Evaluation of Coagulation in the Neurosurgery Patient

George M. Rodgers, MD, PhD

KEYWORDS

• Coagulation testing • Hemostasis • Fibrinolysis • Viscoelastic assays • Thromboelastography • Rotational elastometry • Traumatic brain injury

KEY POINTS

- Bleeding disorders can be categorized as platelet type or coagulation type.
- The bleeding time test is not a reliable assay to diagnose platelet-type bleeding disorders or to predict surgical bleeding.
- The gold standard assay for measuring platelet function is light transmission platelet aggregation.
- The prothrombin time and partial thromboplastin time are the 2 primary screening tests used to assess coagulation. These assays (and the International Normalized Ratio) predict bleeding and mortality in neurosurgical patients.
- Viscoelastic assays are useful in guiding transfusion therapy and diagnosing hyperfibrinolysis in neurosurgical patients. Their use in guiding treatment decisions is controversial.

OVERVIEW OF HEMOSTASIS

Achieving and maintaining adequate hemostasis is critical in management of neurosurgical patients. Even minor bleeding may have severe clinical consequences. This article reviews normal hemostatic mechanisms, summarizes traditional and emerging coagulation tests that are relevant for neurosurgical patients, reviews the clinical usefulness of standard and newer coagulation tests in neurosurgery practice with a focus on patients with traumatic brain injury (TBI), and provides an overview of common bleeding disorders and their laboratory evaluation.

Mechanisms of Normal Hemostasis

The prevention of excessive bleeding after vascular injury relies on normal hemostasis, which provides for balanced interactions between the vessel wall, coagulation proteins, and platelets.[1] After vascular injury, vascular constriction occurs in association with platelet aggregation and fibrin formation.

Normal hemostasis includes primary hemostasis, which involves platelet adhesion and aggregation, and secondary hemostasis, which involves thrombin generation and the formation of a fibrin mesh that reinforces the platelet thrombus. Defects in either hemostatic pathway may result in a bleeding disorder. After hemostasis has been achieved, blood vessel patency is restored by the fibrinolytic mechanism.

Excessive bleeding may result either from defects in primary hemostasis (platelet number or platelet function), defects in secondary hemostasis (coagulation protein deficiency), or excessive fibrinolysis.

Primary Hemostasis

In the absence of vascular injury, the normal vessel wall expresses antiplatelet and anticoagulant

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Division of Hematology and Hematologic Malignancies, University of Utah Health Sciences Center, 30 North 1900 East, Salt Lake City, UT 84132, USA
E-mail address: george.rodgers@hsc.utah.edu

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activities that maintain blood in the fluid state and prevent activation of platelets and the coagulation mechanism.[2] However, with blood vessel injury, subendothelium is exposed that contains collagen fibrils, which induce binding of von Willebrand factor to platelets. Glycoprotein (GP) Ib is the platelet von Willebrand factor receptor required for platelet adhesion. Subsequent platelet activation leads to platelet aggregation, which is mediated by fibrinogen and its receptor, platelet GP IIbIIIa. Therefore, the defects in primary hemostasis that could lead to bleeding include deficiency of platelet GP 1b or GP IIbIIIa, deficiency of von Willebrand factor (von Willebrand disease), thrombocytopenia, or platelet dysfunction.[1]

Secondary Hemostasis

An effective clot requires fibrin consolidation (reinforcement) of the initial platelet thrombus; otherwise, delayed bleeding may occur. Secondary hemostasis involves thrombin generation and fibrin formation to provide this consolidation.

Typically, the blood coagulation mechanism is initiated by vessel trauma that exposes extravascular tissue factor to blood.[1] Tissue factor is present in the subendothelial matrix and fibroblasts; exposure of tissue factor to coagulation factor VII in blood initiates the coagulation pathway, leading to thrombin formation. The coagulation pathway is summarized in **Fig. 1**; it involves sequential enzymatic conversions of precursor coagulation zymogens to proteases that ultimately result in conversion of prothrombin to thrombin. Thrombin then activates platelets and converts soluble fibrinogen to an insoluble fibrin clot. Defects in secondary hemostasis that could result in bleeding include deficiency of or antibody to prothrombin (factor II), fibrinogen, and factors V, VII, VIII, IX, X, XI, and XIII.[1]

Fibrinolysis

After cessation of bleeding by formation of the hemostatic plug, repair of the blood vessel begins with lysis of the fibrin clot.[1] Endothelial cells of the vessel wall secrete tissue plasminogen activator (TPA); activation of plasminogen by TPA produces plasmin, a protease that induces clot lysis. Fibrinolysis is regulated by inhibitors to TPA (plasminogen activator inhibitor) and plasmin (α_2-antiplasmin). Defects in fibrinolysis that could result in bleeding include excessive secretion of TPA or deficiency of plasminogen activator inhibitor or α_2-antiplasmin.[1] **Fig. 2** summarizes hemostatic events that occur after vascular injury, including

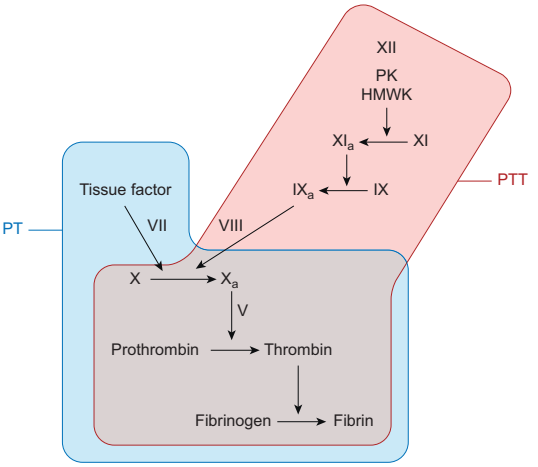

Fig. 1. The coagulation pathway and coagulation assays (prothrombin time [PT], partial thromboplastin time [PTT]) used to measure coagulation factor activities. The PT measures the tissue factor/factor VII pathway and common pathway (fibrinogen, prothrombin, factors V and X); this pathway is initiated in vivo with vascular injury when extravascular tissue factor interacts with factor VII to activate factor X. The PTT measures the common coagulation pathway plus 6 additional coagulation factors, namely, factor XII, PK, HMWK, factor VIII, factor IX, and factor XI. Factor XII, PK, and HMWK are necessary for in vitro coagulation, but not in vivo coagulation. The endpoint of both the PT and PTT assays is conversion of fibrinogen to fibrin. Factor XIII activity (not shown) is not measured by the PT or PTT assays. HMWK, high-molecular-weight kininogen; PK, prekallikrein; PT, prothrombin time; PTT, partial thromboplastin time.

platelet adhesion and aggregation, thrombin generation, and fibrin formation.

APPROACH TO THE BLEEDING PATIENT

Before laboratory testing, historical questions may provide useful information as to the type of bleeding disorder.[3] Asking about the duration of the bleeding tendency can aid in distinguishing inherited versus acquired bleeding disorders. Inquiring about a familial bleeding history can suggest if the bleeding disorder is transmitted in a dominant versus recessive manner. Asking whether bleeding is spontaneous versus requiring surgery or trauma can indicate if the bleeding disorder is severe or mild. The presence of petechial rash and small bruises suggest a platelet-type bleeding disorder, whereas large soft tissue hematomas, visceral bleeding, and hemarthrosis suggest a coagulation-type bleeding disorder. **Table 1** summarizes differences between platelet-type versus coagulation-type bleeding disorders.