Hemostasis and Healing Wounds

Clotting is the term generally applied when discussing hemostasis and it has to do with coagulation factors, platelets, and plasma in blood tissue that begin to act when a vascular injury occurs, working to stop the bleeding and prevent entry of micro-organisms, while still permitting blood to flow through the injured vessel (obviously, a seriously injured vessel may need surgical intervention as well, or be so seriously injured that clotting will not stop the flow of blood). The body's ability to heal its own wounds depend upon several factors, including being in good overall health to begin with, having a sound nutritional status, and being possessed of a good blood supply. Conditions affecting these factors (such as chronic conditions, poor nutrition, and so forth) will affect the body's ability to heal its own wounds, and the amount of contamination in the wound (microbes and foreign bodies) can determine how well or poorly the wound heals, as will the size, shape, and type of wound itself (whether its damaged edges are closely appositional, whether it is septic, how much tissue is missing, and so forth).

Primary healing takes place in wounds where there is minimal damage to tissues, and involves inflammation (clotting and removal of debris), proliferation (epithelial cells build up new tissue to replace damaged tissue, clot eventually separates), and maturation (scar tissue development, strengthening of tissue at wound site).[1]

Figure 1 illustrates a basic overview of the inflammatory response, which is activated at the moment of injury.[2] With tissue injuries involving vascular damage, bleeding also occurs. In this case, the inflammatory response is activated and the "coagulation cascade" is set into motion. Keep in mind that the inflammatory response will be active during the process of coagulation, working in parallel with it, and will remain active until such time that the threat of

[1] Secondary healing follows the same process, but takes longer due to the amount of damaged tissue or the inability of the edges of the wound to come together.

[2] Cursing, another type of involuntary response, sometimes accompanies activation of the inflammatory response.

infection ceases to be of concern. With a splinter-puncture wound as our example, the inflammatory response goes into action, taking care of anything that has entered the tissue, such as pieces of wood from the splinter, dirt and other foreign substances, and any other contaminants, microbes, or antigens that are along for the ride.

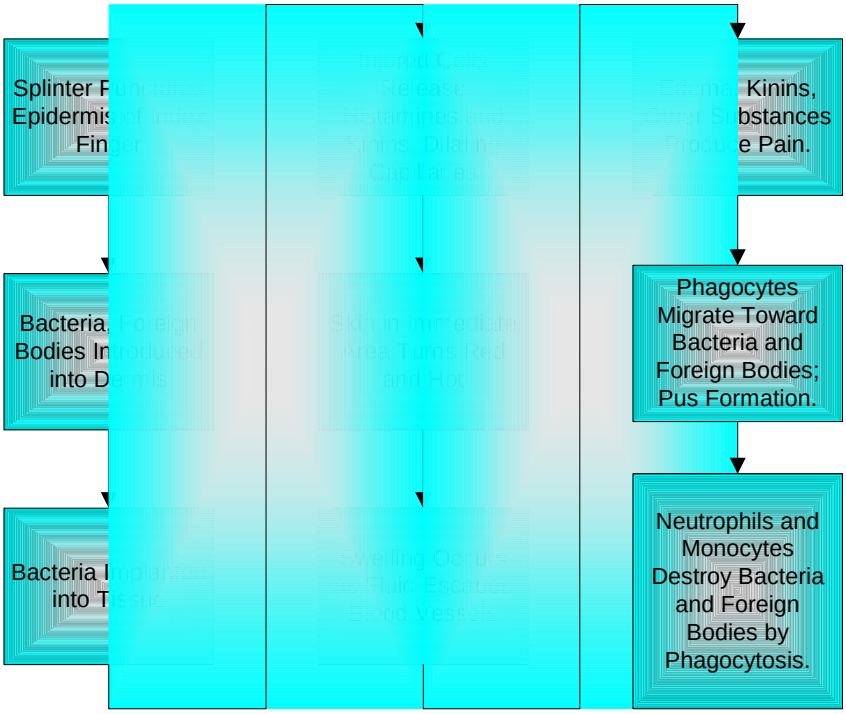

Figure 1: Inflammatory Response

Simultaneously, the hemostasis process begins in order to seal the wound (another way to block invasion) and to stop the bleeding. The forming of a platelet plug, the first stage of coagulation, occurs in the *extrinsic cascade* ("from the tissue"). Thromboplastin is released from damaged cells causing platelet aggregation (sticking together) to close the damaged vessel wall(s), while at the same time vasoconstriction takes place in an attempt to minimize continued hemorrhage from injured vessels. The second stage, clot formation, occurs in the *intrinsic cascade* ("from the blood"), leading to the creation of a fibrin 'net' over the top of the

platelets via the interaction of various clotting factors. This net traps red blood cells, and the continued interaction of clotting factors strengthens and tightens the structure, forming a stable, fibrin clot. The process serves two purposes as previously mentioned:

- to block micro-organisms from invading the body by sealing the wound.
- to stop the bleeding.

The flowchart in figure 2 illustrates this complex process in greater detail:

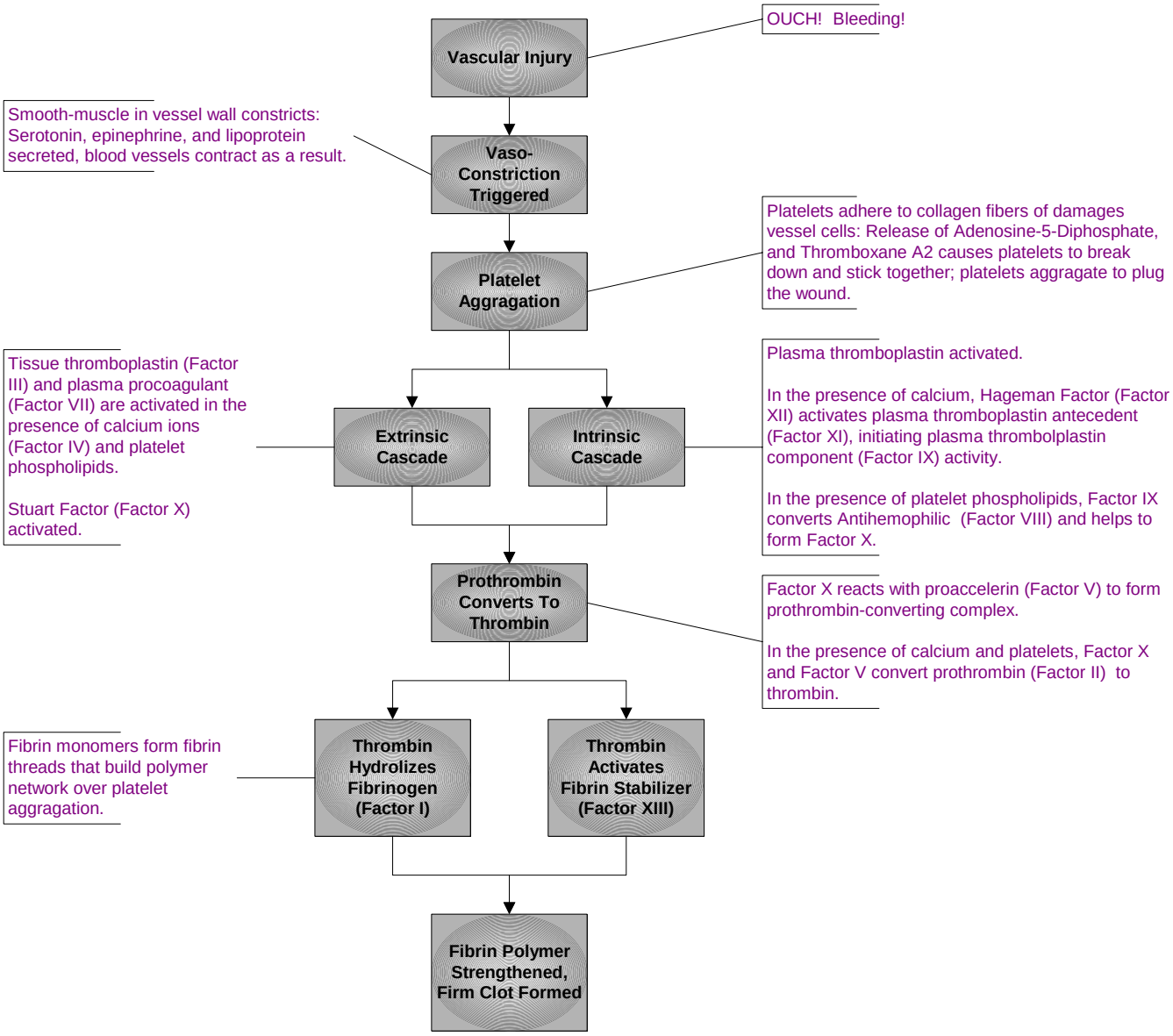

Figure 2: Coagulation Cascade

The “coagulation cascade” begins with the injury to the vessel. Blood platelets are damaged when they come into contact with the collagen fibers exposed in the wall of the vessel. As they break, they release serotonin, which induces vaso-constriction at the site of injury to reduce blood flow in the vessel until it can be repaired. Thromboxane A2 is also released from injured platelets, making them “sticky” so they will aggregate to eventually form a plug. At the same time, another substance (Prostacyclin) prevents platelet aggregation in adjacent areas that are not damaged. Platelets and blood plasma provide materials that accelerate coagulation, carried as precursors, and activated upon injury. The liver and Vitamin K are the “homebase” for synthesis of most of these factors, and when they are activated at the site of an injury, a chain reaction occurs with them that creates the conditions needed for the formation of a platelet plug and the subsequent clot.

- Factor I: Fibrinogen; a high molecular-weight protein synthesized in the liver and converted to Fibrin during the process of hemostasis.
- Factor II: Prothrombin; with action from Vitamin K, synthesized in the liver. Converts to thrombin during coagulation.
- Factor III: Tissue Thromboplastin; required in the first phase of the extrinsic cascade, this is released from damaged tissues and activated in the presence of calcium.
- Factor IV: Calcium Ions; required during the entire process of coagulation.
- Factor V: Proaccelerin; another protein synthesized in the liver, this factor plays a key role in both intrinsic and extrinsic cascades.
- Factor VII (Factor VI is not used): Called Stabilizing Factor, Serum ProThrombin Conversion Accelerator, or Proconvertin. This factor is also synthesized in the presence of Vitamin K in the liver. It is activated with tissue and blood thromboplastin with the help of Factor IV, Calcium.

- Factor VIII: Antihemophilic Globulin; also synthesized in the liver. Plays a role in the activation of Factor X.
- Factor IX: Plasma Thromboplastin Component; used in the first part of the intrinsic phase, this factor is also synthesized in the liver with Vitamin K.
- Factor X: Stuart factor; activated in both phases to activate prothrombin. This factor is also synthesized in the liver with vitamin K.
- Factor XI: Plasma Thromboplastin Antecedent
- Factor XII: Hageman Factor
- Factor XIII: Fibrin Stabilizing Factor; stabilizes and tightens clot, extruding plasma.

There are additional protein factors involved in this very complicated process that are not identified here. Other factors involving the dissolving of the clot are also activated at the appropriate time (plasminogen is converted to plasmin). As the injury heals, plasmin digests the fibrin net and the clot breaks down. What does not fall off will eventually be engulfed and removed by phagocytes.

Bibliography

Kapit, Macey, Meisami. The Physiology Coloring Book. San Francisco: Benjamin/Cummings Science Publishing, 2000.

Lippincott Williams & Wilkins. Anatomy and Physiology. Second Edition. New York: Lippincott Williams & Wilkins, 2002.

Waugh, Anne. Ross and Wilson: Anatomy and Physiology in Health and Illness. Spain: Elsevier Health, 2004.

http://www.indstate.edu/thcme/mwking/blood-coagulation.html

Excellent resource for a very detailed analysis of blood clotting (Website of Indiana State University, Department of Medical BioChemistry)