Hemostasis Cheat Sheet

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Stages of Hemostasis

1. Vessel Spasm	Response to inflammation. Initiated by endothelial injury. Reflex vessel restriction by the smooth muscle layer reducing blood flow. Only last 1 minute. Thromboxane A2 released from platelets contribute to vasoconstriction. This happens locally at the site of the injury
2. Formation of Platelet Plug	Platelets are attracted to damaged vessel wall by the release of von willebrand factor. Once they encounter vWF they activate and change from disk shaped to star shaped then flat sphere like shaped. Then they adhere to collagen and aggregation occurs. Aggregation is mediated by the release of granules- ADP and TXA2 (more of these = more aggregation). Glycoprotein IIb and IIIa receptors bind fibrinogen and link platelets together. This leads to the platelet plus formation.
3. Blood Coagulation	Results in conversion of inactive soluble fibrinogen to insoluble fibrin. *Vitamin K* is necessary for synthesis of factors **VII, IX, X, prothrombin, protein C**. *Calcium* is required by activated factor **X** to convert prothrombin to thrombin. Involves intrinsic, extrinsic and common pathway. Regulated by natural anticoagulants (Antithrombin II, Protein C-inactivates factor V and VIII, plasmin-breaks down fibrin).
4. Clot Retraction	Serum is squeezed out of the clot and the edges of the vessels are joined. Failure of clot retraction is indicative of low platelet count.
5. Clot Dissolution	Needed for permanent tissue repair. Process known as fibrinolysis (getting rid of clot). Plasmin digests fibrin, factors V, VIII, XII, prothrombin. Plasminogen is activated to plasmin by enzymes (one is factor XII or Hageman factor).

These 5 stages are the holy grail of wound healing.
vWF is produced by endothelial cells, platelets and connective tissue. disorder?

Hemostasis

Definition:	The process which causes the bleeding to stop. Maintains blood fluidity and prevents blood from leaving the vascular compartments
Main Factors:	1. Cell membrane 2. Platelets 3. Coagulation cascade

Abnormal function of hemostasis: thrombosis (inappropriate clotting) or bleeding/-hemorrhaging *insufficient clotting)

Coagulation Cascade

Blood Testing for Coagulability (cont)

PTT-Partial thromboplastic time	Tests *intrinsic* pathway. Used to monitor *heparin*. Normal range is 30-50 seconds.

Hypercoagulability (increased platelet function)

Hypercoagulability results in platelet adhesion and formation of clots which leads to disruption of blood flow.

Increased Clotting Activity

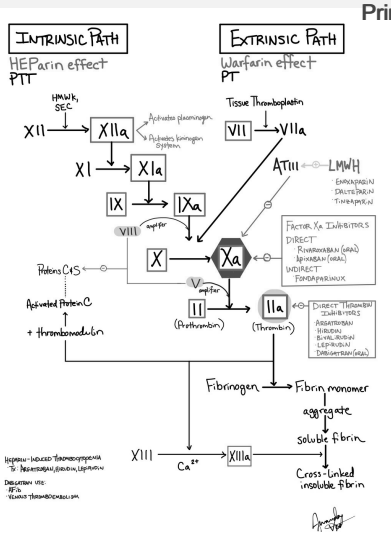
Increased Clotting Activity (cont)

Secondary:	*Acquired*. Stasis due to bed rest (slows normal blood flow and allows accumulation of clotting factors)cancer, birth control, smoking and obesity, MI.
Antiphospholipid Syndrome:	AKA Hughes syndrome. Autoimmune hypercoagulable state caused by antiphospholipid antibodies. Provokes blood clots in arteries in veins. Can be primary or secondary (due to lupus).

Bleeding Disorders

Bleeding Disorders (cont)

Thrombocytopenia:	Low circulating platelets. Due to decreased production by bone marrow (aplastic anemia, leukemia, HIV) or increased pooling of platelets in the spleen, or decreased platelet survival or nutritional deficiencies (B12, iron, folic acid),
	Types: idiopathic, thrombotic or hemolytic uremia syndromes or heparin induced.
Decreased platelet function:	Caused by asprin, uremia (increased urea in blood coats the platelets causing glycoproteins not to function) or genetic disorders



Primary: *Genetics*. Mutations in factor V and prothrombin genes. Results in inability of factor Va to be deactivated by protein C. Examples: Factor V Leiden disorder where clotting persists and predisposes to DVT. Other disorders are inherited deficiencies of antithrombin III, protein C/S.

Platelet Disorders:	normal range: 150,000- 400,00-0/ml. Signs of disorders include:
	Petechia, purpura, ecchmyosis, bleeding from mucous membrane

Blood Testing for Coagulability

PT-Prothrombin time	Tests *extrinsic* and *common* pathway. Looking at time to clot. Used to monitor *warfarin*. Normal is 11-13 seconds. PT is increased with warfarin

Bleeding Disorders (cont)

	Genetic disorders: Bernard Soulier- GpIIb disorder so vWf has nowhere to bind, Von Willebrand Disease-no vWF to bind platelets. Leads to decreased platelet adhesion *Vasopressin can stimulate release of vWF for tx. Glanzmann thrombocytopenia- GpIIb-IIIa so platelets cant bind together
Coagulation Cascade Disorders:	Deficiencies or impairments of one or more coagulation factors due to defective synthesis, inherited disease or increased consumption. Prevents fibrinogen from converting to fibrin. Will see bleeding in deep tissues like hematomas. Elevated PTT and PT.

Bleeding Disorders (cont)

Hemophilia A- Factor VIII deficiency: X-linked recessive disorder, affects mostly males. Soft tissue bleeding of GI, hip, knee, elbow and ankle joints. Can lead to joint fibrosis and contractures. Tx is factor VIII replacement therapy. Only affects intrinsic pathway.

Anticoagulants

Warfarin (Coumadin):	Vitamin K antagonist. Blocks epoxidase reductase, leads to depletion of reduced vit K (which is essential for synthese of factors II, VII,IX,X, protein c/s)
	Uses: Prevention of thrombosis in predisposed patients. AE- bleeding

Anticoagulants (cont)

Heparin(IV)/ LMW Heparin (lovenox):	Induces a conformational change in antithrombin III making it more accessible to proteases -> increase inactivation of thrombin
	Uses: Prophylaxis and tx of thromboembolic diseases, unfractionated (IV heparin) used with antiplatelet agents for tx of acute coronary syndromes. Lovenox is an efficient catalyzation of factor Xa inactivation.
	AE: bleeding and heparin induced thrombocytopenia

Novel Oral Anticoagulants

Apixaban (Eliquis), Rivaroxaban (Xarelto):	Direct inhibitor of free and clot-bound factor Xa which prevents the conversion of prothrombin to thrombin. Prevents clot formation.

Novel Oral Anticoagulants (cont)

	Uses: A- reduces stroke and systemic embolism, prophylaxis of DVT/PE after hip or knee surgery. R- same but prophylaxis of venous thromboembolic events for hip/knee surgery pts.
	AE: easy bruising, bleeding, back or muscle pain, hypotension.
Dabigatran (Pradaxa):	Direct thrombin inhibitor which prevents conversion of fibrinogen to fibrin.
	Uses: Prevents thromboembolism in pts with AF, DVT, PE
Betrixaban (Bevyxxa):	Cofactor-independent direct inhibitor of factor Xa.
	Uses: prophylaxis of VTE in moderate to severe restricted mobility patients.

Rivaroxaban interacts with Aspirin.
All drugs will have bleeding as a side effect!

Inhibition of Anticoagulation

Protamine:	Antagonist of heparin.
	Uses: IV administration if there is life threatening hemorrhage/heparin excess

Thrombolytic Agents

Streptokinase:	Forms a stable complex with plasminogen which then cleaves other plasminogen molecules into plasmin
	Uses: PE, STEMI, arterial thrombosis, DVT. *AE*:systemic fibrinolysis, hemorrhage
Recombinant Tissue Plasminogen Activator:	Binds to newly formed thrombi and makes it a potent activator of plasminogen. Cleaves plasminogen into plasmin which then cleaves fibrin into fibrin degradation products
	Uses: PE,STEMI, Acute ischemia stroke. *AE*: bleeding

Antiplatelet Agents

Aspirin (ASA)	Non selective COX inhibitor. Irreversible inhibition of COX-1= inhibits platelet aggregation for 10 days. Stops conversion of arachidonic acid to thromboxane A2 (potent platelet aggregation inducer).
	Uses: Pain/inflammation/fever, reduces risk of MI/unstable angina, prevents strokes due to blood clots
	AE: hemorrhagic stroke, GI bleeding

PDE Inhibitors

Cilostazol (Pletal)	Antiplatelet and vasodilator. Inhibitors phosphodiesterase II -> suppresses cAMP degradation -> increases cAMP in platelets and blood vessels -> inhibition of platelet aggregation and vasodilation

Antiplatelet Agents (cont)

	Uses: Intermittent claudication symptoms (by widening the vessels in teh legs which helps with blood flow).
	AE, DI: heart failure, tachycardia, interacts with NSAIDs and aspirin.
Pentoxifylline (Trental)	Inhibits erythrocyte phosphodiesterase -> increases cAMP activity, decreases blood viscosity by reducing plasma fibrinogen concentrations and increasing fibrinolytic activity
	Uses: Intermittent claudication, chronic occlusive arterial disease
	AE: muscle aches, headaches, GI discomfort

ADP Receptor Pathway Inhibitor

Clopidogrel (Plavix)	Irreversibly binds to P2Y12 which prevents the binding of ADP receptors on platelets which prevents GPIIb-IIIa activation -> inhibits platelets aggregation

Antiplatelet Agents (cont)

	Uses: reduces risk of MI/stroke, better than aspirin in decreasing CV outcomes
	AE, DI: upper RTI, joint, chest pain, depression, bleeding. DI-Ibuprofen

GPIIb-IIIa Antagonist

Abicixmab (Reopro)	Binds to intact platelet GPIIb/IIIa receptor and blocks access of large molecules to receptor through steric hinderance or conformational change. Prevents cell adhesion
	Uses: prevents cardiac ischemic complications in vascular surgeries or pts w/ unstable angina, intended for use with aspirin and heparin
	AE: N&V, hypotension, vision changes, back pain