NOTES
HYPOCOAGULABLE DISORDERS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Acquired, inherited disorders; defects in coagulation cascade

SIGNS & SYMPTOMS

- Bleeding
- Thrombosis, only disseminated intravascular disease (DIC)

DIAGNOSIS

LAB RESULTS

- Platelet count
- Levels of clotting factors
- Prothrombin time (PT)
- Partial thromboplastin time (aPTT)
- Fibrin degradation products
- Genetic testing

TREATMENT

OTHER INTERVENTIONS

- Supportive therapy

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

osms.it/disseminated-intravascular-coagulation

PATHOLOGY & CAUSES

- Acquired, paradoxical process of thrombosis, bleeding
- Release of procoagulants, tissue factors, bacterial components, enzymes/major endothelial injury → excessive activation of coagulation cascade → thrombosis of small/medium blood vessels → activation of fibrinolysis to resolve clots → fibrin degradation products released into circulation → interfere with platelet aggregation, clot formation
- Depletion of platelets, fibrin, coagulation factors → consumption coagulopathy

CAUSES

- Complication of underlying conditions
- Obstetric complications (e.g. preeclampsia, obstetric hemorrhage, retained dead fetus)
- Critical illness (individuals in intensive care unit)
- Malignancy
  - Mucin-secreting adenocarcinoma (e.g., lungs, pancreas, stomach, prostate, ovaries)
  - Acute promyelocytic leukemia (APL)
- Infection/sepsis, especially gram-negative bacteria
- Massive tissue injury due to trauma,

surgery, burn, fracture
- Intravascular hemolysis due to blood type incompatibility
- Shock
- Snakebites

COMPLICATIONS

- Widespread thrombosis, ischemia, necrosis of brain, heart, kidneys, liver, lungs, adrenals, spleen → organ dysfunction
- Microangiopathic hemolytic anemia (MAHA)
- Paradoxical tendency to life-threatening bleeding, due to consumption of procoagulatory factors

MNEMONIC: DIC TEAR

Common causes of DIC

Delivery **TEAR**: obstetric complications

Infections: gram negative)/ **I**mmunological

Cancer: prostate, pancreas, lung, stomach

Obstretrical complications

Toxemia of pregnancy

Emboli (amniotic)

Abruptio placentae

Retain fetus products

SIGNS & SYMPTOMS

- *Acute:* bleeding episodes (e.g. ecchymoses, petechiae, purpura, blood oozing from gingival/oral mucosa, sites of trauma, catheters, intravenous lines)
- *Chronic:* thromboembolism, tissue hypoxia, infarctions

DIAGNOSIS

LAB RESULTS

- ↓ Platelets
- ↓ Fibrinogen
- ↓ Clotting factors
- ↑ Prothrombin time (PT)
- ↑ Partial thromboplastin time (aPTT)
- ↑ D-dimers (fibrin degradation product)
- Schistocytes, damaged red blood cells (RBCs) due to MAHA
- Physiologic compensation → lab results normal
  - For chronic (solid tumors, large aortic aneurysms)

TREATMENT

MEDICATIONS

- Oxygen, IV fluids

OTHER INTERVENTIONS

- Replace clotting factors with fresh frozen plasma (FFP), cryoprecipitate, fibrinogen
- Platelet transfusions, if platelet count < 30,000
- RBC transfusions for severe bleeding

HEMOPHILIA A

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PATHOLOGY & CAUSES

- Most common inherited clotting factor deficiency; classic hemophilia
- X-linked recessive disorder
- Mutated gene *F8* on X chromosome

CAUSES

- Quantitative/qualitative deficiency of factor VIII → insufficient activation of the intrinsic pathway → defect in common coagulation pathway → increased tendency for bleeding
- Peritoneal dialysis

RISK FACTORS

- More common in individuals who are biologically male; individuals who are biologically female more likely to be carriers

SIGNS & SYMPTOMS

- Varies according to mutation, factor VIII activity
- Asymptomatic/spontaneous bleeding
- < 10% factor VIII
  - Easy bruising
  - Prolonged bleeding, after injury/surgery
  - Hematomas (e.g. muscle hematomas, hemophilic pseudotumors)
  - Gastrointestinal (GI) bleeding
  - Hematuria
  - Severe epistaxis
  - Painful hemarthrosis → progressive joint irregularity, disability (knee most common)
  - Intracerebral hemorrhage

DIAGNOSIS

LAB RESULTS

- Normal platelet count
- Normal prothrombin time (extrinsic pathway not affected)
- Prolonged partial thromboplastin time (intrinsic pathway affected)
- Factor VIII clotting assay
- Genetic testing

TREATMENT

MEDICATIONS

Desmopressin (DDAVP)

- For mild quantitative hemophilia A
  - → stimulates von Willebrand factor (vWF) release → promotes stabilization of residual factor VIII

OTHER INTERVENTIONS

- Recombinant factor VIII infusions
- If severe deficiency, immune system may perceive supplemental factors as foreign → production of antibodies (inhibitors) → elimination of injected factors/anaphylaxis
- Avoid sports, trauma, medications that promote bleeding
- Local measures
  - Treat hemarthrosis, hematomas (e.g. resting of affected part, application of ice)

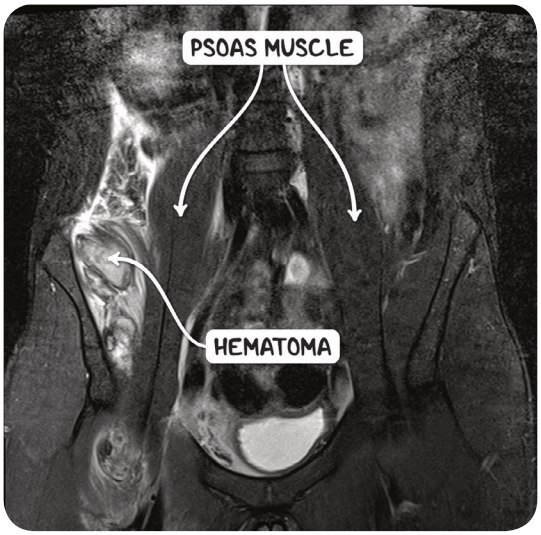

Figure 47.1 An abdominal MRI scan in the coronal plane demonstrating a hematoma of the right psoas muscle in an individual with hemophilia.

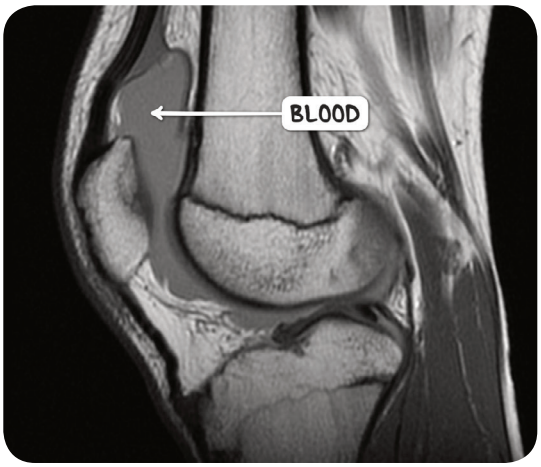

Figure 47.2 An MRI scan of the knee demonstrating hemarthrosis. Individuals with hemophilia are at increased risk of hemarthrosis.

HEMOPHILIA B

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PATHOLOGY & CAUSES

- Mutated gene *F9* on X chromosome
- AKA Christmas disease
- Qualitative/quantitative deficiency of coagulation factor IX → insufficient activation of intrinsic coagulation pathway → impaired hemostasis
- Less common

SIGNS & SYMPTOMS

- Spontaneous bleeding, delayed bleeding after trauma, hemarthrosis, hematomas, epistaxis, intracranial, GI/genitourinary tract bleeding

DIAGNOSIS

LAB RESULTS

- Normal platelet count, prothrombin time (intrinsic pathway affected)
- Factor IX clotting assay/genetic mutation testing

TREATMENT

MEDICATIONS

DDAVP

- Not helpful in hemophilia B; stimulates vWF → stabilizes only factor VIII, not IX

OTHER INTERVENTIONS

- Infusions of recombinant factor IX

VON WILLEBRAND DISEASE

osms.it/von-willebrand-disease

PATHOLOGY & CAUSES

- Most common inherited bleeding disorder of primary hemostasis
- Defective platelet function with normal platelet count
- Quantitative/qualitative deficiency of vWF → impaired platelet aggregation, adhesion, dysfunction of factor VIII → deficiency in coagulation cascade → bleeding tendency
- Hemostatic pressure (e.g. surgery/trauma)

TYPES

Type I
- Most common
- Autosomal dominant, partial quantitative deficiency

Type II
- Autosomal dominant, qualitative deficiency

Type III
- Autosomal recessive, severe quantitative deficiency

SIGNS & SYMPTOMS

- Typically asymptomatic
- Surgery/trauma provoke clinical manifestation
- Spontaneous mucosal, cutaneous bleeding (e.g. epistaxis, easy bruising, excessive bleeding from wounds, bleeding gums)
- Menorrhagia
- GI bleeding
- Internal/joint bleeding (Type III)

DIAGNOSIS

LAB RESULTS

- Abnormal PFA-100 test
- ↓ factor VIII activity
- ↓ vWF
- PTT prolonged
- ↓ platelet aggregation, presence of ristocetin
- Collagen-binding function reduced
- Platelet count normal

TREATMENT

MEDICATIONS

- DDAVP
  - Type I, Type II
- Factor VIII/vWF concentrates
  - After major injury; during operation; Type III, II not responding to DDAVP
- High-purity vWF concentrates

OTHER INTERVENTIONS

- Local measures, tranexamic acid for mild bleeding