Bleeding and Thrombotic Disorders
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Bleeding and Thrombotic Disorders

**Bleeding disorders**
- von Willebrand disease
- Hemophilia
- DIC
- TTP/HUS

**Thrombotic disorders**
- Factor V Leiden
<table>
<thead>
<tr>
<th>“Platelet” bleeding</th>
<th>“Factor” bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial (skin)</td>
<td>Deep (joints)</td>
</tr>
<tr>
<td>Petechiae</td>
<td>Big bleeds</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>History of trauma *</td>
</tr>
</tbody>
</table>

* Includes prolonged bleeding after dental work
Petechiae vs. purpura
Bleeding and Thrombotic Disorders

Bleeding disorders
  • von Willebrand disease
Von Willebrand Disease

Things you must know

- Most common hereditary bleeding disorder
- Autosomal dominant
- vW factor decreased (or abnormal)
- Variable severity
What’s von Willebrand Factor?

- Huge multimeric protein
- Made by megakaryocytes and endothelial cells
- Two functions:
  - Glues platelets to subendothelium
  - Carries factor VIII (prevents its degradation)
vWF is the “glue” that sticks platelets to subendothelial proteins
vWF also carries FVIII, preventing it from degrading
Symptoms of Von Willebrand Disease

- Mucosal bleeding in most patients (due to decreased platelet adhesion)
- Deep joint bleeding in severe cases (due to decreased fibrin formation)
Von Willebrand Disease

Diagnosis
• Bleeding time: prolonged
• PTT: prolonged (in severe cases)
• PT/INR: normal

Treatment
• Desmopressin (↑ release of vWF and VIII)
• Cryoprecipitate (contains vWF and VIII)
Bleeding and Thrombotic Disorders

Bleeding disorders

- von Willebrand disease
- Hemophilia
Hemophilia

Things you must know

- Most common factor deficiency
- X-linked recessive in most cases (30% are spontaneous mutations)
- Hemophilia A = ↓ VIII (more common)
  Hemophilia B = ↓ IX
- Variable amount of “factor” bleeding
Hemophilic arthropathy of knee
Joint deformity in hemophilia
Hemophilia

Diagnosis

• PTT: prolonged
• PT/INR: normal
• Bleeding time: NORMAL!

Treatment of hemophilia A

• Desmopressin
• Recombinant Factor VIII

Treatment of hemophilia B

• Recombinant Factor IX
Bleeding and Thrombotic Disorders

Bleeding disorders
- von Willebrand disease
- Hemophilia
- DIC
Disseminated Intravascular Coagulation (DIC)

Things you must know

- Excessive clotting and bleeding
- Many potential causes
- Blood: MAHA and thrombocytopenia
- PT/INR, PTT, and bleeding time prolonged
What’s going on in DIC?
Symptoms of DIC

Thrombosis

Hemorrhage
Remember these causes of DIC:

- Malignancy
- OB complications
- Sepsis
- Trauma
Bleeding and Thrombotic Disorders

Bleeding disorders

- von Willebrand disease
- Hemophilia
- DIC
- TTP/HUS
Thrombotic Thrombocytopenic Purpura/
Hemolytic-Uremic Syndrome

Things you must know

• Both have widespread clotting (± bleeding)
• Cause: ADAMTS13 deficiency (TTP) or E. coli (HUS)
• Symptoms: renal failure, neurologic symptoms
• Coagulation factors (and tests) are normal!
Deficiency of ADAMTS 13 in TTP
Nasty creatures in TTP

Rodent of unusual size (ROUS)
- *The Princess Bride*, 1987

Von Willebrand multimer of unusual size (MOUS)
- *NEJM*, 1982
Bleeding and Thrombotic Disorders

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Thrombotic disorders
  • Factor V Leiden
Thrombosis Risk Factors

**Endothelial damage**
- Atherosclerosis

**Stasis**
- Immobilization
- Varicose veins
- Cardiac dysfunction

**Hypercoagulability**
- Surgery
- Carcinoma
- Estrogen/postpartum
- Thrombotic disorders
When should you worry about a hereditary disorder?

- no obvious cause
- family history
- weird location
- recurrent
- patient is young
- miscarriages
Factor V Leiden

Things you must know

- Most common cause of unexplained thromboses
- Inherited point mutation in factor V gene
- Mutated factor V can’t be turned off!
- Diagnosis requires genetic testing
Intrinsic

IX

VIII

X

thrombin

fibrin

Extrinsic

TF VII
Intrinsic

VIII

IX

V Leiden → VLa

Extrinsic

TF VII

X

thrombin

fibrin

protein C
Factor V Leiden

**Diagnosis**
- PT/INR and PTT: normal!
- Need genetic testing

**Treatment**
- Don’t! Unless there is a thrombosis.
- Then give oral anticoagulants