

Module 2

14.	Clinical symptoms of blood system affection: anemia and erithrocytosis. Leukopenias and leukocytosis. Methods of clinical, laboratory and instrumental examination.	2	26.12.16
15.	Clinical syndroms and symptoms of gastrointestinal tract diseases (syndromes of esophagus motility disorders and stomach diseases).	2	2.01.17
16.	Clinical syndroms and symptoms of gastrointestinal tract diseases (syndromes of large and small intestine motility disorders, syndromes of malgigestion and malabsorption).	2	9.01.17
17.	Clinical syndroms and symptoms of hepato-biliary system diseases (syndroms of gallbladder motility disorders, syndrome of jaundice).	2	16.01.17

Clinical Symptoms of Blood System Affection: Anemia and Polycythemia; Leukopenias and Leukocytosis; Leukemia; Hemorrhagic Syndrome.

LECTURE IN INTERNAL MEDICINE PROPAEDEUTICS

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Anemia

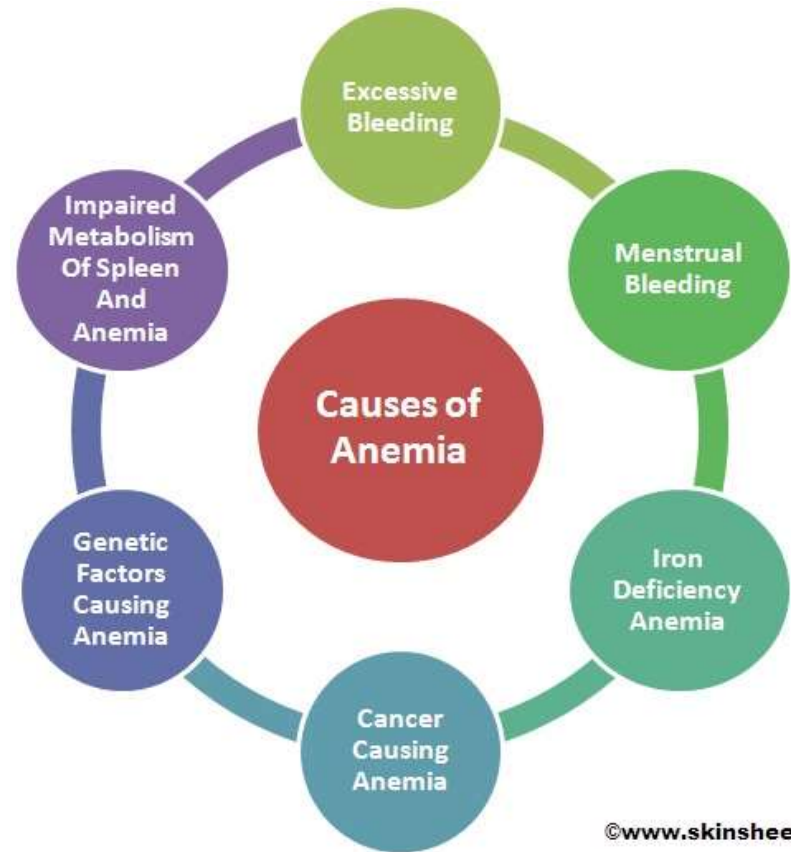
Definition

Anemia (anaemia) is a decrease in the amount of RBCs or hemoglobin in the blood or a lowered ability of the blood to carry oxygen

Anemia

Causes

- Impaired RBC production
- Increased RBC destruction
- Blood loss
- Fluid overload



Anemia

Causes: Impaired production 1

- Disturbance of proliferation and differentiation of stem cells (Pure red cell aplasia, Aplastic anemia, Anemia of renal failure, Anemia of endocrine disorders)
- Disturbance of proliferation and maturation of erythroblasts (Pernicious anemia, Anemia of folic acid deficiency, Megaloblastic anemia, Anemia of prematurity, Iron deficiency anemia, Thalassemias, Congenital dyserythropoietic anemias, atc.)

Anemia

Causes: Impaired production 2

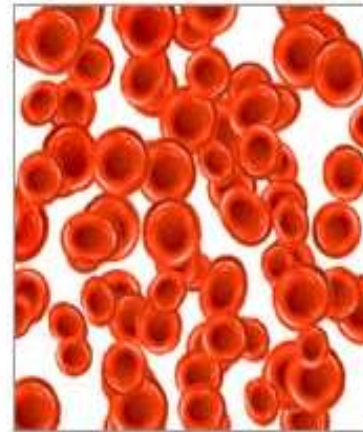
- Other mechanisms of impaired RBCs production (Myelophthisic anemia, Myelodysplastic syndrome, Anemia of chronic inflammation)

Anemia

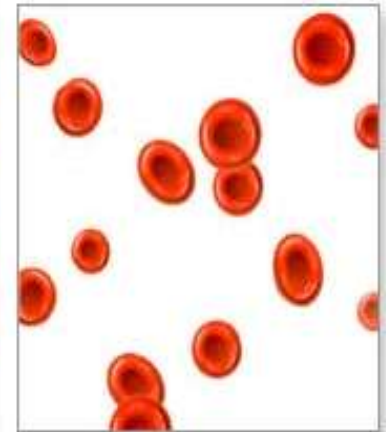
Causes: Increased RBCs 1
destruction (hemolytic
anemias)

- Intrinsic (intracorpuseular) abnormalities cause premature destruction (except paroxysmal nocturnal hemoglobinuria, are hereditary genetic disorders)

Normal amount of
red blood cells



Anemic amount of
red blood cells

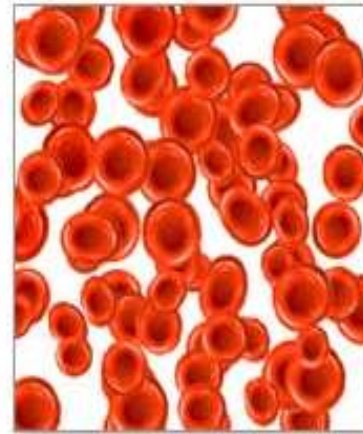


Anemia

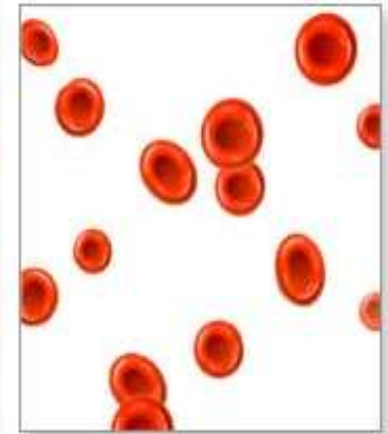
Causes: Increased RBCs 2
destruction (hemolytic
anemias)

- Extrinsic (extracorporeal)
abnormalities (antibody-
mediated, mechanical
trauma to red cells)

Normal amount of
red blood cells



Anemic amount of
red blood cells



Anemia

Causes: Blood loss

- Anemia of prematurity
- Trauma or surgery, causing acute blood loss
- Gastrointestinal tract lesions (acute bleeds: peptic ulcers, chronic blood loss (angiodysplasia))
- Gynecologic disturbances (chronic blood loss)
- Menstruation, among young women or older women with fibroids
- Infection by intestinal nematodes feeding on blood

Anemia

Hydremia

Causes: Fluid overload (hypervolemia with hemodilution, normal total amount of Hb and RBCs in the body)

- Excessive sodium or fluid intake, sodium or water retention and fluid shift into the intravascular space
- Anemia of pregnancy (induced by blood volume expansion experienced in pregnancy)



Anemia

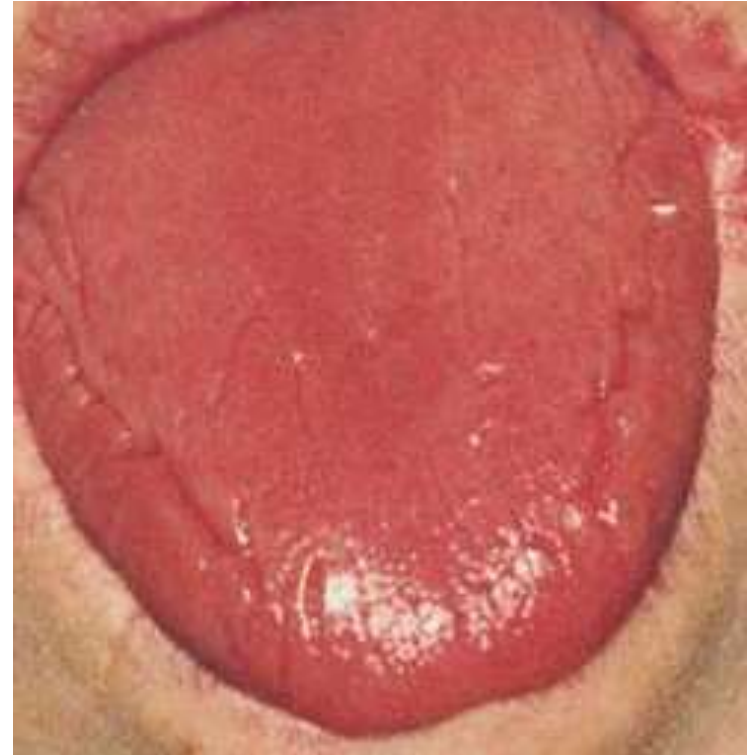
Diagnostic steps

- Clinical manifestations
- Hematological syndromes (blood tests abnormalities)
- Blood biochemistry abnormalities
- Bone marrow abnormalities

Anemia

Signs and symptoms 1

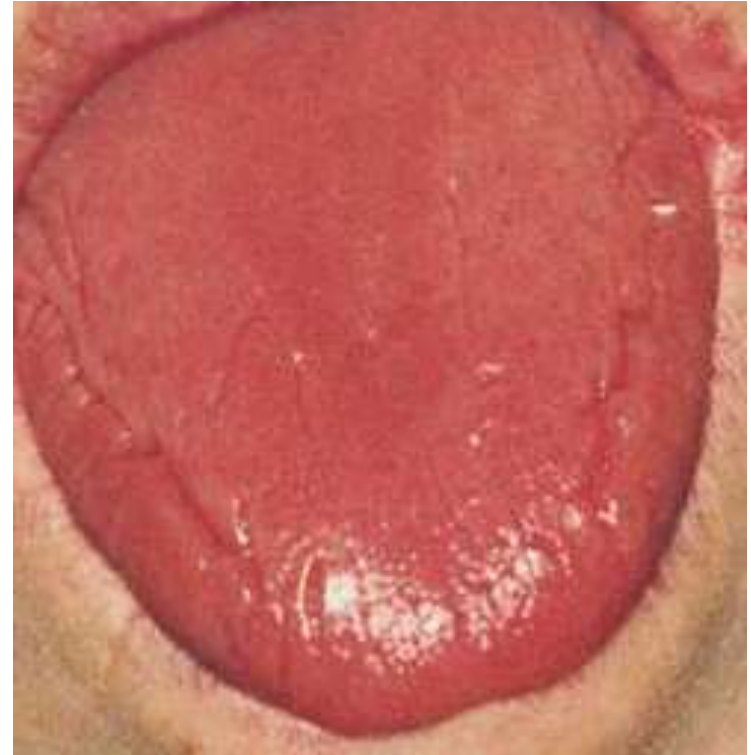
- weakness, fatigue, general malaise, poor concentration
- dyspnea (shortness of breath) on exertion
- increasing cardiac output, palpitations, angina (if pre-existing heart disease is present), heart failure



Anemia

Signs and symptoms 2

- intermittent claudication
- pallor (pale skin, lining mucosa, conjunctiva and nail beds)



Anemia

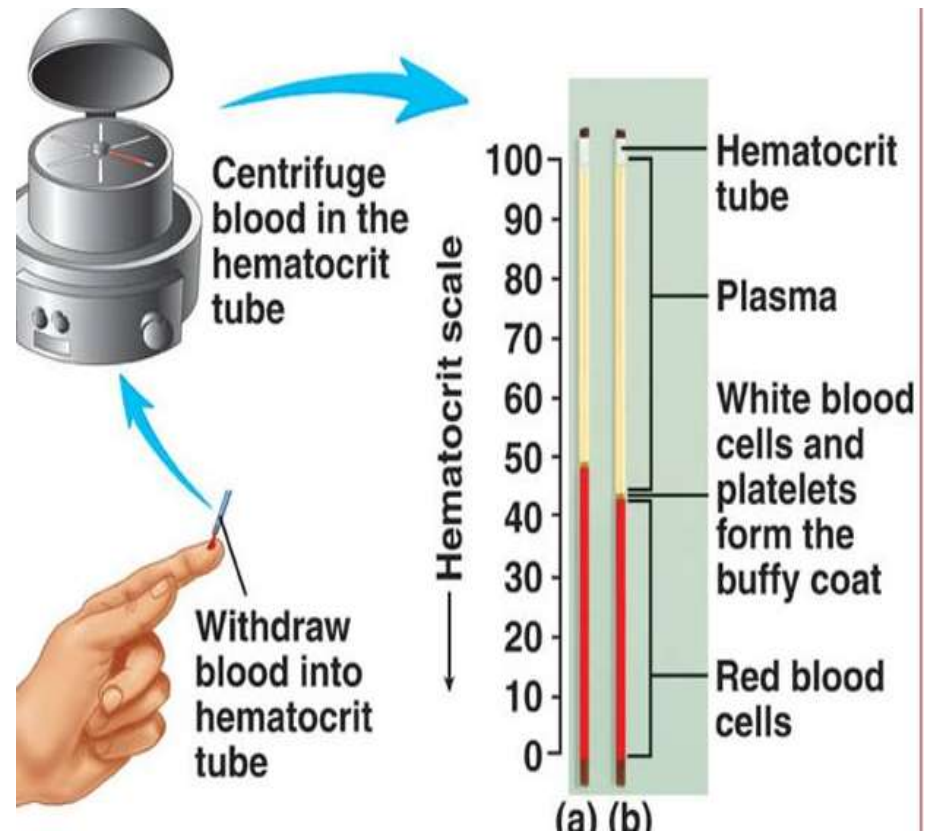
Additional signs of severe anemia

- hyper dynamic circulation (tachycardia, bounding pulse, flow murmurs, cardiac ventricular hypertrophy)
- heart failure
- pica
- restless legs syndrome (iron-deficiency anemia)

Anemia

Diagnosis

- Complete blood count
- Blood smear
- Hemoglobin
- Hematocrit
- Red blood cell size
- Reticulocyte count
- Reticulocyte production index



Anemia

WHO's Hemoglobin Thresholds used to define Anemia

Age, Gender	Hb threshold (g/dl)	Hb threshold (mmol/l)
Children (0.5–5.0 yrs)	11.0	6.8
Children (5–12 yrs)	11.5	7.1
Teens (12–15 yrs)	12.0	7.4
Women, non-pregnant (>15yrs)	12.0	7.4
Women, pregnant	11.0	6.8
Men (>15yrs)	13.0	8.1

Anemia

Color index

- Hypochromic ($<0,85$) – e. g chronic posthemorrhagic, Fe-deficient
- Normochromic ($0,85 - 1,05$) – e. g acute posthemorrhagic, hemolytic
- Hyperchromic ($>1,05$) – e.g. B12-deficient, folate-deficient, aplastic

Anemia

Types of red blood cells size

- The cells are small - microcytic anemia (MCV < 80 fL) - e.g Fe deficient anemia
- The cells are large - macrocytic anemia (MCV > 100 fL) – e.g B12-folate deficient anemia
- The cells are normal - normocytic anemia - e.g anemia if chronic diseases



Anemia

Regenerative abilities of bone marrow-
reticulocytes, $\% / 100$

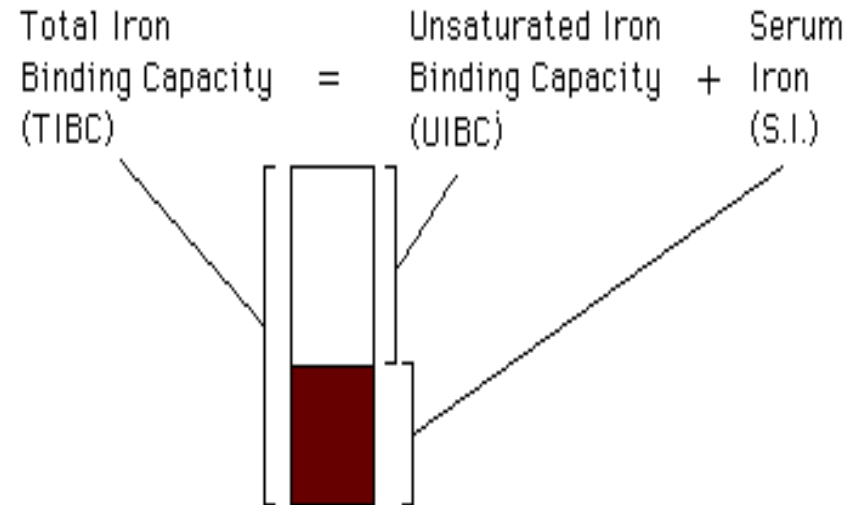
- Normoregenerative (6 – 12) – anemias due to deficiency (Fe, B12-folate, etc)
- Hyperregenerative (> 12) – hemolytic,
acute posthemorrhagic
- Hyporegenerative (< 6) – aplastic

Anemia

Blood biochemistry 1

- Ferritin (↓ in Fe deficiency)
- Serum iron (↓ in Fe deficiency)
- Transferrin saturation (↓ in Fe deficiency)
- RBC folate level
- Serum vitamin B₁₂

Serum Iron and Iron Binding Capacity

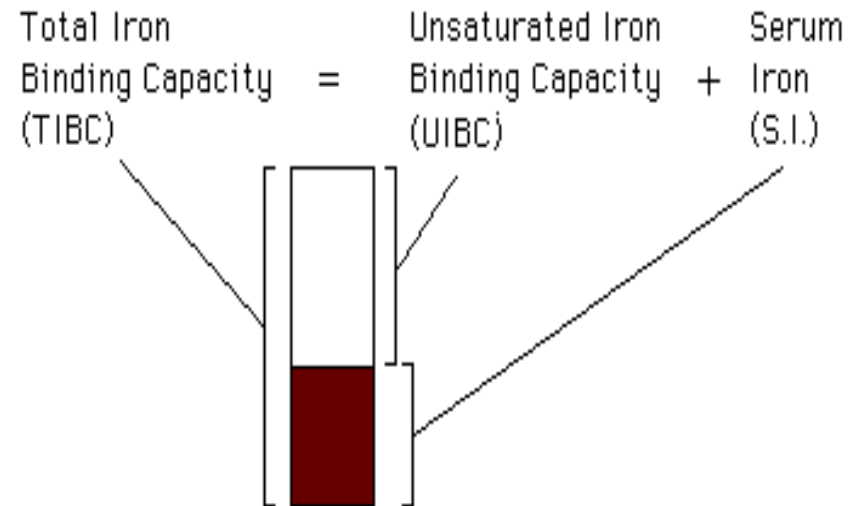


Anemia

Blood biochemistry 2

- Serum methylmalonic acid and homocystein (in B₁₂ def.)
- Renal and liver function tests
- Erythropoietin level

Serum Iron and Iron Binding Capacity



Polycythemia

Definition

Polycythemia is a myeloproliferative condition that results in an increased level of circulating red blood cells in the bloodstream with increase in hematocrit, hemoglobin, or red blood cell count above the normal limits

Polycythemia

Synonyms

Erythremia

Osler-Vaquez disease

Polycythemia rubra vera

Primary polycythemia

Splenomegalic polycythemia

Vaquez-Osler disease

Polyglobulia

Polycythemia

Risk factors:

- Hypoxia from long standing (chronic) lung disease and smoking
- Chronic carbon monoxide (CO) exposure
- People living at high altitudes due to low environmental oxygen levels
- People with genetic mutations and familial types of polycythemia and certain hemoglobin abnormalities

Polycythemia

Causes 1

- Primary (a slow-growing type of blood cancer)
 - Polycythemia Vera
 - Primary familial and congenital polycythemia

Polycythemia

Causes 2

- Secondary 1
 - Physiologically appropriate (adaptation to living at high altitudes, iatrogenic, etc.)
 - Chronic hypoxia (COPD, hypoventilation syndrome, chronic heart diseases, sleep_apnea, pulmonary_hypertension)

Polycythemia

Causes 2

- Secondary 2
 - Erythropoietin secreting tumors (hepatocellular carcinoma, renal cell carcinoma, adenocarcinomas, uterine tumors)
 - Relative polycythemia (the underlying cause is reduced blood plasma)

Polycythemia

Signs and symptoms Polycythemia Vera 1

- Trouble breathing when lying down
- Dizziness
- Excess bleeding
- Full feeling in the left upper abdomen (enlarged spleen)
- Headache

Polycythemia

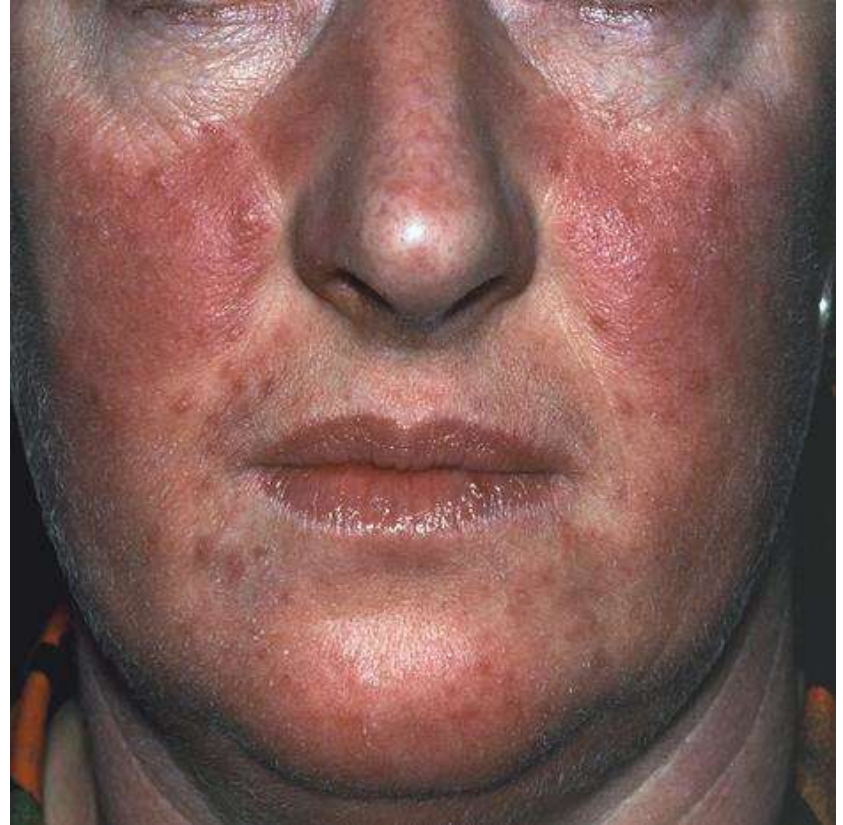
Signs and symptoms Polycythemia Vera 2

- Itchiness, especially after a warm bath
- Red skin coloring, especially of the face
- Shortness of breath
- Phlebitis

Polycythemia

Other symptoms that may occur with Polycythemia Vera

- Bluish skin color
- Fatigue
- Red skin spots
- Vision problems



Polycythemia

Diagnosis 1

- Bone marrow biopsy
- Complete blood count with differential
- Comprehensive metabolic panel
- Erythropoietin level
- Genetic test for the JAK2V617F mutation



Polycythemia

Diagnosis 2

- Oxygen saturation of the blood
- Red blood cell mass
- Vitamin B12 level



Polycythemia

Diagnosis (WHO criteria): 1

- Major criteria
 - Hemoglobin > 18.5 g/dL in men and > 16.5 g/dL in women, or other evidence of increased red blood cell volume
 - Presence of JAK2617V F or other functionally similar mutation, such as *JAK2* exon 12 mutation

Polycythemia

Diagnosis (WHO criteria): 2

- Minor criteria
 - Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis) with prominent erythroid, granulocytic, and megakaryocytic proliferation
 - Serum erythropoietin level below the reference range for normal
 - Endogenous erythroid colony formation in vitro

Polycythemia

Diagnosis (The Polycythemia Vera Study Group criteria : the diagnosis is established if all three category A criteria are present, or if criteria A1 plus A2 plus any two criteria from category B are present):

- Category A criteria
 - Total red blood cell mass ≥ 36 mL/kg in males or ≥ 32 mL/kg in females
 - Arterial oxygen saturation $\geq 92\%$
 - Splenomegaly

Polycythemia

Diagnosis (The Polycythemia Vera Study Group criteria : the diagnosis is established if all three category A criteria are present, or if criteria A1 plus A2 plus any two criteria from category B are present): Category B criteria

- Thrombocytosis, with platelet count $> 400,000/\mu\text{L}$
- Leukocytosis, with a white blood cell count $> 12,000/\mu\text{L}$
- Increased leukocyte alkaline phosphatase (ALP) > 100 U/L
- Serum vitamin B-12 concentration > 900 pg/mL or binding capacity > 2200 pg/mL

Leukopenia

Definition

Leukopenia or leucopenia or leukocytopenia is a decrement in the white blood cells (WBC) or leukocytes present in the blood that places individuals at greater infection risks

Leukopenia

Causes 1

- Viral infections (cold/flu, HIV/AIDS, etc.)
- Microbial infections (sepsis, psittacosis, rickettsial infections, tuberculosis, malaria, dengue, etc.)
- Autoimmune connective tissue diseases (rheumatoid arthritis, systemic lupus erythematosus, etc.)

Leukopenia

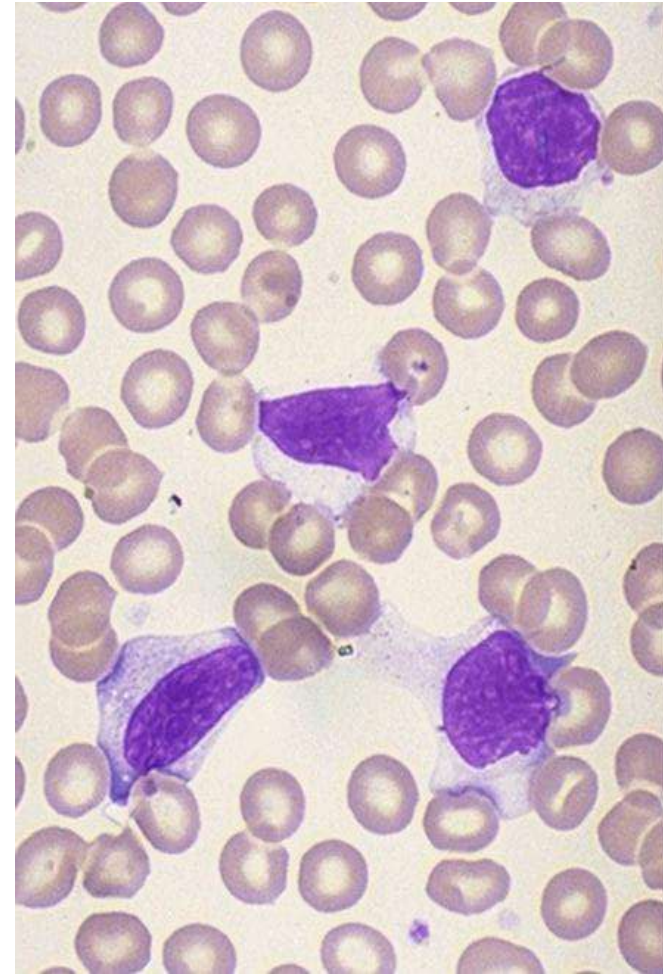
Causes 2

- Cancer or other diseases that damage bone marrow (leukemia, myelofibrosis, Hodgkin's lymphoma)
Congenital disorders (Kostmann's syndrome, Myelokathexis)
- Vitamin deficiencies (folate deficiency, etc.)
- Deficiency of minerals (zinc, copper, etc.)
- Medications and radiation therapy (diuretics , antibiotics, antipsychotics, antidepressants, etc.)

Leukopenia

Signs and symptoms 1

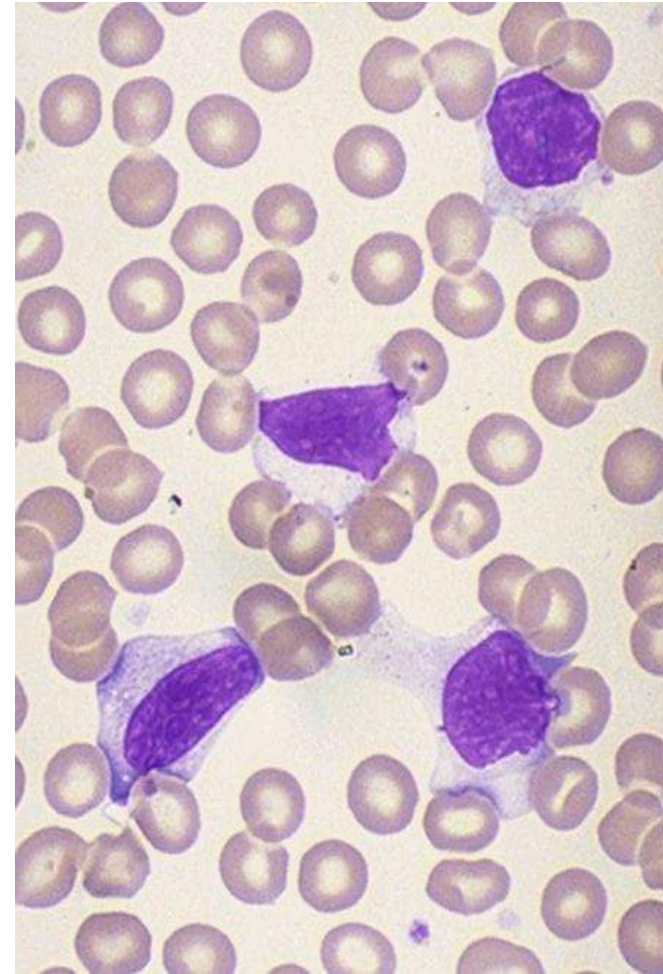
- Anemia
- Thrombocytopenia
- Pneumonia
- Stomatitis, oral ulcer and various infections
- Liver abscesses



Leukopenia

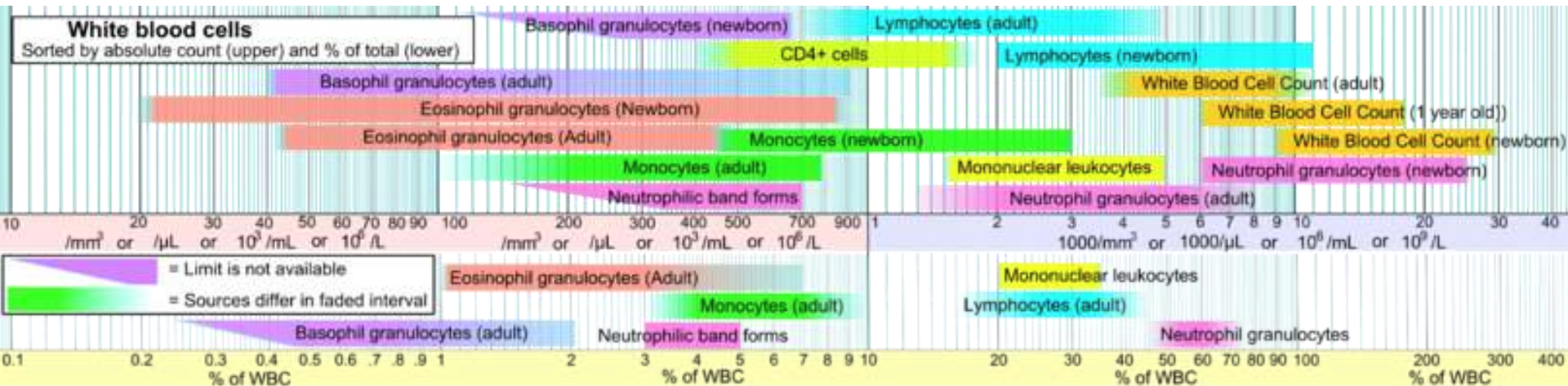
Signs and symptoms 2

- Metrorrhagia, menorrhagia
- Neurasthenia
- Fatigue and hot flashes
- Strong desire to consume hot drinks



Leukopenia

Diagnosis: leukopenia can be identified with a complete blood count



Leukocytosis

Definition

A white blood cell (the leukocyte) count above the normal range ($<50 \times 10^9/L$) in the blood

Leukocytosis

Five principal types and Causes

Neutrophilic leukocytosis (neutrophilia)	Bacterial infections, Tissue necrosis
Eosinophilic leukocytosis (eosinophilia)	Allergic disorders, Parasitic infections, Malignancy, Systemic autoimmune diseases, etc.), Acute stress
Basophilic leukocytosis (basophilia)	Myeloproliferative disease
Monocytosis	Chronic infections (Tuberculosis, Systemic autoimmune diseases, etc.)
Lymphocytosis	Chronic infections (Tuberculosis, Brucellosis, Viral infections, Pertussis, Malignancy)

Leukocytosis

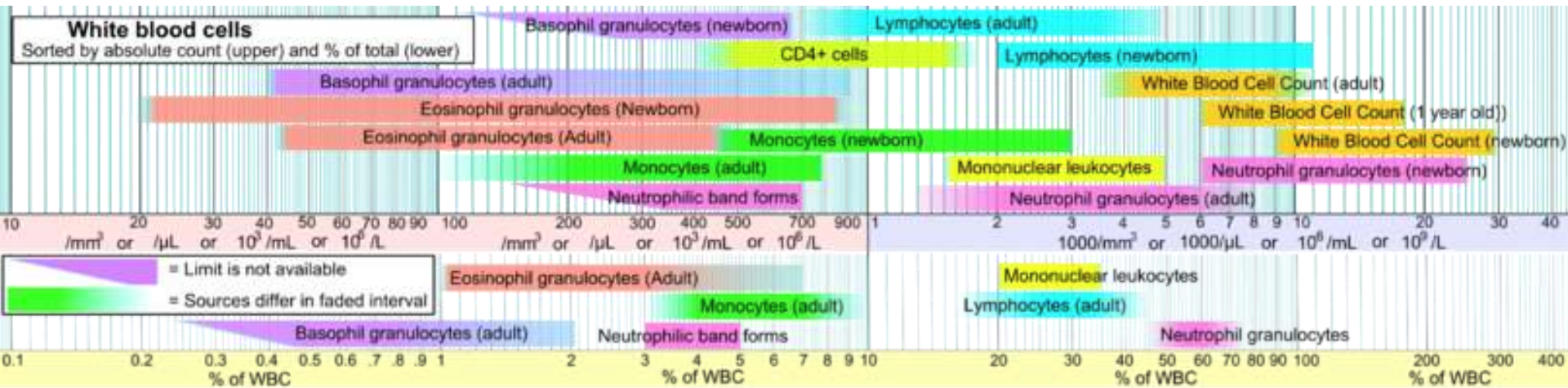
Signs and symptoms

- Fever
- Bleeding or bruising
- Feeling weak, tired, or sick
- Feeling dizzy, faint, or sweaty
- Pain or tingling in arms, legs, or abdomen
- Trouble breathing, thinking, or seeing
- Losing weight without trying, or a poor appetite



Leukocytosis

Diagnosis: leukocytosis can be identified with a complete blood count



Leukocytosis

Comment

- Excessive numbers of white blood cells are most often due to the response of normal bone marrow to infection or inflammation
- In some instances, leukocytosis is a sign of more serious primary bone marrow disease (leukemia or myeloproliferative disorders)

Leukemia

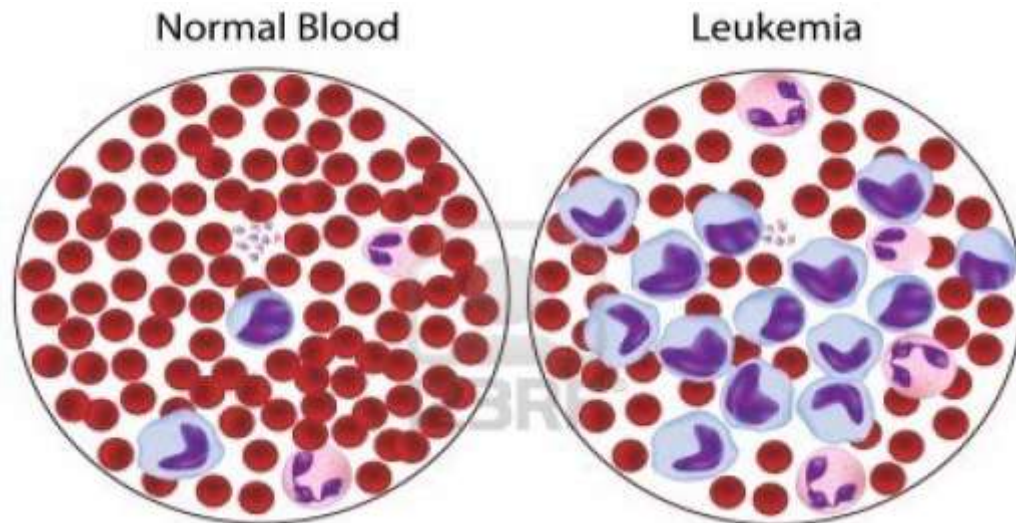
Definition

Abnormal proliferation of the blood-forming tissues that usually begins in the bone marrow and results in high numbers of abnormal white blood cells

Leukemia

Causes

- Mutations in the DNA as a result of exposure to radiation or carcinogenic substance
- A genetic predisposition



Leukemia

Classification

Cell type	Acute	Chronic
Lymphocytic (lymphoblastic) leukemia	Acute lymphoblastic leukemia (ALL)	Chronic lymphocytic leukemia (CLL)
Myelogenous (myeloid) leukemia	Acute myeloblastic leukemia (AML)	Chronic myelogenous leukemia (CML)

Leukemia

Signs and symptoms 1

- Fever or chills
- Persistent fatigue, weakness
- Frequent or severe infections
- Losing weight without trying
- Swollen lymph nodes, enlarged liver or spleen
- Easy bleeding or bruising

Leukemia

Signs and symptoms 2

- Recurrent nosebleeds
- Tiny red spots in skin (petechiae)
- Excessive sweating, especially at night
- Bone pain or tenderness

Leukemia

Acute leukemia is characterized by a rapid increase in the number of immature blood cells (blasts) crowding due to such cells makes the bone marrow unable to produce healthy blood cells immediate treatment is required in acute leukemia due to the rapid progression and accumulation of the malignant cells, which then spill over into the bloodstream and spread to other organs of the body

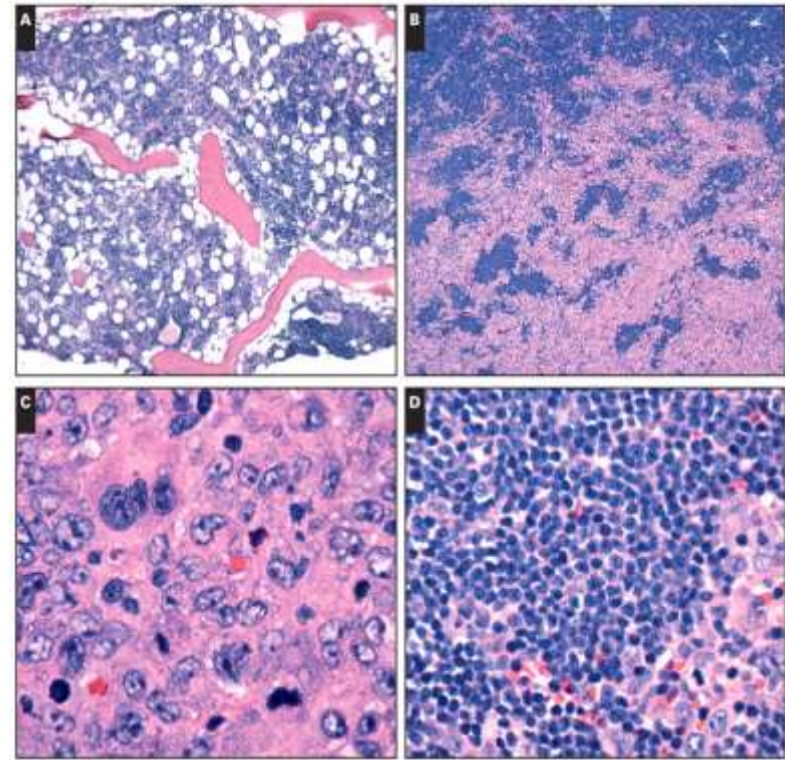
Leukemia

Chronic leukemia is characterized by the excessive buildup of relatively mature, but still abnormal, white blood cells typically taking months or years to progress, the cells are produced at a much higher rate than normal, resulting in many abnormal white blood cells mostly occurs in older people, but can theoretically occur in any age group

Leukemia

Diagnosis

- Repeated complete blood counts and blood films
- Philadelphia chromosome in CML
- Bone marrow examination
- A lymph node biopsy (in lymphoma)
- X-ray, MRI, or ultrasound



Hemorrhagic Syndrome

Definition

The extravasation of red blood cells from the vasculature into the skin and/or subcutaneous tissue in form of petechiae, purpura, and ecchymosis (collectively referred to as purpura) with purpuric rashes formation

Hemorrhagic Syndrome

Appendix for Definition

The extravasation occur internally, where red blood cells leaks from blood vessels inside the body

Hemorrhagic Syndrome

Purpura forms

- Petechiae - pinpoint red lesions less than 2 mm in size
- Purpura - pinpoint red lesions from 2 mm to 10 mm in size
- Ecchymoses pinpoint red lesions more than 10 mm in size



Hemorrhagic Syndrome

Principal types and Causes

Thrombocytopathy	Any of blood disorders characterized by dysfunctional platelets (thrombocytes) with either normal platelet counts (non-thrombocytopenic purpuras) or decreased platelet counts (thrombocytopenic purpuras), which result in prolonged bleeding time, defective clot formation, and a tendency to hemorrhage (Henoch-Schönlein Purpura, von Willebrand disease, thrombasthenia, platelet aggregation, etc.)
Hemophilia	A group of hereditary genetic disorders that impair the body's ability to control blood clotting, which is used to stop bleeding when a blood vessel is broken (Hemophilia A - clotting factor VIII deficiency (the most common form of the disorder) and Hemophilia B - factor IX deficiency (occurs in around 1 in about 20,000–34,000 male births)
Telangiectasia	A small dilated blood vessels near the surface of the skin or mucous membranes, measuring between 0.5 and 1 millimeter in diameter

Hemorrhagic Syndrome

Signs and symptoms 1

- Purpura, sometimes mucosal bleeding (localization, distribution)
- Arthritis and Arthralgia
- Central Nervous, Gastrointestinal, Cardiovascular, Urethral Systems involvement
- Prolonged, heavy menstrual periods (menorrhagia)
- Unexplained nosebleeds

Hemorrhagic Syndrome

Signs and symptoms 2

- Extended bleeding after minor cuts, blood draws or vaccinations, minor surgery or dental procedures
- Bleeding after aspirin

Hemorrhagic Syndrome

WHO' grading scale to measure the severity of bleeding

Grade 0	no bleeding
Grade 1	petechial bleeding
Grade 2	mild blood loss (clinically significant)
Grade 3	gross blood loss, requires transfusion (severe)
Grade 4	debilitating blood loss, retinal or cerebral associated with fatality

Hemorrhagic Syndrome

Diagnosis

- The platelet count
- The platelet function (bleeding time, platelet aggregation studies, von Willebrand Factor studies, specialized tests)
- A coagulation screen (clotting factor deficiencies)
- If the patient is on warfarin, INR (International Normalized Ratio)
- Autoantibody screen for connective tissue disorders

Glossary of blood disorders pathology' terms

[GLOSSARY of BLOOD RELATED TERMS](#)
[BLOOD AND HEMATOLOGY DICTIONARY](#)
[BLOODBOK.COM](#)