Coagulopathy in the Hospital Setting

Coagulopathy, an impairment in the body's ability to form blood clots, is a common and potentially life-threatening condition in hospitalized patients. It can result from various causes, including medications, liver disease, malnutrition, genetic disorders, supplements, and other factors. This pamphlet provides physician assistant (PA) students with a guide to diagnose, evaluate, and manage coagulopathy in the hospital setting, with clinical scenarios to apply the knowledge.

Causes of Coagulopathy

- **Medications:**
  - Anticoagulants:
    - Warfarin (inhibits vitamin K-dependent factors, INR >3), DOACs (dabigatran, rivaroxaban), heparin (aPTT prolongation), LMWH (enoxaparin).
    - Antiplatelets: Aspirin, clopidogrel (inhibit platelet aggregation, bleeding risk).
  - Thrombolytics: Alteplase (tPA), streptokinase (fibrinolysis, risk of bleeding).
- Other Drugs:
  - NSAIDs (e.g., ibuprofen, impair platelet function), chemotherapy (e.g., methotrexate, bone marrow suppression).
- **Liver Disease:**
- Cirrhosis: Reduced synthesis of clotting factors (II, V, VII, IX, X) and proteins C/S, thrombocytopenia (splenomegaly), INR >1.5.
- Acute Liver Failure: Similar mechanism, often more severe (INR >2), risk of bleeding and thrombosis (imbalanced hemostasis).
- **Malnutrition:** Vitamin K Deficiency:
  - Inadequate dietary intake (e.g., prolonged fasting, TPN without vitamin K), malabsorption (e.g., celiac disease, IBD), INR prolongation.
  - General Malnutrition:
    - Protein deficiency (low albumin, impaired clotting factor synthesis), common in critically ill patients.
- **Supplements:**
  - Herbal Supplements:
    - Ginkgo Biloba: Inhibits platelet aggregation, increases bleeding risk.
    - Garlic: Antiplatelet effects, may prolong bleeding time.

        - Ginseng: inhibits platelet aggregation, potentiates warfarin (increases INR).
        - Ginger: Antiplatelet effects, especially at high doses.
        - Turmeric (Curcumin): Mild antiplatelet effect, may enhance bleeding risk with anticoagulants.
        - Dong Quai: contains coumarin-like compounds, increases INR, bleeding risk.
    - Vitamins and Oils:
        - Vitamin E: High doses (>400 IU/day) impair platelet aggregation, prolong INR.
        - Fish Oil: Omega-3 fatty acids (EPA/DHA) have antiplatelet effects, mild bleeding risk.
        - Flaxseed Oil: Similar to fish oil, contains alpha-linolenic acid, mild antiplatelet effect.
    - Other Supplements:
    - Cranberry Extract May potentiate warfarin (increases INR), theoretical bleeding risk.
    - St. John's Wort: Induces CYP450 (decreases warfarin efficacy), but can increase bleeding risk if stopped suddenly (rebound INR elevation).
- **Genetic Causes:**
    - Hemophilia A: Deficiency of factor VIII, X-linked, prolonged aPTT, joint/muscle bleeds, severity based on factor VIII levels (severe: <1%, moderate: 1-5%, mild: 5-40%).
    - Hemophilia B (Christmas Disease): Deficiency of factor IX, X-linked, similar presentation to hemophilia A, prolonged aPTT, treated with factor IX concentrate.
    - Hemophilia C: Deficiency of factor XI, autosomal recessive, more common in Ashkenazi Jews, milder bleeding (e.g., post-surgical), prolonged aPTT, treated with FFP or factor XI concentrate.
    - Von Willebrand Disease (vWD): Deficiency/dysfunction of von Willebrand factor (vWF), most common inherited bleeding disorder, mucocutaneous bleeding (epistaxis, menorrhagia), prolonged bleeding time, low vWF antigen/activity.
        - Type 1: Partial deficiency (most common, 70-80%), mild bleeding.
        - Type 2: Qualitative defect, variable bleeding severity.
        - Type 3: Severe deficiency, rare, severe bleeding similar to hemophilia.
    - Rare Bleeding Disorders (RBDs):
        - Factor II (Prothrombin) Deficiency: Very rare, autosomal recessive, prolonged PT/aPTT, treated with FFP or PCC.
        - Factor V Deficiency: Autosomal recessive, prolonged PT/aPTT, treated with FFP (no specific concentrate).

        - Factor VII Deficiency: Autosomal recessive, prolonged PT, normal aPTT, treated with recombinant factor VIIa.
        - Factor X Deficiency: Autosomal recessive, prolonged PT/aPTT, treated with FFP or PCC, seen in amyloidosis (factor X binds to amyloid fibrils).
        - Factor XIII Deficiency: Autosomal recessive, normal PT/aPTT, delayed bleeding (e.g., umbilical stump in neonates), treated with factor XIII concentrate or cryoprecipitate.
    - Platelet Function Disorders:
        - Glanzmann Thrombasthenia Autosomal recessive, defect in GPIIb/IIIa receptor, normal platelet count, prolonged bleeding time, mucocutaneous bleeding, treated with platelet transfusion.
        - Bernard-Soulier Syndrome: Autosomal recessive, defect in GPIb-IX-V receptor, large platelets, thrombocytopenia, prolonged bleeding time, treated with platelet transfusion.
- **Other Causes:**
    - Disseminated Intravascular Coagulation (DIC): Consumptive coagulopathy (sepsis, trauma, malignancy), low platelets, prolonged PT/aPTT, high D-dimer, schistocytes.
    - Vitamin K Deficiency (Non-Malnutrition):
    - Antibiotics (e.g., cephalosporins, disrupt gut flora producing vitamin K), neonates (hemorrhagic disease of the newborn), INR prolongation. Bone Marrow Suppression:
    - Aplastic anemia, leukemia, chemotherapy (low platelets, anemia, coagulopathy).
    - Renal Disease:
    - Uremia (Cr >3 mg/dL) impairs platelet function, prolonged bleeding time.
    - Hypothermia: Impairs clotting factor activity, common in trauma/surgery, PT/aPTT prolongation.
    - Dilutional Coagulopathy: Massive transfusion (>10 units PRBCs), dilutes clotting factors/platelets, prolonged PT/aPTT.
    - Amyloidosis:
    - Factor X deficiency (binding to amyloid fibrils), prolonged PT/aPTT, bleeding risk.
    - Sepsis: Endotoxin-mediated coagulopathy, low platelets, prolonged PT/aPTT, high D-dimer.
    - Antiphospholipid Syndrome (APS): Paradoxical bleeding risk if over-anticoagulated (e.g., warfarin INR >3), prolonged aPTT (lupus anticoagulant), treated with anticoagulation adjustment.

- Alpha-2-Antiplasmin Deficiency: Rare, autosomal recessive, impaired fibrinolysis regulation, normal PT/aPTT, treated with antifibrinolytics (e.g., tranexamic acid).
- Hereditary Hemorrhagic Telangiectasia (HHT): Autosomal dominant, abnormal blood vessels (telangiectasias), epistaxis, GI bleeding, normal labs, treated with iron supplementation, cauterization.

Causes of Coagulopathy Table

Cause	Mechanism	Key Features	Lab Findings
Medications (Warfarin)	Inhibits vitamin K factors	Bruising, GI bleed	INR >3, prolonged PT
Liver Disease	Reduced clotting factor synthesis	Jaundice, ascites, bleeding	INR >1.5, low platelets, low albumin
Supplements (Ginkgo)	Antiplatelet effect	Epistaxis, bruising	Prolonged bleeding time
Genetic (Hemophilia C)	Factor XI deficiency	Post-surgical bleeding	Prolonged aPTT, normal PT
DIC	Consumptive coagulopathy	Sepsis, bleeding, thrombosis	Low platelets, high D-dimer, schistocytes

Diagnosis and Labs

- **Initial Assessment:**
- History: Bleeding symptoms (bruising, epistaxis, GI bleed, hematuria), medication/supplement use (anticoagulants, ginkgo), diet (vitamin K intake), liver disease, family history (genetic disorders), recent trauma/surgery.
- Physical Exam: Mucocutaneous bleeding (petechiae, purpura, telangiectasias in HHT), joint swelling (hemophilia), jaundice/ascites (liver disease), signs of DIC (petechiae, oozing from IV sites), pallor (anemia).
- **Labs:**
  - Inpatient Testing (Hospital Setting):
    - Purpose: Rapid assessment to guide acute management of bleeding or coagulopathy in the hospital, focusing on immediate, actionable results.
    - Tests Performed:
      - **PT/INR:** Prolonged in warfarin use, liver disease, vitamin K deficiency, DIC, factor VII deficiency (normal INR: 0.8-1.2).
      - **aPTT:** Prolonged in hemophilia A/B/C, heparin use, DIC, vWD, factor XI/XII deficiency (normal: 25-35 sec).

        - **Bleeding Time:** Prolonged in vWD, uremia, antiplatelet drugs, Glanzmann thrombasthenia, Bernard-Soulier syndrome (normal: 2- 7 min); often replaced by PFA-100 (Platelet Function Analyzer) in some centers, though less commonly used in acute settings.
        - **Platelet Count:** Low (<150,000/µL) in DIC, liver disease, bone marrow suppression, sepsis, Bernard-Soulier syndrome.
        - **Fibrinogen:** Low (<150 mg/dL) in DIC, liver disease, thrombolytic therapy, factor XIII deficiency (late).
        - **D-dimer/Fibrin Degradation Products (FDPs):** Elevated in DIC, thrombolytic therapy, VTE, alpha-2-antiplasmin deficiency.
        - **CBC:** Anemia (bleeding, hemolysis in DIC), schistocytes (DIC), Howell-Jolly bodies (splenomegaly in liver disease).
        - **CMP:** Elevated LFTs (liver disease), low albumin (malnutrition, liver disease), elevated Cr (uremia).
        - **Peripheral Smear:** Schistocytes (DIC), large platelets (Bernard-Soulier syndrome).
    - Rationale: These tests are widely available, provide rapid results (often within hours), and are critical for guiding acute interventions (e.g., FFP transfusion, reversal of anticoagulation). Inpatient testing prioritizes speed and practicality over specificity, especially in emergencies (e.g., active bleeding, DIC).
- Outpatient Testing (More Accurate, Diagnostic):
    - Purpose: Detailed and specific testing to confirm the underlying cause of coagulopathy, often requiring specialized labs, and performed in a stable patient for long-term management.
    - Tests Performed:
        - **Specific Factor Assays:** Factor VIII/IX/XI (hemophilia A/B/C), vWF antigen/activity (vWD), factor XIII activity (clot solubility test for factor XIII deficiency).
        - **Genetic Testing:** Confirms hemophilia, vWD, or rare bleeding disorders (e.g., factor II, V, VII, X deficiencies), especially with family history or recurrent bleeds.
        - **Platelet Function Assays:** PFA-100, light transmission aggregometry (LTA) for Glanzmann Thrombasthenia, Bernard- Soulier syndrome (more accurate than bleeding time, which is operator-dependent).
        - **Vitamin K Level:** Confirms deficiency (not routine in hospital, more useful for outpatient workup of malabsorption or dietary causes).
        - **Inhibitor Assays:** Bethesda assay for factor inhibitors (e.g., acquired hemophilia), lupus anticoagulant (APS).
        - **Bone Marrow Biopsy:** Confirms leukemia, aplastic anemia (outpatient if stable, inpatient if urgent pancytopenia).

- Rationale: Outpatient testing is more specific and accurate for diagnosing the exact cause of coagulopathy (e.g., distinguishing vWD types, confirming rare factor deficiencies). These tests often require specialized labs, longer turnaround times (days to weeks), and are not practical in acute inpatient settings where immediate action is needed. Outpatient testing is ideal for stable patients after initial stabilization or for those with recurrent, unexplained bleeding.
- **Diagnostic Workup:**
  - Mixing Studies:
  - PT/aPTT corrects with 1:1 mixing (normal plasma): Factor deficiency (e.g., hemophilia, liver disease).
  - **PT/aPTT does not correct:** Inhibitor (e.g., lupus anticoagulant, acquired hemophilia).
  - **Hospital Setting:** Performed if initial PT/aPTT is prolonged to guide acute management (e.g., FFP for deficiency vs. further workup for inhibitors).
  - **Outpatient Setting:** Follow-up with inhibitor assays (e.g., Bethesda assay) to confirm specific inhibitors.

- Imaging:
  - **Ultrasound/CT:** Liver/spleen (liver disease, splenomegaly), bleeding sites (e.g., retroperitoneal hematoma); typically inpatient for acute bleeding.
  - **Bone Marrow Biopsy:** Inpatient if urgent (e.g., pancytopenia, suspected leukemia); outpatient for stable patients with chronic symptoms.

Diagnosis and Treatment Table

Cause	Diagnostic Approach	Treatment	Notes
Warfarin Overdose	INR >3, prolonged PT	Vitamin K 5-10 mg IV, PCC	Monitor INR q6h, transfuse PRBCs if bleeding.
Liver Disease	INR >1.5, low platelets, LFTs	FFP 10-15 mL/kg IV, vitamin K	Treat underlying cause, monitor for thrombosis.
Supplements (Garlic)	Prolonged bleeding time	Stop supplement, supportive care	Transfuse PRBCs if bleeding, monitor INR.
Hemophilia B	Prolonged aPTT, low factor IX	Factor IX concentrate	Avoid aspirin, monitor for inhibitors.
DIC	Low platelets, high D-dimer, schistocytes	Treat cause, FFP, platelets, cryoprecipitate	Heparin if thrombotic predominance.

Treatment and Overall Management

- **General Principles:**
  - Stabilize: ABCs (airway, breathing, circulation), IV access, telemetry, monitor for bleeding.
  - Identify Cause:
  - Reverse anticoagulation, replace deficiencies, treat underlying disease.
  - Supportive Care:
    - Transfuse blood products, control bleeding, prevent thrombosis.
- **Specific Treatments:**
  - Medications (Anticoagulant Overdose):
    - **Warfarin:** Vitamin K 5-10 mg IV slow infusion (reverses over 12-24h), PCC 25-50 units/kg IV (immediate), FFP 10-15 mL/kg IV if PCC unavailable.
    - **DOACs:** Dabigatran (idarucizumab 5 g IV); rivaroxaban/apixaban (andexanet alfa, per protocol; PCC if unavailable).
    - **Heparin:** Protamine sulfate 1 mg IV per 100 units heparin (UFH), 1 mg per 1 mg enoxaparin (LMWH, partial reversal).
    - **Antiplatelets:** Stop drug, transfuse platelets if bleeding (e.g., 1 unit IV, target >50,000/µL).
  - Liver Disease:
    - **Vitamin K:** 10 mg IV daily x 3 days (if vitamin K deficiency contributes).
    - **FFP:** 10-15 mL/kg IV (replace clotting factors, temporary effect).
    - **Cryoprecipitate:** 1 unit/10 kg IV (if fibrinogen <100 mg/dL).
    - **Treat Underlying Cause:** Manage cirrhosis (e.g., lactulose for encephalopathy), acute liver failure (e.g., NAC for acetaminophen toxicity).
  - Malnutrition/Vitamin K Deficiency:
    - **Vitamin K:** 10 mg IV/PO daily x 3 days (IV for faster effect in bleeding).
    - **Nutritional Support:** Ensure adequate vitamin K intake (e.g., leafy greens), TPN with vitamin K if needed.
    - **Treat Malabsorption:** Manage celiac disease (gluten-free diet), IBD (anti- TNF therapy).
  - Supplements:
    - **Stop Offending Agents:** Discontinue ginkgo biloba, garlic, ginseng, ginger, turmeric, dong quai, vitamin E, fish oil, flaxseed oil, cranberry extract, St. John's wort.
    - **Supportive Care:** Transfuse PRBCs if bleeding, monitor INR (if vitamin K affected), platelets if bleeding time prolonged.

- Genetic Causes:
  - **Hemophilia A:** Factor VIII concentrate (50 units/kg IV for major bleed); DDAVP 0.3 mcg/kg IV (mild cases).
  - **Hemophilia B:** Factor IX concentrate (80 units/kg IV for major bleed).
  - **Hemophilia C:** FFP 10-15 mL/kg IV (no specific factor XI concentrate widely available), antifibrinolytics (e.g., tranexamic acid 1 g IV q8h).
  - **vWD:** DDAVP 0.3 mcg/kg IV (type 1), vWF concentrate (type 2/3 or severe bleeding).
  - **Factor II Deficiency:** PCC 25-50 units/kg IV (contains prothrombin), FFP if PCC unavailable.
  - **Factor V Deficiency:** FFP 10-15 mL/kg IV (no specific concentrate).
  - **Factor VII Deficiency:** Recombinant factor VIIa 15-30 mcg/kg IV q4-6h.
  - **Factor X Deficiency:** PCC 25-50 units/kg IV, FFP as alternative.
  - **Factor XIII Deficiency:** Factor XIII concentrate (20-30 units/kg IV), cryoprecipitate (1 unit/10 kg IV).
  - **Glanzmann Thrombasthenia/Bernard-Soulier Syndrome:** Platelet transfusion (1 unit IV), antifibrinolytics (tranexamic acid 1 g IV q8h).
  - **HHT:** Iron supplementation (chronic epistaxis), cauterization/laser for telangiectasias, antifibrinolytics for GI bleeding.
- DIC:
  - **Treat Underlying Cause:** Sepsis (antibiotics, source control), trauma (surgery), malignancy (chemotherapy).
  - **Replace Factors:** FFP 10-15 mL/kg IV (prolonged PT/aPTT), cryoprecipitate 1 unit/10 kg IV (fibrinogen <100 mg/dL), platelets 1 unit IV (platelets <50,000/µL).
  - **Heparin:** 5-10 units/kg/h IV (if thrombotic predominance, e.g., arterial thrombosis, microthrombi).

- other Causes:
  - **Vitamin K Deficiency (Non-Malnutrition):** Vitamin K 10 mg IV/PO x 3 days, reassess INR.
  - **Bone Marrow Suppression:** Transfuse platelets/PRBCs, treat underlying cause (e.g., chemotherapy hold, G-CSF for neutropenia).
  - **Uremia:** Dialysis (if Cr >3 mg/dL, bleeding), DDAVP 0.3 mcg/kg IV (improves platelet function).
  - **Hypothermia:** Rewarm (target >35°C), transfuse FFP/platelets if bleeding persists.
  - **Dilutional Coagulopathy:** FFP 10-15 mL/kg IV, cryoprecipitate 1 unit/10 kg IV, platelets 1 unit IV.
  - **Amyloidosis:** FFP or PCC for factor X deficiency, treat underlying amyloidosis (e.g., chemotherapy).

- **Monitoring:**
  - Labs: Q6-12h (PT/INR, aPTT, platelets, fibrinogen, D-dimer) until stable.
  - Bleeding: Q1-2h (vital signs, oozing, Hgb drop), imaging if internal bleed suspected (e.g., CT for retroperitoneal hematoma).
- Underlying Cause: Monitor LFTs (liver disease), Cr (uremia), cultures (sepsis).

Key Pearls

- **Coagulopathy:** Identify cause (medications, genetic, liver disease); bleeding risk varies by etiology.
- **Labs:** PT/INR (warfarin, liver disease), aPTT (hemophilia, heparin), platelets/D-dimer (DIC).
- **Supplements:** Ginkgo, garlic, ginger, turmeric increase bleeding risk; stop and monitor.
- **Genetic:** Hemophilia A/B/C (factor VIII/IX/XI replacement), vWD (DDAVP/vWF), rare disorders (PCC, FFP).
- **DIC:** Treat cause, replace factors (FFP, cryoprecipitate), heparin if thrombotic predominance.
- **Testing:** Inpatient (PT/aPTT, platelets for acute management); outpatient (factor assays, genetic testing for diagnosis).
- **Monitor:** Labs q6-12h, bleeding signs q1-2h, address underlying cause (sepsis, liver disease).

References

- **UpToDate:** “Coagulopathy: Diagnosis and Management in the Hospitalized Patient” (2025).
- **NEJM:** “Disseminated Intravascular Coagulation: A Review” (2024).
- **Blood:** “Rare Bleeding Disorders: Diagnosis and Treatment” (2023).
- **J Thromb Haemost:** “Vitamin K Deficiency Bleeding in Adults” (2023).

Clinical Scenarios

Case 1: A 60-Year-Old Male with Liver Cirrhosis

- **Presentation:** A 60-year-old male with cirrhosis presents with epistaxis and melena for 2 days. Exam: BP 100/60 mmHg, HR 90 bpm, jaundice, ascites, melena on rectal exam.
- **Labs:** INR 2.5, PT 20 sec, aPTT 35 sec, platelets 80,000/µL, Hgb 7 g/dL, albumin 2 g/dL, bilirubin 4 mg/dL.

- **Diagnosis:** Coagulopathy Due to Liver Disease → INR 2.5, low platelets, melena, cirrhosis.
- **Management:** NS 1 L IV bolus, transfuse PRBCs 2 units (Hgb <7 g/dL). Vitamin K 10 mg IV daily x 3 days. FFP 10 mL/kg IV (replace clotting factors). GI consult for endoscopy (likely variceal bleed). Octreotide 50 mcg IV bolus, then 50 mcg/h infusion (variceal bleed). Monitor INR q12h, Hgb q6h, platelets. Treat cirrhosis (lactulose for encephalopathy).

Case 2: A 25-Year-Old Male with Joint Bleeding

- **Presentation:** A 25-year-old male with a family history of bleeding presents with right knee swelling and pain after a fall. Exam: BP 120/80 mmHg, HR 80 bpm, right knee hemarthrosis, bruising.
- **Labs:** aPTT 55 sec, PT 12 sec, INR 1.0, factor XI 3% (normal 50-150%).
- **Diagnosis:** Coagulopathy Due to Hemophilia C → Hemarthrosis, prolonged aPTT, low factor XI.
- **Management:** FFP 10-15 mL/kg IV (no specific factor XI concentrate). Elevate leg, ice, avoid weight-bearing. Tranexamic acid 1 g IV q8h (mucosal bleeding risk). Avoid aspirin/NSAIDs. Monitor aPTT q12h, joint swelling. Hematology consult for outpatient genetic testing and long-term management.

Case 3: A 45-Year-Old Female with Sepsis

- **Presentation:** A 45-year-old female with urosepsis presents with oozing from IV sites and petechiae. She takes high-dose fish oil supplements. Exam: BP 90/60 mmHg, HR 120 bpm, Temp 39°C, petechiae, urine culture: E. coli.
- **Labs:** Platelets 30,000/µL, INR 2.0, aPTT 45 sec, fibrinogen 120 mg/dL, D-dimer 3000 ng/mL, schistocytes on smear.
- **Diagnosis:** Coagulopathy Due to DIC (Fish Oil Contribution) → Sepsis, low platelets, high D-dimer, schistocytes, fish oil use.
- **Management:** Stop fish oil. NS 2 L IV bolus, ceftriaxone 1 g IV daily (urosepsis). FFP 10 mL/kg IV (prolonged PT/aPTT), cryoprecipitate 1 unit/10 kg IV (fibrinogen <150 mg/dL), platelets 1 unit IV (platelets <50,000/µL). ICU admission (sepsis, DIC). Monitor labs q6h (platelets, fibrinogen, D-dimer), bleeding q1-2h. Heparin 5 units/kg/h IV if thrombosis develops (e.g., limb ischemia).