

Laboratory Dimensions

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A COAGULATION OVERVIEW

Blood clotting is a vital process that stops bleeding when we have an injury that breaks blood vessels, whether they be in the skin or in the deeper tissues of the body. Our body can both make the clots and break them down once they have done their job.

Coagulation is a fascinating and complex process that involves many steps. Proteins made by the liver are an essential part of this process. These proteins circulate in our blood, ready for action at any time. An external or internal injury activates the proteins and sets the blood clotting process in motion.

The clotting process starts with activation and aggregation of circulating platelets. A stabilizing fibrin clot is then formed through a multi-step process called the **coagulation cascade**, involving the many different proteins. This chain reaction, where one step leads to the next, produces a new protein which acts as an enzyme or cofactor for the next step. To simplify understanding, it is often divided into three pathways—the extrinsic pathway, the intrinsic pathway, and the common pathway.

Extrinsic pathway

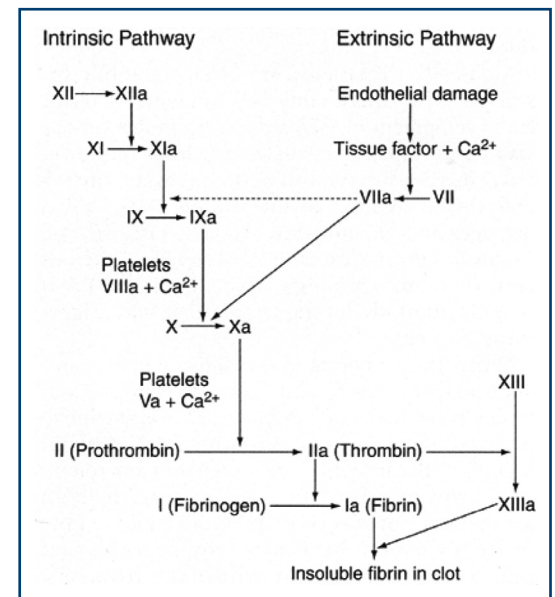
This pathway, also called the *tissue factor* pathway, is triggered by release of tissue factor (thromboplastin) outside the blood vessels when tissue is damaged. The main role of this pathway is to generate a burst of thrombin to eventually form a fibrin clot. It eventually leads to activation of Factor X.

Intrinsic pathway

Triggered by blood coming into contact with collagen fibers in the broken wall of a blood vessel (intrinsic because the factor is *intrinsic* to blood), this is sometimes called the *contact activation* pathway. This pathway also activates Factor X.

Common pathway

Both pathways eventually lead to activation of Factor X which produces a prothrombin activator that begins the common pathway. Prothrombin is converted to thrombin which leads to the conversion of fibrinogen to fibrin. Fibrin forms a stabilizing meshwork cementing the platelet plug in place.



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The proteins involved in the coagulation cascade are called factors and are numbered with Roman numerals. There are twelve clotting factors described and they are numbered in the order in which they were discovered, not in the order in which they react.

The Coagulation (clotting) Process

Coagulation begins almost instantly after an injury to a blood vessel. Exposure of blood to the space under the endothelium lining the blood vessel initiates two simultaneous processes: 1) **primary hemostasis** – the process of platelet activation and aggregation to form a plug at the site of injury, and 2) **secondary hemostasis**, which is simply the coagulation cascade forming fibrin strands to strengthen the platelet plug.

Control

Once the coagulation cascade is activated, it is important to keep the process restricted locally to the site of vascular accident to prevent clotting all over the body. This is done through several mechanisms:

- 1) Protein C/S—vitamin-K dependent proteins; Protein C is activated by thrombin into activated protein C (APC). APC, with Protein S and Factor V as cofactors, degrades activated Factors V and VIII. An abnormal form of factor V (Factor V Leiden) is resistant to inactivation by Protein C. This is an inherited deficiency that is relatively common in our area.
- 2) Antithrombin—a serine protease inhibitor that degrades thrombin, Factors IX, X, XI, and XII.
- 3) Tissue factor pathway inhibitor—limits the action of tissue factor. It also inhibits excessive activation of Factors VII and X by tissue factor.
- 4) Plasmin—cleaves fibrin into fibrin degradation products that inhibit excessive fibrin formation.
- 5) Prostacyclin—leads to decreasing levels of calcium which, in doing so, inhibits the release of granules that would lead to activation of additional platelets and the coagulation cascade.
- 6) Phospholipid—provided by platelet membranes and required for several crucial reactions.
- 7) Dilution, clearance, and consumption of activated factors.

Fibrinolysis

Eventually, the blood clots are resorbed by a process termed fibrinolysis. The main enzyme for this process is plasmin and is regulated by various activators and inhibitors.

Names and Sources of the Clotting or Coagulation Factors

| Coagulation Factor | Common Name | Source |
|------------------------|--|--|
| Factor I | fibrinogen | liver |
| Factor II | prothrombin | liver |
| Factor III | tissue factor or thromboplastin | Damaged tissue cells release tissue thromboplastin. Platelets release platelet thromboplastin. |
| Factor IV | calcium ions | bone, and absorption through the lining of the small intestine |
| Factor V | proaccelerin or labile factor | liver and platelets |
| Factor VI (unassigned) | No longer used after it was discovered that this chemical is Factor Va | N/A |
| Factor VII | proconvertin or stable factor | liver |
| Factor VIII | anti-hemophilic factor | platelets and the lining of blood vessels |
| Factor IX | Christmas factor | liver |
| Factor X | Stuart Prower factor | liver |
| Factor XI | plasma thromboplastin antecedent | liver |
| Factor XII | Hageman factor | liver |
| Factor XIII | fibrin stabilizing factor | liver |

It is interesting that after vessel damage, all of these pathways are activated simultaneously: vasoconstriction, platelet activation, coagulation, and fibrinolysis.

Testing

Primary hemostasis, or platelet activity, can be monitored with various laboratory tests, including a platelet count and several tests assessing aggregation (e.g. platelet function analysis or PFA). The bleeding time is a very poor test of platelet function and should not be used.

For secondary hemostasis, the various pathways can be monitored in the laboratory by measuring the amount of time it takes for blood to clot.

Intrinsic: PTT measures the factors that are part of the intrinsic and common pathways: XII, XI, IX, VIII, X, V, II and fibrinogen as well as prekallikrein and high molecular weight kininogen.

Extrinsic: PT measures the factors that are part of the extrinsic and common pathways: VII, X, V, II and Fibrinogen.

Common: PTT, PT, thrombin time, fibrinogen testing

A healthy body protects us by clotting blood when we are injured, preventing the clots from growing too big, and removing the clots when they are no longer needed. It is an amazing process. Learning more about it may help us discover ways to improve coagulation when it is not working properly and also to prevent it from occurring inappropriately.

<https://owlcation.com/stem/How-Does-Blood-Clot-and-What-Causes-Coagulation> Accessed 9/7/16

<https://en.wikipedia.org/w/index.php?title=coagulation&printable=yes> Accessed 9/7/16

https://labtestonline.org/understanding/analytes/coag-cascade/?show_all=1&printpreview=1 Accessed 9/7/16

Coagulation cascade courtesy of Medscape 10/20/16

The Laboratory, Healthcare Reform, and What It Means to Me?

Have you heard healthcare buzz words like... *Healthcare Reform, Healthcare 2.0, Bending the Cost Curve, Patient Centered or Value-Based Care Models, Volume-to Value, Population Health Management, Test Utilization*, and the list could go on and on, but then ask yourself, ***“Just what in the world is Healthcare Reform and what does it mean for ‘MY Laboratory’?”***

It has been estimated that the annual amount spent for national healthcare expenses is over \$2.7 trillion dollars. Clinical laboratory costs typically are between 3 to 5 percent of total hospital spending and represent less than 2 percent of the overall \$72 billion annual Medicare costs. With upcoming regulation surrounding PAMA, OPSS, MACRA, and other ACA healthcare rulings, CMS estimates there will be a decrease to clinical laboratory payments of nearly \$360 million in 2018 and \$1.7 billion over the next five years.

Key Components

Since 2010, when the Patient Protection and Affordable Care Act (ACA) was signed into law, our healthcare system has been in the midst of significant changes. The ACA can be simplified and broken down into two major parts: 1) health insurance reform, and 2) payment or reimbursement models that require the improvement of healthcare performance while reducing costs.

Healthcare systems have identified three key areas known as the **‘triple aim’** to help accomplish patient healthcare needs. These key aims include:

- 1) Better overall care in a safe environment, equitable to all who seek it and always available when needed;
- 2) improved health accomplishment through the practice of proactive, preventive medicine and chronic care coordination with demonstrated better outcomes;
- 3) lower per capita cost aimed at reducing the trending of medical costs. For the laboratory, the biggest challenge will be transitioning from the current ‘volume-based’ model to a ‘value-based’ testing model, which is sometimes referred to as *‘The Second Curve’*.



Impact on Consumers

Transitions in healthcare practices are being driven by three primary stakeholders: the government, payers, and consumers. The government is mandating the changes, knowing that if the current pace of healthcare spending continues, it will result in out of control spending that negatively impacts each of us. Research is demonstrating that if insurance premiums and out-of-pocket expenses continue to rise, it will result in the majority of household incomes being used to help cover healthcare expenses by the year **2030**. This is resulting in payers taking a more active role impacting reimbursement models that will help manage costs. The healthcare delivery model commonly referred to as *Population Health Management*, involves patients in all aspects of their healthcare decisions aiming for improved outcomes at lower costs. Partnerships between patients, providers, and payers collaboratively working together to promote preventative medicine, the coordination of chronic care treatment, while reducing healthcare costs, is the ultimate goal in Healthcare Reform.

Impact on Laboratories

While most laboratorians know that at least **70% of all medical decisions are based on diagnostic laboratory tests**, they are not certain as to what impact healthcare reform may have on their immediate laboratory. Laboratories are currently in a unique position to help drive the progression of improving the quality of patient care but the success will depend on the ability of laboratories to accept upcoming changes, adapt, and make the commitment to navigating in the new healthcare landscape. Through a collaborative effort between the laboratory and other key healthcare stakeholders, clinical laboratories can make a significant impact on ‘Bending the Cost Curve’ and reducing unnecessary wasteful healthcare expenses.

The laboratory can play a very important role in promoting a culture of continuous improvement that is focused on driving up quality, while at the same time contributing to the reduction of overall costs in healthcare. It will be fundamental for laboratories to seek opportunities to engage physicians in discussions that will help gain a better understanding of how clinical laboratory data can support achieving better patient outcomes. Partnering the patient with their comprehensive healthcare coordination team that focuses on a holistic approach of prevention, treatment, and ongoing improvement of healthier lifestyles will ensure the best outcome for the patient.

The laboratory’s active role in the coordination of care can be demonstrated in a number of ways:

- 1) Offering input of test utilization management to help guide provider ordering practices and determine if the correct tests are being ordered at the correct time;
- 2) encouraging patients to take a more interactive role in their healthcare decisions by taking advantage of preventative screenings and by using patient portals to obtain laboratory and other healthcare data; and
- 3) expanding laboratory availability and services. These can all play a significant role in the alignment of healthcare goals. The laboratory has the clinical data, the ability to identify problems and directly influence the effectiveness in which the data is interpreted and outcomes are driven.

Summary

So the next time there is a conversation regarding healthcare and healthcare reform, take pride in the fact that your laboratory is making a direct impact towards reshaping the way medicine is delivered. *Without you and your laboratory, it would be difficult to improve healthcare outcomes, enhance quality of life, and reduce overall costs in the Healthcare Reform process.* In the ever changing field of healthcare, one can only wait and see what will change under the new administration.



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*Wishing you every happiness
this holiday season and
throughout the coming year.*

Dr. Askeland – New Medical Director

We are pleased to announce the appointment of Ryan Askeland, MD, as Sanford Laboratories' new Medical Director!

Following his undergraduate studies at the University of Northern Iowa (Cedar Falls, IA), Dr. Askeland attended medical school at the University of Iowa Carver College of Medicine (Iowa City, IA). He also completed his pathology residency and fellowships (Surgical Pathology and Cytopathology) at the University of Iowa Carver College of Medicine.

Dr. Askeland is Board Certified by the American Board of Pathology in Anatomic Pathology, Clinical Pathology, and Cytopathology. Throughout his professional career, Dr. Askeland has published over 25 articles, received awards, and continues to actively teach pathology, along with additional responsibilities.

We welcome Dr. Askeland to Sanford Laboratories and value his knowledge in many areas as he assists our organization.



Ryan Askeland, MD