TABLE 180-2 COMMON CAUSES OF PETECHIAL OR PURPURIC RASHES

Enteroviruses
Influenza and other respiratory viruses
Measles virus
Epstein-Barr virus
Cytomegalovirus
Parvovirus
Deficiency of protein C or S (including postvaricella protein S deficiency)
Platelet disorders (e.g., idiopathic thrombocytopenic purpura, drug effects, bone marrow infiltration)
Henoch-Schönlein purpura, connective tissue disorders, trauma (including nonaccidental injuries in children)
Pneumococcal, streptococcal, staphylococcal, or gram-negative bacterial sepsis

level of consciousness, seizures or status epilepticus, and focal neurologic signs. Classic signs of meningitis, such as neck stiffness and photophobia, are often absent in infants and young children with bacterial meningitis, who more usually present with fever and irritability and may have a bulging fontanelle.

While 30–50% of patients present with a meningitis syndrome alone, up to 40% of meningitis patients also present with some features of septicemia. Most deaths from meningococcal meningitis alone (i.e., without septicemia) are associated with raised intracranial pressure presenting as a reduced level of consciousness, relative bradycardia and hypertension, focal neurologic signs, abnormal posturing, and signs of brainstem involvement—e.g., unequal, dilated, or poorly reactive pupils; abnormal eye movement; and impaired corneal responses (Chap. 328).

Septicemia Meningococcal septicemia alone accounts for up to 20% of cases of meningococcal disease. The condition may progress from early nonspecific symptoms to death within hours. Mortality rates among children with this syndrome have been high (25–40%), but early aggressive management (as discussed below) may reduce the figure to <10%. Early symptoms are nonspecific and suggest an influenza-like illness with fever, headache, and myalgia accompanied by vomiting and abdominal pain. As discussed above, the rash, if present, may appear to be viral early in the course until petechiae or purpuric lesions develop. Purpura fulminans occurs in severe cases, with multiple large purpuric lesions and signs of peripheral ischemia. Surveys of patients have indicated that limb pain, pallor (including a mottled appearance and cyanosis), and cold hands and feet may be prominent. Shock is manifested by tachycardia, poor peripheral perfusion, tachypnea, and oliguria. Decreased cerebral perfusion leads to confusion, agitation, or decreased level of consciousness. With progressive shock, multiorgan failure ensues; hypotension is a late sign in children, who more commonly present with compensated shock (tachycardia, poor peripheral perfusion, and normal blood pressure). Poor outcome is associated with an absence of meningism, hypotension, young age, coma, relatively low temperature (<38°C), leukopenia, and thrombocytopenia. Spontaneous hemorrhage (pulmonary, gastric, or cerebral) may result from consumption of coagulation factors and thrombocytopenia.

Chronic Meningococcemia Chronic meningococcemia, which is rarely recognized, presents as repeated episodes of petechial rash associated with fever, joint pain, features of arthritis, and splenomegaly that may progress to acute meningococcal septicemia if untreated. During the relapsing course, bacteremia characteristically clears without treatment and then recurs. The differential diagnosis includes bacterial endocarditis, acute rheumatic fever, Henoch-Schönlein purpura, infectious mononucleosis, disseminated gonococcal infection, and immune-mediated vasculitis. This condition has been associated with complement deficiencies in some cases and with inadequate sulfonamide therapy in others.

A study from the Netherlands found that half of isolates from patients with chronic meningococcemia had an underacylated lipid A (part of the surface LPS molecule) due to an lpxL1 gene mutation, which markedly reduces the inflammatory response to endotoxin.

Postmeningococcal Reactive Disease In a small proportion of patients, an immune complex disease develops ~4–10 days after the onset of meningococcal disease, with manifestations that include a maculopapular or vasculitic rash (2% of cases), arthritis (up to 8% of cases), iritis (1%), pericarditis, and/or polyserositis associated with fever. The immune complexes involve meningococcal polysaccharide antigen and result in immunoglobulin and complement deposition with an inflammatory infiltrate. These features resolve spontaneously without sequelae. It is important to recognize this condition since a new onset of fever and rash can lead to concerns about relapse of meningococcal disease and unnecessarily prolonged antibiotic treatment.

DIAGNOSIS

Like other invasive bacterial infections, meningococcal disease may produce elevations of the white blood cell (WBC) count and of values for inflammatory markers (e.g., C-reactive protein and procalcitonin levels or the erythrocyte sedimentation rate). Values may be normal or low in rapidly progressive disease, and a lack of rise in these laboratory test values does not exclude the diagnosis. However, in the presence of fever and a petechial rash, these elevations are suggestive of meningococcal disease. In patients with severe meningococcal septicemia, common laboratory findings include hypoglycemia, acidosis, hypokalemia, hypocalcemia, hypomagnesemia, hypophosphatemia, anemia, and coagulopathy.

Although meningococcal disease is often diagnosed on clinical grounds, in suspected meningococcal meningitis or meningococcemia, blood should routinely be sent for culture to confirm the diagnosis and to facilitate public health investigations; blood cultures are positive in up to 75% of cases. Culture media containing sodium polyanethol sulfonate, which may inhibit meningococcal growth, should be avoided. Meningococcal viability is reduced if there is a delay in transport of the specimen to the microbiology laboratory for culture or in plating of cerebrospinal fluid (CSF) samples. In countries where treatment with antibiotics before hospitalization is recommended for meningococcal disease, the majority of clinically suspected cases are culture negative. Real-time polymerase chain reaction (PCR) analysis of whole-blood samples increases the diagnostic yield by >40%, and results obtained with this method may remain positive for several days after administration of antibiotics. Indeed, in the United Kingdom, more than half of clinically suspected cases are currently identified by PCR.

Unless contraindications exist (raised intracranial pressure, uncorrected shock, disordered coagulation, thrombocytopenia, respiratory insufficiency, local infection, ongoing convulsions), lumbar puncture should be undertaken to identify and confirm the etiology of suspected meningococcal meningitis, whose presentation cannot be distinguished from that of meningitis of other bacterial causes. Some authorities have recommended a CT brain scan prior to lumbar puncture because of the risk of cerebral herniation in patients with raised intracranial pressure. However, a normal CT scan is not uncommon in the presence of raised intracranial pressure in meningococcal meningitis, and the decision to perform a lumbar puncture should be made on clinical grounds. CSF features of meningococcal meningitis (elevated protein level and WBC count, decreased glucose level) are indistinguishable from those of other types of bacterial meningitis unless a gram-negative diplococcus is identified. (Gram's staining is up to 80% sensitive for meningococcal meningitis.) CSF should be submitted for culture (sensitivity, 90%) and (where available) PCR analysis. CSF antigen testing with latex agglutination is insensitive and should be replaced by molecular diagnosis when possible.

Lumbar puncture should generally be avoided in meningococcal septicemia, as positioning for the procedure may critically compromise the patient's circulation in the context of hypovolemic shock. Delayed lumbar puncture may still be useful when the diagnosis is uncertain, particularly if molecular diagnostic technology is available.

In other types of focal infection, culture and PCR analysis of normally sterile body fluids (e.g., synovial fluid) may aid in the diagnosis. Although some authorities have recommended cultures of scrapings