OVERVIEW

1. General introduction
2. Types:
   - Functions
   - Interpreting changes in blood values
3. Morphological changes
4. General patterns of WBC disorders

1. GENERAL INTRODUCTION
HEMATOPOIESIS

pluripotent stem cell
CFU-Bone marrow (spleen)

myelopoiesis
CFU-GEMM

CFU-MK CFU-E CFU-G CFU-M

thrombocytes

granulocytes
neutrophils eosinophils basophils

erythrocytes monocytes

CFU=colony forming unit, G=granulocytic, E=erythroid, M=myeloid, Mk=megakaryocytic

DISTRIBUTION OF GRANULOCYTES

(three compartments)

- myeloblast
- promyelocyte
- myelocyte

- metamylocyte
- banded granulocytes

- segmented granulocytes

BONE MARROW proliferation pool

PERIPHERAL BLOOD maturation pool

TISSUE mature cell

Storage pool

DISTRIBUTION OF GRANULOCYTES

(three compartments)

BONE MARROW

proliferation pool

maturation pool

storage pool

release

distribution in BLOOD VESSELS

marginalisation, adhesion, transmigration

utilization in TISSUES
DISTRIBUTION OF GRANULOCYTES IN THE PERIPHERAL BLOOD OF RESTING DOGS AND CATS

**Marginated Pool**
- Dog: 50%
- Cat: 25-50%

**Circulating Pool**
- Dog: 50%
- Cat: 50-75%

PRACTICAL APPLICATIONS:
1. Ways to evaluate leukocytes:
   - Bone marrow evaluation: biopsy/aspirate
   - Blood sample
   - Tissue cytology
   - Easier to obtain reflects the equilibrium between different compartments

2. Epinephrine can produce a rapid shift of cells from marginated to circulating pool, especially in the cat

BASIC TESTS FOR LABORATORY EVALUATION OF WBC'S
- Total leukocyte count
  (manually, automated or estimated from a smear)
- Leukocyte evaluation in a stained blood smear
  (differential count for WBC types and morphology evaluation)
2. TYPES OF LEUKOCYTES: FUNCTION & INTERPRETATION OF CHANGES IN BLOOD VALUES

TYPES OF LEUKOCYTES

- GRANULOCYTES:
  - Neutrophils, Eosinophils, Basophils
- MONOCYTES
- LYMPHOCYTES

NEUTROPHILS

FUNCTION:
- Phagocytosis in infectious & inflammatory conditions
- A central role in the inflammatory process with many functions (e.g., release of cytokines)

Usually changes in neutrophils

changes in total WBC numbers
**NEUTROPHILIA (causes)**

- Physiological, non-inflammatory response:
  - Epinephrine effect
  - Glucocorticoid effect

- Reactive, inflammatory response
  - Infection (local – systemic) → Any process which produces an inflammatory response
  - Tissue necrosis/injury
  - Immune-mediated diseases
  - Tumour, myeloproliferative disorders

**NEUTROPHILS IN DIFFERENTIAL BLOOD CELL COUNT**

Cell maturation proceeds from left to right, so a shift to the left means more immature cells, a shift to the right means more mature/aged cells.

<----- left shift ----- right shift ----->

1-myeloblast, 2-promyelocyte, 3-myelocyte, 4-metamyelocyte, 5-band, 6-segmented granulocytes

**NEUTROPHILIC LEFT SHIFT**

An increase in immature neutrophils (e.g. band and metamyelocyte cells) is known as a left shift and is a sign of inflammation.

- If neutrophil numbers are increased it is a regenerative left shift (an appropriate response to acute inflammation)
- If neutrophil numbers are within range or decreased, it is a degenerative left shift (carries a guarded or poor prognosis, except in cattle)
Band neutrophil granulocytes, dog

**NEUTROPENIA (main causes)**

- Decreased bone marrow production
  - Infectious agents (e.g., parvo, FeLV)
  - Drugs
  - Lymphomas

- Marginal compartment sequestration

-Increased destruction or use
  - Overwhelming bacterial infection
  - Toxins

**EOSINOPHILS**

Some functions:
- Inactivate histamine and similar toxic materials
- Inhibit oedema production
- Phagocytosis
- Essential to allergic responses and defence against parasites

Eosinophil, horse. Appearance varies with species.
EOSINOPHILIA (main causes)
- Parasitism + allergy (to flea or food/ hypersensitivity)
- Hypereosinophilic syndrome

EOSINOPENIA (causes)
- increased glucocorticoid levels
- acute infection

BASOPHILS
FUNCTION
release of histamine
(release is modified by eosinophils).

Basophil, horse. Appearance varies with species

BASOPHILS
BASOPHILIA
- usually associated with eosinophilia as part of hypersensitivity reactions
- basophilic leukaemia

BASOPENIA rare and significance unknown
MONOCYTES

FUNCTION
- Phagocytosis, particularly of larger items such as:
  - Tissue debris
  - Fungi
  - Protozoa
  - Bacteria (brucella spp., mycobact. spp)
  - Antigen presentation
  - Secretion of cytokines
  - Become tissue macrophages

MONOCYTOSIS (causes)
- Chronic inflammation particularly some infections, e.g. listeriosis
- Transient monocytosis, perhaps a few days after the onset of acute inflammation
- Increased glucocorticoid levels particularly in dogs
- Monocytic, myelo-monocytic leukaemia/other neoplasias

LYMPHOCYTES

FUNCTIONS
- Humoral (antibody mediated) immunity
- Cell mediated immunity.

B cells and T cells are not distinguishable on morphological grounds
- Short lived lymphocytes (few days)
- Long lived lymphocytes (up to years)
LYMPHOCYTOSIS (causes)

Physiological
- mobilization of cells (lymph drainage)
- epinephrine release (i.e. frightened cats)

Pathological
- recent immune stimulation (i.e. vaccination)
- lymphoid neoplasias

LYMPHO(CYTO)PENIA (main causes)

Decrease in lymphopoiesis:
- increased glucocorticoid levels
- acute infection, sepsis, endotoxaemia
- radiation
- immunodeficiency syndrome
- some neoplasias

3. MORPHOLOGICAL CHANGES
### Morphological Changes

<table>
<thead>
<tr>
<th>Changes</th>
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<tbody>
<tr>
<td>Toxic changes in neutrophils</td>
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<tr>
<td>Neutrophil hypersegmentation</td>
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<tr>
<td>Changes in lymphocytes:</td>
</tr>
<tr>
<td>- reactive lymphocytes</td>
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<tr>
<td>- lymphoblasts</td>
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<tr>
<td>WBC inclusions</td>
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<tr>
<td>Pelger-Huët anomaly</td>
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</tbody>
</table>

### TOXIC CHANGES IN NEUTROPHILS

**toxic neutrophil, nucleated RBC (NRBC), dog**

- Dohle body
- NRBC

### TOXIC CHANGES IN NEUTROPHILS

**basophilic cytoplasm, larger neutrophils, dog**
**TOXIC CHANGES IN NEUTROPHILS**

Toxic neutrophils with basophilic and foamy cytoplasm, Doehle bodies and toxic granulation, dog

**Morphological Changes**

- Toxic changes in neutrophils
- Neutrophil hypersegmentation
- Changes in lymphocytes:
  - reactive lymphocytes
  - lymphoblasts
- WBC inclusions
- Pelger-Huët anomaly

**NEUTROPHIL HYPERSEGMENTATION**

Hypersegmented neutrophil, dog
Toxic changes in neutrophils
Neutrophil hypersegmentation
Changes in lymphocytes:
- reactive lymphocytes
- lymphoblasts
WBC inclusions
Pelger-Huët anomaly

COMPARISON OF NORMAL LYMPHOCYTES AND NUCLEATED RED BLOOD CELLS (NRBC)

lymphocyte - NRBC, dog

CHANGES IN LYMPHOCYTES

reactive lymphocytes, dog

small lymphocyte
CHANGES IN LYMPHOCYTES

- lymphoblasts, dog
- small lymphocyte

Morphological Changes

- Toxic changes in neutrophils
- Neutrophil hypersegmentation
- Changes in lymphocytes:
  - reactive lymphocytes
  - lymphoblasts
- WBC inclusions
- Pelger-Huët anomaly

PARASITES

- hepatozoon, dog
**PARASITES**

*ehrlichia organism in a neutrophil, dog*

**BACTERIA**

*neutrophil with phagocyted bacteria, dog*

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### Morphological Changes

- Toxic changes in neutrophils
- Neutrophil hypersegmentation
- Changes in lymphocytes:
  - reactive lymphocytes
  - lymphoblasts
- Parasites / bacteria
- Pelger-Huët anomaly
4. GENERAL PATTERNS OF LEUKOCYTE DISORDERS

CLINICAL USES OF CHANGES IN WBC VALUES: ADVANTAGES

Changes can help to:
- detect the existence of inflammatory disease.
- determine prognosis and monitor treatment.
- detect some haematopoietic neoplasias.

It is recommended, where possible, to interpret WBC values over the course of several blood counts.
CLINICAL USES OF CHANGES IN WBC VALUES: LIMITATIONS

- Usually does not identify specific aetiological agents
- Cannot indicate the site of inflammation
- May not identify presence of inflammation, i.e.:
  - chronic, non-invasive or mild inflammation
  - generalized inflammation may cause less WBC change, compared with local inflammation.

COMMON CAUSES OF CHANGES IN WBC VALUES

NONINFLAMMATORY CAUSES OF WBC CHANGE:
- Epinephrine-induced leukogram
- Glucocorticoid-induced leukogram
- Red cell regenerative response
- Leukaemias

INFLAMMATORY CAUSES OF WBC CHANGE:
- Inflammatory response. Leukaemoid reaction
- Leukopenias

NON-INFLAMMATORY CAUSES OF CHANGES IN WBC VALUES
### NON-INFLAMMATORY CAUSES OF CHANGES IN WBC VALUES

<table>
<thead>
<tr>
<th>EPINEPHRINE-INDUCED</th>
<th>GLUCOCORTICOID-INDUCED</th>
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</thead>
<tbody>
<tr>
<td><strong>Causes:</strong></td>
<td><strong>Causes:</strong></td>
</tr>
<tr>
<td>- Activity (physiological leukocytosis)</td>
<td>- Increase in exogenous or endogenous glucocorticoids</td>
</tr>
<tr>
<td>- Fear, excitement</td>
<td></td>
</tr>
<tr>
<td><strong>Signs:</strong></td>
<td><strong>Signs:</strong></td>
</tr>
<tr>
<td>- Leukocytosis</td>
<td>- Leukocytosis</td>
</tr>
<tr>
<td>(15.0 - 25.0 (30.0) x 10⁹/L)</td>
<td>(15.0 - 25.0 (30.0) x 10⁹/L)</td>
</tr>
<tr>
<td>- Neutrophilia, without left shift</td>
<td>- Neutrophilia, without left shift</td>
</tr>
<tr>
<td>- Lymphocytes within reference ranges in most species, but lymphocytosis common in cats</td>
<td>- Decrease in lymphocytes and eosinophils</td>
</tr>
<tr>
<td></td>
<td>- In dogs: Monocytosis (mild)</td>
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</tbody>
</table>

### NON-INFLAMMATORY CAUSES OF CHANGES IN WBC VALUES

**RED CELL REGENERATIVE RESPONSE**
- Associated with strongly regenerative anaemias.
- Usually appear as a neutrophilia with left shift, and sometimes thrombocytosis, as a result of non-specific stimulation of the bone marrow by erythropoietin.

### NON-INFLAMMATORY CAUSES OF CHANGES IN WBC VALUES

**LEUKAEMIAS**
In some cases of leukaemia there is a persistent increase of the affected leukocyte type in blood.
INFLAMMATORY CAUSES OF CHANGES IN WBC VALUES

GENERAL INFLAMMATORY RESPONSE

GENERALLY THERE IS:
- Leukocytosis
- Neutrophilia
- Left shift

IN ADDITION, OR INSTEAD, THERE MAY BE:
- Toxic changes in neutrophils
- Monocytosis (especially in chronic inflammation)
- Leukopenia (see slide on causes of leukopenia)

LEUKAEMOID REACTION

Very marked increases in leukocyte number due to an inflammatory response (up to or >100 x 10^9/L) which must be differentiated from Leukaemias!

Some examples:
- Pyometra
- Severe abscession
Differention of Leukaemoid Reactions from Leukaemia:
- Clinical evidence of inflammation (including response to anti-inflammatory treatment)
- Toxic neutrophils may occur in leukaemoid reaction

Leukaemoid reaction
Leukaemia

Leukopenia
In most domesticated animals, the neutrophil is the predominant cell, so leukopenia is often caused by neutropenia. However, in the cow, the lymphocyte is the predominant cell, so leukopenia is often caused by lymphopenia.
Main causes are:
- Excessive tissue consumption in an inflammatory disease: e.g. Peritonitis, Septicaemia
- Bone marrow injury:
  - Infectious agents: FeLV, parovirus, Ehrlichia canis
  - Drugs: oestrogens/chemotherapy
  - Neoplasia

Degree of WBC Response in Several Species

<table>
<thead>
<tr>
<th>Species</th>
<th>Neut/Lym Ratio</th>
<th>Leukopenia (x10^9/L)</th>
<th>Leukocytosis (x10^9/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>dog</td>
<td></td>
<td>Mild</td>
<td>Moderate</td>
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<tr>
<td>cat</td>
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<td></td>
<td></td>
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<tr>
<td>horse</td>
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<td></td>
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<tr>
<td>cattle</td>
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<tr>
<td>LEUKOCYTE RESPONSES IN DOGS AND CATS</td>
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<table>
<thead>
<tr>
<th>Epinephrine induced</th>
<th>WBC Seg</th>
<th>Band</th>
<th>Lymph</th>
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<tr>
<td>↑</td>
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<table>
<thead>
<tr>
<th>Glucocorticoids</th>
<th>WBC Seg</th>
<th>Band</th>
<th>Lymph</th>
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<table>
<thead>
<tr>
<th>Acute Inflammation</th>
<th>WBC Seg</th>
<th>Band</th>
<th>Lymph</th>
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<table>
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<tr>
<th>Chronic Inflammation</th>
<th>WBC Seg</th>
<th>Band</th>
<th>Lymph</th>
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<table>
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<tr>
<th>Overwhelming</th>
<th>WBC Seg</th>
<th>Band</th>
<th>Lymph</th>
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<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
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↑ = increased, ↓ = decreased, - = no change, ↑/- = variable