

## Vesalius SCALpel™ : Coagulation

### Coagulation

injury attracts platelets

chemoattractants: platelet derived growth factor (PDGF), transforming growth factor beta (TGF beta)

platelets release ADP causing additional platelet aggregation, unstable white clot

platelets release calcium and phospholipids which facilitate intrinsic pathway

extrinsic pathway facilitated by tissue thromboplastin

final common pathway factor Xa converts prothrombin to thrombin

thrombin converts fibrinogen (I) to (weak) fibrin

fibrin stabilizing factor (XIII) creates tight fibrin which stabilizes white clot

### Clotting tests

PT: extrinsic pathway, II, V, VII, X, fibrinogen

acted on by warfarin

abnormalities: Vit K deficiency, liver disease, malabsorption (fat)

PTT: intrinsic pathway, everything else but VII and XIII

acted on by heparin

abnormalities: VIII deficiency (hemophilia A), IX (hemophilia B), XII

bleeding time:

measures pl plug formation

nl 8-9m = pl > 50k

low VonWillibrand factor increases bleeding time

the most effective tool to detect coagulation abnormality is history

### Bleeding disorders

**Hemophilia A:** VIII deficiency, sex-linked

spontaneous bleeding: intraarticular, intramuscular, intracranial, GU

PT normal, PTT may be elevated, factor VIII assay definitive Dx

Rx: factor VIII concentrate; use cryo (80u of VIII/unit) if VIII not available; 1/2 life 8-12h, 50% level controls spontaneous bleed

Rx for bleeding: 30% factor VIII level, minor bleeding, 50% joint, muscle, 100% for severe

need 80-100% level pre-op; 40-50u/kg; maintain 30% post op

**Hemophilia B:** rarer, pure Christmas factor/IX deficiency, sex-linked recessive

PT normal, PTT prolonged

Rx: IX concentrate; 1/2 life 24h; pre-op raise level to 60%, 60u/kg, 30% postop

**VonWillibrands:**

VonWillibrand's factor/protein binds to platelets and factor VIII, causes cohesion of clot

VWF gene on chromosome 12 mutation

autosomal dominant, abnormal VWF protein synthesis  
VonWillibrand more common than hemophilia  
70% abnormal platelet adhesion, count may be normal  
affects males and females (v. hemophilia males only)  
platelet dysfunction (v. normal platelet function in hemophilia)  
increased bleeding time, petechiae, purpura, menorrhagia  
Rx: cryoprecipitate (FFP if cryo not available), achieve level >30%  
DDAVP/desmopressin: hormone which causes release of VonWillibrand's factor  
from endothelial cell storage sites

**thrombocytopenia:** most common acquired bleeding disorder  
most common hematological abnormality in critically ill patients  
seen in 20% of ICU patients  
hypothermia prevents clotting, normal platelet life 2-3d  
etiology: decreased production, sequestration, destruction (valve, DIC, HITT), sepsis,  
shock, ASA, NSAIDS, drugs, VWb  
clinical bleeding @ 30K  
bank blood has few platelets, and decreased function of remaining  
1 unit fresh whole blood -> 50k pl in 50cc, no X-match necessary  
platelet pack 5K/u @ 1h, 10pk -> 50K  
FFP contains near normal levels of most clotting factors except platelets  
(3% increase in factors/u FFP)  
plasmapheresis results in 30-60K increase

**heparin-induced thrombocytopenia (HIT),** 5% incidence with any form/route of heparin  
venous thrombosis most common presentation  
pl <150K or 50% of baseline  
onset 4-14 days after start heparin therapy, two types  
mild form (HIT-I):  
transient sequestration of platelets with heparin Rx, 15% incidence  
4d, minimal decrease platelets, direct effect of heparin on platelets  
not immunological, no thrombosis, resolves without discontinuing heparin  
severe/immune HIT (HIT-II): 4-14d, (within hrs if prior exposure to heparin)  
usually due to IV unfractionated heparin  
suspect if > 30% decrease in platelets or level < 100K, thromboembolic  
events, resistance to anticoagulation  
delayed recognition poor outcome  
heparin-associated antiplatelet IgG antibody (HAA) + pl factor 4 -> pl  
activation/aggregation, XS thrombin generation, venous and  
arterial thrombosis  
test for HAA: if negative, can resume heparin  
Rx: stop unfractionated heparin, replace with direct thrombin inhibitor  
(argatroban, lepirudin)  
fondaparinux: similar action to LMWH, does not cause immune  
mediated thrombocytopenia (HIT)

**recombinant VIIa (rVIIa)** hemostatic:  
combines w tissue factor to act on thrombin and activate platelet factor V & VIII  
stimulates thrombosis and platelet thrombus generation

activates IX & X causing thrombin burst, fibrin clot  
bypasses intrinsic cascade and shortens time to clot formation  
prothrombotic for hemophilia A & B  
greatest effect at injury site, not systemic  
use in emergency reversal of coumidin especially with intracerebral hemorrhage,  
bleeding trauma patients (after surgical hemostasis) with coagulopathy,  
perioperative hemorrhage, platelet related bleeds, bone marrow transplant,  
hepatic dysfunction, hepatic transplant, neonatal/pediatric bleeding  
10% incidence of hypertension

### Hypercoagulable states, congenital

**Factor V Leiden:** autosomal dominant (altered amino acid sequence on V)  
20% of patients with thrombosis, 5% of Caucasians, less African, Asian  
heterozygous 7X increased clotting risk, homozygous 80X

**G20210A:** another amino acid in the V chain; autosomal dominant, 4X thrombosis risk  
7% of patients with thrombosis, 3% of caucasians

**antithrombin III deficiency:** **ATIII** inhibits coagulation proteases that inhibit thrombosis,  
inactivates thrombin, Xa, XII, XI & IX; enhanced by heparin; increased risk  
DVT/PE  
congenital form: autosomal dominant, 0.03% of pop, in 5% of pts with DVT  
suspicious: young DVT, idiopathic, FH, recurrent, thrombosis resistant to  
heparin, unusual locations, during pregnancy  
high risk patients: OR, infection, trauma; give prophylaxis  
if AT activity <70% give heparin or coumidin  
if contraindicated, give AT to 80-120% level  
enoxaparin, dextran, heparin not sufficient  
IVC filter if none of the above possible  
acquired: massive thrombosis, DIC, heparin Rx, liver disease, GI/GU protein loss  
Dx: ATIII assay  
Rx: heparin followed by warfarin, antiplatelet Rx

**protein C deficiency:** inhibits the procoagulant system, lack normal ability to prevent clot  
degrades V, VIII; hepatic synthesis requires vit K  
autosomal dominant, variable penetrance; homozygous inheritance early death  
recurrent DVT/PE, test for decreased concentration protein C  
Rx lifelong heparin to warfarin

**protein S deficiency:** cofactor of protein C; vitamin K dependent hepatic synthesis  
autosomal dominant, effects and Rx same as protein C  
increased XII > 90<sup>th</sup> percentile 2X risk of thrombosis; may account for 11% of venous  
thrombotic events

### Hypercoagulable states, acquired (more common than congenital)

disseminated intravascular coagulation (DIC): thromboplastic material in circulation  
general: surgery (1/2 of DVTs start in the OR), trauma, immobility, age, malignancy,  
pregnancy, prior hx DVT/PE

**antiphospholipid antibodies:** most common of the acquired protein defects  
most commonly seen with autoimmune diseases (initially found with SLE)  
associated with 25% of unexplained thrombotic events  
Rx heparin

**thrombocytosis:** myeloproliferative disorders, post-splenectomy (problems when reach 1M),  
inflammatory disease, malignancy  
rarely symptomatic; Rx ASA, rarely plasmapheresis necessary  
platelet inhibitors:

**ASA:** weak inhibitor, blocks only one pathway, arachidonic to thromboxane;  
blocks cyclooxygenase activity of prostaglandin synthetase (COX1) and  
COX2 for the 3-5d life of the platelet

**plavix/clopidogrel:** selective inhibition of ADP receptor-mediated  
aggregation; associated with increased bleeding, transfusion requirement,  
stop 5-7d before OR; in emergency give platelet transfusion

**reopro/abciximab** (-ab indicates monoclonal antibody): inhibit platelet  
glycoprotein IIb/IIIa receptor; most potent  
for high risk for coronary event who undergo intervention (e.g.  
angioplasty) within 2d of hospitalization; severe drop in platelets;  
9d to normal platelet count

**pletal/cilostazol:** reversible phosphodiesterase III inhibition, increases  
availability of camp, causes vasodilatation, platelet inhibition; may  
improve walking distance in claudication; weak inhibitor of platelet  
aggregation; 5-7d

**NSAIDS:** inhibit thromboxane-dependent platelet function by reversibly  
inhibiting COX1 at high dose, not clinically therapeutic, 24h reversal

## **DVT/PE**

anticoagulation: INR 2.5-3 usually adequate, intensive up to 3.5

High risk for DVT/PE: closed head injury (GCS <8), pelvic & long bone fx, multiple long  
bone, spinal cord injury, hx DVT/PE, age, obesity, immobility >3d, femoral V  
catheter >24h, multiple transfusions, abnormal coags on admission

mechanical prophylaxis: foot pump, sequential pressure devices (increase femoral vein  
flow, fibrinolytic activity); pts remove pressure devices because hot, especially when  
sitting and need them most

**low dose heparin:** 5K units 2-3X/d  
reduces DVT from 25% to 9%, PE from 1.2% to 0.5%  
increase minor bleeding 4-6%

no significant difference in major bleeding  
not effective prophylaxis in trauma patients  
low dose anticoagulation decreases cath thrombosis

**low molecular weight heparin:** better than low dose in trauma, 10X cost of unfractionated  
binds to antithrombin III increasing its anti factor Xa activity  
activated PTT not useful for monitoring  
cleared by kidney, adjust dose in renal impaired  
trauma, ortho, general surgery, pelvic fx pts. treated with bed rest

spinal cord injury; continue several weeks if patient remains high risk  
**DVT/PE Rx:** 1<sup>st</sup> episode anticoagulate 6mo; stop at 3mo 25% risk of re clotting  
**lifetime anticoagulation:** ATIII deffic, Protein C, S, homozygous V Leiden, combined thrombophilias, antiplatelet antibody syndrome, G20210  
**therapeutic IVC interruption:** PE, progressive DVT in spite of adequate anticoagulation, ongoing DVT/PE risk, not candidate for anticoagulation (head bleed)  
**prophylactic IVC interruption:** controversial  
free floating clot in IVC or iliac  
after major PE, high risk of death from another PE  
in conjunction with venous embolectomy  
high risk for DVT and bleeding complications  
non-operative treatment of solid organ injury  
pelvic fx, hematoma  
retroperitoneal hematoma  
intraocular hemorrhage  
**IVC filter:** does not increase or prevent DVT (continue prophylaxis)  
reduces but does not eliminate PE risk  
IVC thrombosis in 10%, 50% recanalize, rest chronic venous stasis  
long term IVC patency 95%  
retrievable filters put in from below, retrieved from above, remove up to 1y  
**methemoglobinemia**  
ferrous form of iron capable of combining with oxygen, not when oxidized to ferric  
exposure to chemical oxidizing agent most common etiology  
genetic defect NADH dependent reductase enzyme production  
genetic abnormality of Hb making it susceptible to oxidation  
methylene blue accelerates the enzymatic reduction of methemoglobin by NADP-methemoglobin reductase and its reduction product leukomethylene blue  
directly reduces methemoglobin

## **Transfusion**

bank blood has low 2,3DPG, high O<sub>2</sub> affinity (curve shift to L)  
hemolytic transfusion reaction most commonly from ABO  
first intraop sign diffuse ooze  
fever common