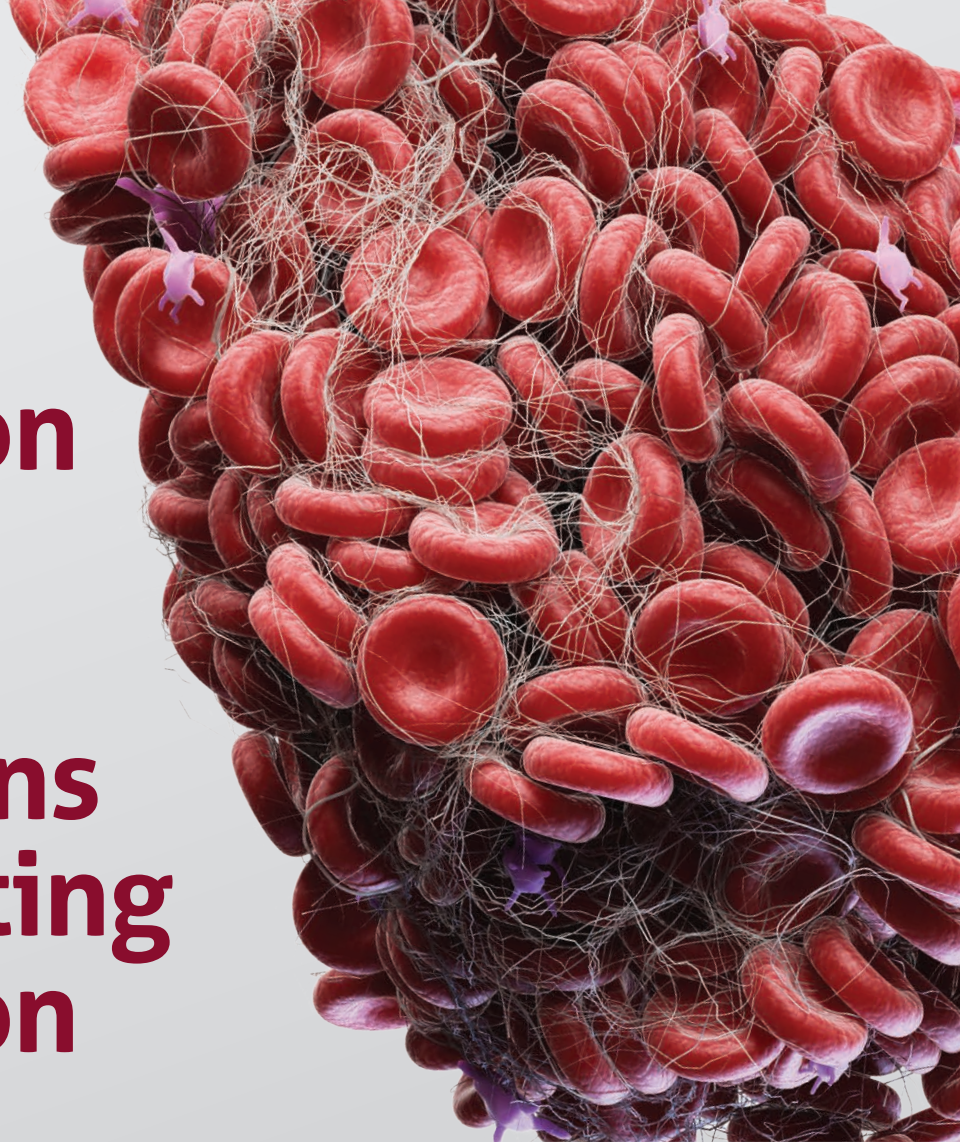
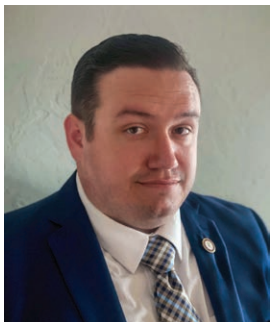
The Coagulation Process & Clinical Applications for Evaluating Coagulation





BRYAN FULTON, M.ED., CER.A.T.T.
THE AMERICAN SOCIETY OF ANESTHESIA TECHNOLOGISTS AND TECHNICIANS

During surgery, it is understood that a resulting factor of the procedure will produce some form of blood loss. Sometimes, this blood loss is severe and can be exacerbated by a patient's coagulation status. For this reason, the anesthesia technologist must have a baseline understanding of hemostasis, fibrinolysis, and laboratory testing to evaluate clotting, particularly the global assay TEG. This paper seeks to provide the reader with an overview of Primary and Secondary Hemostasis, describing the critical elements required for clot formation and focusing on the clotting cascade pathways within secondary hemostasis. Additionally, we will identify the primary roles of clot termination and fibrinolysis. Furthermore, we provide an overview of laboratory testing used to evaluate patient coagulation, explicitly focusing on Thromboelastographic technology (TEG), giving insight into the technology used and methods of analyzing TEG samples.

Hemostasis an Overview

Hemostasis is the process by which our bodies maintain vascular integrity in preserving blood flow through the circulatory system via repair mechanisms primarily in the form of clot formation (Miller & Pardo, 2017, p. 377). Hemostasis is accomplished through two domains, Primary Hemostasis, and Secondary Hemostasis, with the prior characterized by platelet aggregation and platelet plug creation in response to minor vascular injury (Butterworth,

Mackey, & Wasnick, 2022, p.731). Secondary hemostasis activates in response to more considerable vascular intrusion, where platelet plugs are inadequate to stop blood flow from the vascular tear. Successful coagulation results in a thickening of the blood, sealing off the vascular insult (Miller & Pardo, 2017, p. 378). Coagulation, characterized by Secondary Hemostasis, is accomplished via a process known as the clotting cascade. In this systematic process, enzymes, endothelial cells, proteins, and ions activate and organize together to solidify into a state that will preserve blood flow within the circulatory system (Heiner & Nagelhout, 2022, p.898).

Primary Hemostasis

Initially, primary hemostasis relies on a vasoactive response in the endothelial cells. This vascular spasm is followed by a small chain reaction necessary to repair the damaged tissue. Primary hemostasis depends upon the interaction of Platelets, von Willebrand factor (vWF), or collagen aggregating together and adhering to the damaged endothelium (Miller & Pardo, 2017, p. 377). Aggregation is best understood as the ability of the platelets to bind together once activated (Keohane & Walenga, 2019, p.582). Von Willebrand factor is a large glycoprotein and is essential in the role of hemostasis, as it is present in both primary and secondary hemostasis. The glycoprotein is formed inside the endothelial cells. Factor VIII and vWF are the only clotting factors not synthesized in the Liver (Cortes, Moore, & El-Nakeep, 2022). During vascular damage, vWF is released, acting as a triggering agent for platelet adhesion.

It should be noted that inactivated vWF will also be present in the blood plasma, indicating that the process of primary hemostasis is not solely reliant on vWF's interaction with platelets. Before vascular damage, platelets remain inactive; once the endothelial cell is damaged, numerous platelet agonist receptors are altered, signaling the platelets to begin the adhesion process around the injury site (Heiner & Nagelhout, 2022, p.896). One of these agonist receptors is Adenosine Diphosphate (ADP) receptor. ADP is an essential compound for the functioning of normal physiology, responsible for several mechanisms, such as muscular contraction (Klabunde, 2020, p.158). However, ADP is also necessary for primary hemostasis. Within the platelet cell structure resides ADP and, once released, connects with ADP receptors to ignite the platelet aggregation process (Miller & Pardo, 2017, p.377).

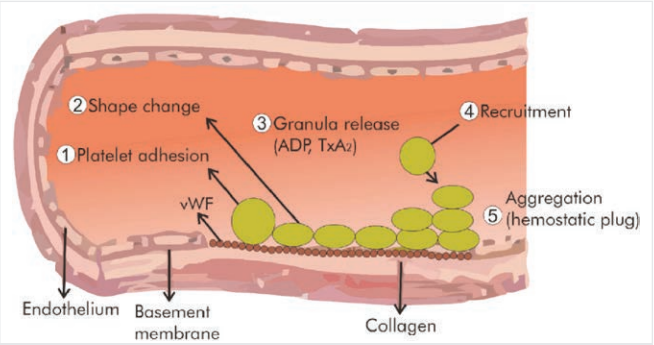


Image details the process of platelet aggregation and ADP degranulation

Amalia, Lisda. (2022). The Role of Platelet-Selectin as a Marker of Thrombocyte Aggregation on Cerebral Sinus Venous Thrombosis. Journal of Blood Medicine. Volume 13. 267-274. 10.2147/JBM.S356028.

The platelet aggregation process is noted by a degranulation, where agonists locked within the platelet are released (Butterworth, Mackey, & Wasnick, 2022, p.730). As mentioned earlier, one of the agonists released from the platelet is ADP, which is responsible for triggering platelet aggregation. Additionally, it is responsible for binding to fibrinogen, which will be necessary later if the vascular injury is severe (Michelson et al., 2007). This process acts as a domino effect speeding up the platelet plug formation. At the same time, the ADP is released during degranulation, resulting in the release of epinephrine, vasopressin, and other agonists, which along with ADP, work to enhance vasoconstriction at the injury site (Miller & Pardo, 2017, p.377).

Primary Hemostasis is the initial response to vascular injury, which relies on a combination of vasoconstriction and platelet aggregation, forming a plug at the injury site. This combination of vasoconstriction from releasing numerous agonists and platelet plugs is effective for minor insults to the vascular system. However, in cases where bleeding is moderate to severe and vascular damage heightened, the body will undergo a process of blood thickening to stave off hypovolemia, hypoperfusion, and restore homeostasis. The coagulation process in response to broader-scale bleeding is known as Secondary Hemostasis.

Secondary Hemostasis

Secondary Hemostasis, also known as the clotting cascade, is the body's response to larger-scale bleeding, where the secondary response is characterized by coagulation. Derived from the Latin word coagulo which refers to the blood's ability to curdle. Coagulation can then be understood as the process by which a liquid changes into a semi-solid or solid state. Concerning the process of Secondary Hemostasis, coagulation relies on a complex arrangement of enzymes,

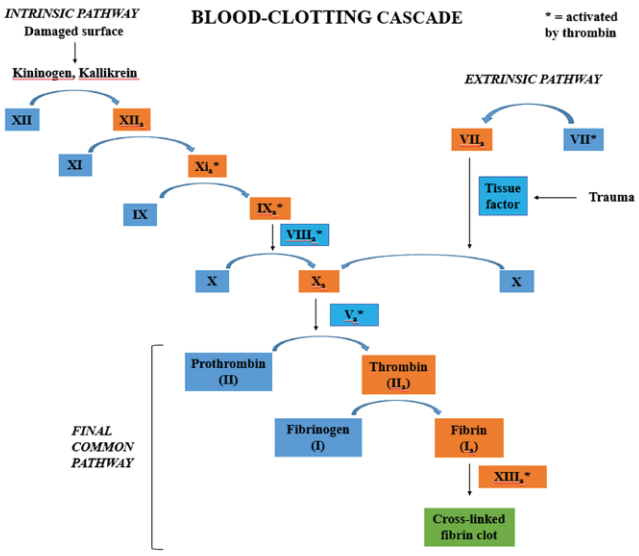


Image details the extrinsic, intrinsic, and common pathways in secondary hemostasis

https://upload.wikimedia.org/wikipedia/commons/0/07/Blood_Clotting_Cascade.png

proteins, ions, and other agonists to alter the blood's state to respond to more severe injury (Miller & Pardo, 2017, p.378). Unlike Primary Hemostasis, which relies on a combination of vasoconstriction and platelet plug formation to resolve damage, Secondary Hemostasis is best understood as a cascade of three events that seek to thicken the blood (Butterworth, Mackey, & Wasnick, 2022, p.730). These cascading events are divided into intrinsic, extrinsic, and common pathways. Like a tree branch, the intrinsic and extrinsic pathways connect at the common pathway, joined by the activated clotting Factor X (Heiner & Nagelhout, 2022, p.899). Ultimately, the cascade aims to form Thrombin, a thickened agent, and Fibrin, a chain-linked complex surrounding platelet plugs and thrombin. The pathways differ in the required factors and speed by which Thrombin and Fibrin are formed (Miller & Pardo, 2017, p.378).

There are several agents necessary to propagate Secondary Hemostasis. The agents can be broken into three large blocks. Zymogens are enzymes and can be found in the plasma. Co-factors work in concert with their respective zymogen counterpart and act to "..bind, stabilize, and enhance" the process of the zymogens (Keohane & Walenga, 2019, p.584). Fibrinogen, a protein called Factor I, is synthesized in the liver and is vital in thrombin formation (Keohane & Walenga, 2019, p.584). The agents are represented along their respective pathways and serve as an illustration of the process of coagulation.

Extrinsic Pathway

The Extrinsic Pathway, also called the tissue factor pathway, starts at the endothelial cells, releasing tissue factors into the plasma, allowing thrombin to form rapidly (Keohane & Walenga, 2019, p.584). The production of thrombin is caused by the rapid release of thromboplastin and enzymes (Chaudhry et al., 2022). The conversion of thromboplastin into thrombin relies on the binding and activation of Factor VII with the eventual binding and activation of Factor X (Miller & Pardo, 2017, p.378). At Factor X, the common pathway activates with assistance from Factor V, Calcium ions, and lipids. Concerning Factor V, this factor is Proaccelerin, a co-factor released into the bloodstream through the degranulation process of platelets discussed earlier in primary hemostasis (Butterworth, Mackey, & Wasnick, 2022, p.731). This rapid Thrombin formation is seen early on in the bleeding process and is where our Prothrombin Time (PT) is derived (Miller & Pardo, 2017, p.384). Along the Common Pathway, the formation of thrombin results in the activation of fibrinogen and conversion into fibrin, or Factor XIII (Smith et al., 2015). The purpose of the common pathway is to quickly form Thrombin and Fibrin as a quick resolution to bleeding, which is necessary for emergencies allowing time for the intrinsic pathway to organize a more extensive enzymatic process producing a more durable clot repose to restore Hemostasis (Heiner & Nagelhout, 2022, p.899).

Intrinsic Pathway

The Intrinsic Pathway, the slower pathway to coagulation, begins with the activation of Factor XII and its interaction with collagen released from the endothelium (Butterworth, Mackey, & Wasnick, 2022, p.731). Factor XII, also called Hageman Factor, is a plasma protein produced in the liver and suspended in the plasma; after activation, it binds to activate Factor XI (Heiner & Nagelhout, 2022, p.899). Factor XI is the thromboplastin antecedent used to activate Factor IX. The thromboplastin antecedent is a serine protease, an enzyme that severs proteins. In this case, Factor IX acts to cleave the protein, thus activating Factor XI. Factor IX is also known as Christmas Factor. This factor is essential in preventing Hemophilia, particularly Hemophilia B (Lichtman et al., 2022, p.563). Like the other factors discussed, it is produced and synthesized in the liver and suspended in the plasma as a deactivated state until activation post-injury (Heiner & Nagelhout, 2022, p.899).

Factor IX is the last activated factor in the intrinsic pathway before its continued activation of the clotting process in the common pathway. Factor X, as mentioned earlier, is the joining point between the intrinsic and extrinsic pathways and is responsible for activating Factor II, which is prothrombin. This process is accomplished by concurrently binding and activating Factor X and Factor V (Miller & Pardo, 2017, p.378). Together, these two agents form a larger prothrombinase complex. As the name suggests, the prothrombinase complex breaks down prothrombin, with the resulting by-product being thrombin. The thrombin then includes a semi-solid component and activates fibrinogen, converting it into fibrin.

Fibrinogen is a complex protein produced in the liver known as Factor I. Through its enzymatic conversion into Fibrin by Thrombin, it becomes a chain-linked complex that stabilizes semi-solid thrombin and platelet plugs. Ultimately, whether the clotting is intrinsic or extrinsic, the goal is to form complexes of Thrombin, Fibrin, and platelets to close off areas of vascular puncture.

Coagulation Breakdown and Fibrinolysis

Regulation of Clots

As with any process where there is a build-up physiologically, there is a process for the removal. Much like the clotting cascade propagated the formation of Fibrin and Thrombin, there are agonists which suspend clotting. The three primary agents responsible for the cessation of coagulation once Hemostasis is restored are antithrombin, tissue factor inhibitor, and the activation of Protein C (Miller & Pardo, 2017, p.378).

Antithrombin, also known as Antithrombin III, is a primary agent preventing and ceasing clotting. Within anesthesia, Antithrombin III is crucial, with its relationship to Heparin. According to Butterworth et al. (2022), *"Heparin exerts its anticoagulant activity by augmenting the activity of antithrombin III"* (Butterworth, Mackey, & Wasnick, 2022, p.731). It accomplishes this by binding to antithrombin-III, but more importantly, it significantly potentiates AT-III's effect. This binding suspends the conversion of prothrombin into thrombin, directly deactivating Factor X (Heiner & Nagelhout, 2022, p.525).

Tissue Factor Pathway inhibitors (TFPI) work to inhibit coagulation by blocking the beginning phases of the clotting cascade, unlike AT-III, which inhibits Factor X much later in the cascade. TFPIs are single-chain proteins that are expressed close to the endothelium tissue surface. This location and molecule formation allow it to inhibit Factor VII. Additionally, due to its similar molecular shape to Factor V, it can bind to Factor V, further inhibiting coagulation. According to the American Heart Association (2016), TFPI is the *"only endogenous protein recognized that inhibits prothrombinase at physiologically relevant rates and protein concentrations,"*—indicating its importance in correcting clotting post-vascular repair (Mast, 2016).

The final component of coagulation termination is protein C (aPC) activation. The essential function behind the activation of aPC relies on the binding of thrombin to thrombomodulin (Miller & Pardo, 2017, p.379). Thrombomodulin (TM) is a membrane protein, meaning it is attached to a cell or organelle. In this case, TM is contained in the endothelial cells functioning as a receptor on the vascular wall membrane. Along with its role in promoting the activation of aPC, it also acts as an anti-inflammatory agent (Weiler & Rezaie, 2021).

The Process of Fibrinolysis

As there is a pathway to fibrin formation, there is a pathway to fibrinolysis. The overall process for fibrinolysis depends on plasminogen converting into plasmin which then breaks down fibrin. Plasminogen is a plasma-based protein that, when activated into plasmin, works as a solvent to degrade fibrin (Miszta et al., 2021). The conversion of plasminogen into plasmin results from tissue plasminogen activator (tPA) and Urokinase merging with activated Factor XI and XII along with kallikrein (Miller & Pardo, 2017, p.379). However, tPA is the more profound activator as it has a high affinity for plasminogen. Hence, why tPA is used clinically for ischemic strokes and pulmonary embolisms as it profoundly activates plasminogen into plasmin to dissolve fibrin clots.

Coagulation Testing

Clinically, several tests evaluate a patient's coagulation performance or lack thereof. The most common are Prothrombin Time (PT), Activated Clotting Time (ACT), and Thromboelastography (TEG), which all evaluate clot performance and are used to diagnose and correct numerous coagulopathies in the perioperative environment.

Prothrombin Time

The prothrombin time evaluates the time it takes to initiate thrombin formation, typically along the extrinsic pathway.

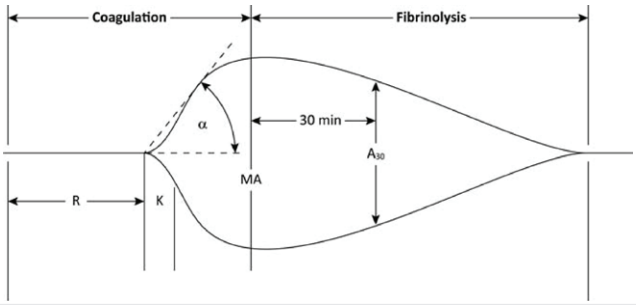
The test provides data on the amount of time it takes thromboplastin to synthesize into thrombin (Miller & Pardo, 2017, p.384). A PT's average clot production time is between 12-14 seconds (Heiner & Nagelhout, 2022, p.902). According to Miller and Pardo (2017), prolonged PT testing can provide insight into certain factor deficiencies, such as factor VII and Factor V. Due to its ability to evaluate vitamin-K-dependent factors, it is often used as a standard test for patients on warfarin (Guimaraes et al., 2018, p.235). PT testing is essential for diagnosing and evaluating several clinical events in the operating room. Its ability to measure the length of clot formation along the extrinsic pathway makes it useful in monitoring disseminated intravascular coagulation (DIC), a condition that overproduces clots which typically block small blood vessels; once the proteins necessary for clot formation are depleted, hemorrhage begins. Additionally, its ability to evaluate the necessary factors along the extrinsic and common pathways is a valuable test for assessing liver function as these factors are synthesized.

Activated Clotting Time

The ACT is a test to evaluate clot formation, and in the operating room is used in cardiovascular suites to monitor the effectiveness of heparin therapies related to cardiopulmonary bypass (Guimaraes et al., 2018, p.352). Clotting data provided to the anesthesia care team and perfusionist are measured in seconds. Blood is mixed exogenously with a reagent, typically kaolin when performing the test (Miller & Pardo, 2017, p.385). The test measures clot formation when the reagent mixes with the sampled blood. The regular ACT will range from 70-120 seconds, whereas when heparin is present, the average clotting time is between 180 and 240 seconds (University of Rochester Medical Center, 2022).

Thromboelastography

Despite the importance of the ACT and PT point-of-care testing, Throbeleastography (TEG) is considered a gold standard for evaluating coagulation and diagnosing coagulopathies. The primary reason for its importance is its ability to provide the same information given by both the ACT and PT, along with other important coagulation information (Butterworth, Mackey, & Wasnick, 2022, p.731). Its use in the perioperative environment can guide the anesthesia care team on its treatment protocols for massive transfusion events. The TEG provides information on the time to form a clot, the strength of the clot, and information on clot lysis, essentially measuring the life cycle of the clot (Heiner & Nagelhout, 2022, p.903). Due to its ability to capture the whole framework of coagulation and fibrinolysis, it is referred to as a global coagulation assay (Miller & Pardo, 2017, p.386).



De Pietri, Lesley & Ragusa, Francesca & Deleuterio, Annalisa & Begliomini, Bruno & Serra, Valentina. (2015). Reduced Transfusion During OLT by POC Coagulation Management and TEG Functional Fibrinogen. Transplantation Direct. 2. 1. 10.1097/TXD.0000000000000559.

https://www.researchgate.net/figure/Normal-TEG-tracing-1-17-a-angle-reflecting-the-rate-of-clot-formation-normal-values_fig1_287391039

The technology behind Thromboelastogram (TEG)

Despite the importance of this global assay in contemporary medicine, the technology behind the TEG goes back to 1948 (Whiting, 2014). The basic principle behind TEG is having a small sample of blood move around a stationary pin. As the angulation of movement continues, the clotting factors in the sample will activate around the pin (Selby, 2020). Like another coagulation test, the sample's ability to begin clot formation relies on a reagent added to the sample, which in the case of the TEG is kaolin (Stettler, 2018). The pin is attached to a transducer and monitors the torque and tension generated by the stiffing clot. Once the clot has been sufficiently formed, the movement will cease for some time, and as the fibrinolysis pathway initiates, the pin will be able to detect the drop-in tension and torque, providing an overall picture of the clotting process. There are two primary ways of measuring the kinetics of the clot. One is via a torsion pin connected to an electromechanical transducer, which relays the information to the computer for visual analysis of the clot (Guimaraes et al., 2018, p.353). The second method does not rely on the cup's movement but rather the pin's movement. The other significant alteration is the transducer. The moving pin is connected to a mirror. As the oscillation occurs, the mirror reflects light generated from a LED light source (Selby, 2020). A transducer captures this reflection. Similar to reflection-based SpO2 monitoring, this analysis relies on the time change to determine the tension and strength of the clot. For example, when the clot is weak, the

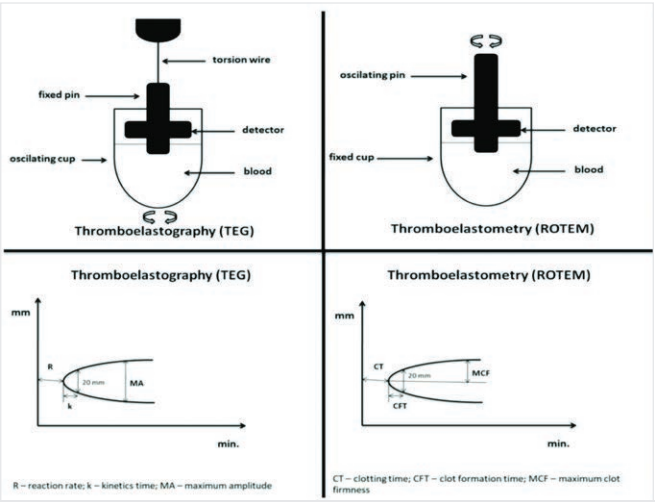
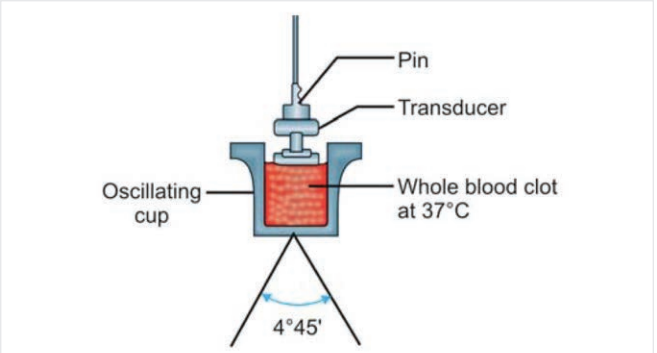


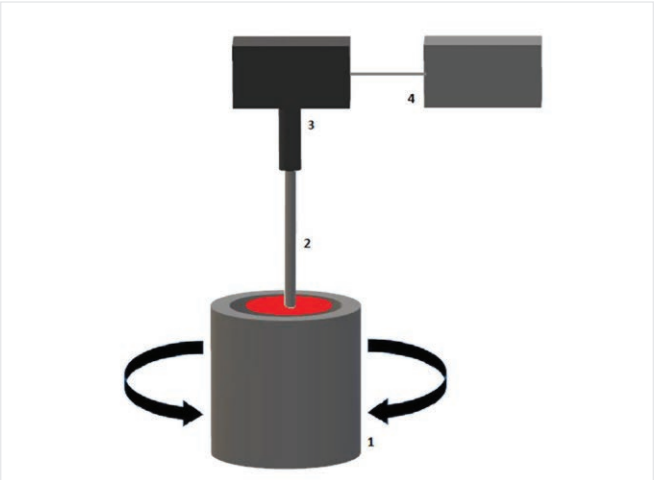
Image describes the process of pin engagement either from cup oscillation or pin oscillation

Samoš, Matej & Skornova, Ingrid & Bolek, Tomáš & Stančiaková, Lucia & Korpallová, Barbora & Galajda, Peter & Staško, Ján & Kubisz, Peter & Mokáň, Marián. (2021). Viscoelastic Hemostatic Assays and Platelet Function Testing in Patients with Atherosclerotic Vascular Diseases. Diagnostics. 11. 143. 10.3390/diagnostics11010143.

https://www.researchgate.net/figure/Thromboelastography-TEG-and-rotational-thromboelastometry-ROTEM_fig1_348617078



Butterworth J. F. Mackey D. C. Wasnick J. D. Morgan G. E. & Mikhail M. S. (2018). Morgan & mikhail's clinical anesthesiology (Sixth). McGraw-Hill Education. Retrieved November 20 2022 from **https://accessanesthesiology.mhmedical.com/book.aspx?bookid=2444**.



Cannata, G., Mariotti Zani, E., Argentiero, A., Caminiti, C., Perrone, S., & Esposito, S. (2021). Teg® and Rotem® traces: Clinical applications of viscoelastic coagulation monitoring in Neonatal Intensive Care Unit. Diagnostics, 11(9), 1642. **https://doi.org/10.3390/diagnostics11091642**

oscillation will cause a rapid light reflection to the detector, visually representing a low-amplitude waveform. As the clot strengthens, the time between reflections will lengthen, and the waveform's amplitude will increase.

Considerations for TEG Sampling

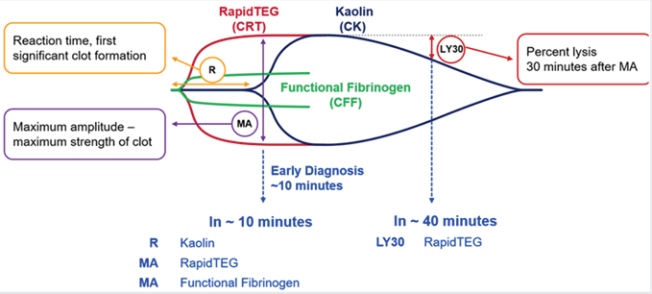
Global blood assays require the analysis of whole blood. Venipuncture is the most common method for acquiring a TEG sample (Shaydakov, Sigmon, Blebea, 2022). However, samples can be drawn from arterial lines. A 2001 study of 40 patients noted that TEG results differed between arterial and venous draws, with recommendations to use a single draw site for TEG sampling (Manspeizer, 2001). Hence it is essential that whatever location is used, changes in the draw site are avoided to maintain consistent testing measures, thus limiting variables in the analysis.

The sample is drawn into a vial buffered with sodium citrate. Sodium citrate pauses the clotting process by binding to Calcium in the blood to ensure the sample is preserved before analysis in the lab (Shaydakov, Sigmon, Blebea, 2022). Once blood is drawn, an inversion technique is done to ensure blood is sufficiently mixed with the citrate; however, rigorous agitation should be avoided to prevent clotting. For this reason, TEG samples should not be sent through pneumatic tube systems. It should be noted that non-citrated blood can be used, but testing needs to be done immediately (Shaydakov, Sigmon, Blebea, 2022).

Depending on the study requested, sampling will be conducted differently. For example, Kaolin TEGs are processed in a transparent study cup. The kaolin TEG provides information on the intrinsic pathway giving insight into the causes of bleeding. In addition, a Kaolin TEG with heparinase will be sampled in a blue cup indicating the study cup is coated with heparinase. The purpose is to inhibit any heparin present in the sample (Haemonetics, 2014). All TEGs are drawn with two blue top vacutainers, with the first tube being used as a waste line to ensure the sampled product is not contaminated with saline solution. If testing requires platelet mapping, sampling should be done with a green top tube (Haemonetics, 2014).

Coagulation - Clinical Analysis Using TEG

Clinical evaluation utilizing TEG provides the anesthesia care team with vital information on the patient's coagulation status. The data can diagnose coagulopathies and provide insight into what treatments should be used intraoperatively.



Cochrane, C., Chinna, S., Um, J. Y., Dias, J. D., Hartmann, J., Bradley, J., & Brooks, A. (2020). Site-of-care viscoelastic assay in major trauma improves outcomes and is cost neutral compared with standard coagulation tests. Diagnostics, 10(7), 486. https://doi.org/10.3390/diagnostics10070486
https://www.mdpi.com/2075-4418/10/7/486/htm

At its base level, TEG analysis allows the anesthesia care team to determine three things, normal hemostasis, hemorrhage, or thrombosis. The analysis is provided to the care team in the form of a real-time visualization of clot performance via thromboelastogram and quantitative analysis. The parameters measured are the reaction time, kinetic time, alpha angle, maximum amplitude, and LY30 time which is the lysis time for the clot.

The reaction time is also called the "R-time," which is the time for initial clot formation or the enzymatic process to generate thrombin. As was mentioned earlier, TEG replaces several coagulation tests (Miller & Pardo, 2017, p.386). In the case of reaction time, the R-time replaces prothrombin testing. Depending on the TEG system you are using and the sample location, reaction times can vary, but the average range is between five (5) and ten (10) minutes (Open Anesthesia, 2022). Similar to Prothrombin time testing, prolonged reaction times indicate a deficiency in clotting factors necessary to trigger the intrinsic and extrinsic pathways.

The kinetic time is understood as the initial strength of the clot. For TEG, this is measured as the time it takes for the clot to reach 20mm on the graph. How does this work with the clotting cascade? The kinetics directly correlate to the initiation of fibrin formation and rapid potentiation of fibrin synthesis (Miller & Pardo, 2017, p.386). Mechanically, this is the point at which the pin is engaged, and torsion can be detected on the electromechanical transducer. Concerning clinical relevance, kinetic times provide the anesthesia care team with information on fibrinogen volume status and the ability of fibrinogen to synthesize into fibrin. For example, a kinetic value longer than four (4) minutes could indicate a hemorrhagic event (Open Anesthesia, 2022). When looking at the reaction time and kinetic times together, the anesthesia care team can make transfusion decisions, such as the transfusion of plasma to replace lost clotting factors; or the administration of cryoprecipitate to improve fibrinogen levels (Butterworth, Mackey, & Wasnick, 2022, p.728). Ultimately, follow-up TEG samples would show a shorter reaction and kinetic times by taking this course of action.

When analyzing a TEG sample, it is essential to review the degree of angulation of the graph, which is referred to as the Alpha angle, closely associated with clot kinetics; alpha angles provide information on the fibrinogen status. A low alpha angle would indicate low levels of fibrinogen in the plasma and, thus, weak fibrin chain formation (Miller & Pardo, 2017, p.386). Again, as with increased kinetic times, alpha angles below 45 degrees indicate the need for cryoprecipitate to improve fibrinogen levels and clot strength (Open Anesthesia, 2022).

The overall clot strength analysis is also assessed via the recorded amplitude on the graph measuring its width. A narrow width on the graph would point to a patient with some hemorrhagic condition, whereas a wide width would indicate a thrombotic state (Butterworth, Mackey, & Wasnick, 2022, p.728). A typical MA will be measured between 50-60mm, indicating a normal hemostatic state (Open Anesthesia, 2022).

The final point of analysis is the LY30 which measures the clot breakdown thirty minutes after Maximum amplitude is reached. This is similar to the kinetics and alpha angle in that it provides information on the strength of the clot, the difference being that it measures the end of the clotting cycle and includes data on the fibrinolytic state of coagulation (Miller & Pardo, 2017, p.386). The MA width change is being measured on the TEG, which is calculated as a percentage. According to Chapman et al. (2013), percentage drops that are 3% or greater would indicate a hyperfibrinolytic state (Chapman et al., 2013). The ability of the TEG to monitor clot breakdown is one of the reasons this test is unique and valuable. For example, in the perioperative environment, if we were to see average reaction time, acute alpha angle (>55 degrees), lowered MA (< 50mm), and rapid degradation of the clot, treatment for fibrinolysis can begin. On the other end of the spectrum, if we were to see a short reaction time, acute alpha angle, increased MA (>60mm), and a clot that breaks down rapidly (>3%), we can recognize DIC and begin treatment promptly (Miller & Pardo, 2017, p.386).

Practical steps in evaluating a Thromboelastography

Beyond the valuable information provided by the TEG

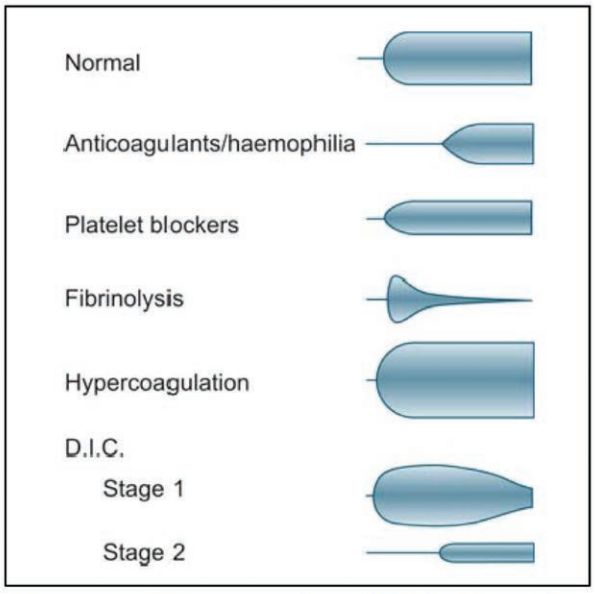


Figure illustrates common TEG read outs seen in the operating room.
http://www.emdocs.net/thromboelastogram-teg-five-minute-primer-emergency-physician/
Butterworth J. F. Mackey D. C. Wasnick J. D. Morgan G. E. & Mikhail M. S. (2018). Morgan & mikhail's clinical anesthesiology (Sixth). McGraw-Hill Education. Retrieved November 20 2022 from https://accessanesthesiology.mhmedical.com/book.aspx?bookid=2444.

sample, which directs perioperative care, the visual display of clot performance provides the anesthesia care team with an ideal way to evaluate a patient and make salient clinical decisions to monitor or correct a patient's coagulation status. There are several methods to assess a TEG sample, but one of the most understandable ways to evaluate the graph is by comparing the shape of the chart to glassware. Normal hemostasis will take the form of a brandy tumbler concerning its kinetics, alpha angle, and maximum amplitude. The only indicator missing is the reaction time provided on the sample readout.

If we carry the glassware example further, we next use a red wine glass as a descriptor of a patient needing plasma. The long stem of the wine glass indicates a prolonged reaction time but is in a similar shape to the brandy glass in every other way (Nickson, 2020). This analysis would show a patient's need for fresh frozen plasma to replace deficit clotting factors. On the opposite end, if you were to see a champagne glass, this would mean a patient needs cryoprecipitate (Miller & Pardo, 2017, p.386). The reason being you have an elongated stem, narrow base (elongated kinetic and diminished alpha angle), a narrow flute (low MA), with a drop further narrowing at the end of the glass (diminished LY30) (Miller & Pardo, 2017, p.386). Another practical glassware example is the martini glass. In this case, though, we use the stem of the glass as our LY30 (Nickson, 2020). In this example, we see a rapid development of the fibrin clot but a rapid devolution of the clot indicating primary fibrinolysis with a recommended treatment of tranexamic acid (TXA). In the final example, we move beyond traditional drinkware and look at a test tube (Miller & Pardo, 2017, p.386). If a sample looks like a test tube, this will indicate that a patient is on a platelet-blocking treatment or has thrombocytopenia, indicating a need to replenish platelet levels (Nickson, 2020). Utilizing these simple examples to explain TEG readouts gives the anesthesia technologist valuable information in managing the patient's transfusion needs intraoperatively.

Closing Thoughts

Maintaining hemostasis in the operating room is imperative; thus, having a cursory understanding of primary and secondary hemostasis is essential for the anesthesia technologist. Over the course of this paper, we focused on the necessary elements for clot formation in both primary and secondary hemostasis. We further described the pathways needed to generate thrombin and fibrin in the secondary hemostasis, tying the hematological concepts to laboratory testing and analysis. Finally, we further explained the importance of global coagulation assays, focusing on Thromboelatographs, providing descriptions of the graph, normal values, and practical methods for evaluation to guide care in the operating room.

References

Butterworth, J. F., Mackey, D. C., & Wasnick, J. D. (2022). *Morgan and Mikhail's Clinical Anesthesiology* (7th ed.). McGraw-Hill Professional. https://bookshelf.vitalsource.com/books/9781260473803

Cortes GA, Moore MJ, El-Nakeep S. (2022) Physiology, Von Willebrand Factor. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559062/

Chapman, M. P., Moore, E. E., Ramos, C. R., Ghasabyan, A., Harr, J. N., Chin, T. L., Stringham, J. R., Sauaia, A., Silliman, C. C., & Banerjee, A. (2013). Fibrinolysis greater than 3% is the critical value for initiation of antifibrinolytic therapy. *The journal of trauma and acute care surgery, 75*(6), 961–967. https://doi.org/10.1097/TA.0b013e3182aa9c9f

Chaudhry R, Usama SM, Babiker HM. Physiology, Coagulation Pathways. [Updated 2022 Aug 29]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482253/

Elisha, S., Heiner, J. S., & Nagelhout, J. J. (2022). *Nurse Anesthesia* (7th ed.). Elsevier Health Sciences (US). https://bookshelf.vitalsource.com/books/9780323778640

Giri, H., Panicker, S. R., Cai, X., Biswas, I., Weiler, H., & Rezaie, A. R. (2021). Thrombomodulin is Essential for maintaining quiescence in vascular endothelial cells. *Proceedings of the National Academy of Sciences of the United States of America, 118*(11), e2022248118. https://doi.org/10.1073/pnas.2022248118

Guimaraes, E., Davis, M., Woodworth, G., & Kirsch, J. R. (2018). The Anesthesia Technologist's Manual (2nd ed.). Wolters Kluwer Health. https://bookshelf.vitalsource. com/books /9781496344342

Haemonetics. (2014). *Hemostasis Analyzer System - Haemonetics.* TEG 5000 Hemostasis analyzer system. Retrieved November 20, 2022, from https://teg.haemonetics.com/~/media/sharepoint/devices/teg/marketing/brochures/teg5000_brochure/col-pp-000078-us_teg_brochure.pdf.ashx

Keohane, E., Otto, C. N., & Walenga, J. (2019). *Rodak's Hematology* (6th ed.). Elsevier Health Sciences (US). https://bookshelf.vitalsource.com/books/9780323549639

Klabunde, R. E. (2020). *Cardiovascular Physiology Concepts* (3rd ed.). Wolters Kluwer Health. https://bookshelf.vitalsource.com/books/9781975150105

Lichtman, M. A., Kaushansky, K., Prchal, J. T., Levi, M. M., Burns, L. J., & C., D. (2022). *Williams Manual of Hematology* (10th ed.). McGraw-Hill Professional. https://bookshelf.vitalsource.com/books/9781264269211

Manspeizer, H. E., Imai, M., Frumento, R. J., Parides, M. K., Mets, B., & Bennett-Guerrero, E. (2001). Arterial and venous Thrombelastograph variables differ during cardiac surgery. *Anesthesia and analgesia, 93*(2). https://doi.org/10.1097/00000539-200108000-00007

Mast, A. E. (2016). Tissue factor pathway inhibitor. *Arteriosclerosis, Thrombosis, and Vascular Biology, 36*(1), 9–14. https://doi.org/10.1161/atvbaha.115.305996

Michelson, A. D., Jennings, L., & White, M. (2007). *Platelets.* Chapter 26 - Platelet Aggregation (2nd ed.). Academic Press, Elsevier. https://www.sciencedirect.com/science/article/pii/B9780123693679507886

Miller, R., & Pardo, M. (2017). *Basics of Anesthesia* (7th ed.). Elsevier Health Sciences (US). https://bookshelf.vitalsource.com/books/9780323401159

Miszta, A., Huskens, D., Donkervoort, D., Roberts, M. J. M., Wolberg, A. S., & de Laat, B. (2021). Assessing Plasmin Generation in Health and Disease. *International journal of molecular sciences, 22*(5), 2758. https://doi.org/10.3390/ijms22052758

Nickson, C. (2020, November 3). *Thromboelastogram (TEG).* Life in the Fast Lane • LITFL. Retrieved November 20, 2022, from https://litfl.com/thromboelastogram-teg/

Open Anesthesia . (2022). *ABA keywords.* OpenAnesthesia. Retrieved November 20, 2022, from https://www.openanesthesia.org/teg_decreased_max_rx/#:~:text=Normal%20is%2045%2D55%20degrees,to%20form%20a%20stable%20clot.

Selby R. (2020). "TEG talk": expanding clinical roles for thromboelastography and rotational thromboelastometry. *Hematology. American Society of Hematology. Education Program, 2020*(1), 67–75.

Shaydakov ME, Sigmon DF, Blebea J. (2022) Thromboelastography. [Updated 2022 Apr 14]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537061/

Stettler, G. R., Sumislawski, J. J., Moore, E. E., Nunns, G. R., Kornblith, L. Z., Conroy, A. S., Callcut, R. A., Silliman, C. C., Banerjee, A., Cohen, M. J., & Sauaia, A. (2018). Citrated kaolin thrombelastography (TEG) thresholds for goal-directed therapy in injured patients receiving massive transfusion. *The journal of trauma and acute care surgery, 85*(4), 734–740. https://doi.org/10.1097/TA.0000000000002037

Smith, S. A., Travers, R. J., & Morrissey, J. H. (2015). How it all starts: Initiation of the clotting cascade. *Critical reviews in biochemistry and molecular biology, 50*(4), 326–336. https://doi.org/10.3109/10409238.2015.1050550

Univ. of Rochester Medical Center. (2022). *Activated coagulation time.* Activated Coagulation Time - Health Encyclopedia - University of Rochester Medical Center. Retrieved November 19, 2022, from https://www.urmc.rochester.edu/encyclopedia/content.aspx?contenttypeid=167&contentid=act

Whiting, D., & DiNardo, J. A. (2014). TEG and ROTEM: technology and clinical applications. *American journal of hematology, 89*(2), 228–232. https://doi.org/10.1002/ajh.23599

Take the QUIZ On The Next Page

Continuing Education Quiz

To test your knowledge on this issue's article, provide correct answers to the following questions on the form below. Follow the instructions carefully.

1. What do platelets bind to help initiate platelet aggregation?
a. Christmas Factor
b. Von Willebrand Factor
c. Proconvertin
d. Fletcher Factor

2. What clotting factor is NOT formed in the Liver?
a. Factor VII
b. Factor II
c. Factor X
d. Factor VIII

3. What is the name of the process where ADP is released from the platelet?
a. Degranulation
b. Cleaving
c. Fusion
d. Aggregation

4. What factor connects the common pathway to the intrinsic and extrinsic pathways?
a. Factor III
b. Factor V
c. Factor X
d. Factor XIII

5. Fibrinogen is converted into.
a. Fibrin
b. Fibrinolysis
c. Prothrombinase
d. Thromboplastin

6. What is the primary factor in the extrinsic pathway?
a. Factor VII
b. Factor II
c. Factor X
d. Factor VIII

7. Factor X and Factor V form.
a. Fibrin
b. Fibrinolysis
c. Prothrombinase
d. Thromboplastin

8. What is a necessary protein in terminating clot formation?
a. TFPI
b. Factor V
c. Fibrin
d. vWF

9. What is needed to start the process of fibrinolysis?
a. Christmas Factor
b. tPA
c. TXA
d. Protein C

10. What drug works by binding to Antithrombin-III?
a. TXA
b. tPA
c. Heparin
d. Protamine

To apply for Continuing Education/ Contact Hours:

1) Provide all the information requested on this form.
2) Provide correct answers to this issue's quiz in this box > > >
3) Mail this form along with $10.00 Member $20 Non-Member *(check or money order, payable to ASATT)*

The answers to the Winter 2022 "Coagulation Testing and Analysis" Quiz are: *(circle answers)*

1: A B C D	**6:** A B C D
2: A B C D	**7:** A B C D
3: A B C D	**8:** A B C D
4: A B C D	**9:** A B C D
5: A B C D	**10:** A B C D

Quiz 1 of 2

Name: _____ ASATT Number: _____
Street Address: _____ Phone Number: _____
City: _____ State: _____ Zip: _____

Signature: _____ Date: _____

SUBMISSIONS FOR THIS ISSUE'S QUIZ EXPIRE **DECEMBER 31, 2023.**
ACHIEVE 80% IN THIS QUIZ TO EARN ONE (1) CONTINUING EDUCATION CREDIT.