The Bruising Child

Dr Beatrice Nolan
Consultant Haematologist

Our Lady's Children's Hospital, Crumlin

How to make a clot
- plug holes so blood can't escape
  - Constrict the blood vessel in the region of the hole
  - Form a platelet plug
  - Seal that plug with fibrin
Stages of Hemostasis

- **Primary hemostasis**
  - von Willebrand factor (vWF), platelets, fibrinogen

- **Secondary hemostasis**
  - Coagulation cascade

- **Tertiary hemostasis**
  - Cross-linking of fibrin strands
  - Clot maturation and wound healing
Platelets

- fragments of cytoplasm shed by gigantic precursor cells in bone marrow
- no nucleus
- number
- life span

Primary haemostasis

Von Willebrand factor has 2 key roles in normal haemostasis

- Glues platelets to the subendothelium
- Serves as a carrier molecule for FVIII (free factor VIII is destroyed)
Secondary haemostasis

Intrinsic pathway
to generate a clot via the intrinsic pathway in a test tube, you only need things that are intrinsic to whole blood

Extrinsic pathway
to generate a clot via the extrinsic pathway in a test tube you need to add things that are extrinsic to whole blood

- In vitro – intrinsic and extrinsic pathways operate separately
- In vivo – co-dependent

Final common pathway

Coagulation Cascade

Intrinsic pathway

Extrinsic pathway

Tissue factor

Prothrombin Time

Prothrombin (II) → Thrombin

Fibrinogen (I) → Fibrin clot (XIII)
Prothrombin time (PT)

- Measures the extrinsic pathway (basically VII)
- Measures the common pathway (X, V, II, I)
- Doesn't measure TF

Factor VII

- Made by the liver
- Activated by vitamin K
- Synthesis is inhibited by warfarin
INR
international normalized ratio

• PT that's been mathematically corrected to allow for differences between laboratories

What prolongs PT

• Deficiency or inhibition of any of the factors in the extrinsic pathway (VII), or the common pathway (X, V, II, and/or fibrinogen)
• Liver disease
• Vitamin K deficiency
• Warfarin - II, VII, IX and X
• Heparin (to some extent) affects factors in all 3 pathways IIa, VIIa, IXa, Xa and Xia
Coagulation Tests

PT

VII

XII

Prekallikrein

XI

HMWK

IX

VIII

Fibrinogen → Fibrin

X

II

V

Thrombin time

Reptilase time

Clot stability test

stable fibrin clot

XIII

HMWK, high-molecular weight kininogen.

APTT

Measures

- intrinsic factor pathway
  (factors XII, XI, IX, VIII)

- common pathway (factors X, V, II, I)
Prolonged APTT

- Deficiency or inhibition of factors in the intrinsic factor pathway (XII, XI, IX and VIII) and the common pathway (X, V, II, I)
- Liver disease
- Vitamin K deficiency
- Unfractionated heparin (IIa, IXa, Xa and Xla)
- Warfarin
  - II, IX and X
  
  By the time the APTT goes up, the patient will be possibly at risk of bleeding

Coagulation Tests

PTT
- Prekallikrein
- HMWK
- XI
- IX
- VII
- X
- II
- V
- XIII
- Stable fibrin clot
- Clot stability test

PT

Fibrinogen → Fibrin

Thrombin time
Reptilase time

HMWK. High-molecular weight kininogen.
Mixing study

- Coagulation factor deficiency
- Inhibitor

Thrombin time

Thrombin time measures conversion of fibrinogen to fibrin
Prolonged thrombin time

- fibrinogen deficiency (qualitative or quantitative)
- D dimers— inhibit the conversion of fibrinogen to fibrin
- Heparin – inactivates thrombin added to the patient plasma

Fibrinogen assay

- Fibrinogen is the final coagulation factor precursor to fibrin
- Made in the liver
- Rapidly depleted during clotting
Reduced fibrinogen

- Afibrinogenaemia
- Hypofibrinogenaeemia
- Hypodysfibrinogenaeemia

Coagulation Tests

PTT

Thrombin time
Reptilase time

Fibrinogen → Fibrin

Stable fibrin clot

Clot stability test

HMWK, high-molecular weight kininogen.
Summary

• APTT - intrinsic pathway
• PT / INR - extrinsic pathway
• TT – fibrinogen to fibrin
• Fibrinogen - measures fibrinogen

Evaluation and diagnosis

History
• Age / sex
• Bleeding
• Haemostatic challenges
• Medical history
• Medication
• Family history

Physical examination
Laboratory tests
Bleeding history

Bruises: extensive, large, indurated, location

Petechiae

Bleeding
- gum bleeding
- epistaxis persistent after 15 minutes of pressure
- menstrual periods >7 days, heavy flow >3 days, soaking of pads, frequent staining of clothing
- umbilical cord stump bleeding

Deep muscle and joint bleeding

Haematemesis, melaena, haematuria, haemoptysis

- Recurrent bleeding from a single site suggests a structural abnormality

- Bleeding at many different sites suggests a systemic haemostatic defect
Medical History

- Liver disease
- Cholestasis, fat malabsorption, antibiotics, vitamin K deficiency
- Uraemia
- Drugs

Laboratory Screening Studies

- FBC and blood film
- Prothrombin time
- Activated partial thromboplastin time
- PT and APTT mixing studies
- Fibrinogen
- Thrombin time
Platelets

- Quantitative: Thrombocytopenia
- Qualitative: Platelet Function Disorders

Platelets

- Decreased Number: Thrombocytopenia
  - Decreased Production
  - Decreased Survival – Immune (ITP)
  - Increased Utilisation – DIC

- Defective Platelet function:
  - Acquired
  - Congenital
Acquired platelet function defects

- Drugs
  - Anti-inflammatories
    - Aspirin, NSAIDs,
  - Specific anti-platelet agents
    - Clopidogrel, Ticlopidine

- Systemic disease
  - Renal failure
  - Liver failure

- Haematological disease
  - MDS, myeloproliferative disorders

Case

- 4 yr old boy
- URTI 2 weeks ago
- Sudden onset bruising/petechiae
- PH: Nil
- FH: Nil
- Physical examination:
Investigations

- **FBC**: Hb 11g/dl; WCC 8x10^6/l; Platelets <10x10^9/l
- **PT** 14 sec; **APTT** 33 sec; **Fibrinogen** 2.0g/l
- **Treatment options**: Nil; IVlg; Steroids
- **Outcome**: 90% recovery; 10% chronic

von Willebrand Disease

The most common hereditary bleeding disorder

A quantitative or qualitative defect of VWF

VWF has two key roles in normal haemostasis

- Glues platelets to the subendothelium
- Serves as a carrier molecule for FVIII (free factor VIII is destroyed)
Haemophilia

deficiency or lack of factor VIII (haemophilia A) or factor IX (haemophilia B)

- 1:10,000 males FVIII > FIX x 6
- X-linked recessive
- severity consistent between family members
- 1/3 no family history / spontaneous mutation in FVIII/FIX genes
- Molecular diagnosis possible > 90%
- Carrier status of mother can be accurately predicted (Antenatal diagnosis via CVS at 11 weeks)

DISEASE SEVERITY

Degrees of severity in haemophilia

- Factor VIII or IX activity
- 50-200% Mild
- 5-50% Moderate
- 2-5% Severe
- <1%
Haemophilia

- When there is no family, infants with moderate/severe disease usually present:
  - post-circumcision bleeding
  - bad “toddler bruising”
  - soft tissue/muscle or joint bleeds at 6-18 months of age
  - RARE, intracranial, ilio-psoas, intra-abdominal, haematuria

Haemophilia - Treatment

**Aims of modern management**
- To prevent chronic joint damage
- To prevent life threatening bleed
- To avoid doing harm in terms of transmission viral / other potentially harmful agents