Polycythemia

Polycythemia denotes an abnormally high red cell count, usually with a corresponding increase in the hemoglobin level. It may be relative when there is hemoconcentration due to decreased plasma volume, or absolute when there is an increase in the total red cell mass. *Relative polycythemia* results from dehydration, such as occurs with deprivation of water, prolonged vomiting or diarrhea, or excessive use of diuretics. It is also associated with an obscure condition of unknown etiology called stress polycythemia, or Gaisböck syndrome. Affected individuals are usually hypertensive, obese, and anxious ("stressed"). *Absolute polycythemia* is *primary* when it results from an intrinsic abnormality of hematopoietic precursors and *secondary* when the red cell progenitors are responding to increased levels of erythropoietin. A pathophysiologic classification of polycythemia divided along these lines is given in Table 14-8.

The most common cause of primary polycythemia is *polycythemia vera*, a myeloproliferative disorder associated with mutations that lead to erythropoietin-independent growth of red cell progenitors (Chapter 13). Much less commonly, primary polycythemia results from familial mutations in the erythropoietin receptor that induce erythropoietin-independent receptor activation. One such individual won Olympic gold medals in cross-country skiing, having benefited from this natural form of blood doping! Secondary polycythemia may be caused by compensatory or pathologic increases in erythropoietin secretion. Causes of the latter include erythropoietin-secreting tumors and rare, but illustrative, inherited defects that lead to the stabilization of HIF-1α, a hypoxia-induced factor that stimulates the transcription of the erythropoietin gene.

Bleeding Disorders: Hemorrhagic Diatheses

Excessive bleeding can result from (1) increased fragility of vessels, (2) platelet deficiency or dysfunction, and (3) derangement of coagulation, alone or in combination. Before discussing specific bleeding disorders, it is helpful to review the common laboratory tests used in the evaluation of a bleeding diathesis. The normal hemostatic response involves the blood vessel wall, the platelets, and the clotting cascade (Chapter 4). Tests used to evaluate different aspects of hemostasis are the following:

- *Prothrombin time (PT).* This test assesses the extrinsic and common coagulation pathways. The clotting of plasma after addition of an exogenous source of tissue thromboplastin (e.g., brain extract) and Ca^{2+} ions is measured in seconds. A prolonged PT can result from deficiency or dysfunction of factor V, factor VII, factor X, prothrombin, or fibrinogen.
- *Partial thromboplastin time (PTT).* This test assesses the intrinsic and common clotting pathways. The clotting of plasma after addition of kaolin, cephalin, and Ca^{2+} ions is measured in seconds. Kaolin activates the contact-dependent factor XII, and cephalin substitutes for platelet phospholipids. Prolongation of the PTT can be due to deficiency or dysfunction of factors V, VIII, IX, X, XI, or XII, prothrombin, or fibrinogen, or to interfering antibodies to phospholipid (Chapter 4).
- *Platelet counts.* These are obtained on anticoagulated blood using an electronic particle counter. The reference range is 150×10^3 to 300×10^3 platelets/μL. Abnormal platelet counts are best confirmed by inspection of a peripheral blood smear, in that clumping of platelets can cause spurious "thrombocytopenia" during automated counting, and high counts may be indicative of a myeloproliferative disorder, such as essential thrombocythemia (Chapter 13).
- *Tests of platelet function.* At present, no single test provides an adequate assessment of the complex functions of platelets. Specialized tests that can be useful in particular clinical settings include tests of platelet aggregation, which measure the ability of platelets to aggregate in response to agonists like thrombin; and quantitative and qualitative tests of von Willebrand factor, which plays an important role in platelet adhesion to the extracellular matrix (Chapter 4). An older test, the bleeding time, has some value but is time-consuming and difficult to standardize and is therefore performed infrequently. Newer instrument-based assays that provide quantitative measures of platelet function show promise but remain imperfect at predicting bleeding risk, presumably because of difficulties in simulating in vivo clotting in the laboratory.

More specialized tests are available to measure the levels of specific clotting factors, fibrinogen, fibrin split products, and the presence of circulating anticoagulants.

Table 14-8 Pathophysiologic Classification of Polycythemia

Relative
Reduced plasma volume (hemoconcentration)
Absolute
Primary (Low Erythropoietin)
Polycythemia vera
Inherited erythropoietin receptor mutations (rare)
Secondary (High Erythropoietin)
Compensatory
Lung disease
High-altitude living
Cyanotic heart disease
Paraneoplastic
Erythropoietin-secreting tumors (e.g., renal cell carcinoma, hepatocellular carcinoma, cerebellar hemangioblastoma)
Hemoglobin mutants with high O_2 affinity
Inherited defects that stabilize HIF-1α
Chuvash polycythemia (homozygous *VHL* mutations)
Prolyl hydroxylase mutations

HIF-1α, Hypoxia-induced factor 1α.

Bleeding Disorders Caused by Vessel Wall Abnormalities

Disorders within this category are relatively common, but do not usually cause serious bleeding problems. Most often, they present with small hemorrhages (petechiae and purpura) in the skin or mucous membranes, particularly the gingivae. On occasion, however, more significant hemorrhages occur into joints, muscles, and subperiosteal