

Disease	Pathophysiology	Genetics	Gross morphology	Micro morphology	Clinical manifestations	Other information
AML	Acquired (rarely inherited) chromosomal abnormalities in relatively undifferentiated blasts of early myeloid differentiation that replace normal marrow elements	Depends on clinical setting: balanced translocations often occur in de novo cases, in particular t(8;21) in the M2 type and t(15;17) associated with M3 type AML that causes the production of a fusion gene <i>PML-RAR</i> which encodes an abnormal retinoic acid receptor that blocks myeloid differentiation; therapy related AMLs often exhibit deletions or monosomies of chromosomes 5 and 7, though some show a translocation involving the <i>MLL</i> gene on chromosome 11q23	Hypercellular bone marrow	>20% myeloblasts in the bone marrow with delicate nuclear chromatin, two to four nucleoli, moderate cytoplasm, and often peroxidase positive granules and Auer rods; Monoblasts have folded or lobated nuclei, lack Auer rods, are usually peroxidase positive and stain for nonspecific esterase	Fatigue, fever, spontaneous cutaneous and mucosal bleeding (petechiae, ecchymoses), possibly DIC, mild lymphadenopathy, mild organomegaly, rapid onset, peripheral leukemic cells	Primarily affects adult FAB classification divided into eight stages (M0-M7) based on degree of maturation and the lineage of leukemic blasts, immunophenotype CD13 and CD33+
Myelodysplastic syndrome	Ineffective hematopoiesis of myeloid precursors that suppresses normal hematopoiesis and causes increased apoptosis of cells in the bone marrow, may be idiopathic or related to cytotoxic chemotherapy	Associated with monosomies of chromosomes 5 and 7, trisomy of chromosome 8, and deletions of 5q, 7q, and 20q	Hypercellular bone marrow, <30% myeloblasts	Abnormal myeloblasts: erythroid precursors may exhibit megaloblastoid maturation, nuclear budding abnormalities, and iron-laden macrophages (ringed sideroblasts); granulocyte precursors may be of the Pseudo-Pelger-Huet type with hyposegmented nuclei; thrombocyte precursors may be of the pawn ball megakaryocyte type (single nuclear lobes or multiple separate nuclei)	Weakness, infection, hemorrhage, fatigue, dyspnea on exertion, peripheral cytopenias	Classified as one of eight WHO categories; primarily affects adult older than 60, increased risk of AML, therapy related subtype has a poorer prognosis
CML	Marrow hypercellularity, increased hematopoiesis, cellular homing to secondary hematopoietic organs, extramedullary hematopoiesis	Philadelphia chromosome: t(9;22) between the <i>BCR</i> gene on chromosome 9 and the <i>ABL</i> gene on chromosome 22 leading to the production and dysregulation of an oncogenic tyrosine kinase, the product of the <i>BCR-ABL</i> fusion gene	Hypercellular bone marrow with increased granulocyte precursors	Storage histiocytes with wrinkled sea blue cytoplasm in the bone marrow; marked peripheral leukocytosis; presence of metamyelocytes, myelocytes, and <10% myeloblasts in the peripheral blood	Insidious onset, may be asymptomatic, fatigue, weight loss, weakness, anorexia, splenomegaly	Presents most often in the fourth and fifth decades, affects pluripotent stem cells; terminates in a blast crisis with or without an intermediate accelerated phase that closely resembles AM

Polycythemia vera	Multipotent stem cells with decreased thresholds for growth factors, especially erythropoietin		Hypercellular bone marrow	Increase in all myeloid progenitor cells, some reticulin fibers in the bone marrow	Slow onset, cyanosis, hypertension, headache, dizziness, GI symptoms, pruritis, peptic ulceration, splenomegaly, hepatomegaly, hyperviscosity, gout, panmyelosis	Affects primarily older adults (median age of onset 60), terminates in a spent phase characterized by marrow fibrosis and extramedullary hematopoiesis, may transform to AML
Essential thrombocytosis	Clonal stem cell disorder of the megakaryocyte line		Mild to moderate marrow hypercellularity	Megakaryocyte hyperplasia, cells are enlarged and have hyperlobated nuclei; minority of cases have reticulin fiber deposition in the bone marrow space, giant platelets in the peripheral blood	One third of cases are asymptomatic, no organomegaly, recurrent spontaneous abortions, fetal growth retardation, frequent manifestations of thrombosis	Affects middle aged to elderly patients equally of both sexes, platelet count >600,000, mild leukocytosis, diagnosis of exclusion
Chronic idiopathic myelofibrosis	Increased collagen deposition by non-neoplastic fibroblasts due to inappropriate secretion of growth factors (potentially PDGF and TGF- β) by neoplastic megakaryocytes		Fibrotic bone marrow, initially hypercellular	Bone marrow, early: atypical megakaryocyte hyperplasia (frequently in clusters), dilated sinusoids with intravascular hematopoiesis; bone marrow, fibrotic phase: diffuse reticulin fiber deposition (starts early in disease); peripheral blood: tear drop RBCs, circulating megakaryocytes	Fatigue, weight loss, night sweats, fever, weakness, gout, splenomegaly	Affects middle aged to elderly patients of both sexes equally