Diseases of RBCs

I. Anaemia:

True or absolute anaemia, may be defined as a decrease in erythrocyte mass in the body. HTC, HB and RBCs mass are usually below their normal range. Anaemia is a sign not a disease; it is a problem not a diagnosis.

Anaemia is classified in various ways to assist in determining its specific cause so that effective treatment can be provided in addition to history, clinical signs, and other lab. Findings and other test procedures (e.g., diagnosing images).

**Classification of anaemia according to the cause:**

a) Blood loss anaemia (Haemorrhagic).

* Theileria parva
* Babesia bigemina
* Canine distemper inclusion
* Lymph smear showing schizonts of Thieleria
* Stage of Babesia bigemina

b) Anaemia due to increase in RBCs destruction (Haemolytic anaemia).

c) Anaemia caused by decrease in RBCS production.

a) Blood loss anaemia(Haemorrhagic):

* May be caused by ,different kind of parasitic infestation as fleas, blood sucking lice, ancylestoma (hookworm), Hemonchus .Trauma, surgery and coagulative disorders- e.g. vit.K deficiency, sweet clover toxicity (dicoumarol) in cattle, inherited coagulation factors deficiency( hemophilia A& B),platelets disorders, neoplasia, gastrointestinal ulcers etc.

b) Anaemia due to increase in RBCs destruction(Haemolytic anaemia):

* Destruction of rbcs or their lyses may be caused by different agents; this may take place within the circulation (Intravascular haemolysis or extracellular haemolysis) it means outside macrophages of the spleen.
* Extravascular haemolysis or intracellular haemolysis; means destruction of rbcs inside splenic macrophages outside the vascular system:

**Haemolytic anaemia associated with immune response(immune mediated ):**

It is caused by the binding of immunoglobulins to the surface of rbcs or their precursors. The two major diseases in animal s are:

1) Neonatal isoerythrolysis (NI) or isoimmune haemolytic anaemia:

* It is a haemolytic disease of horse & mule foals ,rarely calves & kittens, problem arises when a dam is bred more than once to the same stallion which has different blood group; antigens of the male rbcs are transmitted to the fetus; then the dam develop antibodies against the fetal red cells.
* The colostrums then will contain antibodies against rbcs of the new born who ingested them they are then absorbed intact to the circulation, bind to neonatal rbc causing haemagglutination and intravascular haemolysis characterized by haemoglobinuria jaundice pale mucous membranes weakness &collapse, if not treated it is fatal.

2) Autoimmune haemolytic anaemia (AIHA): May be classified as:

* 1. Primary or idiopathic: In the absence of any other clinical condition or disease, it means that it is of unknown cause. Abs is directed against self antigens on rbcs.
	2. Secondary AIHA: When it occurs as a result of concurrent disease e.g. viral, rickettsial, bacterial or protozoal infections, neoplasia especially lymphoma, SLE & different toxin or drug exposure. Parts of the drug, toxin or infectious agent will associate with the rbcs, so they are going to be recognized as foreign by the immune system and Abs are formed against them.

**Laboratory findings in AIHA:**

* Low rbc, Hb & pcv values.
* Presence of spherocytes in stained blood films. Spherocytosis is caused by partial phagocytosis of sensitized rbcs and removal of part of the cell membrane; spherocytes have short half life because of their rigidity.
* Anaemia produced is regenerative in most cases & characterized by reticulocytosis, anisocytosis &increase in MCV.
* If the cause of AIHA leads to injury or inhibition to bone marrow non-regenerative anaemia will result (normocytic normochromic) as in EIA in horses.
* Coomb,s test or direct antiglobulin test(DAT): It is a test used to detect anti-rbcs Abs when visible agglutination is absent,all cases of AIHA are coombs test positive.
* Hyper- bilirubinaemia & bilirubinuria, haemoglobinuria is observed when intravascular rbcs destruction takes place.

**c) Anaemia caused by decrease in RBCS production:**

* Such anaemia lacks evidence of bone marrow response or non-regenerative (nonresponsive).It results from reduced or defective erythropoiesis:

1. Reduced erythropoiesis:

* Chronic renal diseases (decrease in EPO).
* Chronic diseases as inflammation and neoplasia.
* Endocrine diseases as hypothyroidism hypoadrenocorticism.
* cytotoxic damage to bone marrow.
* Infectious agents like Ehrlichiosis.
* feline leukemia virus infection (FeLV),
* myelophthisis as in leukemia, lymphoma, multiple myeloma metastatic tumors etc.

2. Defective erythropoiesis: It means abnormal or incomplete erythropoiesis, it includes:

* + - Disorders of haem synthesis: Mostly due to iron, copper or B6 deficiency all are needed for complete and normal synthesis of haem.
		- Disorders of nucleic acid synthesis: Due to B12 and folic acid deficiency, both are coenzymes needed and are essential for nucleic acid synthesis to accomplish mitosis of the developing rbc, both are rare in domestic animals, in man they cause megaloblastic anaemia characterized by macrocytic normochromic anaemia.
		- Abnormal maturation of rbcs: Caused by erythroleukemia, or myelodysplastic syndrome.

**Classification of anaemia according to erythrocyte indices:**

Anaemia may also be classified using MCV&MCHC values to assist in determining the cause of anaemia.

Terms used to express size:

* Macrocytic = increase in MCV.
* Normocytic = normal MCV.
* Microcytic =decrease in MCV.

Terms used for MCHC (haemoglobin concentration):

* Normochromic = normal MCHC.
* Hypochromic=decreased MCHC.
* Anaemia is not classified as. hyperchromic because high MCHC is an artifact.

**Comparison of classification of anaemia by rbc indices and etiology:**

* Normocytic normochromic: With poor or no bone marrow response associated with:
* Acute haemorrage(after < 3days).
* Acute haemolytic disease (before sufficient time has relapsed for sufficient reticulocyte production).
* Chronic inflammations and neoplasia.
* Chronic renal failure.
* Endocrine insufficiency.
* Selective erythroid aplasia
* Aplastic and hypoplastic bone marrow.
* Macrocytic hypochromic:
* Regenerative anaemia with marked reticulocytosis.
* Hereditary stomatocytosis in dog.
* Macrocytic normochromic:
* Regenerative anaemia (decrease in MCHC is not always present).
* Infection with Feline leukemia virus(FeLV) due to dyserythropoiesis and maturation arrest.
* Normal regenerative response in equine.
* Microcytic normochromic:
* Chronic iron deficiency.
* Anaemia of chronic diseases usually normocytic).
* Portosystemic shunt.
* Copper & pyridoxine (B6) deficiency.

**Classification of anaemia according to bone marrow response:**

a) Regenerative or responsive anaemia: It is characterized by good bone marrow response which is associated with the following lab. Results:

* Reticulocytosis: except in equine they do not release reticulocyte to the peripheral circulation but macrocytes with increase in MCV.
* Examination of stained blood film:
1. Increase in polychromasia which indicate reticulocytosis.
2. Anicocytosis due to the presence of large immature rbcs.
3. Presence of nucleated rbcs ( metarubricytes, rubricytes).
4. Howell- Jolly bodies.

Basophilic stippling, in ruminants rarely other animals

b) Non-responsive or non-regenerative anaemia:

* Bone marrow response is not evident in spite of the presence of anaemia, there is no reticulocytosis or anisocytosis
* anaemia is normocytic normochromic.

Causes:

* Blood loss of < three days.
* Diseases associated with suppression of erythropoiesis e.g. Chronic inflammatory diseases; renal failure, (decrease in EPO), drugs and toxins affecting erythropoiesis selectively in the bone marrow.
* Infections, e.g. Parvo virus infection in dogs.
* Bone marrow diseases e.g. Myelofibrosis, pure red cell aplasia (autoimmune in nature), marrow necrosis, neoplasia .
* Radiation.

**Clinical signs of anaemia:**

* Pale mucous membranes (Icteric if haemolytic).
* Weakness and exercise intolerance.
* Tachycardia and polypnea particularly after exercise.
* Increased sensitivity to cold.
* Syncope and depression.
* Heart murmur caused by decrease in viscosity and increase in turbulence of blood.
* Weak or fluttering pulse.
* Shock, if one third of blood is lost rapidly.

II. ERYTHROSYTOSIS (POLYCYTHEMIA):

* It refers to increase in HCT, Hb and RBC count above the normal reference range.
* Normal reference range can vary between species and breeds. Polycythemia is eitherabsolute or relative.

1) Relative polycythemia: The PCV is high but total RBC mass is normal. It is caused by:

* + 1. splenic contraction (transitory or physiologial polycythemia): As occur in excitement, fear, pain, or exercise after the release of adrenaline from the adrenal medulla.
		2. Dehydration: Causes polycythemia as from water loss after diarrhea vomiting excessive diuresis, sweating or water deprivation. Plasma protein will increase also; clinical signs of dehydration may be detected by examination.

2) Absolute polycythemia: Real polycythemia characterized by real increase in circulating RBC mass, it may be: primary or secondary.

1. Primary absolute polycythemia: Also known as Polycythemia Vera, it is an erythrocytosis that result from myeloproliferative disorder of unknown cause, there is normal or decreased EPO level in the blood. It is EPO- independent Autonomous proliferation of rbcs precursors, mostly observed in man, dogs & cats. Familial erythrocytosis has been described in highly inbred Jersey calves .There is persistence of a moderate or marked increase in pcv. Arterial blood gas is normal.
2. Secondary absolute polycythemia: Mostly characterized by increase in EPO level in the blood & increase in EPO production. It is caused by :
* Chronic hypoxia as seen in chronic lung diseases, heart defects with right to left shunting of blood, living in high altitudes, methaemoglobinaemia.
* Renal disorders: Causing local hypoxia in renal tissue like tumors, renal cysts hydronephrosis.
* EPO – secreting tumors: As nephroma, hepatoma.

This kind of polycythemia is characterized by :

* In chronic hypoxia there is increase in Pco2 in and decrease in Po2 when arterial blood gases are measured.
* There is increase in EPO production. Clinical examination & diagnostic images to
* differentiate between lung and heart diseases.