HAEMOLYTIC ANAEMIAS

There are four general features of haemolytic anaemias.
These include.

(a) Evidence of increased destruction of red cells (haemoglobin) such as haemoglobinuria, haemoglobinuria, haemoglobinaemia (both of which occur only with intravascular haemolysis), hyperbilirubinaemia (unconjugated bilirubin, haemosiderosis. Usually the capacity of the liver to conjugates bilirubin is increased in haemolytic anaemias so that where haemolysis is not severe the plasma bilirubin may remain normal despite haemolysis.

(b) Compensatory increase in red cell production (also seen with haemorrhagic anaemia) such as elevated reticulocytes counts, increased PITR and EITR, polychrosia.

(c) Evidence of red cell damage such as fragmentation (= schistocytes, microspharocytes). and spherocytosis.

(d) Shortened survival of circulation blood cells (also seen in haemorrhagic anaemia).

Haemolytic anaemias are distinguished from haemorrhagic anaemias as follows:

	Haemolytic Anaemias	**Haemorrhagic Anaemias**
(i) Plasma bilirubin	Increased or normal	Normal
(ii) Haemosiderosis	Present	Absent
(iii) Haemoglobinaemia And haemoglobinuria	Present with intravascular Haemolysis only	Absent
(iv) Red cell fragments	May be present	Absent
(v) Plasma protein	Normal or elevated	Decreased

Two types of haemolytic anaemias are recognized based on site of red cell destruction: Intravascular and extravascular haemolysis. The cells may sometimes be destroyed at both sites, but one always predominates in a given disease condition.

INTRAVASCULAR HAEMOLYSIS. Here, the cells are lysed within the circulation leading to presence of free haemoglobin in plasms (i. e. haemoglobinaemia) and in urine (i. e. Haemoglobinuria, "red water"). Most cases occur as peracute or acute episodes; regenerative response (reticulocytes, etc) will not become evident until 3 days after the onset of haemolysis. The cause of intravascular haemolysis include blood parasitism (Babesia sp), bacteria (Leptospira sp, Clostridium haemolyticum Cl. Perfringens Types A), chemical agents (copper, ricin, phenothiazine, onion, methylene blue,

acetaminophen,Phenazopyridine), and immune haemolysis (incompatible transfusion, neonatal isoerythrolysis).

EXTRAVASCULAR HAEMOLYSIS. In this type, there is phagocytosis of the red cells by macrophages in the spleen, liver, and bone marrow. This form is usually chromic and slow in onset, there is absence of haemoglobinaemia or haemoglobinuria, and hyperbilirubinaemia is not common since the rate of red cell destruction and release of bilirubin hardly exceeds the ability of the liver to conjugate bilirubin. A regenerative response is evident; in cases with low grade erythrocyte destruction this response may be adequate to keep the PCV values within normal and the anaemia is then termed compensated haemolytic anaemia.
The causes of extravascular haemolysis include erythrocyte parasites (Anaplasma sp, Eperythrozoon sp, Haemobartonella sp, Plasmodium sp, Theileria mutants, Th.Annulata), iso-immune haemolysis (autoimmune haemolysis, EIA, lupus erythematosis) Intrinsic erythrocyte defect (pyruvate kinase deficiency, porphyria, hereditary Stomatocytosis; as well as sickle cell disease, hereditary spherocytosis in man), and erythrocyte fragmentation in micro-angiopathic haemolysis (DIC).

ANAEMIAS DUE TO NUTRITIONAL DEFICIENCES

A. IRON DEFICIENCY

Iron is a major component of haemoglobin, which contains 4 porphyrin rings and $4Fe^{2+}$ atoms. There is 3.4mg of iron per gm of Hb. Iron is absorted through duodenal mucosal cells, the rate of absorption varying directly with the rate of erythropoiesis and availability, and inversely with the size of iron stores. Plasma iron is oxidized to Fe^{3+} and bound to transferring, a β-globulin. Excess iron is stored in macrophages as ferritin, a soluble complex of Fe3+ and phosphoprotein, and isoluble haemosiderin which is composed of ferritin aggregates; these stores provide ready source of iron for erythropoiesis. Part of transferring bound iron is taken up by normoblasts in the bone marrow for haemoglobin synthesis.

Iron deficiency anaemia is microcytic hypochromic. Hypochrimia and microcytosis are due partly to the reduced production of haemoglobin which forms about 95% of the dry weight of the red blood cells, and partly to the fact that during the accompanying delayed maturation of the red cell, there is further mitosis of the normoblasts producing smaller cells. The bone marrow shows abundance of late normoblasts which have skimpy ragged rim of bluish-staining cytoplasm rather the normal pink or polychromatophilic colour. Prussian blue stain shows depletion of iron stores in the marrow. Usually thrombocytosis and neutrophilia are present. Reticulocytes may be normal or slightly increased, or even reduced.

Iron deficiency in animals can be due to:

(a) Poor dietary supply: encountered in piglets and pups of large breeds of dogs because of the low iron content of milk and the fast growth rate of these animals. The problem in piglets is prevented if they are allowed to graze outside the pen (soil has a high Fe content) or by giving each piglet 100mg of iron on the 4^{th} day of life.

(b) Chronic haemorrhage-due to bleeding neoplasms or blood sucking parasites.

(c) Impaired absorption – due to alkalinity of intestines or precipitation of iron. Iron is better absorbed as Fe^{2+}than as Fe3+.
Iron deficiency anaemia is microcytic hypochromic. Hypochrimia and microcytosis are due partly to the reduced production of haemoglobin which forms about 95% of the dry weight of the red blood cells, and partly to the fact that during the accompanying delayed maturation of the red cell, there is further mitosis of the normoblasts producing smaller cells. The bone marrow shows abundance of late normoblasts which have
skimpy ragged rim of bluish-staining cytoplasm rather the normal pink or
polychromatophilic colour. Prussian blue stain shows depletion of iron stores in the marrow. Usually thrombocytosis and neutrophilia are present. Reticulocytes may be normal or slightly increased, or even
reduced.

B. CORPER DEFICIENCY

Copper plays very important roles in haemoglobin synthesis, firstly, as part of the glycoprotein cereloplasmini which oxidizes Fe2+ to Fe3+, a change that is a prerequisite for binding to transferring, so that with copper deficiency the macrophages fail to release storage iron into plasma secondly as part of the enzyme ALA-dehydrase which catalyse one of the steps in haemoglobin synthesis. Alanine Amino-Acid dehydrase.

Copper deficiency occurs mainly in ruminants and is characterized by microcytic hypochromic anaemia similar to that produced by iron deficiency.

C. Vitamin B12, CABALT, AND FOLIC ACID DEFICIENCIES

Causes include:

(a) Ironizing radiation: This destroys the stem cells of the marrow as well as those of the lymph tissue, so that lymph also develops. Radiation generates free radicals which damage cells. Where the radiation is not fatal, there is regeneration later from surviving, pluripotential stem cells, erythroblasts and myeloblasts; sometime regeneration may be excessive leading to leukemia.

(b) Bracken fern poisoning: Occurs when cattle feed on the plant for 1 to 3 months in times of scarcity of feed. The plant contains an antivitamin, thiaminase, which damages the haemopoietic cells.

(c) Trichloroethylene – extracted soyabean meal, also produces marrow aplasia due to effects of a compound, DICHLOROVINYLCYSTEINE, which is formed between tricholoethylene and cysteine from the beans.
(d) Myelophthisis: In which the marrow is displaced by extramarrow tissue such as Neoplastic cells (e.g. lymphosarcoma), or fibrous (i. e. myelofibrosis).
(e) Infectious agents that destroy marrow cells: including Ehrlichia canis, feline infectious panleukopenia virus and feline leukemia virus.
(f) Drugs, such as chloramphenicol and anti-cancer drugs.

SECONDARY ANAEMIAS

These are associated with primary diseases which affect systems other than haematopoietic. Such diseases include malignant neoplasms, chronic infections, chronic liver and kidney diseases, parastic diseases other than blood sucking parasites and haemoprotozoan parasites, and endocrine deficiencies. The anaemias are usually nonresponsive.

A. CHRONIC INFECTIONS (ANAEMIA OF CHRONIC DISORDERS)

This type of anaemia is produced by chronic in inflammatory diseases such as abscesses, pyometra, pneumonia, tuberculosis, endocarditis, chromic fungal disease, osteomyelitis, arthritis, and myocardial infarction, and malignancies such as carcinoma, lymphosarcomas, leukemia, multiple myelomas, etc.

The anaemias, which is mild, develops within the first 1 to 2 months of disease and then does not progress further; the red cell values are only modestly depressed and may infact remain at the lower levels of the normal range. The severity of the anaemia correlates well with the degree of primary disease. The anaemia is normocytic normochromic, but may be hypochromic in some cases.

There is lack of regenerative response, so that reticulocytosis and Polychromasia are lacking.

The anaemia results because of blockage of the release of iron from the storage depots in the spleen, liver and bone marrow, so that plasma iron levels and iron binding capacity are depressed, which interferes with erythropoiesis. There also appears to be a slight decrease in red cell survival due to a non-specific activation of macrophages which, as one of their effects, destroy some red blood cells.

In neoplasia, the above mechanisms are always operative; however there may be other mechanisms involved which would usually increase the severity of the anaemia. Such mechanisms include myelopthisis, if the Neoplastic cells invade the bone marrow (lymphosarcoma) or originate from the marrow (erythroleukemia, granulocytic leukemias). The neoplasia may also cause haemorrhage which may be chromic or acute. Anti-cancer therapy also induces marrow hypoplasia.

B. CHRONIC HEPATIC DISEASE

Anaemia develops in such conditions as cirrhosis. The anaemia may be macrocytic with formation of leptocytes, but may also be normocytic normochromic. It results from deficiency of erythropoietic factor but haemorrhage may also occur.

C. CHRONIC RENAL DISEASE

Anaemia occurs in chronic nephritis including chronic interstitial nephritis. It is commonly normocytic normochromic. The mechanisms involved include those associated with chronic disorders (see A above), lack of renal erythropietic factor, and the depressant effects on the marrow of toxic metablites associated with the uraemia that often develops.

D. ENDOCRINE DEFICIENCIES

Hypopituitarism and hypothyroidism cause low grade normocytic normochromic anaemia. Leptocytes commonly are present in hypothyroidism.

E. PARASITISM

Trichostrongyliosis (except haemonchosis) produces normocytic normochromic anaemia in sheep and cattle, with absence of responsiveness. Some of the underlying mechanisms include protein leakage and malabsorbtion which are associated with enteritis.

Some specific diseases in domestic animals and poultry

1. **Babesiosis**
2. **Trypanomosis**
3. **Anaplasmosis**
4. **Leptosprirosis**
5. **Ancylostomiasis**
6. **Haemonchosis**
7. **Canine Erhlichiosis**
8. **Coccidiosis**