Thrombosis

Jeffrey S. Jiang, M.D.
Assistant Professor of Clinical Pathology

Overview of Normal Thrombosis
- Perturbation of endothelial cells
- Exposure of subendothelial components
- Adherence, Activation and Aggregation of Platelets
- Activation of Coagulation
- Inhibition by Fibrinolysis
- Stasis

Protective Mechanisms
- Endothelial Antithrombotic factors
- Regulation
  - Anticoagulation factors: plasma protease inhibitors
  - Degradation of coagulation factors
- Dissolution of thrombi (Fibrinolysis)
Primary Hemostasis

- Adhesion
  - Platelet GPIb binds to vWF
  - Platelet GPVI binds to collagen

- Activation & Recruitment
  - Spreading; phospholipid exposure
  - Secretion of vasoactive substances

- Aggregation
  - Platelet to platelet bridging by GPIIb/IIIa binding to fibrinogen

Adhesion

- Collagen
- Thrombin
- IIb/IIIa ligands
- Thromboxane
- ADP
- Serotonin
- Epinephrine

Platelet Plug Formation

- Activating
- Extension
- Permeability

Prostaglandin and Thromboxane Synthesis
Antithrombotic Factors

Virchow’s Triad

- Endothelial Injury
- Stasis or Turbulence of Blood
- Blood Hypercoagulability
**Inherited Hypercoagulable States**

**Common**
- Factor V Leiden (resistance to activated protein C)
- Prothrombin 20210A Polymorphism
- Methyleradonfolate gene polymorphism (MTHFR)
- Homozygous cystathionine-β-synthase deficiency
- Increased FVIII Levels

**Rare**
- Antithrombin Deficiency
- Protein S Deficiency
- Protein C Deficiency

**Acquired Hypercoagulable States**
- Antiphospholipid Antibody Syndrome
- Malignancy
- Heparin-Induced Thrombocytopenia
- Abnormalities of Vessel Wall
- Disturbances of blood flow
- Central Venous Catheters
- Immobilization
- Disseminated Intravascular Coagulation
- Oral contraceptives
- Sickle cell disease
- Smoking
- Myocardial Infarction
- Atrial Fibrillation
- Prosthetic Heart Valves
Pulmonary Thromboembolism

Antithrombotic Therapy: Heparin

NEJM 337(10):689
Anti-thrombotic Therapy: © Coumadin ©

- Oral anti-coagulant
- Vitamin K-dependent carboxylase.
- gamma carboxy-glutamic acid on coagulation factors
- Coumadin affects newly synthesized enzymes
- Vitamin K-dependent Factors
  - Factor II, VII, IX, X
  - Protein C and S
- Reversed with Vitamin K

Anti-platelet Therapy: © Aspirin ©

Anti-platelet Therapy: clopidogrel