



Basic Clinician Training

Module 1

An Overview of Hemostasis

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An introduction and overview of hemostasis. Advance to the next slide to begin the presentation, or click on an underlined link to jump to a specific topic.



Hemostatic System

 **Menu**

Introduction

- Define hemostasis
- Why monitor hemostasis?

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The introduction defines hemostasis and discusses the importance of monitoring it.



Definition of Hemostasis

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- Balance between procoagulant and anticoagulant systems
 - Liquid blood in normal blood vessels
 - Rapid creation of hemostatic plug at site of injury
- Self regulation of complex, dynamic, interactive elements for controlled clot formation and lysis

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A simple definition of hemostasis is the stoppage of bleeding or hemorrhage by controlled clot formation. The clot is the single end product of this complex, dynamic, highly regulated system involving more than 50 interactive elements. When functioning properly in healthy blood vessels, a dynamic balance is maintained between the procoagulant and anticoagulant elements, keeping the blood in a liquid state.

In the case of microvascular damage, a balanced system will react and regulate the process of localized clot formation while the damage undergoes repair and clot lysis upon completion of the repair.

An unbalanced system, due to disease state or pharmacological agents, will result in either hemorrhage or thrombosis, depending on which way the balance is tipped.



Why Monitor Hemostasis?

 Menu

Clinical		Administrative
• Assess risk of bleeding or thrombotic event • Personalize hemostatic therapy • Monitor efficacy of hemostatic therapy		• Improve patient care • Use hemostatic drugs appropriately • Lower costs ▪ Reduce blood product use ▪ Reduce re-operations ▪ Reduce thrombotic events ▪ Reduce length of stay

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Clinically, hemostasis is monitored to assess the risk of bleeding or thrombosis, to allow personalized hemostatic therapy, and to monitor efficacy of hemostatic therapy.

Monitoring hemostasis in a timely fashion provides clinicians with the information necessary to:

- Improve patient care
- More appropriately use hemostatic drugs
- Reduce health care and hospital costs

Costs can be lowered by a reduction in:

- Blood product usage
- Number of re-operations to explore for causes of bleeding
- Long term care due to thrombotic events
- Length of stay



The Hemostatic Process: A System Perspective


Menu

- At least six systems
 - Proteins
 - Coagulation pathways
 - Fibrinolytic pathway
 - Extra-vascular matrix and tissues
 - Cells
 - Platelets
 - Endothelium
 - Inflammatory cells
- Interdependent components
- Highly regulated process



Source: Diagnostica Stago

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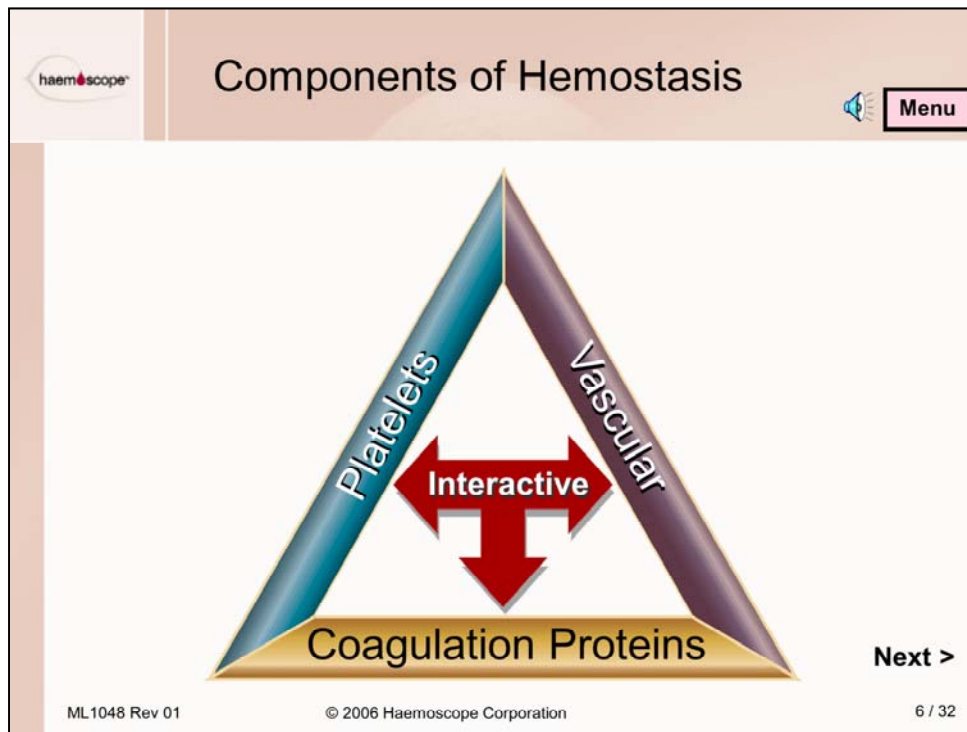
Hemostasis is monitored to identify the balance or imbalance of the system, and if an imbalance exists, to determine its cause and magnitude.

The system perspective considers the interaction of all components currently known to be associated with the function and regulation of hemostasis. Currently, at least six systems are known to be involved. These include:

- Platelets
- Coagulation pathways
- Fibrinolytic pathway
- Vascular endothelium
- Subendothelium or extra-cellular matrix
- Inflammatory cells and mediators.

The role of inflammation in the hemostatic process is best demonstrated in sepsis; however, any disease state with an inflammatory component will have an important hemostatic role. Two examples are coronary artery disease and cancer.

The components of these systems are interdependent. A change in one part of the system will result in changes in the others. These systems are typically highly regulated, and always try to maintain an internal balance. A system's loss of interdependency or of its self-regulating capacity results in a system that is out of balance, leading to a higher risk of bleeding or thrombosis.



Understanding how hemostasis is regulated requires an understanding of the balance among three highly interactive primary components. These are:

- The vascular system
- The coagulation proteins
- The platelets

For example, changes in the vascular system can influence the function of platelets and coagulation proteins.

Understanding this interaction is important for accurately monitoring hemostasis. Most routine tests such as PT, aPTT, and platelet aggregation monitor the *function* of isolated components, but not the *interaction* of these components.

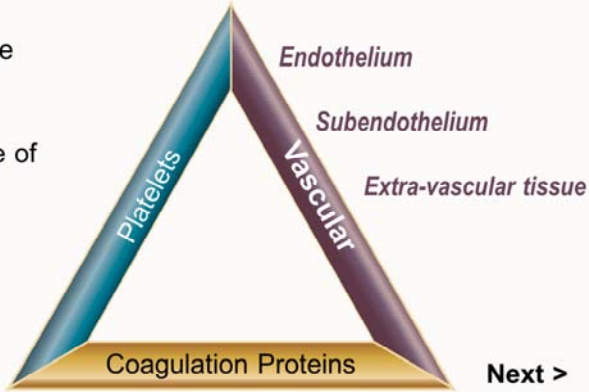


Components: Vascular System



Menu

- Intact Endothelium**
 - Releases prostacyclin, nitric oxide
 - Expresses heparin-like molecules and thrombomodulin
 - Synthesis and release of tPA



The diagram illustrates the components of the vascular system as a triangle. The left side is labeled 'Platelets', the right side is 'Vascular', and the bottom is 'Coagulation Proteins'. The top of the triangle is divided into 'Endothelium' and 'Subendothelium'. The area outside the triangle is labeled 'Extra-vascular tissue'.

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The vascular system is composed of the vascular endothelium, the extracellular matrix or subendothelium, and the extravascular tissue, which expresses tissue factor, a potent activator of the coagulation pathways.

The endothelium also directly modulates several aspects of hemostasis. Quiescent endothelium is non-thrombogenic in nature due to its anti-platelet, anticoagulant, and pro-fibrinolytic properties. These anti-thrombotic properties include:

- Secretion or release of prostacyclin and nitric oxide, which inhibit platelet aggregation
- Expression of heparin-like molecules and thrombomodulin, which indirectly inhibit thrombin and thrombin production
- Synthesis and release of tPA (tissue plasminogen activator), which promotes fibrinolysis

Components: Vascular System Endothelium

Menu

- Damaged endothelium
 - Von Willebrand factor
 - Tissue factor
 - Fibrinolytic inhibitor (PAI)
- Endothelial cells activated by inflammatory mediators
 - Express tissue factor
 - Express binding sites for factors IXa and Xa

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When injured or activated, the endothelium expresses procoagulant properties in an effort to augment local clot formation. The endothelium may be activated or injured by excessive exposure to stress hormones, trauma, surgery, plaque rupture, inflammatory mediators such as cytokines, infectious agents, and hemodynamic factors.

The procoagulant properties of the endothelium include:

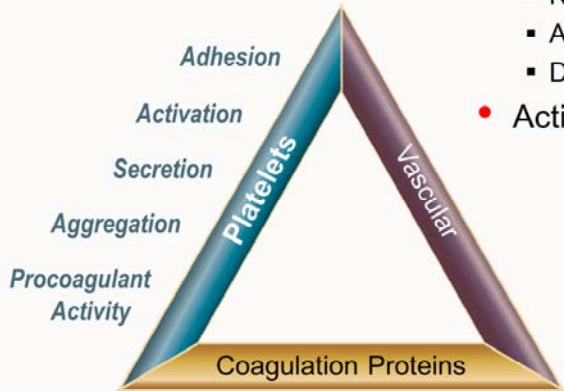
- The release of von Willebrand factor (vWF), a platelet binding protein
- The expression of tissue factor, an activator of the extrinsic pathway
- The secretion of fibrinolytic inhibitors, such as plasminogen activator inhibitor (PAI)

Endothelial cells are also able to synthesize and express tissue factor when activated by bacterial endotoxin or cytokines such as tumor necrosis factor (TNF) or interleukin I (IL-1); this endothelial expression of tissue factor activates the extrinsic pathway. Activated endothelial cells also bind factors IXa and Xa, further enhancing and localizing hemostatic activity.



Components: Platelets


Menu



- Platelets
 - Normally inactive
 - Activated by vascular injury
 - Deform upon activation
- Activated platelets

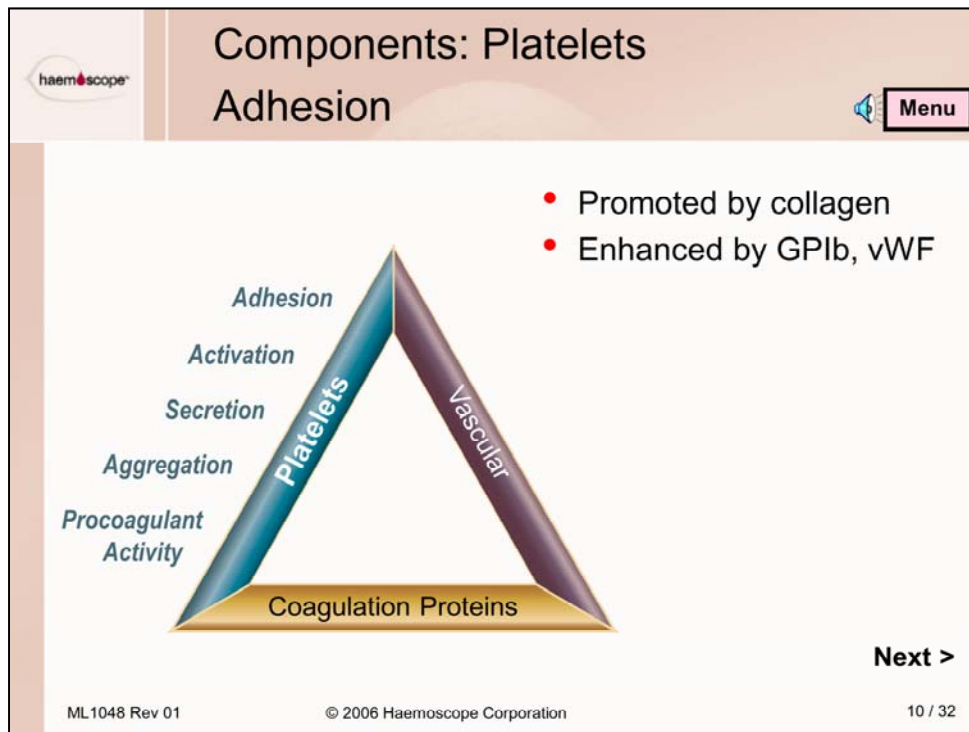
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Platelets are small spherical cells, with smooth surfaces, that circulate in liquid blood in an inactive state until activated at the location of a vascular injury. The activated platelets deform, losing their smooth surface, and bind to the subendothelium forming a center for massive thrombin generation and clot formation.

Platelet activation:

- Initiates the pathways associated with platelet release reactions
- Expresses phospholipids on the platelet surface required for the assembly of coagulation complexes and subsequent thrombin generation,
- Expresses adhesion molecules allowing interaction with other cells and surfaces
- Expresses the receptors required for platelet adhesion



Injury to the vascular wall exposes platelets to proteins in the extracellular matrix that enhance platelet adhesion. These proteins include collagen (most important), proteoglycans, fibronectin, and other adhesive glycoproteins.

Contact with the extracellular matrix activates platelets to undergo three types of reactions:

- Platelet adhesion and shape change
- Secretion
- Aggregation.

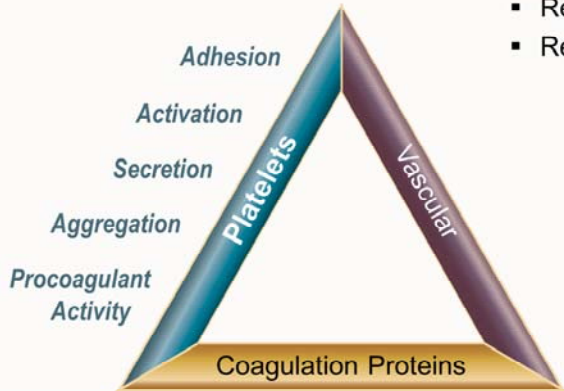
Collagen promotes adhesion of the platelets to the vascular extracellular matrix. Adhesion is subsequently enhanced by interaction between platelet surface receptors such as glycoprotein Ib (GPIb) and von Willebrand factor (vWF). This interaction stabilizes platelet adhesion against the shear forces of flowing blood.



Components: Platelets

Secretion


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- Enhances process
 - Release of dense bodies
 - Release of α -granules

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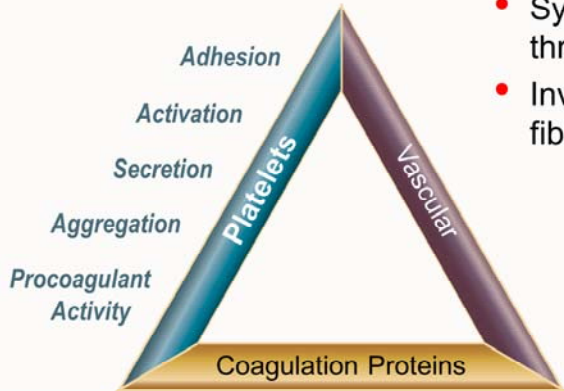
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The secretion reaction results in release of the contents of the dense bodies and alpha granules contained within the platelets. These dense bodies and alpha granules contain adenine nucleotides (ADP, ATP), ionized calcium, histamine, serotonin, and epinephrine. The alpha granules, also contain fibrinogen, fibronectin, factor V, von Willebrand factor, platelet-derived growth factor, and transforming growth factor alpha. The release of the contents of these granules enhances the local hemostatic process by further activating platelets, the vascular endothelium, and the coagulation pathways.



Components: Platelets Aggregation

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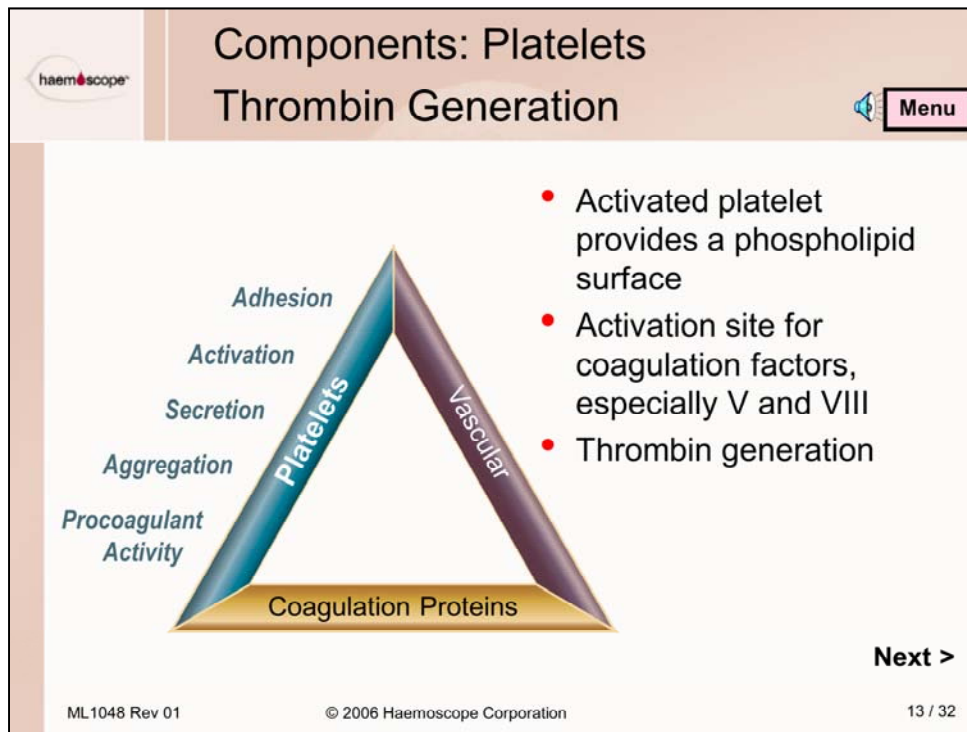


- Release of ADP
- Synthesis and release of thromboxane
- Involves GP IIb/IIIa and fibrinogen

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Platelet aggregation follows platelet adhesion, activation, and secretion. Aggregation also results from stimulation of locally produced thrombin. The release of ADP, plus the synthesis and release of thromboxane (TxA₂) from platelets, stimulates platelet aggregation and the subsequent formation of the primary hemostatic plug, or white clot. Platelet aggregation involves the interaction between the fibrinogen and glycoprotein IIb/IIIa receptors expressed on activated platelets.



Platelet activation also results in the expression of specific phospholipids on the platelet surface, providing a binding and activation site for coagulation factors, specifically factor VIII and factor V. Calcium is also an important cofactor in this binding/activation reaction. Thus, platelets also display procoagulant activity, and are considered the primary surface upon which thrombin is generated during normal hemostasis.

The thrombin-mediated conversion of fibrinogen to fibrin, plus thrombin activation of platelets, results in platelet contraction and the formation of the platelet-fibrin plug, or secondary hemostatic plug.

In summary, platelets play a major role in both localizing and controlling the generation of thrombin and subsequent clot formation. The mechanisms associated with this procoagulant activity of platelets include:

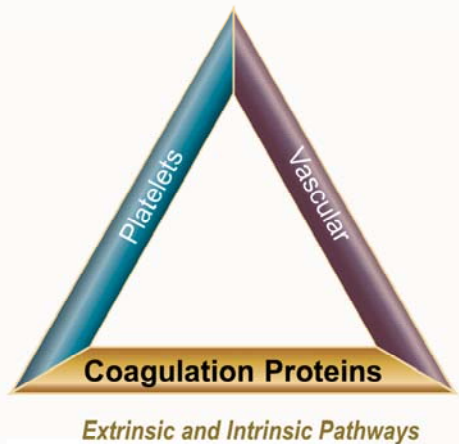
- Alterations in the phospholipid composition of platelet surface membranes
- Expression of binding proteins that permit binding of factors VIIIa and Va
- Expression of glycoprotein receptors which promote localization of the hemostatic reaction through adhesion and aggregation.



Components: Coagulation Proteins

Menu

- Tissue factor activates factor VII (extrinsic pathway)
- Extrinsic and intrinsic pathways
 - Converge at factor X
 - Models well *in vitro*
 - Do not model well *in vivo*
 - Extrinsic initiates thrombin generation
 - Intrinsic amplifies thrombin generation (factor V and VIII)



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The coagulation proteins normally circulate in an inactive form. Damage to the endothelium exposes blood to tissue factor, which in combination with activated Factor VII, begins the sequential activation of the remaining coagulation proteins in the extrinsic pathway, leading to the initial generation of thrombin.

As already discussed in conjunction with platelets and vascular components, the coagulation proteins and pathways are responsible for the generation of thrombin. Traditionally, coagulation has been viewed as extrinsic and intrinsic pathways, which converge at factor X to form the final common pathway.

For *in vitro* settings, the separation works relatively well; however, for *in vivo* settings, the separation is obscured, and the pathways appear to serve different functions in thrombin generation. The extrinsic pathway is responsible for initiating thrombin generation upon exposure or expression of tissue factor, whereas the intrinsic pathway is responsible for amplifying thrombin generation through thrombin-mediated activation of factors V and VIII.



Components: Coagulation Proteins

Thrombin Generation


Menu

- **Thrombin generation**
 - Pivotal point for coagulation (PT, aPTT measure only 5% of total thrombin production)
 - Self promoting (activates Factor XI)
 - Self limiting (thrombin activates thrombomodulin)



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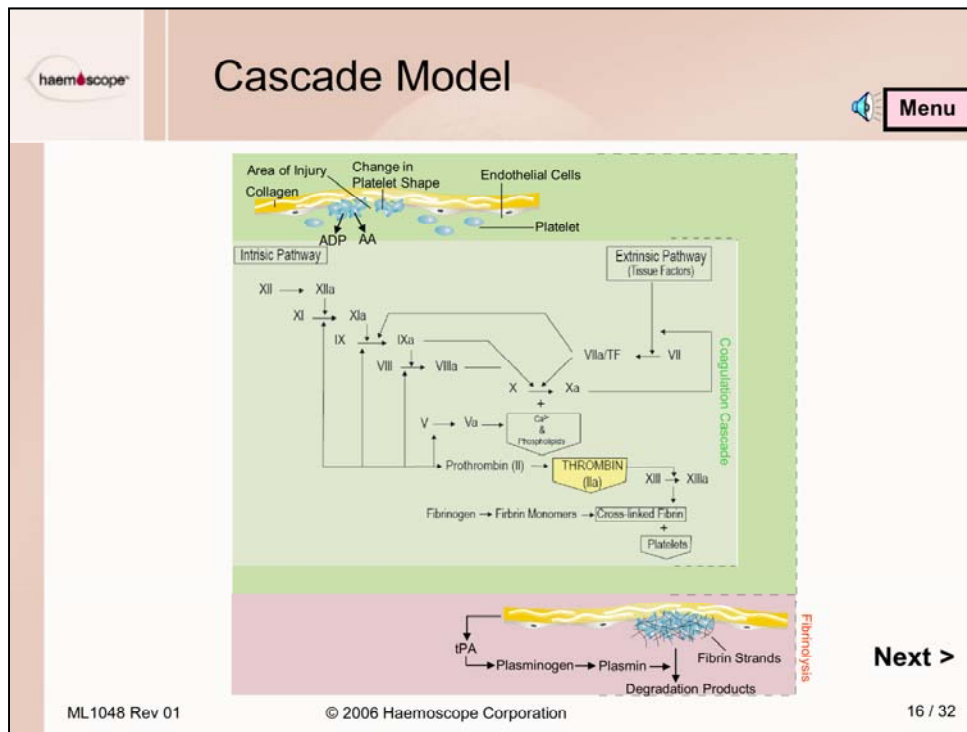
Thrombin generation is considered to be the pivotal point of coagulation. In addition to catalyzing the conversion of fibrinogen to fibrin, thrombin is also a potent activator of platelets, leading to further platelet activation and aggregation. PT and aPTT tests measure only 5% of total thrombin production.

In addition, thrombin also amplifies its own production by activating factor XI, leading to a rapid increase its concentration. This overwhelms the antithrombotic characteristics of the endothelium, allowing clot formation to proceed to completion.

Thrombin also affects both the local vasculature and inflammation, which influence the magnitude of the hemostatic response.

Finally, thrombin displays antithrombotic activity through interaction with thrombomodulin, a protein expressed on the surface of vascular endothelium.

Thus, thrombin both promotes and limits the extent of the hemostatic process.



These components come together and are reflected in the cascade model of hemostasis, represented in this graphic. This model works well for processes observed in the laboratory, where the components are isolated and the processes occur in plasma. However, by isolating the components, this model ignores their interactivity and balance as well as the contribution of platelets.

In vivo, the hemostatic reactions occur in whole blood, and are localized to a phospholipid surface.



Components: Cellular Elements

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- Subendothelial cells and leukocytes
 - Express tissue factor
 - Provide reaction surface for coagulation protein activation and binding (TF/VIIa complex formed)
 - Lead to thrombin generation (Factor X, IX, VIII, V, and XI)
- Phospholipid surface

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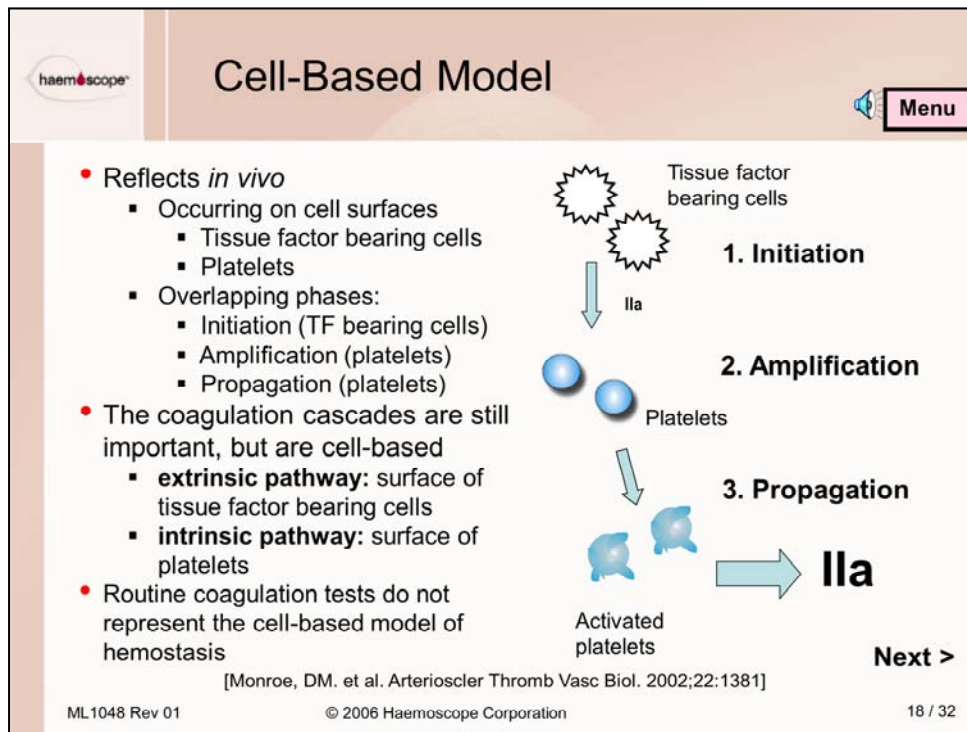
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Cellular elements play a significant role in hemostasis. The subendothelial cells and leukocytes express tissue factor, which activates coagulation proteins. Leukocytes contain an encrypted version of tissue factor that becomes active under certain conditions.

Upon exposure of the blood to tissue factor (TF), a tissue factor/factor VIIa complex is formed on the tissue factor bearing cell. In vitro tests suggest that this TF/VIIa complex activates factors X and IX, leading to the generation of thrombin in the vicinity of the cell. This thrombin can then activate both platelets and factors VIII, V, and XI.

These cells also provide a phospholipid surface on which the coagulation proteins can bind and activate. Activation of the coagulation proteins involves multiple pathways that converge to produce an explosive generation of thrombin — the final active enzyme in the coagulation pathway.

Once again, thrombin generation is considered the pivotal point in hemostasis due to thrombin's interaction with platelets, its further activation of coagulation proteins, and its effects on the vascular endothelium.



A newer hemostasis paradigm is presented in the cell-based model. The addition of cellular elements is reflected in the cell-based model of hemostasis. This model represents thrombin generation as a process occurring on two types of cell surfaces — tissue factor bearing cells and platelets. It occurs in three overlapping phases:

- Initiation
- Amplification
- Propagation

During the initiation phase, factor VII interacts with the tissue factor expressed on the surface of cells, such as extravascular tissue cells, endothelial cells, or monocytes. This interaction activates the extrinsic pathway, which leads to the generation of a small amount of thrombin which in turn activates platelets and factors V, VIII, and XI of the intrinsic pathway during the amplification phase.

In the propagation phase, the combination of platelet and coagulation factor activation generates a burst of thrombin sufficient to form a stable hemostatic platelet-fibrin clot.

The coagulation cascade still plays a role in hemostasis, but the pathways are dependent on interactions at a cellular surface, rather than in plasma. In the cell-based model, the extrinsic pathway works on the surface of tissue factor bearing cells, and the intrinsic pathway works on the surface of platelets.

The waterfall coagulation cascade model still plays a role in hemostasis, but the pathways are dependent on

interactions at a cellular surface, rather than in plasma. In the cell-based model, the extrinsic pathway works on the surface of tissue factor bearing cells, and the intrinsic pathway works on the surface of platelets.

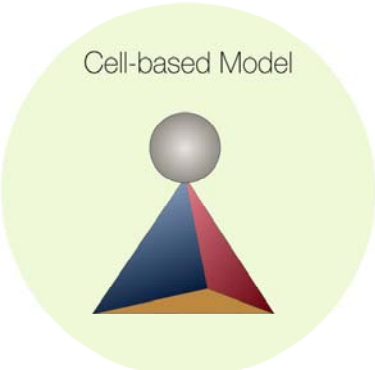


Normal/Balanced Hemostasis

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- Multiple feedback mechanisms maintain balance

Cell-based Model



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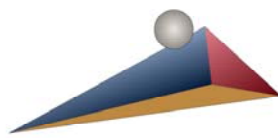
An important point regarding hemostasis is that under normal conditions, the activities and interactions among these four components function to maintain balance through a multitude of regulatory and feedback mechanisms. For example, a change in platelet activity will generate a change in the vascular, coagulation protein, and cellular components, keeping the whole system in balance.



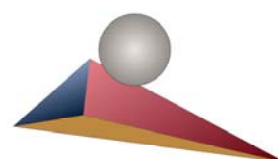
Abnormal/Unbalanced Hemostasis

 Menu

- Imbalance when mechanisms are overwhelmed
 - Surgery
 - Trauma
 - Disease
 - Drugs



Hypocoagulable



Hypercoagulable

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Surgical interventions, trauma, disease states, or drugs may overwhelm these regulatory mechanisms, causing a hemostatic imbalance and resulting either in a risk of bleeding or thrombosis. Abnormal hemostasis occurs when the activities and interactions of the hemostatic components are out of balance.



Hemostasis

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- Clot: The end product of hemostasis
 - Platelet plug formation (white clot)
 - Platelet-fibrin(ogen) clot formation (red clot)
 - Fibrinolysis

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When all the hemostasis processes are put together, the end product is clot formation. The process consists of three separate but highly interrelated steps:

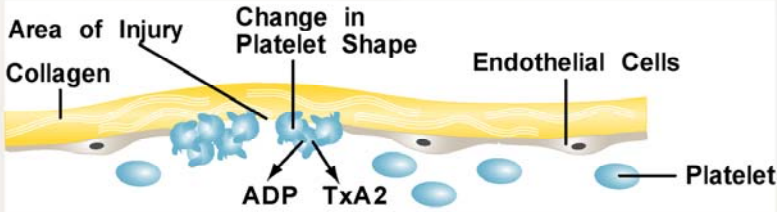
- Platelet plug formation
- Platelet-fibrin(ogen) clot formation
- Clot breakdown or fibrinolysis.



Platelet Plug Formation


Menu

- Endothelial damage: exposure to collagen
 - Promotes platelet adherence and activation
 - Platelet recruitment
 - Platelet aggregation
 - Results in formation of platelet plug (white clot)



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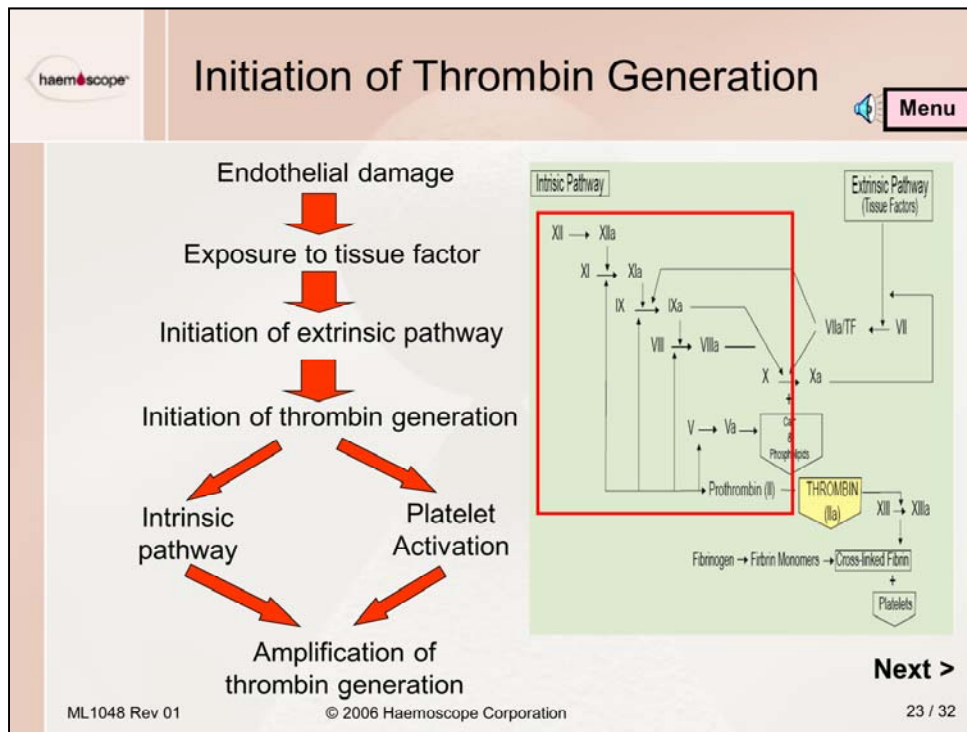
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Platelet plug formation is initiated by damage to the endothelium. This damage can occur through:

- Physical trauma to the vessel
- Chronic overexposure to stress hormones or inflammatory mediators
- Physical rupture of plaque, such as in coronary artery disease

Endothelial damage results in the exposure of platelets to collagen, which in turn promotes platelet adherence and activation.

Activated platelets secrete both ADP from dense granules and thromboxane, which is synthesized via the arachidonic acid pathway. ADP and thromboxane both promote further platelet recruitment and aggregation. A weak structure forms resulting in the formation of a platelet plug, or white clot.



Endothelial damage also results in exposure of the blood to tissue factor, which is found in the extra-vascular tissues.

After the initial generation of a small amount of thrombin, the tissue factor pathway is rapidly inhibited by activation of tissue factor pathway inhibitor. However, the thrombin that is generated is sufficient to activate platelets to build more platelet surface through aggregation and to produce a surface conducive to procoagulant activity through the expression of phospholipids. In addition, the initial amount of thrombin activates factors V, VIII, and XI in the intrinsic pathway. Activation of these factors, along with the creation of a platelet procoagulant surface, allows an explosion or amplification of thrombin generation.

Intravascular sources of tissue factor have also been demonstrated; these include endothelial cells and monocytes. They are especially important in diseases which involve a strong inflammatory component, such as sepsis. Exposure of tissue factor initiates the activation of the extrinsic or tissue factor pathway, which in turn initiates thrombin generation.



Fibrin-Platelet Clot Formation

 Menu

- Thrombin generation the pivotal point of the coagulation process
- Thrombin prothrombotic actions
 - Platelet activation
 - Amplification of thrombin generation
 - Fibrin clot development through conversion of fibrinogen to fibrin
- Result: Platelet-fibrin(ogen) clot (red clot)

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Thrombin generation is the pivotal point of the coagulation process. The prothrombotic characteristics of thrombin include:

- Platelet activation
- Amplification of thrombin generation
- Fibrin clot development through conversion of fibrinogen into fibrin and activation of the three-dimensional cross-linking of fibrin.

The interaction of platelets and thrombin generation results in formation of the platelet-fibrin(ogen) clot (red clot), a mechanical device that impedes blood loss from the vasculature. Both white and red blood cells are also mixed within the clot matrix. The importance of these blood cells to clot structure and function is still under investigation, and may change depending on different disease states and drug interventions.

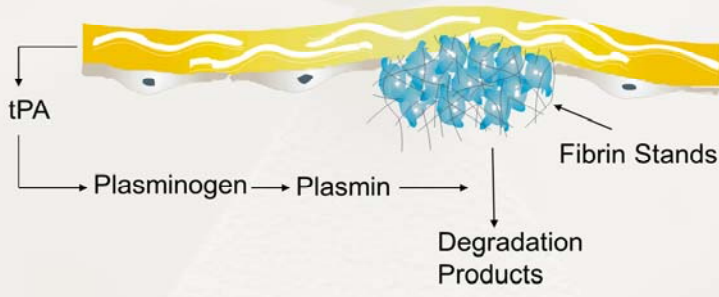
The structure and physical properties of the clot play an important role in the effectiveness of blood coagulation and clot breakdown.



Fibrin Formation: Initiation of Fibrinolysis


Menu

- Tissue plasminogen activator binds to fibrin
 - Converts plasminogen to plasmin
- Plasmin breaks down fibrin



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Clots play an important role in the healing process; they are temporary structures, dissolving once vascular repair occurs.

The clot breaks down in the process of fibrinolysis. This is initiated simultaneously with fibrin formation in the early phases of hemostasis. Tissue plasminogen activator (tPA) is continually released into the blood by endothelial cells. Free tPA has low plasminogen activating ability, but the binding of tPA to fibrin significantly increases tPA's activity. Activation of tPA converts plasminogen, a proenzyme, to plasmin, a catalytic enzyme that breaks down the fibrin network.

Plasmin breaks down fibrin, resulting in the formation of fibrin degradation products. Fibrinolytic activity is regulated by the ability of tPA to bind to fibrin. The clot gradually breaks down, starting with fibrin in contact with tPA near the outside of the clot. Fibrin within the clot is initially protected from exposure to tPA.

Fibrinolysis is also regulated by the release of plasminogen activator inhibitor (PAI-1) from the endothelium.

The slide features a light beige background with a faint, large image of a blood clot. The layout includes a header bar with the 'haemoscope' logo on the left, the title 'Hemostasis' in the center, and a 'Menu' button with a speaker icon on the right. The main content area displays the title 'Monitoring Hemostasis' in the center. At the bottom, there is a 'Next >' button on the right and footer text on the left: 'ML1048 Rev 01', '© 2006 Haemoscope Corporation', and '26 / 32'.

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Hemostasis

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Monitoring Hemostasis

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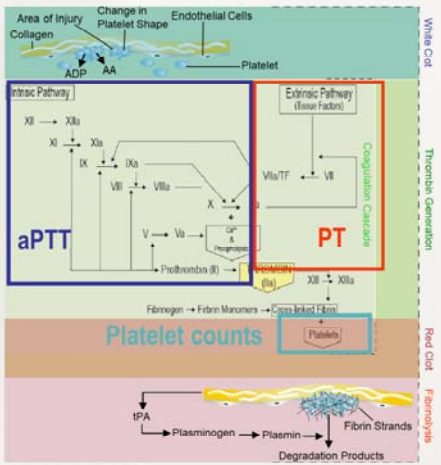
Various tests have been developed to monitor hemostasis. However, because hemostasis is a complex process, many of these tests reflect only a part of it.



Cascade Model: Tests


Menu

- Represents hemostasis
 - Two independent activation pathways
 - Pathways converge at the final common pathway
- PT, aPTT: based on cascade model
 - Measure coagulation factor interaction in solution
 - Determine if adequate levels of coagulation factors are present for clot formation



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In the cascade model, hemostasis is represented as two somewhat independent coagulation protein activation pathways that converge at the final common pathway, resulting in thrombin generation and fibrin formation.

Two of the routine coagulation tests, PT and aPTT, are based on this cascade model; in these tests, components are separated and tested in isolation. The end point for both tests is initial fibrin generation (5% of the fibrin to be generated), and thus the tests measure only a minor part of the entire hemostatic process — the lag phase until initial thrombin generation. In addition, the tests measure only how coagulation factors interact in solution, rather than on a cellular surface.

Finally, PT and aPTT determine only if the coagulation factors are present at levels adequate for clot formation. Platelet counts provide the number of platelets available, but not the functionality of the platelets. D-DIMER and FDP levels provide a quantitative rather than a functional description of fibrinolysis.



Monitoring: Cell Based Model

Menu

- Whole blood sample
 - Platelets
 - Coagulation factors
 - Cellular/plasmatic factors
- TEG® analysis
 - Coagulation factors
 - Fibrinogen
 - Platelets
 - Fibrinolytic factors
 - Inflammatory cells
 - Mediators

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Monitoring hemostasis using the cell-based model requires a whole blood test, as in TEG® analysis, in order to measure the effect of the interactions among platelets, coagulation factors, and other cellular or plasmatic elements. *In vitro* tests use plasma, and are not able to measure the effect of the vascular endothelium on hemostasis, a limitation in all plasma tests. PT, aPTT, TT, D-DIMER, and many other laboratory tests are plasma-based assays that miss the impact of the cellular elements of platelet activation on thrombin generation, and so do not represent the cell-based model.

Because the TEG analyzer uses a whole blood sample, it reflects the cell-based model of hemostasis. The TEG system measures the net effect of all the blood-borne components of hemostasis, such as coagulation factors, fibrinogen, platelets, fibrinolytic factors, inflammatory cells, and mediators.



Monitoring: Hemostatic Process

Menu

- Hemostatic process: cell based model plus red blood cells, white blood cells, etc.
- Activation → clot formation → clot lysis
- Entire process: TEG system

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The hemostatic process extends beyond the cell-based model, which does not include interaction with white blood cells, red blood cells, and other elements that are measured by TEG analysis; but these are not measured by PT, aPTT, TT, D-DIMER, and platelet counts.

Also, the hemostatic process is dynamic, and the components interact differently as the process moves from activation to clot formation to clot lysis. Monitoring hemostasis should look at all components of the system from start to finish. Most tests like PT, aPTT, TT, and platelet count tend to focus on one component at a specific point in the process, whereas the TEG system monitors the interaction of all components throughout the process.



Monitoring Insights

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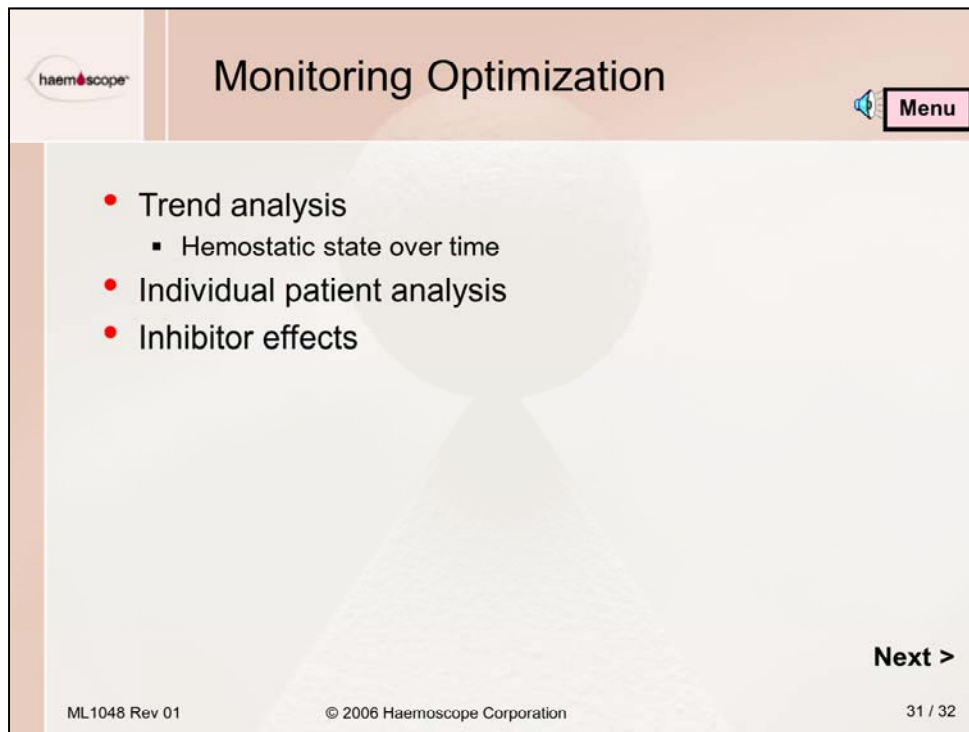
- Results are used in conjunction with patient status:
 - Patient clinical condition (bleeding/not bleeding)
 - Phase in medical intervention
 - Type and dose of drug therapy
 - Patient history
- TEG testing shows net effect “whole picture” of hemostasis at that point in time:
 - Identifies a “factor deficiency,” but not which factor
 - Identifies a platelet defect, but does not distinguish between platelet deficiency and platelet dysfunction

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As with any *in vitro* test, interpretation of results must be done in conjunction with the patient's status to fully understand how the results fit in with the clinical picture. The interpretation of a TEG analysis for a patient who is bleeding may be completely different from the interpretation for someone who is not bleeding. Other factors that may influence the meaning of a TEG analysis include the phase of a medical intervention, the patient's clinical condition and history, the type and dose of a specific drug therapy.

Also, a TEG analysis provides results only for the net effect of blood-borne hemostatic factors at a given point in time. Although it identifies a factor deficiency in general, it does not identify which factor or factors are deficient. The same principle applies to platelets; a TEG analysis identifies a platelet defect, but it does not differentiate between a platelet deficiency and a platelet dysfunction.

The slide is titled "Monitoring Optimization" and features the Haemoscope logo in the top left corner. A "Menu" button with a speaker icon is in the top right. The main content area lists three bullet points: "Trend analysis" (with a sub-bullet "Hemostatic state over time"), "Individual patient analysis", and "Inhibitor effects". A "Next >" button is in the bottom right. The footer contains the text "ML1048 Rev 01", "© 2006 Haemoscope Corporation", and "31 / 32".

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Monitoring Optimization

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- Trend analysis
 - Hemostatic state over time
- Individual patient analysis
- Inhibitor effects

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Another important aspect in monitoring hemostasis is trend analysis, since many clinical procedures cause alterations in the hemostatic state over time. Also, not all patients respond to a clinical procedure or treatment in exactly the same way. With any hemostasis monitoring, it is important to obtain a baseline profile prior to a procedure or treatment, so that the magnitude of any change can be determined.

Optimal outcomes are achieved when hemostatic treatments or interventions can be personalized to the individual patient, rather than to a “standard” patient. Since the TEG analyzer can be used as a point of care instrument, it can be used to monitor changes in the hemostatic status of a patient at the bed side both before and after treatment or intervention, providing a means to deliver an optimal outcome.

Identifying the effects of different classes of inhibitors on platelet function allows the clinician to make well-informed decisions for administering personalized antiplatelet therapy. The addition of PlateletMapping™ assays to the set of TEG analyzer tests provides the clinician with results that aid in making such decisions.



Summary

Menu

- Hemostasis
 - Interactive components
 - Balance
- Hemostatic tests
 - Cascade model: limited (PT, aPTT)
 - Cell-based model: whole blood (TEG)
- Monitoring hemostasis
 - Appropriate drugs
 - Reduction in health care costs
- Personalized treatment → improved patient care

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In summary, when looking at hemostasis, it is important to remember that it is a system with highly interactive components. In normal hemostasis, these components maintain a balance. An imbalance can cause either excessive bleeding or thrombosis.

Many of the hemostatic tests are plasma tests based on the cascade model, and have limitations because they test only part of the system; they do not test the interactivity of the components. The cell-based model provides a more comprehensive view of hemostasis; it requires testing of a whole blood sample, as with the TEG system.

Monitoring hemostasis in its entirety provides clinicians with the information necessary to:

- Provide personalized treatment and improve patient care
- Use hemostatic drugs more appropriately
- Reduce health care and hospital costs.

Costs can be lowered by a reduction in:

- Blood product usage
- Number of re-operations to explore for bleeding
- Long term care due to post-thrombotic events
- Length of hospital stay.



Basic Clinician Training

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Hemostasis Hemostatic Monitoring

Test your knowledge of hemostasis by answering the questions in the slides that follow.

[Begin Exercises](#)[Skip Exercises](#)

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Exercise 1

Normal hemostasis is characterized by a functional _____ between the procoagulant pathways/components and the antithrombotic and anticoagulant pathways/components.

[Answer](#)[Next](#)[Menu](#)

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Exercise 2

What is the typical initiating event of the hemostatic process?

- a) Platelet activation
- b) Thrombin generation
- c) Endothelial damage
- d) Plasmin generation

Answer

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Exercise 3

What is the pivotal point in the activation of the coagulation pathways?

- a) Tissue factor expression
- b) FXII activation
- c) FXa generation
- d) Thrombin generation
- e) Fibrin formation
- f) Platelet activation

[Answer](#)[Next](#)[Menu](#)

Exercise 4

Which coagulation pathway is responsible for the *initiation* of thrombin generation?

- a) Intrinsic
- b) Extrinsic

Which coagulation pathway is responsible for the *amplification* of thrombin generation?

- a) Intrinsic
- b) Extrinsic

[Answer](#)[Next](#)[Menu](#)

Exercise 5

In the cell-based model of hemostasis, where do the intrinsic and extrinsic pathway activities occur?

- a) On neutrophils
- b) On the tissue-factor bearing cells and platelets
- c) In the plasma
- d) On endothelial cells

[Answer](#)[Next](#)[Menu](#)



Exercise 6

Which of the following statements does **not** describe PT and aPTT tests?

- a) They both measure how coagulation factors interact in solution.
- b) They both use fibrin formation as a static end point.
- c) They both demonstrate the effect of thrombin generation on platelet function.
- d) They both demonstrate the function of the extrinsic and intrinsic pathways, respectively.

[Answer](#)[Next](#)[Menu](#)

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Exercise 7

The TEG system is a whole blood hemostasis analyzer that can measure the contribution of which of the following hemostatic components? (select all that apply)

- a) Enzymatic factor
- b) Fibrinogen
- c) Platelets
- d) Fibrinolytic pathway
- e) Endothelial cells

[Answer](#)[Next](#)[Menu](#)

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Exercise 8

The TEG analyzer provides results that help distinguish between surgical bleeding and bleeding due to a coagulopathy.

True or False?

Answer

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Answer to Exercise 1

Normal hemostasis is characterized by a functional **balance** between the procoagulant pathways/components and the antithrombotic and anticoagulant pathways/components.

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Answer to Exercise 2

What is the typical initiating event of the hemostatic process?

- a) Platelet activation
- b) Thrombin generation
- c) Endothelial damage**
- d) Plasmin generation

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Answer to Exercise 3

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- d) Thrombin generation**
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Answer to Exercise 4

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Answer to Exercise 5

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Answer to Exercise 6

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Answer to Exercise 7

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- c) Platelets**
- d) Fibrinolytic pathway**
- e) Endothelial cells

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Answer to Exercise 8

The TEG analyzer provides results that help distinguish between surgical bleeding and bleeding due to a coagulopathy.

True

End

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