DEFINITION

Anaemia is a decrease below normal of the erythrocyte count and/or haemoglobin concentration. It is not a disease in itself, but a sign of disease. This condition arises as a result of excessive loss of blood and/or decreased production. Anaemia may occur in 2 major ways.

1. A loss from the vascular system by haemorrhage or haemolysis (Red Cell Lysis).
2. Inadequate production of red cells by the bone marrow, this also falls into 2 categories. (a) Reduced proliferation of red cell precursors.
   (b) Defective synthesis of haemoglobin.

GENERAL CONSIDERATIONS: In the health individual, the production of erythrocytes equals their destruction so that circulating read blood cell (RBC) value remains fairly stable. Anaemia arises when RBC production falls or its destruction rises above normal, but it may occasionally be due both factors. Anaemia is a syndrome which the practicing veterinarian encounters commonly in his practice. It is of utmost importance in Nigeria because many of the causative agents abound in our environment due partly to the suitability of the climatic factors for their proliferation and partly to the poor level of our animal management practices which usually fail to apply established control measures that help to limit the spread of infectious disease agents.

Despite the simple nature of its definition, it is important and necessary that the **nature** of the anaemia is defined because successful treatment of anaemia depends on this characterization. Such Characterization of anaemia depends on accumulation of some basic data: Heamatocrit (i.e. PCV%), Haemoglobin concentration (Hb g/dl) and erythrocyte (RBC) count $X10^6/\mu l$

CLINICAL MANIFESTATIONS OF ANAEMIA

Several features are associated with anaemia, but will vary with the nature of the cause(s).

(a) Pallor of mucous membranes of the mouth and pharynx, and of the conjunctivae and lips is common in anaemia. It may however be masked by jaundice, cyanosis and dilation of peripheral vessels as occurs in shock.

(b) Tachycardia and polypnoea, particularly after exercise; there is low exercise tolerance.

(c) Weakness and poor stamina

(d) Fever may be present particularly in anaemias due to infectious agents. It may be lacking in anaemias due to blood sucking parasites such as Haemonohus sp and Ancylostoma sp.

(e) Icterus, haemoglobinaemia and haemoglobinaria may be present depending on the cause; they usually occur in haemolytic anaemias but are lacking in anaemias due to haemorrhage or bone marrow hypofunction.

(f) Heart murmurs, due to reduced viscocity of blood and turbulence, and in severe cases due additionally to mitral and tricuspid valve insufficiency arising from cardiac dilation.

(g) Shock may also occur if more than one-third of the blood is lost.

(h) Relative depression, lethargy and anorexia, all of which may be made more severe by the primary cause.

Diagnosis

(a) Haematologic data: Heamatocrit (i.e. PCV), Haemoglobin concentration (Hb), erythrocyte count, erythrocyte sedimentation rate, reticulocytes count, leucocyte and platelet counts, and examination of stained blood films for such features as alterations of red cell morphology and presence of causative agents. Red cell indices (MCV, MCH) need to be calculated from accurate values of PCV, Hb conc. and RBC count.

(b) Bone marrow function evaluation. Usually made from biopsies, and will reveal underlying cause of anaemia such as marrow hypoplasia and toxicity, as well as its response to the anaemia. Marrow function can also be evaluated using ^{59}Fe to estimate erythropoiesis.

(c) Faeces: The colour consistency, presence of occult blood, And of parasites and their eggs should be noted.

(d) Urinalysis: Evaluation for presence of occult blood, Haemoglobin, conjugated bilirubin, urobilinogen and protein.

While the collection of the above data is ideal and essential for a definitive diagnosis of anaemia to be made, it is obvious that laboratory facilities are very inadequate in most establishments in Nigeria. It is however necessary that data listed in (a), (b) and (d) should at least be collecte

CLASSIFICATION OF ANAEMIAS

There are 3 main ways of classifying anaemias:

(i) Morphological Classification
(ii) Aetiologic or Pathogenetic Classification
(iii) Responsiveness (or Erythrokinetic Classification).

MORPHOLOGICAL CLASSIFICATION

This is based on the average size and average haemoglobin content of the red blood cell. The underlying reason for variation in these parameters is that reductions in the PCV, Hb concentration and red cell counts are not always proportionate. This method of

classification is based on calculation of red blood cell indices and the results are usually corroborated by examination of stained thin blood smears. The indices used are as follows:

(a) Mean Corpuscular volume, MCV, (i. e. average size of the red cell) =

$$\frac{\text{PCV\% X 10}}{\text{RBC (mill per ul)}} \text{ fl}$$

(fl = femtolitre)

(b) Mean corpuscular Haemoglobin Concentration, MCHC, (i. e. the average weight of haeoglobin per volume of the red blood cell).

$$\frac{\text{Hb gm\% x 100}}{\text{PCV (\%)}} \text{ gm per dl}$$

(c) Mean Corpuscular Haemoglobin, MCH, (i.e. the average weight of haemoglobin per red blood cell)

$$\frac{\text{Hb gm\% x 100}}{\text{RBC (mill per ul)}} \text{ pg (pg = picogram)}$$

The accuracy of these indices depends on the accuracy of the measurements of the blood cell values (PCV, Hb, RBC). (normal MCV), macrocytic (elevated MCV) or microcytic (decreased MCV). It may also be normochromic (normal MCHC or MCV) hypochromic (decreased MCHC i. e Subnormal haemoglobin content).

MCHC value cannot normally be above normal, i. e. anaemia cannot be hyperchromic because the normochromic red cell already has a maximal haemoglobin content which cannot be exceeded. However, an elevated MCHC or MCH can be recorded if there is in vitro or in vivo haemolysis of red cells in the sample. Such lysed red cells are not counted but their free haemoglobin is measured. Using these indices there are 3 types of anaemias.

A. MACROCYTIC ANAEMIAS: Two types are described

(i) Macrocytic hypochromic (= non-megaloblastic):
Assocciated with early post-haemolytic or post-haemorrhagic anaemias. In these states, reticulocytes, which are larger than mature red cells, enter the blood before full haemoglobination. May also be associated with production of RBC with increased surface area, as in liver disease, obstructive jaundice and post-splenectomy.

(ii) Macrocytic normochromic (=megaloblastic):

1. Associated with defective DNA synthesis, occurs in cobalt, Vit B^{12} and or folate deficiencies. Animals make their own Vit B^{12} and deficiency occurs if cobalt is lacking

2. Other causes include erythroleukemia and congenital porphyrinuria.

B. **NORMOCYTIC NORMOCHROMIC** (may manifest as normocytic normochromic): Observed in a variety of conditions, include:

1. Immediately after haemorrhage or acute haemolysis (up to 3 or 4 days) prior to arrival of immature RBCs from bone marrow.
2. Chromic disorders such as neoplasia and inflammatory disease.
3. Nephritis
4. Liver disease
5. Marrow hypoplasia due to destruction of marrow cells (e. g. by irradiation, bracken fern poisoning) or myelophthisis (i. e. displacement)
6. Stomach worm infestation (excluding haemonchosis).
7. Haemodilution due to excessive expansion of plasma volume.

C. MICROCYTIC HYPOCHROMIC:

1. Iron deficiency, due to low dietary intake, excessive demands in growing young animals such as piglets, chronic blood loss associated with bleeding ulcers or neoplasm, or with blood sucking parasites (Haemonchus sp. Ancylostoma sp etc).

2. Defective utilization of iron associated with copper deficiency and molybdenum poisoning.

AETIOLOGICAL/ PATHOGENETIC CLASSIFICATION

This is based on the cause of the anaemia. The broad classification includes:

A. Anaenias due to marrow hypofunction
   (i) Reduced erythrocyte production
   (ii) Reduced haemoglobin synthesis.

B. Increased loss of red blood cells due to:
   (i) Haemorrhage (ii) Haemolysis
   (Details are given in Table 1)

	REDUCED RBC PRODUCTION	**REDUCED Hb SYNTHESIS**
A.	Nutritional Causes - Vit B^{12} deficiency - Folic acid deficiency	- Fe deficiency - Cu - Cobalt

	- Protein deficiency	- Vit E
B.	Marrow Hypoplasia/Aplasia with stem Cell injury: - Irradiation - Bracken fern poisoning - Chloramphenicol poisoning	
C.	Myelophthisis (= marrow displacement) - Myelofibrosis - Neoplasia e. g. Iymphosarcoma	
D.	Secondary Anaemias - Chronic infections - Neplasia - Nephritis	

INCREASED BLOOD LOSS

	HAEMORRHAGIC BLOOD LOSS:	**HAEMOLYTIC BLOOD LOSS:**
A.	Acute Blood Loss - Trauma include surgery - Bracken fern poisoning - Sweet clover (dicoumarol) - Warfarin poisoning - Pathological rupture of vessel	Red cell Parasitism - Anaplasma, Babesia, EIA, Theileria, Haemobartonella, Eperythrozoon, Leptospira, Trypanosoma.
B.	Chronic Haemorrhage - GIT lesions (-ulcers, coccidiosis, Neoplasms) - Vit. K and prothrombin deficiencies, Haemopintus A - Thrombocytopenia - Bleeding neoplasms - Ectoparasites: ticks, lice, fleas. - Endoparasites: Haemonchrosis, Ancylostoma, Bunostomum.	Hypersplenism
C.		Toxins - Chronic Cu poisoning - lead, phenothiazine - Snake venom - Bacteria toxin (Cl, haemolyticium,Staph, pyogenes) - Ricin (castor oil) - Chemical oxidants (=

		methylene blue, Tylenol, phenothiazing onion).
D.		Antibody-antigen Reactions - Isoimmunization - Autoimmunity - Incompatible Transfusion
E.		Genetically defective RBC: - Pyruvate kinesa deficiency - Glucose – 6 – PO^4 deficiency - Hereditary spherocytosis - Sickle cell anaemia (Hb S)
F.		Microangiopathy (RBC fragmentation).

CLASSIFICATION BASED ON RESPONSIVENESS

Two forms of anaemias are recognized by this classification:

A. Responsive or Regenerative anaemias: Occur as a result of factors that are extramarrow, i. e. haemolysis or haemorrhage. The bone marrow responds actively by accelerating the rate of erythropoiesis and this results in the appearance of reticulocytes and nucleated red cells in circulation. The marrow itself becomes hypercellular, and shows increases in erythropoietic cells so that the me ratio drops. The first reticulocytes appear in blood 3 to 4 days after the blood loss or haemolysis, attains at peak 4 to 7 days and then declines if the emergency is over. In some cases, however, the anaemia is persistent despite increased erythropoiesis, production lags behind destruction or loss. The reticulocytes index or count is the most simple and accurate method of estimating erythropoiesis; ferrokinetic studies (PITR and EITR) are also very accurate, but more laborious. However while most domestic animals (sheep, goat, swine, dogs, cats) readily release reticulocytes into the circulation in responsive anaemias, cattle do so less readily except in severe acute situations. Horses never release reticulocytes no matter the severit of anaemia and the only evidence of responsiveness in the peripheral blood is the appearance of macrocytic fully haemoglobinated mature red cells. PITR and EITR values would seem the only accurate of estimating erythropoiesis in horses.

Responsive anaemias are usually also associated with neutrophilic leukocytosis and thrombocytosis, beginning a few hours after blood loss or haemolysis.

B. Non-responsive or Non-regenerative Anaemias: The underlying mechanism is a defect of the bone marrow so that it cannot respond by increased erythropoiesis, or deficiency of an essential substance (e. g. Fe, Cu) may prevent a normal marrow from responding. There is insufficient erythropoiesis due to hypoplasma of the marrow precipitated by a variety of factors such as toxic necrosis of the marrow cells (by irradiation, plant toxins, infectious agents such as Ehrichia

canis), myelophthisis by neoplastic cells and fibrosis. Non-responsiveness may also co-exist with normal cellularity of the marrow, as in renal disease and chromic disorders (neoplasia and inflammatory conditions). Another form of non-responsive anaemia is that associated with ineffective erythropoiesisi in which the erythrocytes produced are abnormal and are destroyed before they leave the marrow e. g. as occur in megaloblastic anaemias and in human thalasemia syndrome.

In non-responsive anaemia, there is neither Polychromasia nor reticulocytosis. Ferrokinetic studies also show reduced PITR and EITR. Bone marrow examination will illuminate the cause of the non-responsiveness.

While most non-responsive anaemias coexist with low leucocyte and thrombocyte values, i. e. there is pancytopenia, it should be noted that there are cases of pure red cell aplasia in which only erythrocyte precursors in the bone marrow are depressed. It is also to be noted that non-responsive anaemias will exist for the first 3 days after acute haemolysis or haemorrhage prior to onset of mobilization of reticulocytes into the circulation.

HAEMORRHAGIC ANAEMIAS (BLOOD LOSS ANAEMIAS)

The nature of haemorrhagic anaemias depends on whether haeorrhage is acute or chronic, and whether it is internal or external.

With external haemorrhage, which include gastrointestinal bleeding, there is loss of utilizeable blood constituents such as iron and protein, while these are reabsorbed and re-utilized (about 80%) in internal haemorrhage such as occurs into serous cavities. Consequently, marrow haemorrhage. Plasma protein level may be normal or only slightly depressed with internal haemorrhage while it is markedly decreased with external haemorrhage.

ACUTE HAEMORRHAGE

Immediate post-haemorrhagic haemogram is usually normal because both plasma and RBC are lost in similar proportions. Affected animals may develop hypovolemic shock and may die. Shortly after, splenic contraction released RBC stored in the spleen and this will temporarily slightly elevate PCV values. Thrombocytosis and neutrophilic leukocytosis develop within 3 hours of haemorrhage.

The body attempts to maintain blood volume beginning about 2 to 3 hours after bleeding by withdrawing fluid from the interstitial fluid, and this continues for the next 48 to 72 hours; once this process starts there is dilution of the blood so that decreases in PCV, Hb and RBC count become obvious; the anaemia at this time is normocytic and normochromic since the RBC are the original population existing prior to blood loss.

Reticulocytes and usually normoblasts enter the circulation 3 to 4 days post-haemorrhage, so that Polychromasia becomes evident in blood smears; this time lag represents the time taken for the chain reaction: haemorrhage – anaemia – tissue anoxia – renal erythropoietic factor – erythropoietin – stimulation of bone marrow with mobilization of reticulocytes into the circulation and increased erythropoiesis: to be completed. Reticulocytosis attains maximum level about 7 days post-bleeding if only a single episode has occurred; if however the high reticulocytes response persists, it indicates that further episodes of haemorrhage have occurred. The anaemia is macrocytic hypochromic

because of the presence or many reticulocytes. The haemogram returns to normal within 1 to 2 weeks if only a single episode of haemorrhage has occurred.
The reticulocytes response is always higher in haemolytic anaemias than in haemorrhagic anaemias because with haemolysis,the ingredients for erythropoiesis are immediately available after the RBC is haemolysed for utilization in the production of new RBCs, whereas loss of materials such as iron and protein occurs with haemorrhage.
Acute haemorrhage is produced by trauma (e. g. automobile accidents, gunshot wounds, pelvic fractures, uterine rupture at parturition, surgery), large gastro-intestinal ulcers, and haemostatic defects such ad DIC, sweet clover poisoning, warfarin poisoning, bracken fern poisoning, and factor X deficiency.

CHRONIC HAEMORRHAGE

Chronic haemorrhage sets in slowly allowing the body to adapt, so that hypovolemia does not occur. The anaemia is initially responsive with development of reticulocytosis and appearance of normoblasts. With time, however, the iron stores are depleted, particularly in fast-growing young animals with their usually low status of storage iron deficiency supervenes and the anaemia becomes microcytic and the regeneration become less marked. In prolonged cases the iron lack ultimately leads to marrow hypoplasia and end of responsiveness.
The causes of chronic haemorrhage include parasites (Ancylostoma duodenale-man, A. caninum – dogs, Necator americanus – man, Bunostomum phlebotomun – cattle, Haemonchus contortus – sheep and goats, H. placei-cattle, coccidiosis – several species), smaller gastrointestinal ulcers, bleeding neoplasia, haemophilia, thrombocytopenia, excessive menstrual flow-man. Fasciola hepatica and F. gigantica cause haemorrhage by erosion of bile duct and additionally induce dyshaemopoiesis.

IMPORTANT CAUSES OF HAEMORRHAGIC ANAEMIA IN NIGERIAS

Acute haemorrhagic anaemia due to automobile accidents occur occasionally in small animals (dogs and cats). Chronic haemorrhagic anaemias are common in young animals due to ancylostomiasis (dogs), haemonchosis (sheep, cattle, goats), and bunostomiasis (cattle); the high incidence in these young animals is associated with the suitability of our climate to the proliferation of the parasites, the low level of animal management practices and the poor state of veterinary care. Older animals are less susceptible to the parasites because of development of immunity; hence the incidence of severe anaemia due to these parasites is rare. More commonly the low grade infections of adult animals produces only a slight depression of erythrocyte value, but nevertheless the affected animals may appear normal. A further point of note is that range management of animals prevents the acquisition of heavy Helminth burdens, and severe blood-sucking-helminth infestations are more of a feature of settle herds using permanent grazing pastures and or watering points.