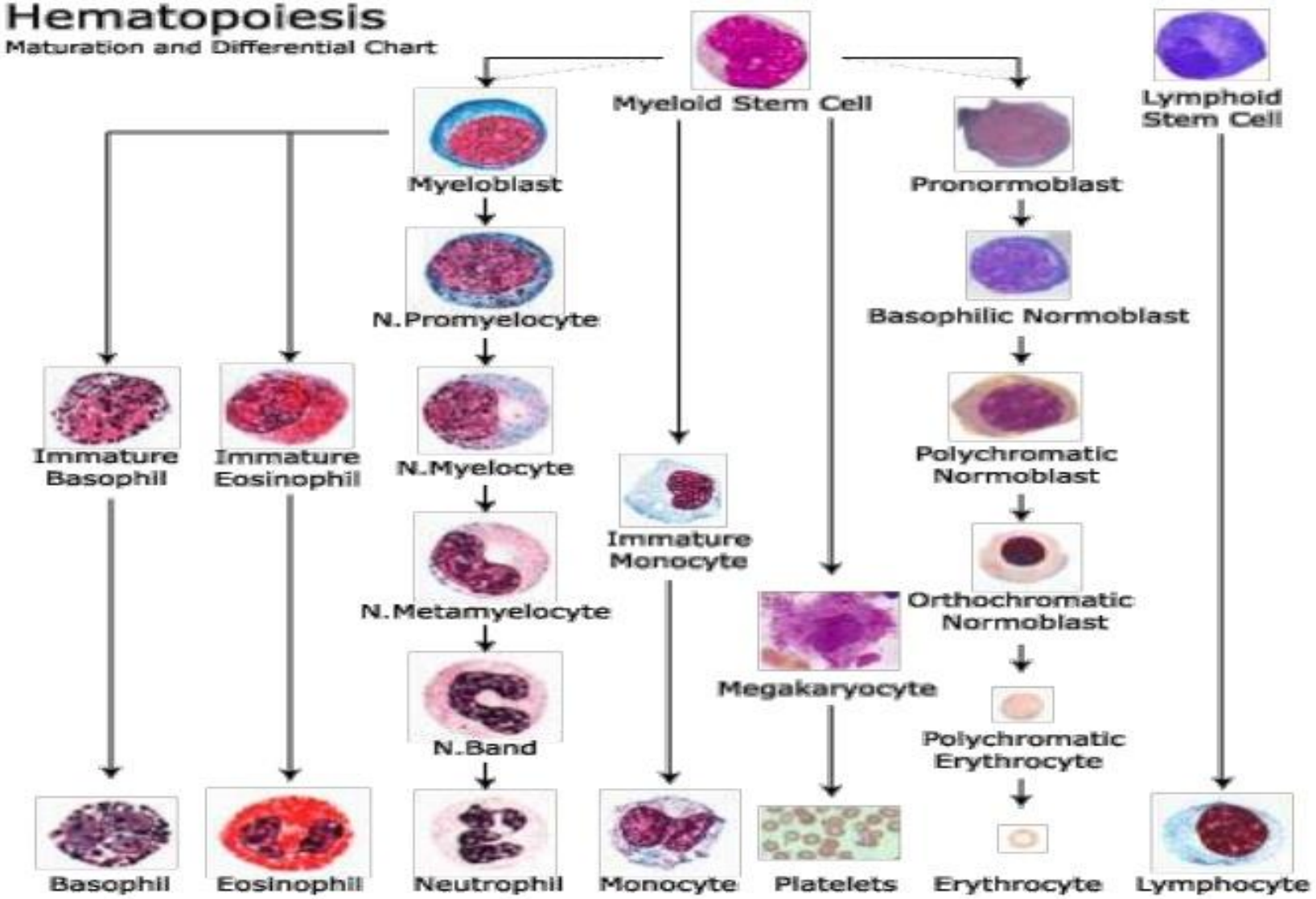
MJF COLLEGE OF VETERINARY AND ANIMAL SCIENCE, CHOMU, JAIPUR

DEPARTMENT OF VETERINARY PATHOLOGY

Haemopoeitic system

tree_hematopoiesis2



TERMINOLOGY

Erythrocyte

Normal erythrocyte

- Normocytic, normochromic erythrocyte is reddish coloured with central depression (biconcave disc) and palor not more than 1/3 of the surface area.
- Avian erythrocytes are nucleated

Hyperchromasia

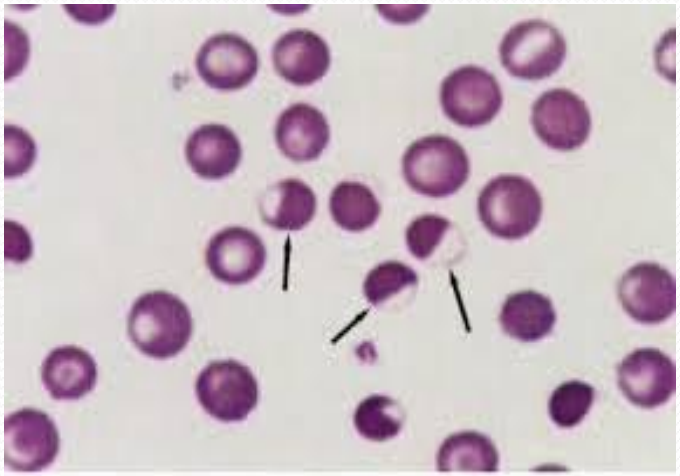
- This is **not due to increased hemoglobin** content but due to increased thickness of erythrocyte.

Hypochromasia

- This is decreased staining intensity of erythrocyte which may be either due to decreased thickness of erythrocyte or decreased hemoglobin content.
- This is seen in iron and copper deficiency.

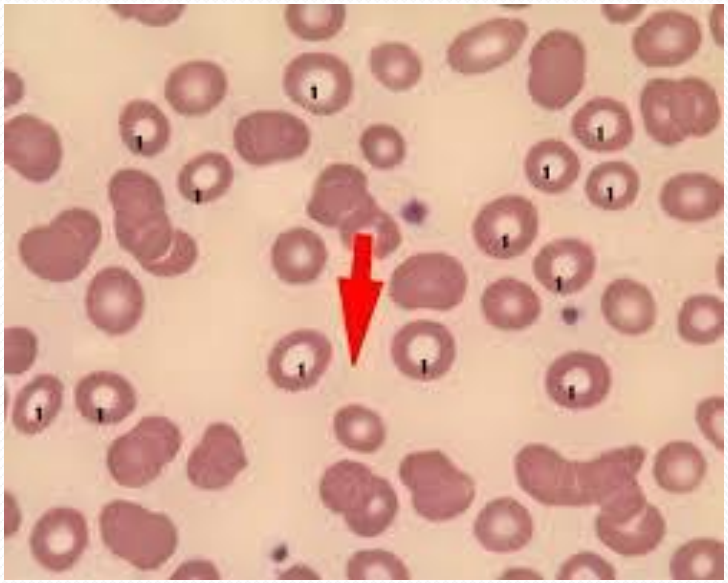
Eccentrocyte

- Here the erythrocyte has hemoglobin on one side.
- This is seen in hemolytic anemia.



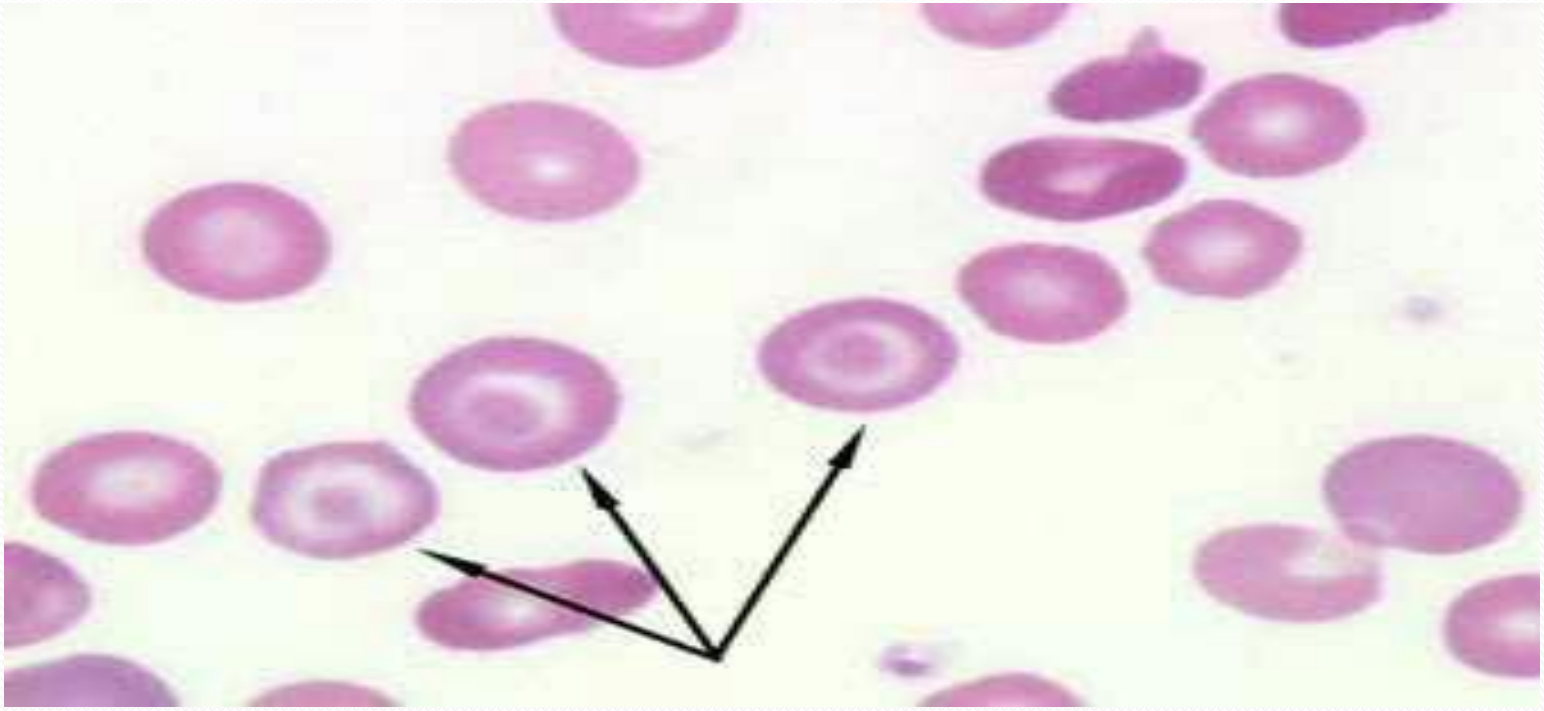
Annulocyte (Pessary cell)

- Here the erythrocytes have a narrow rim of hemoglobin surrounding a large central pale area



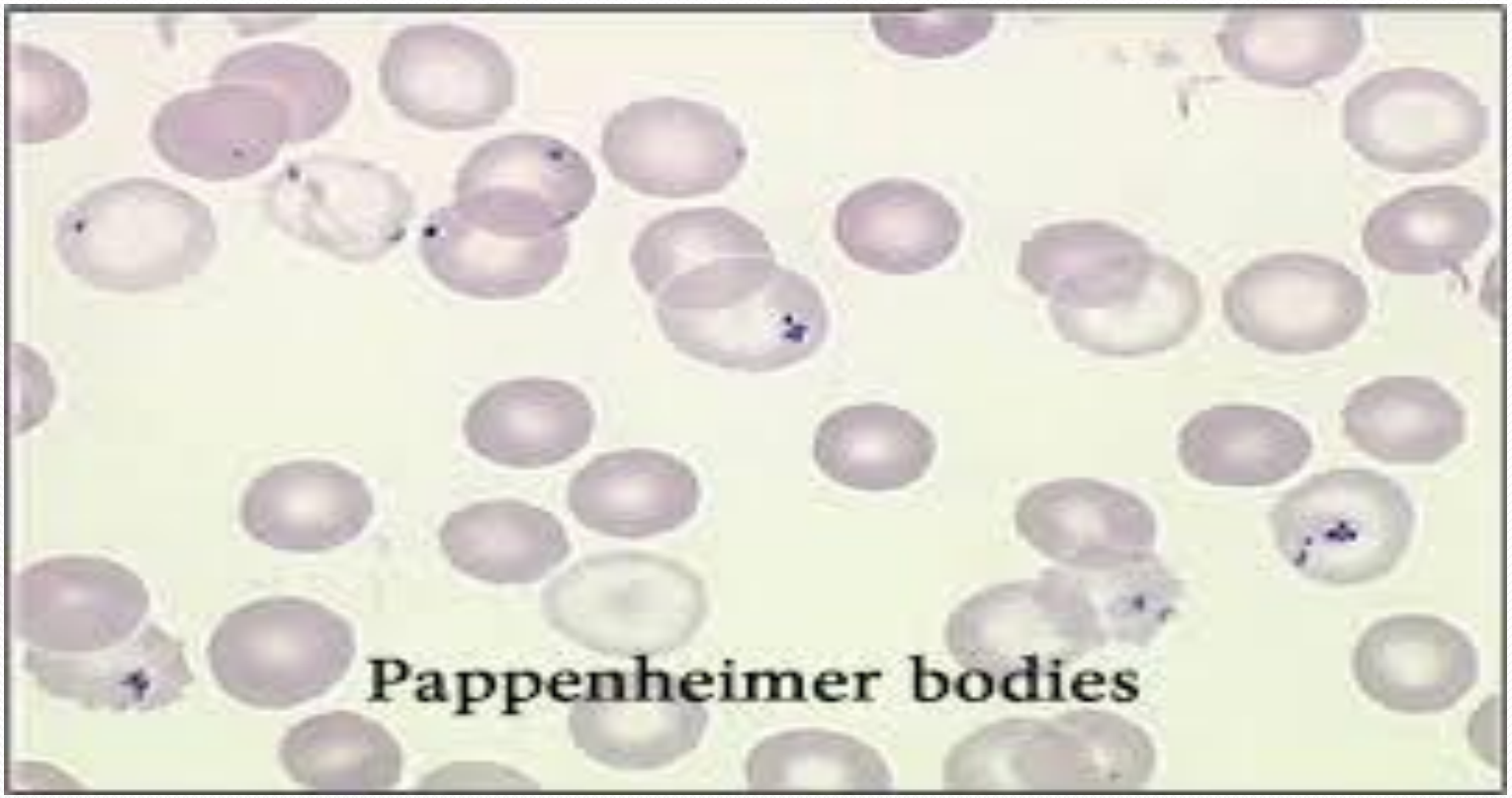
Target cell

- Here the erythrocyte has central pigmented material surrounded by a clear unpigmented area and the outside border has haemoglobin pigmentation (resembles a bull's eye).
- These are seen in chronic disease, liver diseases and lead poisoning



Pappenheimer bodies (Siderotic granules)

- These are purplish coccoid granules seen at the periphery of erythrocytes in anemias due to impaired heme synthesis (sideroachrestic anemias).
- The granules contain iron in ferritin.



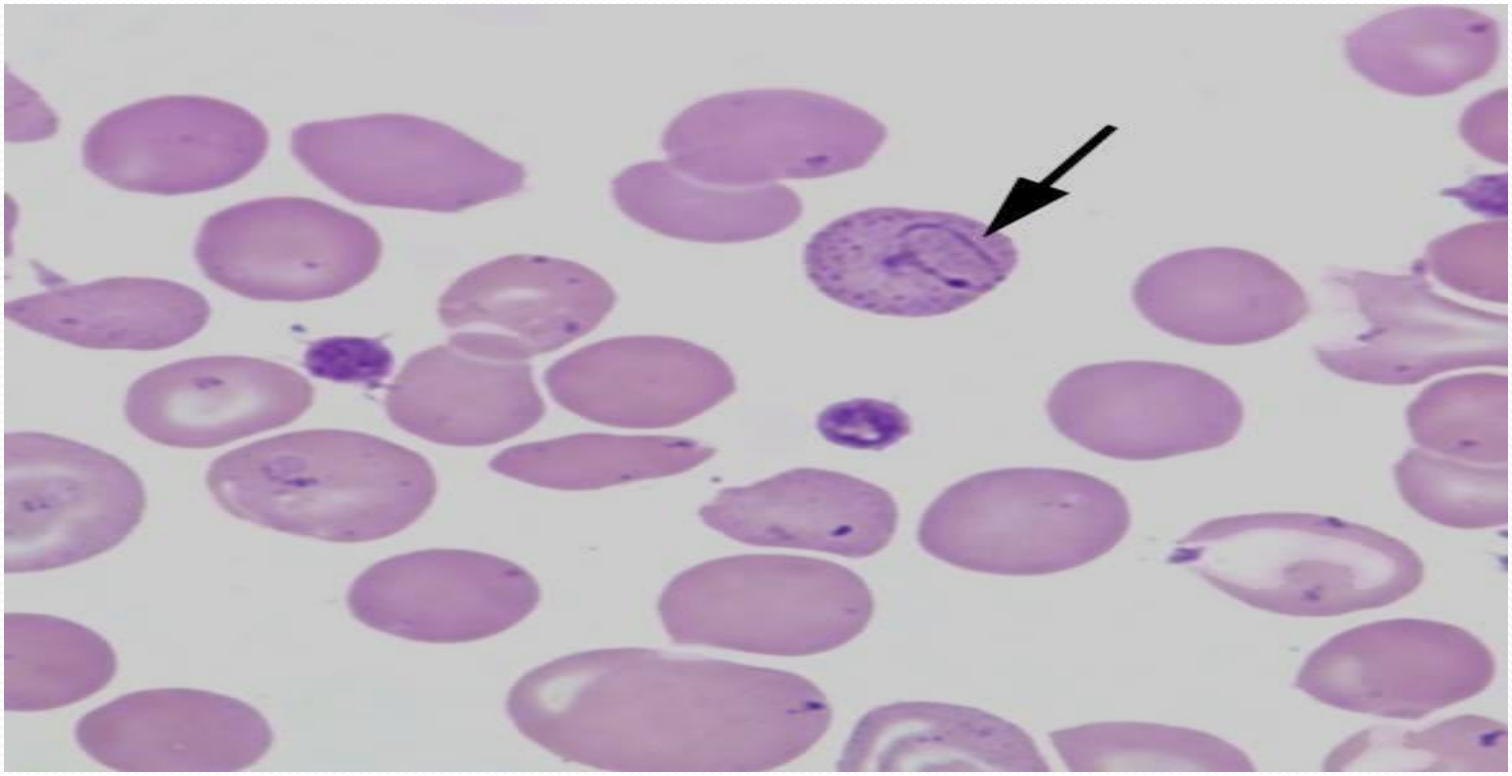
Polychromasia (Polychromatophilia)

- This denotes staining of erythrocytes with many colors i.e. red, blue and intermediate colours.

- This may be an immature cell or it may be seen in blood loss.

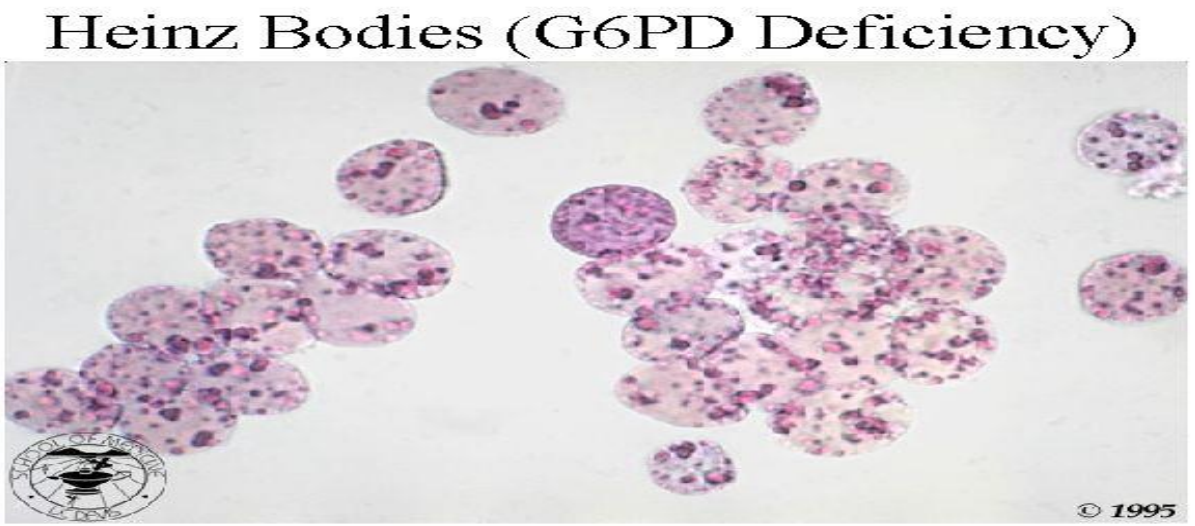
Cabot rings

- Cabot rings are bluish thread like rings seen in the erythrocytes.
- These are seen in hemolytic and toxic anemias and lead poisoning



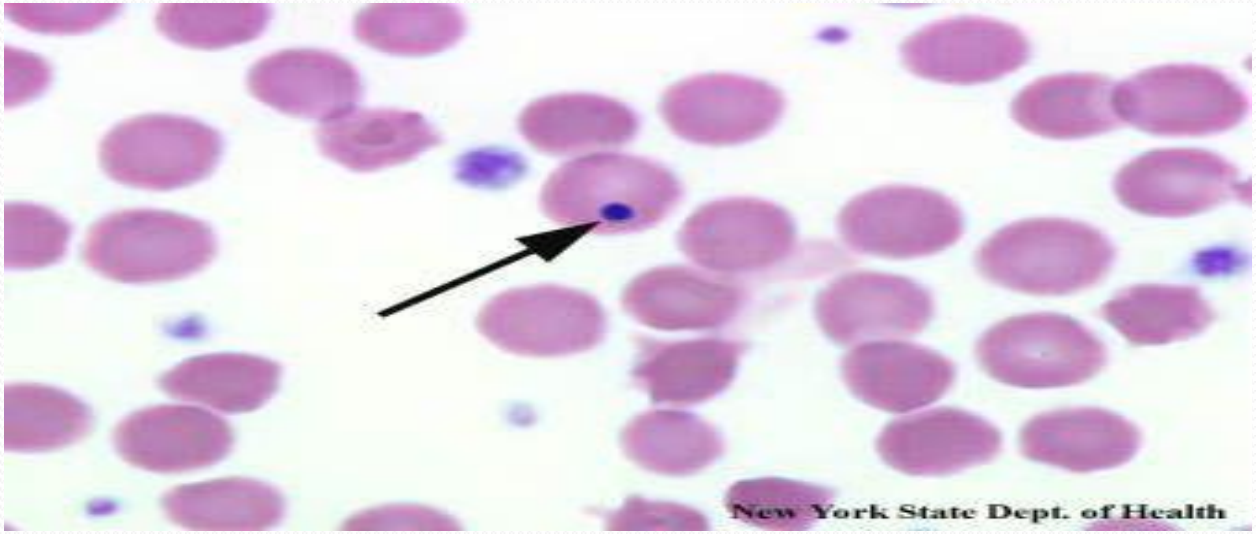
Heinz bodies

- These are refractile inclusions found in the erythrocytes.
- These are associated with denatured protein.
- These are seen hemolytic anaemia and in horses undergoing phenothiazine therapy.
- They are not visible when the blood smear is fixed in methanol.



Howell – Jolly bodies

- These are single or double spherical bluish bodies situated eccentrically usually.These are remnants of nuclear material.
- These are normally seen in young pigs and dogs. Horse blood also contains these bodies in one per cent of erythrocytes.
- In bovine these should be differentiated from *Anaplasma marginale*. The *Anaplasma marginale* is uniform in size while Howell – Jolly bodies vary in size.
- These are seen in hemolytic anaemia, splenectomy and lead poisoning.

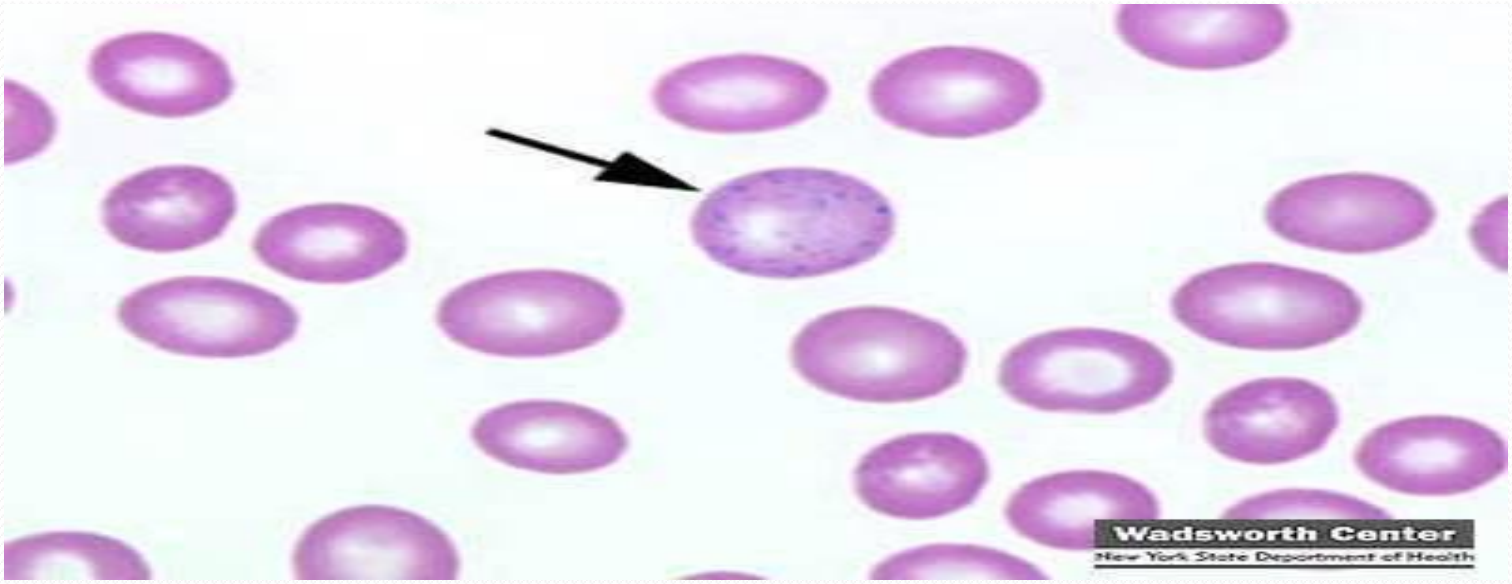


Basophilia

- Here the erythrocytes take a pale bluish or bluish stain instead of red stain.
- This is because of retention of ribonucleic acid which takes up bluish stain.
- This indicates incomplete maturation of erythrocytes, lack or deficiency of hemoglobin. This is seen in anemia.

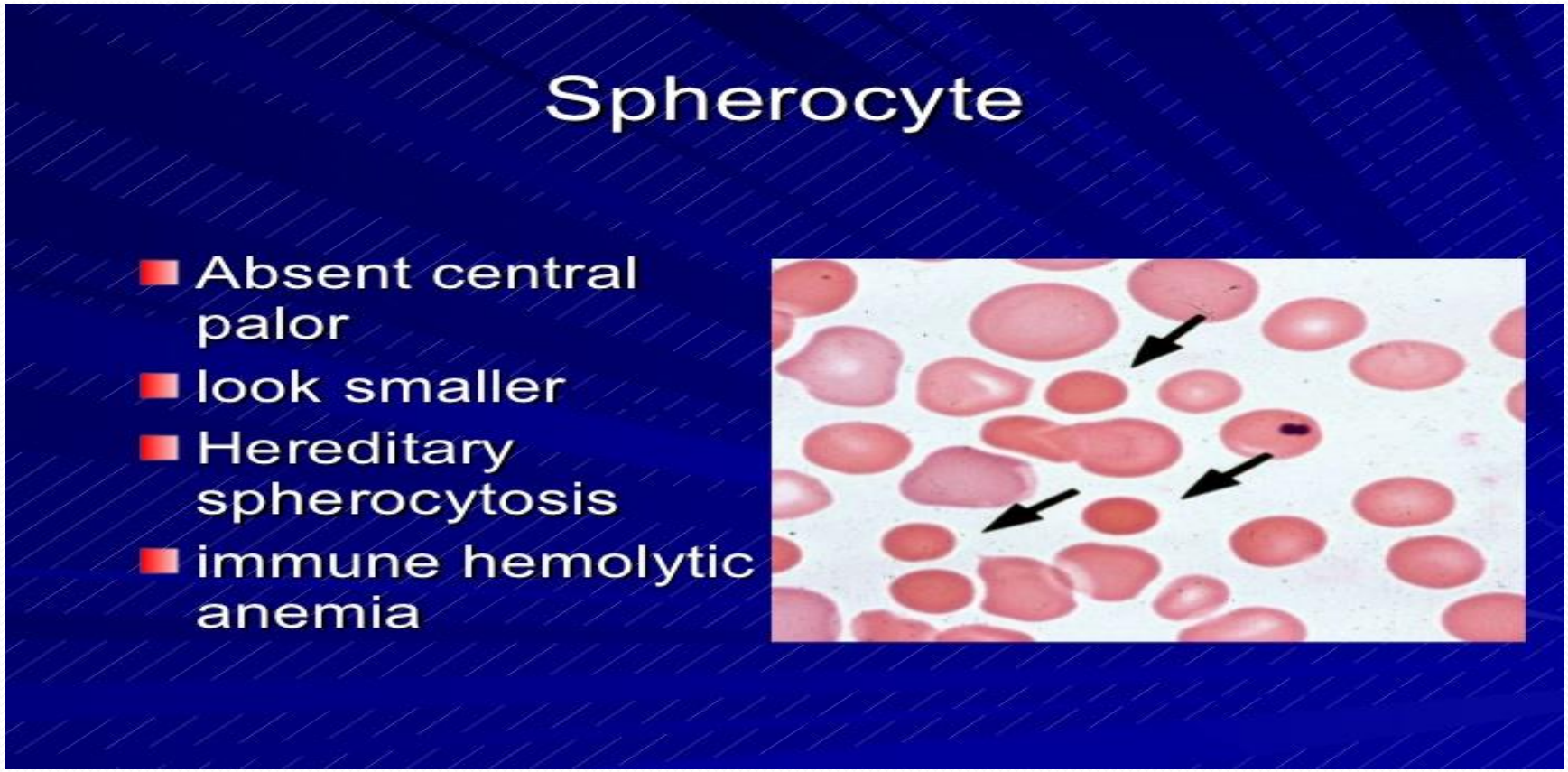
Basophilic stippling (Punctate basophilia)

- Here the erythrocyte has blue staining granules scattered through out.
- These are remnants of RNA. This condition is seen in anaplasmosis in bovines, haemonchosis in sheep and in lead poisoning.

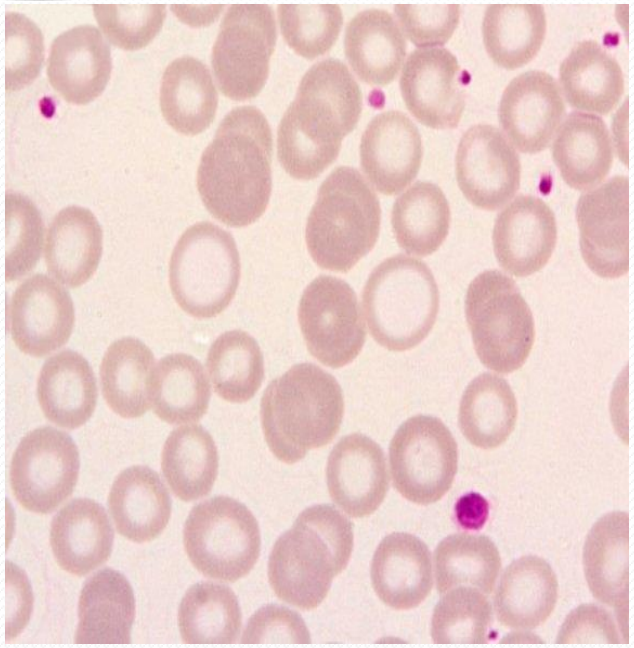


Spherocyte

- These are dome shaped, thick erythrocytes.
- These are seen in immune mediated hemolysis and blood loss.
- These are not seen in animals.



Leptocyte



- Leptocytes are thin erythrocytes with larger surface without increase in volume.
- These are seen in chronic diseases and liver diseases.

Megaloblast

- This is an immature erythrocyte comparable to prorubricyte.
- This is seen in Vitamin B_{12} or folic acid deficiency.

Macrocyte

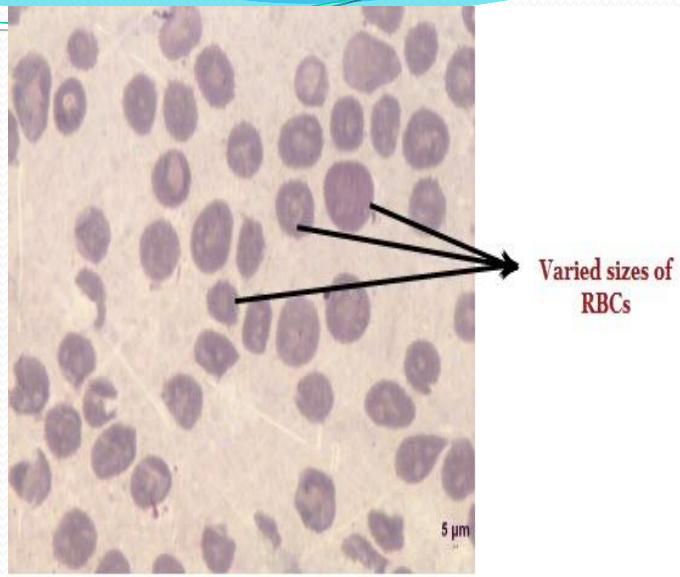
- The erythrocyte has larger diameter than the normal erythrocyte.
- Hence the mean corpuscular volume is higher.
- This is an immature cell and is seen in blood loss.

Microcyte

- Here the erythrocyte has smaller diameter than the normal.
- This is seen in iron deficiency.

Anisocytosis

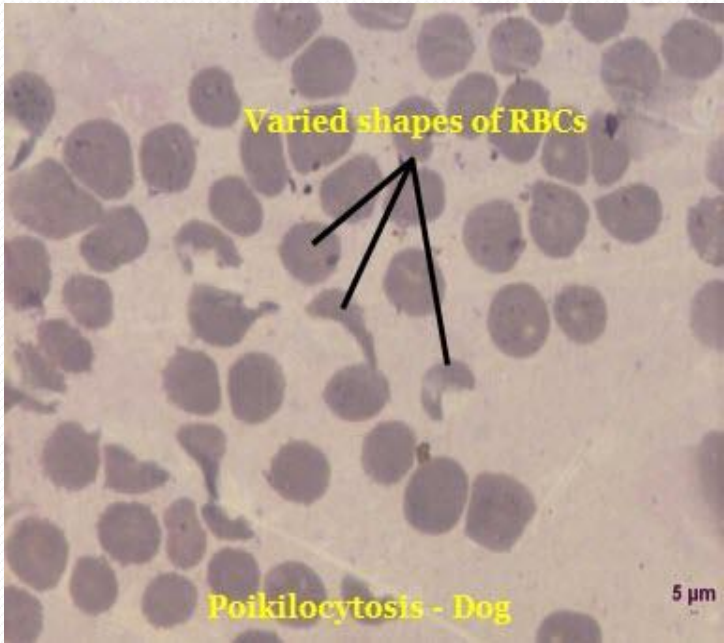
- Anisocytosis means variation in the size of erythrocytes.
- In cattle blood slight anisocytosis is common



Anisocytosis

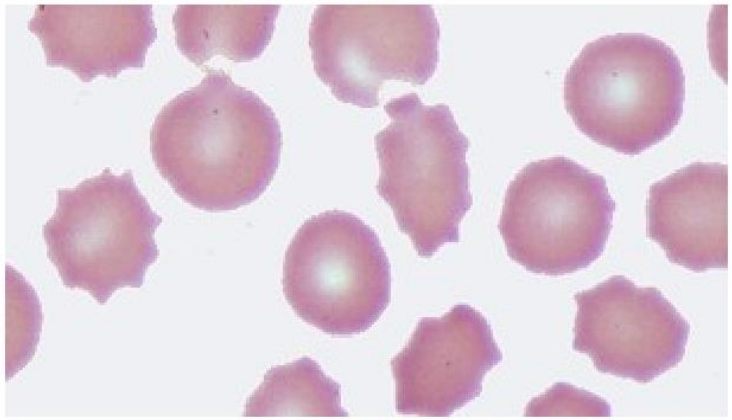
Poikilocyte

- Here the erythrocytes have varied shapes



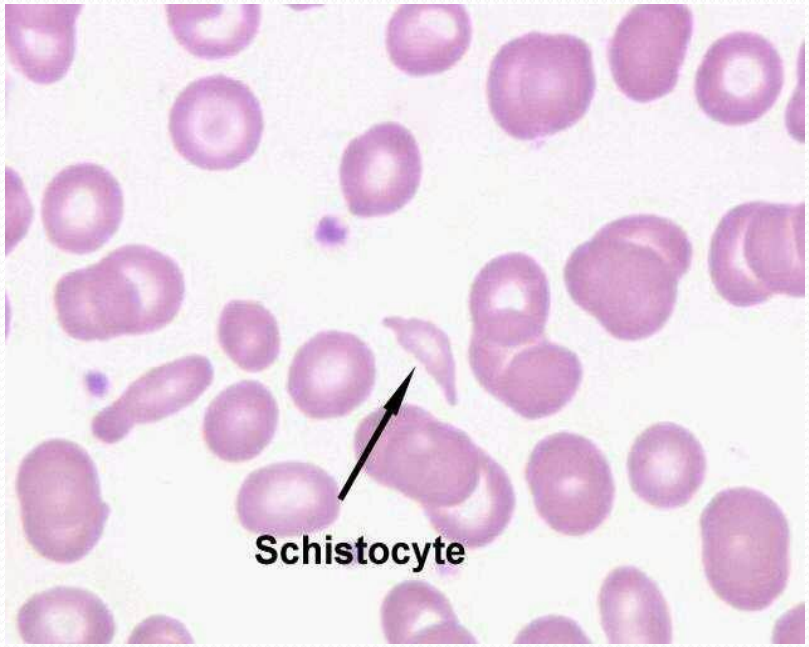
Crenation

- Here the erythrocytes have abnormal notching.
- This is seen in splenic disease and haemangiosarcoma.



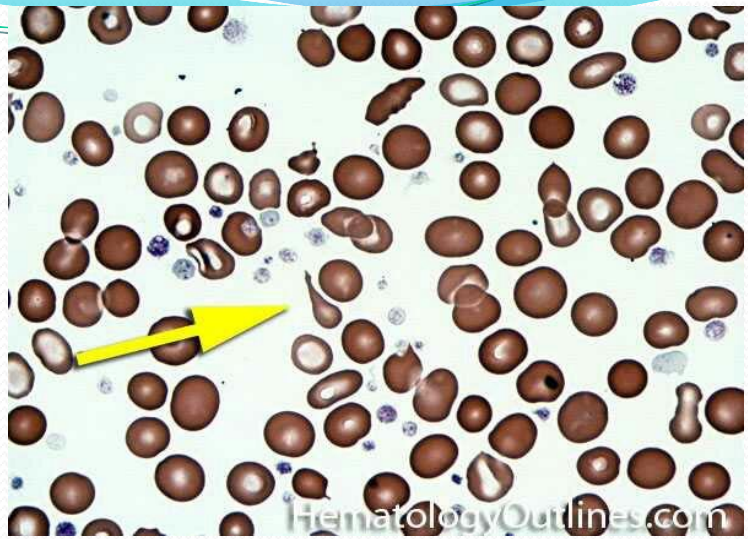
Schizocyte

- This is a small irregular erythrocyte fragment that may have two or three pointed extremities.
- This is seen in intravascular coagulation and vasculitis.



Dacrocyte

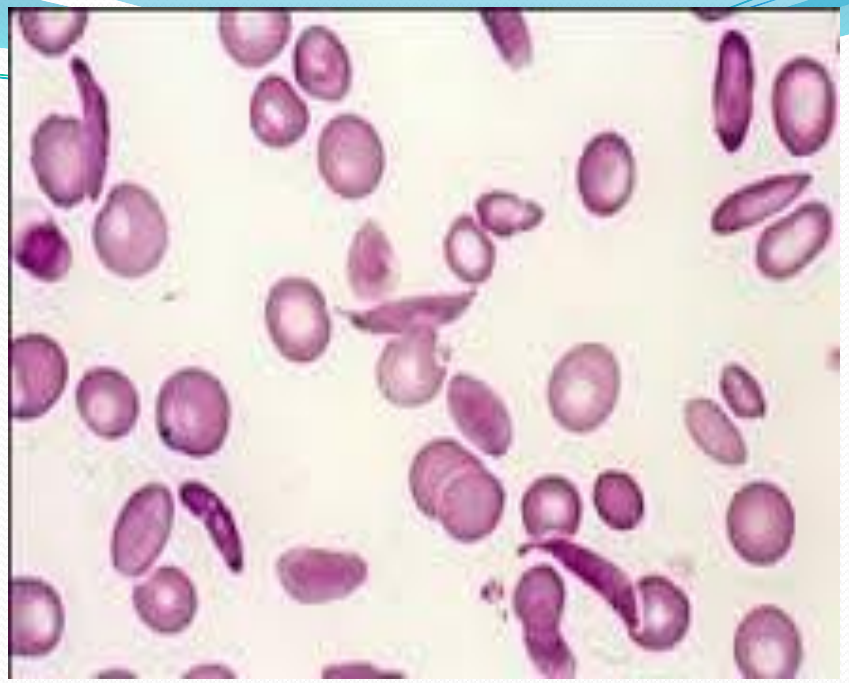
- This is a tear drop shaped erythrocyte.
- This is seen in myelofibrosis



Keratocyte

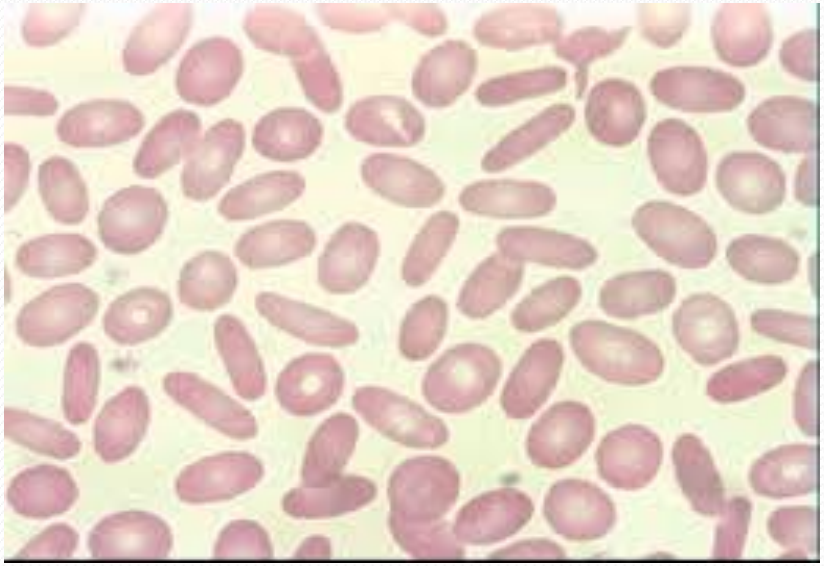
- Here the erythrocyte has half-moon shape with spicules.
- This is seen in intravascular coagulation

Meniscocyte (Drepanocyte)



- These are crescent shaped erythrocyte.
- This is seen in sickle cell anemia

Ovulocyte



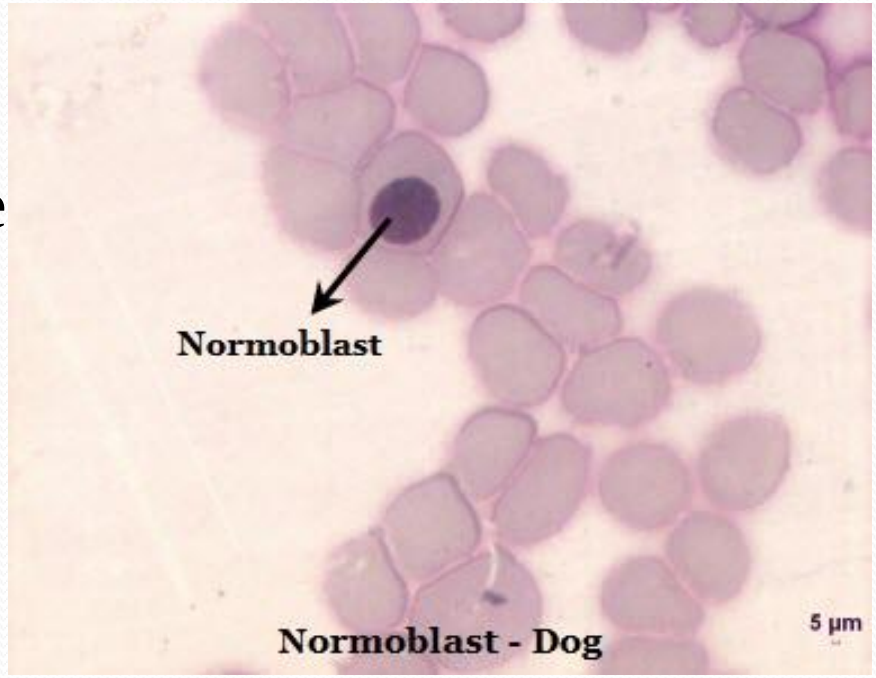
- These are elliptical erythrocytes.
- These may be seen in advanced anemia with poikilocytosis

Reticulocyte

- Reticulocyte is a precursor of erythrocyte and can not divide but can undergo maturation.

Normoblast

- Normoblast will have the remnant of nuclear material



RED BLOOD CELL MORPHOLOGY

Size variation

- Normal
- Microcyte
- Macrocyte
- Oval macrocyte
- Hypochromic macrocyte

Hemoglobin distribution

- Hypochromia
  - 1+
  - 2+
  - 3+
  - 4+
- Polychromasia (Reticulocyte)

Shape variation

- Target cell
- Acanthocyte
- Spherocyte
- Helmet cell (fragmented cell)
- Ovalocyte
- Schistocyte (fragmented cell)
- Stomatocyte
- Tear drop
- Sickle cell
- Burr cell

Inclusions

- Pappenheimer bodies (siderotic granules)
- Cabot's ring
- Basophilic stippling (coarse)
- Howell-Jolly

Red cell distribution

- Agglutination
- Rouleaux

Crystal formation

- HbSC
- HbC

POLYCYTHEMIA

Definition

- Polycythemia means increase in the circulating erythrocyte.
- Blood picture: Normocytic, normochromic

Types

- ***Relative polycythemia***
  - This is seen when there is reduction in the circulating blood volume.
  - Hence there is increased concentration of normal number (hemoconcentration).
  - This is seen in excessive fluids loss as in dehydration due to continued vomiting, diarrhea, sweating, shock and collapse.

Absolute polycythemia

Blood volume is normal but the erythrocyte number is more.

- This condition may be primary, secondary or due to pathological causes.
- Primary – **Polycythemia Vera** – a tumor of bone marrow may cause polycythemia.
- *Secondary* – Physiological: Seen permanently in high altitude
- Temporary: Seen in splenic contraction.

  e.g. Sporting dogs, racing horses
- Neonates have more number of erythrocytes
- Pathological – Prolonged anoxia e.g. Cardiac and pulmonary disease, Tetralogy of Fallot

OLIGOCYTHEMIA

Definition

- This is decrease in the quantity of erythrocytes in the peripheral blood.

Types

- ***Relative oligocythemia***
  - Here is increase in the blood volume (hemodilution) with normal number of erythrocyte.
- ***Absolute oligocythemia***
  - This is otherwise called as anemia.

ANAEMIA

Definition

- Anaemia means decrease in the quantity or quality of erythrocytes below normal.

Clinical signs

- Visible mucous membrane will be pale

Types

- Production is low but destruction is normal: **Dyshaemopoietic anemia**
- Production is normal but destruction is high: This is seen in **haemolytic and haemorrhagic anemia**.

Conjuctiva pale - Anemia - Goat

DYSHAEMOPOIETIC ANEMIA

Definition

There is defect in the formation of haemoglobin.

- The defect may be either in the formation of protein or hemoglobin.
- Decreased heme synthesis

Porphyrinopathy

- Porphyrins are needed for the synthesis of heme.
- If certain enzymes are lacking, then heme is not synthesized .
- So excessive amounts of porphyrins are found in the body (Porphyria)and in urine (Porpyrinuria).
- Congenital porphyriea occurs in bovines and pigs.
- Porphyrins are photosensitive.

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- The following changes are seen
- Skin undergoes photosensitization (Photosensitive dermatitis)
- Teeth looks pink (Pink tooth)
- In bone, ostoheamochromatosis occurs.
- In kidneys, porphyrins are deposited in the tubular epithelium and interstitium. Urine also contains porphyrins (porphyrinuria). The urine turns red on exposure to light

Decreased protein formation

- Blood picture is macrocytic and normochromic or hypochromic.
- Bone marrow shows numerous megaloblasts and giant metamyelocytes

Dietetic deficiency of extrinsic factor

- Cobalt is needed for the synthesis of Vitamin B_{12} by the microbes in the rumen. Vitamin B_{12} and folic acid deficiency causes arrest of maturation of prorubricyte and metamyelocytes. As Vitamin B_{12} is needed for the synthesis of DNA and RNA, its deficiency leads to delayed maturation of nucleus whereas hemoglobin synthesis continues. When hemoglobin synthesis reaches a certain concentration in the erythrocytes, the nucleus leaves them and so macrocytes result giving rise to macrocytic anemia.
- Dietetic deficiency of folic acid: As folic acid is essential for the maturation of erythrocytes, in its absence maturation is slowed and so macrocytic anemia occurs.

- ***Deficiency of the intrinsic factor***
  - Gastric mucosa secretes an enzyme which helps in the absorption of Vitamin $B_{12.}$
  - In its absence (gastritis), Vitamin B_{12} may not be absorbed and so results in macrocytic anemia.
- ***Failure to store the erythrocyte maturation factor***
  - The erythrocyte maturation factor i.e. Vitamin B_{12} is normally stored in the liver.
- In diseases of liver, this vitamin is not stored hence there is deficiency of Vitamin B_{12} which in turn causes macrocytic anemia.

- ***Failure to use the erythrocyte maturation factor***
  - Failure of mobilization of erythrocyte maturation factor

    i.e. Vitamin B_{12} or its utilization leads to macrocytic anemia.
  - This is called **achrestic anemia** (Achrestic means failure to utilize).
- ***Hypopituitarism***
  - Anterior pituitary seems to exert a potent influence in erythropoiesis directly or through the thyroid which influences metabolism of carbohydrates, releasing energy.

Decreased hemoglobin formation

- Blood picture is initially normocytic and hypochromic, but later becomes microcytic hypochromic.

- ***Iron deficiency***
  - Iron deficiency may occur in the following conditions
    - Deficient intake: Milk of sows is deficient in iron. If piglets are not allowed for access to iron in soil, they suffer from iron deficiency.
    - Defective absorption: Excessive phosphorus and phytic acid forms insoluble complexes with iron which are excreted through the feces.
    - Increased requirement: Young growing animals and pregnant animals require more iron

Copper deficiency

- Copper acts as a catalyst in the utilization of iron in hemoglobin synthesis, hence its deficiency leads to iron deficiency.
- Some cells undergo additional mitosis and so microcytic erythrocytes occur.

Dietetic deficiency of ascorbic acid

- Vitamin C is dietary reducing agent and so facilitates the reduction of Fe+++ to Fe++ which is easily absorbed.
- It is also needed for the synthesis of folic acid and its further conversion to more active folinic acid.

Dietetic deficiency of pyridoxine

- Pyridoxine is required for the utilization of iron in hemoglobin synthesis.
- So its deficiency leads to iron deficiency.

Dietetic deficiency of nicotinic acid

- Nicotinic acid interferes with respiration of immature red cells.

Dietetic deficiency of riboflavin

- Riboflavin is needed for the metabolism and arrangement of amino acids of hemoglobin.

Deficiency of thyroxine

- Thyroxine along with vitamin C is required for the conversion of folic acid to folinic acid.
- In myxedema, the secretion of intrinsic factor is depressed as well as absorption of Vitamin B_{12}.
- So a normocytic or macrocytic anemia may be encountered.

Toxic inhibition

- Bone marrow is normal and active but is unable to utilize haematinics.
- The blood picture is microcytic normochromic and no regenerative forms are seen.

Etiology

Physical - Irradiation can damage the hemopoietic system.

Chemical - Nitrogen mustard, hair dyes

Metals - Arsenic, bismuth and gold

- Bacteria - In chronic infections like tuberculosis and brucellosis normocytic normochromic anemia is seen. In these conditions there is hypoferremia. In these chronic diseases there is **greater utilization of iron by the tissue hence the iron is sided tracked instead of to the bone marrow, so hemoglobin is not formed and anemia results**.
- Parasite - *Esophagastomiasis* causes decreased absorption from the intestine
- Pathological - Chronic interstitial nephritis leads to decreased erythropoietin production
- Poisons – Insecticides

  Drugs - Sulpha, streptomycin and chloromycetins

Aplastic anaemia

- Here the bone marrow is aplastic and inactive.
- The blood picture is normocytic normochromic.
- No regenerative forms are seen.

- ***Etiology*** *-Types*
  - **Primary**
    - Idiopathic and is rare
  - **Secondary**
    - Exhaustion caused by chronic haemorrhage due to gastric and intestinal ulcer, blood sucking worms, neoplasm and deficiency of vitamin K, vitamin C and prothrombin.
    - Toxic agents which cause toxic inhibition also cause aplastic anemia.
    - Metabolic: A type anemia occurs in piglets born of sows which suffered from protein malnutrition during pregnancy.

Myelophthisic anaemia

- Myelophthesic anemia means anaemia resulting from replacement of bone marrow by other tissues.

- *Blood picture*
  - Erythroblasts and immature granulocytes are seen. Hence, it is also called leuco-erythroblastic anaemia .
- *Etiology*
  - Myelophthesic anemia may occur in the following conditions
    - Replacement of myeloid tissue by connective tissue which occurs in osteodystrophy
    - Primary tumour like Hodgkin's disease
    - Metastatic tumour - lymphatic leukemia in dog and cat
- *Sequelae of dyshemopoietic anemia*
  - After restitution of hematinics, reticulocyte number increase

  (Reticulocyte shower).
  - This is called as regenerative anemia .

HEMOLYTIC ANAEMIA

Definition

- In hemolytic anemia, there is intravascular destruction of RBCs.

Blood picture

- Blood picture is macrocytic normochromic which becomes microcytic and hypochromic as iron stored is used up.
- Many regenerative forms and spherocytes are also seen.

Etiology

Hemolytic anemia may occur in the following conditions

- Poisoning - Copper poisoning
- As copper is poorly excreted if excessive quantities are ingested, the excess copper is stored in the liver and poisoning may result.
- Excessive dose of copper given for deworming
- Ingestion of large quantities of salt lick containing copper sulphate
- Eating forage contaminated with copper from mines or having too much concentration of copper from soil
- Too much of supplemental mineral mixture containing copper sulphate
- In stress conditions more amount of copper is released and may cause hemolysis.
- Lead poisoning

- Poisons – Onion poisoning (n- propyl disulphide); Castor seeds (ricin) toxicity
- Naphthalein balls accidentally ingested by pets
- Drugs – Phenothiazine poisoning- In horses with usual dosage, phenothiazine may be toxic. Cattle may also be susceptible.
- Snake venom which contains lecthinase acts on lecithin and converts it into lyolecithin which is highly hemolytic

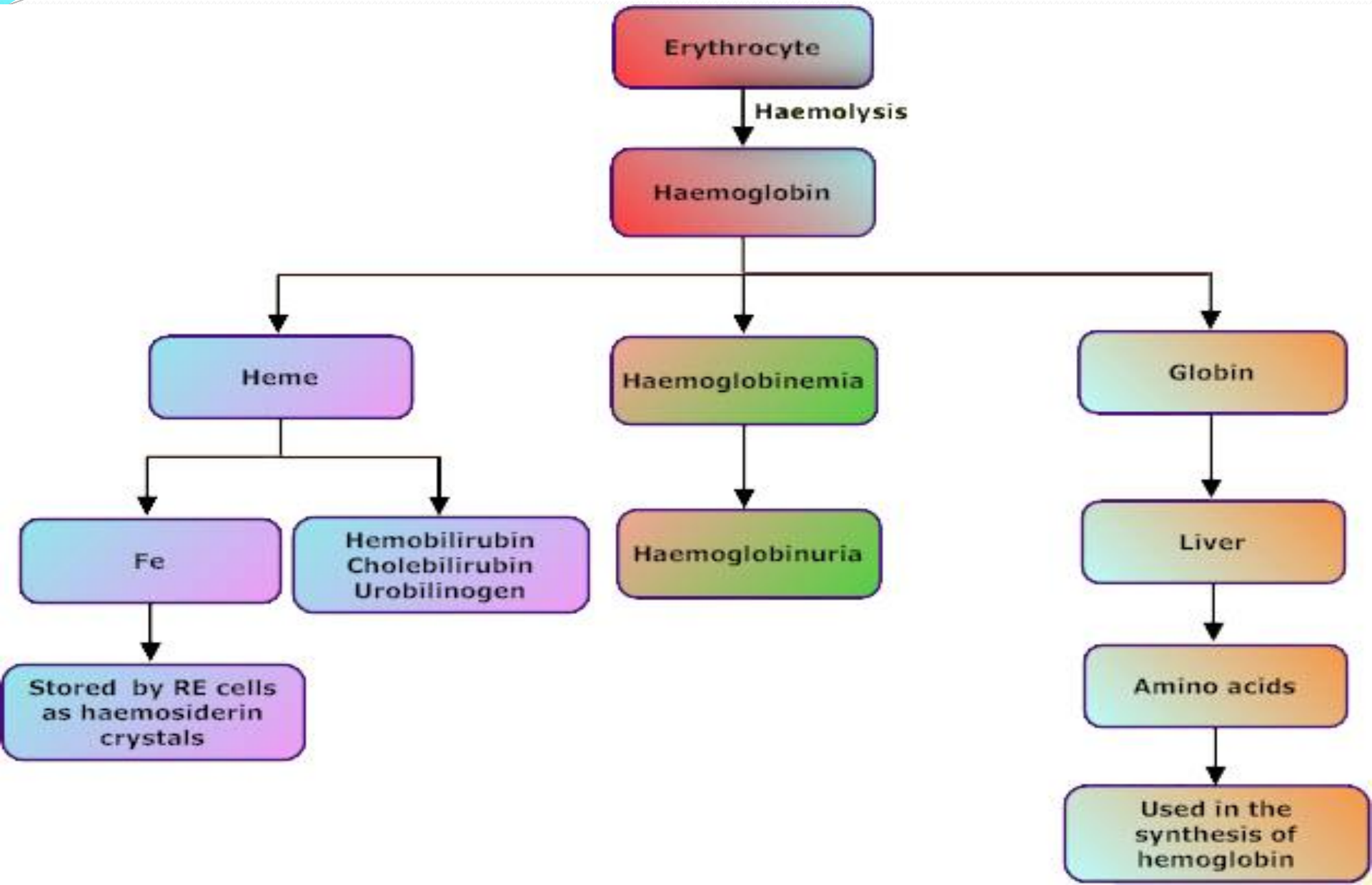
- Hypersensitivity
- Hypersensitivity to certain drugs like sulphanilamide, quinine, paraaminosalicylic acid and some antipyretic drugs may cause hemolytic anemia.
- Nutritional
- Hypophosphatemia in cows leads to postparturient haemoglobinuria and postparturient hemoglobinemia.
- Cold water – Ingestion of excessive quantities of cold water in calves leads to intravenous hemolysis and haemoglobinuria
- Infections
- Bacteria – *Leptospira, Staphylococci, Streptococci* and *Clostridium*
- Virus – Equine infectious anemia and feline infectious anemia
- Protozoa – *Anaplasma, Babesia, Ehrlichia canis,* eperythrozoonosis and haemobartonellosis

- Pathological
- Hypersplenism in dogs leads to severe anaemia of macrocytic or normocytic type.
- Abnormal auto-antibodies to
- malignancy – Lymphatic neoplasms, ovarian tumours and gastrointestinal carcinomas.
- Collagen disease – Disseminated lupus erythematosis
- Idiopathic cause
- Abnormal iso-antibodies

  Haemolysins in plasma may be produced by incompatible blood transfusion, blood products and in icterus neonatorum.
- In icterus neonatorum, the blood group antigen of the foetus pass into the dam's blood and so isoantibodies are produced.
  - Eg . Icterus neonatorum
  - Incompatible blood transfusion
  - Blood products

Pathogenesis

- Here break down of hemoglobin occurs at a faster rate.



Clinical signs

- Anemia
- Icterus
- Hemoglobinuria
- Dyspnoea
- In postparturient hemogobinuria, signs of phosphorus deficiency are seen viz. pica shifting lameness, decreased productivity and lordosis
- In cold hemoglobinuria in calves, there is cardiac insufficiency.

Clinical pathology

- Erythrocytes show increased hypotonic fragility

Gross pathology

- Carcass smells of onion in case of onion toxicity
- Mucosa – Icteric
- Spleen – swollen and darker
- Liver – yellowish and friable; shrunken in later stages.
- Kidneys – Dark brown
- Ur . Bladder – distended with blood coloured urine
- Bone marrow is active

In postparturient hemoglobinuria

- Liver – pale and slightly enlarged
- Kidney is black coloured due to deposition of hemoglobin
- Body cavities – contain excessive fluid
- Lung shows edema
- Hypersplenism in dogs
- Spleen is enlarged
- In cold hemoglobinuria in calves, there is pulmonary edema.

Histopathology -

- In postparturient hemoglobinuria

  Liver – Centrilobular necrosis

HAEMORRHAGIC ANEMIA

- In haemorrhagic anemia, there is extravascular destruction of RBCs and blood loss is greater than production.
- Anaemia depends on
  - Amount of blood lost
  - Rate at which blood is lost
  - Diet controlling the balance between blood loss and production

- If there is balance between blood loss and production, the blood picture is normocytic-normochromic anemia with many regenerative forms.
- If the balance of blood loss and production is maintained with difficulty, then the bone marrow works faster and macrocytes appears.
- Later if there is depletion of iron stores, microcytic-hypochromic anaemia results with numerous regenerative forms.
- Ultimately if the bone marrow is exhausted aplastic anemia with normocytic - normochromic anemic picture is observed but with out any regenerative forms.

- Types
- Acute haemorrhagic anaemia
- Chronic haemorrhagic anaemia
- Purpura and haemorrhagic disease

- Acute haemorrhagic anaemia
- Acute haemorrhagic anaemia may be due to
  - Injury
  - Stomach ulcers in pigs; Abomasal ulcers in cows
  - Ancylostomiasis and haemonchosis
  - Coccidiosis in poultry
  - Bovine enzootic hematuria
  - Poisoning by warfarin, sweet clover and bracken fern:
- In bracken fern poisoning, there is acute thrombocytopenia which is the direct cause of hemorrhage.
- Bracken fern is also a cumulative poison and cause granulocytopenia which leads to bacteremia and bacterial embolism

Gross pathology

- Gastrointestinal tract shows submucosal haemorrhages which may lead to ulcers
- Myocardium, liver and kidney show haemorrhages.
- In cumulative poisoning, there are haemorrhages and infarcts in the heart and kidneys.
- **Chronic haemorrhagic anaemia**
- Chronic haemorrhagic anemia may be due to
  - Ectoparasite - ticks, lice, fleas
  - Protozoa - coccidiosis in dogs
  - Nematode - *Haemonchus, Fasciola, Bunostomum* in cattle and sheep; Strongyles in horses; *Ancylstomum* in dogs.
  - Haemorrhagic disease - Chronic bovine hematuria
  - Gastrointestinal ulcers and vascular tumours

Purpura and haemorrhagic diseases

- Purpura is accumulation of blood under the skin due to spontaneous rupture of the capillaries.
- Haemorrhages result even due to mild damage.
- It is a syndrome and not a disease. The causes are
  - Vascular disorders
  - Impaired clotting mechanism
  - Other coagulation defects
  - Unknown cause

VASCULAR DISORDERS

- **Purpuric infection (Symptomatic purpura)**
  - This is seen in various diseases characterized by petechiae viz. anthrax, haemorrhagic septicaemia.
  - Here the cause is injury to the endothelium of blood vessels by bacterial toxins.
  - In viremic diseases like infectious canine hepatitis and hog cholera, the viruses directly damage the endothelium by their multiplication in the endothelial cells.
- **Allergic purpura or purpura haemorrhagica**
  - This is a symptom of post-infectious toxaemia as in strangles, fistulous withers, poll evil and empyema of guttural pouches.
  - Here the defect is due to development of allergy resulting in increased capillary permeability.

Gross pathology

- Mucous membranes shows haemorrhages
- Subcutis, peritoneal cavity and muscles show edema

Congenital purpura

- Congenital purpura may develop in the foetus.
- Here iso-agglutinins formed against the platelets of the mother pass via placenta and produce thrombocytopenia in the foetus.

Senile purpura

- This is seen in old men.
- The skin is very much atrophied.
- There is no subcutaneous fat.
- Vessels of skin are easily injured and haemorrhage occurs.
- Vitamin C deficiency
- In vitamin C deficiency of human beings, there is increased capillary permeability

- Vitamin C deficiency
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- and fragility since cement substance of the capillary wall is not synthesized