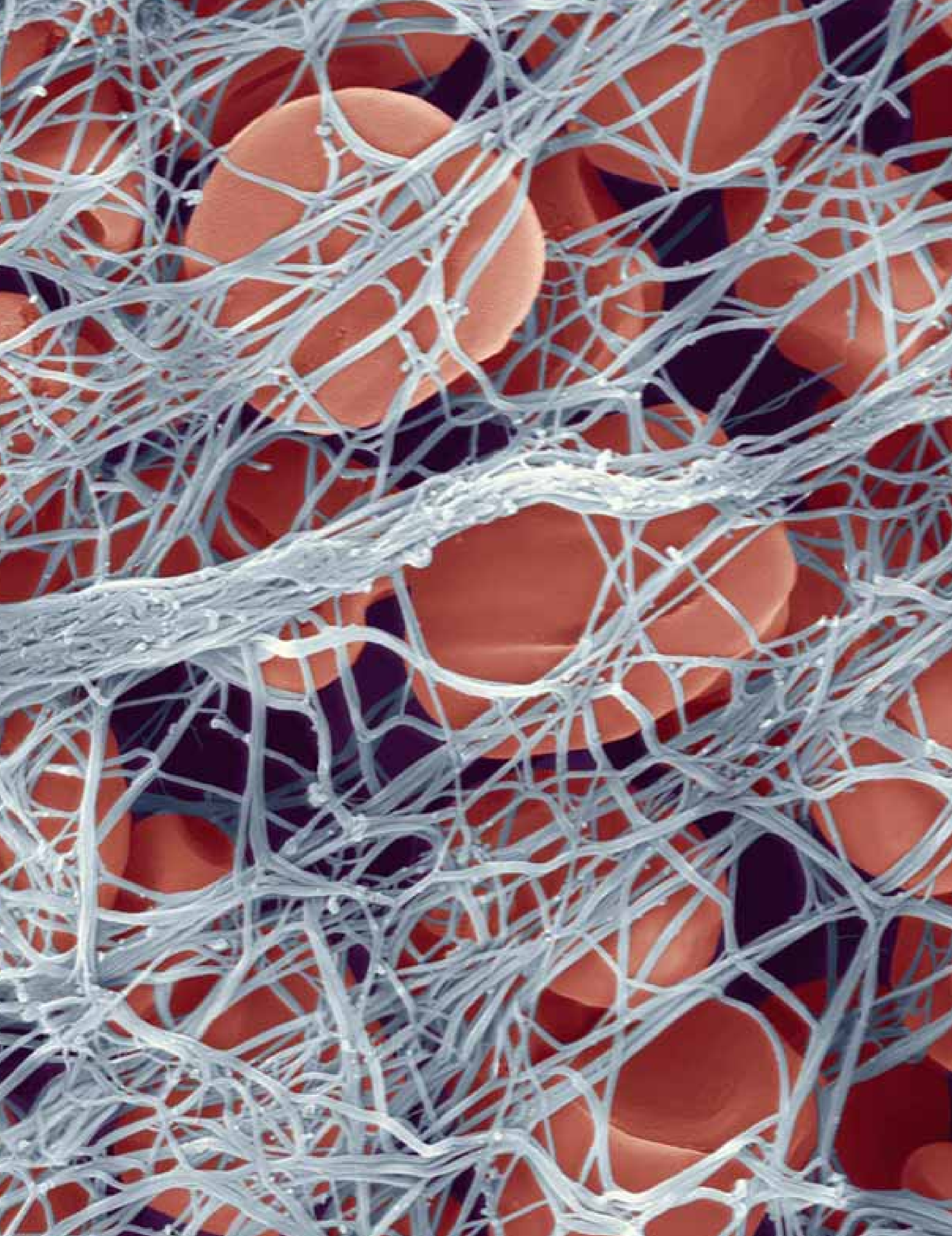

HEMOSTASIS

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There is nothing more important for the successful outcome of an operation than maintenance of hemostasis. Literally translated, hemostasis means stoppage of blood. In the operating room, it denotes prevention of blood loss from the intravascular space. Thus the main events of hemostasis are initiated and then develop in the internal environment of blood vessels.

In the case of penetrating trauma, this space may be violated by a traumatic rupture of the integrity of the endothelial lining of an artery or vein. In elective surgery, this lining is usually violated with a scalpel. In either case, the response of the body is the same. It will try to stem the flow of blood from the damaged vessels and thus preserve the organism. This hemostatic response is highly coordinated, protective, and complicated. It has developed because of the critical importance of blood for all organisms with a circulation.

Blood

Blood is made up of solid elements, cells, suspended in a fluid matrix, serum. Its importance derives from the fact that its cells are extremely important for bodily functions and its serum is the essential means of delivery of multiple substances (eg cells, hormones, cytokines, medications) to all parts of the body. The serum component of blood is rather easy to replace and can be substituted by a variety of intravenous fluids, such as saline or lactated ringers solution. The blood cells are harder to replace and loss of blood cells usually has dire consequences.

The most important cells are the red blood cells, which carry and deliver oxygen. If a human is deprived of oxygen for a matter of minutes, the result is usually reversible organ failure. If the time of deprivation is longer, the organ failure becomes irreversible and with longer periods of deprivation, the result is uniformly fatal. Rapid replacement of lost blood is obviously of paramount importance. Unfortunately, the source of replaced blood is usually allogeneic (from another person), and transfusion of allogeneic blood carries significant risks, including transmission of viral illnesses, such as HIV and hepatitis.[1] The complete list of transfusion risks ranges from the fairly common febrile reactions to rare viral diseases (Table 1).

Substitution of red blood cells by a variety of chemicals, such as fluorocarbons (eg Fluosol), has been researched for more than 20 years, and the results have been disappointing. Although fluorocarbons have been used with limited success in unusual circumstances, such as patients refusing blood products for religious reasons, the toxicities and difficulties in transporting oxygen with a fluorocarbon molecule have severely limited their use.

The key to the red blood cell's ability to transport oxygen lies in the hemoglobin molecules contained within each cell.[2] Substitution of red blood cells with hemoglobin-based solutions seems to hold some promise, but there are still no hemoglobin-based blood substitutes that have gained wide acceptance or that are commercially available.

The white blood cells (WBC) are a heterogeneous group of cells that serve a largely protective function by fighting bacteria, allergens, and a variety of other foreign invaders. Although the absence of WBCs can be devastating, such as in HIV disease, the effect of WBC loss is usually not an acute problem during active bleeding.

The platelets are the last major classification of blood cells. They are usually present in large enough numbers that acute blood loss and hemodilution do not present problems with thrombocytopenia (lack of platelets). Platelets are extremely important for the process of hemostasis, so when their numbers drop below 50,000/cmm (normal levels are 150,000–375,000/cmm) and the patient is actively bleeding, platelets are usually transfused. Without active bleeding, their numbers may be as low as 10,000/cmm without clinical consequences.

Clot formation

When the integrity of the endothelial lining of the blood vessels is disrupted, the first blood element on the scene is the platelet.[3] The platelet is exposed to the collagen of the vessel wall, which causes the usually smooth-surfaced platelet to become irregular and "sticky" (Figure 1). The platelet adheres to the area of the injury and becomes activated. The activated platelet secretes a number of factors, including von Willebrand Factor (vWF), which recruits more platelets to the area of injury and stimulates them to adhere. Other factors released by the platelets initiate the coagulation cascade.

Coagulation occurs via two main pathways, the intrinsic and extrinsic.[4] The intrinsic pathway is primarily involved in situations where there is no disruption of vessel integrity, such as hypercoagulable states and deep venous thrombosis. The extrinsic pathway is involved when there has been vessel injury and exposure of the blood to tissue factors in the vessel wall. Regardless of which pathway initiates coagulation, the final common event is the conversion of prothrombin to thrombin, which catalyzes the conversion of soluble fibrinogen to insoluble fibrin filaments (Figure 2). These filaments form a net

TABLE 1 **Transfusion risks**

Risk	Incidence
ABO reaction—hemolytic	1:13,000
Febrile reaction—plasma, leukocyte, etc	1:500
CMV	Unknown
Hepatitis B	1:50,000
Hepatitis C	1:3,000,000
HIV/AIDS	1:4,000,000

that traps more blood cells, such as red blood cells, and causes a clot to form, grow, and mature (shown on cover and page 10). Coagulation is often compromised by an inherited lack of coagulation factors (eg hemophilia A and B) or a lack of von Willebrand Factor (von Willebrand Disease). Treatment of these disorders usually involves replacement of the missing factors and is briefly discussed below.

Like many other physiologic responses in the body, the clotting system has its own negative feedback controls. Almost as soon as clot formation begins, other processes begin to turn off (or down regulate) clotting and dissolve the already formed blood clots. Under the direction of plasmin, the formed fibrin network is broken down into fibrin split products. Excessive or untimely activity of plasmin may not only dissolve needed clots, but it may cause unwanted bleeding in areas subjected to minor repeated injury, such as the mucosal lining of the GI tract. Obviously, the important elements of clotting and clot dissolution are proper regulation and correct timing. The body should form a clot in response to an injury that causes loss of blood from the vascular system, but should also be able to dissolve that clot when it has served its purpose. It should not form unwanted clots, such as those that cause heart attacks or deep venous thrombosis, and should be able to dissolve these unwanted clots when they do occur. Importantly, it should not dissolve a clot that is needed to plug holes in the vasculature until the body heals the injury.

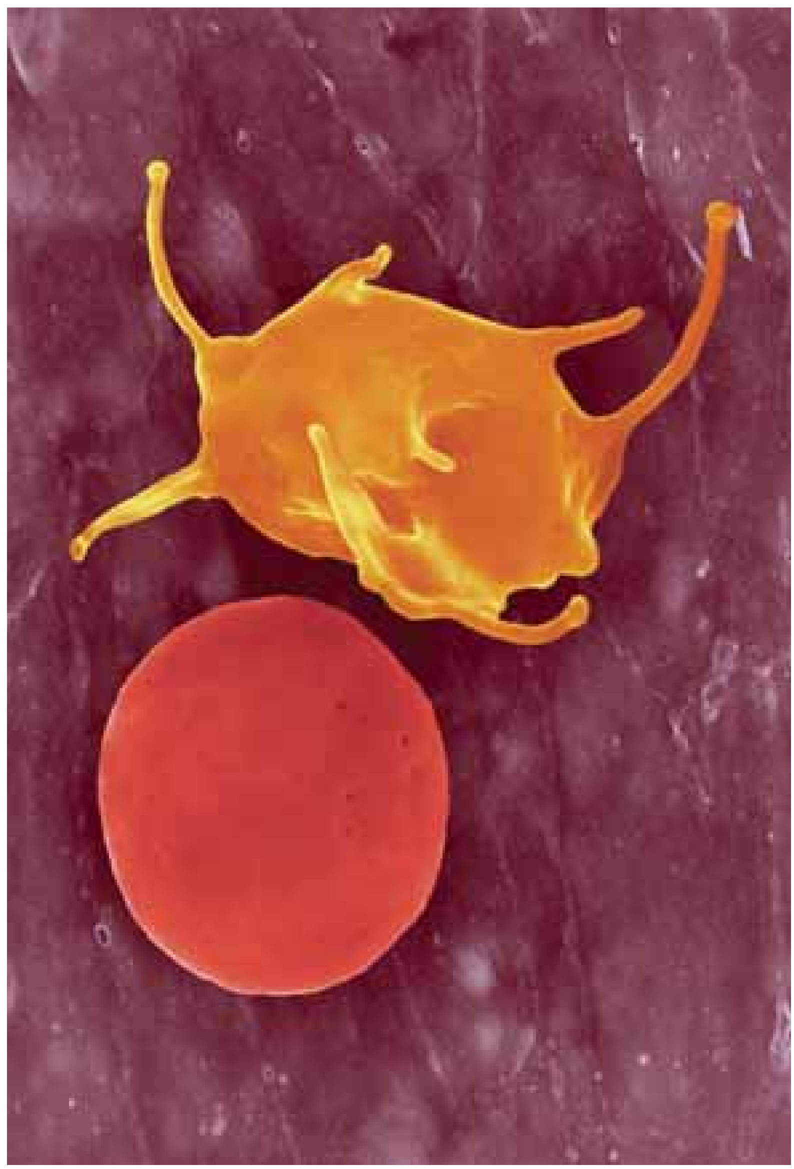
Operative considerations

Hemostasis is critically important in the operating room, and for this reason, a thorough evaluation of the body's ability to form blood clots must be determined prior to beginning any operation. The preoperative history and physical exam are important. This should include a history of easy bruising, excessive bleeding from minor trauma (eg tooth brushing), and most importantly, drug ingestion (certain drugs such as aspirin compromise clotting). The physical exam should focus on the presence of bruises, petechiae, and blood in the stool.

Another important aspect of the preoperative evaluation is lab testing. Most patients going to the operating room have a complete blood count,

FIGURE 1

Activated (top) and inactivated (bottom) platelets.



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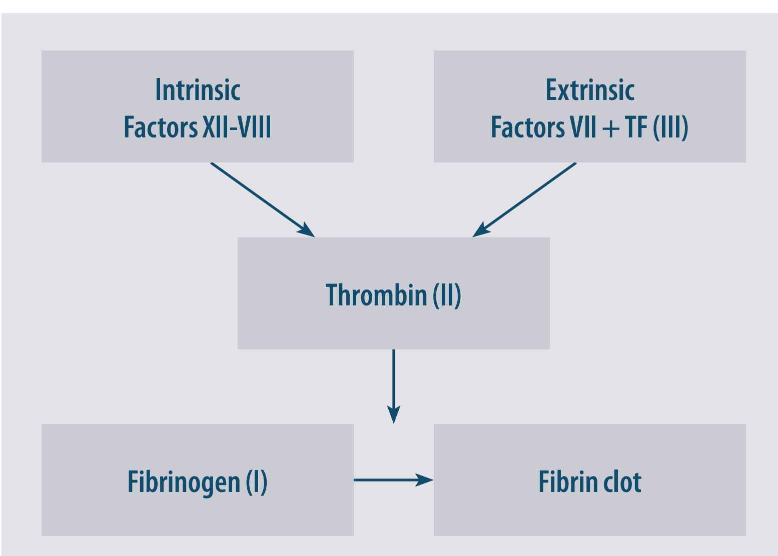
prothrombin time, and a partial thromboplastin time. These three lab tests cover the majority of bleeding disorders that are encountered.[5] If one or more of these baseline tests are abnormal or if the history and physical examination have uncovered a bleeding disorder, a consultation with a hematologist and additional tests—such as a bleeding time, thrombin time, or specific factor levels—may be needed. Pretreatment of bleeding disorders depends on the specific disorder and must be done prior to surgery.

As soon as the patient enters the operating room, preparations should be made for treating expected blood loss. Typed and cross-matched blood should be available from the blood bank for transfusion. Devices to keep the patient warm during the procedure, such as warm air suits or warming blankets, should be applied, because patients get cold during long, open procedures and blood clots best at normal body temperatures. For cases in which a large amount of blood may be lost, equipment to reuse blood (cell savers) or heat massively transfused blood must be set up. Compression stockings must be placed to prevent unwanted clotting, which may be as devastating as insufficient clotting.

Once the operation has started, all operating room personnel should make an effort to monitor blood loss, monitor the patient's vital signs, replace lost blood, and to move as quickly as possible without making mistakes. This last point is critical, because speed is important to minimize the time a patient spends in the operating room. Minimizing the time in the operating room and, specifically, the time that any major body cavity is open will also minimize heat loss, which is a major factor in perioperative morbidity. Body temperature will also drop with the infusion of room-temperature or colder intravenous fluids. Using warmed fluids helps, but the major effort on the part of the operating team should be to complete the operation and close all body cavities as expeditiously as possible.

FIGURE 2

Coagulation cascade.



Hemostatic material, equipment, and techniques

Materials such as collagen and cellulose-based powders, sheets, and sponges are used in the operating room to promote healing[6] (Table 2). Not only do these materials provide a matrix on which clots form, but they provide collagen, which stimulates platelet activation and adherence.

The newer clotting materials are available in the form of glues. In general, they work like epoxies, using coagulation factors found in plasma and mixing them with a procoagulant, such as thrombin. As soon as the two components mix, a solid clot is formed. The advantage of the glues over the sheets and sponges is that the liquid components may be squirted or sprayed on areas of active blood loss. Because they are liquid, until they solidify, they can penetrate small crevices and conform exactly to the irregular contours of actively bleeding surfaces.

Most cutting in surgery is still done with a scalpel or scissors. The introduction of electrocautery in the operating room reduced blood loss by allowing planes to be cauterized as they were cut. Large raw surface areas created by blunt dissection can also be cauterized to limit blood loss.

More recently, laser technology has also allowed tissue to be cut precisely and with little blood loss. Argon laser beam coagulation cauterizes and fulgurates, as does electrocautery, but with less depth of tissue damage and less smoke generation. Other types of lasers include the carbon dioxide laser and the Nd:YAG laser. Although all lasers create thermal injury, they are somewhat more precise than electrocautery.

TABLE 2 **Hemostatic material**

• Collagen, cellulose, gelatin (powder, sponge, sheets)
• Impregnated with procoagulants (thrombin, fibrin, fibrinogen)
• Glue (BSA + glutaraldehyde)
• Fibrin glue (fibrin + cryoprecipitate)

TABLE 3 **Damage control**

Stop operating
Repair life-threatening injuries
Pack bleeders, close holes
Rapid closure
ICU—warm, correct pH
Return in 24-48 hours

Low power ultrasonic dissection, such as the CUSA (cavitational ultrasonic aspirator), was introduced decades ago. It is good for dividing tissue but does not coagulate blood vessels. More recently, higher power ultrasonic systems, such as the harmonic scalpel,[7] generate more heat, which is useful in coagulating small blood vessels. High-velocity, high-pressure water dissection produces clean dissections but poor hemostasis.

New techniques for surgical ablation have been developed that don't involve cutting and, therefore, don't result in blood loss. Cryotherapy destroys tissue (eg tumors) by rapidly freezing it to -40° or lower. In radiofrequency ablation, a radiofrequency current heats the target tissue and destroys it.

A variety of intraoperative techniques have been developed to address the problem of blood loss due to excessive body cooling. One of the most important strategies is "damage control," a technique developed by trauma and military surgeons for dealing with the inevitable blood and heat loss during surgery for extensive and devastating injuries[8] (Table 3).

The strategy used in damage control is to abort the operation when it becomes apparent that a patient undergoing surgery is becoming too cold and losing too much blood to survive the operation. The surgical team should forego any immediate reconstructive efforts and focus their attention on stopping life-threatening hemorrhage and preventing further contamination (eg closing holes in the GI tract). The peritoneal cavity or other incisions are rapidly but temporarily closed with a single layer of suture or with towel clamps. The patient is then brought to the intensive care unit where he or she can be stabilized, warmed, and transfused. After stabilization has been achieved, which may be one or two days later, the patient is brought back to the O.R. to finish the initial operative objectives—such as debridement of nonviable tissue, resection of tumors, biliary reconstruction, restoration of bowel continuity, and/or formal closure of the abdomen.

This technique has been especially useful on the battlefields, where the initial stabilization is done in a field hospital and the definitive surgery is done in a large referral hospital. It has also been adapted for civilian trauma and even for large elective cases, where major blood loss and core body cooling compromise the operation.

Another very important technique for minimizing intraoperative cooling and blood loss is the newly defined area of minimally invasive surgery. This term encompasses a variety of technologies, such as laparoscopic, endoscopic, thoracoscopic, cystoscopic, and arthroscopic surgery. Although some of these techniques have been used for decades, over the last 10 years they have become more prevalent, and pioneering surgeons are now using minimally invasive techniques for almost every kind of operation. By not opening major body cavities, blood loss is minimized and body temperature is preserved. Most recently, the use of surgical robots has allowed minimally invasive techniques to be used in areas that were previously inaccessible.

Postoperative considerations

After the operation, continued surveillance of the patient's temperature, pH, vital signs, and blood loss is mandatory. Continued blood loss and hemodynamic changes are common for six to 12 hours after surgery. In the case of large operations or situations when the primary pathology has not been completely resolved with the operation (eg severe trauma or infections), blood loss may continue for days. Blood levels and coagulation parameters should be kept close to normal until the threat of postoperative hemorrhage is minimal.

The future

The distant future undoubtedly holds surprises and technologies that are difficult if not impossible to predict. There are some developments on the horizon that will probably be available in the next few years.

The wide use of blood substitutes made of hemoglobin molecules obtained from red blood cells or made with recombinant technology seems to be a very achievable goal.[9] Insofar as manufactured or cell-free blood would not carry the infectious risk of donated blood, it could replace blood donation completely. Coagulation factors for bleeding disorders, such as hemophilia and von Willebrand Disease, which are still occasionally obtained from donated blood will also be more available as recombinant products in the near future.

Development of materials for intraoperative hemostasis seems to be pointing in the direction of the epoxy-like products such as fibrin glue. Several products are now commercially available and their use will probably become more prevalent.

The world of minimally invasive surgery, after an inexplicably long dormant period, has virtually exploded on the scene and threatens to replace almost every surgical procedure that involves opening a major body cavity. It has spawned other techniques, such as robotic surgery and telesurgery, which once were considered the province of science fiction novels and are now being trialed in major medical centers around the country.

Hemostasis has always been a major concern of surgeons, and many of the new technologies that are being developed today to obviate the morbidity associated with large incisions have the added benefit of minimizing blood loss. Hemostasis has always been and will remain one of the principal goals of every surgical procedure. It is at the core of any safe operation.

About the author

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References

1. (Adverse effects of transfusion. Calgary Laboratory Services. ***www.calgarylabservices.com/?LabTests/TransfusionMedicine/TransfusionGuidelines/?AdverseEffects.htm*** (accessed 4/27/2004)
2. Schimmeyer S. The search for a blood substitute. Illumin [online] vol. 5, issue iii. USC Viterbi School of Engineering. ***engrwp.usc.edu/?illumin/article.php?articleID=62&page=1*** (accessed on 4/29/2004)
3. Blood clotting. Natural Toxins Research Center. Texas A&M University-Kingsville. ***ntri.tamuk.edu/homepage-ntri/lectures/clotting.html*** (accessed 5/12/04)
4. King MW and Marchesini S. Blood coagulation. University of Brescia. ***www.med.unibs.?it/~marchesi/blood.html*** (accessed 5/12/04)
5. Clinical laboratory procedures. Natural Toxins Research Center. Texas A&M University-Kingsville. ***ntri.tamuk.edu/homepage-ntri/lectures/?clinical.html*** (accessed 5/12/04)
6. Biological hemostasis. Medcompare: the buyers guide for medical professionals. ***medcom-?pare.com/matrix.asp?catid=727*** (accessed 4/27/04)
7. The harmonic scalpel. The Heartburn Center of San Diego. ***www.sdheartburn.com/pages/har-?monic.html*** (accessed 7/27/04)
8. Moore EE, Burch JM, Franciose RJ, et al. Staged physiologic restoration and damage control surgery. *World J Surg.* 1998 Dec;22(12):1184-1191.
9. Corwin HL, Gettinger A, Pearl RG, et al. Efficacy of recombinant human erythropoietin in critically ill patients: a randomized controlled trial. *JAMA.* 2002 Dec 11;288(22):2827-2835.