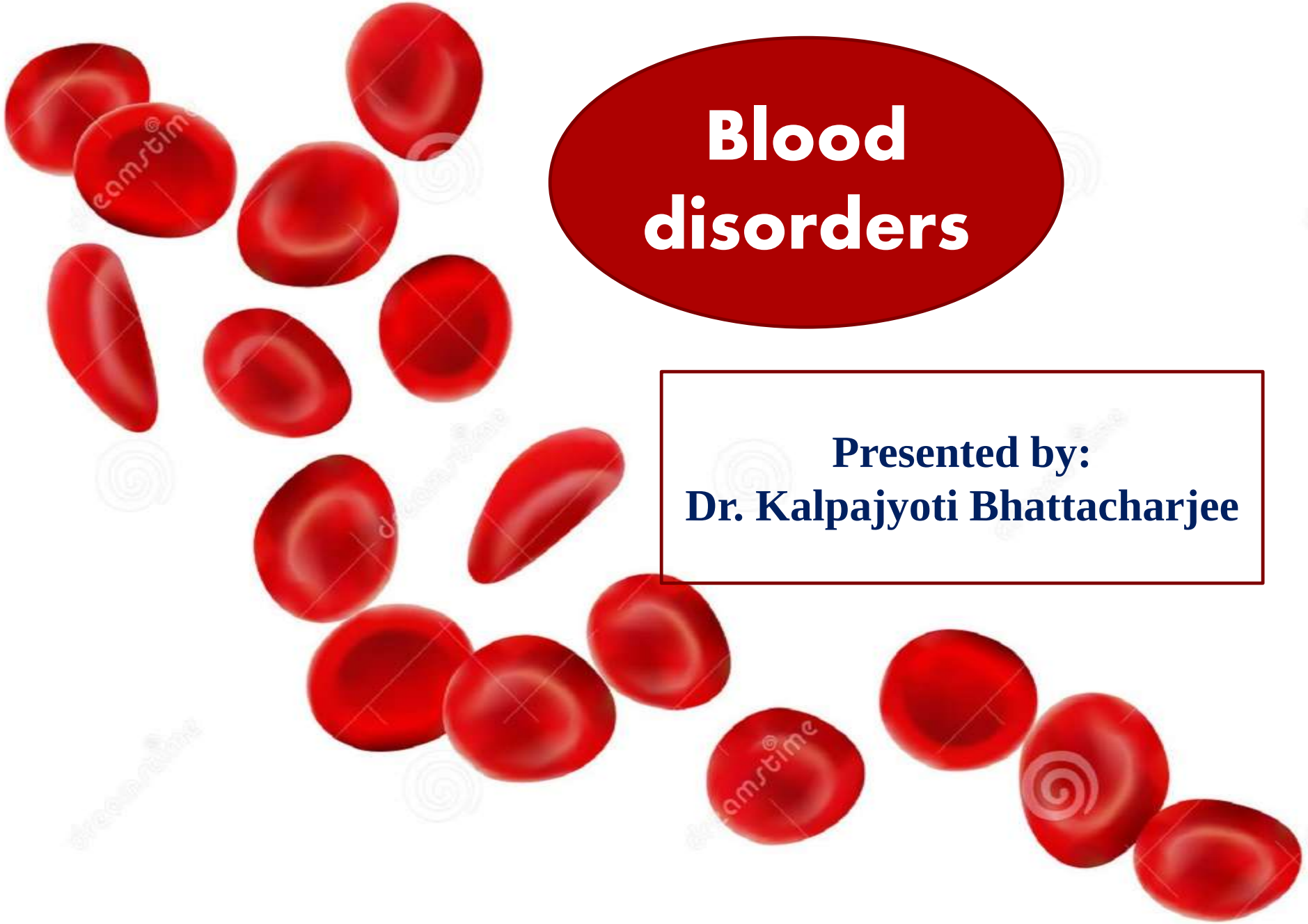

Blood disorders

Presented by:
Dr. Kalpajyoti Bhattacharjee

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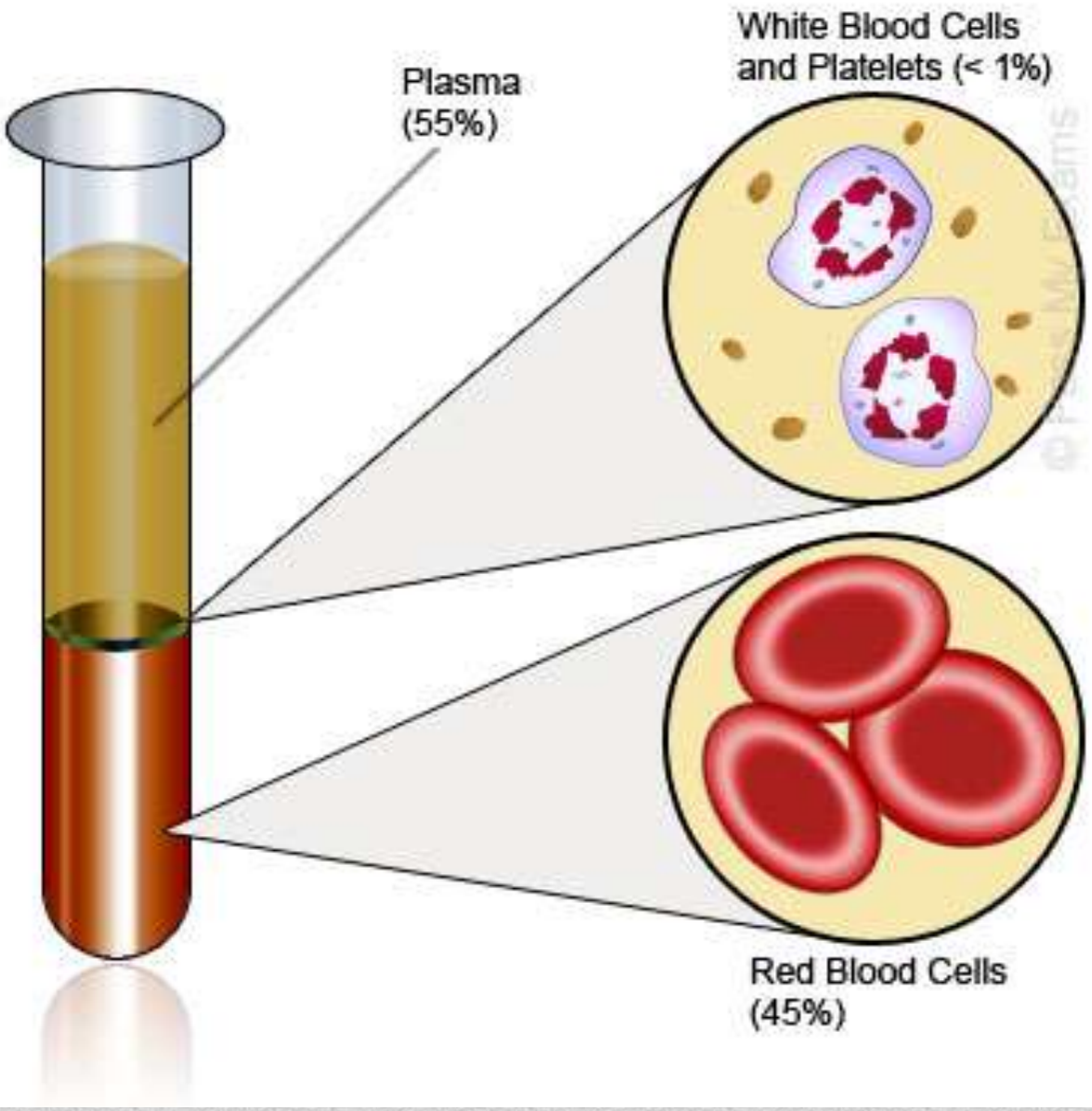
- Red blood cell and its disorders
- White blood cell and its disorders
- Platelet and its disorders
- Coagulation disorders
- Anticoagulant-Related Coagulopathies
- Disease-Related Coagulopathies
- Conclusion

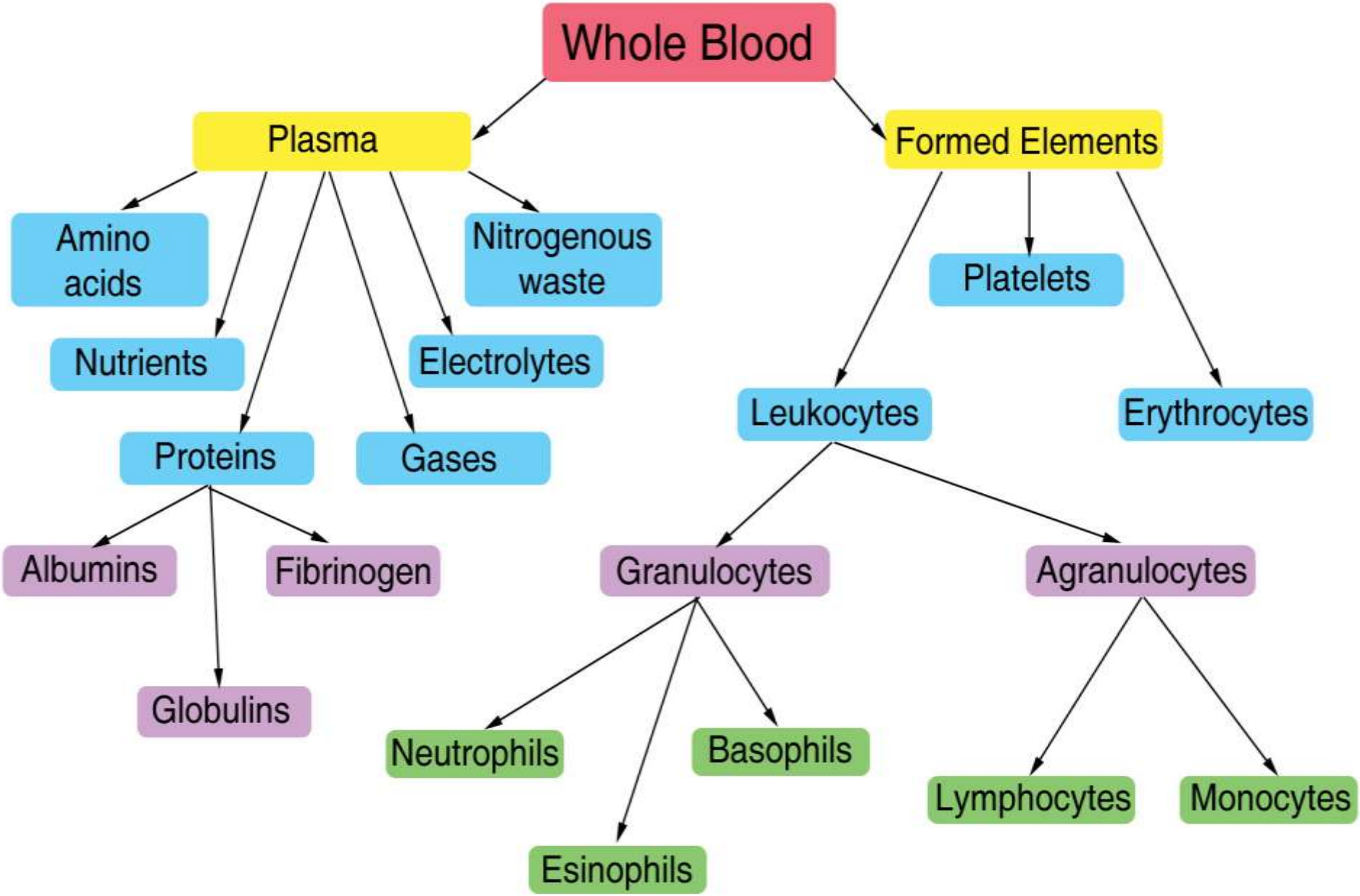
INTRODUCTION

- **William Harvey-** father of physiology discovered blood circulated through the body in 1628.
- Blood is fluid connective tissue present in circulatory system
- **FLUID OF LIFE-** because it carries oxygen from lungs to all parts of the body and carbon dioxide from all parts of the body to the lungs.

- **FLUID OF GROWTH-** because it carries nutritive substances from the digestive system and hormones from endocrine gland to all the tissues.

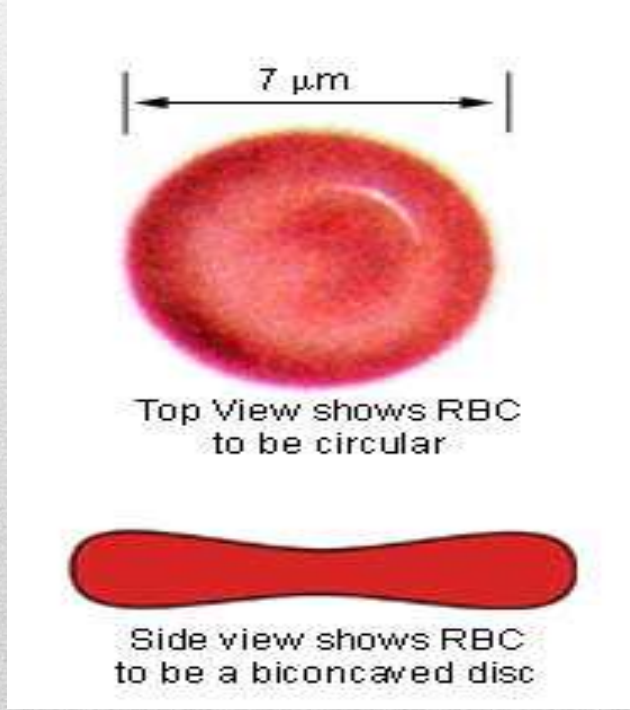
- **FLUID OF HEALTH-** because it protects the body against the diseases and gets rid of the waste products and unwanted substances by transporting them to the excretory organ like kidney.


White Blood Cells
and Platelets (< 1%)
Plasma
(55%)
Red Blood Cells
(45%)



RED BLOOD CELL AND ITS DISORDERS

- Erythrocytes or red blood cells are the non nucleated formed elements in the blood.
- Red color- due to hemoglobin.



Variations in the number of red blood cells

- **Physiological variations**

A. Increase in RBC:

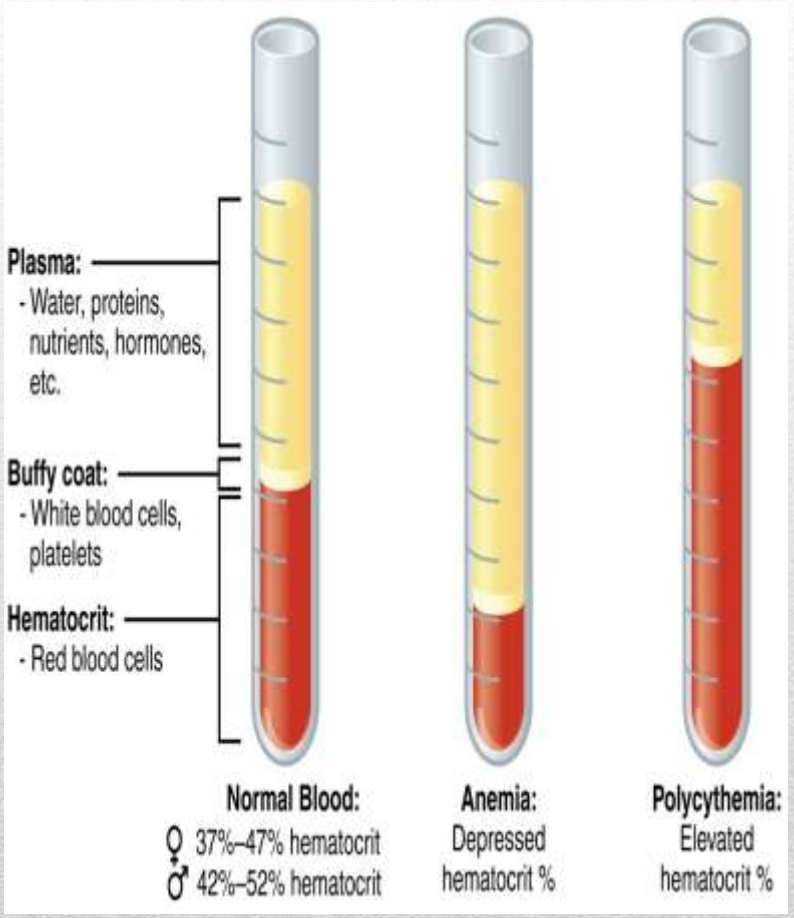
1. Age
2. Sex
3. High altitude
4. Muscular exercise
5. Emotional conditions
6. Increase environmental temperature
7. After meals

B. Decrease in RBC:

1. High barometric pressures
2. After sleep
3. Pregnancy

- **Pathological variation:**

1. Polycythemia
2. Anemia



RED BLOOD CELL DISORDERS

- Erythrocytoses
- Polycythemia vera
- Anemia

✓ Iron deficiency anemia

✓ Anemia owing to hemolysis

✓ Sickle cell anemia

✓ Erythroblastosis fetalis

✓ Thalassemia

✓ Pernicious anemia

✓ Aplastic anemia

Erythrocytoses

- A conditions with an increase in circulating red blood cells (RBCs), characterized by a increased hemoglobin level.
- 2 types- relative and absolute

- **Relative polycythemia**: Occur as a result of loss of fluid with hemoconcentration of cells.

  -Seen in: vomiting, diarrhea or loss of electrolytes with accompanying loss of water.

  -Increase in number of RBC is only relative to the total blood volume.

- **Absolute erythrocytoses**
- **Primary polycythemia:** ***True idiopathic increase*** in the number of circulating RBC and of the hemoglobin level.

  - Bone marrow with an inherited increased proliferative activity.

- **Secondary polycythemia:** known etiology
- **A**bsolute increase in RBC mass resultant ***to enhanced stimulation of RBC production***.
- Bone marrow anoxia – pulmonary dysfunction, high altitude, CO poisoning.
- Production of an erythropoietic stimulating factor- drugs and chemicals such as coal-tar, mercury, iron, bismuth.

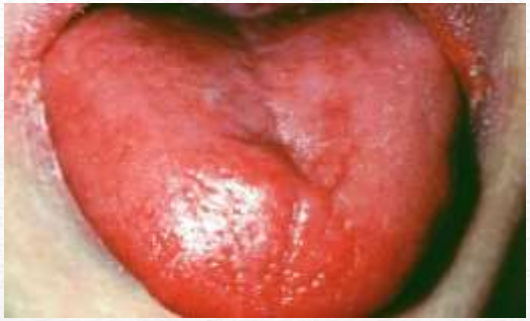
POLYCYTHEMIA VERA

- Chronic stem cell disorder with an insidious onset characterized as a panhyperplastic, malignant and neoplastic marrow disorder.
- Absolute increase in the number of circulating RBC and in the total blood volume because of uncontrolled RBC production.
- Accompanied by increase in WBC and platelet production.

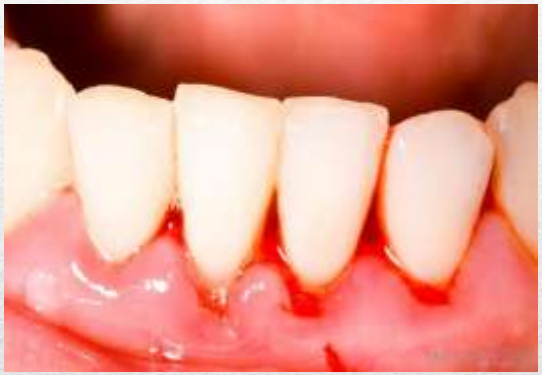
Clinical Manifestations

- Asymptomatic
- Pruritis
- Vertigo
- Gastrointestinal pain
- Headache
- Paresthesias, fatigue, weakness,
- visual disturbances, tinnitus,

Oral Manifestations



- Erythema (red-purple color) of mucosa,
- Glossitis,
- Erythematous & edematous gingiva
- Spontaneous gingival bleeding



Laboratory findings

- RBC- normochromic normocytic- >10,000.000/cubic mm
- HEMOGLOBIN: >20gm/dl
- PLATELETS- 400,000-800,000/dl
- BONE MARROW- hypercellular, megakaryocytes are increased

TREATMENT

- Phlebotomy
- Chemotherapy
- Radioactive phosphorus

Oral health consideration:

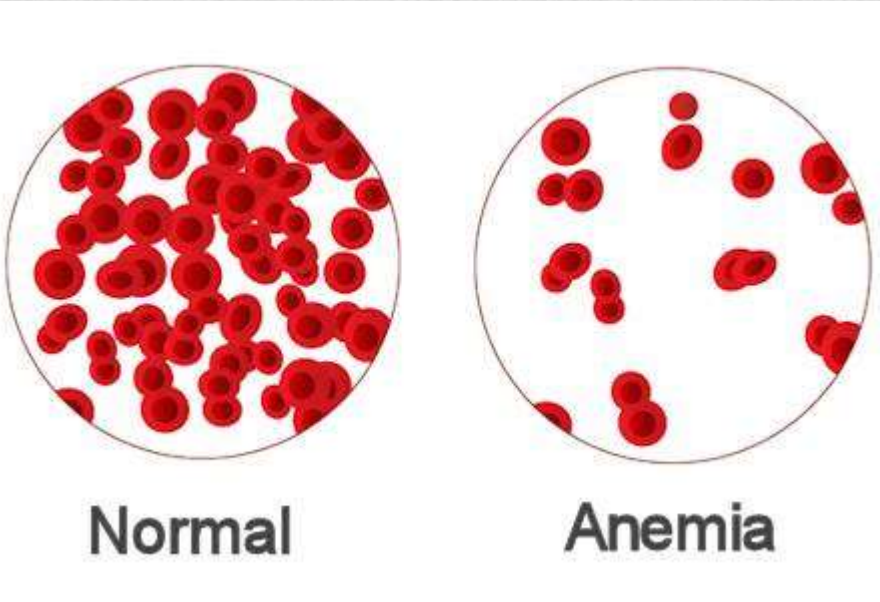
- Clinically significant bleeding may paradoxically require platelet transfusion
- Tranexamic acid can be used
- Adjustment of any concomitant antiplatelet and/or anticoagulant therapy

ANEMIA

- Anemia refers to reduction in

1. Red blood cell count
2. Hemoglobin content
3. Packed cell volume

- It can also be defined as a lowered ability of the blood to carry oxygen.



Etiologic classification of Anemia:

1. **Loss of blood:**

- Acute posthemorragic anemia
- Chronic posthemorrhagic anemia

2. **Excessive destruction of RBC:**

a) Extra corpuscular causes: Antibodies, Infection(malaria),

- Splenic sequestration and destruction
- Drugs, chemicals and physical agents

b) Intracorpuscular haemolytic disease

1) Hereditary

- Disorder of glycolysis, abnormalities in RBC membrane.
- Abnormalities in synthesis of globin

2) Acquired – lead poisonong

3. Impaired blood production resulting from deficiency of substances essential for erythropoiesis

a. Iron deficiency
b. Deficiency of vitamin B12 , folic acid and Protein deficiency

4. Inadequate production of mature erythrocytes

a) Deficiency of erythroblasts
b) Pure red cell aplasia
c) Infiltration of bone marrow- Leukemia, lymphoma, Multiple myeloma
d) Endocrine abnormality- myxedema
e) Chronic renal disease
f) Chronic inflammatory disease
g) Cirrohisis of liver

- **Normocytic** - occurs when the overall hemoglobin levels are decreased, but the red blood cell size (mean corpuscular volume) remains normal. Causes include: Acute blood loss, Anemia of chronic disease
- **Microcytic-** result of hemoglobin synthesis failure/insufficiency. Iron deficiency anemia, thalassemia.
- **Macrocytic**- Megaloblastic anemia, the most common cause of macrocytic anemia, is due to a deficiency of either vitamin B_{12}, folic acid, or both. Also seen in hypothyroidism, alcoholism.
- **Hypochromic microcytic-** iron deficiency anemia.

Anemia owing to blood loss- Iron deficiency anemia

- Iron deficiency is defined as a reduction in total body iron to an extent that iron stores are fully exhausted and some degree of tissue iron deficiency is present.
- Females are mostly affected.

Etiology

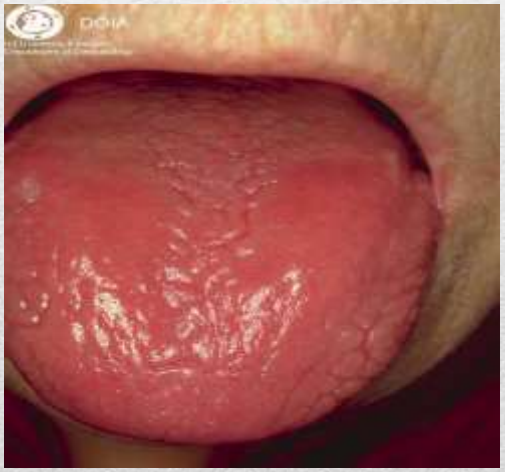
- Chronic blood loss
- Inadequate dietary intake
- Faulty iron absorption
- Increased requirements for iron- infancy, childhood, pregnancy.

Clinical Manifestations

- Chronic fatigue
- Pallor of the conjunctiva, lips, and oral mucosa;
- Brittle nails with spooning, cracking,
- Splitting of nail beds, koilonychia
- Palmar creases
- Palpitations
- Shortness of breath, numbness
- Bone pain

Oral Manifestations

- Angular cheilitis,
- Glossitis with different degrees of atrophy of fungiform and filliform papillae
- Pale oral mucosa
- Oral candidiasis
- Recurrent aphthous stomatitis
- Erythematous mucositis
- Burning mouth



Laboratory findings

- Microcytic hypochromic anemia due to inadequate supply of iron for normal hemoglobin synthesis.
- RBC- 3,000,000-4,000,000/cubic mm
- Low hemoglobin
- Low serum iron and ferritin with an elevated total iron binding capacity (TIBC)

Treatment

- Oral iron supplementation - Ferrous sulfate.
- High protein diet.

Oral Health Considerations

- Low hemoglobin levels - physician consultation prior to surgical treatment.
- If Hemoglobin is less than 8 gm/dL, general anesthesia should be avoided.
- Narcotic use should be limited.
- Increased risk for ischemic heart disease

Plummer-Vinson Syndrome/ Paterson-Kelly syndrome

- Rare syndrome , middle-aged white women
- Classic triad : Dysphagia,
  Iron deficiency anemia
  Upper esophageal webs or strictures.

Etiopathogenesis :

- Unknown - iron deficiency.
- Malnutrition,
- Genetic predisposition and Autoimmune processes.

Treatment: Iron supplementation

Anemia Owing to Hemolysis

- Normal RBC life span - 90 to 120 days.
- Hemolytic diseases result in anemia if the bone marrow is not able to replenish adequately the prematurely destroyed RBCs.
- Either inherited or acquired.

3 mechanism for accelerated destruction of RBCs:

1. Molecular defect inside the red cell
2. Abnormality in membrane structure and function
3. Environmental factor- mechanical trauma

Clinical Manifestations

- Signs and symptoms depend on the mechanism that leads to red cell destruction.
- Acute back pain,
- Renal failure.
- Fatigue
- Loss of stamina
- Breathlessness
- Tachycardia
- Hemoglobinuria
- Physical findings : jaundice of skin and mucosae, splenomegaly

Oral Manifestations

- Pallor or jaundice of oral mucosa,
- Paresthesia of mucosa, and,
- Hyperplastic marrow spaces in the mandible, maxilla, and facial bones

Laboratory findings:

- An elevated reticulocyte count is the most useful indicator of hemolysis, reflecting erythroid hyperplasia of the bone marrow.

Sickle Cell Disease/Sickle Cell Anemia

- Hereditary type of chronic hemolytic anemia transmitted as a mendalian dominant, nongender linked characteristic.
- Exclusively in blacks and in whites of Mediterranean origin.
- A concordance exists between the prevalence of malaria and HbS

HbA is genetically altered to produce HbS,

Substituition of valine for glutamine at the sixth position of the β globin chain

- Erythrocytes have their normal biconcave discoid shape distorted, generally presenting a sickle-like shape.
- Reduces both their plasticity and lifetime from the normal 120 days average down to 14 days.
- This results in the underlying anemia and hypertrophic bone marrow.
- In heterozygote- 40% of hemoglobin is HbS
- In homozygote- nearly all hemoglobin is HbS

Deoxygenation of the heme moiety of HbS

↓

Hydrophobic interactions between adjacent Hbs molecule

↓

Aggregate into larger polymer

↓

Distorting the RBC into

↓

Classic sickle shape

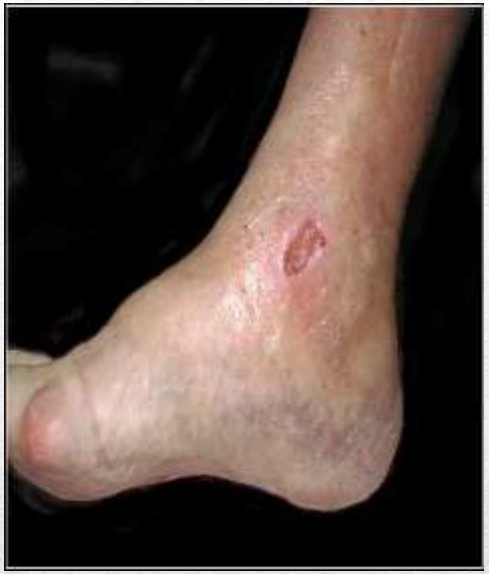
↓

Obstructs microcirculation

↓

Hypoxia → promotes sickling

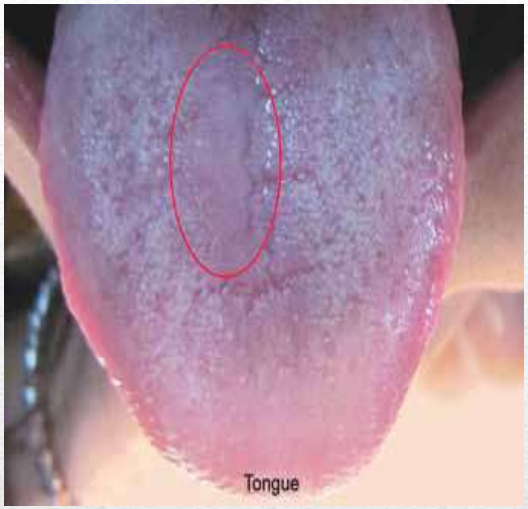
Clinical Manifestations



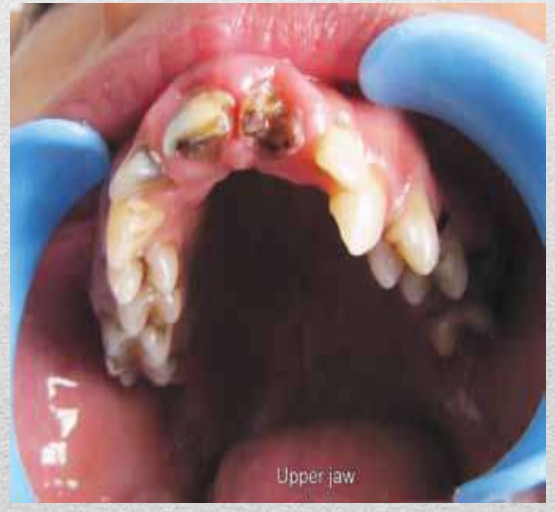
- Common in females, before the age of 30 years
- Cerebrovascular accidents/ strokes,
- Aplastic crises leading to severe anemia,
- chronic leg ulcers,
- Hematuria,
- Aseptic osteonecrosis,
- Retinitis leading to blindness
- Splenic sequestration,
- Renal failure
- **Acute chest syndrome** - fever, cough, sputum production, dyspnea, or hypoxia.

Oral Manifestations

- Significant bone change in dental radiograph
- Mild to severe generalized osteoporosis
- Loss of trabeculation of the jaw bone
- Enamel hypomineralization
- Increased overjet and overbite
- Pallor of the oral mucosa
- Delayed eruption of the teeth
- Pulpal necrosis

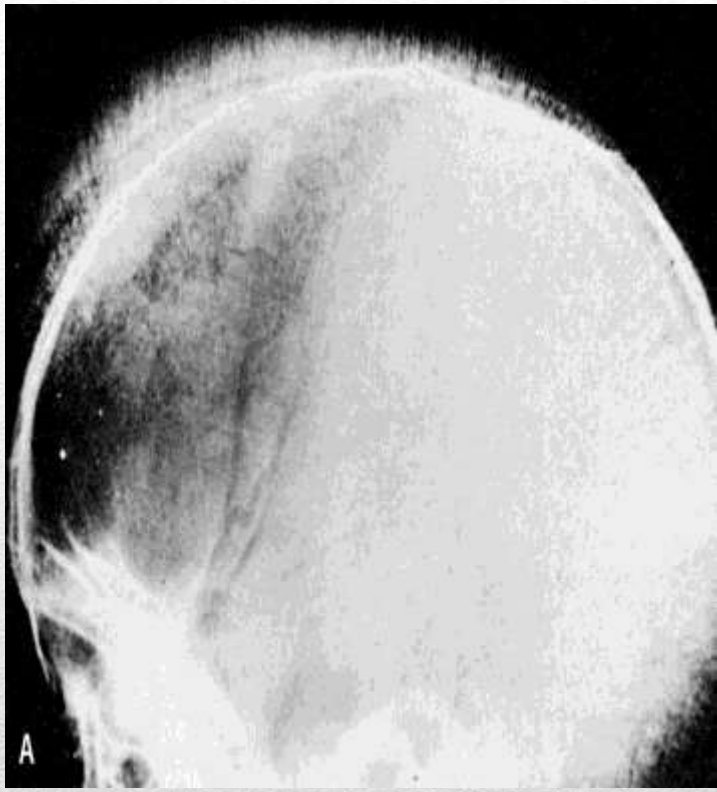


Smooth tongue



Radiographic features

- **HAIR – ON – END:** perpendicular trabeculations radiating outward from the inner table.
- Outer table of bone may appear absent and the diploe thickened.
- Generalized osteoporosis
- Enlarged medullary cavities with thin cortices

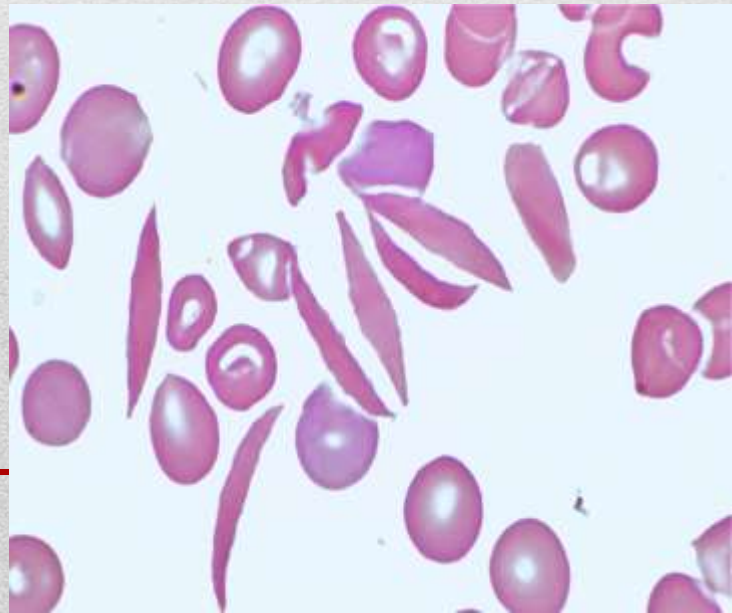


Laboratory findings

- RBC- may reach a level of 1,000,000 cells per cubic mm.
- Decreased hemoglobin level.
- High reticulocyte count- Anemia
- Increased marrow response.
- Elevated lactic dehydrogenase and decreased levels of hepatoglobin- confirms hemolysis

Blood smear:

- Typical sickle- shaped RBCs seen



Treatment :

- Management of vaso-occlusive crisis
- Management of chronic pain syndrome
- Management of chronic hemolytic anemia
- Prevention and treatment of infections
- Management of the complications.

Oral Health Considerations:

- Amoxicillin was the most commonly chosen antibiotic
- Maintaining good oral hygiene, routine care needed,
- Aggressive treatment of oral infection,
- Avoidance of long, stressful dental visits

Erythroblastosis fetalis

- Congenital hemolytic anemia due to Rh incompatibility results from the destruction of fetal blood brought about by a reaction between maternal and fetal blood factors.
- Rh factor, named after the rhesus monkey, was discovered by Landsteiner and wiener in 1940 as a factor in human RBC that would react with rabbit antiserum produced by administration of RBC from the rhesus monkey.

Pathogenesis

- EF is essentially due to inheritance by the fetus of a blood factor from the father that acts as a foreign antigen to the mother.

Transplacental transfer of this antigen, transplacental leaks of RBC

↓

From the fetus to the mother

↓

Immunization of the mother, formation of antibodies which

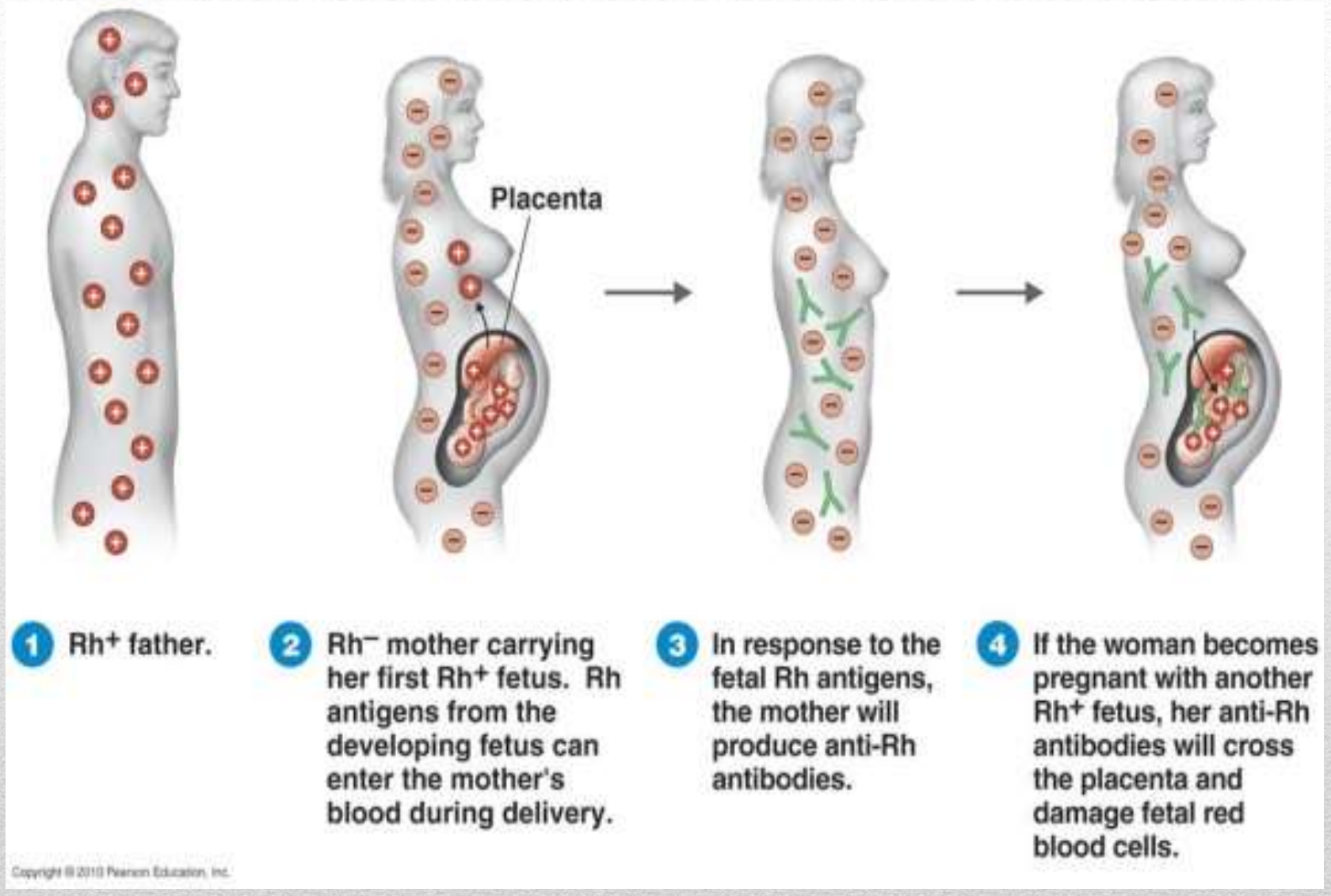
↓

When transferred back to the fetus by the same route

↓

Produce fetal hemolysis

- If both parents are homozygously Rh positive→ infant will be Rh positive → no maternal immunization.
- If mother is homozygously positive but father is Rh-negative → no maternal immunization.
- If father is Rh- positive and mother is Rh- negative → fetus inherits parental factor, which may act as an antigen to the mother and immunize her with resultant antibody formation.

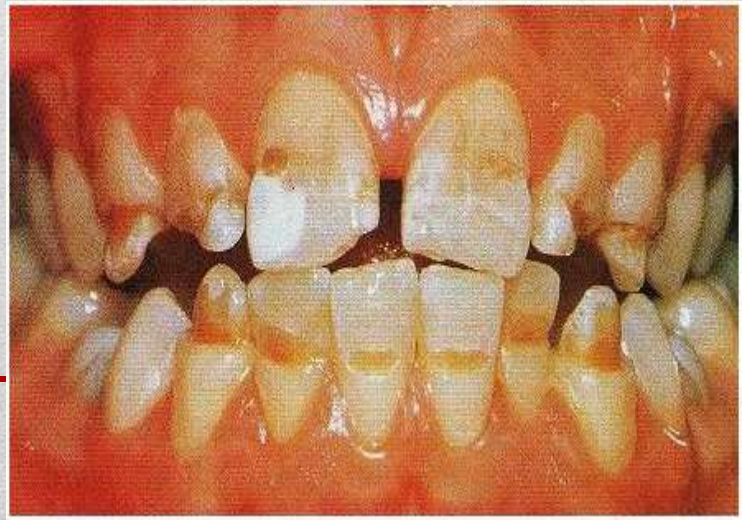


Clinical features

- Some infants are stillborn.
- Anemia with pallor
- Jaundice
- Compensatory erythropoiesis
- Fetal hydrops

Oral manifestation

- Deposition of blood pigments in the enamel and dentin
- Ground sections- positive test for bilirubin
- Intrinsic stains
- Enamel hypoplasia
- Rh hump



Laboratory findings

- RBC count decreased, large number of normoblasts or nucleated red cells
- Icterus index high
- Positive direct coombs test on cord blood

Treatment

- At present, Rh-negative mothers are being given anti-D gamma globulin to prevent immunization

Thalassemias

- Thalassemia is a group of genetic disorders of hemoglobin synthesis characterized by a disturbance of either alpha (α) or beta (β) hemoglobin chain production.
- An estimated 900,000 births are expected to occur in the next 20 years with clinically significant thalassemia disorders
- First described by Thomas B Cooley in 1925.
- Thalassa means ‘sea’in Greek.

Pathogenesis:

- **Normal adult hemoglobin (HbA)-** heme is conjugated to globin.
- Globin- 2 pairs of α chain and β chain.

In thalassemia group of anemias,

- Heterogenous group- diminished synthesis of α chain and β chain of hemoglobinA.
- Thalassemia α- deficient synthesis of α chain.
- Thalassemia β – deficient synthesis of β chain.

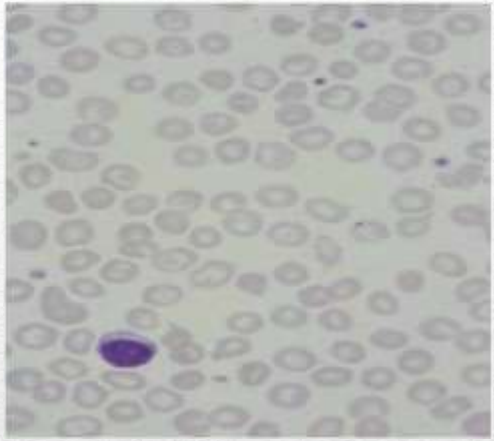
  - an excess of α- chains, producing **'unstable hemoglobins'.**

Damage the erythocytes → vulnerability to destruction

- **In heterozygotes**, the disease is mild and is called as **Thalassemia minor or thalassemia trait**
- Represent both α and β thalassemia.

- **In homozygote,** severe form, called **Thalassemia major or β - thalassemia/ Cooley's anemia**
- Production of β chain is markedly decreased or absent.
- Consequent decrease in synthesis of total hemoglobin occurs → severe hypochromic anemia
- Furthermore, excess α chain which synthesize at normal rate , precipitate as insoluble inclusion bodies within the erythrocytes and their precursors.

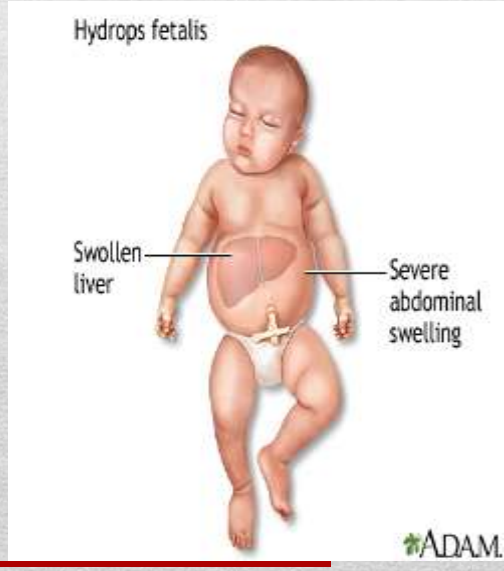
- **FESSAS BODIES:** **I**ntracellular inclussion bodies, leads to increased erythrocyte hemolysis and severe ineffective hematopoiesis.



2 other forms of thalassemia major that represent α- thelasemia are:

Hemoglobin H disease- very mild form

Hemoglobin Bart's disease- with hydrops fetalis, in which infants are stillborn or die shortly after birth



Clinical Manifestations

- Occurs within the first 2 years of life.
- Siblings are commonly affected.
- Yellowish pallor of the skin
- Fever, chills, malaise,
- Generalized weakness
- Splenomegaly and hepatomegaly

- **RODENT FACIES-** develops mongoloid features due to prominence of the cheeks, protrusion of the maxillary anterior teeth, depression of the bridge of the nose.

Oral manifestation

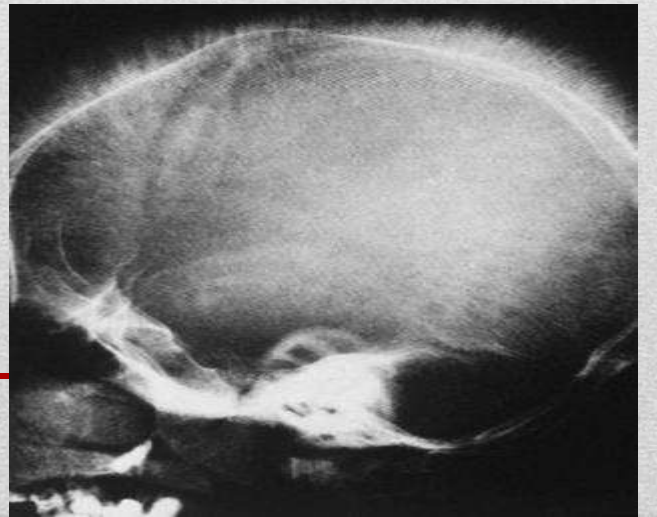
- Unusual prominance of the premaxilla
- Anemic pallor observed

Laboratory findings

- Hypochromic microcytic
- RBC- exhibiting Poikilocytosis and Anisocytosis.
- Safety pin cells and nucleated RBCs in the circulating RBC is also a characteristic feature.
- WBC- frequently elevated.
- Bone marrow- cellular hyperplasia with large number of immature, primitive and stem form of RBCs.
- Supravital staining- Methyl blue demonstrate inclusion bodies.

Radiographic findings

- RIB- WITHIN- A- RIB: noted in middle and anterior portion of the ribs. Long linear density within or overlapping the medullary space of the rib and running parallel to its long axis.
- HAIR- ON- END appearance.
- SALT AND PEPPER EFFECT: peculiar trabeculae pattern of maxilla and mandible, apparent coarsening of some trabeculae and the blurring and disappearance of others.



Treatment

- Blood transfusion- temporary remission
- Bone marrow transplantation.

Anemia Owing to Decreased Production of RBCs

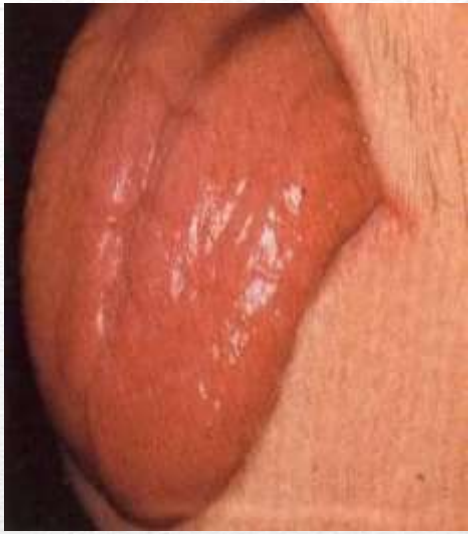
Megaloblastic (Pernicious) Anemia and Vitamin B12 (Cobalamin) Deficiency

- It is adult form of anemia that is associated with gastric atrophy and a loss of intrinsic factor production in gastric secretions.
- Rare congenital autosomal recessive form.
- Autoimmune disease resulting from autoantibodies directed against intrinsic factor (a substance needed to absorb vitamin B12 from the gastrointestinal tract) and gastric parietal cells.
- Vitamin B12 → erythrocyte – maturing factor.

Clinical Manifestations

Hematologic	Megaloblastic (macrocytic) anemia
	Pancytopenia (leukopenia, thrombocytopenia)
Neurologic	Paresthesias, tingling and numbness of hands and feet
	Peripheral neuropathy
	Muscle weakness
	Impaired sense of smell
	Syncope
Psychiatric	Fatigue
	Irritability, personality changes
	Mild memory impairment
	Depression
Cardiovascular	increased risk of myocardial infarction and stroke

Oral Manifestations



- Burning sensation in the tongue, lips, buccal mucosa, and other mucosal sites.
- The tongue is generally inflammed often described as **'beefy red'**in color.
- Characteristically with the glossitis, glossodynia and glossopyrosis there is gradual atrophy of the papillae tongue that eventuates in a smooth or bald tongue → **Hunter's glossitis or Moeller's glossitis.**
- Fiery red appearance of the tongue may undergo periods of remission, recurrent attacks are common.
- Dysphagia and taste alterations have been reported.

Laboratory findings

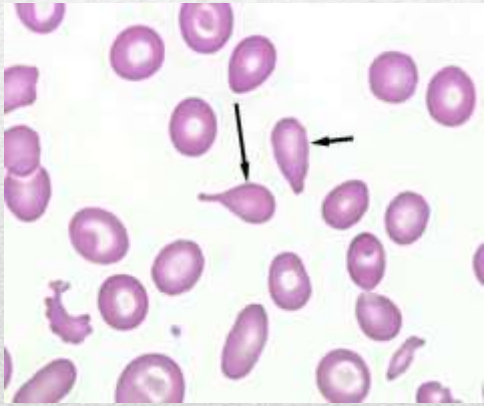
- **BLOOD:** RBC count is seriously decreased, often to 1,000,000 or less per cubic mm.

  -Macrocytosis is one of the chief characteristic feature, although poikilocytosis or variation in shape of cells present.

  - pear or tear drop shape erythrocytes are present.

  - increased hemoglobin content.

  - mild to moderate thrombocytopenia is noticed.



- **SERUM:** Indirect bilirubin may be elevated.

  serum lactic dehydrogenase is markedly increased.

  ↓- serum potassium, cholesterol and alkaline phosphatase

- **BONE MARROW-** hypercellular and show trilineage differentiation.

TREATMENT:

- Weekly intramuscular injections of 1,000 μg of vitamin B12 for the initial 4 to 6 weeks, followed by 1,000 μg per week indefinitely.
- Delayed treatment permits progression of the anemia and neurological complication

Aplastic Anemia

- Aplastic anemia (AA) is a rare blood dyscrasia in which peripheral blood pancytopenia results from reduced or absent blood cell production in the bone marrow and normal hematopoietic tissue in the bone marrow has been replaced by fatty marrow.
- Paul Ehrlich, introduced the concept of aplastic anemia in 1888.
- 1n 1904 it was termed as aplastic anemia by Chauffard.
- Environmental exposures, such as to drugs, viruses, and toxins, are thought to trigger the aberrant immune response in some patients, but most cases are classified as idiopathic

2 chief forms:

- **Primary aplastic anemia**: unknown etiology.

  young adults, develops rapidly and terminates fatally.

  FANCONI'S SYNDROME: congenital, sometimes familial, aplastic anemia is associated with other congenital defects including bone abnormalities, microcephaly, hypogenitalism and generalized olive brown pigmentation of the skin.

- **Secondary aplastic anemia-** known etiology

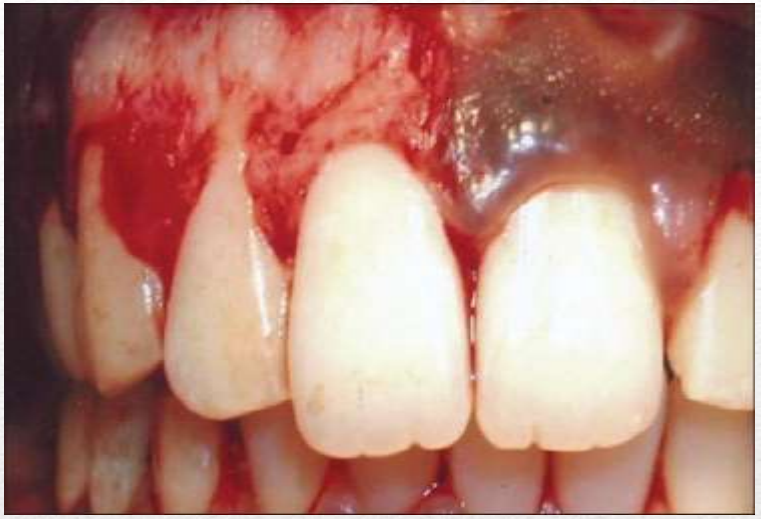
  Exposure of the patient to various drugs or chemical substances or to radiant energy in the form of x-rays, radium or radioactive isotopes.

Clinical Manifestations

- Pancytopenia
- Anemia→ such as fatigue and malaise, chest pain, or shortness of breath.
- More sudden onset of bleeding caused by thrombocytopenia, manifest as increased bruising, evident by purpura and petechiae, and epistaxis or gingival bleeding.
- Leukopenia, particularly neutropenia, can result in fever and infection.
- Preceded by infections by hepatitis viruses, EBV, HIV parvovirus, mycobacterial infections.

Oral Manifestations

- Hemorrhage,
- Candidiasis,
- Viral infections,
- Gingival bleedings



Laboratory findings

- RBC- diminished as low as 1,000,000 cells per cubic mm
- ↓ in hemoglobin level.
- A paucity of granulocytes, monocytes and reticulocytes is found.
- Prolonged bleeding time
- Tourniquet test is positive.

BONE MARROW SMEAR:

- **Anemia:** erythropoietic depression, marrow appears normal or even hyperplastic.
- **Pancytopenia**- hypoplasia of all marrow element
- **Severe cases-** hypocellular bone marrow with fatty replacement and relatively increased nonhematopoietic element such as plasma cell and mast cell.

Treatment

- Blood transfusions to correct anemia and thrombocytopenia
- Immunosuppression with antithymocyte globulins and cyclosporine is effective at restoring blood cell production

Oral Health Considerations

- Neutropenia leads to an increased susceptibility to infection,
- Thrombocytopenia leads to bruising and mucosal bleeding.
- Neutropenic fevers must be treated aggressively with parenteral, broad-spectrum antibiotics.
- Antifungal therapy should be added
- Attention to details of oral hygiene and hand washing and avoidance of minor injuries or casual exposure to infectious agents can reduce the risk of serious complications.

WHITE BLOOD CELLS AND ITS DISORDERS

- **White blood cells** (**WBCs**), also called **leukocytes** or **leucocytes**, are the cells of the immune system that are involved in protecting the body against both infectious disease and foreign invaders.
- All white blood cells are produced and derived from multipotent cells in the bone marrow known as hematopoietic stem cells.
- Leukocytes are found throughout the body, including the blood and lymphatic system
- 2 types: granulocytes and agranulocytes


neutrophil
eosinophil
basophil
monocyte
lymphocyte

Variations in the number of white blood cells

❑PHYSIOLOGICAL VARIATIONS:

- Age
- Sex
- Diurnal variations
- Exercise
- Emotional condition
- Pregnancy
- Sleep

❑PATHOLOGICAL VARIATIONS

- Leukopania
- Leukocytosis
- Neutrophilia
- Eosinophilia
- Basophilia
- Monocytosis
- Lymphocytosis
- Leukemia

Disorders

- Leukocytosis
- Leukopenia
- Agranulocytosis
- Neutropenia
- Chediak – Higashi Syndrome
- Acute Leukemia
- Chronic leukemia

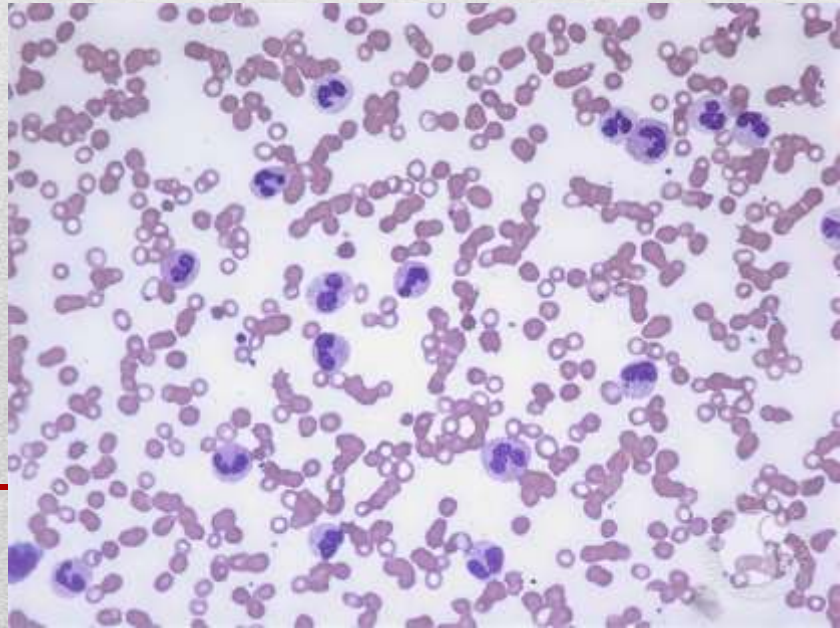
LEUKOCYTOSIS

- Defined as abnormal increase in the number of circulating WBCs.
- Considered to be a manifestation of the reaction of the body to a pathologic situation.
- It may also occur after exercise, convulsions such as epilepsy, emotional stress, pregnancy, anesthesia, and epinephrine administration.
- There are five principal types of leukocytosis:

1. Neutrophilia (the most common form)
2. Lymphocytosis
3. Monocytosis
4. Eosinophilia
5. Basophilia

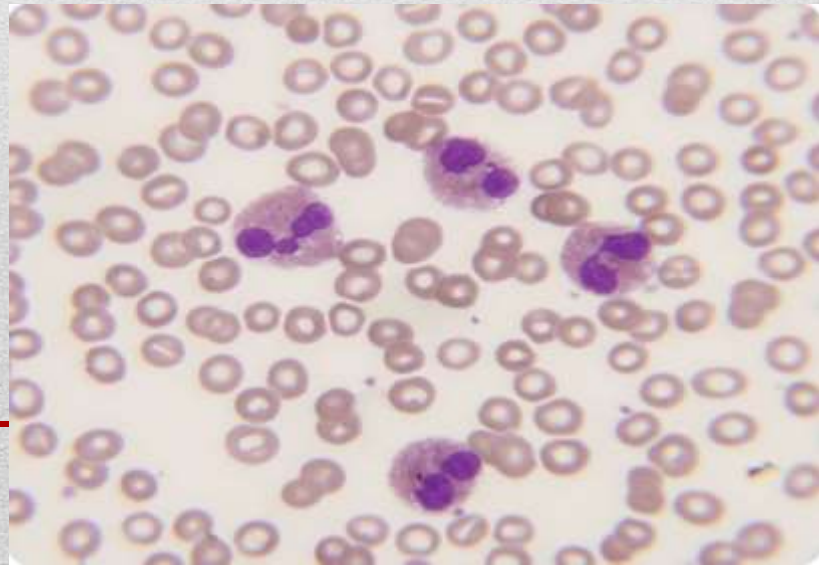
Neutrophilia

- **Physiologic**- in new born, during labor, after exercise, convulsions
- **Acute infections-** certain bacilli, fungi, viruses, parasites.
- **Inflammatory conditions-** Gout, Burns, Vascular disease, Hypersensitivity reactions
- **Intoxications-** Uremia, Poisoning by chemicals and drugs- lead, mercury.
- Acute hemorrhage
- Acute hemolysis
- Polycythemia, myelotic leukemia.



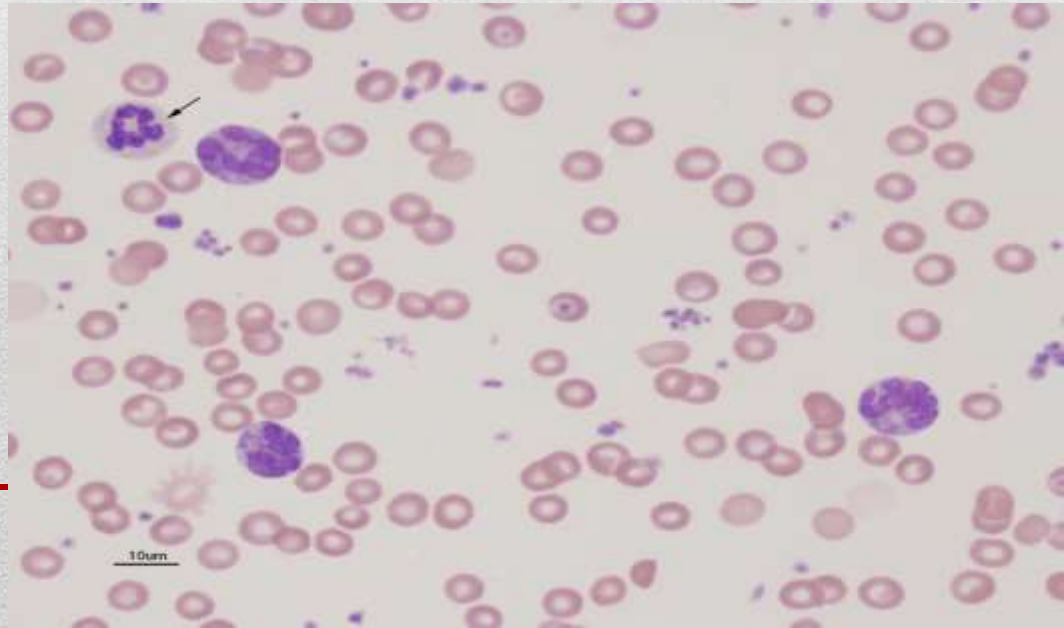
Eosinophilia

- **Allergic disorders-** bronchial asthma, hay fever
- **Skin disease-** phemphigus, erythema multiforme
- Scarlet fever,
- **Parasitic infection-** malaria.
- **Diseases of the hemopoietic system-** chronic myeloid leukemia, polycythema vera, hodgkins disease, pernicious anemia
- Following irradiation
- Sarcoidosis, rheumatoid arthritis.



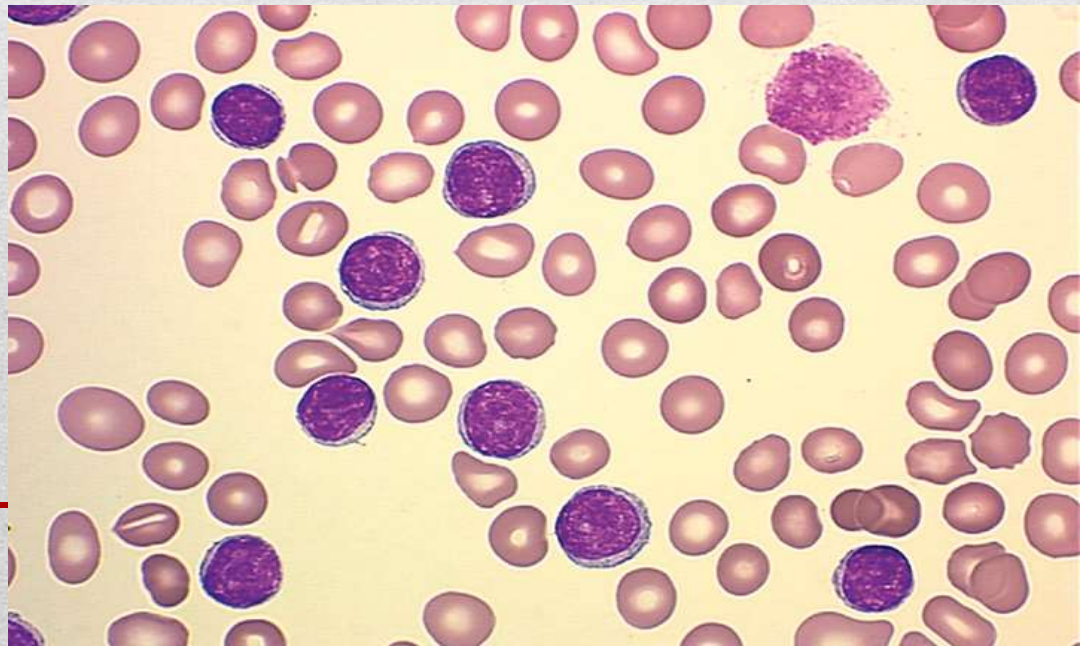
Basophilia

- Splenectomy
- **Blood disease-** CML, polycythemia vera, hodgkin's anemia
- **Infection**- smallpox, chickenpox
- After injection of foreign proteins



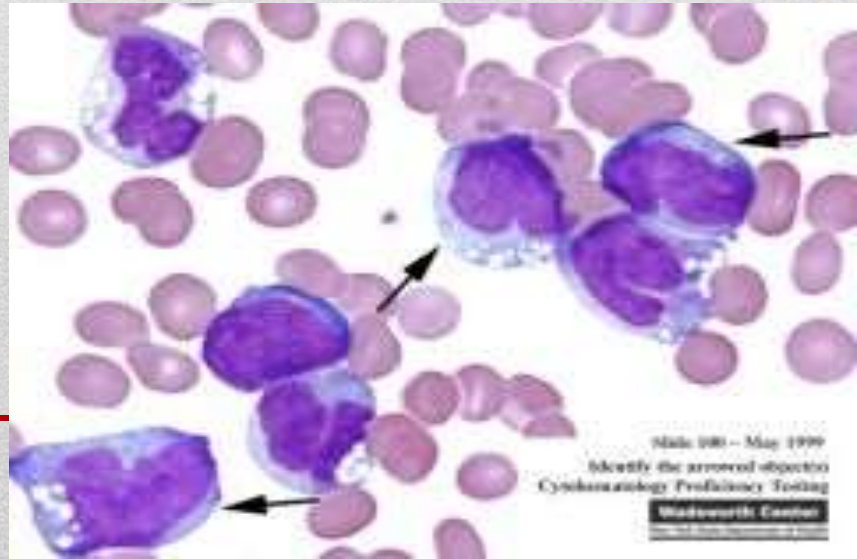
Lymphocytosis

- **Acute Infections-** infectious mononucleosis,
- **Chronic Infections-** tuberculosis, syphilis,
- Lymphocytic leukemia, lymphosarcoma
- **Hemopoietic disorders-** lymphocytosis,
- Mumps, german measles, thyrotoxicosis.



Monocytosis

- **Bacterial infections-** tuberculosis, SABE, syphilis,
- **Protozoal and Rickettsial-** malaria, typhus, kala-azar
- CML, hodgkin's disease, multiple myeloma
- **Lipid storage disease-** Gaucher's disease
- Granulomatous disease- sarcoidosis, ulcerative colitis
- Collagen vascular disease- lupus erythematosus, rheumatoid arthritis.



LEUKOPENIA

- Leukopenia is a decrease in the number of white blood cells (leukocytes) found in the blood, which places individuals at increased risk of infection.

CAUSES:

1) Infections:

- A) **Bacterial** – typhoid fever, Paratyphoid fever, Brucellosis
- B) **Viral and Rickettsial-** Influenza, Measles, Chickenpox, Dengue, Infectious Hepatitis
- C) **Protozoal-** Malaria, Kala-azar

2) Hemopoietic disorders**:**

- Gaucher's disease, Pernicious anemia, Aplastic anemia, Chronic hypochromic anemia, Agranuocytosis

3) Chemical agents:

- Mustards, Benzene, Urethane.
- Analgesics, Anticonvulsants, Sulfonamides, Antihistamines, Antithyroid drugs.

4) X-ray radiations

5) Anaphylactid shock

6) Liver cirrhosis, DLE

Agranulocytosis (Neutropenia/Granulocytopenia)

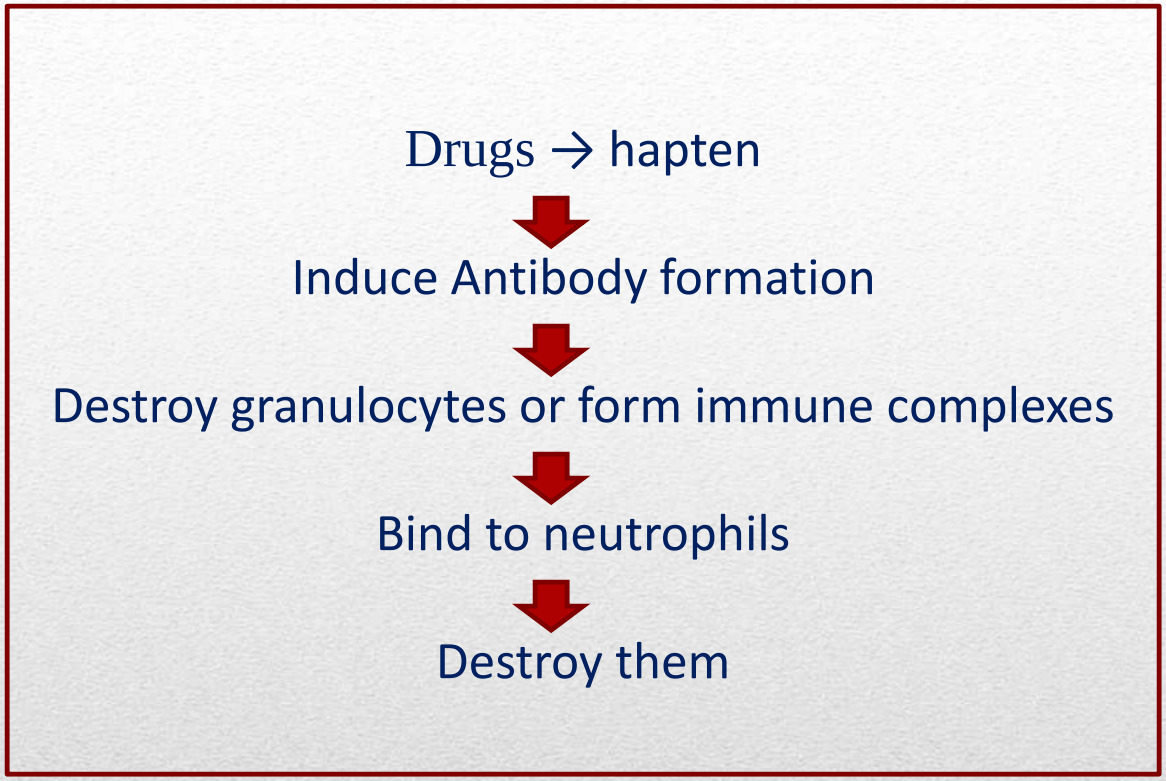
- Serious disease involving the WBC and is characterized by decrease in the number of circulating granulocytes.
- The terms agranulocytosis, neutropenia, and granulocytopenia are commonly used interchangeably for a reduced quantity of leukocytes.

Types:

- Primary Agranulocytosis- unknown etiology
- Secondary Agranulocytosis- known etiology.

ETIOLOGY

- Antineoplastics,
- Antibiotics,
- Anticonvulsants,
- Antiinflammatories,
- Antithyroid agents,
- Diuretics, and
- Phenothiazines



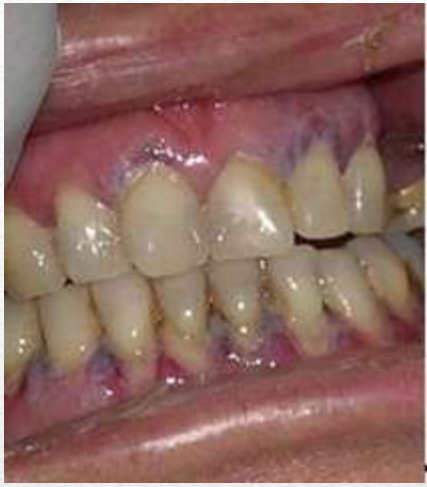
Kostmann syndrome is a group of diseases that affect myelopoiesis, causing a congenital form of neutropenia , usually without other physical malformations.

- manifests in infancy with life-threatening bacterial infections

Clinical features

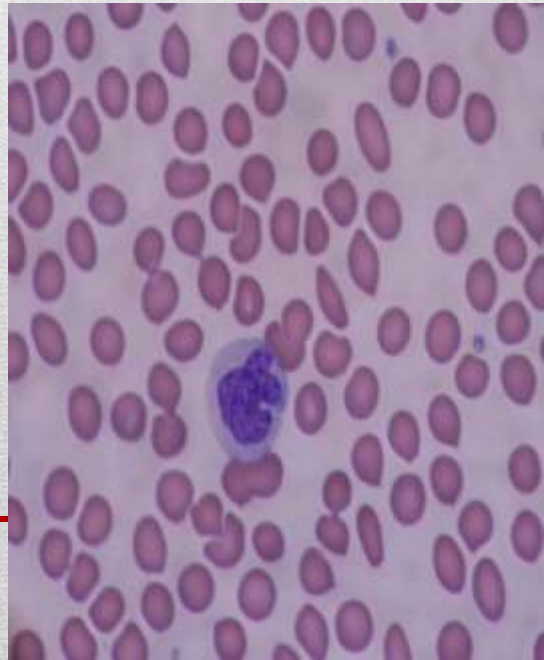
- Occur at any age- particularly among adults
- Women are more affected.
- High fever, chills, sore throat,
- Malaise, weakness
- Skin appears pale and anemic,
- **Presence of infections**
- Regional lymphadenitis,
- **Complication**- Generalized sepsis.

Oral manifestations



- Necrotizing ulceration of the oral cavity, tonsils and pharynx particularly gingiva and palate.
- Necrotic ulcers are covered by gray or even black membrane.
- No purulent discharge are noted.
- Excessive salivation.
- Oral surgical procedures are contraindicated.

Laboratory findings



- WBC are often below 2000 cells per cubic mm
- **Almost complete absence of granulocytes or PMNs.**
- RBC and platelet counts are normal

Treatment

- Recognition and withdrawal of the causative drugs
- Oral hygiene should be meticulous to foster an immaculate oral environment.

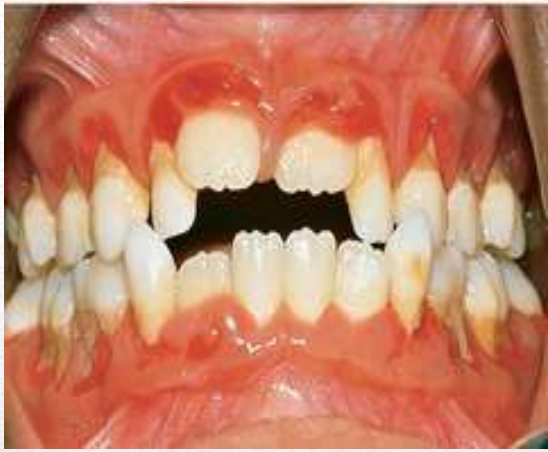
Cyclic Neutropenia

- Cyclic neutropenia is a rare hematologic disorder, characterized by repetitive episodes of fever, mouth ulcers, and infections attributable to recurrent severe neutropenia.
- Characterized by periodic or cyclic diminution in circulating PMNs as a result of bone marrow maturation arrest.
- Neutropenia recurs with a regular periodicity of 21 days, persists for 3 to 5 days, and is characterized by infectious events that are usually less severe than in severe chronic neutropenia.
- Autosomal dominant cyclic neutropenia is caused by a mutation of the gene for neutrophil elastase, *ELA2*, *located at 19p13.3*

Clinical features

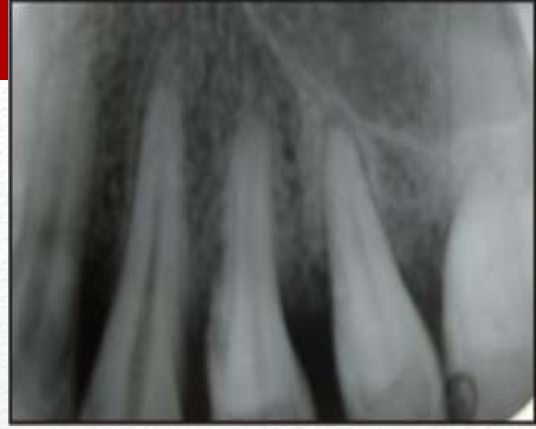
- Occurs at any age, infants or young adults.
- Symptoms are milder
- Fever, malaise, sore throat, stomatitis
- Regional lymphadenopathy
- Headache, arthritis,
- Cutaneous infections,
- conjunctivitis

Oral manifestations



- Severe gingivitis
- Stomatitis with Ulceration
- Isolated painful ulcers- lasts for 10-14 days , heals with scarring.
- With return of the neutrophil count to normal, gingiva appears normal

Radiographic features



- Mild to severe loss of superficial alveolar bone.
- Prepubertal periodontitis- in children, loss of bone around multiple teeth.

Laboratory findings:

- Patient exhibit a normal blood count which, over a period of 4-5 days, begins to show a precipitous decline in neutrophil count compensated by an increase in monocytes and lymphocytes.
- Neutrophil count completely disappear for 1-2 days, however cells begins to reappear within 4-5 days.

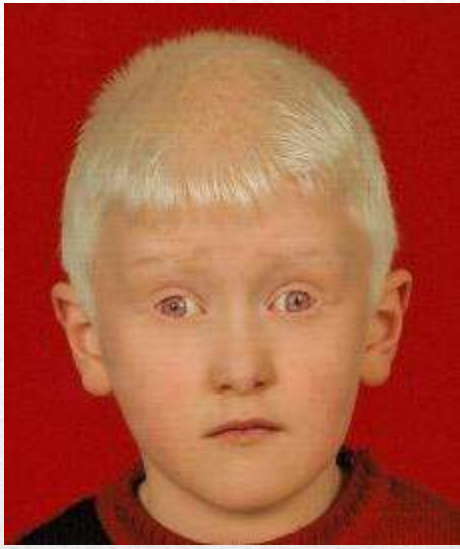
Treatment

- No specific treatment
- Splenectomy may be beneficial.

Chédiak-Higashi Syndrome

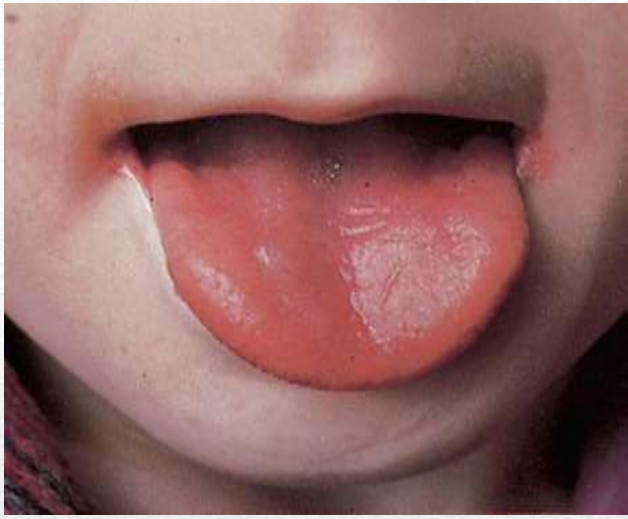
- Chediak-Higashi syndrome (CHS) is a rare autosomal recessive immunodeficiency disorder characterized by abnormal intercellular protein transport.
- Described by Steinbrinck in 1948, Chediak in 1952 and Higashi in 1954.
- Epstein – Barr virus

Clinical Manifestations



- Immune deficiency
- Oculocutaneous albinism
- Neurologic features- peripheral neuropathy,
- Recurrent infections, and
- Easy bruisability and bleeding
- Abnormalities can be found in the hematopoietic tissues, hair, ocular pigment, skin, adrenal and pituitary glands, gastrointestinal organs, peripheral nerves, and elsewhere.
- Infections are caused by S. aureus, S. pyogenes.

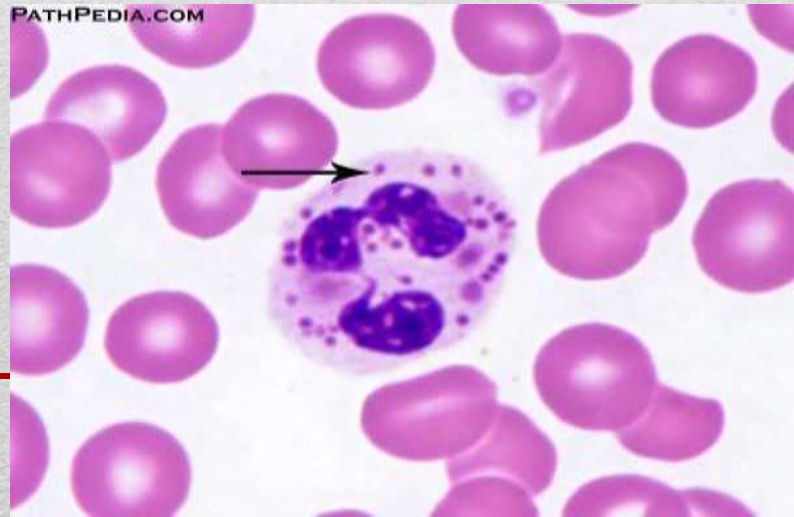
Oral manifestation



- Ulceration of the oral mucosa,
- Severe gingivitis and glossitis
- Periodontal breakdown

Laboratory findings

- **Exhibit giant abnormal granules** in the peripheral circulating leukocytes and in the marrow precursors.
- Granules represent abnormal lysosomes bear resemblanc to toxic granulations and Dohle bodies.
- Pancytopenia may be present.



Treatment

- No specific treatment
- Most of the therapy available in CHS is symptomatic, such as childhood immunizations and antibiotics for infections.

Oral Health Considerations

- When oral surgical procedures are planned, excessive operative blood loss should be anticipated secondary to qualitive defects in platelet function.
- Intramuscular injections should be avoided.
- Patients often have photophobia and may be sensitive to the bright operatory lights.
- Patients can be encouraged to bring sunglasses to dental appointments.

Leukemia

- Leukemia is a disease characterized by the progressive overproduction of WBCs which usually appear in the circulating blood in an immature form.
- **True malignant neoplasm-** proliferation of WBC or their precursors occurs in such as uncoordinated and independent fashion.
- Leukemic cells multiply at the expense of normal hematopoietic cell lines, resulting in marrow failure, altered blood cell counts, and, when untreated, death from infection, bleeding, or both.

Leukemia is classified into:

- **Lymphoid (lymphoblastic, lymphocytic) leukemia-** involving the lymphocytic series.
- **Myeloid (myelogenous) leukemia**- involving progenitor cells that gives rise to terminally differentiated cells of the myeloid series (erythrocytes, granulocytes, monocytes, platelets).

Classification may be modified to indicate the course of the disease- **acute** –survival is less than 6 months

subacute- survival is between acute and chronic

chronic- survival of over 1 year

Etiology

- Combination of environmental and genetic factors.
- Certain syndromes are associated with an increased risk. These genetic disorders include the following:

❖Down syndrome

❖ Bloom syndrome

❖ Neurofibromatosis

❖Ataxia- telangiectasia syndrome

❖Klinefelter syndrome

❖Fanconi's anemia

❖Myelodysplasia syndromes

- Certain types of leukemia show specific chromosomal abnormalities.
- **Chronic myeloid leukemia** has a genetic alteration called the **Philadelphia chromosome** which represents a translocation of the chromosomal material between the long arms of chromosomes 22 and 9.
- Exposure to pesticides, benzene, and benzene like chemicals, Ionizing radiation has been associated with an increased risk of developing leukemia.
- **EBV, Polyoma virus, Human T-cell leukemia virus- 1 (HTLV-1)** is known to be associated.

ACUTE LEUKEMIA

Acute Lymphocytic/Lymphoblastic Leukemia

- ALL is the clonal proliferation of lymphoid cells that have undergone maturational arrest in early differentiation.
- General mechanisms: aberrant expression of proto-oncogenes, chromosomal translocations that create fusion genes encoding active kinases and altered transcription factors.
- Philadelphia chromosome–positive ALL is the most common subtype of ALL in adults

Acute Myelogenous (Nonlymphocytic) Leukemia

- AML is a heterogeneous clonal disorder of hematopoietic progenitor cells (“blasts”) that lose the ability to differentiate normally and to respond to normal regulators of proliferation.
- In the absence of treatment, bone marrow failure and fatal infection, bleeding, or organ infiltration may occur within 1 year of diagnosis.
- The median age at presentation for patients with AML is 70 years.
- Risk factor- exposure to ionizing radiation, benzene, and cytotoxic chemotherapy.

Clinical features of acute leukemia

- Weakness,
- Fever, headache
- Generalized swelling of lymph node
- Petechial or ecchymotic hemorrhages in the skin and mucous membrane
- Anemia
- Spleen, liver and kidney become enlarged owing to leukemic infiltration.
- Hemorrhage

CHRONIC LEUKEMIA

Chronic Myelogenous leukemias

- Less pronounced marrow failure than acute leukemias.
- Indolent course, median age of 53 years at diagnosis.
- **Risk factors:** older age, male gender, and exposure to ionizing radiation and benzene and benzene-containing products.
- Most patients with CML have an acquired mutation called the **Philadelphia chromosome** that results from a translocation between chromosomes 9 and 22, producing the Bcr-Abl abnormal gene → causes the excess WBCs typical of CML.

Chronic Lymphocytic Leukemia

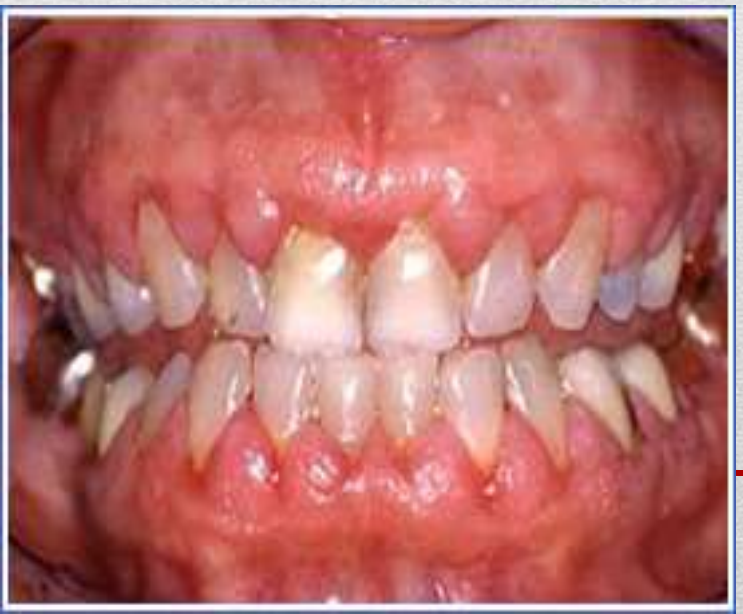
- CLL results from the slow accumulation of clonal B lymphocytes in 95% of patients.
- Median age at diagnosis of CLL is 65 years
- Etiology: unknown, although an abnormality of chromosome 12 is noted
- Lymphocytosis >5,000/mL for a month, with at least 30% of nucleated marrow granulocytes being well-differentiated lymphocytes, in an adult is diagnostic for CLL.

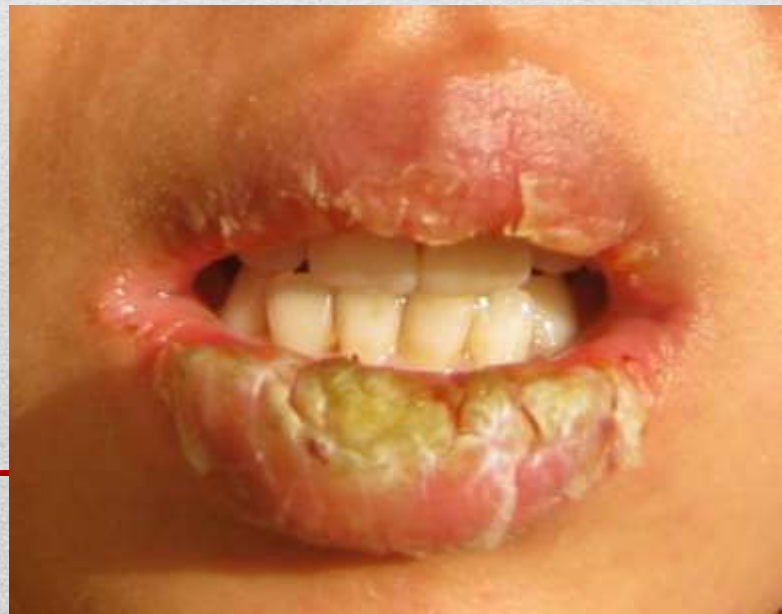
Clinical features

- Develop insidiously that the disease may be present for months or even several years before the symptoms lead to discovery.
- Anemic pallor
- Lymph node enlargement
- Splenomegaly, hepatomegaly
- Enlargement of the salivary gland and tonsils
- Xerostomia

Oral manifestations

- Gingivitis, gingival hyperplasia
- Hemorrhage, petechiae and ulceration of the mucosa
- Rapid loosening of the tooth due to necrosis of the PDL
- Destruction of the alveolar bone
- Oral mucositis, exfoliative cheilitis
- Infection with herpes and candida





Laboratory findings

Acute leukemia

- Both bleeding and coagulation time are prolonged. Tourniquet test is positive.
- Leukocyte count- may rise upto 1,000,000 cells per cubic mm
- In AML- predominant cells resemble myeloblast.
- ALL- cells exhibit considerable variation in degree of differentiation.
- Monocyte leukemia- poorly differentiated cells

Chronic leukemia

- Anemia and thrombocytemia are common
- WBC count over 5,000,000 cells per cubic mm

Treatment

- Chemotherapy
- Radiation therapy
- Corticosteroids
- If bcr-abl fusion is identified- Tyrosine kinase inhibitor is appropriate.
- Supportive care
- Optimal oral hygiene care

PLATELET AND ITS DISORDERS

- Platelets or thrombocytes are small colorless, nonnucleated and moderately refractive bodies.
- Considered to be fragments of cytoplasm
- Spherical or rod shaped, becomes oval or disc shaped when inactivated.

Properties:

1. Adhesiveness
2. Aggregation
3. Agglutination

Normal count and its variation

- Normal platelet count- 2,00,000-4,00,000/cu mm of blood

❑Physiological variation

- Age
- Sex
- High altitude
- After meals

❑Pathological variation

Thrombocytopenia-

- acute infections,
- acute leukemia,
- aplastic and pernicious anemia,
- chickenpox,
- smallpox,
- splenomegaly,
- scarlet fever, typhoid,
- tuberculosis

Thrombocytosis-

- allergic conditions,
- hemorrhage,
- bone fracture,
- surgical operations,
- splenectomy,
- rheumatic fever,
- trauma.

Thrombocythemia-

- carcinoma,
- chrinic leukemia,
- hodgkin’s disease

Platelet Disorders

- Platelet disorders may be divided into two categories by etiology— congenital and acquired—
- Two additional categories by type—thrombocytopenias and thrombocytopathies.

- **Thrombocytopenias** occur when platelet quantity is reduced and are caused by one of three mechanisms:

1. decreased production in the bone marrow,
2. Increased sequestration in the spleen, or
3. accelerated destruction.

- **Thrombocytopathies,** or qualitative platelet disorders-

  -Characterized by dysfunctional platelets (thrombocytes), which result in prolonged bleeding time, defective clot formation, and a tendency to hemorrhage
- May result from defects in any of the three critical platelet reactions:

1. Adhesion,
2. Aggregation, or
3. Granule release.

Purpura

- Purpura is defined as a purplish discoloration of the skin and mucous membrane due to spontaneous extravasation of blood.
- Symptoms rather than a disease entity.

Classification:

- Nonthrombocytic purpura
- Thrombocytic purpua

a) Primary or essential purpura
b) Secondary or symptomatic purpura

Nonthrombocytopenic purpura

- Heterogeneous group of disease
- Not mediated through changes in blood platelets
- Due to alterations in the capillaries themselves that results in many instances in increased permeability.

Bleeding disorders due to Nonthrombocytopenic purpura

Autoimmune

- Allergic purpuras
- Drug- induced vascular purpuras

Infections

- Bacterial- typhoid fever, scarlet fever, tuberculosis
- Viral- smallpox, influenza, measles
- Rickettsial- typhus
- Protozoal- malaria, toxoplasmosis

Structural malformations

- Hereditary hemorrhagic telangiectasia, Ehlers- Danlos syndrome, Osteogenesis Imperfecta, scurvy.

Thrombocytic purpura

- Abnormal reduction in the number of circulating blood platelets.
- Patient develops focal hemorrhages in to various tissues and organs, including skin and mucous membranes.

2 basic forms-

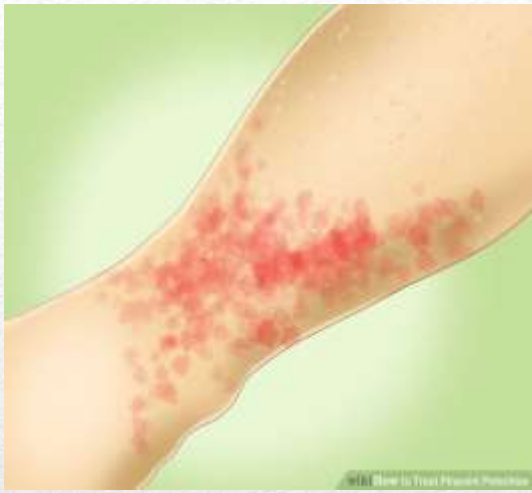
- Primary- unknown etiology
- Secondary- known etiology

Idiopathic purpura/ Primary thrombocytopenia

- Autoimmune disorder in which person becomes immunized and develops antibodies against his/her own platelet.
- An antiplatelet globulin which results in a decrease in the number of circulating platelets when administered to normal patients.
- **Acute form-** children, often following certain viral infections
- **Chronic type-** adults

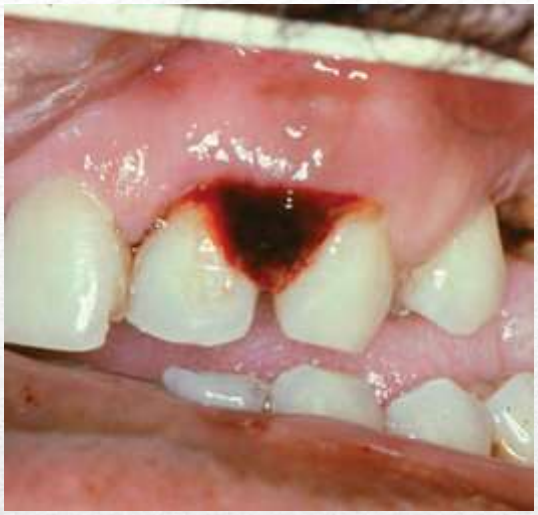
Clinical features:

- Spontaneous appearance of purpuric or hemorrhagic lesions of the skin which vary in size – tiny red pinpoint petechiae to large purplish ecchymoses.
- Massive hemartomas
- Bruising tendency
- Epistaxis
- Hematuria
- Malena
- **Complications**- intracranial hemorrhage, hemiplagia.



Oral manifestations

- Severe and profuse gingival bleeding
- Hemorrhage may be spontaneous
- Petechiae- palate
- Ecchymosis



Laboratory findings

- Platelet count is usually below 60,000 platelets/cubic mm
- Bleeding time is prolonged
- Coagulation time- normal

Treatment

- No specific treatment
- Splenomegaly
- Corticosteroids

- Oral surgical procedures are contraindicated until the deficiency has been compensated.

Thrombotic thrombocytopenic purpura

- Uncommon form, life-threatening multisystem disorder of an obscure nature but may be immunologically mediated.
- First described by Eli Moschowitz in 1924.
- More common in adults, and is associated with pregnancy, disease such as HIV, cancer, bacterial infections, vasculitis.
- **Characterized by**: microangiopathic hemolysis and platelet agggregation/hyaline thrombi in microcirculation.

Clinical features

- Young adults, more common in females
- Thrombocytopenia
- Hemolytic anemia
- Fever,
- Renal failure

Laboratory findings

- Fragmented RBCs consistent with hemolysis are noted in the peripheral smear.
- Reticulocyte count is also elevated
- PT and PTT are within normal limits
- LDH levels are increased
- Urinalysis- proteinuria and hematuria

Histologic features

- Widespread microthrombi in the arterioles, venules and capillaries.
- Intravascular thrombi are composed of loose aggregates of platelets that become organized into amorphous plugs which are than replaced by fibrins.

Treatment

- Corticosteroids
- Platelet aggregation inhibitors
- Splenectomy
- Exchange transfusion

Thrombocytasthenia

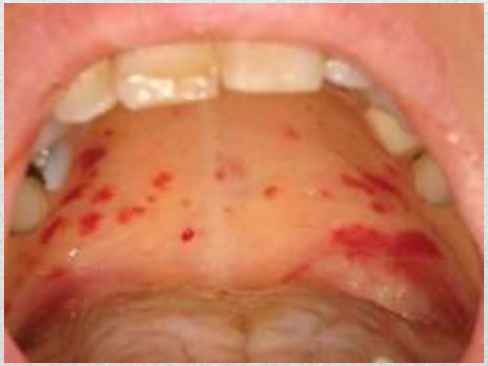
- A variety of diseases characterized by a qualitative defect in the blood platelets.
- Congenital and/or familial
- Acquired

Thrombocytopathic purpura

- A group of rare disease of unknown etiology.
- Patient manifests a bleeding tendency referable to **qualitative defects** in the blood platelets.
- Platelet count is usually normal.
- Defective platelet aggregation.

Clinical features

- Severe bleeding tendency and bruise easily after only minor trauma.
- Spontaneous ecchymoses
- Epistaxis
- Bleeding into GIT are frequent
- Menstrual bleeding is severe- may require blood transfusion



Oral manifestation

- Spontaneous gingival bleeding
- Mucosal ecchymosis
- Excessive and prolonged bleeding from extraction socket

Laboratory findings

- Platelet count- nearly normal
- Bleeding time- is either normal or prolonged
- Normal capillary plugging is impaired

Treatment

- Conventional hemostatic agents
- Blood transfusion

Thrombocythemia/ Thrombocytosis

- Condition characterized by an increase in the number of circulating blood platelets.
- 2 types:
- **Primary-** unknown etiology
- **Secondary-** occur after traumatic injury, inflammatory conditions, surgical procedures, parturition.

  - may be due to the overproduction of proinflammatory cytokines such as IL-1, IL-6, IL-11, that occurs in chronic inflammatory, infective, and malignant states.

Clinical features

- No gender or age predilection is seen
- Bleeding tendency in spite of the fact that their platelet count is elevated.
- Epistaxis
- Bleeding into- Genitourinary tract and CNS

Oral manifestations

- Spontaneous gingival bleeding
- Excessive and prolonged bleeding

Laboratory findings

- Platelet count is increased
- Clotting time, PT, clot retraction and tourniquet test- all are normal

Treatment

- Radioactive phosphorus
- Blood transfusion
- Corticosteroids
- Aspirin, heparin

Congenital coagulopathies

Hemophilia

- Blood disease characterized by prolonged coagulation time and hemorrhagic tendencies.
- Hereditary disease, defect being carried by x-chromosome,
- Transmitted as a gender-linked Mendelian recessive trait.
- Occurs only in males, transmitted through an unaffected daughter to a grandson.

Etiology

- Hemophilia A- Plasma Thromboplastinogen (AHG factor VIII)
- Hemophilia B- Plasma Thromboplastin component (PTC factor IX)
- Hemophilia C- Plasma Thromboplastin antecedent (PTA factor XI)

Hemophilia A

- A deficiency of F VIII, the antihemophilic factor, is inherited as an X-linked recessive trait that affects males. The trait is carried in the female without clinical evidence of the disease.

Clinical signs:

- hematomas, hemarthroses, hematuria,
- gastrointestinal bleeding, and
- bleeding from lacerations
- head trauma or spontaneous intracranial bleeding
- Joint synovitis, hemophilic arthropathies
- Intramuscular bleed and pseudotumors

Hemophilia B

- Due to PTC deficiency also known as Christmas disease.
- 2 forms- apparently normal levels of the inactive protein and another in which there is deficient level of the coagulant factor.

Hemophilia C

- Mild disorder seen in pedigrees of Jewish descent; it is transmitted as an autosomal dominant trait.
- Bleeding symptoms do occur but are usually mild.

Oral manifeststions

- Gingival Hemorrhage- massive and prolonged
- Pseudotumor

Laboratory findings

- Prolonged coagulation time
- Bleeding time- normal
- PTT is prolonged

Treatment

- Preoperative transfusion of whole blood
- Administration of antihemophilic factor
- Protected from traumatic injuries

von Willebrand's Disease

- vWD, a unique disorder that was described originally by Erik von Willebrand in 1926, can result from inherited defects in the concentration, structure, or function of von Willebrand's factor (vWF).
- It promotes its function in two ways:

❑(1) by supporting platelet adhesion to the injured vessel wall under conditions of high shear forces and

❑(2) by its carrier function for factor VIIIc in plasma.

- Transmitted as an autosomal dominant trait.

vWD is classified into four primary categories.

1. **Type 1 (85% of all vWD)** includes partial quantitative deficiency,
2. **Type 2 (10–15% of all vWD)** includes qualitative defects,
3. **Type 3 (rare)** includes virtually complete deficiency of vWF
4. **pseudo- or platelet-type vWD,** and it is a primary platelet disorder that mimics vWD.

Clinical features

- Usually mild and include mucosal bleeding,
- soft tissue hemorrhage, menorrhagia in women, and hemarthrosis.

Laboratory findings

- Clotting time- usually normal, may be slightly prolonged
- Bleeding time- shows variation
- Prothrombin time- normal
- Tourniquet test- positive

Treatment

- Transfusion of plasma
- Antihemophilic factor
- Local control of hemostasis

Anticoagulant-Related Coagulopathies

- **Heparin** - short duration of action of 3 to 4 hours
- acute anticoagulation.
- Binds with antithrombin III to significantly inhibit activation of Fs IX, X, and XI, thereby reducing thrombin generation and fibrin formation.
- **Indications** - prophylaxis or treatment for venous thromboembolism, including prophylaxis in medical and surgical patients
- **Dose-** intravenous infusion of 1,000 units unfractionated heparin per hour.

- **Coumarin anticoagulants-** which include warfarin and dicumarol
- **Indication** - prevent recurrent thromboembolic events, such as pulmonary embolism, venous thrombosis, stroke, and myocardial infarction.
- They slow thrombin production and clot formation by blocking the action of vitamin K.

- **Ethylenediaminetetraaetic (EDTA)-** strong anticoagulants. It prevents blood clotting by removing calcium from blood.

Disease-Related Coagulopathies

- **Liver disease-** Owing to impaired protein synthesis, important factors and inhibitors of the clotting and the fibrinolytic systems are markedly reduced. Additionally, abnormal vitamin K–dependent factor and fibrinogen molecules have been encountered.
- Thrombocytopenia and thrombocytopathy are common.

- **Vitamin k deficiency-** plays an important role in hemostasis. Vitamin K deficiency is associated with the production of poorly functioning vitamin K–dependent Fs II,VII, IX, and X.
- When vitamin K deficiency results in coagulopathy, supplemental vitamin K by injection restores the integrity of the clotting mechanism

- **Disseminated Intravascular Coagulation-** triggered by potent stimuli that activate both F XII and tissue factor to initially form microthrombi and emboli throughout the microvasculature.
- DIC can produce massive hemorrhage and be life threatening.

- **Fibrinolytic Disorders-** lead to hemorrhage when clot breakdown is enhanced or excessive clotting and thrombosis when clot breakdown mechanisms are retarded.
- Deficiency in plasminogen activator inhibitors, natural proteins that turn off activation of the fibrinolytic system.

Procoagulants

1. Thrombin
2. Snake venom
3. Extracts of lungs and thymus
4. Sodium or calcium alginate
5. Oxidized cellulose

PHYSICAL METHODS TO PREVENT BLOOD CLOTTING

- Cold
- Collecting blood in a container with smooth surface

Identification of the Dental Patient with a Bleeding Disorder

- Begins with a thorough review of the medical history.
- A family history of bleeding problems may help to identify inherited disorders of hemostasis.
- Past history of bleeding following surgical procedures, including dental extractions, can help identify a risk.
- Identification of medications with hemostatic effect-coumarin anticoagulants, heparin, aspirin.
- Active medical conditions, including hepatitis or cirrhosis, renal disease, hematologic malignancy, and thrombocytopenia, may predispose patients to bleeding problems.
- History and the review of systems suggest increased bleeding propensity, laboratory studies are warranted.

Conclusion

- A wide array of disorders of blood and hemostasis encountered in internal medicine has manifestations in the oral cavity and the facial region.
- It is important that all clinicians are aware of the physiopathology and oral manifestations of blood disorders .
- Dental surgeons should carefully obtain the patient's clinical history and information about particular features so that they can plan any dental treatment such that it is appropriate to the patient's limitations and needs.
- Proper diagnosis is essential to initiate the correct treatment.

References

- Guyton and Hall, textbook of medical physiology, 11th edition.
- K. sembulingam, Essentials of medical physiology, 3rd edition.
- Burket's oral medicine, 11th edition.
- Shafer's textbook of oral pathology, 6th edition.
- Oral and maxillofacial pathology, 3rd edition, Neville

THANK YOU!