Evidence-Based Patient Safety Advisory: Blood Dyscrasias

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Summary: Rarely, patients with blood disorders may seek to undergo plastic surgery. Although plastic surgeons are not expected to diagnose or manage blood disorders, they should be able to recognize which patients are suitable for surgery and which should be referred to a hematologist before a procedure. This practice advisory provides an overview of the perioperative steps that should be completed to ensure appropriate care for patients with blood disorders. (*Plast. Reconstr. Surg.* 124 (Suppl.): 82S, 2009.)

The term "blood dyscrasia" refers to any pathologic condition of the blood involving disorders of the blood's cellular components (platelets, white blood cells, or red blood cells) or soluble plasma components required for proper coagulation (coagulation factors). In general, most of these blood disorders can be broken down into two basic categories based on the patient's coagulation phenotype: hypocoagulable (hemorrhagic) states and hypercoagulable (thrombotic) states. Each category includes heritable and acquired causes.

During normal hemostasis, various factors operate in combination to arrest bleeding after vascular injury. Early in the coagulation response, platelets aggregate to form a plug at the site of the ruptured vessel. After initial bleeding control has been achieved, the platelet plug is stabilized by means of fibrin deposition, effectively sealing the break in the vessel and preventing further bleeding. Fibrin deposition is initiated by a cascading series of proteolytic events involving coagulation factors (Fig. 1). This efficient coagulation system is controlled at several steps by means of anticoagulant mechanisms to ensure that the clotting process remains localized to the area of damage.

Hypocoagulable patients typically have difficulty controlling bleeding as a result of decreased platelet numbers or loss-of-function mutations affecting specific clotting factors. By contrast, hypercoagulable patients typically exhibit excessive thrombus formation resulting from hyperactive platelet aggregation, increased platelet numbers, or mutations affecting the function of specific clotting factors (Fig. 1). Whatever the source of the defect in the coagulation cascade, these patients' risks of bleeding or thrombosis during surgery is increased significantly over the normal patient, and complications may result if they are not diagnosed or treated appropriately.

There is a paucity of published clinical research pertaining to the perioperative care of surgical patients with blood dyscrasias. In an effort to ensure patient safety, the American Society of Plastic Surgeons (ASPS) Patient Safety Committee sought to develop a practice advisory to assist decision-making for patients with blood disorders who seek to undergo elective surgical procedures. The current practice advisory thus provides an overview of the perioperative steps that should be completed to ensure appropriate care for these patients. These guidelines are designed for use by

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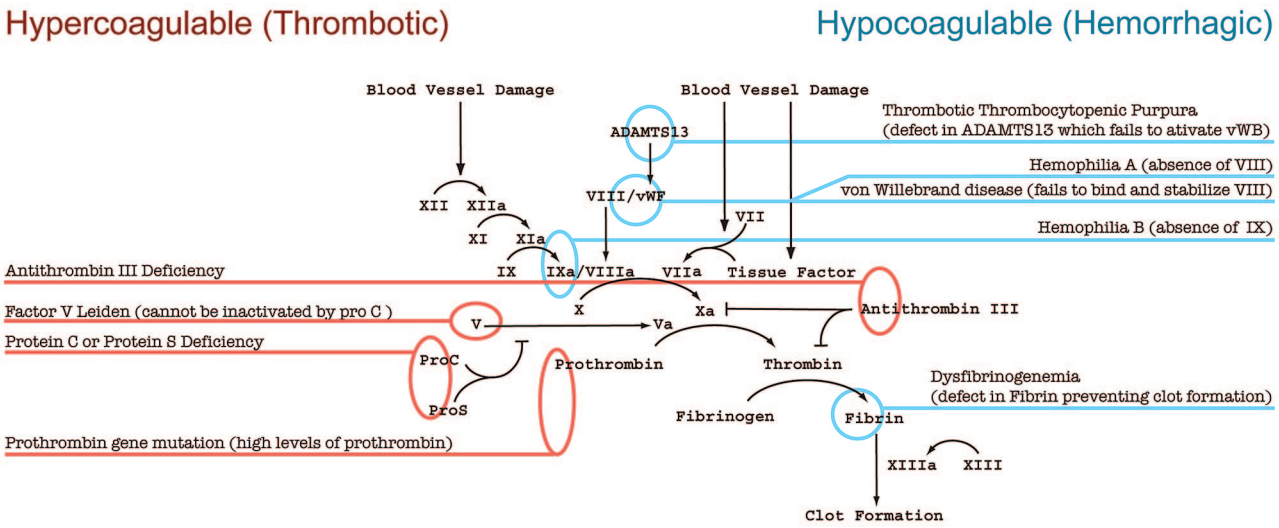

Fig. 1. The coagulation cascade and associated defects.

any health care practitioner managing the perioperative care of patients with bleeding disorders. Although plastic surgeons are not expected to manage hypocoagulable and hypercoagulable disorders, they should be able to recognize which patients are suitable for surgery and which should be referred to a hematologist before a procedure.

This patient safety advisory was developed through a comprehensive review of the scientific literature and a consensus of the Patient Safety Committee. The supporting literature was critically appraised for study quality according to criteria referenced in key publications on evidence-based medicine.[1–5] Depending on study design and quality, each reference was assigned a corresponding level of evidence (I through V) with the ASPS Evidence Rating Scale (Table 1),[6] and the evidence was synthesized into practice recommendations. The recommendations were then graded (A through D) with the ASPS Grades of Recommendation Scale (Table 2)[7]; grades correspond to the levels of evidence provided by the supporting literature for that recommendation. Practice recommendations are discussed throughout this document, and graded recommendations are summarized in Appendix A.

Table 1. Evidence Rating Scale for Studies Reviewed

Level of Evidence	Qualifying Studies
I	High-quality, multicentered or single-centered, randomized controlled trial with adequate power; or systematic review of these studies
II	Lesser quality, randomized controlled trial; prospective cohort study; or systematic review of these studies
III	Retrospective comparative study; case-control study; or systematic review of these studies
IV	Case series
V	Expert opinion; case report or clinical example; or evidence based on physiology, bench research, or "first principles"

DISCLAIMER

Practice advisories are strategies for patient management, developed to assist physicians in clinical decision-making. This practice advisory, based on a thorough evaluation of the present scientific literature and relevant clinical experience, describes a range of generally acceptable approaches to diagnosis, management, or prevention of specific diseases or conditions. This practice advisory attempts to define principles of practice that should generally meet the needs of most patients in most circumstances. However, this practice advisory should not be construed as a rule, nor should it be deemed inclusive of all proper methods of care or exclusive of other methods of care reasonably directed at obtaining the appropriate results. It is anticipated that it will be necessary to approach some patients' needs in different ways. The ultimate judgment regarding the care of a particular patient must be made by the physician in light of all the circumstances presented by the patient, the diagnostic and treatment options available, and available resources.

This practice advisory is not intended to define or serve as the standard of medical care. Standards of medical care are determined on the basis of all the facts or circumstances involved in an individual case and are subject to change as scien-

Table 2. Scale for Grading Recommendations

Grade	Descriptor	Qualifying Evidence	Implications for Practice
A	Strong recommendation	Level I evidence or consistent findings from multiple studies of levels II, III, or IV	Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
B	Recommendation	Levels II, III, or IV evidence and findings are generally consistent	Generally, clinicians should follow a recommendation but should remain alert to new information and sensitive to patient preferences.
C	Option	Levels II, III, or IV evidence, but findings are inconsistent	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role.
D	Option	Level V: Little or no systematic empirical evidence	Clinicians should consider all options in their decision-making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role.

tific knowledge and technology advance, and as practice patterns evolve. This practice advisory reflects the state of knowledge current at the time of publication. Given the inevitable changes in the state of scientific information and technology, periodic review and revision will be necessary.

PATIENT SELECTION

Medical care has become sufficiently advanced that patients with complex blood disorders can safely undergo a variety of surgical procedures. However, there remain inherent risks associated with any surgical procedure, and these can be exacerbated in patients with blood dyscrasias. The literature is unclear about whether patients with blood dyscrasias are appropriate candidates for ambulatory surgery. Only minor outpatient procedures (e.g., dental) have been described in the literature. Most patients with hypocoagulable or hypercoagulable states need close monitoring for many days following surgery; however, this can now be accomplished with outpatient testing.

During the preoperative assessment, patients should be evaluated for a history of bleeding, bruising, or thrombosis, including any family history of these conditions. Evidence of unusual postsurgical bleeding, epistaxis, gingival bleeding, and (in women) menorrhagia and a history of pregnancy complications such as stillbirth, preterm delivery, and recurrent miscarriages may be signs of an undiagnosed blood dyscrasia.[8–15] In addition, patients should be asked about their use of antithrombotic drugs and other drugs/supplements (i.e., over-the-counter and herbal) that may affect coagulation.[8] In its evidence-based guidelines for managing patients with bleeding disorders,[16] the National Heart, Lung, and Blood Institute has provided appropriate questions to ask patients during the preoperative assessment (Appendix B).

Although routine screening of all patients is not recommended, patients who have a positive history for bleeding, bruising, or thrombosis should undergo preoperative coagulation and/or thrombophilia screening.[8,16,17] Initial hemostasis laboratory tests may include platelet count and complete blood count, activated partial thromboplastin time, prothrombin time, and optionally either a fibrinogen level or a thrombin time.[8,16] Bleeding time may be useful to detect severe blood disorders, but is often unreliable for detecting mild or moderate cases.[8,16] If initial tests are positive or inconclusive, referral may be necessary for further evaluation.

PERIOPERATIVE MANAGEMENT

For patients with hypocoagulable or hypercoagulable states who are candidates for surgical procedures, the following points should be taken into consideration when preparing a detailed preoperative plan for the treatment of local bleeding/thrombi formation:

- Hemostatic laboratory monitoring.
- The choice of treatment for the disorder.
- Preoperative confirmation of the treatment's effectiveness in the specific patient.
- The dose and duration of the treatment.
- Anticipated side effects of the treatment.

HYPOCOAGULABLE (HEMORRHAGIC) STATES

Hypocoagulable, or hemorrhagic, states are characterized by inappropriate or excessive bleeding and a failure to form blood clots. As with any

medical procedure, there are several possible complications that may arise in association with surgical treatment; however, in patients with hypocoagulable states, the risk of excessive bleeding is the primary concern.

Patients with hypocoagulable disorders taking prophylactic coagulation factors in combination with anticoagulants need to be closely monitored before, during, and after surgery. Medications administered for a particular disorder are often monitored to determine the effectiveness of the coagulation therapy. Coagulation is often monitored by activated partial thromboplastin time, prothrombin time, and other methods, similar to full coagulation workups typically performed preoperatively. Thrombin generation assays, which measure clotting time, the amount of thrombin that forms, and the time it remains active, have also been used to monitor coagulation efficiency in patients.[18] Thromboelastographic assessment, which determines the kinetics of clot formation and the strength and stability of the formed clot, has also been used to monitor coagulation in patients with these disorders.[19,20]

There are two sequelae of coagulation therapy that need to be considered. First, patients undergoing coagulation-factor replacement therapy to control bleeding need to be monitored closely and treated for possible thrombi formation.[21,22] Second, the development of inhibitors (antibodies) against human-derived factors is a common and serious complication of factor replacement therapy. Because of the complexity of controlling coagulation in patients who have developed inhibitors, the risks of elective procedures should be considered carefully, and these patients may not be candidates for elective surgery. If surgery is necessary, patients should undergo surgical procedures in centers with personnel well skilled in perioperative inhibitor management.[23,24]

The treatment of patients with hypocoagulable states depends on the cause and nature of the procedure. For patients with mild disease who are undergoing minor surgical procedures, desmopressin and/or antifibrinolytic agents may facilitate local hemostasis.[12,25,26] However, bleeding episodes and surgical procedures typically require the use of blood-derived or recombinant replacement factors (Fig. 2).[18,27–38] For patients who have developed inhibitors against standard factor replacements, therapies that bypass the inhibitors have been used.[23,39–46] Other treatments such as platelet concentrate, red blood cells, fresh frozen plasma, plasmapheresis, and cryoprecipitate have been described but depend on the type and severity of bleeding disorder.[20,47–50]

There are several specific conditions, either inherited or acquired, that can cause excessive bleeding. Below are descriptions of the most common bleeding disorders followed by recommendations for perioperative management. Because von Willebrand disease and hemophilia often require similar management, treatment/prophylactic options are discussed concurrently after their descriptions.

von Willebrand Disease

The von Willebrand factor, a multimeric plasma glycoprotein, normally functions to me-

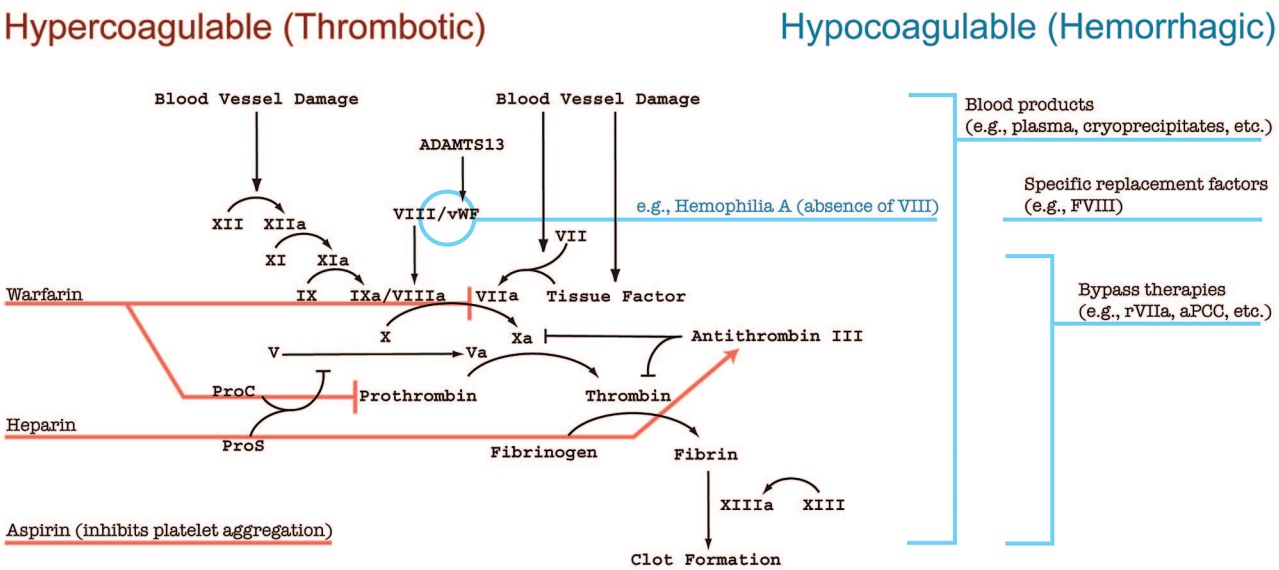

Fig. 2. Action of blood products and replacement factors on the coagulation cascade.

diate the initial adhesion of platelets and transport factor VIII to the site of vascular injury, promoting the activation of thrombin. The disease is typically characterized by defects in von Willebrand factor that cause low platelet adhesion and increased turnover of factor VIII, which results in the inhibition of normal blood-clotting mechanisms and an increased risk of bleeding.[51,52] Defects in von Willebrand factor can be attributable to a variety of mutations and/or abnormal multimer patterns.[51] After initial coagulation tests have been performed, specific tests for diagnosing or excluding the disease include von Willebrand factor ristocetin cofactor activity, von Willebrand factor antigen, and factor VIII activity. Additional tests may include evaluation of the ratio of von Willebrand factor activity (von Willebrand factor ristocetin cofactor activity and/or von Willebrand factor collagen binding) to von Willebrand factor antigen, ristocetin-induced platelet aggregation, and analysis of von Willebrand factor multimers.[16,53]

Von Willebrand disease cannot be attributed to one particular defect, as several distinct mechanisms have been identified, resulting in different forms of the disease. Three main types of the disease have been defined: type 1, the most common form, represents partial deficiency of von Willebrand factor; type 2 variants represent qualitative abnormalities of von Willebrand factor; and type 3 represents severe deficiency of von Willebrand factor (Table 3).[51] It is important to identify the type of von Willebrand disease, as each has important clinical features requiring specific therapeutic approaches.

Table 3. Classification of von Willebrand Disease*

Type	Description
1	Partial quantitative deficiency of vWF
2	Qualitative vWF defects
A	Decreased vWF-dependent platelet adhesion and a selective deficiency of high-molecular-weight vWF multimers
B	Increased affinity for platelet glycoprotein Ib
M	Decreased vWF-dependent platelet adhesion without a selective deficiency of high-molecular-weight vWF multimers
N	Markedly decreased binding affinity for factor VIII
3	Virtually complete deficiency of vWF

vWF, von Willebrand factor.
*From Sadler JE, Budde U, Eikenboom J, et al. Update on the pathophysiology and classification of von Willebrand disease: A report of the Subcommittee on von Willebrand Factor. *J Thromb Haemost.* 2006;4:2103–2114.

Hemophilia

Hemophilia is an inherited X-chromosome-linked disorder characterized by deficiencies of factor VIII (hemophilia A) and factor IX (hemophilia B). These factors normally act to promote the formation of active thrombin. Hemophilia results in decreased thrombin activation, which can inhibit normal blood-clotting mechanisms, thus increasing the risk of bleeding. Hemophilia is diagnosed with initial coagulation tests and specific factor assays, and is classified by bleeding risk (mild, moderate, or severe), which typically correlates with coagulation factor activity (Table 4).[54,55]

Prophylaxis and Treatment for von Willebrand Disease and Hemophilia

Desmopressin

1-Deamino-8-D-argenine vasopressin (desmopressin) is the first-line approach to prophylaxis and treatment in patients with von Willebrand disease and hemophilia A.[16,56]A synthetic analogue of vasopressin, desmopressin releases bound stores of von Willebrand factor and factor VIII from the vascular endothelium, thereby increasing the plasma concentration of these coagulation factors. Approximately 80 percent of patients with the disease respond favorably to desmopressin[57]; however, the response depends on the specific type and location of mutations and the multimeric pattern of von Willebrand factor.[52,58] Desmopressin is effective in most type 1 and some type 2 patients. Because type 3 patients are completely deficient in von Willebrand factor and have no bound stores to release, they are completely unresponsive to desmopressin.[16,57] In patients with hemophilia, response rates depend on the type and severity of disease. Patients with mild hemophilia A respond

Table 4. Classification of Hemophilia*

Classification	Residual Factor Concentration	Description
Mild	0.05–0.35 IU/ml or 5–35%	No spontaneous bleeding; delayed-onset bleeding after trauma, surgery, or dental extractions
Moderate	0.01–0.05 IU/ml or 1–5%	Bleeding into joints or muscles with minor trauma; excessive bleeding with surgery
Severe	<0.01 IU/ml or <1%	Spontaneous joint, muscle, and internal bleeding; excessive bleeding with trauma or surgery

*From Israels S, Schwetz N, Boyar R, McNicol A. Bleeding disorders: Characterization, dental considerations and management. *J Can Dent Assoc.* 2006;72:827.

favorably to the drug; patients with moderate to severe hemophilia A or any form of hemophilia B typically are unresponsive.[56,57]

The standard dosing of injectable desmopressin is 0.3 μg/kg administered intravenously in 30 to 50 ml of normal saline over 30 minutes, with peak increments of factor VIII and von Willebrand factor 30 to 90 minutes after infusion. Although desmopressin is also available in a nasal spray, intravenous administration is recommended for surgical procedures. Before surgery, a test infusion should be considered to evaluate the patient's response to desmopressin.[16,52,59]

Coagulation Factor Replacement

For patients who do not respond to desmopressin, the next approach involves replacement of deficient coagulation factors. Patients with von Willebrand disease often receive von Willebrand factor, typically by infusion of exogenous von Willebrand factor contained in plasma-derived von Willebrand factor/factor VIII concentrates.[22,27,28,30–32,50,60–62] Perioperative management with von Willebrand factor concentrates depends on the invasiveness of surgery. Table 5 lists the National Heart, Lung, and Blood Institute evidence-based guidelines for the perioperative use of von Willebrand factor concentrate in major and minor surgery.

Patients with hemophilia can be treated with plasma-derived or recombinant factor VIII or factor IX concentrates.[18,21,33,34,36–38,63–65] For perioperative management, recommended dosages vary by product but generally are 35 to 50 U/kg for factor VIII and 70 to 100 U/kg for factor IX, both with a target factor activity level of 0.7 to 1.0 U/ml (70 to 100 percent).[57]

Adjunctive Agents

Adjunctive agents, such as antifibrinolytics (e.g., tranexamic acid or ε-aminocaproic acid) and topical thrombin and fibrin sealants, can be used with desmopressin or replacement factors and may further facilitate hemostasis.[26,57] In some cases (dental and minor skin wounds), these agents may even be used alone to treat local bleeding.[66]

Patients with Inhibitors

Development of inhibitors against coagulation factors is the most common and serious complication of replacement therapy in patients with bleeding disorders. Although rare in patients with von Willebrand disease and hemophilia A, inhibitors develop in approximately 25 to 33 percent of patients with hemophilia B.[24,56,67] Newly and previously treated patients can develop inhibitors, justifying the need for frequent screening, especially before surgical procedures. Patients are diagnosed by inhibitor type (low or high-responding) and titer [measured in Bethesda units (BU)] as follows[24,67]:

- Low responders: patients have low titers (≤5 BU), even despite immunologic challenges.
- High responders, low titer: patients have low titers at evaluation that become high (>5 BU) in response to immunologic challenges.
- High responder, high titer: patients have high titer on evaluation; titers can decrease over time in some patients.

There are several hemostatic products available for patients with inhibitors; however, treatment depends on the type and current titer of the inhibitor. Typically, low-responding inhibitors can be overcome by high doses of plasma-derived or recombinant factor VIII or factor IX. High-responding inhibitors of low or high titer typically require bypassing agents including activated pro-

Table 5. NHLBI Evidence-Based Guidelines for the Perioperative Use of vWF Concentrate*

	Type of Surgery	
Perioperative Period	**Major**	**Minor**
Loading dose (vWF: RCo IU/dl)	40–60 U/kg	30–60 U/kg
Maintenance dose	20–40 U/kg every 8–24 hr	20–40 U/kg every 12–48 hr
Monitoring	vWF:RCo and factor VIII trough and peak, at least daily	vWF:RCo and factor VIII trough and peak, at least once
Therapeutic goal	Trough vWF:RCo and factor VIII >50 IU/dl for 7–14 days	Trough vWF:RCo and factor VIII >50 IU/dl for 3–5 days
Safety parameter	Do not exceed vWF:RCo 200 IU/dl or factor VIII 250–300 IU/dl	Do not exceed vWF:RCo 200 IU/dl or factor VIII 250–300 IU/dl
Other	May alternate with DDAVP for latter part of treatment	May alternate with DDAVP for latter part of treatment

NHLBI, National Heart, Lung, and Blood Institute; vWF, von Willebrand factor; RCo, ristocetin cofactor; DDAVP, desmopressin.
*Modified from Nichols W; Expert Panel, and National Hemophilia Foundation. The diagnosis, evaluation and management of von Willebrand disease. Available at: http://www.nhlbi.nih.gov/guidelines/vwd/vwd.pdf. Accessed September 22, 2008.

thrombin complex concentrates, such as factor VIII inhibitor bypassing activity (factor VIII inhibitor bypassing activity)[39,42,68] or recombinant factor VIIa, alone or in combination with antifibrinolytic agents.[23,29,35,40–46,66,69–72] The recommended starting dose for factor VIII inhibitor bypassing activity is 50 to 100 μg/kg; for recombinant factor VIIa, 90 μg/kg. Additional doses should be administered perioperatively as needed.[24]

Thrombocytopenia

Thrombocytopenias are characterized by reduced levels of blood platelets, and can be inherited or acquired. Inherited thrombocytopenias are often attributed to defects in platelet size, whereas acquired forms typically result from an autoimmune condition, drug toxicity, or underlying disease. Normally, the level of platelets is maintained by the balance of production in the bone marrow and removal by the spleen. When this balance is disrupted, thrombocytopenia develops. Management of the condition depends on cause, but most thrombocytopenias are effectively managed by increasing the total number of platelets before surgery, usually by platelet transfusion, total plasma exchange, or immunosuppressant therapy.

In patients with idiopathic thrombocytopenia, platelet concentrate, red blood cells, fresh frozen plasma,[48,49] corticosteroids, and immunoglobulin G[73,74] have been used to control bleeding during surgery. Vinca alkaloids have been used successfully in idiopathic thrombocytopenia patients who fail to respond to corticosteroids.[74] Of note, acute heart failure may represent an extremely important clinical risk in patients with thrombotic thrombocytopenia who are undergoing surgery. Therefore, thrombotic thrombocytopenia patients with active-phase disease should undergo a preoperative cardiac workup, including an electrocardiogram, echocardiogram, determination of cardiac enzymes levels, and invasive arterial blood pressure monitoring.[75]

HYPERCOAGULABLE (THROMBOTIC) STATES

Hypercoagulable, or thrombotic, states are characterized by an increased risk of inappropriate or excessive blood clot formation. These conditions may be attributable to lifestyle risks, such as obesity, smoking, and inadequate exercise; prothrombotic states such as malignancy or pregnancy; or genetic risk factors. Table 6 lists genetic conditions associated with thrombosis formation.

In patients with hypercoagulation, the risk of venous thromboembolism is the greatest perioperative concern.[76–78] Several studies support preoperative testing for heritable thrombophilic defects to aid in the prediction of first-time and recurrent venous thromboembolism episodes. One study showed that venous thromboembolism recurrence rates were significantly increased in patients with hypercoagulable disorders.[76] In another study, patients who had thrombotic events after total hip arthroplasty were more likely than matched control patients to have hypercoagulable disorders, including the prothrombin gene mutation, protein C deficiency, or antithrombin III deficiency.[77] In addition, patients with polycythemia vera and essential thrombocythemia were five times as likely as patients without blood disorders to develop venous thromboembolism after major surgery.[78]

Table 6. Genetic Hypercoagulable (Thrombotic) States

Characteristic	Condition
Anticoagulant deficiency or defect	Antithrombin
	Protein C
	Protein S
Abnormal coagulant protein	Factor V Leiden
	Prothrombin gene mutation (20210)
	Dysfibrinogenemia
Increased procoagulant	Prothrombin factor VIII
Abnormal metabolism	Hyperhomocysteinemia

The literature includes case reports of plastic surgery patients who developed venous thromboembolism events that may have been related to the prothrombin gene mutation. One patient undergoing reconstruction for squamous cell carcinoma developed multiple thromboses, resulting in venous microvascular anastomotic failure.[12] Another developed pulmonary thromboembolism after a face lift, despite normal preoperative coagulation tests.[79] Consideration should be made, however, to one study reporting that venous thromboembolism recurrence rates were not related to the presence of heritable thrombophilia ($p = 0.187$).[80]

Use of oral contraceptives or hormone replacement therapy may further increase venous thromboembolism risk in patients with hypercoagulable disorders. For oral contraceptive use, significant associations of venous thromboembolism risk were found in women with factor V Leiden; deficiencies of antithrombin, protein C, or protein S; elevated levels of factor VIIIc; and factor V Leiden and prothrombin G20210A.[17,81] In addition, use of oral contraceptives in patients with factor V Leiden, the prothrombin gene mutation, or hyperhomocysteinemia may increase risk of re-

current thrombi formation.[76] A significant association was also found between factor V Leiden and use of hormone replacement therapy.[17] In general, it is up to the physician to decide whether to discontinue usage of hormone replacement therapy and oral contraceptives and to discuss this with his or her patients when discussing these risks.

In patients with hypercoagulable states, the use of prophylactic anticoagulants (e.g., heparin, warfarin) constitutes the primary management approach before, during, and after surgery (Fig. 2). Because anticoagulant therapy can lead to excessive bleeding, patients receiving such prophylaxis must be monitored closely. As mentioned previously, activated partial thromboplastin time, thrombin generation assays, and thromboelastographic assessment represent the spectrum of available monitoring modalities.[18–20,82] As with normal patients, postoperative graduated compression stockings, intermittent pneumatic compression devices, and early mobilization are used in hypercoagulable patients to prevent thrombosis.[77,83,84] For more information on prophylaxis, see Haeck et al., "Evidence-Based Patient Safety Advisory: Patient Selection and Procedures in Ambulatory Surgery," in this issue.

Additional therapeutic measures may include coagulation factor replacement (e.g., total volume exchange transfusions, plasmapheresis, or fresh frozen plasma)[19,85,86]; however, coagulation factor/blood product replacement therapy is not typically performed for patients with hypercoagulable disorders (as they are in hypocoagulable states) because of the inherent risks associated with blood products and the possibility of inhibitor formation.[87] Intravenous immunoglobulin G can also be used in the case of hypercoagulable states derived from autoimmune disorders.[87] Patients with myeloproliferative disorders that result in increased platelet counts can be treated with phlebotomy and/or cytoreductive therapy (e.g., hydroxyurea, anagrelide, and interferon).[78,88,89]

CONCLUSIONS

Patients with blood dyscrasias can safely undergo elective surgical procedures; however, because of their inherent bleeding and thrombotic risks, these patients may or may not be suitable candidates for outpatient surgery. The surgeon should conduct a thorough medical history, including family history, to identify any possible blood disorders, and refer patients for further coagulation testing as needed. It is recommended that the surgeon consult with a hematologist to determine whether a patient is suitable for outpatient surgery, to develop an appropriate plan for perioperative treatment/monitoring, and to ensure proper hemostasis and prevention of thrombi formation.

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Appendix A. Summary of Recommendations

Recommendation	Supporting Evidence	Grade
PATIENT SELECTION		
Medical history (see Appendix B)	8–17	B
It is recommended that the medical history include questions about:		
• Personal and family history of recurrent bleeding, bruising, or thrombosis		
• In women, a history of menorrhagia and/or pregnancy complications		
• Previous excessive posttraumatic or postsurgical bleeding		
• Use of antithrombotic drugs and other drugs/supplements that may affect coagulation (i.e., herbal remedies, HRT, oral contraceptives).		
PREOPERATIVE TESTING	8, 16, 17	B
• If bleeding and thrombosis history is negative, preoperative coagulation testing is not recommended.		
• If bleeding and thrombosis history is positive or there is a clear clinical indication (e.g., liver disease), preoperative coagulation testing is recommended.		
• For patients requiring coagulation tests, first-line clotting tests may include activated partial thromboplastin time and prothrombin time. Bleeding time may or may not be helpful, depending on severity of blood disorder.		
PERIOPERATIVE MANAGEMENT		
Hypocoagulable (hemorrhagic) states		
von Willebrand disease		
• Determine type of vWD: type 1, type 2 (A, B, M, or N), or type 3.	16, 52, 58	B
• Consider desmopressin as first approach to bleeding prophylaxis (most type 1; some type 2 patients; type 3 patients do not respond to desmopressin).	16, 25, 50, 52, 57, 58, 90	B
• For patients who do not respond to desmopressin (most type 2 and all type 3), consider replacement factors, vWF/VIII plasma-derived concentrates.	16, 27, 30, 32, 50, 57, 60, 90–98	B
• If patients have an inadequate response to factor concentrates, additional tests should be considered to test for inhibitors.	16, 57	B
• Adjunctive agents (e.g., antifibrinolytics, topical thrombin or fibrin) can be considered, as needed.	16, 26, 50, 57, 99	D
• Before surgery, the patient's response to therapies should be evaluated to ensure adequate hemostasis.	16, 52, 57, 58	B
Hemophilia		
• For patients with hemophilia A, consider desmopressin as first approach to bleeding prophylaxis (desmopressin is not effective in patients with hemophilia B).	56, 57	D
• For patients who do not respond to desmopressin, consider plasma-derived or recombinant replacement factor concentrates, factor VIII (hemophilia A), and factor IX (hemophilia B).	18, 29, 33–38, 56, 57, 64, 65, 72	B
• If patients have an inadequate response to factor concentrates, additional tests should be considered to test for inhibitors.	24, 56, 57	B
• Adjunctive agents (e.g., antifibrinolytics, topical thrombin or fibrin) can be considered, as needed.	24, 46, 56, 65, 66	D
• Before surgery, the patient's response to therapies should be evaluated to ensure adequate hemostasis.	56, 57	D

(*Continued*)

Appendix A. (*Continued*)

Recommendation	Supporting Evidence	Grade
Patients with inhibitors		
• For patients with low-responding inhibitors, consider high doses of recombinant factor concentrates, or plasma-derived concentrates if recombinant forms are unavailable.	24, 57	D
• For high-responding inhibitors, either low or high titer, consider recombinant factor VIII or factor IX, or bypass therapies, aPCC (e.g., FEIBA) or recombinant factor VIIa.	12, 23, 24, 39–46, 57, 66, 69–72, 100	B
• Adjunctive agents (e.g., antifibrinolytics, topical thrombin or fibrin) can be considered, as needed.	24, 44, 46, 57	D
• Before surgery, the patient's response to therapies should be evaluated to ensure adequate hemostasis.	24, 57	D
Thrombocytopenias		
• Increase platelet count preoperatively.	48	D
• Consider the use of corticosteroids or IgG.	73	D
• Consider vinca alkaloids for patients who do not respond to corticosteroids.	74	D
• Consider platelet concentrate, red blood cells, fresh frozen plasma, and plasmapheresis.	48, 49, 75	D
Hypercoagulable (thrombotic) states		
• Presence of thrombophilia disorders is considered a significant risk for the development of VTE.	12, 17, 77–79	B
• It is unclear whether presence of thrombophilia increases risk for *recurrent* VTE.	76, 80	C
• Prophylactic anticoagulants (e.g., heparin, warfarin, aspirin) should be considered before, during, and after surgery; medications should be adjusted as needed to prevent hemorrhage.	18–20, 82, 83	D
• Postoperative graduated compression stockings, intermittent pneumatic compression devices, and early mobilization are recommended after surgery to prevent thrombosis.	77, 83, 84	D
For more information on DVT/PE prophylaxis, consult "Evidence-Based Patient Safety Advisory: Patient Selection and Procedures in Ambulatory Surgery," in this issue.		

HRT, hormone replacement therapy; vWD, von Willebrand disease; vWF, von Willebrand factor; aPCC, activated prothrombin complex concentrates; FEIBA, factor VIII inhibitor bypassing activity; IgG, immunoglobulin G; VTE, venous thromboembolism; DVT, deep vein thrombosis; PE, pulmonary embolism.

APPENDIX B. SUGGESTED QUESTIONS FOR SCREENING PERSONS FOR A BLEEDING DISORDER*

*Adapted from Nichols W; Expert Panel, and National Hemophilia Foundation. The diagnosis, evaluation and management of von Willebrand disease. Available at: http://www.nhlbi.nih.gov/guidelines/vwd/vwd.pdf. Accessed September 22, 2008.

1. Have you or a blood relative ever needed medical attention for a bleeding problem or been told you have a bleeding disorder or problem:
   - During/after surgery?
   - With dental procedures, extractions?
   - With trauma?
   - During childbirth or for heavy menses?
   - Ever had bruises with lumps?
2. Do you have or have you ever had:
   - Liver or kidney disease, a blood or bone marrow disorder; a high or low platelet count?
3. Do you take aspirin, NSAIDs (provide common names), clopidogrel (Plavix; Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership, Bridgewater, N.J.), warfarin, heparin, or other drugs/supplements (i.e., other over-the-counter and/or herbal remedies)?

If any of the answers to questionquestions *and* obtain history of treatment and examine patient for signs of bleeding or underlying disease.

1. Do you have a blood relative who has a bleeding disorder, such as von Willebrand disease or hemophilia?
2. Have you ever had prolonged bleeding from trivial wounds, lasting more than 15 minutes or recurring spontaneously during the 7 days after the wound?
3. Have you ever had heavy, prolonged, or recurrent bleeding after surgical procedures, such as tonsillectomy?
4. Have you ever had bruising, with minimal or

no apparent trauma, especially if you could feel a lump under the bruise?
5. Have you ever had a spontaneous nosebleed that required more than 10 minutes to stop or needed medical attention?
6. Have you ever had heavy, prolonged, or recurrent bleeding after dental extractions that required medical attention?
7. Have you ever had blood in your stool, unexplained by a specific anatomical lesion (such as an ulcer in the stomach or a polyp in the colon), that required medical attention?
8. Have you ever had anemia requiring treatment or received blood transfusion?
9. For women, have you ever had heavy menses, characterized by the presence of clots greater than 1 inch in diameter and/or changing a pad or tampon more than hourly, or resulting in anemia or low iron level?

If the bleeding history is positive, initial laboratory tests and possible referral are recommended.