# Prolonged Bleeding After Surgery

# 10

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## Abbreviations

| | |
|---|---|
| aPTT | Activated partial thromboplastin time |
| ASA | Acetylsalicylic acid |
| CBC | Complete blood count |
| CI | Confidence interval |
| DIC | Disseminated intravascular coagulation |
| NSAIDs | Nonsteroid anti-inflammatory agents |
| PBAC | Pictorial bleeding assessment chart |
| PCC | Prothrombin complex concentrate |
| PT | Prothrombin time |
| rFVIIa | Recombinant activated factor VIIa |
| TCT | Thrombin clotting time |
| VWD | von Willebrand disease |

**Clinical Vignette**

A 14-year-old male has continued to bleed on and off for 10 days after tonsillectomy. He spits out clots and blood. He has taken aspirin 325 mg when needed for pain after the surgery. Hemoglobin has now dropped from 141 to 75 g/L and we are contemplating blood transfusion. Platelet count and prothrombin time (PT) are normal, activated partial thromboplastin time (aPTT) is borderline, 40 s. The patient does not have a history of bleeding or any family history thereof, except that his father required multiple transfusions after open-heart surgery.

## Epidemiology

Bleeding after surgery or a procedure can be a normal occurrence, e.g., transient hematuria after transurethral prostate resection or collection of half a liter of blood in the drain after hip replacement. Increased bleeding during and after surgery can often be explained by *aggravating circumstances* (see examples below) and would then also be expected (Schulman et al. 2010).

- Extensive surgery
- Infection
- Tumor invasion
- Anomalous blood vessels
- Accidental operative vascular injury
- Revision surgery
- Concomitant antithrombotic medication
- Known congenital bleeding disorder
- Liver or kidney disease

The risk for unexpected bleeding after surgery varies widely depending on the type of procedure

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but also on the experience of the surgeon. In a systematic review of studies with patients who stopped their anticoagulant treatment for invasive procedures and either received or did not receive bridging anticoagulation with heparin, major bleeding occurred in the latter group in 18 of 2104 (0.9 %; 95 % confidence interval [CI], 0.2–1.6) and overall bleeding in 3.4 % (95 % CI, 1.1–5.8) (Siegal et al. 2012). The risk increases dramatically for emergency surgery as seen in an analysis of the population in the RE-LY study that compared dabigatran with warfarin for stroke prophylaxis in atrial fibrillation. Major bleeding was described here in 17.7–21.6 % of emergent procedures compared to 2.8–3.8 % after elective surgery (Healey et al. 2012). This could obviously reflect insufficient delay from the last dose of the anticoagulant drug. After adenoidectomy or tonsillectomy, major bleeding is observed in 0.5 % (Tomkinson et al. 2012) and any bleeding in approximately 5 % (Shargorodsky et al. 2012).

## Definitions

The terms "major bleeding" or "prolonged bleeding" have until recently been very heterogeneous, even in the setting of clinical trials. An attempt to harmonize the definition of major bleeding was made through the International Society on Thrombosis and Haemostasis, both for medical patients (Schulman and Kearon 2005) and for surgical patients (Schulman et al. 2010). Any detailed definition of "prolonged" bleeding has been carefully avoided. It is thus up to the surgeon to determine whether the duration of bleeding was longer than expected under the circumstances.

## Investigation: Medical History

For patients with unexpected postoperative bleeding, the investigation starts with a careful *review of the medical history*, which should include the following items:

1. Previous bleeding events
   (a) Spontaneous or after challenges
   - Tooth extractions
   - Major surgery, child delivery
   - Menstruation
   - If spontaneous—from mucosa, skin, muscle, and joint
     – Recent onset or lifelong history
     (b) Immediate or delayed onset after challenge
     (c) Requiring reoperation, transfusion, or other treatment
2. Renal or hepatic disease, hypothyroidism, and autoimmune disorder
3. Concomitant medications and dietary supplements
   (d) What is the patient using for pain?
4. Family history
   (e) First-degree relative or more distant
   (f) On father's or mother's side

Typical for a *disorder of the primary hemostasis* (platelet disorder or von Willebrand disease (VWD)) is the pattern of immediate onset and mainly mucosal bleeding and ecchymoses. Conversely, a *disorder of the secondary hemostasis* (coagulation factor defect) is characterized by a delayed onset and often internal bleeding, typically in muscles and joints, although skin bruising is also common. Spontaneous bleeding with recent onset can be a sign of development of autoantibodies against any component in the hemostatic system, whereas a lifelong history suggests a congenital deficiency. Delayed onset (or secondary) hemorrhage appears to be at least as common as early (primary) hemorrhage after tonsillectomy and is probably related to premature discharge of the eschar (Wei et al. 2000).

A first-degree relative with bleeding diathesis raises the suspicion of a hereditary bleeding disorder, whereas a second-degree relative on the maternal side and bleeding exclusively among males is almost pathognomonic for hemophilia A or B (deficiency of factor VIII or IX). A diagnosis of hemophilia is sometimes established in patients with a negative family history. The reason is either a de novo mutation or that the genetic defect has been passed on entirely by females for several generations (Peyvandi et al. 2006). De novo mutations are responsible for one third of the hemophilia cases.

It is important to note that a negative bleeding history by no means excludes a congenital bleeding disorder. Every now and then patients are diagnosed with the mild form of hemophilia at an advanced age, after their first surgical challenge or major trauma in life, as already reported in 1964 (Pappas et al. 1964). Postoperative bleeding in combination with a negative history for any bleeding despite surgical challenges could be either due to an acquired defect (medication, autoantibodies, consumption coagulopathy) or to local pathology.

Excessive bleeding is a highly subjective observation by patients, e.g., assessment of menorrhagia, where the patient often compares her experiences with her mother—who may have the same primary hemostatic disorder. It is often helpful to use a standardized questionnaire to try and quantify more objectively the bleeding diathesis (Rodeghiero et al. 2010) or specifically a pictorial bleeding assessment chart (PBAC) for suspected menorrhagia (Philipp et al. 2011). The sensitivity of the PBAC as a screening tool for hemostatic defects was 89 % in a recent study (Philipp et al. 2011).

Patients will, when questioned about their medications, at best provide an account for their prescriptional drugs but they will usually omit the over-the-counter medications. In order to capture sporadic use of acetylsalicylic acid (ASA) or nonsteroid anti-inflammatory agents (NSAIDs), the patients should be asked what they would use for headache and other pain. Low-dose ASA impairs the platelet function for about 3 days whereas 325 mg ASA inhibits the platelet aggregation for 7–10 days. For NSAIDs the duration of their platelet inhibition parallels their half-life, which is a few hours for ibuprofen and diclofenac and 1–2 days for naproxen. Clopidogrel and warfarin should be stopped for 5 days before surgery, though some surgeons prefer a longer duration off clopidogrel.

## Physical Examination

This part of the investigation should include inspection of the skin. Large and palpable bruises are typical for coagulopathies. Petechiae are mainly a manifestation of vascular disorders on the capillary level but to some extent also a manifestation of platelet disorders.

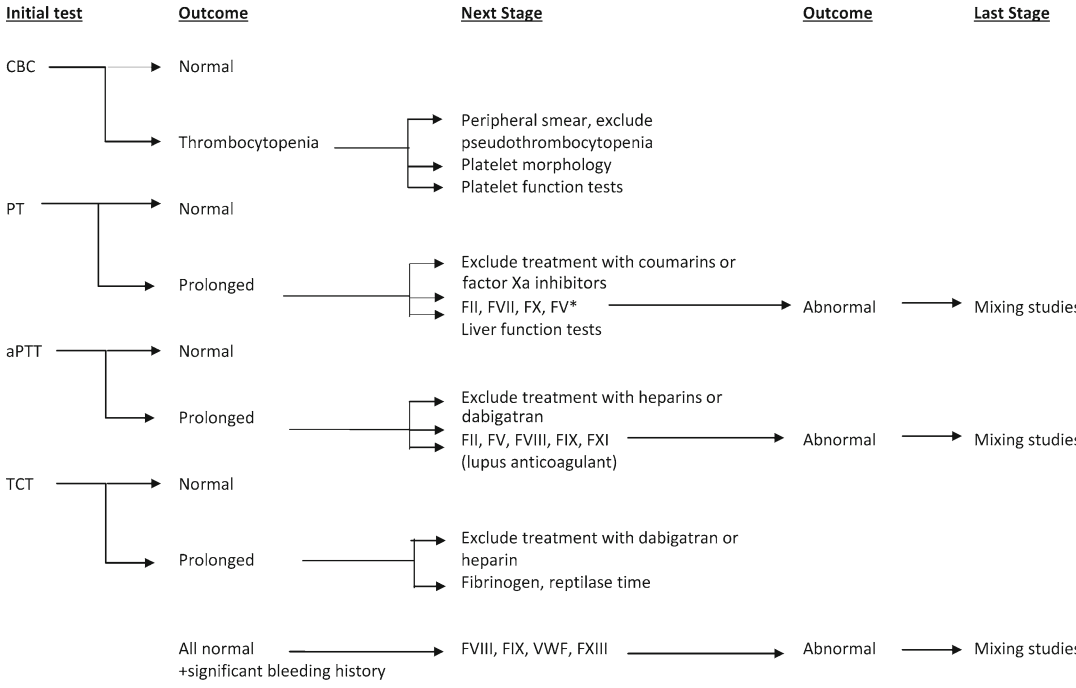
If the surgical area lends itself to inspection, it should be possible to assess whether there is rapid (pulsating) or slow diffuse bleeding and also whether the bleeding is confined to the surgical wound area or also has other localizations. The latter could indicate disseminated intravascular coagulation (DIC). Rapid bleeding could be due to arterial injury or from operation in an area with abnormal blood vessels, e.g., hemangioma or tumor.

The joints are also examined. Synovitis or a reduced range of motion are typical for hemophilia-associated arthropathy but can be seen with other coagulopathies. Conversely, hyperextension of the joints is a cardinal sign of Ehlers-Danlos collagen disorder.

Signs of liver or kidney disease should lead to further evaluation of the severity of the respective condition. Liver disease can be associated with the whole spectrum of bleeding manifestations since most of the coagulation factors are synthesized by the hepatocytes and are reduced in severe liver cirrhosis. The platelet count is also reduced by hypersplenism secondary to portal hypertension and this is often combined with a platelet function defect. In severe renal failure there is also a platelet function defect that has been ascribed to the blockage of surface receptors by uremic toxins such as guanidinosuccinic acid.

## Laboratory Investigation

Preoperative screening for hemostatic disorders in asymptomatic patients is not helpful to predict bleeding events after surgery, as shown in a prospective French study with more than 3,000 patients (Houry et al. 1995) and in a systematic review (Eckman et al. 2003). In patients with a history of bleeding diathesis or in the acute situation with a patient with prolonged bleeding after surgery, the investigation should start with the simple screening tests: complete blood count (CBC), PT, aPTT, and thrombin clotting time (TCT). Thereafter, an algorithm can be used (Fig. 10.1).




*FV deficiency is only deleted with PT using the Quick method, which is the most disseminated, but not with the Owren method.

**Fig. 10.1** Algorithm for laboratory investigation of postoperative bleeding

Platelet function tests should be performed at a specialized hemostasis laboratory with the blood samples obtained on site. There are instruments for global analysis of platelet function, such as PFA-100® (Siemens Healthcare Diagnostics, Deerfield, IL), but they are not very sensitive for the common, mild functional defects. Pseudothrombocytopenia is a laboratory artifact related to ethylenediaminetetraacetic acid (EDTA)-induced platelet clumping. This is usually revealed on a peripheral blood smear, and when the blood instead is drawn into a test tube with citrate as anticoagulant, the platelet count becomes normal. Several platelet function defects are combined with abnormalities in the platelet morphology, both regarding size and appearance.

In case of a low level of a specific coagulation factor, the laboratory should be asked to perform mixing studies. Patient plasma is then mixed with an equal volume of normal plasma and analyzed again with the screening test that was prolonged (PT or aPTT) without as well as after incubation at 37 °C for 30, 60, and/or 120 min. The interpretation of results is shown in Table 10.1.

**Table 10.1** Interpretation of the screening test (PT or aPTT) in mixing tests

| | Without incubation | After incubation |
|---|---|---|
| Isolated deficiency of a factor | Normalized screening test | Normalized screening test |
| Specific factor inhibitor | Normalized or prolonged screening test | Prolonged screening test |
| Lupus anticoagulant | Prolonged screening test | Prolonged screening test |

A prolonged TCT in combination with a normal reptilase time identifies the presence of heparin in the sample. Dabigatran at therapeutic levels causes an excessive TCT.

If DIC is suspected, the platelet count will be reduced; the PT, aPTT, and TCT may be prolonged; and the fibrinogen level is low for the circumstances. Since fibrinogen is an acute phase reactant, levels within the reference range in a patient with sepsis

should be interpreted as abnormal. Fibrin D-dimer is high or very high in DIC.

Patients with the mild form of hemophilia A or B may have normal screening tests, and in case of clinical suspicion, the factor assays should be performed. The screening tests do not identify deficiencies of von Willebrand factor (vWF) in mild or moderate form or factor XIII or the components of the fibrinolytic system. Of these only VWD is common, with a prevalence of about 2 % in population studies.

### Hyperacute Analyses

Abnormal bleeding during surgery requires immediate investigation in order to provide adequate therapy for hemostasis so that the procedure can be safely concluded. The screening tests that are performed by all hospital laboratories (platelet count as part of CBC, aPTT, PT, fibrinogen, and D-dimer) are helpful, but there is a delay that can result in suboptimal treatment while awaiting the results. Point-of-care analysis with thromboelastography, of which there are several variants, provides results within 10–15 min. The results inform the clinician on which component(s) of the hemostatic system is/are deranged and whether the bleeding is best treated with platelets, plasma (or factor concentrates), or antifibrinolytic agents. Several randomized studies have demonstrated that with the use of this type of instrument, the blood loss seems to be reduced and with significantly lower utilization of red cell, platelet, and plasma transfusions (Ak et al. 2009; Avidan et al. 2004; Cui et al. 2010; Shore-Lesserson et al. 1999; Westbrook et al. 2009).

## Treatment Options

### Local Hemostatic Measures

There are several options for local or regional hemostasis, as listed below:

- Compression
- Astringent agents (cold temperature, alum, adrenalin)
- Chemical barriers (gelatin, cellulose, collagen, inorganic films)
- Procoagulants (topical thrombin, fibrin sealant—a combination of fibrinogen and thrombin)
- Cauterization, argon plasma coagulation
- Interventional procedures such as coiling or arterial embolization

Potential side effects are tissue necrosis or formation of alloantibodies to components in the fibrin sealant, e.g., against factor V or thrombin. These antibodies may cross-react with the patient's own coagulation factor although this is a rare phenomenon (see Chap. 5).

### General Supportive Measures

When the bleeding causes a rapid reduction of the circulating blood volume of at least 30 %, the patient becomes hypotensive. The American Association of Blood Banks suggests that the decision to transfuse *red cells* be based on both symptoms and the level of hemoglobin (Carson et al. 2012). They strongly endorse a restrictive transfusion policy for hospitalized and stable patients, using a threshold of 70–80 g/L. For patients with preexisting cardiovascular disease, a restrictive threshold of 80 g/L and occurrence of symptoms are suggested to trigger transfusion. The "symptoms" should be expanded to a "clinical picture," which includes patient age, cardiorespiratory signs and symptoms, mental status, and other signs of organ ischemia as well as the risk of further reduced oxygenation (Practice Guidelines 2006). Elderly patients with acute myocardial infarction seem to benefit from being transfused up to hemoglobin of at least 100 g/L (Hebert et al. 1999). It is also interesting to note that when the hemoglobin drops below this level, the platelet function becomes increasingly impaired. The reason is that platelets, instead of rolling along the endothelium and identifying damages, find room to move centrally in the blood flow.

Improved oxygenation can obviously also be provided by adequate ventilation and the use of oxygen. Other supportive measures include volume substitution and withholding or reversing any antithrombotic agent.

## Systemic Hemostatic Treatments

*Platelet* transfusions are indicated in the following situations when there is bleeding (Practice Guidelines 2006):

1. Platelet count of less than 80–100/mL in case of life-threatening bleeding (e.g., central nervous system, other internal, and severe bleeding) or of less than 50/mL for major but less serious bleeding
2. Severe platelet dysfunction, even with normal platelet count
   - Congenital disorders such as Glanzmann's thrombasthenia or Bernard-Soulier's disease, where pharmacological agents may not work
   - Iatrogenic platelet dysfunction due to
     - Irreversible antiaggregants (clopidogrel, prasugrel, abciximab)
     - Hemodilution in massive transfusion

Patients with immune thrombocytopenia are often refractory to platelet transfusion. It has been discussed whether in DIC, platelet transfusions may actually aggravate the condition but this has not been proven. Thus, for patients with DIC, active bleeding and low platelet count (<50,000/μL) transfusion of platelets can be considered in conjunction with other corrective therapy and elimination of the cause of DIC.

The expected rise in platelet count of 30,000/μL after transfusion of six single donor units or one apheresis unit may not be seen in DIC, sepsis, immune thrombocytopenia, or splenomegaly due to consumption/sequestration.

Platelet transfusions do not seem to reverse bleeding caused by the $P_2Y_{12}$-receptor blocker ticagrelor, as long as the drug, which is active without any prior metabolic step, is present in the circulation.

*Plasma* transfusion is indicated when there is no information on a specific coagulation factor defect for which a purified concentrate is available or when there is a general deficiency of these factors due to poor synthesis (liver failure), dilution, or consumption (DIC). Abnormal global coagulations tests, such as aPTT and PT in a bleeding patient, support the need for plasma transfusion, whereas asymptomatic patients with such deranged tests rarely have an indication for replacement therapy. On the other hand, if a bleeding patient has normal aPTT and PT, plasma is unlikely to be effective.

For patients with congenital factor V deficiency, there is no specific concentrate and plasma should be given in case of hemorrhage. Conversely, for patients with bleeding in association with treatment with vitamin K antagonists, it is preferable to use a concentrate of the deficient factors—prothrombin complex concentrate (PCC), see below.

In massive transfusion (usually defined as ≥10 units red cells within 24 h) there is a high risk for dilution coagulopathy, but it is debated how early and in what internal proportion units of plasma and platelets versus red cells should be transfused to these patients. There is a recent tendency, based on positive observations in the military setting, to increase the proportion of these hemostatic blood components to *1 unit red cells/1 unit plasma/1 apheresis unit* (or six single donor units) platelets.

Plasma can be treated with viral inactivation, for example, using solvent-detergent, and this is commercially available in some countries.

*Cryoprecipitate* can be used for substitution of fibrinogen when specific fibrinogen concentrates are unavailable (see Fibrinogen below). A fibrinogen level of ≤100 mg/dL in a bleeding patient calls for treatment to raise the level (Practice Guidelines 2006). In addition, cryoprecipitate contains factor VIII, VWF, and factor XIII, but there are purified concentrates available for each of those factors. Cryoprecipitate is used at some hospitals for bleeding after cardiac surgery. The volume needed to replace fibrinogen is smaller than with plasma. Drawbacks of cryoprecipitate are the lack of viral inactivation and the relatively high risk of allergic reactions due to the low degree of purification from other plasma proteins.

*Fibrinogen* concentrate at a dose of 2 g has, in a small randomized controlled trial in patients with coronary artery bypass surgery with a preoperative level of <3.8 g/L, been shown to reduce postoperative blood loss (Karlsson et al. 2009). The concentrate is virally inactivated, and the risk of transfusion reactions is much smaller than with cryoprecipitate.

**Table 10.2** Calculation of the dose of prothrombin complex concentrate based on the prothrombin time, expressed as international normalized ratio (INR)

| Current INR | Target INR = 1.5 | Target INR = 1.1–1.2 |
|---|---|---|
| "Therapeutic" = 2–3.0 | 20 IU/kg | 30 IU/kg |
| "High" = 3.0–5.0 | 30 IU/kg | 40 IU/kg |
| "Extremely high" >5.0 | 40 IU/kg | 50 IU/kg |

*Prothrombin complex concentrate* (PCC) contains factors II, IX, and X (3-factor concentrate) and some of them also factor VII (4-factor concentrate), i.e., the vitamin K-dependent coagulation factors, which are reduced by coumarin anticoagulants in liver failure, DIC, and dilution coagulopathy. PCC is 20 times more concentrated than plasma and thus there is, as opposed to plasma transfusions, no risk for volume overload. This permits a more effective and much faster normalization of the PT. The required dose can be quite precisely estimated from the difference between the current and the desired PT and adjusted for the body weight (Schulman 2003). A simplified calculation strategy is shown in Table 10.2. The potential risk associated with PCC is thromboembolism, the risk for which in a meta-analysis was estimated at 1.4 % (95 % confidence interval (CI), 0.8–2.1 %) (Dentali et al. 2011). This event rate is, however, not significantly different from what is seen in patients who have their vitamin K antagonist treatment interrupted for surgery and receive bridging anticoagulation with heparin (0.9 %; 95 % CI, 0.0–3.4 %) (Siegal et al. 2012). It is thus possible that the unmasking of the underlying thrombogenic condition or the activation of coagulation by surgery or trauma is the major risk factor rather than PCC.

*Recombinant activated factor VIIa* (rFVIIa) is only indicated for hemophilia with inhibitors or certain severe platelet function disorders, such as Glanzmann's thrombasthenia (in Europe). But it has been evaluated and also used extensively for bleeding in patients without preexisting bleeding disorders. The results from clinical trials in patients with intracranial hemorrhage, trauma-related hemorrhage, and postpartum bleeding or in cardiac surgery have not been convincing regarding net benefit. Nevertheless, it is difficult for the hematologist to explain to the surgeon or anesthesiologist why this drug should not be used when there is massive hemorrhage and other measures have failed.

Problem areas include uncertainty regarding the optimal dose, since this is not an example of replacement to physiological levels. Typically, the standard dose for patients with hemophilia of 90 μg/kg is given and repeated after approximately 2 h. Second, there is no coagulation parameter that has demonstrated utility in monitoring the treatment or in predicting the effect. Third, a meta-analysis demonstrated an increased risk for arterial thromboembolic events versus placebo (odds ratio 1.68; 95 % CI, 1.20–2.36), which was pronounced in the elderly subpopulation and for the off-label indications (Levi et al. 2010).

Other *single factor concentrates* should be used for the respective factor deficiencies in case of bleeding or as prophylaxis before surgery. For factor II (prothrombin) deficiency and often also for factor X deficiency, PCC is used, although there is a factor IX-X concentrate available from one manufacturer (Factor IX Behring, Marburg, Germany). Some factor XI concentrates were associated with thromboembolic events (Bolton-Maggs et al. 1994), and the patients with congenital factor XI deficiency and bleeding may do best with a very low dose of rFVIIa (Schulman and Nemeth 2006). For patients with VWD and postoperative bleeding, a combined VWF-factor VIII concentrate is better than a pure VWF concentrate. The reason is that factor VIII becomes unprotected against and degraded by proteases in the absence of VWF. After infusion of pure VWF, there is a delayed increase in factor VIII, which also is needed to halt the bleeding.

Hyperfibrinolytic conditions are mostly treated effectively with *antifibrinolytic agents* such as tranexamic acid or epsilon aminocaproic acid. These conditions are seen with bleeding after pregnancy complications and prostate surgery. Importantly, prophylaxis with antifibrinolytic agents has been demonstrated to reduce bleeding after knee or hip replacement (Alshryda et al. 2011;

Gill and Rosenstein 2006), hip fracture surgery (Zufferey et al. 2010), spine surgery (Gill et al. 2008), and cardiac surgery (Henry et al. 2009). The dose of these agents has varied widely between trials. Although fibrinolytic activity mainly has been localized to mucosal membranes, the examples above highlight the efficacy of antifibrinolytics in a variety of organs.

Another synthetic agent that can improve hemostasis in a number of conditions is the vasopressin analogue d-arginine-deaminovasopressin (*desmopressin*), which acts by releasing VWF from the endothelium and also increases the levels of factor VIII as well as tissue-plasminogen activator to some extent. It has been demonstrated to reduce bleeding in:

- Many congenital platelet function disorders (not the most severe types)
- Acquired platelet function disorders due to
  - Aspirin, clopidogrel
  - Liver or kidney disease
- Mild form of VWD or hemophilia A
- Hemophilia A with inhibitor and a residual level of factor VIII

The dose is 0.3 μg/kg intravenously or subcutaneously and can be repeated after several hours. There is, however, a risk for tachyphylaxis, water retention, and hyponatremia after repeated dosing. Desmopressin is often combined with tranexamic acid to counteract further activation of fibrinolytic system.

## Postoperative Bleeding Associated with Residual Anticoagulant Effect

Ideally, anticoagulants should have been held for a number of days before surgery, which is required to normalize hemostasis. In emergency surgery, this is not possible and knowledge as well as availability of effective reversal agents are of paramount importance (Schulman and Bijsterveld 2007). Patients with postoperative bleeding related to heparin should be treated with *protamine* sulfate, which neutralizes heparin by forming a stable salt complex. This works fully with unfractionated heparin whereas low-molecular-weight heparin is partly reversed. The dose is 1 mg per 100 units of circulating heparin and usually up to 50 mg is given at a time and may be repeated after 15 min, depending upon the PTT. When protamine is injected too fast, it can cause hypotension and bronchoconstriction due to release of histamine. It is better to give protamine sparingly since an excessive dose can result in platelet aggregation, consumption, and paradoxically increased bleeding.

In rare cases, when bleeding continues due to insufficient reversal of low-molecular-weight heparin (Lewis et al. 2001) or for fondaparinux-related bleeding (Lisman et al. 2003), *rFVIIa* seems to be effective.

Vitamin K antagonists should be reversed with *PCC* or, if unavailable, with rFVIIa or plasma. At the same time, a dose of *vitamin K* should be injected slowly intravenously to eliminate the risk for rebound when any of the above-mentioned agents wears off. That dose should be 1–2 mg only if the plan is to resume anticoagulation as soon as the bleeding has stopped or 5–10 mg when a longer lasting neutralization is desirable and anticoagulation will be resumed at a later stage.

The new oral anticoagulants have so far no antidotes. Ex vivo studies in human volunteers indicate that *PCC* may be effective to treat factor Xa inhibitor-associated bleeding (Eerenberg et al. 2011), although this remains to be verified in clinical situations. The oral thrombin inhibitor, dabigatran, is dialyzable (Stangier et al. 2010; Warkentin et al. 2012). It is also possible that activated PCC can reverse the effect of dabigatran (Dager and Roberts 2011; Marlu et al. 2012). Giving activated charcoal may help absorb dabigatran. Again more clinical data is desperately needed.

## Practice Guidelines

Most of the published guidelines on management of postoperative bleeding are limited to one type of surgery or invasive procedure, to bleeding associated with a specific risk factor, or written in a non-English language. A task force of the American Society of Anesthesiologists published

a more general practice guideline in 2006 (Practice Guidelines 2006). The level of evidence is in many cases low, and it does not seem possible to provide exact criteria for transfusion of any of the blood components.

**The case in the Clinical Vignette**

The initially described young man had bled longer than what can be considered normal after tonsillectomy. He had started bleeding at home the first night after the surgery. Clearly, the pain medication with aspirin has contributed to the bleeding. The information that his father required transfusion after heart surgery is probably irrelevant, but there is a possibility that the patient has a mild form of an autosomal inherited coagulopathy. A normal PT and borderline aPTT exclude deficiency of factor VII. Further investigation with factor assays confirmed that the patient has hemophilia A in mild form with a factor VIII level of 15 % (0.15 IU/mL). Since this young patient did not demonstrate signs of poor oxygenation, blood transfusions were not given. The bleeding stopped after infusion of factor VIII concentrate to reach a level of 70 %. It was combined with tranexamic acid, 20 mg/kg orally every 8 h for 5 days. Two more doses of factor VIII were given. Desmopressin might not have been sufficiently effective in this case, requiring more than a threefold rise from the baseline factor VIII level. A patient with a new diagnosis of hemophilia should be referred to a hemophilia treatment center for registration, education, and follow-up.

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