

### 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
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hypo cellular marrow (immunologic/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) → anemias, infections, bleeding

collagen deposition in marrow, JAK2/C-ALR/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%)
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### Plasma Proteins (cont)

large, stays intravascular: maintains colloid oncotic pressure

α-globulins → bilirubin & steroids

soluble: thrombin converts to insoluble fibrin → coagulation mesh

β-globulins → iron (transferrin) & copper (ceruloplasmin)

γ-globulins → immunoglobulins (antibodies)

myeloproliferative neoplasms (myeloproliferative syndrome, polycythemia / CML)

↓ albumin (nephrosis, nephrotic syndrome, malnutrition, edema, drug fraction)

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

### Diagnostic Cornerstones

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

Hb	distinguis	height	posterior
	underp	RBC	iliac
	roductio	falls in 1	crest
	vs	hr	standard
	peripheral		
	loss		
	hemoly		
	sis/bleed		

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 reconver 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



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Page 1 of 2.

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### 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 (cont)

common: Xa + Va + Ca<sup>2+</sup> + phospholipid  
 → prothrombin → thrombin: thrombin  
 converts fibrinogen → fibrin, activates V, VIII, XIII and platelets

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

### Normal Hemostatic Sequence

1.	2.	3.	4.	5.
Vascular Spasm	Platelet Activation	Platelet Activation + Aggregation	Coagulation Cascade	Clot Retraction & Fibrinolysis
endothelin-1 (endothelium), thromboxane A <sub>2</sub> & serotonin (platelets) ↓ blood flow	vWF binds exposed collagen, links to platelet GP Ib	shape change: dense granule release (ADP, Ca <sup>2+</sup> , serotonin): GP IIb/IIIa binds fibrinogen → primary plug	intrinsic (contact): XII → XI → IX (+VIII) → Xa	platelet actin-myosin contracts: tPA converts plasminogen → plasmin: plasmin degrades fibrin → D-dimers

extrinsic (tissue factor): TF + VIIa → Xa (fast)



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