

Pathology Tables

Anemia of Low Production

Type of Anemia	Cause / Mechanism	Pathophysiology	Lab Findings	Blood Smear & Morphology	Clinical Features / Notes
1. Iron Deficiency Anemia (IDA)	Nutritional deficiency, chronic blood loss, <u>decreased absorption</u> (gastrectomy, elderly, intestinal disease, hypochlorhydria), <u>increased demand</u> (pregnancy, growth, neoplasms), <u>hypotransferritinemia</u> (2nd to liver disease, protein deficiency, loss in urine), enzyme defects	↓ iron → ↓ Hb synthesis → microcytic, hypochromic RBCs; low iron shifts marrow progenitors from erythroid to megakaryocytic lineage, Hepcidin becomes low to compensate.	↓ Serum ferritin, ↓ Serum iron, ↑ Total iron binding capacity (TIBC), ↓ Reticulocyte Hb (CHr), ↓ Mean reticulocyte volume (MRV), Bone marrow iron ↓ (Perl's Prussian Blue Stain)	Microcytic hypochromic RBCs, poikilocytosis, target cells , low reticulocytes, high EPO, Thrombocytosis	Most common, Chronic anemia, pica, glossitis, stomatitis, koilonychia (spoon nails) , restless legs, hair loss, blue sclera, cognitive impairment, weakened immunity.
2. Anemia of Chronic Disease (ACD)	Chronic infections, cancer, autoimmune/inflammatory diseases	↑ IL-6 → ↑ hepcidin → degradation of ferroportin → iron trapped in macrophages. ↓ erythropoietin secretion.	↓ Serum iron, ↑ Serum ferritin , ↑ Bone marrow iron , ↓ <u>Reticulocytes</u>	Initially normocytic → later microcytic, hypochromic	Symptoms of anemia, seen in chronic illness; most common anemia in hospitalized patients

3. Megaloblastic Anemia	1. Vitamin B12 or Folate deficiency → impaired DNA synthesis (↓ thymidine), abnormalities occur in all rapidly dividing cells 2. Pernicious Anemia (Autoimmune gastritis, Autoreactive T-lymphocytes > parietal cell injury, Activates B-cells > Autoantibodies, >> Block Vit B12 binding to intrinsic factors.)	Ineffective erythropoiesis (maturation of RBC progenitors is deranged) >> apoptosis, mild hemolysis, delayed RBC maturation	↑ MCV (macrocytic), ↓ Reticulocytes, possible pancytopenia Symptoms: glossitis, mild jaundice, pancytopenia, neuro symptoms only in B12 deficiency (paresthesia, loss of proprioception, psychosis, peripheral neuropathy)	Megaloblastoid, Macro-ovalocytes, hypersegmented neutrophils	Folate deficiency: dietary deficiency, <u>increased demand</u> (pregnancy, chronic hemolytic anemia), intestinal diseases, <u>malabsorption</u> (beans, legume, alcohol, phenytoin), <u>methotrexate</u>: inhibit metabolism. B12 deficiency: pernicious anemia, gastrectomy, small bowel disease, <u>metformin</u>: inhibit absorption, elderly (decreased pepsin).
4. Aplastic Anemia	Bone marrow stem cell failure Extrinsic: Ag cross reactivity with stem cells, Activated lymphocytes destroy stem cells. Intrinsic: Inherited defects in telomerase, Stem cells die early, genetically altered= might express abnormal Ag	Damage to multipotent stem cells → bone marrow depletion → pancytopenia	Pancytopenia in peripheral blood, normochromic or macrocytic anemia, ↓ Reticulocytes, bone marrow replaced by fat	Few hematopoietic cells, hypocellular marrow	Severe infections, bleeding, anemia symptoms; Extrinsic factors: idiopathic or secondary to drugs (chloramphenicol, NSAIDs, gold), hepatitis viruses, pregnancy; 70% respond to immunosuppressants

Special Bone Marrow Failure Types	Fanconi anemia: rare inherited DNA repair proteins defect Pure red cell aplasia: selective erythroid absence	—	Pancytopenia Only erythroid cells are absent in BM	—	Predisposition to leukemia and aplastic anemia in early life Congenital: Diamond-Blackfan Anemia, Acquired: Autoimmune, Parvovirus B19
5. Myelophthasic Anemia	Bone marrow infiltration by tumors, granulomas (TB), or storage diseases (e.g., Gaucher)	Physical replacement and damage of marrow → release of immature cells	Leukoerythroblastic picture, immature precursors in blood	Immature granulocytes, nucleated RBCs	Common causes: metastatic cancer, acute leukemia, advanced lymphoma, TB, Gaucher
6. Anemia of Renal Disease	Chronic kidney disease → ↓ erythropoietin	Low EPO → low RBC production	↓ Reticulocyte count, normocytic anemia	Echinocytes (Burr cells)	Patients w/ uremia = Bleeding due to platelet dysfunction, does not correlate with serum creatinine
7. Anemia of Liver Disease	Chronic liver disease → multiple mechanisms	↓ clotting factor synthesis (bleeding), ↓ transferrin synthesis	↓ Transferrin, abnormal coagulation	Acanthocytes (spur cells)	Bleeding from varices , macrocytosis common
8. Anemia of Hypothyroidism	↓ T3/ T4 → ↓ erythropoiesis ↓ EPO	—	Usually normocytic , or macrocytic	Normal or macrocytic RBCs	Fatigue, bradycardia, anemia symptoms

9. Myelodysplastic Syndrome (MDS)	Acquired neoplastic disorder of bone marrow stem cells (elderly)	Mutated BM stem cells → ineffective hematopoiesis, <u>prolonged survival</u> , <u>abnormal maturation</u>	Cytopenias (anemia, neutropenia , thrombocytopenia), refractory anemia	Macrocytes , dysplastic precursors	Elderly, anemia unresponsive to therapy
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Hemolytic Anemia

Type of Hemolytic Anemia	Cause / Inheritance	Mechanism (Site & Pathogenesis)	Key Triggers / Associations	Peripheral Blood / Lab Findings	Clinical Features	Special Notes
1. Extravascular vs. Intravascular (General Classification)	Extravascular : spleen, macrophage destruction	Abnormal shape / antibody-coated RBCs removed by macrophages	—	Spherocytes, ↑ unconjugated bilirubin	Jaundice, splenomegaly, pigmented gallstones	Serum haptoglobin ↓ in both Note: other classification: Acc. to cause: Extracorpuscular/ Intracorpuscular
	Intravascular: circulation, RBC rupture	Direct rupture in vessels → sudden release of free Hb in plasma		Hemoglobinemia, hemoglobinuria, hemosiderinuria	Hemoglobinuria, iron deficiency	

2. G6PD Deficiency	X-linked Recessive (↓ G6PD enzyme → ↓ glutathione → ↓ protection against ROS)	Inability to neutralize oxidants → Hb denaturation → Heinz bodies → membrane damage → intra + extravascular hemolysis	Infections, <u>drugs</u> (sulfonamides, nitrofurantoin, aspirin, vit K, primaquine), fava beans, large number of oxidants.	Heinz bodies (on supravital stain, denatured Hb membrane-bound dark spots), Bite cells (partially phagocytosed inside spleen), reticulocytosis, ↓ haptoglobin	Sudden anemia 2–3 days after trigger (Massive hemolysis), jaundice, dark urine	Both Extra & Intravascular. Types: G6PD-A (mild), G6PD-Mediterranean (severe), Females can show symptoms if X-inactivation affects normal allele.
3. Warm Autoimmune Hemolytic Anemia (WAIHA)	Autoimmune 60% = idiopathic, 25% = SLE, 15% = drugs (<u>α-methyldopa</u> , <u>penicillin</u>)	High affinity IgG binds RBCs at 37°C → macrophages in spleen remove them (extravascular) → <u>spherocytes develop</u> → destroyed by spleen	Autoantibody formation against RBC membrane protein.	<u>Spherocytes</u> , positive Direct Coombs test , reticulocytosis	Mild chronic anemia, splenomegaly	Warm antibody = IgG, extravascular; treated by steroids or splenectomy
4. Cold Autoimmune Hemolytic Anemia (CAIHA)	Autoimmune (transient : secondary to infections or Chronic : lymphoma,) 	Low affinity IgM binds RBCs at <30°C in peripheral areas → complement (C3b, C3d) binds → partial removal by spleen (extravascular)	Mycoplasma pneumoniae, infectious mononucleosis, B-cell lymphoma, idiopathic	RBC agglutination, <u>spherocytes</u> , positive Coombs (for C3d)	Acrocyanosis, <u>Raynaud phenomenon</u> : IgM binds 5 RBCs = block small capillaries in fingers/toes, mild	—

5. Hereditary Spherocytosis (HS)	Autosomal dominant (mutations in ankyrin, band 3, spectrin)	Membrane instability → gradual membrane loss → spherical RBCs (non-deformable) → trapped in spleen, engulfed by histiocytes and destroyed (extravascular)	Genetic mutation (family history)	Spherocytes, ↑ MCHC, normal MCH, ↓ MCV, ↑ osmotic fragility	Variable anemia, splenomegaly	Splenectomy corrects anemia (RBCs persist in peripheral blood with no destruction)
6. Paroxysmal Nocturnal Hemoglobinuria (PNH)	Rare, Acquired mutation in PIGA gene (stem cell level)	Defective PIG anchor → loss of CD55/CD59 (protective proteins) → complement-mediated spontaneous intravascular hemolysis	Non-specific (RBCs > WBCs); worsens during sleep (↓pH, ↑CO ₂ = more active complement system)	Hemoglobinuria (esp. morning), pancytopenia, <u>flow cytometry: absence of CD55/CD59</u>	Episodes of dark urine, fatigue, anemia, thrombosis is common	—
7. Traumatic Hemolysis (Microangiopathic / Mechanical)	Physical damage to RBCs	RBC fragmentation by mechanical stress (prosthetic valves, thrombi, trauma) → intravascular hemolysis	Marathon running, boxing, prosthetic valves, DIC, TTP	Schistocytes (fragmented RBCs), reticulocytosis, ↓ haptoglobin	Fatigue, anemia, sometimes jaundice	Schistocytes = hallmark; treat underlying mechanical cause, Disseminated Thrombi = Microangiopathic hemolytic Anemia

8. Chronic Hemolytic Anemia	Clinical Symptoms: Jaundice, Pigmented Gallbladder Stones, Red Urine.
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Anemia of Blood Loss

Type of Hemolytic Anemia	Cause	Mechanism	Body Response	Morphology
1. Anemia of Acute Blood Loss	Sudden blood loss in significant amounts	If >20% lost, decreases intravascular volume, hypovolemic shock and death.	Shifting fluid from interstitial to intravascular space, causing Dilutional Anemia & worse Hypoxia (for 2-3d). EPO is stimulated, activating erythropoiesis (5-7d) If Internal Hemorrhage = Fe Reused, If External/GIT = Fe Lost.	Normocytic, Normochromic, Reticulocytosis
2. Anemia of Chronic Blood Loss	Rate of RBC loss exceeds regeneration, small amounts lost over a long time	Gastrointestinal Diseases, Excessive Menstruation	—	Microcytic, Hypochromic, Reticulocytopenic
3. Special Types	Clinical Symptoms: Extramedullary Hematopoiesis: Splenomegaly, Hepatomegal Thalassemia Major & Sickle Cell Anemia: Growth Retardation, Bone Deformity, Secondary Hemochromatosis			

Polycythemia

Polycythemia Type	Definition / Mechanism	Erythropoietin (EPO) Level	Causes / Associations	Bone Marrow Activity	Notes / Clinical Features
Relative Polycythemia	Apparent increase in RBC secondary due to decreased plasma volume , not an actual rise in RBC mass.	Normal or slightly high (secondary to dehydration).	- Water deprivation - Severe diarrhea - Use of diuretics	Normal (no true increase in RBC production).	Not a true erythrocytosis; resolves when plasma volume is restored. No Splenomegaly
Absolute Polycythemia	True increase in total RBC mass due to increased bone marrow production.	Variable: depends on cause (see primary vs secondary).	Two main subtypes: → Primary (Polycythemia Vera) & Secondary Polycythemia	Increased (true over- production).	Labs: ↑Hb Con, ↑HTCT, ↑RBCs, Masked if Fe Deficiency develops. Variable Splenomegaly
Primary Polycythemia (Polycythemia Vera)	Autonomous proliferation of bone marrow stem cells due to JAK2 mutation → cells become less dependent on growth factors → uncontrolled erythrocyte production.	Low (negative feedback inhibition).	- JAK2 tyrosine kinase mutation. - Classified as a myeloproliferative neoplasm.	Markedly increased, panmyelosis (erythroid is most prominent, myeloid, megakaryocytic lineages). Leukocytosis & thrombocytosis = common.	Pruritus (aquagenic), Peptic Ulcer, Secondary Gout (arthritis, kidney stones, tophi), Chronic Disease, Spent phase : BM fibrosis, extramedullary hematopoiesis (esp. spleen). Rarely progresses to acute myeloid leukemia (blast crisis). Splenomegaly is common PLUS the 2nd symptoms

Secondary Polycythemia	Increased EPO secretion secondary to systemic hypoxia or EPO-producing tumors → stimulates bone marrow → increased RBC production. Considered a compensatory or secondary response, not autonomous.	High, to compensate.	Adaptive causes: (High altitude, Cyanotic heart disease, Chronic pulmonary diseases, Sleep apnea) Paraneoplastic causes: (Renal or liver cancer), Surreptitious causes: (blood doping; athletes), Alcohol (frequent urination = relative, depressed respiration), Smoking.	Increased (stimulated by EPO).	Plethora/ Cyanosis. Headache & Dizziness from HTN. Hyperviscosity > slow circulation > cyanosis, blurred vision, tissue ischemia. Thrombosis, or bleeding. (vWF) No Splenomegaly