K. J. Lee: Essential Otolaryngology and Head and Neck Surgery (IIIrd Ed)

Chapter 33: Surgical Hemostasis

Excessive surgical bleeding can result from vascular injury or may be secondary to a defect in the hemostatic mechanism. If damage to local tissue or vascular integrity is not the apparent cause for excessive bleeding, then such patients should be evaluated for a defect in platelets or the blood coagulation process. It is a mistake to assume that all patients with bleeding and a local anatomic defect do not also have an undetected bleeding disorder. Therefore, all bleeding patients should be screened for the common bleeding disorders. Likewise, all patients in whom surgery is anticipated should undergo a similar screening evaluation for clinically undetected bleeding disorders.

Hemostasis results from a complex interaction of plasma coagulation factors, platelets, and blood vessels. Tissue injury results in vasoconstriction, exposure of the blood to collagen and connective tissue, as well as to the procoagulant thromboplastin. Thromboplastin or tissue factor causes activation of the coagulation system through what is known as the extrinsic system. Through a final common pathway fibrin is formed. Simultaneously, platelets begin to adhere to exposed collagen. Once this happens, platelets aggregate, release ADP, and form the platelet plug. The release of phospholipids from platelets, as well as the formation of fibrin, triggers the more complex intrinsic coagulation system with continued formation of the fibrin net. Figure 33-1 shows a simplified coagulation cascade. Adequate functional levels of coagulation factors are necessary for the formation of a fibrin clot. In addition, adequate numbers of functioning platelets are necessary for hemostasis by both plugging blood vessel holes and by providing phospholipids necessary for the coagulation cascade.

Clinical Evaluation of the Bleeding Patient

In the patient who is bleeding, it must be determined if the problem is a local one alone or if it is related to a defect in the hemostatic system. A careful history and physical examination in conjunction with several screening laboratory tests will usually clarify this problem and indicatge whether it is congenital or acquired. A history of easy bruisability, spontaneous bleeding, especially from mucous membranes, and excessive bleeding after trauma, all suggest either an acquired or congenital bleeding disorder. A family history of bleeding suggests an inherited coagulation disorder such as hemophilia or von Willebrand's disease. For example, the description of bleeding following a dental extraction may be an important clue to a bleeding disorder. Normal patients typically bleed for up to 12 hours after a dental extraction and may have some slight oozing for an additional 1-2 days. Patients with platelet disorders usually have immediate and chronic bleeding while patients with disorders of blood coagulation typically have delayed bleeding. The phenomenon of delayed bleeding in patients with coagulation defects may be explained by the fact that these patients form a normal platelet plug which prevents immediate bleeding following a dental extraction. However, an inadequate coagulation system will allow bleeding to restart after 1-8 days. Therefore, bleeding occurring later than 3 days after surgery should alert one to the possibility of a secondary hemorrhagic diathesis. Physical examination may reveal petechiae suggesting a platelet disorder or significant bruising (especially greater than 6 cm) suggesting a coagulation defect. Bleeding from multiple sites is seen with disseminated intravascular coagulation with defibrination.

Laboratory Evaluation

The most common tests used to evaluate the hemostatic and coagulation systems are outlined below. Table 33-1 summarizes the relationship between different bleeding disorders and specific laboratory abnormalities.

Screening Tests

Platelet Count

The platelet count is a measurement of the number of circulating platelets. The normal platelet count is 150.000-350.000/mm^3. A platelet estimate is usually adequate and is obtained from evaluation of the peripheral blood smear by an experienced technician. A formal platelet count is more accurate and should be done when an exact platelet count is needed.

Prothrombin Time (PT)

This test evaluates the extrinsic coagulation system as well as the final common pathway. The test is prolonged secondarily to hereditary deficiencies of Factors V, VII, X, prothrombin, and fibrinogen. It is most frequently abnormal with acquired disorders of coagulation such as vitamin K deficiency, warfarin (Coumadin) ingestion, liver disease, and disseminated intravascular coagulation.

Activated Partial Thromboplastin Time (PTT)

This test evaluates all of the coagulation factors in the intrinsic coagulation system and final common pathway. The PTT is prolonged by reduced levels of Factors VIII, IX, XI, and XII. To a lesser extent, it also is affected by defects in the final common pathway. Heparin prolongs the PTT by its antithrombin action and this test is a useful monitor of heparin activity. Mixing studies using equal parts of normal plasm and the patient's plasma may help to determine whether prolongation of the PTT is secondary to a coagulation factor deficiency or a circulating anticoagulant.

Additional Tests

Bleeding Time

This test specifically evaluates platelet function. The bleeding time will be prolonged if the platelet count falls below 100.000 or when there is a defect in platelet function. The normal value for the modified Ivy bleeding time is 2.5-10 minutes with a mean of 5 minutes. Despite a normal platelet count, certain drugs such as aspirin and the nonsteroidal anti-inflammatory drugs will prolong the bleeding time by affecting platelet function. This test is also abnormal in uremia and in von Willebrand's disease.

Platelet Aggregation Studies

These tests further define platelet function and may be abnormal with both congenital and acquired platelet function disorders. They are useful in separating out the different problems that can prolong a bleeding time.

Fibrinogen Level

Low levels of fibrinogen may be seen with disseminated intravascular coagulation, fibrinolysis, and a severe liver disease.

Thrombin Time

This test measures clot formation when thrombin is added to plasma. It is prolonged in clinical states manifesting very low levels of fibrinogen. It also is prolonged by elevated levels of fibrin degradation products, disseminated intravascular coagulation (DIC), and with heparin use.

Fibrin Degradation Products

These are circulating fragments of fibrin or fibrinogen. They are typically increased with liver disease, DIC, and fibrinolysis.

Specific Coagulation Factor Assays

The measurement of plasma levels of specific coagulation factors can be obtained. These assays can help to define specific coagulation factor deficiencies.

The platelet count, PT, and PTT are used as initial screening tests. A prolonged PTT will detect most patients (greater than 90%) with hereditary coagulation factor deficiencies while a prolongation of the PT usually suggests an acquired disorder of coagulation such as vitamin K deficiency or DIC. These tests will be normal in patients with vascular abnormalities such as hereditary hemorrhagic telangiectasia, senile purpura, cryoglobulinemia, and allergic purpura. The PT and PTT may be prolonged secondary to improperly collected and stored blood samples, and abnormal results should always be repeated. Unfortunately, some patients with mild coagulation factor deficiencies or with mild von Willebrand's disease who have significant bleeding may have normal screening tests.

Patients with no bleeding history and normal screening tests are assumed to have no bleeding problem. Alternatively, a defect in hemostasis can be assured if abnormal screening tests are associated with a history of abnormal bleeding. The most difficult patients to evaluate are those in whom there is a history suggestive of abnormal bleeding but the primary screening tests are normal. Such patients need further evaluation especially if surgery is contemplated. Mild coagulation factor deficiencies and von Willebrand's disease may fall into this group. Additional studies that might be done are a bleeding time, specific coagulation factor assays, and platelet aggregation studies. The latter test is especially important if the bleeding time is found to be prolonged as is typically the case in von Willebrand's disease.

It should be remembered that a clear-cut history of bleeding may be more significant than a normal laboratory evaluation.

Specific Hemostatic and Coagulation Abnormalities

Platelet Abnormalities

Normally, platelet counts range between 150.000-350.000/mm^3. In addition to a low platelet count, defects in platelet function or extraordinarily high platelet counts may all be associated with bleeding. Bleeding secondary to platelet disorders is usually small-vessel bleeding, and one frequently sees petechial hemorrhages on the skin and mucous membranes. A low platelet count or abnormal platelet function will prolong the bleeding time, and this test is therefore useful in the evaluation of platelet function.

Thrombocytopenia

Thrombocytopenia is the most common cause of abnormal bleeding. While spontaneous bleeding typically is not seen until the platelet count falls below 20.000/m^3, platelet levels below 100.000/mm^3 can cause bleeding during surgery (assuming platelet function is normal). A low platelet count may be secondary to reduced platelet production as seen with bone marrow infiltrative processes, ineffective thrombopoiesis as in megaloblastic defects (vitamin B12 or folic acid deficiency), primary disorders of the bone marrow, and by hematopoietic suppression secondary to drugs. Increased destruction of platelets as seen with idiopathic thrombocytopenic purpura (ITP), drug allergy, hypersplenism, and DIC also cause a reduction in the number of circulating platelets. Bleeding is typically more severe in disorders caused by decreased platelet production. Syndromes associated with increased platelet destruction are accompanied by younger circulating platelets which are homeostatically most effective. Older functionally senescent platelets predominate in the circulation of patients with decreased platelet production. A bone marrow aspiration is required to evaluate thrombocytopenia since the number of megakaryocytes may suggest either decreased platelet production or increased destruction as the cause for the thrombocytopenia.

Another significant and important cause of thrombocytopenia is platelet loss. This should be looked for in a bleeding patient who has received more than 10 units of red cells, since banked red cells do not contain significant numbers of viable platelets. Thrombocytopenia is treated by the administration of platelet concentrates.

Platelet transfusions should be given prophylactically to patients with platelet counts less than 20.000/mm^3, especially when the thrombocytopenia is caused by reduced platelet production. All patients with hemorrhage and thrombocytopenia also should be given platelet transfusions though they may not be of value if the thrombocytopenia is secondary to accelerated platelet destruction as is the case with immune thrombocytopenia.

Qualitative Platelet Disorders

Abnormal platelet function also may cause bleeding. A normal platelet count in the presence of a prolonged bleeding time suggests platelet dysfunction. Platelet aggregation

studies are available in many hospitals to further evaluate this problem. Although congenital defects in platelet function are rare, acquired defects in platelet function are not uncommon. This may result from the ingestion of drugs such as aspirin and the non-steroidal anti-inflammatory agents. Other causes of platelet dysfunction include uremia, the myeloproliferative disorders, and paraproteinemias. Treatment may be with the transfusion of platelet concentrates or by the removal of the offending agent.

Thrombocytosis

Bleeding also may become a problem if the platelet count rises above 1 million/mm^3 especially when this occurs secondary to a myeloproliferative disorder. Treatment is directed toward the underlying cause of the thrombocytosis. Occasionally, however, in an emergency situation, plateletpheresis can be done.

Coagulation Factor Deficiencies

The most common hereditary coagulation factor deficiencies are typically associated with a prolongation of the PTT. Von Willebrand's disease is the most common of these disorders followed by hemophilia A (Factor VIII deficiency), Factor IX, and Factor XI deficiency. Together these four disorders comprise greater than 90% of the congenital coagulation factor deficiencies. Other hereditary coagulation factor deficiencies are quite rare and will be mentioned only for completeness. Rarely, patients develop acquired deficiencies of coagulation factors, usually secondary to an underlying immunologic disorder.

There is no difficulty in diagnosing the patient with a severe hereditary coagulation factor deficiency. These patients have lifelong bleeding at times including disabling hemarthrosis. Mild to moderate deficiencies of the coagulation factors are more of a diagnostic problem. These disorders are at times unsuspected yet bleeding after surgery or trauma may be quite severe. It is these mild deficiencies which are clinically unsuspected that we hope to detect by our screening coagulation tests.

Factor VIII Deficiency (Hemophilia A)

Factor VIII deficiency and Factor IX deficiency (hemophilia B or Christmas disease) are both inherited as sex-linked recessive traits. In Facor VIII deficiency the actual coagulation protein is not absent. Rather, its is qualitatively abnormal. This explains the classic findings of low Factor VIII coagulation activity in the presence of normal levels of immunologically measured Factor VIII antigen. As will be seen below, a normal level of Factor VIII antigen distinguishes hemophilia A from von Willebrand's disease where both Factor VIII activity and antigen are decreased.

When Factor VIII levels are very low, the activated partial thromboplastin time is markedly prolonged. The severity of the hemophilic disorders correlates directly with coagulation factor activity. In hemophilia A, Factor VIII activity is typically less than 2%. Crippling hemarthroses and other severe spontaneous bleeding develops. As the level of Factor VIII activity increases from 2-25%, episodes of hemarthrosis become less frequent and spontaneous bleeding occurs less often. The PTT which was markedly prolonged when Factor VIII activity was less than 5% approaches the normal range. It is specifically this group of

patients with mild hemophilia and Factor VIII levels between 5-40% who may have a normal PTT yet may have serious bleeding after trauma or with surgery. For this reason, a Factor VIII level is obtained when there is a significant bleeding history and the PTT is borderline or normal. The PT and bleeding time are both normal in this disorder.

The goal of therapy for these patients is to restore Factor VIII activity to a hemostatically safe range. Cryoprecipitate has high levels of Factor VIII activity and is the blood product of choice for this disorder. A reasonable therapeutic regimen for patients with bleeding or who are undergoing major surgery consists of a loading dose of 3.5 bags of cryoprecipitate per 10 kg of weight. Maintenance therapy is started 8 hours later with cryoprecipitate 1.75 bags per 10 kg every 8 hours for 1-2 days, followed by cryoprecipitate given every 12 hours. The duration of therapy should be 10-14 days following major surgery or trauma. The exact dose of cryoprecipitate is determined by measuring blood levels of Factor VIII activity and enough cryoprecipitate should be given to prevent Factor VIII activity from falling below 50%. These patients cannot be monitored by the PTT alone since as stated above, this test may be normal with low levels of Factor VIII activity.

Factor IX Deficiency (Hemophilia B or Christmas Disease)

This disorder is seven times less common than Factor VIII deficiency. As with Factor VIII deficiency, the severity of the disease directly correlates with the level of Factor IX activity. The PTT is prolonged while the PT and bleeding time are both normal. The treatment strategy for this disease is similar to that used in the treatment of Factor VIII deficiency except that one generally uses plasma or Factor IX concentrates. The serum half-life of Factor IX is longer than that of Factor VIII and one can usually administer this product at less frequent intervals. Care must be taken in the administration of Factor IX concentrates since they may be associated with potentially dangerous side effects.

Von Willebrand's Syndrome

This illness is now the most commonly recognized congenital factor deficiency. First described in 1926 it is an autosomal-dominant trait with variable expressivity. One generally sees a triad of a mild bleeding history associated with a prolongation of the bleeding time and moderate Factor VIII deficiency. Unlike classic hemophilia where the Factor VIII activity is low but Factor VIII antigen is normal, both coagulation activity and Factor VIII are proportionally reduced in this illness. In addition, there are two biologically related activities, one being coagulant activity (VIIIAHF) and the second correlating with a platelet defect (VIIIvWF) which are reduced in von Willebrand's disease. Platelets do not function normally in this disorder, thus accounting for the prolonged bleeding time. The platelet defect can be corrected with the transfusion of normal platelet-poor plasma.

The clinical history is an important clue in detecting patients with von Willebrand's syndrome. Symptoms usually begin in childhood when one frequently sees mucosal bleeding such as epistaxis. These patients usually are noted to have easy bruisability and have excessive bleeding with surgery. Petechiae are rare despite the fact that there is a platelet defect. The laboratory evaluation of these patients usually reveals a slightly prolonged PTT and a prolonged bleeding time. These patients also have abnormal platelet aggregation studies specifically when platelets are tested in the presence of ristocetin. Patients with classic

hemophilia have a normal bleeding time. Measurements of Factor VIII activity are low, though typically not as low as is seen with hemophilia A.

It is very important to realize that there are several variations to this syndrome and at times a screening PTT may be normal. It is for this reason that patients who have a suggestive bleeding history or a strong family history should have additional studies to investigate the possibility of von Willebrand's disease. Additional tests should include specific measurements of plasma Factor VIII activity and Factor VIII antigen, and platelet aggregation studies. At times it may be impossible to differentiate in the laboratory mild variations of von Willebrand's syndrome from normal patients. In this group, if there is a strong bleeding history and surgery is anticipated, one should consider treatment with cryoprecipitate.

An interesting phenomenon has been observed in this disorder whereby normal plasma or even plasma from true haemophilacs will induce new Factor VIII synthesis. It is for this reason that replacement therapy should be started 24 hours before a planned surgical procedure. Another important therapeutic principle to be remembered is that both Factor VIII coagulant activity and the Factor VIII-related plateled defect must be corrected in these patients in order to establish normal hemostasis. Cryoprecipitate contains both of these activities and is the treatment of choice for this disorder. Commercially available Factor VIII concentrations contain only Factor VIII coagulant activity and if these product must be used, additional plasma must be given to correct the Factor VIII-dependent platelet defect.

Factor XI Deficiency

This disorder is typically mild and is seen predominantly but not exclusively in those of Jewish ancestry. Many of these patients present with persistent bleeding after a dental extraction or a tonsillectomy. Since this factor is involved in the intrinsic coagulation system, the PTT is prolonged while other coagulation tests and the bleeding time are normal. Treatment of this disorder is with fresh-frozen plasma. Replacement therapy usually can be given at less frequent intervals since the plasma half-life of this factor is approximately 60 hours. As with other factor deficiencies, the specific amount of replacement therapy should be determined by measurements of plasma Factor XI activity.

Factor XII Deficiency (Hageman Factor)

Factor XII deficiency is associated with a prolongation of the PTT. It is important to separate this factor deficiency from deficiencies of Factors VIII, IX, and XI since it is not associated with abnormal bleeding and no therapy is required.

Deficiencies of Factors II (Prothrombin), V, VII, and X

Congenital deficiencies of these coagulation factors are quite rare. As a group they are associated with prolongation of the PT. In addition, the PTT is typically abnormal in all but Factor VII deficiency. Treatment is with fresh-frozen plasma. However, Factor IX concentrates also may be used since these products contain significant levels of Factors II, VII, and X activity.

Acquired Disorders of Coagulation

As a group the acquired disorders of coagulation are more common than congenital coagulation factor deficiencies. In addition, these are typically associated primarily with a prolongation of the PT.

Disseminated Intravascular Coagulation (DIC)

This is a syndrome characterized by the intravascular consumption of platelets and coagulation factors. It may be an acute process caused by shock, infection, or trauma, or may be a chronic process as is typically the case when associated with a disseminated neoplasm. In this syndrome, fibrin deposition may lead to tissue ischemia while depletion of platelets and coagulation factors may cause excessive bleeding. The peripheral blood smear may be helpful in establishing the diagnosis of DIC and may reveal fragmented red blood cells (schistocytes) in addition to thrombocytopenia. In acute DIC the diagnosis may be readily established by noting a low platelet count and serum fibrinogen in association with a prolonged PT and PTT. In addition, fibrin degradation products will generally be increased either secondary to the disseminated intravascular coagulation or the accompanying fibrinolysis which is frequently present. The diagnosis of chronic DIC may be more difficult to establish with certainty, and at times the only laboratory abnormalities may be a reduction in the platelet count and an increase in the amount of circulating fibrin degradation products.

Treatment of DIC is directed at the underlying cause. If bleeding is severe, blood replacement must be given to prevent shock. Cryoprecipitate should be given to replace Factor VIII and fibrinogen which are consumed by the intravascular coagulation and fresh-frozen plasma is given to replace coagulation factors. The use of heparin has been recommended in certain circumstances as a means of inhibiting intravascular coagulation. However, it is actually used infrequently, specifically in certain life-threatening circumstances.

Acquired Inhibitors of Coagulant Factors

Rarely, patients will develop inhibitors to specific coagulation factors. These disorders are detected by the usual screening tests (PT and PTT). More specific tests (PT and PTT mixing studies) will usually separate these disorders from congenital factor deficiencies. Acquired Factor VIII inhibitors may be associated with acute bleeding episodes and require the administration of very large quantities of Factor VIII. Systemic lupus erythematosus, specifically, may be associated with an acquired circulating anticoagulant which can cause a prolongation of either the PT or the PTT. Bleeding is unusual with this disorder and treatment is directed at the underlying illness. Several cases of acquired von Willebrand's disease also have been reported.

Liver Disease

There are many different coagulation problems that may develop in association with liver disease. With severe liver disease, there can be a decrease in the synthesis of the vitamin K-dependent coagulant factors (prothrombin, VII, IX, and X). Patients with steatorrhea and obstructive jaundice also have a reduced absorption of vitamin K from the gastrointestinal tract. In addition, Factors V and fibrinogen will be diminished in patients with very severe

liver disease. Thrombocytopenia also is seen frequently in patients with liver disease and may at times suggest the presence of hypersplenism. Both DIC and fibrinolysis also may be seen, especially when the liver disease is severe. Treatment is generally directed at replacing of blood loss in the bleeding patient and fresh-frozen plasm may be given to correct coagulation factor deficiencies. If there is a prolongation of the PT, vitamin K should always be given because of the possibility of concurrent vitamin K deficiency. Thrombocytopenia can be corrected by the administration of platelet concentrates.

Vitamin K Deficiency and Oral Anticoagulants

The vitamin K-dependent coagulation factors (prothrombin, VII, IX, and X) are all synthesized in the liver and are diminished when there is vitamin K deficiency. Vitamin K is a fat-soluble vitamin synthesized by intestinal bacteria. Broad-spectra antibiotics with secondary intestinal sterilization can cause reduced synthesis of vitamin K. This problem may be a specific complication of hospital antibiotic administration, and may contribute to bleeding when there is poor dietary intake. Obstructive jaundice with an inability to absorb the fat-soluble vitamins also is associated with vitamin K malabsorption. The coagulation factors affected by vitamin K deficiency are part of the extrinsic and common coagulation pathway, and it is the PT which is characteristically prolonged in this disorder. Warfarin (Coumadin), an oral anticoagulant, impairs hepatic synthesis of the vitamin K-dependent coagulant factors and is similarly associated with a prolongation of the PT.

It can be seen that vitamin K deficiency, liver disease, and DIC may be present simultaneously, yet each can itself cause a prolongation of the PT. Specific coagulation factor assays (Factors V, VII, and VIII) may help distinguish between these three disorders. Vitamin K deficiency will reduce Factors II, VII, IX, and X with Factor VII generally the first to be reduced. Factors V and VIII are unaffected by vitamin K deficiency or by oral anticoagulants. DIC causes a consumption of the coagulation factors. Factors V and VIII typically have a short plasma half-life and are reduced early in this disorder while Factor VII is variably affected. Severe liver disease (without DIC) will reduce Factor V and the vitamin K-dependent coagulant factors. Factor VIII however is unaffected by liver disease since it is not synthesized in liver.

Therapy of vitamin K deficiency is dependent on the severity of the hemostatic defect. One can administer vitamin K1 (Aquamephyton) which will stimulate synthesis of the reduced coagulation factors within 6-12 hours, or one can administer fresh-frozen plasma which will immediately replace the deficient coagulation factors. Fresh-frozen plasma should be given specifically when there is bleeding and more rapid correction of the PT is required. The starting dose of fresh-frozen plasma is 15-20 mL/kg. Additional therapy may be required if bleeding continues and the PT has not completely corrected.

Heparin

Heparin is the most common anticoagulant administered to hospitalized patients and has potent antithrombin activity. Its administration caused prolongation of the PTT and thrombin time. Performing a thrombin time in the presence of toluidine blue can be used to differentiate the heparin effect from other circulating anticoagulants. Heparin has a short serum half-life and the anticoagulant effect of this drug is usually lost within 4 hours after

it is discontinued. In patients with severe bleeding while on heparin, protamine sulphate can be administered to neutralize the heparin effect while carefully monitoring the PTT.

Estimation of Blood Volume

In the physiology laboratory it is possible to measure blood volume accurately with radioactive isotopes or with dye. However, in a clinical situation the following formulas will help the surgeon estimate the blood volume quickly.

1. Blood volume of children in mL = 7.5-8.5% of body weight in grams.

2. Blood volume of adult male in mL = 6-7.5% of body weight in grams.

3. Blood volume of adult female in mL = 5.5-7% of body weight in grams.

For example: A 75 kg male has: 7/100 x 75.000 g = 5250 mL.

Twenty to thirty percent loss of total blood volume is significant and may need replacement. No bloor or plasma transfusion is needed for any blood loss under 20% of total blood volume.