Role of blood and blood cells in homeostasis

Astrid Oscos Snowball

marja.oscossnowball@unimelb.edu.au

Learning Objectives:

1. Describe the components of blood (cells, ions, proteins, platelets), giving their normal values, and explain how blood is essential for maintaining homeostasis

2. Describe the leukocytes found in the blood of normal animals and the differences in appearance between common domestic species

3. Describe the normal balance of leukocyte turnover and how this can alter in response to infection

Blood

- Plasma 55% by volume
  - Water about 90%
  - Protein about 7%
    - Albumin, globulin, immunoglobulins
    - Hormones and other chemical messengers
    - Fibrin for clot formation
  - Electrolytes 2-3%
  - Gases and other solutes
- Cells or formed elements 45%
  - Red blood cells (RBC)
    - 5-10 x 10^9/ml
  - White blood cells (WBC) or leukocytes
    - About 5 x 10^6/ml
  - Platelets
    - 200-1000 x 10^6/ml
- Delivers nutrients and oxygen to tissues and removes metabolic wastes.
- Vital for maintaining body temperature and pH and delivering chemical messengers to tissues and organs.

Red blood cell (RBC) shape

- A normal mammalian RBC is about 7-8µm in diameter and about 2.5µm thick
- Most mammalian RBCs are a biconcave disc
  - Maximises the cell's surface area to volume ratio to facilitate the gas transfer
- In some ungulates (sheep, cattle, deer), there is less of a central depression
- Llamas and camels have oval-shaped RBCs.
- Mature mammalian RBCs lose their nucleus, while those of birds, reptiles, amphibians, and fish do not.

Red blood cell function

- The primary function of RBC is to transport O_2 from the lungs to the tissues and CO_2 from the tissues to the lungs
- Also involved in pH balance
- The functional molecule in RBC is haemoglobin (Hb).
  - Each Hb molecule has four haem units, each with an iron atom that can bind 1 O_2 molecule; hence four molecules of O_2 can be carried/Hb molecule
  - The binding is loose and reversible, allowing O_2 to dissociate in the low O_2 tension found in tissues.
  - RBCs are vital for CO_2 transport back to the lungs, either combined with Hb (21%) as bicarbonate ions within the cell (64%) or dissolved in the cytoplasm (4%). The remainder is carried as CO_2 or bicarbonate ions in the blood plasma.
  - Hb also binds H^+ ions, which has a buffering effect.

Platelets

- Small cytoplasmic pieces (2µm) budded off from megakaryocytes in the bone marrow
- Involved in haemostasis or clotting of blood
- Damage to blood vessels activates platelets, and these are deposited at the injury site
- Activated platelets bind serum thrombin, which in turn converts soluble plasma fibrinogen into insoluble fibrin, forming a mesh of fibres over the platelet plug

Identification of leucocytes in domestic species

Five main types of leukocytes or white blood cells (WBC) can be identified in common domestic species using haematoxylin and eosin, or Wright's stain:

- Lymphocytes are round cells with a nucleus that takes up most of the cell and often has a slight indentation. The cytoplasm stains pale blue. These are the next most common blood leukocyte type in domestic species and the most common type in ruminant blood. Immunostaining is required to identify the B and T lymphocyte subsets and the NK cells.
- Monocytes are larger cells with a nucleus ranging from oval to varying degrees of indentation, from single kidney bean shape to multiple indentations and lobular shapes. Monocytes usually are less than 10% of the blood leukocytes. The cytoplasm is blue- grey and can contain vacuoles, especially after activation.
- Neutrophils generally have a segmented or multi-lobed nucleus and neutral staining cytoplasm. Mature neutrophils have multiple lobes or segments, while immature neutrophils (band neutrophils) have simpler, less-segmented nuclei. These are the most common leukocytes in the blood of most domestic species other than ruminants.
- Eosinophils have a segmented or multi-lobed nucleus that is less defined than a neutrophil nucleus. The cytoplasm stains pale blue but is generally obscured by granules that stain reddish to orange (eosin-loving). The shape and colour of the granules differ between species. Eosinophils are rare in the normal blood of most species.
    - Dog granules are round and variable in number
    - Cat granules are rod-shaped and fill the cytoplasm
    - Horse granules are large, round, or oblong and fill the cytoplasm, often hiding the nucleus
    - Ruminant granules are small, and round and fill the cytoplasm
- Basophils – similar in size to neutrophils but very rare in the blood of most species. They have a segmented nucleus and a light purple cytoplasm (basic staining). The granules may or may not be visible, depending on the stain used and the species.
    - Dog granules may have low numbers of small purple granules or be invisible.
    - Cat granules are small, round, and lavender coloured
    - Horse granules are small, numerous, and purple. They may hide the nucleus

- Ruminant basophil granules are small, numerous, and purple

White blood cell functions

Lymphocytes are involved in the adaptive immune system. B lymphocytes or B cells produce antibodies to antigens (molecules recognised as foreign), referred to as humoral or antibody-mediated immunity. T lymphocytes or T cells have several functions. T helper cells are involved in activating B cells and other T cells. Cytotoxic T cells induce apoptosis or programmed cell death in other cells that express foreign antigens on their surface (such as virus-infected cells). This is referred to as cell-mediated immunity.

Monocytes are phagocytic and antigen-presenting cells – they process antigen and present it to T and B lymphocytes. They are the immature form of tissue macrophages.

Neutrophils are often associated with bacterial infections. They are phagocytic and are the first line of defence against pathogens.

Eosinophils are often associated with helminth parasite infections such as intestinal roundworm and tapeworm infections and may also be involved in allergic responses.

Basophils are most often associated with allergic responses. They bind IgE, an immunoglobulin associated with allergic responses, and release histamine in response to allergens that the IgE recognises.

Most WBC exerts their functions in tissues rather than blood, so they need to migrate out of the blood and into tissue sites of infection. They do this by emigrating from the blood into sites of inflammation, following cytokine and chemokine gradients produced by the infected tissues. WBC express adhesion molecules on their surface, which bind to complementary adhesion receptors on blood vessel endothelial cells, slowing them down in the blood flow and allowing the WBC to migrate between the endothelial cells into sites of inflammation.

Haemopoiesis (Haematopoiesis)

- The cellular elements are all produced from haematopoietic stem cells (HSC) in the bone marrow
- The production and regulation of mature blood cells (haemopoiesis) is vital to the homeostasis of animals, and the role of the haemopoietic system is to maintain adequate numbers of RBC, platelets, and WBC
- Blood cells display certain distinctive features.
    - The short lifespan of most mature blood cells requires continuous new blood

cell formation throughout life

- Total new blood cell production (RBC and WBC) is around 3×10^{11}/day.

- This rate of production must be maintained without pause for the lifespan of the individual
    - In humans, the bone marrow will have released > 10^{16} mature blood cells during a 70-year lifespan
- The multiplicity of blood cell types: myeloid and lymphoid, need to be produced.
- The short lifespan of some Leukocytes limits their ability to damage the animal's tissues.

Suggested references

1. Schalm's Veterinary Haematology. 5th edition. 2010. 6th edition. 2010. D. J. Weiss & K. J. Wardrop. Wiley-Blackwell.
2. Essential Haematology 5th edition 2006. V. Hoffbrand, P. Moss and J. Pettit 2006. Blackwell Science