locations, or take the form of menorrhagia, nosebleeds, gastrointestinal bleeding, or hematuria. The platelet count and tests of coagulation (PT, PTT) are usually normal, pointing by exclusion to the underlying problem.

The varied clinical conditions in which abnormalities in the vessel wall cause bleeding include the following:

- *Infections* often induce petechial and purpuric hemorrhages, particularly meningococcemia, other forms of septicemia, infective endocarditis, and several of the rickettsioses. The involved mechanisms include microbial damage to the microvasculature (vasculitis) and disseminated intravascular coagulation. Failure to recognize meningococcemia as a cause of petechiae and purpura can be catastrophic for the patient.
- *Drug reactions* sometimes induce cutaneous petechiae and purpura without causing thrombocytopenia. In many instances the vascular injury is mediated by the deposition of drug-induced immune complexes in vessel walls, which leads to hypersensitivity (*leukocytoclastic*) vasculitis (Chapter 11).
- *Scurvy* and the *Ehlers-Danlos syndrome* are associated with microvascular bleeding that results from collagen defects that weaken vessel walls. The same mechanism may account for the spontaneous purpura that are commonly seen in older adults and the skin hemorrhages that are seen with *Cushing syndrome,* in which the protein-wasting effects of excessive corticosteroid production cause loss of perivascular supporting tissue.
- *Henoch-Schönlein purpura* is a systemic immune disorder of unknown cause that is characterized by a purpuric rash, colicky abdominal pain, polyarthralgia, and acute glomerulonephritis (Chapter 20). All these changes result from the deposition of circulating immune complexes within vessels throughout the body and within the glomerular mesangial regions.
- *Hereditary hemorrhagic telangiectasia* (also known as *Weber-Osler-Rendu syndrome*) is an autosomal dominant disorder that can be caused by mutations in at least five different genes, most of which modulate TGF-β signaling. It is characterized by dilated, tortuous blood vessels with thin walls that bleed readily. Bleeding can occur anywhere, but it is most common under the mucous membranes of the nose (epistaxis), tongue, mouth, and eyes, and throughout the gastrointestinal tract.
- *Perivascular amyloidosis* can weaken blood vessel walls and cause bleeding. This complication is most common with amyloid light-chain (AL) amyloidosis (Chapter 6) and often manifests as mucocutaneous petechiae.

Among these conditions, serious bleeding is most often associated with hereditary hemorrhagic telangiectasia. The bleeding in each is nonspecific, and the diagnosis of these entities is based on the recognition of other more specific associated findings.

Bleeding Related to Reduced Platelet Number: Thrombocytopenia

Reduction in platelet number (*thrombocytopenia*) constitutes an important cause of generalized bleeding. A count less than 100,000 platelets/μL is generally considered to constitute thrombocytopenia. Platelet counts in the range of 20,000 to 50,000 platelets/μL can aggravate posttraumatic bleeding, while platelet counts less than 20,000 platelets/μL may be associated with spontaneous (nontraumatic) bleeding. Bleeding resulting from thrombocytopenia is associated with a normal PT and PTT.

Table 14-9 Causes of Thrombocytopenia

Decreased Production of Platelets
Selective impairment of platelet production
Drug-induced: alcohol, thiazides, cytotoxic drugs
Infections: measles, human immunodeficiency virus (HIV)
Nutritional deficiencies
B_{12}, folate deficiency (megaloblastic leukemia)
Bone marrow failure
Aplastic anemia (see Table 14-7)
Bone marrow replacement
Leukemia, disseminated cancer, granulomatous disease
Ineffective hematopoiesis
Myelodysplastic syndromes (Chapter 13)
Decreased Platelet Survival
Immunologic destruction
Primary autoimmune
Chromic immune thrombocytopenic purpura
Acute immune thrombocytopenic purpura
Secondary autoimmune
Systemic lupus erythematosus, B-cell lymphoid neoplasms
Alloimmune: posttransfusion and neonatal
Drug-associated: quinidine, heparin, sulfa compounds
Infections: HIV, infectious mononucleosis (transient, mild), dengue fever
Nonimmunologic destruction
Disseminated intravascular coagulation
Thrombotic microangiopathies
Giant hemangiomas
Sequestration
Hypersplenism
Dilution
Transfusions

Platelets are critical for hemostasis, in that they form temporary plugs that stop bleeding and promote key reactions in the coagulation cascade (Chapter 4). Spontaneous bleeding associated with thrombocytopenia most often involves small vessels. Common sites for such hemorrhages are the skin and the mucous membranes of the gastrointestinal and genitourinary tracts. Most feared, however, is *intracranial bleeding*, which is a threat to any patient with a markedly depressed platelet count.

The causes of thrombocytopenia fall into four major categories (Table 14-9).

- *Decreased platelet production.* This can result from conditions that depress marrow output generally (such as aplastic anemia and leukemia) or affect megakaryocytes somewhat selectively. Examples of the latter include certain drugs and alcohol, which may suppress platelet production through uncertain mechanisms when taken in large amounts; HIV, which may infect megakaryocytes and inhibit platelet production; and myelodysplastic syndromes (Chapter 13), which may occasionally present with isolated thrombocytopenia.