Clinical Volume Pearls

30% acute loss: hypovolemic shock
Hemodilution (massive crystalloids / sepsis): protein drop → edema / drug binding changes

Marrow / Stem-Cell Disorders

Aplastic Anemia	Myelodysplastic Syndromes	Leukemias	Myelofibrosis
hypocellular marrow (immune/drug/toxin) → pancytopenia, low retic, empty biopsy	cellular marrow with dysplasia & ineffective hematopoiesis → cytopenias, macrocytic indices, risk of AML	malignant blast proliferation (> 20% blasts in marrow) → anemia, infections, bleeding	collagen deposition in marrow, JAK2/CALR/MPL mutations → EMH, massive spleen, teardrops

Hypercoagulability

↑ platelet function → endothelial injury (atherosclerosis, DM, smoking, hyperlipidemia)
↑ clotting activity
- inherited: factor V leiden (APC resistance), prothrombin G20210A, protein C/S or ATIII deficiency
- acquired: pregnancy/OCPs, stasis (immobility, CHF), malignancy, antiphospholipid syndrome, inflammation/sepsis

Plasma Proteins

Albumin (54%)	Globulins (38%)	Fibrinogen (7%)
large, stays intravascular: maintains colloid oncotic pressure	α-globulins → bilirubin & steroids	soluble: thrombin converts to insoluble fibrin → coagulation mesh
carrier for bilirubin, hormones, FFAs, many drugs	β-globulins → iron (transferrin) & copper (ceruloplasmin)	when removed, remaining fluid = serum
↓ albumin (cirrhosis, nephrotic syndrome, malnutrition) → edema, ↑ free drug fraction	γ-globulins → immunoglobulins (antibodies)	

Lab distinction: order plasma for coagulation studies (contains fibrinogen) vs serum for chemistries / antibodies

Plasma Proteins (cont)

Polycythemia Vera, Essential Thrombocythemia / CML	myeloproliferative neoplasms with overproduction of mature myeloid elements

Diagnostic Cornerstones

CBC & Differential	Reticulocyte Count / Index	ESR	Bone-Marrow Aspiration (cell morphology, iron stores, blast %), Core Biopsy (cellularity, fibrosis, architecture)	Peripheral Smear Clues

Diagnostic Cornerstones (cont)

Hb	distinguishes underproduction vs peripheral loss hemolysis/bleed	height RBC falls in 1 hr	posterior iliac crest standard
Hct		trend in RA, temporal arteritis, SLE	
MCV (micro- vs macrocytic)			
MCHC			
RDW			
WBC absolute counts			
platelets & MPV			

Hematopoiesis

Developmental migration → yolk sac (wk 2-8) → liver + spleen (wk 8-7 mo gestation) → bone marrow (≧7 mo fetal & post-natal)
Adult active (red) marrow restricted to axial skeleton & proximal long bones: yellow marrow = fat (can reconvert under stress)
Pluripotent hematopoietic stem cell (HSC): self-renewing: differentiates to:
- Common myeloid progenitor → CFU-E (erythroid), CFU-GM (granulocyte/monocyte), CFU-Meg (megakaryocyte)
- Common lymphoid progenitor → pro-B, pro-T, NK
Cytokine / growth-factor regulation:
- Erythropoietin (EPO) — renal peritubular cells respond to hypoxia → ↑ RBC proliferation & Hb synthesis

Hematopoiesis (cont)

- Granulocyte-CSF / GM-CSF — drive neutrophil & monocyte lines: pharmacologic G-CSF (filgrastim) for chemo induced neutropenia
- Thrombopoietin (TPO) — hepatic & renal origin: binds megakaryocytes & platelets → controls platelet mass
- IL-3, IL-5, IL-7 fine-tune lineage commitment

Extramedullary hematopoiesis (EMH):

- Occurs when marrow incapable (fibrosis, infiltration, hemolytic stress) → liver & spleen resume fetal role → splenomegaly, leuko--erythroblastic smear, tear-drop RBCs

Normal Hemostatic Sequence

1. Vascular Spasm	2. Platelet Activation	3. Platelet Activation + Aggreg-ation	4. Coagul-ation Cascade	5. Clot Retraction & Fibrin-olysis
endoth-elin-1 (endot-helium), thromb-oxane A2 & serotonin (plate-lets) ↓ blood flow	vWF binds exposed collagen, links to platelet GP Ib	shape change: dense--granule release (ADP, Ca2+, seroto-nin): GP IIb/IIIa binds fibrinogen → primary plug	intrinsic (contact): XII → XI → IX (+VIII) → Xa	platelet actin--myosin contracts: tPA converts plasmi-nogen → plasmin: plasmin degrades fibrin → D-dimers
			extrinsic (tissue factor): TF + VIIa → Xa (fast)	

Normal Hemostatic Sequence (cont)

common: Xa + Va + Ca2+ + phospholipid → prothrombin → thrombin: thrombin converts fibrinogen → fibrin, activates V, VIII, XIII and platelets

anticoagulant safeguards: ATIII (heparin--cofactor), protein C/S, TFPI