TABLE 72-16 CAUSES OF PURPURA

- I. Primary cutaneous disorders
  - A. Nonpalpable
    - 1. Trauma
    - 2. Solar (actinic, senile) purpura
    - 3. Steroid purpura
    - 4. Capillaritis
    - 5. Livedoid vasculopathy in the setting of venous hypertension[a]
- II. Systemic diseases
  - A. Nonpalpable
    - 1. Clotting disturbances
      - a. Thrombocytopenia (including ITP)
      - b. Abnormal platelet function
      - c. Clotting factor defects
    - 2. Vascular fragility
      - a. Amyloidosis (within normal-appearing skin)
      - b. Ehlers-Danlos syndrome
      - c. Scurvy
    - 3. Thrombi
      - a. Disseminated intravascular coagulation
      - b. Warfarin (Coumadin)-induced necrosis
      - c. Heparin-induced thrombocytopenia and thrombosis
      - d. Antiphospholipid antibody syndrome
      - e. Monoclonal cryoglobulinemia
      - f. Vasculopathy induced by levamisole-adulterated cocaine
      - g. Thrombotic thrombocytopenic purpura
      - h. Thrombocytosis
      - i Homozygous protein C or protein S deficiency
    - 4. Emboli
      - a. Cholesterol
      - b. Fat
    - 5. Possible immune complex
      - a. Gardner-Diamond syndrome (autoerythrocyte sensitivity)
      - b. Waldenström's hypergammaglobulinemic purpura
  - B. Palpable
    - 1. Vasculitis
      - a. Cutaneous small-vessel vasculitis, including in the setting of systemic vasculitides
      - b. Polyarteritis nodosa
    - 2. Emboli[b]
      - a. Acute meningococcemia
      - b. Disseminated gonococcal infection
      - c. Rocky Mountain spotted fever
      - d. Ecthyma gangrenosum

[a]Also associated with underlying disorders that lead to hypercoagulability, e.g., factor V Leiden, protein C dysfunction/deficiency. [b]Bacterial (including rickettsial), fungal, or parasitic.

Abbreviation: ITP, idiopathic thrombocytopenic purpura.

In contrast to the previous group of disorders, the purpura (noninflammatory with a retiform outline) seen in the following group of diseases are associated with thrombi formation within vessels. It is important to note that these thrombi are demonstrable in skin biopsy specimens. This group of disorders includes disseminated intravascular coagulation (DIC), monoclonal cryoglobulinemia, thrombocytosis, thrombotic thrombocytopenic purpura, antiphospholipid antibody syndrome, and reactions to warfarin and heparin (heparin-induced thrombocytopenia and thrombosis). DIC is triggered by several types of infection (gram-negative, gram-positive, viral, and rickettsial) as well as by tissue injury and neoplasms. Widespread purpura and hemorrhagic infarcts of the distal extremities are seen. Similar lesions are found in purpura fulminans, which is a form of DIC associated with fever and hypotension that occurs more commonly in children following an infectious illness such as varicella, scarlet fever, or an upper respiratory tract infection. In both disorders, hemorrhagic bullae can develop in involved skin.

Monoclonal cryoglobulinemia is associated with plasma cell dyscrasias, chronic lymphocytic leukemia, and lymphoma. Purpura, primarily of the lower extremities, and hemorrhagic infarcts of the fingers, toes, and ears are seen in these patients. Exacerbations of disease activity can follow cold exposure or an increase in serum viscosity. Biopsy specimens show precipitates of the cryoglobulin within dermal vessels. Similar deposits have been found in the lung, brain, and renal glomeruli. Patients with *thrombotic thrombocytopenic purpura* can also have hemorrhagic infarcts as a result of intravascular thromboses. Additional signs include microangiopathic hemolytic anemia and fluctuating neurologic abnormalities, especially headaches and confusion.

Administration of *warfarin* can result in painful areas of erythema that become purpuric and then necrotic with an adherent black eschar; the condition is referred to as warfarin-induced necrosis. This reaction is seen more often in women and in areas with abundant subcutaneous fat—breasts, abdomen, buttocks, thighs, and calves. The erythema and purpura develop between the third and tenth day of therapy, most likely as a result of a transient imbalance in the levels of anticoagulant and procoagulant vitamin K–dependent factors. Continued therapy does not exacerbate preexisting lesions, and patients with an inherited or acquired deficiency of protein C are at increased risk for this particular reaction as well as for purpura fulminans and calciphylaxis.

Purpura secondary to *cholesterol emboli* are usually seen on the lower extremities of patients with atherosclerotic vascular disease. They often follow anticoagulant therapy or an invasive vascular procedure such as an arteriogram but also occur spontaneously from disintegration of atheromatous plaques. Associated findings include livedo reticularis, gangrene, cyanosis, and ischemic ulcerations. Multiple step sections of the biopsy specimen may be necessary to demonstrate the cholesterol clefts within the vessels. Petechiae are also an important sign of *fat embolism* and occur primarily on the upper body 2–3 days after a major injury. By using special fixatives, the emboli can be demonstrated in biopsy specimens of the petechiae. Emboli of tumor or thrombus are seen in patients with atrial myxomas and marantic endocarditis.

In the *Gardner-Diamond syndrome* (autoerythrocyte sensitivity), female patients develop large ecchymoses within areas of painful, warm erythema. Intradermal injections of autologous erythrocytes or phosphatidyl serine derived from the red cell membrane can reproduce the lesions in some patients; however, there are instances where a reaction is seen at an injection site of the forearm but not in the midback region. The latter has led some observers to view Gardner-Diamond syndrome as a cutaneous manifestation of severe emotional stress. More recently, the possibility of platelet dysfunction (as assessed via aggregation studies) has been raised. *Waldenström's hypergammaglobulinemic purpura* is a chronic disorder characterized by petechiae on the lower extremities. There are circulating complexes of IgG–anti-IgG molecules, and exacerbations are associated with prolonged standing or walking.

Palpable purpura are further subdivided into vasculitic and embolic. In the group of vasculitic disorders, cutaneous small-vessel vasculitis, also known as *leukocytoclastic vasculitis* (LCV), is the one most commonly associated with palpable purpura (Chap. 385). Underlying etiologies include drugs (e.g., antibiotics), infections (e.g., hepatitis C virus), and autoimmune connective tissue diseases (e.g., rheumatoid arthritis, Sjögren's syndrome, lupus). *Henoch-Schönlein purpura* (HSP) is a subtype of acute LCV that is seen more commonly in children and adolescents following an upper respiratory infection. The majority of lesions are found on the lower extremities and buttocks. Systemic manifestations include fever, arthralgias (primarily of the knees and ankles), abdominal pain, gastrointestinal bleeding, and nephritis. Direct immunofluorescence examination shows deposits of IgA within dermal blood vessel walls. Renal disease is of particular concern in adults with HSP. In *polyarteritis nodosa*, specific cutaneous lesions result from a vasculitis of arterial vessels (arteritis), or there