and abdominal tenderness (4–5%).

Early physical findings of enteric fever include rash ("rose spots"; 30%), hepatosplenomegaly (3–6%), epistaxis, and relative bradycardia at the peak of high fever (<50%). Rose spots **(Fig. 190-2; see also Fig. 25e-9)** make up a faint, salmon-colored, blanching, maculopapular rash located primarily on the trunk and chest. The rash is evident in ~30% of patients at the end of the first week and resolves without a trace after 2–5 days. Patients can have two or three crops of lesions, and *Salmonella* can be cultured from punch biopsies of these lesions. The faintness of the rash makes it difficult to detect in highly pigmented patients.

The development of severe disease (which occurs in ~10–15% of patients) depends on host factors (immunosuppression, antacid therapy, previous exposure, and vaccination), strain virulence and inoculum, and choice of antibiotic therapy. Gastrointestinal bleeding (10–20%) and intestinal perforation (1–3%) most commonly occur in the third and fourth weeks of illness and result from hyperplasia, ulceration, and necrosis of the ileocecal Peyer's patches at the initial site of *Salmonella* infiltration **(Fig. 190-3)**. Both complications are life-threatening and require immediate fluid resuscitation and surgical intervention, with broadened antibiotic coverage for polymicrobial peritonitis **(Chap. 159)** and treatment of gastrointestinal hemorrhages, including bowel resection. Neurologic manifestations occur in 2–40% of patients and include meningitis, Guillain-Barré syndrome, neuritis, and neuropsychiatric symptoms (described as "muttering delirium" or "coma vigil"), with picking at bedclothes or imaginary objects.

Rare complications whose incidences are reduced by prompt antibiotic treatment include disseminated intravascular coagulation, hematophagocytic syndrome, pancreatitis, hepatic and splenic abscesses and granulomas, endocarditis, pericarditis, myocarditis, orchitis, hepatitis, glomerulonephritis, pyelonephritis and hemolytic-uremic syndrome, severe pneumonia, arthritis, osteomyelitis, endophthalmitis, and parotitis. Up to 10% of patients develop mild relapse, usually within 2–3 weeks of fever resolution and in association with the same strain type and susceptibility profile.

Up to 10% of untreated patients with typhoid fever excrete *S. typhi* in the feces for up to 3 months, and 1–4% develop chronic asymptomatic carriage, shedding *S. typhi* in either urine or stool for >1 year. Chronic carriage is more common among women, infants, and persons who have biliary abnormalities or concurrent bladder infection with *Schistosoma haematobium*. The anatomic abnormalities associated with the latter conditions presumably allow prolonged colonization.

DIAGNOSIS

Because the clinical presentation of enteric fever is relatively nonspecific, the diagnosis needs to be considered in any febrile traveler returning from a developing region, especially the Indian subcontinent, the Philippines, or Latin America. Other diagnoses that should be considered in these travelers include malaria, hepatitis, bacterial enteritis, dengue fever, rickettsial infections, leptospirosis, amebic liver abscesses, and acute HIV infection **(Chap. 149)**. Other than a positive culture, no specific laboratory test is diagnostic for enteric fever. In 15–25% of cases, leukopenia and neutropenia are detectable. Leukocytosis is more common among children, during the first 10 days of illness, and in cases complicated by intestinal perforation or secondary infection. Other nonspecific laboratory findings include moderately elevated values in liver function tests and muscle enzyme levels.

The definitive diagnosis of enteric fever requires the isolation of *S. typhi* or *S. paratyphi* from blood, bone marrow, other sterile sites, rose spots, stool, or intestinal secretions. The sensitivity of blood culture is only 40–80%, probably because of high rates of antibiotic use in endemic areas and the small number of *S. typhi* organisms (i.e., <15/mL) typically present in the blood. Because almost all *S. typhi* organisms in blood are associated with the mononuclear cell/platelet fraction, centrifugation of blood and culture of the buffy coat can substantially reduce the time to isolation of the organism but do not increase sensitivity.

Bone marrow culture is 55–90% sensitive, and, unlike that of blood culture, its yield is not reduced by up to 5 days of prior antibiotic therapy. Culture of intestinal secretions (best obtained by a noninvasive duodenal string test) can be positive despite a negative bone marrow culture. If blood, bone marrow, and intestinal secretions are all cultured, the yield is >90%. Stool cultures, although negative in 60–70% of cases during the first week, can become positive during the third week of infection in untreated patients.

Serologic tests, including the classic Widal test for "febrile agglutinins," and rapid tests to detect antibodies to outer-membrane proteins or O:9 antigen are available for detection of *S. typhi* in developing countries but have lower positive predictive values than blood culture. More sensitive antigen and nucleic acid amplification tests have been developed to detect *S. typhi* and