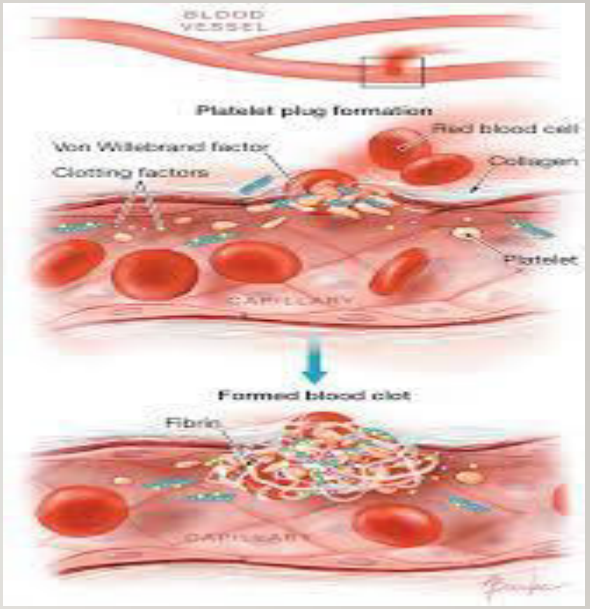
COAGULOPATHIES



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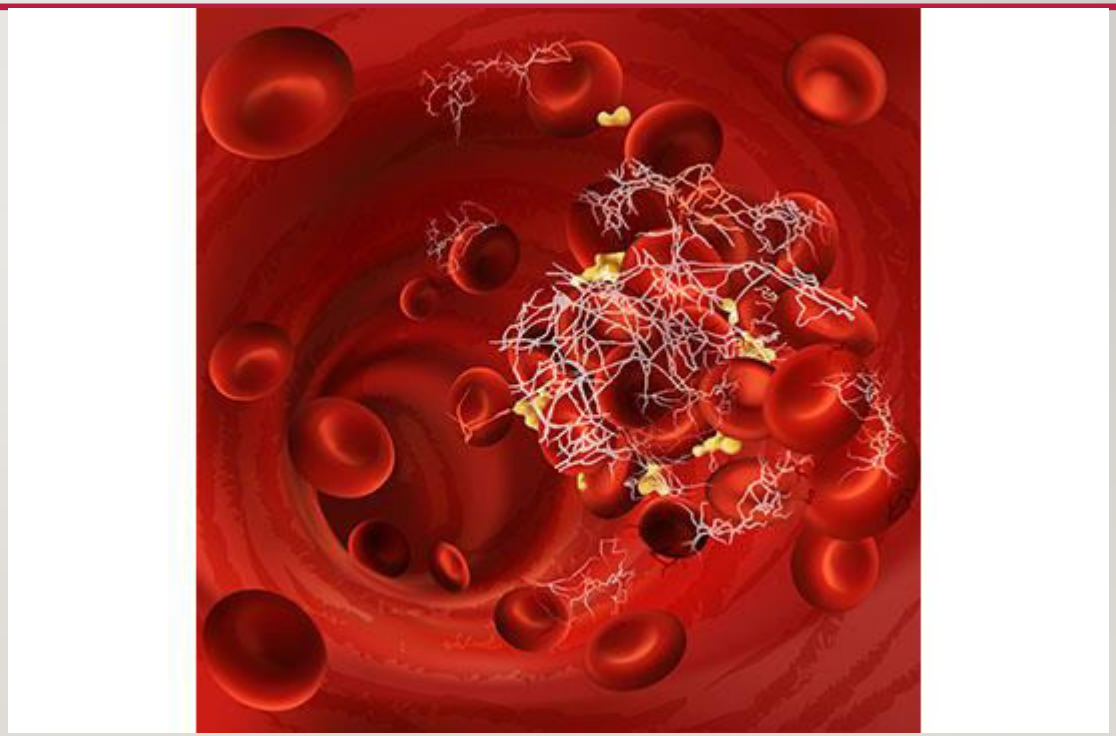
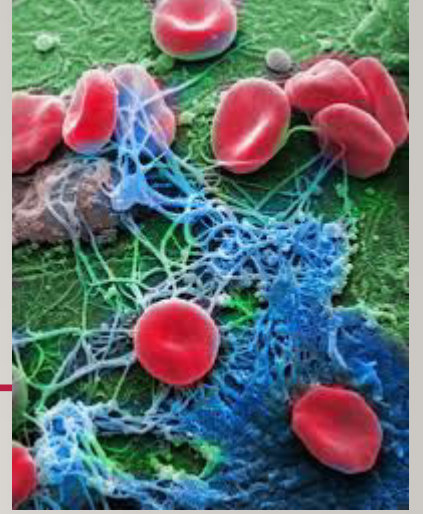
IN THE NAME OF GOD

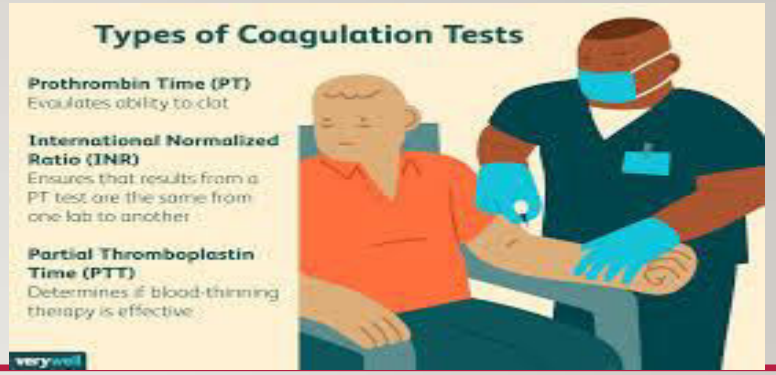


HYPOCOAGULABLE STATES

- Hypocoagulable states may be either inherited (e.g., hemophilia) or acquired (e.g., liver disease, malnutrition, drug exposure).
- To determine the diagnosis and associated bleeding risk, the anesthesiologist should inquire about known diagnoses, tests, treatments, previous bleeding episodes, and family history
- excessive bruising, prolonged bleeding after cuts, heavy menstrual cycles, and bleeding gums
- Petechiae, multiple bruises, hematomas, jaundice, and frank bleeding
- A change in these symptoms is likely more meaningful than a long-term history



- Diagnostic testing may include a CBC (including platelet count), INR, and aPTT; however, routine preoperative screening for coagulopathies is not indicated.
- Clinical indications include a known bleeding disorder, hepatic disease, and anticoagulant use.
- National guidelines in the United Kingdom also recommend coagulation testing only in patients who are (1) ASA physical status class III or IV; (2) undergoing intermediate, major, or complex surgical procedures; and (3) known to take anticoagulant medications or have chronic liver disease.
- If a specific cause of bleeding is suspected or known (e.g., liver disease, malnutrition), then additional targeted testing (e.g., liver function tests, protein, albumin) may be needed.



- Patients may occasionally have abnormal INR or aPTT results on preoperative screening bloodwork
- In patients without a history of vitamin K antagonist use, the most common causes of a prolonged INR are laboratory error, liver disease, and malnutrition
- the test should initially be repeated. If the repeat test result remains abnormal, both liver function tests and a hepatitis panel are warranted, with possible referral to a hematologist
- A prolonged aPTT can result from both hypocoagulable and hypercoagulable (e.g., factor V Leiden, anticardiolipin antibody, lupus anticoagulant, antiphospholipid antibody syndrome) conditions. The first steps are to repeat the test and ascertain possible exposure to heparin. Even small amounts of heparin in indwelling catheters can prolong the aPTT, especially if the blood is drawn from that site. Other than heparin exposure, other causes of a prolonged aPTT include von Willebrand disease (vWD; see section on von Willebrand Disease) and hemophilias

- Elective surgical procedures should be postponed until the etiology of abnormal tests is determined and corrections are made

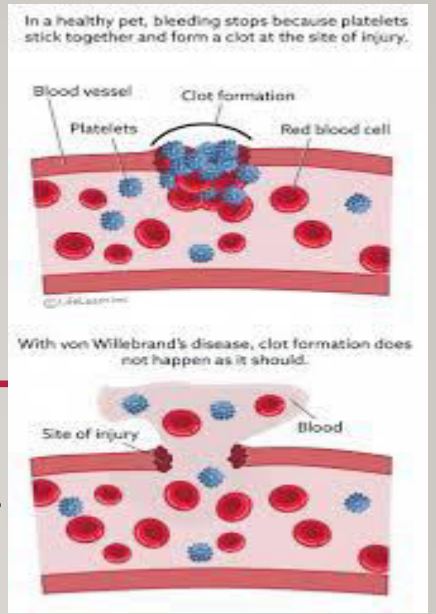
HEMOPHILIAS

- Hemophilia A (factor VIII deficiency)
- Hemophilia B (factor IX deficiency) ,"Christmas disease"
- Hemophilia C (deficiency of factor XI) , Rosenthal syndrome
- Severe hemophilia is characterized by less than 1% factor activity, moderate hemophilia by 1% to 5% activity, and mild hemophilia by more than 5% to under 40% activity
- Patients with hemophilia have a prolonged aPTT, but a normal INR and platelet count
- A hematologist must be involved in the perioperative care of patients with hemophilia

- in the setting of major surgery, factor replacement be used to increase preoperative levels to 80% to 100% for hemophilia A and 60% to 80% for hemophilia B
- After surgery, the target factor level is 50%, until the surgical wound is healed
- The dose required to increase factor VIII levels is:

  Factor VIII dose=weight(kg)×0.5 ×(desired absolute % increase in factor levels)
- Factor IX dose=weight(kg) ×(desired absolute % increase in factor levels)
- To rapidly increase factor levels to close to 100%, the usual dose required is 50 units/kg for factor VIII and 100 to 120 units/kg for factor IX. Intramuscular injections are to be avoided in these patients

VON WILLEBRAND DISEASE



- the most common congenital coagulopathy, occurring in approximately 1% of individuals
- quantitative and qualitative vWF deficiencies
- have a normal INR and platelet count (although type 2B can have a mild thrombocytopenia), but typically elevated aPTT (although patients with mild disease may have normal aPTT)
- Indeed, vWD is the most common cause of a prolonged aPTT in patients not taking heparin

- A hematologist should be involved in the care of patients with vWD
- Treatment options for vWD include desmopressin acetate (1-desamino-8-d-arginine vasopressin [DDAVP]) and vWF replacement therapy
- DDAVP increases the release of factor VIII, vWF, and plasminogen activator from endothelial cells. It is contraindicated in patients with type 2B disease because it increases abnormal vWF release and may cause thrombocytopenia

THROMBOCYTOPENIA

- a platelet count less than 150,000/mm
- decreased production, increased destruction, or sequestration
- Causes include malignant diseases, primary immune thrombocytopenia (ITP), drug-induced thrombocytopenia (e.g., quinine, sulfonamides, ampicillin), rheumatological autoimmune disorders (e.g., SLE, rheumatoid arthritis), pregnancy (i.e., gestational thrombocytopenia, preeclampsia), chronic liver disease (i.e., hypersplenism), alcohol, nutritional deficiencies, infection (e.g., hepatitis C, sepsis), hereditary disease, and disseminated intravascular coagulation
- A patient with newly discovered thrombocytopenia may require a hematology consultation before elective surgery.

- Thrombocytopenia within the context of recent heparin exposure should raise a concern regarding potential heparin-induced thrombocytopenia (HIT), which generally occurs within 5 to 10 days after heparin exposure.
- While HIT is characterized by thrombocytopenia, affected patients are at risk for arterial thromboses, venous thromboses, stroke, skin necrosis, limb gangrene, and organ infarction
- In otherwise healthy individuals (i.e., no other basis for elevated bleeding risks) neuraxial anesthesia is generally considered safe once the platelet count exceeds 50,000 to 80,000 per mm3

- Surgery can be safely performed in patients with platelet counts higher than 50,000/mm3.
- The risk of bleeding increases progressively as the count falls further, to less than 50,000/mm3
- When platelet transfusions are used to treat thrombocytopenia, the platelet count generally rises by 10,000/mm3 for every unit transfused.

THROMBOCYTOSIS

- Thrombocytosis is a platelet count more than 450,000/mm3
- It may be physiologic (i.e., exercise, pregnancy), primary (e.g., myeloproliferative disorder), or secondary (e.g., iron deficiency, neoplasm, surgery, chronic inflammation).
- Increasing levels of thrombocytosis can increase risks for thrombotic events, such as strokes, myocardial infarction, pulmonary emboli, mesenteric emboli, and venous clots
- Treatments include medications (e.g., hydroxyurea, anagrelide, pegylated interferon) that decrease platelet production and thereby reduce platelet counts over 7 to 10 days.
- Plasmapheresis, which removes platelets from the circulation
- normalization of the platelet count.

POLYCYTHEMIA

- increased number of circulating RBCs and increased hemoglobin concentration. It can be defined based on hematocrit (>48% in females and >49% in males) and hemoglobin concentration (>160 g/L in females and > 165 g/L in males)
- a primary disorder (i.e., polycythemia vera) or secondary to conditions typically associated with chronic hypoxia (e.g., COPD, high altitude, cyanotic congenital heart disease).
- A steep increase in blood viscosity occurs once the hematocrit increases to more than 50%, resulting in an increased thrombogenic risk.
- increased atherosclerosis (e.g., carotid stenosis, stroke) and cardiac disease (e.g., heart failure, myocardial infarction).

- The preoperative evaluation should focus on the pulmonary and cardiovascular systems. On physical examination, the anesthesiologist should examine for cyanosis, clubbing, wheezing, murmurs, and oxygen saturation (via pulse oximetry). Useful laboratory tests include an ECG, arterial blood gases, and chest radiograph.
- elective surgery should be postponed pending a consultation by a hematologist.

VENOUS THROMBOEMBOLIC DISORDERS

- The expected risk of postoperative VTE depends on both patient-related (e.g., inflammatory bowel disease, acute illness, smoking, malignant disease, obesity, increased age, prior VTE, estrogen use, hypercoagulable state, inherited thrombophilia) and procedure-related (e.g., invasiveness, trauma, immobilization) factors.
- For individuals with a very recent VTE episode, elective surgery should be delayed until 3 or more months have elapsed since the episode (during which time they should be anticoagulated).
- the risk of recurrent VTE is highest during the first 3 to 4 weeks after the initial episode; this risk then decreases over the next 2 months

MODIFIED CAPRINI RISK ASSESSMENT MODEL FOR VENOUS THROMBOEMBOLISM

1 Point Each/ Age 41–60 years Minor surgery BMI > 25 kg/m2 Swollen legs Varicose veins Pregnancy or postpartum History of unexplained or recurrent spontaneous abortion Oral contraceptives or hormone replacement Sepsis (<1 month) Serious lung disease, including pneumonia (<1 month) Abnormal pulmonary function Acute myocardial infarction Heart failure (<1 month) History of inflammatory bowel disease Medical patient at bed rest

2 Points Each/ Age 61–74 years Arthroscopic surgery Major open surgery (>45 min) Laparoscopic surgery (>45 min) Malignancy Confined to bed (>72 h) Immobilizing plaster cast Central venous access

3 Points Each/ Age ≥ 75 years History of VTE Family history of VTE Factor V Leiden mutation Prothrombin 20210A mutation Lupus anticoagulant Anticardiolipin antibodies Elevated serum homocysteine Heparin-induced thrombocytopenia Other congenital or acquired thrombophilia

5 Points Each/ Stroke (<1 month) Elective arthroplasty Hip, pelvis, or leg fracture Acute spinal cord injury (<1 month)

- Patients having minor procedures such as dental, endoscopic, cataract, or superficial operations usually do not require interruption of anticoagulant therapy
- In other individuals, withholding warfarin for 5 days typically allows the INR to decrease to normal if the baseline INR is in the usual therapeutic target (2.0 and 3.0).
- During the time without warfarin, patients may be at risk for recurrent thromboembolism; however, the risk is relatively small in all but the highest-risk patients (i.e., VTE in prior 3 months, or VTE with high-risk inherited thrombophilia).
- The decision to bridge with intravenous unfractionated heparin or with LMWH subcutaneously in high-risk patients must be made collaboratively with the treating physician.

PREOPERATIVE ANTICOAGULANT THERAPY

- vitamin K antagonists (e.g., warfarin) and DOACs
- These agents increase perioperative bleeding, except in the case of very minor procedures
- they should only be continued perioperatively if an individual does not have patient-related risk factors for bleeding (e.g., liver disease, abnormal renal function, prior bleeding complications), is scheduled for procedures without important bleeding risk (e.g., dental extraction, simple cutaneous procedures, cataract surgery without bulbar blocks)

- vitamin K antagonists (e.g., warfarin) should be stopped 5 days before surgery, with consideration for a longer discontinuation period if the initial INR value is more than 3.0
- INR should be rechecked within 24 hours before surgery
- a low dose of oral vitamin K (1 to 5 mg administrated orally or subcutaneously) administered for any INR result greater than 1.5.
- Vitamin K has an effect within 6 to 10 hours after oral or subcutaneous administration (more predictable with oral administration), and it peaks within 24 hours to 48 hours
- Administration of higher doses may lead to warfarin resistance when therapy is initiated again

- Some patients undergoing elective lower extremity joint replacement surgery may also receive an initial dose of warfarin before surgery for perioperative thromboprophylaxis
- The 2018 American Society of Regional Anesthesiologists (ASRA) guidelines state that neuraxial anesthesia can still be performed in these patients when only a single dose of warfarin has been administered within a period of 24 hours or less before surgery.

- DOACs for long-term anticoagulation, typically for non valvular atrial fibrillation, although some individuals may be prescribed low dose DOAC therapy for IHD
- The timing of preoperative discontinuation of DOACs should be guided by the specific drug prescribed, expected procedural bleeding risk, renal function (based on estimated GFR), and planned use of neuraxial anesthesia
- Patients may require temporary bridging therapy during the intervening period between discontinuation of vitamin K antagonist therapy and the date of surgery
- Such bridging therapy is generally not needed after interruption of DOACs because of their relatively short half lives.

- Most patients with nonvalvular atrial fibrillation do not require bridging therapy if their anticoagulant therapy is temporarily discontinued before surgery
- many patients with mechanical heart valves will require bridging therapy, with the decision based on the location of the mechanical heart valve and nature of planned surgery
- some patients who are at very high risk for recurrent VTE (e.g., VTE episode within prior 3 months) may also require bridging therapy
- If bridging is planned, either LMWH or intravenous unfractionated heparin can be started 2 or more days after the last administrated dose of vitamin K antagonist (e.g., warfarin).

- Bridging therapy should be started once the INR drops to under 2.0
- options for LMWH (e.g., enoxaparin, dalteparin)
- For patients with impaired renal function (eGFR < 30 mL/min), intravenous heparin bridging is preferable, although some LMWH dosing adjustments remain possible if eGFR is in the range between 15 and 30 mL/min
- Intravenous unfractionated heparin is usually discontinued approximately 6 hours before the surgery to allow for normal intraoperative coagulation
- The last dose of bridging dose LMWH should be given 24 hours preoperatively to allow normalization of coagulation by the time of surgery

- Both unfractionated heparin and LMWH are contraindicated in patients with an allergy to heparin or a history of HIT
- argatroban (intravenous infusion), bivalirudin (intravenous infusion), fondaparinux (subcutaneous), or oral DOACs
- 2018 ASRA guidelines recommend that warfarin should be discontinued 5 or more days before surgery, and a repeat preoperative INR should confirm a normalized value before neuraxial blocks are performed.
- The last prophylactic dose of LMWH should be 12 or more hours before any planned neuraxial block, whereas the last therapeutic dose (including bridging therapy) of LMWH should be 24 or more hours beforehand

- Preoperative unfractionated intravenous heparin should be stopped 6 or more hours before planned spinal or epidural anesthesia
- Though the safety of performing neuraxial techniques in the presence of low-dose subcutaneous unfractionated heparin (i.e., 5000 units twice daily) has been described, the 2018 ASRA guidelines include a Grade 2C recommendation for waiting 4 to 6 hours after subcutaneous injection before performing neuraxial blocks in patients receiving subcutaneous unfractionated heparin (i.e., 5000 units 2 or 3 times daily)
- Any patients receiving fibrinolytic and thrombolytic drugs should not receive neuraxial anesthesia.

PREOPERATIVE ANTIPLATELET THERAPY

- A withdrawal period of 7 to 10 days is likely excessive, especially because new platelets formed after aspirin discontinuation (half-life ≈15 minutes) are not inhibited. Since 10% of platelets are turned over every 24 hours, and about 50,000/mm3 of normal functioning platelets are needed to control surgical bleeding, it is likely that aspirin need only be stopped 3 days before surgery to mitigate risks of increased bleeding.
- Continuation of aspirin until the time of surgery leads to increased bleeding during major noncardiac surgery but not during cardiac surgery
- Therefore, a reasonable standard approach for most surgical patients is to discontinue aspirin temporarily 3 days before surgery

- aspirin should be continued in any patient with a prior PCI, high-grade IHD, or high-risk CVD (e.g., stroke within prior 9 months)
- Continuation of aspirin is not a contraindication to performance of neuraxial blocks.
- P2Y12 inhibitors are the other relatively common type of antiplatelet medications that might be encountered during preoperative evaluation, especially among patients with known IHD or CVD.
- These medications include oral medications (clopidogrel, ticagrelor, prasugrel, ticlopidine) and an intravenous formulation (cangrelor).

- Aside from the case of patients with a recent PCI ,P2Y12 inhibitor therapy should be temporarily discontinued before elective surgery.
- The usual recommended time interval for discontinuing these medications before surgery (including cases where neuraxial blocks are planned) is 5 to 7 days for clopidogrel, 5 to 7 days for ticagrelor, 7 to 10 days for prasugrel, 10 days for ticlopidine, and 3 hours for cangrelor.
- Some patients with either PAD or CVD may be on long term therapy with dipyridamole, which causes vasodilation and impairment of platelet function.

- There are minimal data on the safety of continuing dipyridamole in patients undergoing surgery; current ASRA guidelines recommend discontinuing extended-release dipyridamole 24 hours before performing any neuraxial block.
- Information on the perioperative safety of other antiplatelet therapies (e.g., glycoprotein IIb/IIIa inhibitors) is also limited. Platelet glycoprotein IIb/IIIa inhibitors (e.g., abciximab, eptifibatide, tirofiban) exert profound effects on platelet aggregation. Following administration, the time to restoration of normal platelet aggregation is 24 to 48 hours for abciximab, and 4 to 8 hours for eptifibatide and tirofiban. Neuraxial techniques should be avoided until platelet function has recovered after platelet glycoprotein IIb/IIIa inhibitor administration.


THANK YOU