TABLE 78-3 RISK FACTORS FOR THROMBOSIS

Venous	Venous and Arterial
Inherited	**Inherited**
Factor V Leiden	Homocystinuria
Prothrombin G20210A	Dysfibrinogenemia
Antithrombin deficiency	**Mixed (inherited and acquired)**
Protein C deficiency	Hyperhomocysteinemia
Protein S deficiency	**Acquired**
Elevated factor VIII	Malignancy
Acquired	Antiphospholipid antibody syndrome
Age	Hormonal therapy
Previous thrombosis	Polycythemia vera
Immobilization	Essential thrombocythemia
Major surgery	Paroxysmal nocturnal hemoglobinuria
Pregnancy and puerperium	Thrombotic thrombocytopenic purpura
Hospitalization	Heparin-induced thrombocytopenia
Obesity	Disseminated intravascular coagulation
Infection	
APC resistance, nongenetic	
Smoking	
Unknown[a]	
Elevated factor II, IX, XI	
Elevated TAFI levels	
Low levels of TFPI	

[a]Unknown whether risk is inherited or acquired.

Abbreviations: APC, activated protein C; TAFI, thrombin-activatable fibrinolysis inhibitor; TFPI, tissue factor pathway inhibitor.

undergoing a high-risk surgical procedure. As illustrated in Fig. 78-5, a thrombotic event usually has more than one contributing factor. Predisposing factors must be carefully assessed to determine the risk of recurrent thrombosis and, with consideration of the patient's bleeding risk, determine the length of anticoagulation.

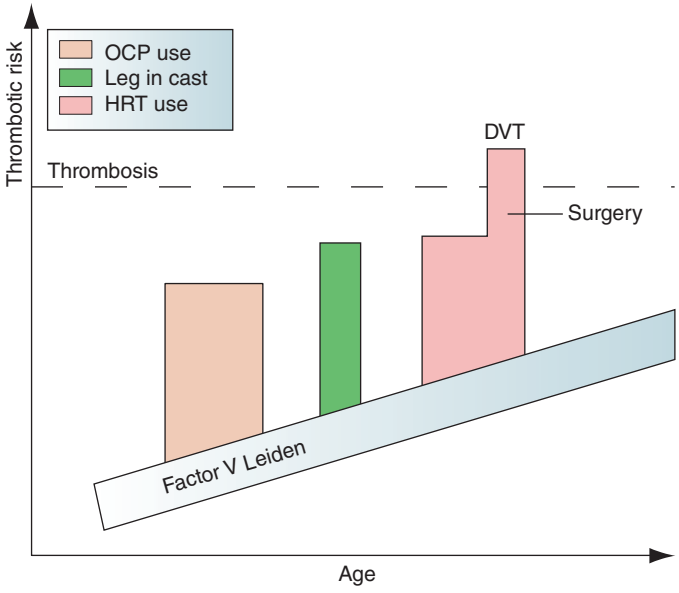

FIGURE 78-5 Thrombotic risk over time. Shown schematically is an individual's thrombotic risk over time. An underlying factor V Leiden mutation provides a "theoretically" constant increased risk. The thrombotic risk increases with age and, intermittently, with oral contraceptive (OCP) or hormone replacement therapy (HRT) use; other events may increase the risk further. At some point, the cumulative risk may increase to the threshold for thrombosis and result in deep venous thrombosis (DVT). Note: The magnitude and duration of risk portrayed in the figure are meant for example only and may not precisely reflect the relative risk determined by clinical study. *(From BA Konkle, A Schafer, in DP Zipes et al [eds]: Braunwald's Heart Disease, 7th ed. Philadelphia, Saunders, 2005; modified with permission from FR Rosendaal: Venous thrombosis: A multicausal disease. Lancet 353:1167, 1999.)*

Similar consideration should be given in determining the need, if any, to test the patient and family members for thrombophilias.

LABORATORY EVALUATION

Careful history taking and clinical examination are essential components in the assessment of bleeding and thrombotic risk. The use of laboratory tests of coagulation complement, but cannot substitute for, clinical assessment. No test exists that provides a global assessment of hemostasis. The bleeding time has been used to assess bleeding risk; however, it does not predict bleeding risk with surgery and it is not recommended for this indication. The PFA-100, an instrument that measures platelet-dependent coagulation under flow conditions, is more sensitive and specific for VWD than the bleeding time; however, it is not sensitive enough to rule out mild bleeding disorders. PFA-100 closure times are prolonged in patients with some, but not all, inherited platelet disorders. Also, its utility in predicting bleeding risk has not been determined.

For routine preoperative and preprocedure testing, an abnormal prothrombin time (PT) may detect liver disease or vitamin K deficiency that had not been previously appreciated. Studies have not confirmed the usefulness of an aPTT in preoperative evaluations in patients with a negative bleeding history. The primary use of coagulation testing should be to confirm the presence and type of bleeding disorder in a patient with a suspicious clinical history.

Because of the nature of coagulation assays, proper sample acquisition and handling is critical to obtaining valid results. In patients with abnormal coagulation assays who have no bleeding history, repeat studies with attention to these factors frequently results in normal values. Most coagulation assays are performed in sodium citrate anticoagulated plasma that is recalcified for the assay. Because the anticoagulant is in liquid solution and needs to be added to blood in proportion to the plasma volume, incorrectly filled or inadequately mixed blood collection tubes will give erroneous results. Vacutainer tubes should be filled to >90% of the recommended fill, which is usually denoted by a line on the tube. An elevated hematocrit (>55%) can result in a false value due to a decreased plasma-to-anticoagulant ratio.

Screening Assays The most commonly used screening tests are the PT, aPTT, and platelet count. The PT assesses the factors I (fibrinogen), II (prothrombin), V, VII, and X (Fig. 78-6). The PT measures the time for clot formation of the citrated plasma after recalcification and addition of thromboplastin, a mixture of TF and phospholipids. The sensitivity of the assay varies by the source of thromboplastin. The relationship between defects in secondary hemostasis (fibrin formation) and coagulation test abnormalities is shown in Table 78-4. To adjust for this variability, the overall sensitivity of different thromboplastins to reduction of the vitamin K–dependent clotting factors II, VII, IX, and X in anticoagulation patients is now expressed as the International Sensitivity Index (ISI). An inverse relationship exists between ISI and thromboplastin sensitivity. The international normalized ratio (INR) is then determined based on the formula: $\text{INR} = (\text{PT}_{\text{patient}}/\text{PT}_{\text{normal mean}})^{\text{ISI}}$.

The INR was developed to assess stable anticoagulation due to reduction of vitamin K–dependent coagulation factors; it is commonly used in the evaluation of patients with liver disease. Although it does allow comparison between laboratories, reagent sensitivity as used to determine the ISI is not the same in liver disease as with warfarin anticoagulation. In addition, progressive liver failure is associated with variable changes in coagulation factors; the degree of prolongation of either the PT or the INR only roughly predicts the bleeding risk. Thrombin generation has been shown to be normal in many patients with mild to moderate liver dysfunction. Because the PT only measures one aspect of hemostasis affected by liver dysfunction, we likely overestimate the bleeding risk of a mildly elevated INR in this setting.

The aPTT assesses the intrinsic and common coagulation pathways; factors XI, IX, VIII, X, V, and II; fibrinogen; prekallikrein;