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Polycythemia

An increase above normal in the total red blood cell count, hemoglobin, and the PCV.

Absolute Polycythemia

May be physiologic or pathologic, although change may be only slight or transitory.

Physiologic

Seen in splenic contraction where reserve blood cells are released into circulation. Most common in cats and horses due to epinephrine release associated with fear, excitement and exercise. The total protein value is not affected and should remain normal. May also be seen in animals at high altitude due to decreased atmospheric oxygen.

Pathologic

Hypoxia observed in heart and lung disease will stimulate the production of erythropoietin and therefore produce polycythemia. Polycythemia rubra vera is a rare disease that has been reported in dogs, cats, cattle and man. All cellular elements of the bone marrow are affected. There is an absolute increase in the numbers of erythrocytes and total blood volume; however, the total protein remains the same.

Relative Polycythemia (HEMOCONCENTRATION)

An increase in the PCV, red blood cell count and hemoglobin due to a loss of water from the blood **(decrease in plasma volume**). The plasma protein concentration is elevated. May be observed in clinical dehydration associated with vomiting, diarrhea, reduced water intake, diuresis and shock.

Oligocythemia

- Reduction in the number of erythrocytes in the circulation.
- Physiological oligocythemia occurs due to hemodilution; RBC number per unit volume is reduced. **(** pregnancy).
- Pathological oligocythemia is also known as anaemia.

ANEMIA

It is a reduction below normal in the total number of red blood cells, **PCV,** hemoglobin concentration or all three.

- It is not a diagnosis but rather a symptom of an underlying disease process.
- Treatment should not be directed at the anemia except as an emergency matter.

Clinical signs of anemia are related to the decrease in oxygen carrying capacity of the blood. Signs and symptoms include:

- 1)Pale mucous membranes
- 2)Weakness or loss of stamina
- 3)Tachycardia, heart murmur
- 4)Shock if one-third of the blood volume is lost
- Signs are less marked if onset is gradual. The animal adapts to the decreased erythron.

- Icterus, hemoglobinuria, hemorrhage, edema or fever may be observed depending on the pathophysiologic mechanism involved.

CLASSIFICATIONS OF ANEMIA

1 CLASSIFICATION OF ANEMIA ACCORDING TO MORPHOLOGY

1 Red Blood Cell Size:

The size of the red cell is determined by visual interpretation on a stained blood smear or more accurately by the mean corpuscular value.

1 MACROCYTIC (Increased MCV): Transitory macrocytic condition is observed in cases where the marrow is responding to increased red blood cell need and discharging more immature cells (reticulocytes and nucleated red cells), which are larger, into the peripheral blood. e.g. Blood loss or hemolysis.

True macrocytic is observed in conditions where there is interference with maturation in the prorubicyte - rubricyte stage and reduced cell division resulting in large cells being released into the blood. e.g. B12, folic acid like deficiency seen in miniature poodles.

2 NORMOCYTIC (Normal MCV): There is interference with erythropoiesis at the stem cell level resulting in fewer cells entering the maturation process. Those that do enter the process develop normally and are released at the normal time. e.g. selective anemias of chronic infections, chronic renal disease, chronic liver disease and aplastic anemias.

3 MICROCYTIC (Reduced MCV): This is the type seen in iron deficiency anemia. A deficiency in iron results in less Hb being formed. Since the cell stops division when a certain critical hemoglobin concentration is reached, in iron deficiency there is often an extra division resulting in smaller cells. e.g. iron, copper and pyridoxine deficiency.

2 HEMOGLOBIN CONCENTRATION: Determined by prominence of central pallor in stained smear and more accurately by the mean corpuscular hemoglobin concentration (MCHC) and mean corpuscular hemoglobin (MCH)

1 .Hyperchromic: The cell cannot become supersaturated with Hb so this state does not actually exist. The MCH may be increased in cases where the MCV is elevated but not the MCHC. Elevated MCHC may indicate free hemoglobin in the plasma due to hemolysis, Heinz bodies in RBCs, or to excessive amounts of EDTA which cause shrinkage of RBCs.

2 Normochromic: Normal Hb concentration is found in most anemias of animals.

3Hypochromic: Reduced Hb concentration is characteristic of iron, copper and pyridoxine deficiency anemias, and in blood loss and hemolysis where the number of immature cells greatly exceeds the number of mature red blood cells.

2 CLASSIFICATION OF ANEMIA ACCORDING TO RESPONSE

1 REGENERATIVE: The bone marrow is capable of responding to the anemia by increasing its production of red blood cells. The ability to respond with increased activity indicates that the site of pathologic alteration is not in the bone marrow. i.e. blood loss and hemolytic anemias. Signs of increased erythrocyte production by the bone marrow may include:

- **Reticulocytosis**
- **Polychromasia**
- **Basophilic stippling**
- **Anisocytosis**
- **Nucleated red cells**
- **Howell-jolly bodie**s

2 NON-REGENERATIVE: The bone marrow is not able to respond to the anemic state. In fact, the inability of the marrow to produce red blood cells is the reason for the anemia. Therefore regenerative signs are absent. Red Cell morphology is normal in depression anemias and aplastic anemias.

3 Classification of anemia by pathophysiologic mechanism

Blood loss anemia

1 Acute Blood Loss: the type Anemia occurs when 25-40% of the circulating blood volume is lost.

Causes

- Trauma - ruptured liver or spleen
- Surgery
- Vascular neoplasm (hemangiosarcoma)
- Coagulation defects
- Severe parasitism - hookworms, Haemonchus
- Gastrointestinal ulceration

  External vs Internal Acute Blood Loss : External blood loss results in a reduction of red blood cells, plasma proteins, and plasma volume. Iron is lost to the exterior and not available for utilization.

Acute blood loss seldom results in iron deficiency since adults generally have sufficient iron stores to regenerate 2-3 times the total blood volume of red blood cells.

Internal blood loss is primarily into body cavities, **2/3** of the blood is reabsorbed by the lymphatics **(completed in 24-72 hours)** while **1/3** is broken down by the **RE** system. If a large amount of blood is broken down it may simulate a hemolytic anemia **(hyperbilirubinemia).**

2 Chronic Blood loss

- Chronic blood loss - Small amount of blood lost over a long period. Common in domestic animals.

Causes:

a)Parasitism

- Hookworms
- Strongyles **(large)**
- Haemonchus (cattle and sheep)
- Coccidia
- Lice, fleas, and ticks

b)GI ulcers

c)Vascular neoplasia

d)Coagulation defects

- Hemophilia
- Thrombocytopenia
- Vitamin K, prothrombin deficiency

2 Anemias due to accelerated erythrocyte destruction (hemolytic anemia)

Causes

1)Intrinsic - Hemolysis stems from a defect in the patient's red blood cells.

- a)Abnormal hemoglobins - not described in animals.
- b)Red blood cell enzymes deficiencies - PK deficiency of Basenji dogs.
- c)Membrane abnormalities - not described in animals

2)Extrinsic - Red blood cells damaged by some external factor

- a)Antibodies
- b)Toxins
- c)Parasites
- d)Chemicals
- e)Mechanical

Site of destruction

Damaged red blood cells (**by intrinsic or extrinsic means**) may lyse within the circulation **(intravascular hemolysis)** or be phagocytized by the reticuloendothelial cells (**extravascular**

hemolysis). In many cases, hemolysis takes place in both locations but one will usually predominate.

1)Intravascular hemolysis - more acute, seen in:

- a)Leptospirosis - particularly in cattle
- b)Clostridium perfringes Type A
- c)Clostridium hemolyticium (**bacillary hemoglo-binuria**) - sheep and cattle
- d)Piroplasmosis (**Babesiosis**) horse and dog
- e)Chronic copper poisoning - sheep and cow - acute hemolytic crisis resulting from stress precipitated release of copper stored in abnormal concentration in the liver.
- f)Phenothiazine poisoning -horse - Heinz bodies in red blood cells.
- g)Onion poisoning - cattle, sheep, horse and dog.
- h)Lead poisoning - canine - characterized by large numbers of basophilic stippled red blood cells and metarubricytes in the presence of a normal or slightly lowered PCV. Polychromia and reticulo-cytosis.
- i)Post-parturient hemoglobinuria - bovine
- j)Porphyria
- k)Isoimmune hemolytic disease
- l)Incompatible transfusions

2) Extravascular hemolysis

- a)Anaplasmosis - the peak of parasitemia occurs before the appearance of anemia and clinical signs, therefore the organism may not be present when you examine the blood.
- b)Hemobartonellosis
- c)Eperythrozoonosis
- d)Equine infectious anemia
- e)PK deficiency - inherited, autosomal recessive disease of Basenji dogs, anemia evident early in life.
- f)Autoimmune hemolytic anemia

3 Reduced or Defective Erythropoiesis

Site of the problem is in the bone marrow in contrast to peripheral blood, as is the case in hemorrhagic and hemolytic anemias.

a.Secondary Anemia (Anemias of chronic disorders) - Selective depression of erythropoiesis.

1) Chronic Inflammatory Disease - Chronic suppurative diseases. The anemia does not respond to hematinics and improves only when the underlying disorder improves. The anemia is mild to moderately severe.

- a)Normocytic, normochromic (**rarely microcytic, hypochromic mild)**
- b)Non-regenerative
- c)Both serum iron and transferring levels are reduced. Iron binding capacity is low. Tissue iron stores are increased. There is an impairment of release of iron from the RE cell. Low serum iron seems to make the bone marrow less responsive to erythropoietin

2) Chronic renal disease

- a)Gradual onset
- b)Normocytic, normochromic anemia
- c)Non-regenerative anemia
- d)Shortened red blood cell survival time (**usually proportional to degree of azotemia)** - erythrophagia evident in RE system. Reduced erythropoietin production by the kidney andresulting lack of stem cell stimulation

3)Neoplastic Disease - **(non-marrow infiltrating**)

- a)Particularly in disseminated malignancies and/or necrotic neoplastic situations.
- b)Similar to secondary anemias associated with chronic inflammatory disease in its pathogenesis and blood picture.

4)Endocrine Disturbances

- a)Hypopituitarism
- b)Hypothyroidism

5) Trichostrongylosis of cattle

4 Aplastic Anemia

Characterized by pancytopenia (granulo-cytopenia, thrombocytopenia and anemia)

- 1)Damage is to the multipotential stem cell
- 2)Normocytic, normochromic, non-regenerative anemia
- 3)Hypocellular bone marrow - fat replacement. M/E ratio usually normal
- 4)Since the life span of white blood cells and platelets are short **(7-10 days)**, severe neutropenia and thrombocytopenia precede the anemia **(red blood cell life span - 120 days in the dog)**.
- 5)Overwhelming infection or uncontrollable hemorrhage is a frequent complication

Causes

1)Irradiation - lymphocytes and bone marrow cells highly sensitive. Mature red blood cells are resistant

2)Bracken fern poisoning - **(Cattle)** a thiaminase appears to be the etiologic component

3)Chemicals

- a)Alkylating Agents, antimetabolites, and other classes of cancer chemotherapeutic drugs
- b)Benzene and cyclic hydrocarbons
- c)Insecticides
- d)Chloramphenicol, sulfonamides, estradiol, Anti-convulsive agents, Phenylbutazone and others. Must be administered over a long period of time. Individual idiosyncrasy is often involved.
- e)Infectious feline enteritis **(panleuko-penia)** due to the usual short course, death may often occur before the anemia is obvious.

4)Chronic blood loss over a long period of time; abrupt aplasia in terminal stages.

5)Myelophthisis anemia - physical replacement of hematopoietic marrow.

a)Neoplasia - Myeloproliferative disorders and other infiltrating neoplasms

b)Osteodystrophia fibrosa and other bone diseases rarely severe enough.

5 Nutritional Anemias

The bone marrow can usually respond but in an ineffective manner. Red blood cell size and Hb content may vary.

a.B12 Deficiency

- 1)Common in man.
- 2)B12 is prepared for absorption by an intrinsic factor in the stomach, a lack of which causes pernicious anemia, a macrocytic anemia associated with leukopenia and thrombocytopenia.
- 3)Removal of 7/8 of the stomach, the entire duodenum and 30 cm of anterior jejunum in the dog does not produce anemia.
- 4)In cattle and sheep B12 deficiency develops in animals on cobalt deficient pasture **(Florida, Northern Wisconsin and Michigan)**. Cobalt is essential in the molecular structure of B12.
- 5)Whether true B12 deficiency occurs in dogs is in question but there are reports of anemia in the dog with some of the characteristics of B12 and folic acid deficiency that respond to treatment. The hematologic picture is that of macrocytic anemia, large macrocytic erythroid cells in the marrow, large hypersegmented neutrophils, and large megakaryocytes occurring in groups in the bone marrow.
- 6)The pathogenesis of the anemia is via B12 nucleic acid synthesis. In the deficient state there is not enough nucleic acid for cell division in the prorubricyte and rubricyte stages resulting in fewer divisions and therefore, the final cell is larger **(macrocyte**).

b.Folic acid deficiency - similar to B12.

Functions in nucleic acid metabolism. Results in a macrocytic anemia.

c.Cobalt deficiency

Required for B12 synthesis in the ruminant.

d.Iron deficiency - 1/2 to 3/4 of the body iron is in Hb.

The remainder is in myoglobin, enzymes of the cytochrome oxidase system and stored iron.

- 1)Absorption of iron from the gut is controlled by need. A high pH and low HCl concentration impair absorption. Transported in blood bound to transferring and stored as ferritin or hemosiderin.
- 2)Most of the Hb iron is re-utilized.
- 3)Because normal daily iron requirement is so low it would take years to deplete the body stores of iron and produce anemia. Iron deficiency in the adult means abnormal chronic blood loss (***see blood loss anemia)***.
- 4)True nutritional iron deficiency anemia occurs only in the young animal. There is a correlation between growth rate and propensity for iron deficiency anemia; i.e. pig **(high)** vs. cat **(low)**.
- 5)Milk has a low iron content.
- 6)Blood picture
- a)Microcytic, hypochromic anemia.
- b)Since accumulation of Hb in the cell is one of the means of halting division. A deficiency of iron (**Hb)** would result in additional divisions and therefore smaller cells with reduced hemoglobin.
- c)Low PCV and Hb but red blood cell count may be normal.
- d)May see regenerative signs of anemia.
- e)Poikilocytosis is common
- f)Erythroid hyperplasia in marrow. Higher numbers of late rubricytes and metarubricytes.
- g)Low serum iron
- h)Absence of hemosiderin in marrow and other RE tissues **(in contrast to increased hemosiderin associated with low serum iron in anemias of chronic disease processes).**
- e.Copper deficiency and/or Pyridoxine **(B6)** deficiency. Both are essential for the utilization of iron and can cause an anemia similar to iron deficiency anemia.

6 MYELOPROLIFERATIVE DISORDERS IN CATS

An abnormal proliferation of a variety of bone marrow cells that leads to a profound non-regenerative anemia. It is primarily a bone marrow disease and believe to be caused by a C-type leukemia virus. See large numbers of nucleated red blood cells without reticulocytes or polychromatophilic cells.

AUTOIMMUNE HEMOLYTIC ANEMIA (AIHA)

Definition

An acquired hemolytic disease in which the life span of the **RBC** is shortened due to the coating of the cell by an abnormal globulin. The animal **(primarily in the dog)** forms antibodies **(autoantibodies)** against its own **RBC's.** The membrane of these RBC's is altered and the cell is removed prematurely by the **RE** system **(extravascular hemolysis)**. Two main forms of **AIHA** are noted in the dog.

- 1.Hemolytic anemia unaccompanied by any coexisting disease.
- 2.Hemolytic anemia accompanied by thrombocytopenia or thrombocytopenic purpura. Approximately **1/3** of the cases are of this type.

CLINICAL SIGNS

- 1.Seen in dogs and cats, more common in females
- 2.Sudden onset, course variable, usually fatal
- 3.Signs referable to anemia
    - a.Pallor
    - b.Weakness
    - c.Shortness of breath
    - d.Tachycardia, heart murmur
- 4.Signs referable to hemolysis
    - a.Very slight icterus in some cases
    - b.Dark orange feces
    - c.Dark urine
    - d.Splenomegaly
    - e.Hepatomegally
    - f.Increased body temperature - **102.5-106'F**
- 5.Signs referable to thrombocytopenia
    - a.Epistaxis
    - b.Gingival, ocular, oral hemorrhages
    - c.Petechial hemorrhages in the skin
    - d.Melena

CLINICAL PATHOLOGIC FINDINGS

- 1.Regenerative anemia--hypochromia in some cases.
- 2.Neutrophilic leukocytosis **(20-40,000)** with left shift, lymphopenia.

- 3.Spherocytosis - Not present in all cases. Difficult to observe in cats. Small, dark **RBC's** with unaltered volume but reduced diameter. should have no central pallor - removed by **RE** system.
- 4.May disappear with therapy or remission.
- 5.Spontaneous agglutination of **RBC's** may occur - usually involves spherocytes.
- 6.Hemolysed plasma - intravascular hemolysis is not characteristic of **AIHA** but fragile spherocytes may rupture intravascular or when blood is drawn.
- 7.Positive Coombs' test or absence of spherocytes does not rule out the disease. Often becomes negative with treatment.