🧬 HEMATOLOGY AND ONCOLOGY FOR USMLE 🧬

IMPORTANT PATHOLOGIES

Leukopenias | Heme | Porphyrias | Lead and Iron Poisoning | Coagulation Disorders | Platelet Disorders | Thrombotic Microangiopathies | Mixed Platelet and Coagulation Disorders | Hereditary Thromophilias | Blood Transfusion | Acute and Chronic Leukemias

---

LEUKOPENIAS

Leukopenia refers to a decrease in total white blood cell (WBC) count, predisposing the patient to infections. It is classified based on which WBC lineage is reduced.

---

1. Neutropenia

Definition

- Absolute neutrophil count (ANC) < 1500 cells/mm^3
- Severe neutropenia: ANC < 500 cells/mm^3 → high risk of life-threatening infections ⚠️

Why neutrophils matter

- Neutrophils are the first line of defense against bacterial and fungal infections.
- Severe neutropenia commonly presents with sepsis and recurrent infections 🦠

Causes

- Sepsis / post-infection: consumption and exhaustion of neutrophils
- Drugs: especially chemotherapy, antithyroid drugs, antibiotics
- Aplastic anemia: bone marrow failure → ↓ production
- Autoimmune diseases: e.g., SLE
- Radiation exposure: marrow suppression

- Congenital neutropenia: inherited defects in neutrophil production

---

2. Lymphopenia

Definition

- Absolute lymphocyte count < 1500 cells/mm^3
- Children: < 3000 cells/mm^3 (higher normal baseline)

Why lymphocytes matter

- Lymphocytes are crucial for adaptive immunity (T cells, B cells, NK cells).
- Lymphopenia leads to viral, fungal, and opportunistic infections 🧠

Causes

- HIV infection: destruction of $CD4^+$ T cells
- Congenital immunodeficiencies:
    - DiGeorge syndrome (thymic aplasia)

    - SCID (combined B and T cell deficiency)
- Autoimmune disorders: e.g., SLE
- Glucocorticoid therapy
- Radiation
- Sepsis and postoperative stress

---

3. Eosinopenia

Definition

- Absolute eosinophil count < 30 cells/mm³

Causes

- Cushing syndrome
- Exogenous glucocorticoids

> Eosinopenia itself is usually clinically insignificant, but it helps indicate steroid excess 💊

Effect of Glucocorticoids on WBCs ⚡

- Cause neutrophilia, despite causing leukopenia of other cells
- Mechanism:
  - ↓ activation of neutrophil adhesion molecules
  - Neutrophils remain in circulation instead of migrating to tissues
- Cause lymphopenia:
  - Induce apoptosis of lymphocytes
- Cause eosinopenia:
  - Sequestration in lymph nodes

📌 Key concept:

Glucocorticoids increase neutrophils in blood but impair immune function overall

---

HEME SYNTHESIS, PORPHYRIAS & LEAD POISONING

Porphyrias are disorders of defective heme synthesis, leading to accumulation of toxic heme precursors.

Lead poisoning mimics porphyrias by inhibiting key enzymes ⚙️

---

1. Lead Poisoning

Affected Enzymes

- ALA dehydratase
- Ferrochelatase

Accumulated Substrates

- δ-Aminolevulinic acid (ALA)
- Protoporphyrin

Hematologic Findings

- Microcytic anemia
- Basophilic stippling on peripheral smear
- Ringed sideroblasts in bone marrow 🔬

Clinical Features

- GI symptoms: abdominal pain

- Renal disease
- Children: lead paint exposure → neurodevelopmental delay
- Adults: batteries, ammunition → headache, memory loss, peripheral neuropathy

---

2. Acute Intermittent Porphyria (AIP)

Enzyme Defect

- Porphobilinogen deaminase
- Autosomal dominant

Accumulated Substrates

- Porphobilinogen
- ALA

Classic Symptoms – "5 P's" 🧠

1. Painful abdomen
2. Port wine–colored urine

3. Polyneuropathy
4. Psychological disturbances
5. Precipitated by ↑ ALA synthase

Triggers

- CYP450-inducing drugs
- Alcohol
- Starvation

Treatment

- Hemin
- Glucose (↓ ALA synthase activity)

📌 Important:

No photosensitivity in AIP ❌☀️

---

3. Porphyria Cutanea Tarda (PCT)

Enzyme Defect

- Uroporphyrinogen decarboxylase

Accumulated Substrate

- Uroporphyrin → tea-colored urine ☕

Clinical Features

- Blistering photosensitivity
- Hyperpigmentation
- Most common porphyria

Exacerbating Factors

- Alcohol
- Hepatitis C

Treatment

- Phlebotomy
- Sun avoidance
- Antimalarials (e.g., hydroxychloroquine)

Heme Synthesis Pathway

- Succinyl-CoA + Glycine
  - ↓ *(ALA synthase – rate-limiting step)*
- ALA
  - ↓ *(ALA dehydratase – inhibited by lead)*
- Porphobilinogen
  - ↓ *(Porphobilinogen deaminase – AIP)*
- Hydroxymethylbilane
  - ↓
- Uroporphyrinogen III
  - ↓ *(Uroporphyrinogen decarboxylase – PCT)*
- Protoporphyrin
  - ↓ *(Ferrochelatase – inhibited by lead)*
- Heme (Fe^{2+} added) 🩸

IRON POISONING

Iron poisoning can present as acute (usually accidental) or chronic (due to iron overload states).

1. Acute Iron Poisoning

Key Findings

- High mortality rate, especially in children
- Occurs due to accidental ingestion of iron tablets
- Adult iron tablets may look like candy 🍬 → common cause in pediatrics

Mechanism

- Excess iron causes free radical formation
- Leads to lipid peroxidation of cell membranes
- Result: direct cellular injury and cell death ⚠️

Symptoms and Signs

- Severe abdominal pain
- Vomiting
- GI bleeding
- Radiopaque iron pills visible on abdominal X-ray 📸
- May progress to:

    - Anion gap metabolic acidosis
    - Multiorgan failure
- Late complication:
    - GI scarring → intestinal obstruction

Treatment

- Chelation therapy
    - Deferoxamine
    - Deferasirox
- Gastric lavage (early cases)

📌 Exam pearl:

Acute iron poisoning = GI symptoms + metabolic acidosis + radiopaque pills

---

2. Chronic Iron Poisoning (Iron Overload)

Seen In

- Primary (hereditary) hemochromatosis
- Secondary hemochromatosis, e.g.:

    - Chronic blood transfusions (thalassemia, sickle cell disease)

Mechanism

- Progressive iron deposition in tissues
- Causes organ dysfunction due to oxidative damage

Symptoms and Signs

- Arthropathy
- Cirrhosis of liver
- Cardiomyopathy
- Diabetes mellitus
- Skin hyperpigmentation
    - Classic: "Bronze diabetes" 🟤
- Hypogonadism

Treatment

- Phlebotomy (if patient is not anemic)
- Chelation therapy (if phlebotomy not possible)

COAGULATION DISORDERS – BASIC TESTS 🧠

---

1. Prothrombin Time (PT)

What it Tests

- Extrinsic pathway + common pathway
- Factors: I, II, V, VII, X

Key Point

- Defect → ↑ PT

🧠 Mnemonic:
"Play Tennis Outside" → Extrinsic pathway 🎾

---

2. INR (International Normalized Ratio)

- INR = Patient PT / Control PT
- Normal INR = 1
- INR > 1 → prolonged clotting

Clinical Use

- Most common test to monitor warfarin therapy
- Warfarin → ↑ INR

---

3. Partial Thromboplastin Time (PTT)

What it Tests

- Intrinsic pathway + common pathway
- Tests all factors except VII and XIII

Key Point

- Defect → ↑ PTT

🧠 Mnemonic:
"Play Table Tennis Inside" 🏓

---

4. Thrombin Time (TT)

What it Measures

- Conversion of fibrinogen → fibrin

Prolonged In

- Anticoagulant therapy
- Hypofibrinogenemia
- DIC
- Liver disease

MIXING STUDY

Used to differentiate between:

- Clotting factor deficiency
- Factor inhibitor

How it Works

- Normal plasma is mixed with patient plasma

Interpretation

- Correction of PT/PTT → Factor deficiency

- No correction → Factor inhibitor
    - Most commonly anti-factor VIII

SPECIFIC COAGULATION DISORDERS

Hemophilia A, B, and C

PT / PTT Pattern

- PT: Normal
- PTT: Increased

Mechanism

- Intrinsic pathway defect

Types

- Hemophilia A
    - Factor VIII deficiency
    - X-linked recessive
    - Pronounced: *"hemophilia ate (eight)"* 🍽️
- Hemophilia B

    - Factor IX deficiency
    - X-linked recessive
- Hemophilia C
    - Factor XI deficiency
    - Autosomal recessive

Clinical Features

- Hemarthroses (bleeding into joints, esp. knee)
- Easy bruising
- Excessive bleeding after trauma or surgery (e.g., dental extraction) 🦷

Treatment

- Hemophilia A
    - Desmopressin
    - Factor VIII concentrate
    - Emicizumab
- Hemophilia B
    - Factor IX concentrate
- Hemophilia C

- Factor XI concentrate

Vitamin K Deficiency

PT / PTT Pattern

- ↑ PT
- ↑ PTT
- Bleeding time: Normal

Mechanism

- ↓ activity of vitamin K–dependent factors
  - II, VII, IX, X
  - Protein C and Protein S

📌 Key exam line:

Vitamin K deficiency affects both intrinsic and extrinsic pathways

---

PLATELET DISORDERS – GENERAL FEATURES

All platelet disorders share some core clinical features:

- ↑ Bleeding time (BT) ⏱️
- Mucocutaneous bleeding
  - Epistaxis
  - Gum bleeding
  - Menorrhagia
- Microhemorrhages
  - Petechiae
  - Purpura

Platelet Count (PC)

- Usually decreased
- May be normal in qualitative platelet disorders (function defect, not number)

📌 Key concept:

Platelet disorders → bleeding from skin & mucous membranes, not deep muscle bleeds

SPECIFIC PLATELET DISORDERS

1. Bernard-Soulier Syndrome

Platelet Count / Bleeding Time

- Platelet count: ↓ or normal
- Bleeding time: ↑

Pathophysiology

- Autosomal recessive
- Defect in platelet adhesion
- ↓ GpIb receptor
  - Normally binds vWF
  - Required for platelet adhesion to damaged endothelium

➡️ Result: Impaired platelet-vWF adhesion

Laboratory Findings

- Decreased platelet aggregation

- Giant (big) platelets on blood smear 🔬

📌 One-liner:

Bernard-Soulier = GpIb defect → adhesion problem

---

2. Glanzmann Thrombasthenia

Platelet Count / Bleeding Time

- Platelet count: ↓ or normal
- Bleeding time: ↑

Pathophysiology

- Autosomal recessive
- Defect in platelet aggregation
- ↓ GpIIb/IIIa (integrin αIIbβ3)

➡️ Platelets cannot bind fibrinogen
➡️ Platelet-to-platelet aggregation fails ❌

Laboratory Findings

- Blood smear shows no platelet clumping

📌 One-liner:

Glanzmann = GpIIb/IIIa defect → aggregation problem

---

3. Immune Thrombocytopenia (ITP)

Platelet Count / Bleeding Time

- Platelet count: ↓
- Bleeding time: ↑

Pathophysiology

- Autoimmune destruction of platelets
- Anti-GpIIb/IIIa antibodies
- Antibody-coated platelets are phagocytosed by splenic macrophages 🧠

Causes

- Idiopathic

- Secondary to:
    - Autoimmune diseases (e.g., SLE)
    - Viral infections (HIV, HCV)
    - Malignancies (e.g., CLL)
    - Drug reactions

Laboratory Findings

- ↓ Platelet count
- ↑ Megakaryocytes in bone marrow (compensatory response)

Treatment

- First line: Glucocorticoids
- Others:
    - IVIG
    - Rituximab
    - TPO receptor agonists (eltrombopag, romiplostim)
- Refractory cases: Splenectomy 🩺

📌 Exam pearl:

ITP = low platelets + increased megakaryocytes

---

4. Uremic Platelet Dysfunction

Platelet Count / Bleeding Time

- Platelet count: Normal
- Bleeding time: ↑

Mechanism

- Occurs in chronic renal failure
- Accumulation of uremic toxins
- Toxins interfere with platelet adhesion and aggregation

📌 Important:

Platelet number is normal, but function is impaired

THROMBOTIC MICROANGIOPATHIES (TMA)

These disorders:

- Share overlapping features
- Can resemble DIC
- DO NOT show consumptive coagulopathy

Key Difference from DIC

- Normal PT and PTT
- Normal fibrinogen
- Clotting cascade is not activated ⚠️

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

Epidemiology

- Typically adult females

Pathophysiology

- Deficiency or inhibition of ADAMTS13

    - ADAMTS13 = vWF metalloprotease
- ↓ cleavage of large vWF multimers
- Accumulation of large vWF multimers
- → Excessive platelet adhesion and aggregation
- → Microthrombi formation

HEMOLYTIC UREMIC SYNDROME (HUS)

Epidemiology

- Typically children

Pathophysiology

- Most commonly caused by Shiga toxin–producing E. coli
    - Serotype O157:H7
- Toxin causes severe endothelial damage
- Leads to platelet activation and microthrombi

COMMON PRESENTATION (Triad) – TTP & HUS

Classic Triad 🩸

1. Thrombocytopenia (↓ platelets)
2. Microangiopathic hemolytic anemia
    - ↓ Hemoglobin
    - Schistocytes on smear
    - ↑ LDH
3. Acute kidney injury
    - ↑ Creatinine

Differentiating Features

Feature	TTP	HUS
Additional symptoms	Fever + neurologic symptoms 🧠	Bloody diarrhea
PT / PTT	Normal	Normal

📌 Key exam line:

Normal PT & PTT help distinguish TTP/HUS from DIC

Treatment

TTP

- Plasma exchange (treatment of choice)
- Glucocorticoids
- Rituximab

HUS

- Supportive care only
  - Fluids
  - Dialysis if needed

MIXED PLATELET AND COAGULATION DISORDERS

These disorders affect both primary hemostasis (platelets) and secondary hemostasis (coagulation cascade).
Hence, abnormalities are seen in bleeding time (BT) *and* sometimes PT / PTT.

VON WILLEBRAND DISEASE (vWD)

Platelet Count / Bleeding Time / PT / PTT

- Platelet count: Normal
- Bleeding time: ↑
- PT: Normal
- PTT: Normal or ↑

Pathophysiology (Two Key Defects ⚠️)

1. Platelet Plug Formation Defect

- ↓ von Willebrand factor (vWF)

- vWF is needed for platelet adhesion to exposed collagen via GpIb
- Result → defective platelet–vWF adhesion 🩹

2. Intrinsic Pathway Coagulation Defect

- vWF carries and protects factor VIII
- ↓ vWF → ↓ factor VIII
- Result → ↑ PTT

📌 Key concept:

vWD affects both platelets and coagulation

Genetics

- Most common inherited bleeding disorder
- Usually autosomal dominant
- Generally mild

Clinical Presentation

- Menorrhagia
- Epistaxis
- Easy bruising
- Mucocutaneous bleeding

Treatment

- Desmopressin
    - Releases vWF stored in endothelial cells
- vWF-containing factor VIII concentrates

DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

A consumptive coagulopathy caused by widespread activation of the coagulation cascade.

Platelet Count / Bleeding Time / PT / PTT

- Platelet count: ↓

- Bleeding time: ↑
- PT: ↑
- PTT: ↑

Pathophysiology

- Systemic activation of clotting factors → microthrombi formation
- Rapid consumption of:
  - Platelets
  - Clotting factors
- Leads to simultaneous thrombosis and bleeding ⚠️

📌 Classic description:

"Clot everywhere, bleed everywhere"

Clinical Features

- Thromboses
- Hemorrhages

    - Oozing from IV lines or puncture sites
- May be:
    - Acute (life-threatening)
    - Chronic (if liver compensates)

Causes – SSSTOP 🧠

- Sepsis (especially gram-negative)
- Snake bites
- Stroke (heat stroke)
- Trauma
- Obstetric complications
- Pancreatitis (acute)
- Also: malignancy, nephrotic syndrome, massive transfusion

Laboratory Findings

- Schistocytes on blood smear

- ↑ D-dimers (fibrin degradation products)
- ↓ Fibrinogen
- ↓ Factors V and VIII

HEREDITARY THROMBOPHILIAS

These are autosomal dominant disorders causing a hypercoagulable state, i.e., ↑ tendency to form clots 🧬

---

1. Antithrombin Deficiency

Mechanism

- Antithrombin normally inhibits:
  - Factor IIa (thrombin)
  - Factor Xa
- Deficiency → excess clot formation

Lab

- PT, PTT, TT: Normal

- Heparin resistance
    - Heparin works by activating antithrombin
    - Deficiency → ↓ rise in PTT after heparin

Acquired Causes

- Nephrotic syndrome / renal failure
- Loss of antithrombin in urine 🚰

---

2. Factor V Leiden Mutation

Mechanism

- Point mutation: Arg506Gln
- Factor V becomes resistant to activated protein C
- Failure to inactivate Va

Clinical Complications

- Deep vein thrombosis (DVT)
- Cerebral vein thrombosis
- Recurrent pregnancy loss

📌 Most common inherited thrombophilia

---

3. Protein C or Protein S Deficiency

Mechanism

- Normally:
  - Protein C cancels
  - Protein S stops coagulation 🛑
- Deficiency → ↓ inactivation of factors Va and VIIIa

Clinical Significance

- Hypercoagulable state
- ↑ risk of warfarin-induced skin necrosis
  - Due to early loss of protein C (short half-life)

---

4. Prothrombin G20210A Mutation

Mechanism

- Point mutation in 3´ untranslated region

- Leads to ↑ prothrombin production
- ↑ plasma prothrombin → ↑ clot risk

Clinical Feature

- Venous thrombosis

Summary Line 🔥

vWD = platelet + intrinsic pathway defect
DIC = consumption of platelets and clotting factors
Thrombophilias = normal labs, abnormal clotting tendency

BLOOD TRANSFUSION THERAPY

Blood transfusion is used to restore oxygen-carrying capacity, hemostasis, or intravascular volume, depending on the component transfused.

1. Packed Red Blood Cells (PRBCs)

Dose & Effect

- ↑ Hemoglobin ~1 g/dL per unit
- ↑ Hematocrit ~3% per unit
- Improves oxygen-carrying capacity 🫁

Clinical Uses

- Acute blood loss
- Severe or symptomatic anemia

📌 Key point:

PRBCs are preferred over whole blood to avoid volume overload.

---

2. Platelets

Dose & Effect

- ↑ Platelet count ~30,000/μL per unit
  - (≈ ↑ 5,000/mm³ per unit)

Clinical Uses

- Active or significant bleeding
- Thrombocytopenia
- Qualitative platelet defects

📌 Exam tip:

Platelets are given based on bleeding risk, not just platelet number.

---

3. Fresh Frozen Plasma (FFP) / Prothrombin Complex Concentrate (PCC)

Contents

- FFP
  - All coagulation factors
  - Plasma proteins
- PCC
  - Factors II, VII, IX, X
  - Proteins C and S

Effect

- ↑ Coagulation factor levels

Clinical Uses

- Cirrhosis
- Immediate reversal of anticoagulation (especially warfarin)

📌 High-yield:

PCC acts faster and requires less volume than FFP ⚡

---

4. Cryoprecipitate

Contents

- Fibrinogen
- Factor VIII
- Factor XIII
- von Willebrand factor

- Fibronectin

Clinical Uses

- Hypofibrinogenemia
- Factor VIII deficiency
- Certain bleeding disorders

🧠 Mnemonic:

Cryo = "F8, F13, vWF, fibrinogen"

S. Albumin

Effect

- ↑ Intravascular volume
- ↑ Oncotic pressure

Clinical Uses

- Post-paracentesis
- Therapeutic plasmapheresis

RISKS OF BLOOD TRANSFUSION ⚠️

Although generally safe, transfusions carry important risks:

- Infection transmission (very low risk)
- Transfusion reactions
- TACO (Transfusion-Associated Circulatory Overload)
    - Volume overload → pulmonary edema, hypertension
- TRALI (Transfusion-Related Acute Lung Injury)
    - Hypoxia + inflammation
    - Noncardiogenic pulmonary edema
    - Hypotension
- Iron overload
    - Chronic transfusions → secondary hemochromatosis
- Hypocalcemia
    - Citrate chelates Ca^{2+}

- Hyperkalemia
    - RBC lysis in stored blood 🧂

LEUKEMIA vs LYMPHOMA

Leukemia

- Myeloid or lymphoid neoplasm
- Diffuse bone marrow involvement
- Tumor cells commonly found in peripheral blood

Lymphoma

- Discrete solid tumor
- Arises from lymph nodes
- May have:
    - Extranodal involvement
    - Leukemic presentation

HODGKIN vs NON-HODGKIN LYMPHOMA

Shared Features

- May have B symptoms:
  - Low-grade fever
  - Night sweats 🌙
  - Weight loss

Hodgkin Lymphoma

- Localized
- Single lymph node group
- Contiguous spread
- Stage = strongest prognostic factor
- Better prognosis overall
- Characterized by Reed-Sternberg cells
- Mostly B-cell origin
- Bimodal age distribution
  - Young adults
  - 55 years
- Associated with EBV

- May be associated with autoimmune diseases

Non-Hodgkin Lymphoma

- Multiple lymph nodes involved
- Noncontiguous spread
- Extranodal involvement common
- Worse prognosis
- May arise from B or T cells
- Associated with:
    - HIV
    - EBV
    - HTLV

LEUKEMIAS

Definition

- Malignant disorders with unregulated proliferation of WBCs in bone marrow

- → Marrow failure, causing:
  - Anemia (↓ RBCs)
  - Infections (↓ functional mature WBCs)
  - Hemorrhage (↓ platelets)

Peripheral blood

- Usually ↑ circulating WBCs (malignant leukocytes)
- Sometimes normal or ↓ WBC count

Organ infiltration

- Liver
- Spleen
- Lymph nodes
- Skin → Leukemia cutis

LYMPHOID NEOPLASMS

ACUTE LYMPHOBLASTIC LEUKEMIA / LYMPHOMA (ALL)

Epidemiology

- Most common childhood leukemia
- Less common in adults → worse prognosis
- Associated with Down syndrome

Clinical features

- T-cell ALL → mediastinal mass
    - May cause SVC-like syndrome
- May spread to:
    - CNS
    - Testes

Peripheral blood & bone marrow

- ↑ ↑ ↑ lymphoblasts

Immunophenotype

- TdT+ (marker of pre-B & pre-T cells)
- CD10+ (pre-B cell marker)

Genetics & prognosis

- t(12;21) → good prognosis
- t(9;22) (Philadelphia chromosome) → poor prognosis

Treatment response

- Most responsive leukemia to therapy

CHRONIC LYMPHOCYTIC LEUKEMIA / SMALL LYMPHOCYTIC LYMPHOMA (CLL/SLL)

Epidemiology

- Age >60 years
- Most common adult leukemia

Cell type & markers

- Mature B-cell neoplasm
- CD20+, CD23+, CD5+

Clinical features

- Often asymptomatic
- Slow progression
- Autoimmune hemolytic anemia

Peripheral smear

- Smudge cells
- Mnemonic: CLL = Crushed Little Lymphocytes

Complication

- Richter transformation
    - CLL/SLL → Diffuse large B-cell lymphoma (DLBCL)

HAIRY CELL LEUKEMIA

Epidemiology

- Adult males
- Mature B-cell tumor

Morphology

- Cells with hair-like cytoplasmic projections
- "Fuzzy" appearance on LM
- Peripheral lymphadenopathy uncommon

Bone marrow

- Marrow fibrosis
- → Dry tap on aspiration

Clinical features

- Massive splenomegaly
- Pancytopenia

Stains & genetics

- TRAP positive
    - (TRAPped in a hairy situation)
- TRAP largely replaced by flow cytometry
- Associated with BRAF mutation

Treatment

- Purine analogs
    - Cladribine
    - Pentostatin

MYELOID NEOPLASMS

ACUTE MYELOGENOUS LEUKEMIA (AML)

Epidemiology

- Median age ~65 years

Peripheral smear

- ↑ ↑ ↑ myeloblasts
- Auer rods
- Myeloperoxidase positive

Special subtype — APL (M3 AML)

- Promyelocytes
- t(15;17) → PML-RAR α
- High risk of DIC
- Treatment:
  - All-trans retinoic acid (ATRA)
  - Arsenic trioxide
  - → induces differentiation

Clinical complication

- Leukostasis
    - Capillary occlusion by rigid malignant cells
    - → organ damage

Risk factors

- Alkylating chemotherapy
- Radiation
- Benzene exposure
- Myeloproliferative disorders
- Down syndrome
    - Typically acute megakaryoblastic leukemia (M7)

CHRONIC MYELOGENOUS LEUKEMIA (CML)

Epidemiology

- Peak: 45–85 years
- Median age: 64 years

Genetics

- Philadelphia chromosome
- t(9;22) → BCR-ABL

Pathophysiology

- Myeloid stem cell proliferation
- Dysregulated production of:
    - Neutrophils
    - Myelocytes
    - Metamyelocytes
    - Basophils

Clinical features

- Splenomegaly
- Fatigue, weight loss

Disease course

- May progress to:
    - AML
    - ALL

- → called blast crisis

Treatment

- BCR-ABL tyrosine kinase inhibitors
  - Imatinib

LEUKEMOID REACTION VS CHRONIC MYELOGENOUS LEUKEMIA (CML)

Feature	Leukemoid Reaction	CML
Definition	Reactive neutrophilia (>50,000 cells/mm^3)	Clonal myeloproliferative neoplasm
Neutrophil morphology	Toxic granulation, Döhle bodies, cytoplasmic vacuoles	Pseudo-Pelger-Huët anomaly
LAP score	↑ (high)	↓ (low; LAP enzyme ↓ in malignant neutrophils)

Basophils & eosinophils	Normal	↑

Notes / Mnemonics

- PV & ET → JAK2 mutation common
- Myelofibrosis → "Bone marrow cries" = fibrosis + dry tap
- Leukemoid reaction → reactive, LAP ↑
- CML → BCR-ABL + LAP ↓, basophilia characteristic

-> The End <-