It is of critical importance that clinicians who provide care to surgical patients understand the dynamic interplay of the coagulation and fibrinolytic systems. An appreciation for the relevant underlying biologic mechanisms is central to the diagnosis and appropriate management of patients who present with bleeding diatheses in both the operative and the postoperative setting. Surgery provides the most significant challenge to the integrity of the hemostatic system, and the fidelity of the coagulation system serves as the homeostatic defense mechanism that abrogates the proclivity for bleeding in this context.

To expeditiously manage a critically ill patient experiencing life-threatening hemorrhage, it is crucial that a defined approach for prompt recognition of the underlying cause is used. First, attention is directed toward stabilizing the patient. This includes securing an adequate airway, ventilation, vascular access, and restoring intravascular volume. Second, there should be immediate dialogue with individuals involved in the intraoperative management of the patient. This may provide pertinent information regarding the intraoperative course of the patient, specifically regarding any observed characteristics of bleeding that may suggest an underlying coagulation disorder. A generalized slow oozing of blood from raw surfaces (often termed “nonsurgical bleeding”) is often a manifestation of a systemic disorder of hemostasis (1–3). On the other hand, bleeding related to technical factors that can be associated with the conduct of any surgical procedure (often termed “surgical bleeding”) is localized and is the most common cause of postoperative bleeding. Dialogue with the surgical team should include consideration for re-exploration. The evolving coagulopathy may proceed swiftly in critically ill patients. Qualitative abnormalities of platelet function, depletion of both platelets and plasmatic coagulation factors, and hypothermia are major contributors to the underlying pathophysiology responsible for the coagulopathy that manifests in the critical care setting (2–9). Moreover, previously undiagnosed, rare, at times clinically latent, congenital coagulation disorders may be unmasked by the physiologic stress resulting from a surgical procedure. Familial coagulation defects that may be encountered in a bleeding postoperative patient include von Willebrand disease, factor VIII deficiency (hemophilia A, or classic hemophilia), and factor IX deficiency (hemophilia B or Christmas disease) (10–14).

The initial phase of assessment must include an immediate reconciliation of intravascular volume status to appropriately guide resuscitation and to assist in decision making for early operative intervention. Although signs of an expanding hematoma or saturated dressings are indicative of localized bleeding, there is considerable overlap, and coagulation system defects may present in a similar fashion postoperatively. In terms of management, however, early recognition of the clinical symptoms and signs attributable to hypovolemia (restlessness, anxiety, shortness of breath, pallor, tachycardia, and oliguria) is compulsory. Adjunctive estimates of intravascular volume status may be obtained using both noninvasive and invasive monitoring, as is common in the critical care setting. Systemic hypotension is a late sign of significant hypovolemia, and expeditious resuscitation is paramount to avert the disastrous consequences of an unrecognized and inappropriately triaged patient with ongoing, potentially life-threatening hemorrhage.

It is important to differentiate the inherited (primary) coagulation disorders, which are associated with a history of bleeding diatheses, from the more commonly acquired (secondary) coagulation disorders, which are the consequence of pathologic conditions and numerous medications (1,3,15). This nomenclature (primary vs. secondary) is distinct from and should not be confused with the traditional nomenclature used to describe the hemostatic process itself. In the formation of a stable clot, the hemostatic process was classically described as comprising two phases, a primary phase (also called primary hemostasis) and a secondary phase (also called secondary hemostasis). The primary phase of hemostasis involves vascular or tissue injury, initiating platelet adhesion and aggregation to form the platelet plug. The secondary phase involves the activation of the plasmatic coagulation protein cascade (both the extrinsic and the intrinsic systems), which results in formation of the stable fibrin clot. Disorders involving platelet number or function, or vascular interactions, are classified as disorders of primary hemostasis, and disorders involving the plasmatic coagulation factors are classified as disorders of secondary hemostasis. This serves the purpose of an operational definition, since in vivo these events are not separate processes but highly integrated.

Hemostatic disorders, whether primary (inherited) or secondary (acquired), can both be manifest by diffuse bleeding from the operative site, puncture wounds, vascular access sites, or traumatized tissue outside of the operative field. Surgical and postsurgical bleeding may therefore result from either quantitative (thrombocytopenia) or qualitative (abnormal function) platelet disorders.
Thrombocytopenia may be further attributed to a decrease in production of platelets (asplastic anemia, hypoplastic bone marrow failure, chemotherapy, or neo-occurring lesions of the bone marrow as seen with malignancy), ineffective production (vitamin B₁₂ or folic acid deficiency states), platelet sequestration (primary or secondary hyperplenism), increased destruction or consumption of platelets (hemorrhagic conditions; microangiopathic processes such as thrombotic thrombocytopenic purpura [TTP]; disseminated intravascular coagulation [DIC]), hemolytic-uremic syndrome [HUS]; immune destruction due to antplatelet antibodies, such as in posttransfusion purpura or idiopathic thrombocytopenic purpura], or dilution of circulating platelet volume (massive blood transfusion) (1–4,6–9,16–18).

Qualitative platelet disorders may be inherited [Bernard–Soulier syndrome, abnormal release mechanism, Glanzmann thrombasthenia, storage pool disease, or von Willebrand disease] or acquired [uremia, drug interactions, myeloproliferative disorders]. Disorders involving plasmatic coagulation factors are generally caused by either a decrease in production of clotting factors (commonly associated with hepatic insufficiency, cirrhosis, vitamin K deficiency, obstructive jaundice) or by an increase in consumption of circulating coagulation factors (such as in DIC) (5,6–9,18,19). Coagulopathy manifested in the critically ill patient is often a result of a combination of both platelet and plasmatic coagulation factor defects. Well-known examples include obstructive biliary tract disease or chronic liver disease, which results in diminished production of coagulation factors given that the liver is the major site of synthesis of all coagulation factors with the exception of factor VIII. In addition, platelet sequestration may occur from secondary hyperplenism (18). Massive trauma often results in decreases of both platelets and coagulation factors as a result of secretion secondary to ongoing bleeding or hemorrhage (4). If shock and acidosis develop, there is further decrease in coagulation factor synthesis due to impairment in liver function (22). This results from a combination of dilution of plasmatic coagulation factors and platelets, chelating of ionized calcium (a necessary component of the coagulation cascade) by the anticoagulant (citrate) present in banked blood, acidosis that often attends the underlying disease, hypothermia, or the condition that made massive blood transfusion necessary in the first place. Hypothermia significantly impairs both platelet and plasmatic coagulation functions (5,21). Last, transient platelet dysfunction, responsive to desmopressin (DDAVP, 1-desamino-8-d-arginine vasopressin), is a well-recognized phenomenon in patients after cardiopulmonary bypass (23–26).

In parallel with the ongoing resuscitation of the bleeding patient, attention must be directed toward expeditiously determining the need for surgical re-exploration. All bleeding patients must be considered candidates for reoperation. A comprehensive assessment must take into account the degree and the duration of active bleeding, the anatomic site of involvement, and the potential for additional morbidity or mortality (for example, evolving acidosis, myocardial ischemia, diminished mental status, oliguria, or a progressive neck wound hematoma with impending acute airway obstruction). Physiologic reserve is also a compelling variable to consider, for patients with significant comorbidities, such as the elderly, pediatric, obese and diabetic patients are attended by less reserve. Hence, vigilant observation to recognize early postoperative bleeding is crucial, before hemodynamic instability and shock become manifest. In these patients, consideration for early operative intervention may be necessary because this cohort may not be able to readily tolerate even mild degrees of anemia, hypovolemia, and hyperperfusion. Consideration of other modalities of hemorrhage control (interventional radiology and embolization) may be entertained in appropriate situations.

An important caveat is that not every instance of bleeding requires surgical intervention, and conversely, patients who may initially appear to have clinically self-limited bleeding postoperatively may still require reoperation for control of bleeding. Major pelvic fractures are contemporaneously managed by either fracture stabilization or arteriography with embolization of the culprit bleeding pelvic vessels. In contrast, the natural history of a contained perioperative vascular anastomotic dehiscence is characterized by the evolution of a false aneurysm. In this setting, immediate re-exploration with operative repair is indicated to avert the potentially catastrophic consequence of free rupture and death from exsanguinating hemorrhage.

**EVALUATION OF BLEEDING: CLINICAL HISTORY AND THE UTILITY OF DIAGNOSTIC TESTING**

A detailed history and physical examination is the most important preliminary step in elucidating the cause of surgical bleeding and should be done simultaneously with resuscitative efforts (1). Collateral history from family members and previous medical records is a helpful adjunct to determine if a primary, congenital defect in the coagulation system is present. A history of easy bruising, excessive gingival bleeding after brushing of teeth, bleeding diathesis with dental extractions, hypermenorrhea, frequent spontaneous epistaxis, melena stools or spontaneous hematuria, petechiae or purpura, hemorrhhoses, and a family history of bleeding disorders may indicate a congenital or familial coagulation disorder, such as hemophilia A or B or von Willebrand disease. The family pedigree may provide important clues as to the presumptive disease process based on the pattern of inheritance, whether autosomal or sex linked, dominant or recessive. Suspicion for a congenital disorder of coagulation is further raised by a history of blood transfusions required for common ambulatory procedures such as dental extractions, circumcision, tonsillectomies, or biopsies. Due to differences in gene penetrance, not all individuals affected with inherited coagulation disorders are diagnosed at an early age, and clinically latent, attenuated bleeding disorders may be unmasked when confronted by a major surgical procedure or trauma. A past history of liver disease or heavy ethanol consumption should alert the clinician to the possibility of acquired plasmatic factor deficiencies, in addition to thrombocytopenia resulting from secondary hyperplenism with platelet sequestration.

A thorough medication history is essential (including soliciting information on the use of dietary supplements or herbal tonics, and over-the-counter medications), to determine if the patient has been on any medication that interferes
with hemostasis (common examples include aspirin, other non-
steroidal anti-inflammatory agents, ticlopidine, clopidogrel, or anticoagulant
regimens) (15-25). Poplar supplements that may aggravate bleeding are ginkgo, garlic, ginger, ginseng,
feverfew, and vitamin E. A history of anticoagulation therapy is
equally important in this regard (19-27). Nutritional assess-
ment is paramount, and careful evaluation for the presence of a
vitamin K deficiency is obligatory, as this may occur in patients
on parenteral nutrition or with cancer cachexia in those with
malignancies. Other variables that may affect the integrity of
the coagulation system include previous irradiation, renal fail-
ure, and sepsis, which affect the coagulation cascade at multiple
points.

Physical examination often provides an index of the severity
and the extent of the disease and may provide additional clues
that assist in distinguishing localized surgical bleeding from sys-
temic bleeding resulting from a coagulopathy. For example, the
presence of petechiae, purpura, and mucosal bleeding is often
indicative of thrombocytopenia, a qualitative functional dis-
order of platelets, or increased vascular fragility. Ecchymoses
or spontaneous, nontraumatic hemorrhage is consistent with
plasmatic coagulation factor abnormalities or deficiencies such as
hemophilia. Both platelet and plasmatic coagulation disor-
ders are associated with hematomas. Hepatic insufficiency or
failure can be presumptively identified by recognizing jaun-
dice, ascites, angorias, palmar erythema, arteriosclerosis, congestive
splenomegaly, and testicular atrophy. Splenomegaly itself may
also be associated with hematologic dyscrasias and malignan-
cies associated with hematostatic abnormalities (lymphomas and
leukemias). Connective tissue or collagen vascular disorders
disrupt the usual normal vascular fragility, or with pe-
techiae, joint abnormalities, and a history of delayed wound healing.
These conditions focus attention on the increased risk
for a perioperative bleeding complication, which underscores
the need for vigilance both intraoperatively and postopera-
tively. Last, the possibility of sepsis as an underlying cause for
the development of a coagulopathy must always be entertained in
the postoperative, critically ill patient (9).

The establishment of a definitive diagnosis of a coagula-
tion disorder rests on selective use of a limited battery of
laboratory tests guided by information derived from the his-
tory and physical examination. These assays are selected to
broadly screen the hemostatic system. These tests are, for the
most part, automated (except for the bleeding time), readily
available, and amenable to point-of-care testing methodology.
The tests most commonly used include the template bleeding
time, quantitative platelet count, prothrombin time (PT), ac-

tivated partial thromboplastin time (PTT), fibrinogen level,
and thrombin time (TT). The template bleeding time is the
only test that screens for qualitative platelet function abnor-
malities, a frequent cause of abnormal bleeding. This test also

evaluates platelet number and vascular fragility, demonstrat-
ing abnormal prolongation in thrombocytopenic states and in
conditions associated with increased vascular fragility (exam-

ples include connective tissue disorders such as senile purpura,
Ehlers-Danlos syndrome, steroid-induced purpura, or Mar-
fan syndrome; scurvy; amyloidosis; or hereditary hemorrhagic
telangectasia/Osler-Weber-Rendu disease). Therefore, if both
the platelet count and the template bleeding time are normal,
the presumptive differential diagnosis is directed toward a plas-
matic coagulation factor abnormality. Measurement of both
the PT and PTT will serve to further define the abnormality,
given that each test is more sensitive to changes in procoagu-
lants in the initial phases of the extrinsic and intrinsic pathways,
respectively. The PTT provides a global measure of the activ-
ity of factors XII, XI, IX, and VIII in addition to the common
pathway factors shared by the extrinsic system (factors X, V, II,
and I) and, therefore, identifies many of the inherited disorders
of bleeding, typically a deficiency of factor VIII (hemophilia A),
IX (hemophilia B), or von Willebrand factor, vWF (von Wille-
brand disease). It is worth noting that factor XII deficiency is
not associated with any significant bleeding tendency despite
abnormal prolongation of the PTT. Enzymatically active vWF
is a necessary cofactor for optimum functioning of the factor
VIII procoagulant protein. The PTT exclusively evaluates factor
VII, which is one of the vitamin K–dependent factors (in addi-
tion to factors II, IX, and X). Therefore, the PTT is prolonged
in individuals on Coumadin (warfarin) therapy, and this test is
used to measure therapeutic efficacy of this form of oral antico-
gulation therapy. Liver disease is another common cause for a
prolonged PT; perhaps most notably because factor VII has the
shortest half-life of the plasmatic coagulation factors. Liver
disease, by virtue of the diminished synthesis of all plasmatic
coagulation factors (with the exception of vWF) also results in
prolongation of the PTT in addition to the PT. Due to the sensi-
tivity of factors XII, XI, IX, and VIII to the effects of heparin
(in the presence of antithrombin III), heparin therapy primarily
is reflected by abnormal prolongation of the PTT. In conditions
associated with prolongation of both the PT and the PTT, quan-
titative measurement of the fibrinogen (factor I) level may be
useful to determine if the coagulation disorder is a result of a
defect or deficiency of multiple coagulation factors, which may
be associated with liver disease or may manifest with hep-
titis, joint abnormalities, and a history of delayed wound healing.
These conditions focus attention on the increased risk
for a perioperative bleeding complication, which underscores
the need for vigilance both intraoperatively and postopera-
tively. Last, the possibility of sepsis as an underlying cause for
the development of a coagulopathy must always be entertained in
the postoperative, critically ill patient (9).

The establishment of a definitive diagnosis of a coagula-
tion disorder rests on selective use of a limited battery of
laboratory tests guided by information derived from the his-
tory and physical examination. These assays are selected to
broadly screen the hemostatic system. These tests are, for the
most part, automated (except for the bleeding time), readily
available, and amenable to point-of-care testing methodology.
The tests most commonly used include the template bleeding
time, quantitative platelet count, prothrombin time (PT), ac-


tivated partial thromboplastin time (PTT), fibrinogen level,
and thrombin time (TT). The template bleeding time is the
only test that screens for qualitative platelet function abnor-
malities, a frequent cause of abnormal bleeding. This test also

evaluates platelet number and vascular fragility, demonstrat-
ing abnormal prolongation in thrombocytopenic states and in
conditions associated with increased vascular fragility (exam-

ples include connective tissue disorders such as senile purpura,
Ehlers-Danlos syndrome, steroid-induced purpura, or Mar-
fan syndrome; scurvy; amyloidosis; or hereditary hemorrhagic
telangectasia/Osler-Weber-Rendu disease). Therefore, if both
the platelet count and the template bleeding time are normal,
the presumptive differential diagnosis is directed toward a plas-
matic coagulation factor abnormality. Measurement of both
the PT and PTT will serve to further define the abnormality,
Post-operative bleeding, often termed local hemostatic failure or surgical bleeding, is a known potential complication of any surgical procedure. When associated with evolving hypovolemia, mental status changes, restlessness, anxiety, tachycardia, dyspnea, and oliguria or are commonly associated manifestations. Hypotension is a late finding, and aggressive attempts must be made to avert this serious consequence with expeditious concurrent resuscitation as identification of the source of bleeding is confirmed. The vast majority of patients affected typically present within the immediate perioperative period. Subtle signs may be evident in the postanesthesia care unit, and generally become apparent within the first 8 hours after surgery. A high index of suspicion is necessary to render an early diagnosis of post-operative bleeding, and meticulous attention to look for any evidence of bleeding must be applied, given that many signs of evolving hypovolemia are nonspecific and may also be observed in nonbleeding patients after major thoracic or abdominal procedures (tachycardia associated with post-operative pain, anxiety and restlessness, mental status changes secondary to narcotic analgesic administration, or oliguria resulting from anticipated third-space fluid sequestration after major abdominal surgery). Blood in the peritoneal cavity ordinarily does not result in a significant inflammatory response unless associated with secondary bacterial contamination and therefore is not associated with obvious peritoneal signs. On occasion, localized symptoms may be elicited that are attributable to irritation caused by a collection of blood, exemplified by the Kehr sign. This is referred pain to the right shoulder ascribed to an accumulation of blood under the right hemidiaphragm. Serial hemoglobin and hematocrit levels may assist in determining the degree of bleeding, but isolated, single values can be difficult to interpret. It is difficult to quantitatively account for the effects of isotonic fluid sequestration (third-spacing) after major abdominal procedures that may result in hemococoncentration and elevated hemoglobin and hematocrit levels, or the effects of isotonic fluid administration in the perioperative period that may contribute to hemodilution and lower hemoglobin and hematocrit levels.

Certain surgical procedures are not associated with exacerbating hemorrhage or hypotension but can be life threatening. Prototypic examples include neck operations for en-docrine diseases (thyroid, parathyroid surgery), lymphadenectomies (radical neck dissections), major composite resections for tumors of the neck, and carotid surgery. From a pathophysiologic perspective, an expanding neck hematoma results in airway obstruction from both mechanical compression and from mural edema caused by hypovolemic shock. The cause is frequently venous bleeding, compounded by hypertension and liberal preoperative use of antplatelet medications in those undergoing carotid surgery. Acutely re-exploiting the incision and evacuating the hematoma is often life-saving, although endotracheal intubation or cricothyroidotomy may be required as a temporizing measure until the airway edema resolves. Nearly all patients who develop neck hematomas require operative re-exploitation. It is common practice to place drains in the operative field at the time of surgery prior to closure, and surgical procedural anthologies are replete with instructions substantiating this approach. Caution must be exercised in interpreting drain output as an accurate index of early perioperative bleeding, and it is correspondingly crucial to recognize that placement of a drain is not an appropriate substitute for ensuring meticulous surgical hemostasis (30).

There is no single criterion available to directly re-exploitation for control of post-operative bleeding, and this decision is based on considering a number of variables. The timing of the active bleed relative to the operative procedure, its duration, its rate, the potential for additional morbidity, the patient’s age as a surrogate for physiologic reserve, and other comorbid diseases (such as underlying cardiac or pulmonary disease, renal disease, diabetes, or obesity) must all be taken into consideration when deciding on the need for reoperation. Timing of re-exploitation is of significant concern in conditions associated with limited or poor physiologic reserve as these patients are often quite ill and require judicious resuscitation and expeditious definitive surgical intervention prior to the inception of irreversible shock. The most conservative treatment is to return to the operating room with early control of surgical bleeding. Often times the need to return emergently to the operating room is quite...
Disorders of Plasmatic Coagulation Factors: Overview

Hemostasis involves a complex interplay between elements of the vascular endothelium, plasmatic coagulation factors, platelets, and the fibrinolytic system. Primary isolated disorders of the fibrinolytic system as a cause of major bleeding are rare in the critically ill patient and are covered elsewhere (31,32). Disorders of the clotting system can be broadly classified as congenital or acquired, and a comprehensive history and physical examination often assists in determining the nature of the coagulopathy because of rapid ongoing consumption of coagulation factors and platelets. In these instances, operant intervention is paramount, and the decision to reoperate must not be unduly delayed while awaiting normalization of coagulation parameters. Second, as stated earlier, some subscribe to the notion that drains placed at the time of surgery are a useful adjunct to alert the surgical team to early signs of postoperative bleeding and to gauge the amount and rate of bleeding when it does occur. Caution with this practice must be promulgated, as it is a well-accepted observation that the absence of blood in a drain is not conclusive evidence that bleeding is not occurring, because the drain tip may be dislodged or may have migrated from its original position and this may not be readily apparent externally, or the drain may be obstructed with clot.

There are certain circumstances where operative re-exploration is obligatory, despite the fact that the bleeding may be self-limiting. A vascular anastomosis with a contained leak, even if seemingly small and hemodynamically inconsequential, must be repaired to avert the consequences of false aneurysm formation and later rupture. Small contained leaks may be difficult to recognize and pose a diagnostic dilemma. A duplex study may be helpful in further elucidating anastomotic integrity, but an arteriogram should be performed if any doubt exists.

Last, the surgeon must also be cognizant of the fact that there are some instances where bleeding is optimally addressed without surgical intervention. The prototypic illustration is the severe pelvic fracture with signs of ongoing hemorrhage, as alluded to earlier. In accordance with the Advanced Trauma Life Support protocol, associated injuries and additional sources of obvious bleeding must first be excluded. Once hemoperitoneum and hemorthorax have been excluded, the pelvis is stabilized by external fixation, followed by arteriography with embolization of any bleeding pelvic or retroperitoneal blood vessels.

Quantitative Platelet Disorders: Thrombocytopenia

Thrombocytopenia, defined as a platelet count less than 140 x 10^3/L, results from decreased production, ineffective thrombopoiesis, sequestration, or an associated consumptive process. There are some instances where bleeding is optimally addressed without surgical intervention. The prototypic illustration is the severe pelvic fracture with signs of ongoing hemorrhage, as alluded to earlier. In accordance with the Advanced Trauma Life Support protocol, associated injuries and additional sources of obvious bleeding must first be excluded. Once hemoperitoneum and hemorthorax have been excluded, the pelvis is stabilized by external fixation, followed by arteriography with embolization of any bleeding pelvic or retroperitoneal blood vessels.

Chapter 74: Surgical and Post-Surgical Bleeding

Thus, post-operative bleeding can be a result of quantitative abnormalities (thrombocytopenia), due to decreased production, ineffective thrombopoiesis, sequestration, or an associated consumptive process. There are some instances where bleeding is optimally addressed without surgical intervention. The prototypic illustration is the severe pelvic fracture with signs of ongoing hemorrhage, as alluded to earlier. In accordance with the Advanced Trauma Life Support protocol, associated injuries and additional sources of obvious bleeding must first be excluded. Once hemoperitoneum and hemorthorax have been excluded, the pelvis is stabilized by external fixation, followed by arteriography with embolization of any bleeding pelvic or retroperitoneal blood vessels.

There are several circumstances where operative re-exploration is obligatory, despite the fact that the bleeding may be self-limiting. A vascular anastomosis with a contained leak, even if seemingly small and hemodynamically inconsequential, must be repaired to avert the consequences of false aneurysm formation and later rupture. Small contained leaks may be difficult to recognize and pose a diagnostic dilemma. A duplex study may be helpful in further elucidating anastomotic integrity, but an arteriogram should be performed if any doubt exists.

Last, the surgeon must also be cognizant of the fact that there are some instances where bleeding is optimally addressed without surgical intervention. The prototypic illustration is the severe pelvic fracture with signs of ongoing hemorrhage, as alluded to earlier. In accordance with the Advanced Trauma Life Support protocol, associated injuries and additional sources of obvious bleeding must first be excluded. Once hemoperitoneum and hemorthorax have been excluded, the pelvis is stabilized by external fixation, followed by arteriography with embolization of any bleeding pelvic or retroperitoneal blood vessels.

Disorders of Plasmatic Coagulation Factors: Overview

Hemostasis involves a complex interplay between elements of the vascular endothelium, plasmatic coagulation factors, platelets, and the fibrinolytic system. Primary isolated disorders of the fibrinolytic system as a cause of major bleeding are rare in the critically ill patient and are covered elsewhere (31,32). Disorders of the clotting system can be broadly classified as congenital or acquired, and a comprehensive history and physical examination often assists in determining the nature of the coagulopathy because of rapid ongoing consumption of coagulation factors and platelets. In these instances, operant intervention is paramount, and the decision to reoperate must not be unduly delayed while awaiting normalization of coagulation parameters. Second, as stated earlier, some subscribe to the notion that drains placed at the time of surgery are a useful adjunct to alert the surgical team to early signs of postoperative bleeding and to gauge the amount and rate of bleeding when it does occur. Caution with this practice must be promulgated, as it is a well-accepted observation that the absence of blood in a drain is not conclusive evidence that bleeding is not occurring, because the drain tip may be dislodged or may have migrated from its original position and this may not be readily apparent externally, or the drain may be obstructed with clot.

There are certain circumstances where operative re-exploration is obligatory, despite the fact that the bleeding may be self-limiting. A vascular anastomosis with a contained leak, even if seemingly small and hemodynamically inconsequential, must be repaired to avert the consequences of false aneurysm formation and later rupture. Small contained leaks may be difficult to recognize and pose a diagnostic dilemma. A duplex study may be helpful in further elucidating anastomotic integrity, but an arteriogram should be performed if any doubt exists.

Last, the surgeon must also be cognizant of the fact that there are some instances where bleeding is optimally addressed without surgical intervention. The prototypic illustration is the severe pelvic fracture with signs of ongoing hemorrhage, as alluded to earlier. In accordance with the Advanced Trauma Life Support protocol, associated injuries and additional sources of obvious bleeding must first be excluded. Once hemoperitoneum and hemorthorax have been excluded, the pelvis is stabilized by external fixation, followed by arteriography with embolization of any bleeding pelvic or retroperitoneal blood vessels.

Quantitative Platelet Disorders: Thrombocytopenia

Thrombocytopenia, defined as a platelet count less than 140 x 10^3/L, results from decreased production, ineffective thrombopoiesis, sequestration, or an associated consumptive process. There are some instances where bleeding is optimally addressed without surgical intervention. The prototypic illustration is the severe pelvic fracture with signs of ongoing hemorrhage, as alluded to earlier. In accordance with the Advanced Trauma Life Support protocol, associated injuries and additional sources of obvious bleeding must first be excluded. Once hemoperitoneum and hemorthorax have been excluded, the pelvis is stabilized by external fixation, followed by arteriography with embolization of any bleeding pelvic or retroperitoneal blood vessels.

There are several circumstances where operative re-exploration is obligatory, despite the fact that the bleeding may be self-limiting. A vascular anastomosis with a contained leak, even if seemingly small and hemodynamically inconsequential, must be repaired to avert the consequences of false aneurysm formation and later rupture. Small contained leaks may be difficult to recognize and pose a diagnostic dilemma. A duplex study may be helpful in further elucidating anastomotic integrity, but an arteriogram should be performed if any doubt exists.

Last, the surgeon must also be cognizant of the fact that there are some instances where bleeding is optimally addressed without surgical intervention. The prototypic illustration is the severe pelvic fracture with signs of ongoing hemorrhage, as alluded to earlier. In accordance with the Advanced Trauma Life Support protocol, associated injuries and additional sources of obvious bleeding must first be excluded. Once hemoperitoneum and hemorthorax have been excluded, the pelvis is stabilized by external fixation, followed by arteriography with embolization of any bleeding pelvic or retroperitoneal blood vessels.
manifestations are minimal, but the renal impairment is more pronounced. Central to the treatment of both these entities is supportive care, with particular attention given to management of the renal dysfunction (35–37). Plasma exchange is often efficacious in treating these diseases, and hemodialysis may also be required in some instances for support of renal failure.

Immune-mediated destruction of platelets is observed in several clinical conditions. Alloimmune antibodies are believed to account for posttransfusion purpura observed primarily in women, who may have been previously immunized by fetal-derived platelets since there is a significant association with a prior history of pregnancy (38). Immunizations to a number of candidate alloantigens have been reported in the literature, the most common being the PL antigens. The antibodies induced are generally of the IgG class and therefore are also able to cross the placenta, as a described cause of neonatal thrombocytopenia. The purpura becomes apparent approximately 7 to 10 days after blood transfusion, presumably attributed to an anamnestic response, and can last several months. The population at risk has been estimated to be approximately 1% to 3%, and the condition tends to be self-limiting and responds to intravenous immune globulin. Idiopathic thrombocytopenic purpura is one of the more common examples of immune-mediated platelet destruction (17). It tends to occur in otherwise healthy individuals, and both an acute and a chronic form have been described. Mechanistically, platelets coated with autoantibodies are removed by the reticuloendothelial cells in the spleen (and to an extent in the liver). The diagnosis is one of exclusion after other causes of thrombocytopenia have been ruled out. A similar mechanism may account for the thrombocytopenia associated with collagen vascular diseases, such as systemic lupus erythematosus, lymphoreticular diseases, and in some infectious diseases, such as infectious mononucleosis or human immunodeficiency virus infections. It is noteworthy in this regard that the acute form, often observed in the pediatric population, is often preceded by a viral syndrome. Splenectomy is required in a third of patients if immune globulin, corticosteroids, or plasmapheresis is unable to control the condition (17,39,40). In this context, significant bleeding may not occur until platelet counts decrease as low as $10^4$, because most of the circulating platelet pool consists of younger, more functionally active platelets. The significance of this impacts on the operative approach traditionally adopted during splenectomy. During splenectomy, platelets are hung by the anesthesiologist but not administered until the splenic artery is clamped or splenectomy completed. There is by and large minimal bleeding encountered despite the pronounced degree of thrombocytopenia, if platelets are infused prior to control of the splenic arterial inflow, the infused platelets will merely be consumed by the spleen and not available for the hemostatic process. Immune-mediated destruction of platelets can also be caused by several drugs that can induce antibodies to platelets via hapten-mediated, or by immune complex-mediated, “innocent bystander” mechanisms. Quinine, amiodarone, sulfa drugs, cimetidine, ranitidine, phenytoin, and semisynthetic penicillins are some examples that may be encountered in the critical care environment (3). Heparin-induced thrombocytopenia is an unusual example of drug-induced thrombocytopenia in this context because a hypercoagulable condition is actually created characterized by thrombotic complications with the manifestation of the “white clot syndrome” (41). This syndrome typically becomes apparent after 1 week of therapy but may present within a few hours after implementing heparin therapy in already sensitized patients. Discontinuation of the offending agent is the appropriate treatment approach central to all causes of drug-induced, immune-mediated thrombocytopenia.

Qualitative Platelet Function Disorders

Acquired disorders are the leading cause of qualitative platelet function abnormalities in the critically ill patient. It is vital to be aware that qualitative bleeding disorders are not measured by the standard battery of coagulation tests described above, with the exception of the template bleeding time. This test is not commonly used, given that this does not lend itself to automatic testing and still requires the laboratory technologist to remain at the patient’s bedside. Furthermore, this test has been attended by poor reproducibility, particularly in conditions associated with significant peripheral edema. Nevertheless, when a qualitative platelet function abnormality is suspected, the bleeding time is an appropriate first screening test to guide discriminate use of additional testing to further elucidate the underlying cause. Ingestion of numerous drugs has been associated with inhibition of platelet function (3,16,42). Among these, aspirin is the most well described and best characterized. Aspirin interferes with cyclo-oxygenase-mediated prostaglandin and thromboxane synthesis and has profound effects at multiple steps in the formation of the hemostatic platelet plug. It decreases the platelet response to aggregation in response to collagen, inhibits the second phase of aggregation in response to adenosine diphosphate (ADP) and epinephrine, and irreversibly injures platelets for the duration of their lifespan. It is generally recommended that antplatelet medications, such as aspirin, ticlopidine, and clopidogrel, are discontinued approximately 7 days prior to surgery. For nonsteroidal anti-inflammatory agents other than aspirin, ticlopidine, or clopidogrel, some investigators advocate 2 days of abstinence. It is important to recognize that many over-the-counter medications contain aspirin (e.g., Alka-Seltzer, Excorin, Anacin) and many patients are not aware of this, so it is imperative to obtain a comprehensive drug history, specifically querying for use of aspirin-containing products. Discontinuing the antplatelet drug combined with use of desmopressin and platelet transfusions have been beneficial in treating bleeding encountered in these situations (10,12,14,16).

Another common cause of acquired qualitative defects in platelet function is hypothermia (32,43). Massive blood transfusions or crystalloid infusions without attention to use of blood warmers, lack of attention to maintaining a warm ambient environment in the operating room, especially during long procedures and for individuals at the extremes of age, and prolonged extractions and exposure time in the field in the patient with multiple traumatic injuries are all too familiar causes of hypothermia. Vigilant awareness must be directed toward maintaining normothermia to avert the potentially disastrous consequences of hypothermia in the already bleeding critically ill patient. Rewarming patients reverses the effects of hypothermia on the hemostatic system.

Renal failure is not uncommon in the critical care setting. In its acute form, bleeding is a common manifestation, most often from the gastrointestinal tract. The underlying mechanism is probably multifactorial, as there clearly is a qualitative
platelet function defect related to the degree of uremia, in combination with abnormalities in the plasmatic coagulation system (18-45). The presence of acidosis also contributes to both the platelet and coagulation factor dysfunction. The fundamental approach to therapy centers on dialysis, which results in abatement of the bleeding diathesis. Use of desmopressin and cryoprecipitate, as temporizing measures to transiently stop the bleeding while awaiting institution of dialysis, have been reported to be successful. Conjugated estrogens have also been used with some success, albeit the effects are not as rapid but more durable, but any positive outcomes are balanced by undesirable consequences of hormonal side effects. In its chronic form, renal failure is still attended by a mild qualitative platelet function defect, but significant impact on hemostatic homeostasis is usually not seen.

---

**Acquired Disorders of the Coagulation System Decreased Production**

Decreased production of circulating plasmatic coagulation factors occurs secondary to liver failure (with the exception of factor VIII), vitamin K deficiency (seen with oral antibiotic usage, which depresses gut flora in the setting of nutritional deficiency; malabsorption syndromes, such as celiac sprue or chronic diarrheal conditions; or obstructive jaundice), and use of warfarin (Coumadin) (18,19). In these situations, therapy is acutely centered on replacement of coagulation factors, most commonly with use of FFP. Vitamin K is administered parenterally in patients with deficient states or to reverse the effects of Coumadin. Approaches targeting altered coagulation factor synthesis (in the presence of normal hepatic synthetic function) is not generally seen for 24 to 36 hours after administration of parenteral vitamin K (19,27).

---

**Impaired Function**

The effect of hypothermia on antagonizing normal functioning of the hemostatic mechanism globally has been described under qualitative platelet abnormalities (2,5,21,43). It is important to bear in mind that all enzymatic processes in biologic systems are governed to an extent by the necessity to function in an optimal, typically narrow, temperature range. The coagulation factors are enzymes, and therefore function best under normothermic conditions. Platelets, too, function optimally under normothermic conditions. Platelet dysfunction may be caused by primary platelet dysfunction, which affects normal protein products, or accumulation of proteinaceous breakdown products that affect the normal function of coagulation proteins. Collagen vascular diseases, such as systemic lupus erythematosus, as one example (48,49). In these patients an antibody is produced (lupus anticoagulant) that affects the coagulation cascade at the juncture of the intrinsic and extrinsic systems, resulting in prolongation of both the PT and PTT in vitro. Paradoxically, these patients tend to be hypercoagulable, and if clinically significant bleeding is noted, it is attributable to associated thrombocytopenia and increased vascular fragility. When there are elevated titers of either the lupus anticoagulant or anticardiolipin antibodies, or both, these patients may present with manifestation of the antiphospholipid antibody syndrome with generalized microvascular thrombosis, thrombocytopenia, gangrene of the extremities, multorgan failure, and death. Plasmapheresis, anticoagulation, and immunosuppressive therapy serve as the foundation of treatment (48,49). Other commonly acquired inhibitors or circulating anticoagulants include factor VIII inhibitors and factor IX inhibitors, related primarily to prior frequency of transfusion with plasma-derived blood concentrates and alloimmunization (30-52). Exogenously administered heparin, the prototype for anticoagulation therapy, binds to circulating antithrombin III and catalyzes its ability to neutralize the action of a number of coagulation factors. The end result is interference with the normal coagulation cascade. Disorders characterized by the production of abnormal globulins, often referred to collectively as the paraproteinemias (associated with multiple myeloma and Waldenstrom macroglobulinemia), also result in interference with coagulation proteins and inhibition of fibrin polymerization. In these conditions the PT, PTT, and TT are prolonged. Fibrinogen/fibrin degradation products also inhibit fibrin polymerization, as does uremia, with prolongation of the PT, PTT, and TT. Treatment of the coagulopathy associated with all of these conditions consists of replacement of deficient coagulation factors when bleeding is dominant and definitive treatment directed at the underlying disease process.

---

**Increased Destruction or Consumption**

The most common cause of increased destruction of plasmatic coagulation factors has been variously termed DIC, disseminated intravascular coagulation syndrome, or consumptive coagulopathy (6-9). This syndrome is characterized by a hemorrhagic diathesis with unrestrained clotting and fibrinolysis in the vascular microcirculation, initiated by activation of the intrinsic or the extrinsic system, or both (6-9,37). Release of tissue thromboplastin, from injured tissue or from leukocytes, activates the extrinsic system, whereas damage to vascular endothelium (in addition to releasing tissue thromboplastin) results in activation of the intrinsic system via collagen exposure (8). Exposed collagen initiates platelet aggregation with release of platelet factor III and also activates factor XII directly. The net result is deposition of fibrin in the microvasculature. This results in a microangiopathic hemolytic anemia with fragmentation of red blood cells as they traverse these vascular beds. These fragmented red blood cells, Normal physiologic processes (fibrinolytic system) exist to control for unremitting clot formation and are described in several reviews (1,31,32). Inherited function of the coagulation cascade may be the result of various disorders that are characterized by the genesis of circulating anticoagulants, abnormal protein products, or accumulation of proteolytic breakdown products that affect the normal function of coagulation proteins. Collagen vascular diseases, such as systemic lupus erythematosus, as one example (48,49). In these patients an antibody is produced (lupus anticoagulant) that affects the coagulation cascade at the juncture of the intrinsic and extrinsic systems, resulting in prolongation of both the PT and PTT in vitro. Paradoxically, these patients tend to be hypercoagulable, and if clinically significant bleeding is noted, it is attributable to associated thrombocytopenia and increased vascular fragility. When there are elevated titers of either the lupus anticoagulant or anticardiolipin antibodies, or both, these patients may present with manifestation of the antiphospholipid antibody syndrome with generalized microvascular thrombosis, thrombocytopenia, gangrene of the extremities, multiorgan failure, and death. Plasmapheresis, anticoagulation, and immunosuppressive therapy serve as the foundation of treatment (48,49). Other commonly acquired inhibitors or circulating anticoagulants include factor VIII inhibitors and factor IX inhibitors, related primarily to prior frequency of transfusion with plasma-derived blood concentrates and alloimmunization (30-52). Exogenously administered heparin, the prototype for anticoagulation therapy, binds to circulating antithrombin III and catalyzes its ability to neutralize the action of a number of coagulation factors. The end result is interference with the normal coagulation cascade. Disorders characterized by the production of abnormal globulins, often referred to collectively as the paraproteinemias (associated with multiple myeloma and Waldenstrom macroglobulinemia), also result in interference with coagulation proteins and inhibition of fibrin polymerization. In these conditions the PT, PTT, and TT are prolonged. Fibrinogen/fibrin degradation products also inhibit fibrin polymerization, as does uremia, with prolongation of the PT, PTT, and TT. Treatment of the coagulopathy associated with all of these conditions consists of replacement of deficient coagulation factors when bleeding is dominant and definitive treatment directed at the underlying disease process.
or schistocytes, seen on the peripheral blood smear are a clas-
sic finding in this syndrome. Additionally, microthrombi cause
stasis throughout as well as number of capillary beds, manifest-
ing as renal insufficiency or failure with kidney involvement,
Browninsufficiency with lung involvement, mental status
together with skin involvement. Stasis itself can result in further activation of clot-
ting factors. Fibrin deposition and endothelial wall damage
both bring about the release of plasminogen activator, which
causes the conversion of circulating plasminogen to plas-
min. Plasmin proteolytically hydrolyzes both fibrinogen and
fibrin (secondary fibrinolysis), resulting in fibrinogen and fib-
rin degradation (or “split”) products. These degradation prod-
ucts then interfere with fibrin polymerization through the for-
mation of complexes, further contributing to the hemorhagic
state. Additionally, these degradation products also interfere
with platelet function, impairing both adhesion and aggrega-
tion. The number of disorders associated with DIC is substan-
tial, but the unifying approach to management is supportive
therapy with replacement of coagulation factors and platelets
with attention focused on treating the underlying disease pro-
cess. The end point is normalization of the PT, PTT, TT, and
platelet count. Both acute and chronic forms have been iden-
tified. In the acute form patients are critically ill, whereas in
the chronic form the natural history is more indolent and pro-
tracted, and thrombotic complications may be the predominant
features.

In the postoperative patient in the ICU, infection is the
principle cause for DIC (9). Several causative organisms have
been implicated, including Gram-negative bacteria, such as the
Enterobacteriaceae group, as well as facultative fermentation, Gram-
positive bacteria; rickettsial organisms (Rocky Mountain
spotted fever); mycotic infections, such as disseminated as-
pergillus; parasitic agents, such as malaria; and viruses.

The underlying pathophysiology has been best elucidated
with Gram-negative infections, with endotoxin (cell wall
lipopolysaccharide) triggering the intrinsic system by activa-
tion of factor XII directly and by factor XII exposure to suben-
dothelial collagen, as a result of endotoxin-mediated damage
to vascular endothelium. Endotoxin may also trigger the coagu-
lation cascade by inducing expression of procoagulant activity
in circulating leukocytes, hepatic macrophages, and endothe-
rial cells, and by activating the extrinsic system mediated by the
release of tissue thromboplastin from damaged leukocytes and
vascular endothelium (53–55).

Traumatic injuries (particularly involving brain, bone, or
liver), thermal injuries, and severe crush injuries, as well as
surgical procedures may produce a consumptive coagulopathy
(6–9,56–58). Secondary infection and hemorrhagic shock fur-
ther serve to aggravate the coagulopathy, especially if acidosis,
hypothermia, or tissue ischemia and necrosis develops.

Acute pancreatitis, arising from various causes, may be asso-
ciated with DIC due to release of enzymes that may directly ac-
ivate a number of coagulation factors (59). In many instances,
there is associated multiorgan dysfunction involving cardiovap-
nary, renal, and hepatic function. In addition, pancreatic se-
quelae, such as the development of infected pancreatic necrosis
or abscess formation, may result in DIC attributable to sep-
sis. Treatment is primarily supportive, with aggressive resus-
citation, replacement of deficient coagulation factors if there
is associated bleeding, appropriate use of broad-spectrum an-
tibiotics, and surgical debridement and drainage for control
of infectious complications.

Obstetric complications can result in some of the most pro-
found and challenging instances of DIC. Well-recognized exam-
pies include amniotic fluid embolism, abruptio placentae, re-
tained dead fetuses, and eclampsia (6–8). In these circumstances,
the culprit is massive systemic release of tissue thromboplastin
that generates a fulminating course characterized by bilateral re-
nal cortical necrosis to frank cardiopulmonary collapse, shock,
multinorgan failure, and, at times, death even if aggressive at-
ttempts are made to treat these individuals.

The laboratory diagnosis of DIC is readily established with
routinely available tests. The PT, PTT, and TT are all pro-
longed, and the platelet count is decreased. Depending on the
severity of the disease process, fibrinogen may not be de-
tectable. Fibrinogen/fibrin degradation products are elevated,
and the peripheral blood smear often reveals the presence of
schistocytes. Factors I (fibrinogen), V, VIII, and XIII tend to be
markedly depressed. In milder forms, fibrinogen levels may not be
significantly decreased, particularly in the presence of ade-
quite hepatic function. Radiospecific assay of fibrinopeptide
A, a by-product of the action of thrombin on fibrinogen, may
be useful in these situations to establish the correct diagnosis
and management approach (60). Although rare, primary fibrin-
olysis differs from DIC (where secondary fibrinolysis occurs)
in the following ways. In primary fibrinolysis, (a) platelet count
is normal, (b) soluble fibrin monomers are not present (mea-
sured by the plasma paracoagulation test), (c) schistocytes (red
cell fragments) are not seen, and (d) tests for increased levels
of plasmin activity are strongly positive (euglobulin clot lysis
time, whole blood clot lysis time).

Optimum management of DIC requires aggressive treat-
ment of the underlying disease process and supportive ther-
apy with coagulation factor and platelet replacement. FFP and
platelet concentrates are the two most common blood products
used as a temporary measure (10–14,34). Stored or bailed
whole blood is a reasonable source of most clotting factors if
the units are less than 24 hours old (10,14,61). The biologic
half-life of factors V, VII, VIII, and IX are on the order of
24 hours or less; hence whole blood stored for longer than
24 hours may not provide adequate amounts of these coagula-
tion factors. Heparin had been used in the past in a theoretical
attempt to abrogate the clotting cascade, but its contempo-
raneous use for this purpose is at best controversial, may be
contraindicated in the perioperative period, and is not sup-
ported by evidence-based data (6–8,62). In septic patients with
or without DIC, treatment with recombinant activated pro-
cerinhibits mortality, and this may be attributable in part to
its profibrinolytic, anti-inflammatory, and antiaggregating
effects (6,63).

### COMPLEX POST-OPERATIVE BLEEDING PROBLEMS

#### Hepatobiliary Disease

Hepatic parenchymal and biliary obstructive disease results in
diverse manifestations of hemostatic abnormalities (18). Extra-
hepatic biliary obstruction results in diminished absorption of
vitamin K due to lack of bile salts necessary for gastrointestinal
absorption of lipid-soluble vitamins. Decreased synthesis of
the vitamin K–dependent factors II, VII, IX, and X occurs
with abnormal prolongation of the PT and eventually the PTT.
Parenchymal diseases such as cirrhosis, chronic active hepaticitis, fulminant hepatic failure, or metastatic carcinoma impact on the hemostatic system in a heterogeneous manner. Most coagulation factors, naturally occurring anticoagulants (such as antithrombin III), fibrinolysins precursors (plasminogen), and inhibitors of the fibrinolytic system (antiplasmins) are synthesized by the liver. In severe liver disease, acquired dysfibrinogenemia has also been reported (18,28). This impairs polymerization of soluble fibrin monomers and is suggested by a prolonged TT on purified fibrinogen, which is generally done in a research laboratory. The liver also removes activated coagulation factors from the circulation, but it is speculative to conclude that this results in a coagulopathy by itself, despite the fact that this increased consumption of activated factors by the liver lowers coagulation factors already depressed by decreased production in a diseased liver. Clearance of fibrinogen/fibrin degradation products is reduced in chronic liver disease. These breakdown products inhibit both fibrin polymerization and platelet function and thus contribute to a defective hemostatic system, as discussed earlier. Thrombocytopenia occurs secondary to hypersplenism, potentially exacerbated by vitamin deficiencies associated with decreased thrombopoiesis. Additionally, alcohol has a direct toxic effect on megakaryocytes, which contributes to prevailing vitamin deficiencies and decreased bone marrow production of platelets. Treatment of bleeding in liver failure with vitamin K usually is not successful given the lack of hepatic synthetic function. Whole blood both corrects the red blood cell deficit and is as effective as fresh frozen plasma in correcting coagulation factor deficits if the units of blood have not been banked for an extended period of time (14,61). Platelet transfusions should be judiciously used to raise the platelet count to above 100 x 10^9/L if bleeding is encountered in this setting, and FFP should be provided to correct deficits in plasma coagulation factors (10,11,12,14).

Transfusion-Induced Bleeding

Major trauma, major orthopedic (spine, hip, or pelvis) or hepatic resections, liver transplantation, or other causes of potentially life-threatening, exsanguinating hemorrhage is often associated with the need for what has been termed massive blood transfusion (21,22,61). This term has been variously defined but generally refers to administration of the equivalent of one total blood volume or more to a patient in less than a 24-hour period. Due to consumption of soluble fibrin monomers and is suggested by a prolonged TT on purified fibrinogen, which is generally done in a research laboratory. The liver also removes activated coagulation factors from the circulation, but it is speculative to conclude that this results in a coagulopathy by itself, despite the fact that this increased consumption of activated factors by the liver lowers coagulation factors already depressed by decreased production in a diseased liver. Clearance of fibrinogen/fibrin degradation products is reduced in chronic liver disease. These breakdown products inhibit both fibrin polymerization and platelet function and thus contribute to a defective hemostatic system, as discussed earlier. Thrombocytopenia occurs secondary to hypersplenism, potentially exacerbated by vitamin deficiencies associated with decreased thrombopoiesis. Additionally, alcohol has a direct toxic effect on megakaryocytes, which contributes to prevailing vitamin deficiencies and decreased bone marrow production of platelets. Treatment of bleeding in liver failure with vitamin K usually is not successful given the lack of hepatic synthetic function. Whole blood both corrects the red blood cell deficit and is as effective as fresh frozen plasma in correcting coagulation factor deficits if the units of blood have not been banked for an extended period of time (14,61). Platelet transfusions should be judiciously used to raise the platelet count to above 100 x 10^9/L if bleeding is encountered in this setting, and FFP should be provided to correct deficits in plasma coagulation factors (10,11,12,14).

Cardiopulmonary Bypass

Post-operative bleeding is a frequent impediment of cardiopulmonary bypass. Numerous mechanisms are apparently...
involved, which include contact factor (factors XII and XI) activation, elevations of tissue plasminogen activator level and tissue type plasminogen activator, dilution of plasmatic coagulation factors, residual effects of systemic heparinization, hypothermia, platelet function defects, and failure of surgical hemostasis (23–26).

Some investigations have demonstrated a 30% to 50% decrement in platelet count attributable to the shearing forces that are encountered in the bypass apparatus. The routine use of antplatelet agents in patients with cardiac disease, such as aspirin and thienopyridine derivatives (clopidogrel or ticlopidine), also contributes to the increased risk for bleeding. The combined effects of aspirin and a thienopyridine derivative, such as clopidogrel, on bleeding complications is synergistic and not additive. In approximately 4% to 5% of patients, surgical re-exploration of the mediastinum is necessary, which varies based on the original procedure performed (23,25,79).

Several criteria for re-exploration have been proposed that have in common the rate of blood loss from mediastinal or chest tubes. Criteria vary used include blood loss from chest or mediastinal tubes of 300 mL/hour within the first 3 hours; total blood loss of 1,000 mL after 4 hours; a sudden increase in bleeding (>300 mL/hour) in a patient who previously had minimal drainage; or evidence of cardiac tamponade. A coagulopathy must never be presumed to be the cause of bleeding postoperatively unless surgical causes of bleeding have first been excluded. A site of localized bleeding (surgical failure) is identified in more than 50% of patients re-explored based on these types of criteria (23,25,80).

Despite multiple contributing factors to the bleeding that occurs in these patients, the prime offender is collectively believed to be secondary to qualitative platelet function defects (1,23–26,79,80). The bypass circuitry results in platelet activation with degranulation and aggregation. Although this function normally is transient, increased time on bypass, hypothermia, and antplatelet medications significantly exacerbates this condition. Laboratory analysis reveals a prolongation of the bleeding time with impaired adhesion and aggregation, particularly in the presence of adenosine diphosphate (ADP) and ristocetin. This latter finding is believed to be linked to low levels of vWF found in plasma after cardiopulmonary bypass.

Hence, some investigators have proposed use of desmopressin in this circumstance (and in patients with a history of proceeding use of aspirin), to increase levels of vWF by stimulating release from endothelial cells, increasing the glycoprotein receptors on platelets, and increasing the level of factor VIII and tissue plasminogen activator. However, others believe that this practice increases the risk of graft thrombosis and coronary occlusion (2,79,80). Additionally, peer-reviewed, reported outcome data in this circumstance are indeterminate (2). Usually the acquired qualitative platelet function defect resolves within 4 hours of completion of cardiopulmonary bypass without any intervention. In instances where there is prolonged nonsurgical postoperative bleeding, platelet transfusions are often beneficial (10,14,80).

Many pharmacologic agents have proven efficacy in the management of nonsurgical bleeding, particularly in the post-cardiopulmonary bypass setting. Desmopressin has already been described. Antifibrinolytic agents constitute a heterogeneous group of drugs with proven efficacy in cardiac surgery patients. Aprotinin, a bovine serine protease inhibitor, inhibits plasmin and has been shown to reduce the need for red blood cell transfusions in several randomized trials and reduces the need for reoperation for nonsurgical bleeding (1,2,4,26,80–82). There are several adverse side effects that limit its usefulness. Thromboembolic phenomena, renal insufficiency, allergic reactions (probably due to its bovine origin) have all been reported. The occurrence of serious anaphylactic reactions has been the impetus for the full implementation of the agent (2,80). Aprotinin has been removed from FDA approval until further studies are done confirming safety. Epsilon aminocaproic acid (EACA) and tranexamic acid are lysine analogues that inhibit binding of plasmin to fibrin. EACA appears to have the weakest antifibrinolytic effect compared to tranexamic acid and aprotinin, but nevertheless has been used in the cardiopulmonary bypass patient with some success. Tranexamic acid has met with considerable success in the reduction of postoperative blood loss and the reduced need for red blood cell transfusion in cardiac surgery, total knee arthroplasty, transurethral prostate surgery, and in oral surgery procedures. Neither EACA nor tranexamic acid are associated with thrombotic complications or anaphylactic reactions. The most commonly reported adverse reactions include nausea, diarrhea, and orthostatic reactions (83). Considering efficacy, side effect profile, and lower cost, tranexamic acid has several advantages over aprotinin (26,80–83).

Monitoring for increased risks of hemorrhage commences during surgery (84–86). The activated clotting time, which measures the effect of heparin on fibrin clot formation, has been traditionally used for intraoperative management of anti-coagulation therapy. Thromboelastography, an assay popularized in Europe, can be used to determine if there is a platelet function abnormality, a deficit in plasmatic coagulation factors, the presence of circulating fibrinogen, or fibrinolysis. It is rapidly gaining attention as a valuable adjunct to managing complex coagulation disorders. It has been efficacious in decreasing blood transfusion requirements during cardiac surgery and in liver transplantation (87,88). The effect of hypothermia on a patient’s coagulation profile can also be determined simply by adjusting the temperature of the apparatus to correspond with the patient’s core body temperature. Several automated analyzers are available commercially.

**SUMMARY**

Postoperative bleeding requires immediate recognition of early shock, reexploration, and differentiation between surgical and nonsurgical bleed. Knowledge of coagulation and appropriate replacement of blood and blood products is essential. Careful evaluation of the patient to identify primary or secondary coagulation disorders is necessary.

**References**

Chapter 74: Surgical and Post-Surgical Bleeding

1139

Although some patients may arrive in the ICU in extremis necessitating continued resuscitation without a thorough history and physical examination, the majority should undergo a complete assessment promptly, and it should not be assumed that the ED evaluation was comprehensive and accurate. Such an evaluation, often termed the tertiary survey, is a repeated history and physical examination performed in light of imaging studies and pertinent intraoperative findings (1,2). Additionally, the evaluation is more detailed than that performed in the ED, because all the diagnostic results should be available, further information is obtained from family members, and the physician has time for a more meticulous physical examination, particularly of final imaging results, can be done through a standardized form and facilitates communication among care providers (Fig. 75.1).

The reliability of clinical examination in these patients after ICU admission is often questioned. The clinical exam is...