



Leiden University
Medical Center

Een bloedstollend onderwerp



- De werking van de stolling begrijpen
- Welke rol speelt het laboratorium

Prof. Dr H.C.J. Eikenboom

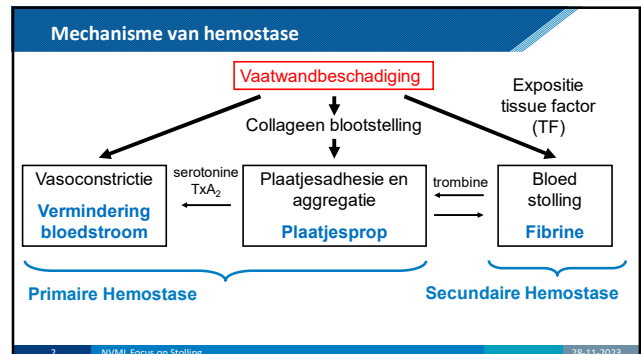
Trombose en Hemostase

LEIDEN

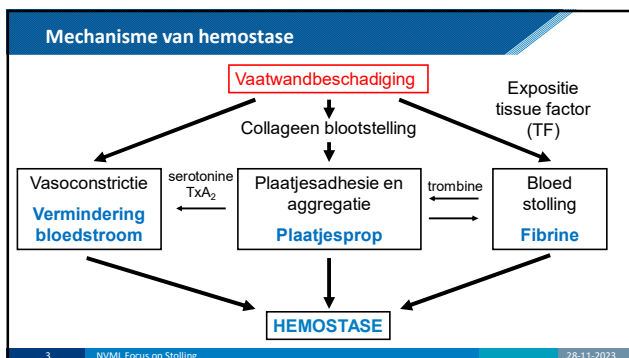
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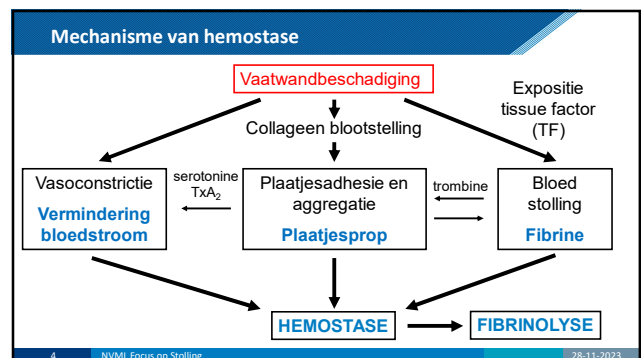
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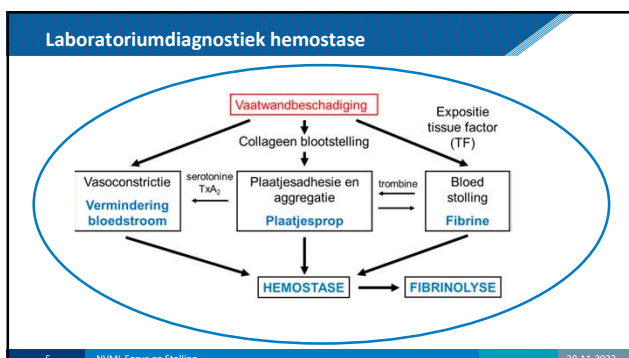
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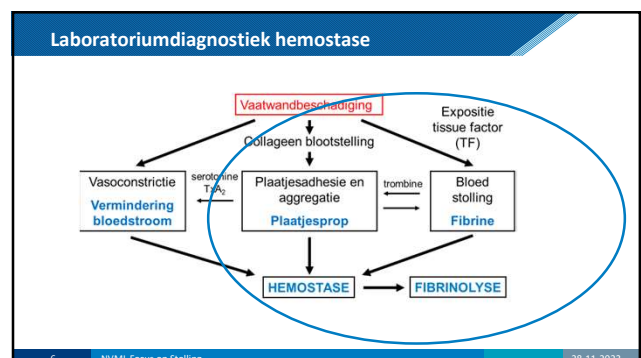
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Laboratoriumdiagnostiek hemostase

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graph TD
    A[Vaatswandbeschadiging] --> B[Collageen blootstelling]
    A --> C[Expositie tissue factor TF]
    B --> D[Plaatjesadhesie en aggregatie  
Plaatjesprosp]
    C --> E[Bloed stolling  
Fibrine]
    D --> F[HEMOSTASE]
    E --> F
    E --> G[FIBRINOLYSE]
    F --> G
    D --> H[Vasoconstrictie  
Vermindering bloedstroom]
    H --> I[serotonine  
TxA2]
    I --> D
    D --> J[thrombine]
    J --> E
    
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The diagram illustrates the physiological processes of hemostasis and fibrinolysis. It begins with 'Vaatswandbeschadiging' (Vessel wall damage), which triggers 'Collageen blootstelling' (Collagen exposure) and 'Expositie tissue factor TF' (Exposure of tissue factor). 'Collageen blootstelling' leads to 'Plaatjesadhesie en aggregatie' (Platelet adhesion and aggregation), which results in 'Plaatjesprosp' (Platelet plug). 'Expositie tissue factor TF' leads to 'Bloed stolling' (Blood clotting), which results in 'Fibrine'. Both 'Plaatjesprosp' and 'Fibrine' contribute to 'HEMOSTASE' (Hemostasis). 'Fibrine' also leads to 'FIBRINOLYSE' (Fibrinolysis). 'HEMOSTASE' also leads to 'FIBRINOLYSE'. 'Plaatjesadhesie en aggregatie' leads to 'Vasoconstrictie' (Vasoconstriction), which results in 'Vermindering bloedstroom' (Reduction of blood flow). 'Vasoconstrictie' is mediated by 'serotonine' and 'TxA2', which in turn lead to 'Plaatjesadhesie en aggregatie'. 'Plaatjesadhesie en aggregatie' also leads to 'thrombine', which leads to 'Bloed stolling'.

Plaatjesadhesie en aggregatie

The diagram illustrates the process of platelet adhesion and aggregation. It shows an endothelial cell with subendothelial collagen. Von Willebrand Factor (VWF) is shown in a coiled, inactive state near the endothelial cell and an uncoiled, active state near platelets. An inactivated platelet is shown with GPIb and collagen receptors. An activated platelet is shown with GPIIb/IIIa receptors. The flow of blood is indicated by a red arrow.

Labels in the diagram include: GPIb, Collagen receptor, Inactive $\alpha_v\beta_3$, Coiled, inactive VWF, Von Willebrand Factor (VWF), ENDOTHELIAL CELL, Subendothelial collagen, INACTIVATED PLATELET, Uncoiled active VWF, ACTIVATED PLATELET, Active $\alpha_v\beta_3$, and FLOW OF BLOOD.

Source: Leebeek and Eikenboom; N Engl J Med 2016;375:2067-80

Plaatjesadhesie en aggregatie

Laboratoriumdiagnostiek hemostase

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graph TD; A[Vaotwandbeschadiging] --> B[Collageen blootstelling]; A --> C[Expositie tissue factor TF]; B --> D[Vasocostrictie Vermindering bloedstroom]; B --> E[Plaatjesadhesie en aggregatie Plaatjesprop]; C --> E; C --> F[Bloed stolling Fibrine]; E --> D; E --> G[HEMOSTASE]; E --> F; F --> G; F --> H[FIBRINOLYSE]; D --> G; G --> H; I[serotonine TxA2] --> E; J[trombine] --> F;
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The diagram illustrates the physiological process of hemostasis and its laboratory diagnosis. It starts with 'Vaotwandbeschadiging' (Vessel wall damage), which leads to 'Collageen blootstelling' (Collagen exposure) and 'Expositie tissue factor TF' (Exposure of tissue factor). 'Collageen blootstelling' leads to 'Vasocostrictie Vermindering bloedstroom' (Vasoconstriction, reduced blood flow) and 'Plaatjesadhesie en aggregatie Plaatjesprop' (Platelet adhesion and aggregation, platelet plug). 'Expositie tissue factor TF' leads to 'Plaatjesadhesie en aggregatie Plaatjesprop' and 'Bloed stolling Fibrine' (Blood clotting, fibrin). 'Plaatjesadhesie en aggregatie Plaatjesprop' leads to 'Vasocostrictie Vermindering bloedstroom', 'HEMOSTASE' (Hemostasis), and 'Bloed stolling Fibrine'. 'Bloed stolling Fibrine' leads to 'HEMOSTASE' and 'FIBRINOLYSE' (Fibrinolysis). 'HEMOSTASE' leads to 'FIBRINOLYSE'. 'serotonine TxA2' (serotonin, TXA2) is shown as a factor in platelet adhesion and aggregation. 'trombine' (thrombin) is shown as a factor in blood clotting. The 'Bloed stolling Fibrine' box is circled in blue.

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Secundaire hemostase

The diagram illustrates the secondary hemostatic cascade. At the bottom, the endothelium is shown with subendothelium below it. A 'TF' (Tissue Factor) molecule is located near the endothelium. Above the endothelium, a 'poly P' (polyphosphate) molecule is shown. The cascade involves several clotting factors: VIIa, Xa, IXa, and Xa. These factors are activated by the 'TF' and 'poly P' molecules. The activated factors then interact with 'platelets' (represented by yellow, irregular shapes) and 'fibrin' (represented by a network of fibers). The final product is a 'poly P' molecule, which is released from the platelets. The diagram also shows 'subendothelium' and 'endothelium' layers.

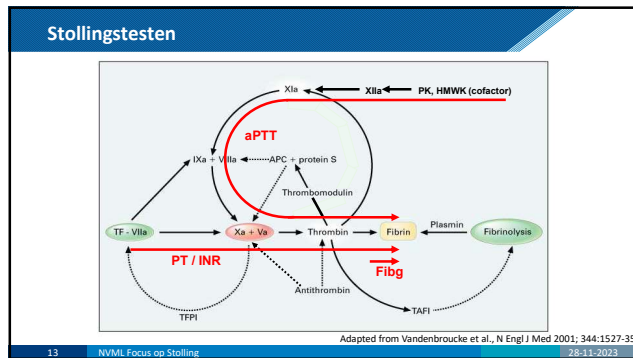
- Start met tissue factor (TF)
- Opeenvolgende proteolytische reacties
- Op het oppervlak van geactiveerde bloedplaatjes
- Pro-enzyme worden omgezet in enzymen
- Bij veel reacties ook cofactoren belangrijk

Versteeg et al., Physiol Rev 2013;93:327-58

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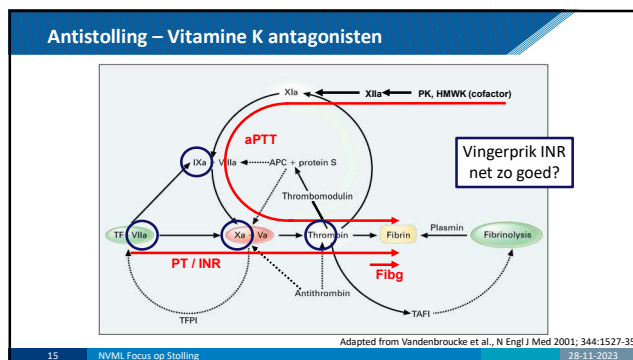


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Antistolling

Vitamine K antagonisten
"gas loslaten"

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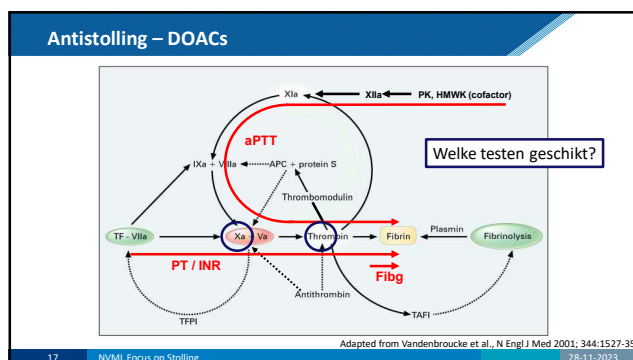
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Antistolling

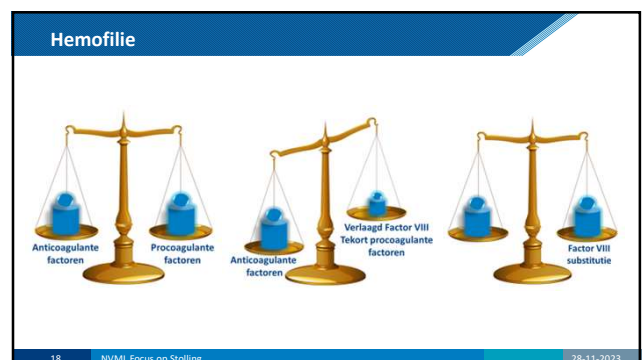
Vitamine K antagonisten
"gas loslaten"

Heparine/LMWH
Directe orale anticoagulantia
"remmen"

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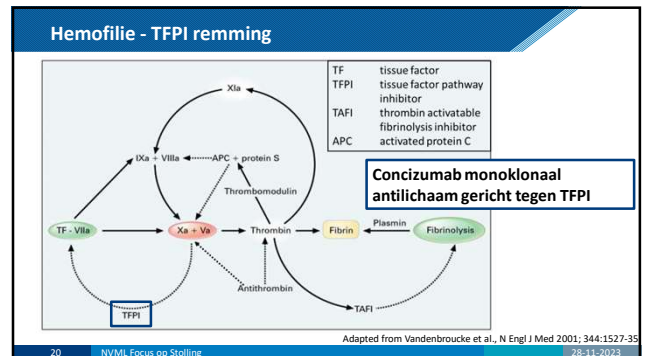
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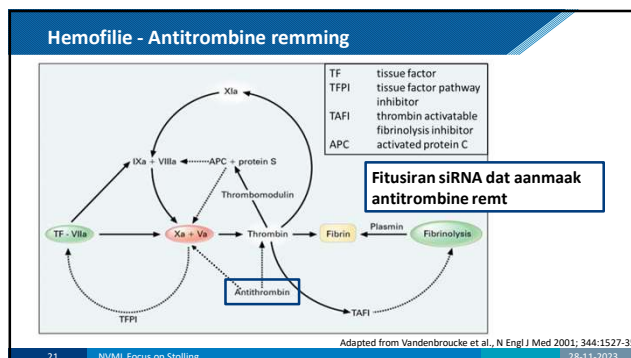
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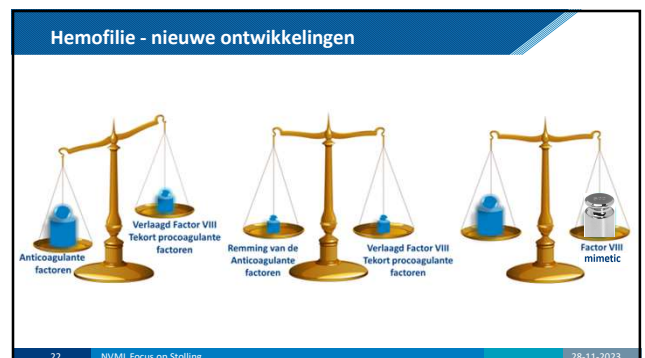
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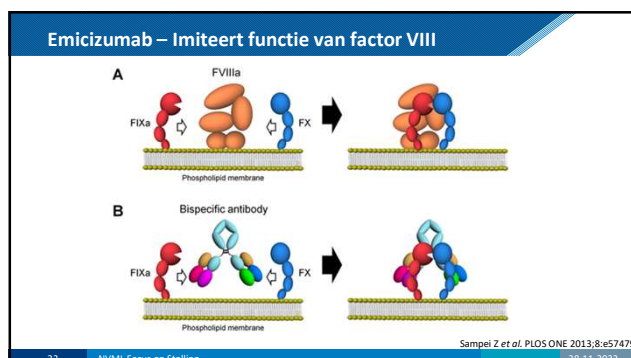
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Take home messages

- Goed begrip van complexe stolling essentieel
- Veel nieuwe (anti)stollingsmedicijnen
- Uitdagingen voor het laboratorium
- De juiste test op het goede moment

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