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Melbourne Veterinary School

Veterinary Bioscience: Cells to Systems
Role of blood and blood cells in homeostasis

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VETS30015 / VETS90121

Intended Learning Outcomes

At the end of this lecture you should be able to:

- Describe the components of blood (cells, ions, proteins, platelets) giving their normal values
- Describe the main functions of blood in homeostasis of the body
- Identify the cells in blood and their species variations
- Discuss the normal balance of blood cell turnover and how this enables an animal to respond to infection

Components of Blood

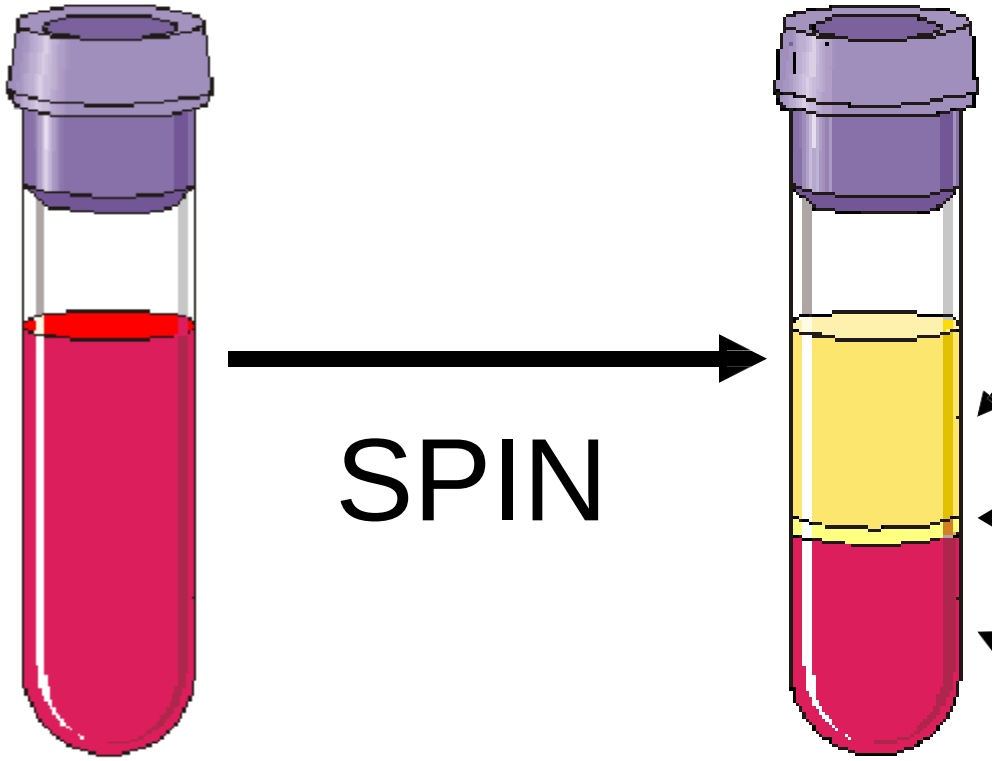
- Blood is a specialised body fluid with 4 main components
  - Plasma
  - Red blood cells (erythrocytes, RBC)
  - White blood cells (leukocytes, WBC)
  - Platelets

Plasma accounts for ~55% of blood volume

Cells account for ~45% of blood volume

- Plasma components
  - Water (~90%)
  - Ions/Salts e.g. Na, Cl, K, HCO3, PO4
  - Protein - albumin, globulins e.g. antibodies, clotting proteins e.g. fibrinogen, hormones
  - Nutrients e.g. glucose
  - Enzymes
  - Waste products e.g. urea
  - Dissolved gases e.g. O2, CO2

Components of Blood



SPIN

Blood sample
with anti-coagulant
e.g. EDTA, Heparin

PLASMA ~ 55% of total blood volume

BUFFY COAT Leukocytes (WBCs) ~ $8x10^9$/L and Platelets (~ $250x10^9$/L)

RED BLOOD CELLS (RBCS)
45% (~ $5x10^{12}$ /L)

Plasma versus Serum

Plasma = Serum + coagulation factors (including fibrinogen)

Plasma collection tubes

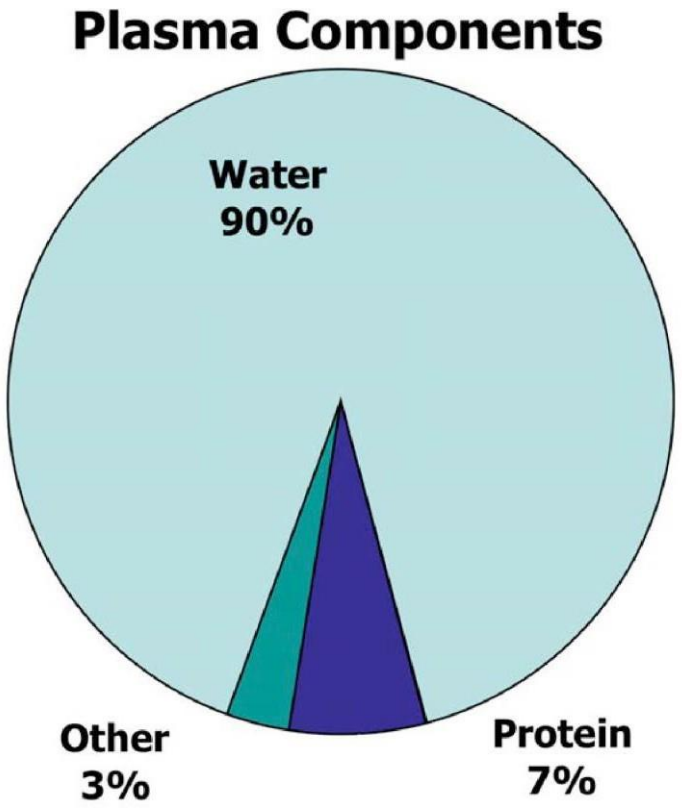
Heparin EDTA

Serum collection tubes

SST, gel separation tubes, plain

Components of Plasma

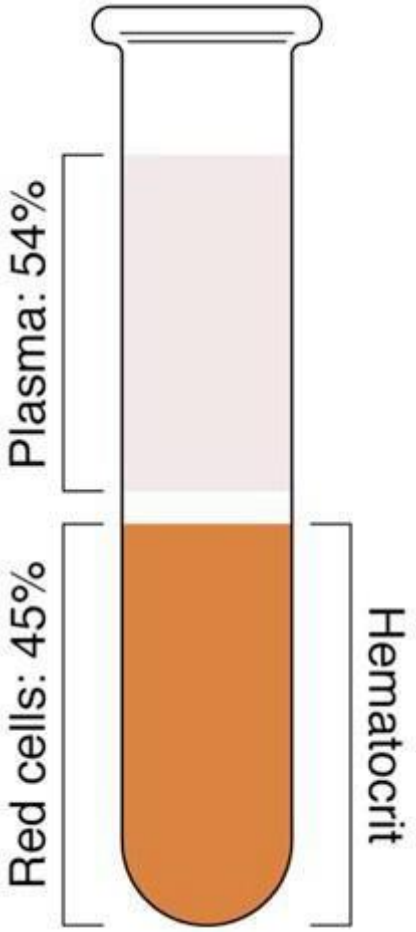
- 90-92% water
- 6-7% proteins
  - Albumin – colloid osmotic pressure
  - Globulin – enzymes, antibodies
  - Fibrinogen – polymerizes into fibrin during coagulation or clot formation
- 2-3% other
  - Fats
  - Carbohydrates (glucose)
  - Electrolytes
    - » Bicarbonate, calcium, chloride, magnesium, phosphorus, potassium, sodium
  - Gases (O_2, CO_2)
  - Chemical messengers



Laboratory analysis of blood cells

- Red blood cell count (RBC)
- White blood cell count
  - Differential counts
- Platelets
- Haematocrit (Hct) or PCV
- Haemoglobin (Hb)
- Hct, RBC count and Hb should be proportional

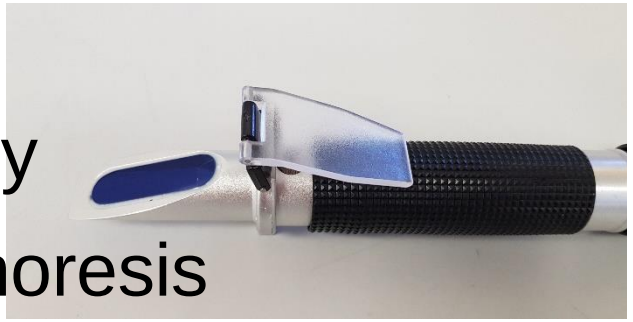
  Plasma levels change due to other factors
  - » Dehydration – can mask anaemia
  - » Increased fluid in pregnancy – can mimic anaemia



Laboratory analysis of plasma

Protein

- Total protein – refractometer or biochemistry
- Albumin – biochemistry or protein electrophoresis



- Globulins

Electrolytes

- Na, K, Cl, HCO_3 – ion specific electrode or biochemical method

Enzymes – biochemical methods

Lipids – triglycerides, cholesterol – biochemistry

Glucose – glucometer or biochemistry

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Clinical laboratory analysis of blood

Haematology		Results	Reference Values
Red cell count	x 10^{12}/L	6.9	5.5 – 8.5
Haemoglobin	g/L	154	120 – 180
PCV	L/L	0.43	0.37 – 0.55
MCV	fL	63	60 - 75
MCH	pg	22	19 - 24
MCHC	g/L	355	320 - 380
Platelets	x 10^{9}/L	263	200 - 500
White cell count	x 10^{9}/L	15.3	6.0 – 17.0
Neutrophils	x 10^{9}/L	10.6	3.0 – 11.5
Lymphocytes	x 10^{9}/L	3.4	1.0 – 4.8
Monocytes	x 10^{9}/L	1.0	0.2 – 1.4
Eosinophils	x 10^{9}/L	0.3	0.1 – 1.3
Basophils	x 10^{9}/L	0	Rare
NRBC	/100 WBC	0	Rare
Reticulocytes	x 10^{9}/L	40	10 - 110
Refractometer protein	g/L	80	60 - 80

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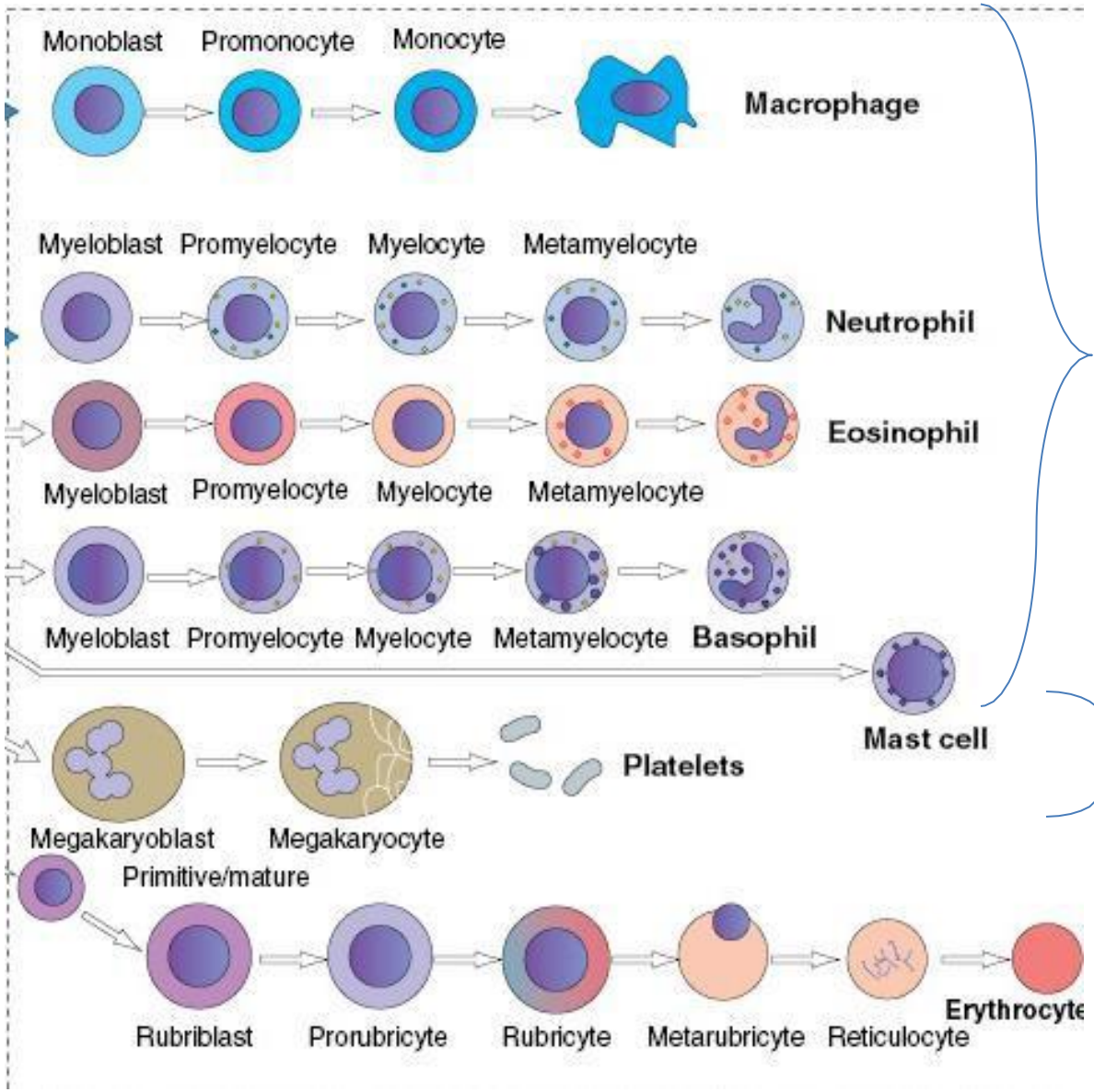
What are Haemopoietic Stem Cells?

- Morphologically indistinguishable from a small lymphocytes
- Multipotent - not pluripotent
  - Can differentiate into any of the mature haemopoietic cell precursors – myeloblastis, monoblasts, rubriblasts, megakaryoblasts
- Rare in bone marrow
  - < 0.2% of haemopoietic cells
- Very potent:
  - as few as 30 cells can repopulate the haemopoietic system of an irradiated mouse
  - One HSC can produce up to 700,000 progeny by clonal expansion

Haematopoiesis – production of blood cells



Leukopoiesis

Thrombopoiesis

Erythropoiesis

Pathologic basis of veterinary disease. Ed JF Zachary and M.D McGavin. Elsevier Mosby 2017

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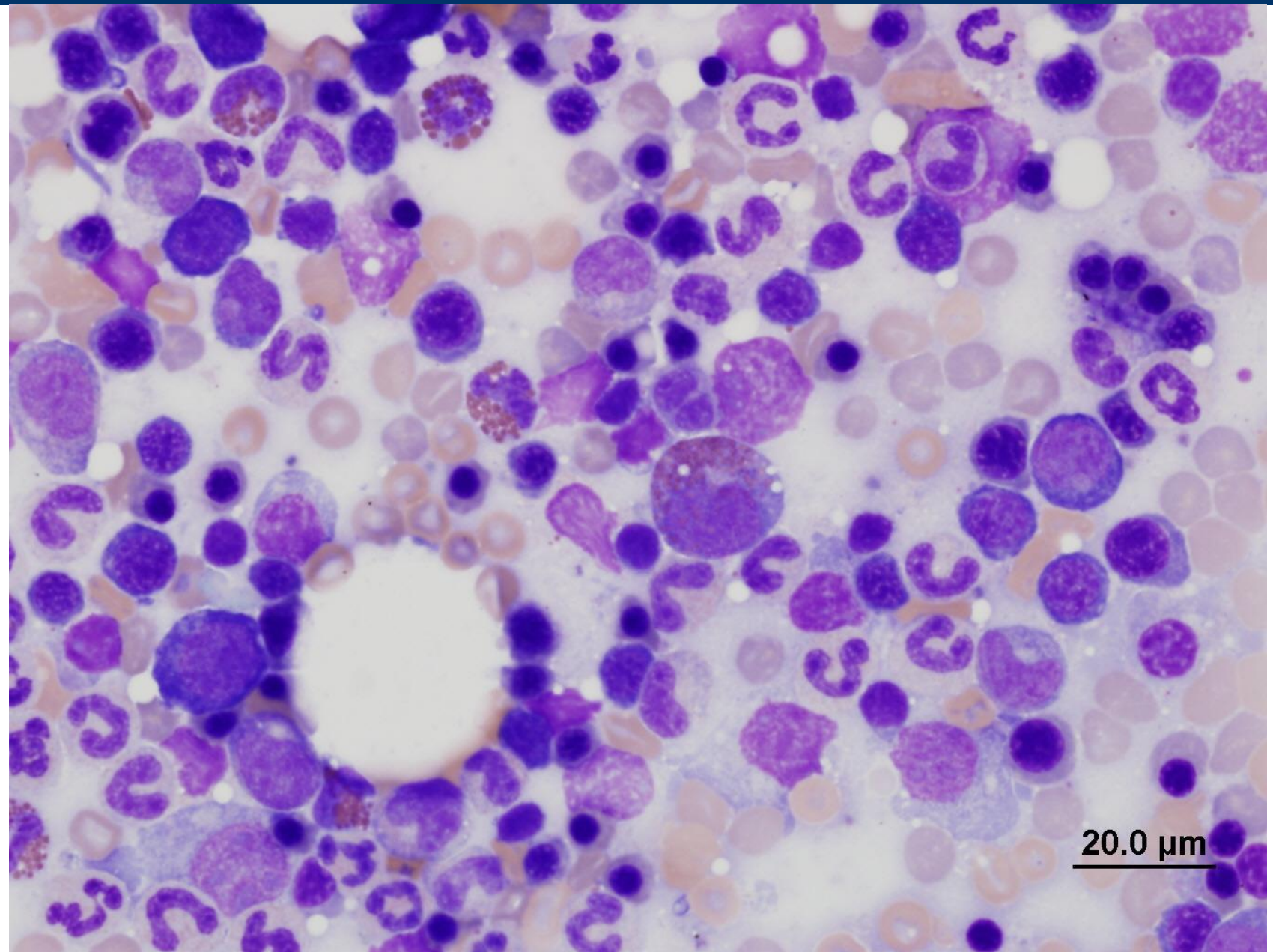
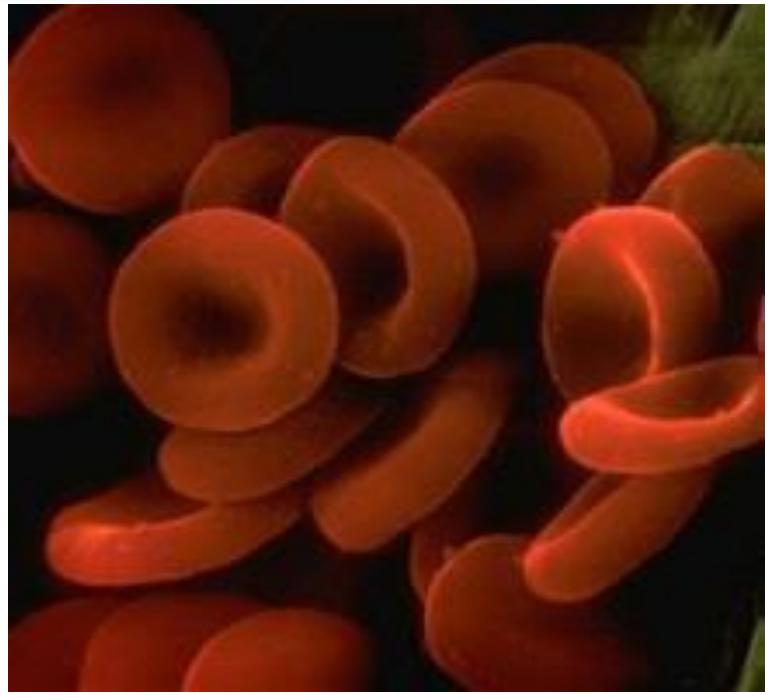
Bone marrow cells



Red blood cell morphology and function



Structure and composition:

- Most common blood cell, 4-10 μm
- Contents - Water (60%) + haemoglobin (40%)
- Biconcave disk – maximises surface area
- Anucleate in mammals, nucleated in birds and reptiles and fish
- Stain eosinophilic (pink)

Ultrastructure:

- homogenous, electron dense
- no organelles in mature mammalian RBC (present in immature RBCs)

Haemoglobin functions - carry O2, CO2 & H+ (buffering role)

Life-span is about 80 d in cats; 100-120 d in dogs & humans; 150 d in horses, cattle & sheep

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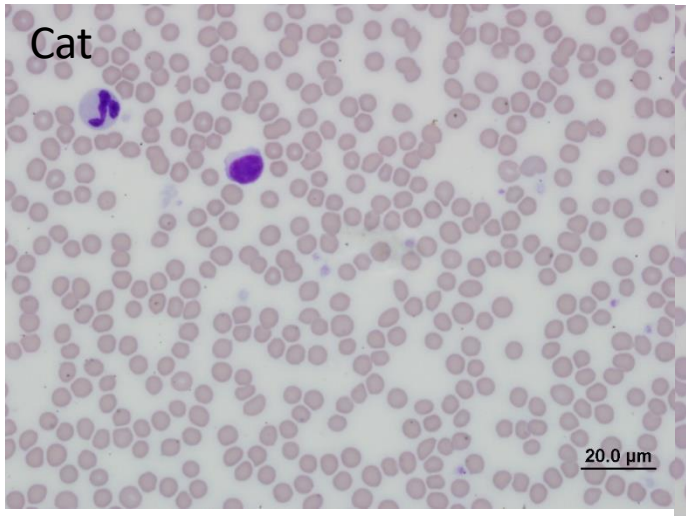
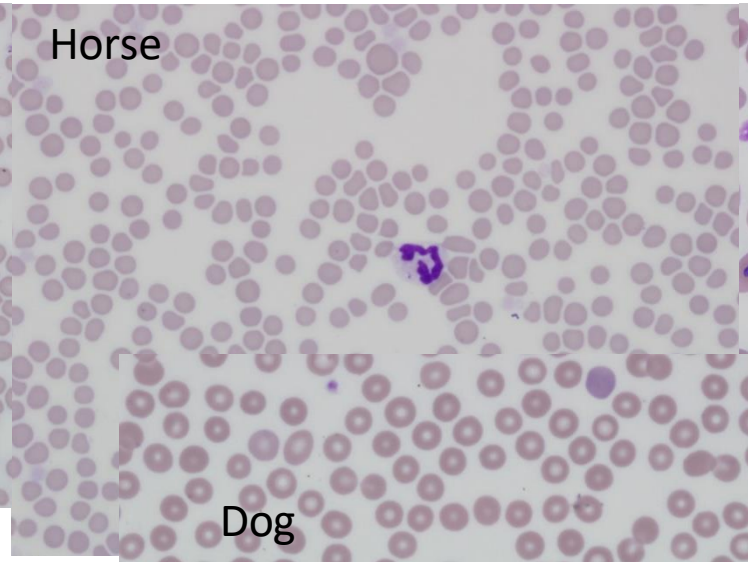
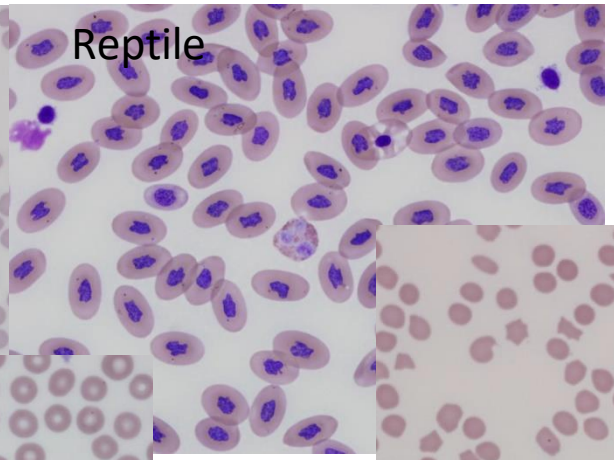
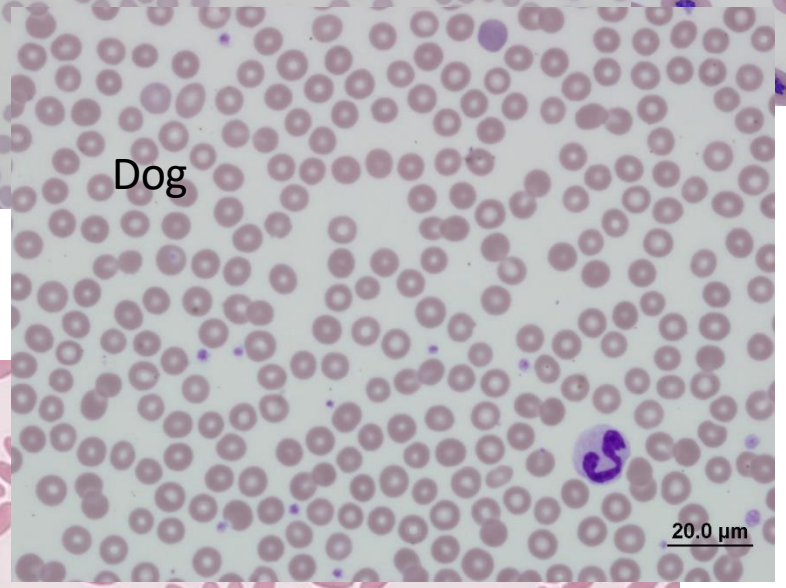
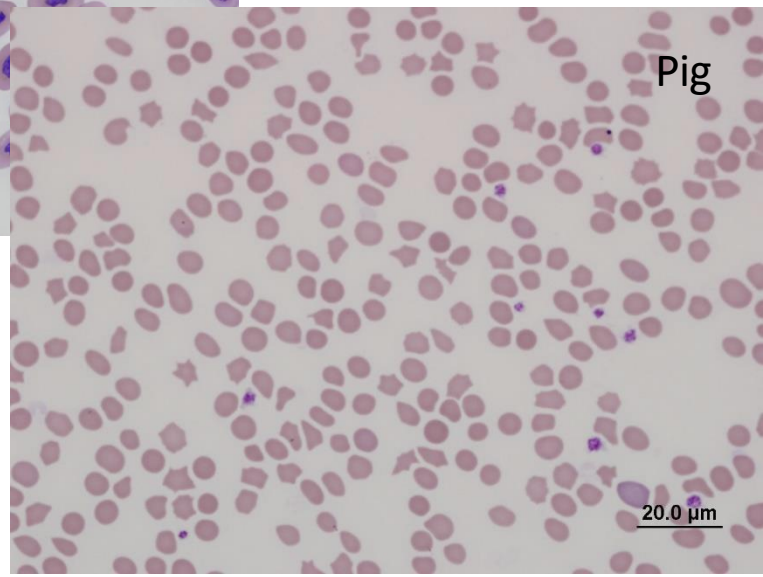
Red Blood Cells – Species Variation

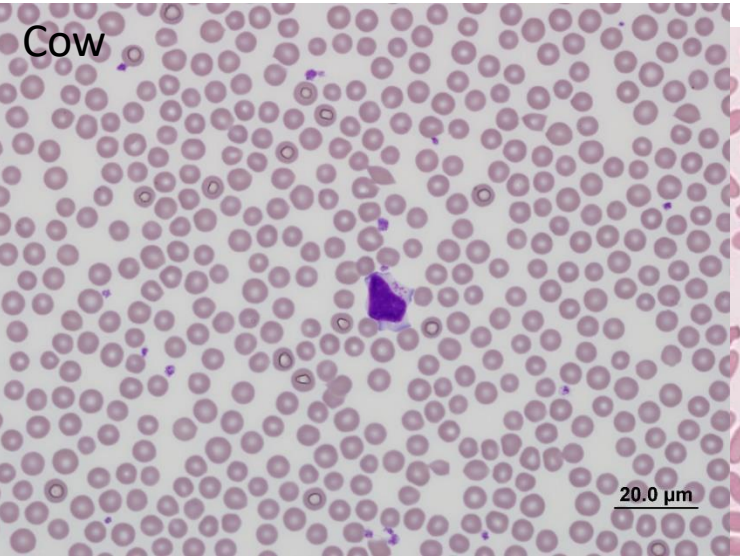


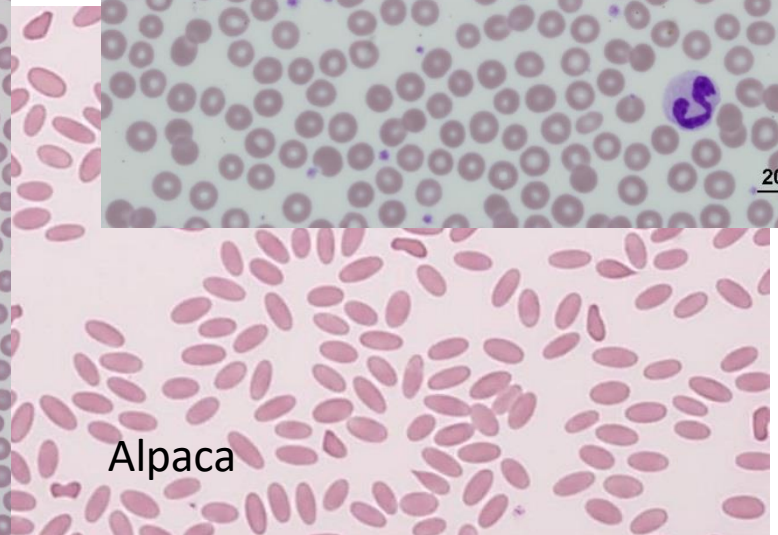


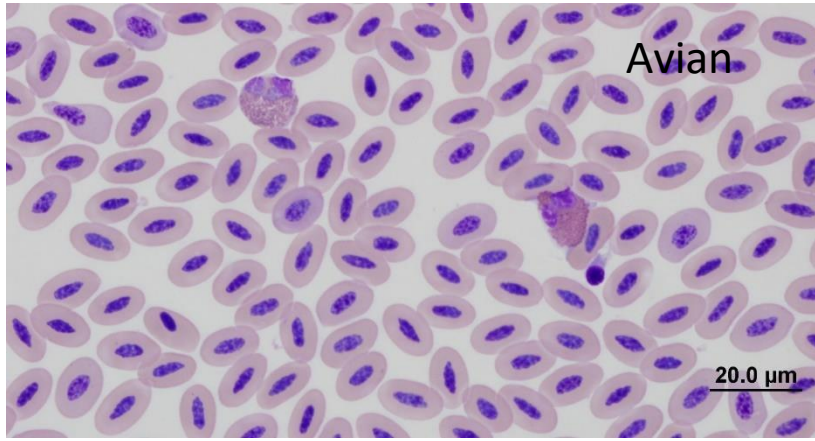












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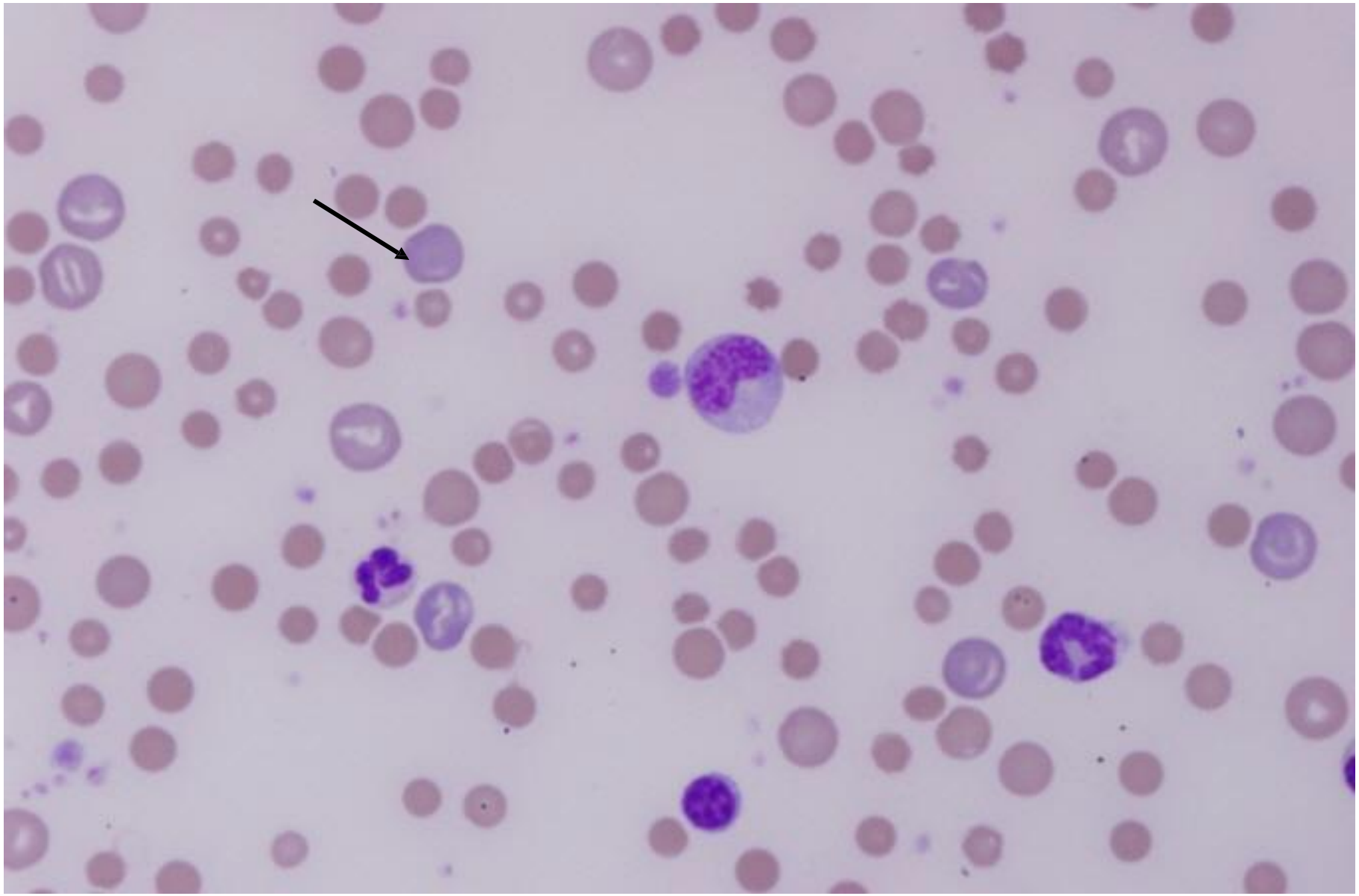
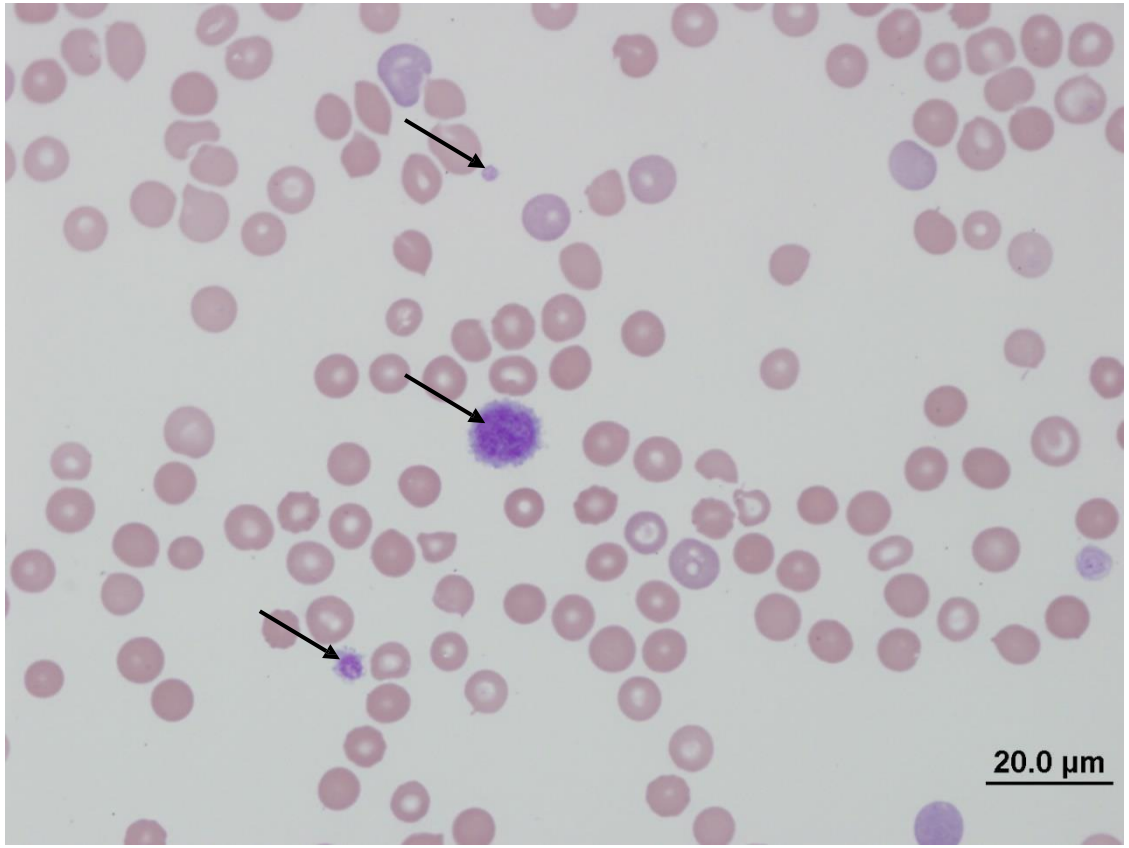
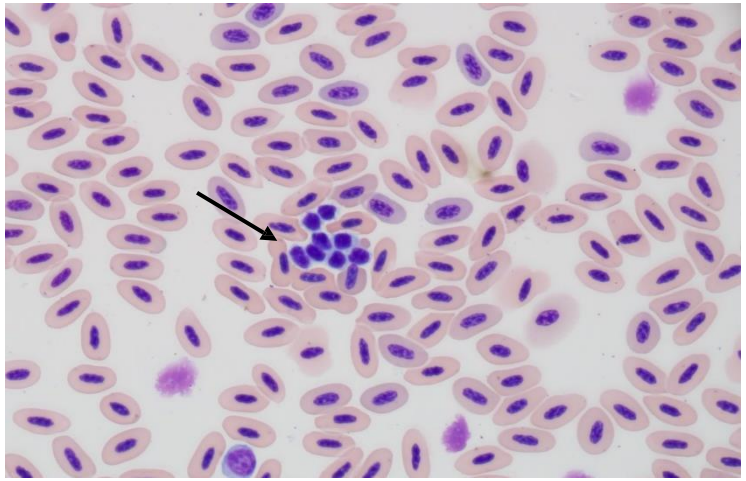
Quick Quiz - What is this cell?



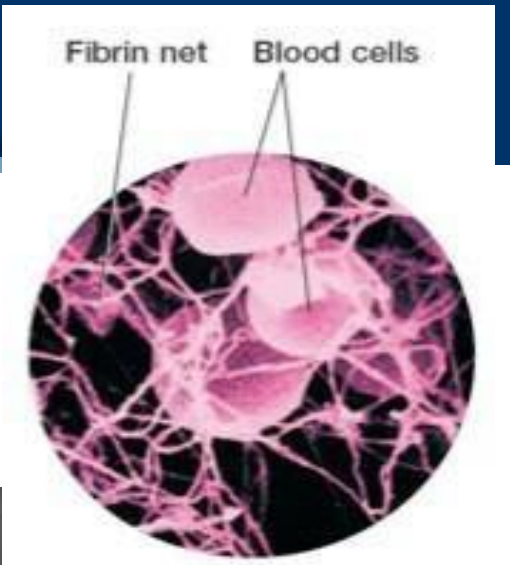
Platelets (thrombocytes) – Species Variation

- Small, round to ovoid bodies in mammals, nucleated in birds (thrombocytes)
- Cytoplasmic pieces ‘budded off’ from megakaryocyte
- ~ 2 μm diameter, disc shaped
- Produced in bone marrow
- Lifespan 8-10 days (sequestered in the spleen)

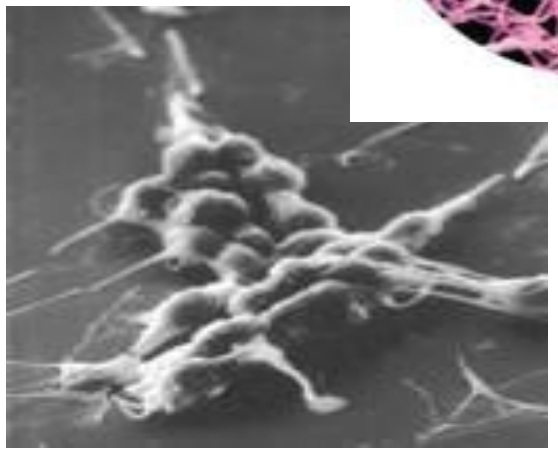




Platelet function



- Blood clotting
  - Aggregation – platelet adherence
  - Coagulation – fibrin formation

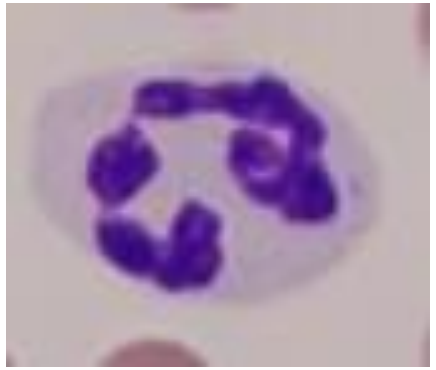


- Aggregation – associated with endothelial cell injury; formation of platelet plug
- Coagulation – initiated at larger sites of injury;

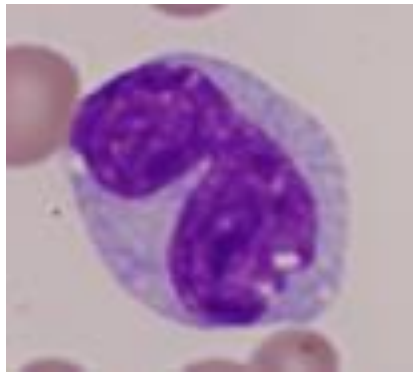
  formation of a clot (thrombus)
- Clotting is tightly regulated

White Blood Cells - Leukocytes

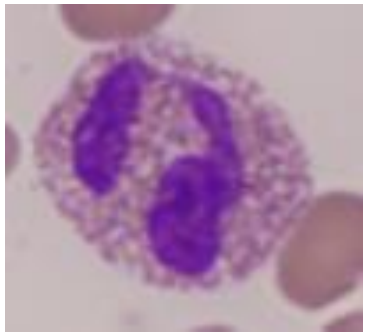
Neutrophils



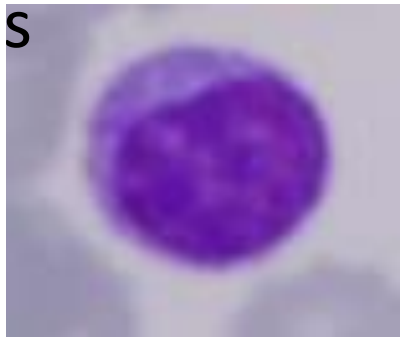
Monocytes



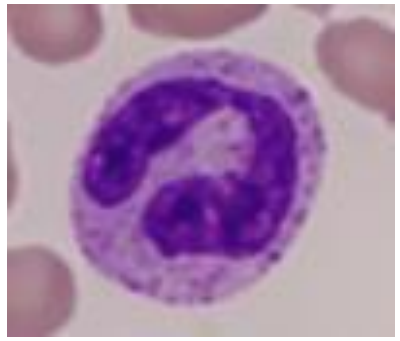
Eosinophils



Lymphocytes



Basophils

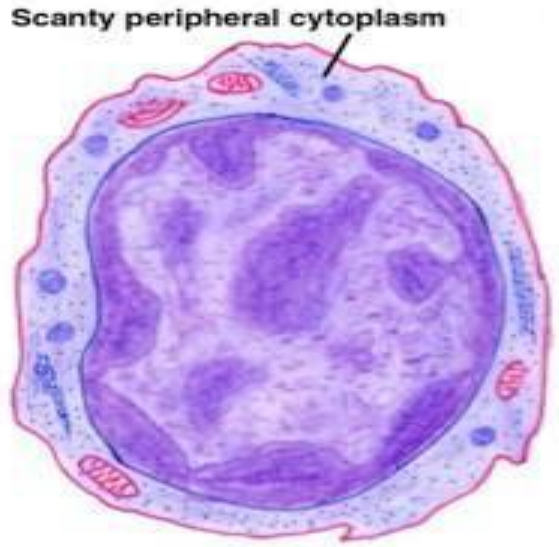


Leukocyte classification:

- 5 main types of WBC
- Granulocytes
  - Neutrophils
  - Eosinophils
  - Basophils
- Monocytes
- Lymphocytes

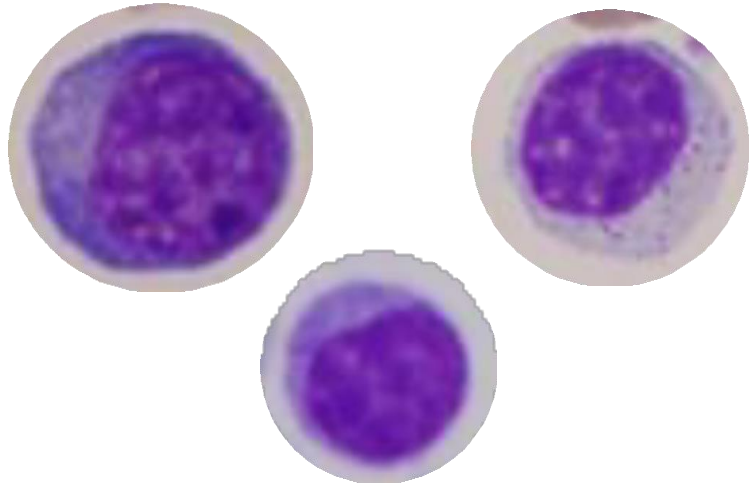
Lymphocytes

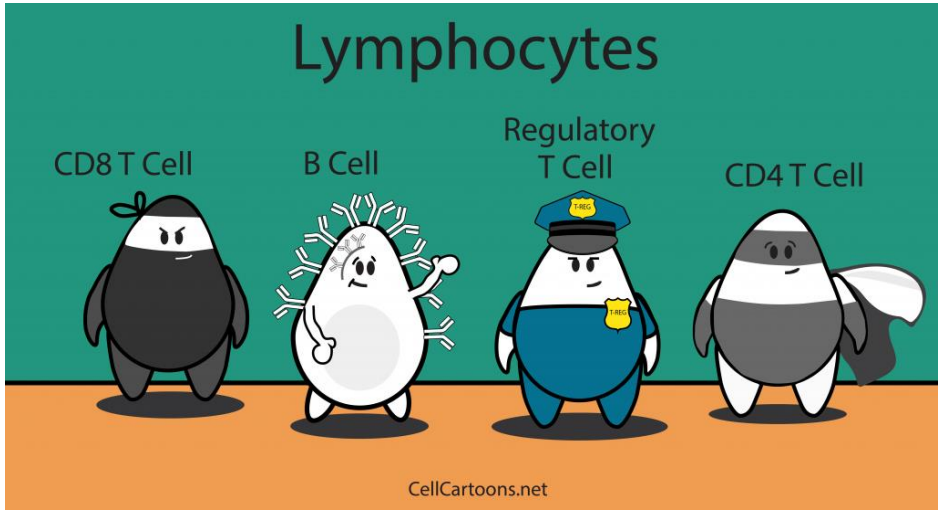
- Most are small (~92%) size 7-8 μm
- Less intermediate and large (~8%) size 9-20 μm
- Round to indented nuclei, clumped chromatin, small rim of blue cytoplasm, some have granules
- Long life span – weeks to years
- Produced in thymus, bone marrow and lymphoid tissue



Lymphocyte Functions

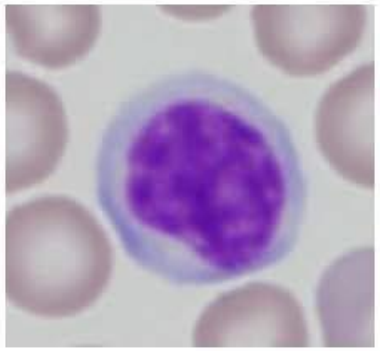
- Antibody production (humoral immune response - B lymphocytes
- Regulate immune response - Helper T cells (CD4+)
- Cytotoxicity (contain cytotoxic granules)
  - T cells (CD8+)
  - NK cells



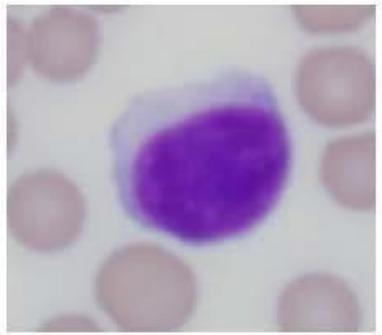


Lymphocytes

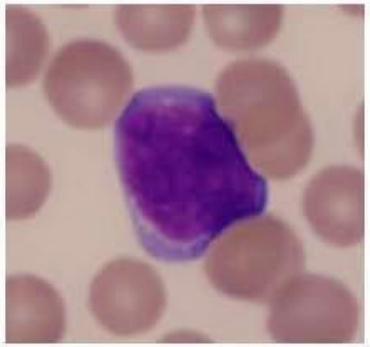
Dog



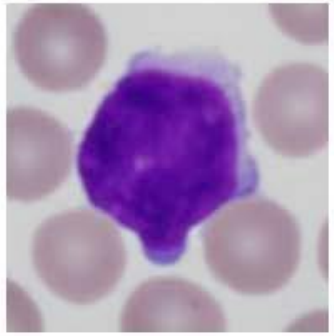
Cat



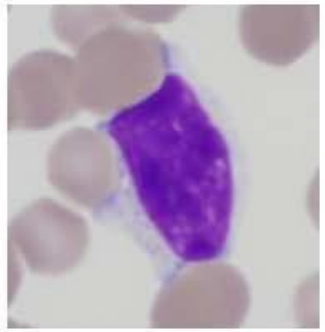
Cow



Sheep

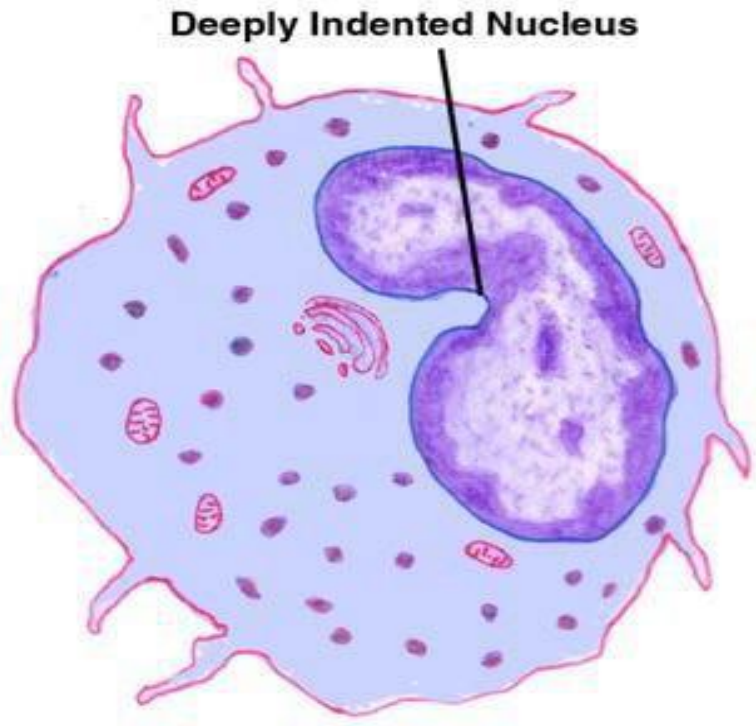


Horse



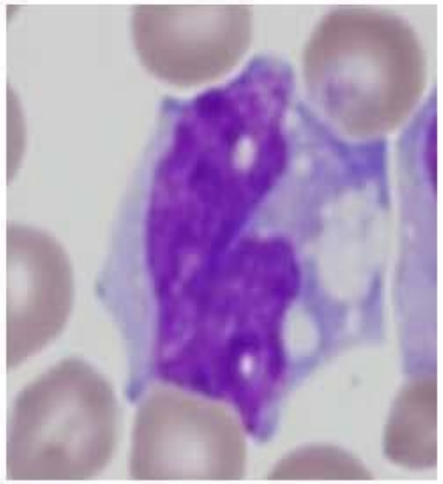
Monocytes

- Size 15-25 μm (largest leukocyte)
- Round/oval/bean-shaped/trilobed nuclei of clumped chromatin
- Abundant blue cytoplasm, may contain vacuoles
- Phagocytic
- Numbers are elevated during chronic bacterial infections & protozoan infections
- Life-span is 20-40h in blood
- Macrophage precursors

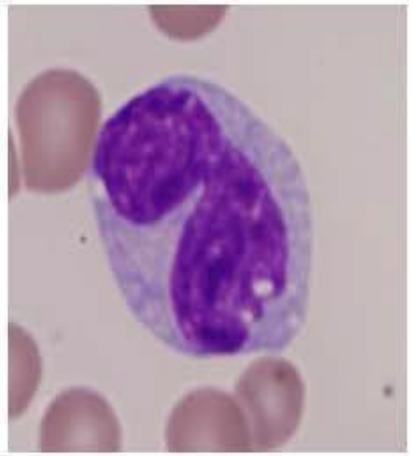


Monocytes

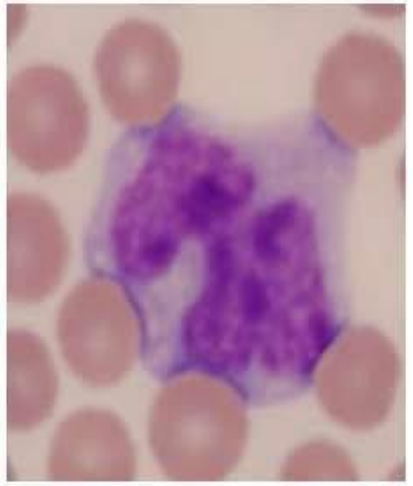
Dog



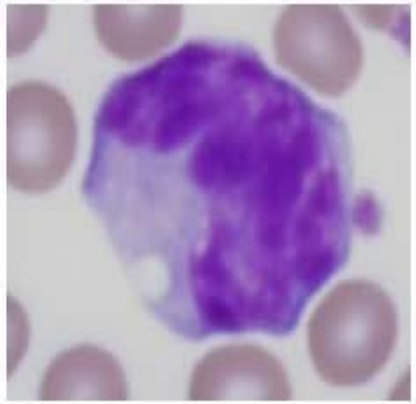
Cat



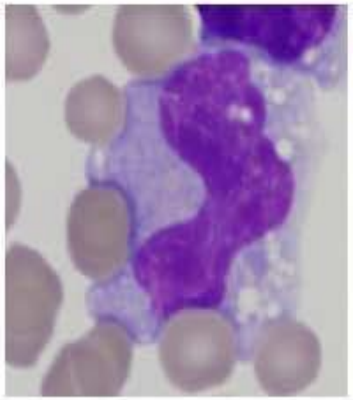
Cow



Sheep

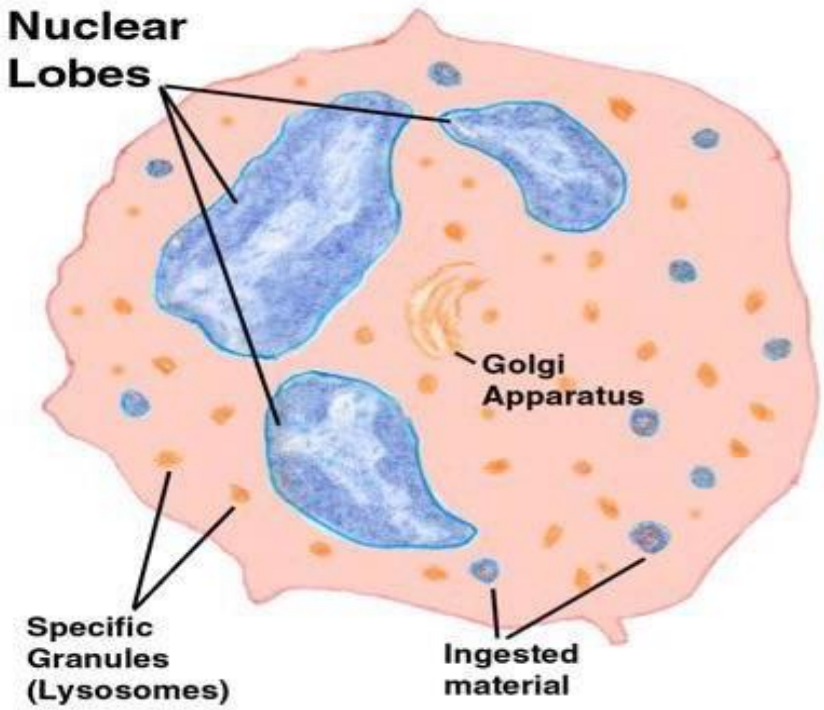


Horse



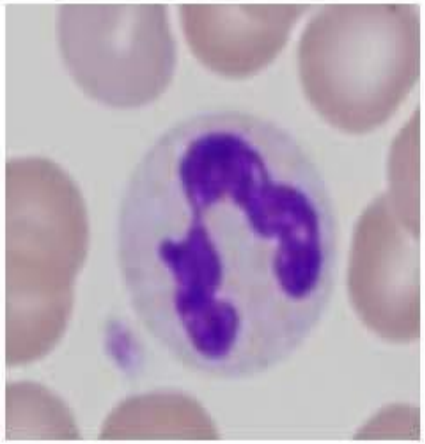
Granulocytes - Neutrophils

- Size 10-12 μm
- Multi-lobed nucleus (polymorphonuclear)
- Clear cytoplasm with clear granules in most species
- Pale pink granules in some species e.g. rabbits, primates, avian, reptiles) - heterophils
- Form first line of defence against microbial infection
- Life-span is 4-12h in blood & 1-2 days in tissues
- Produced in bone marrow in adults
- Numbers are elevated during bacterial infections

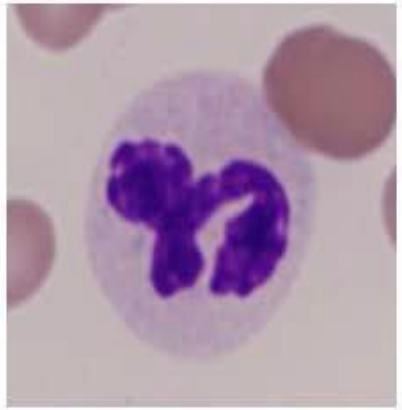


Neutrophils

Dog

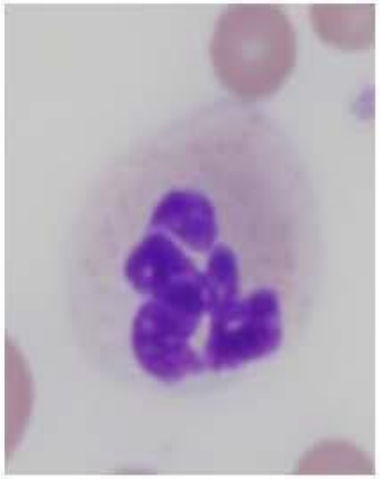


Cat



Cow

Sheep



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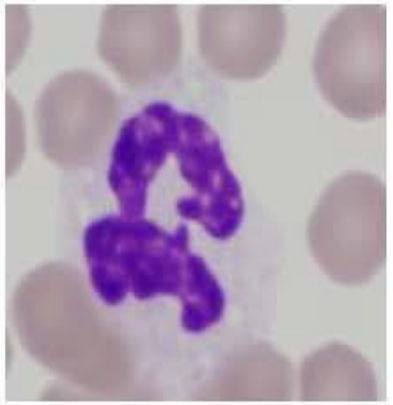
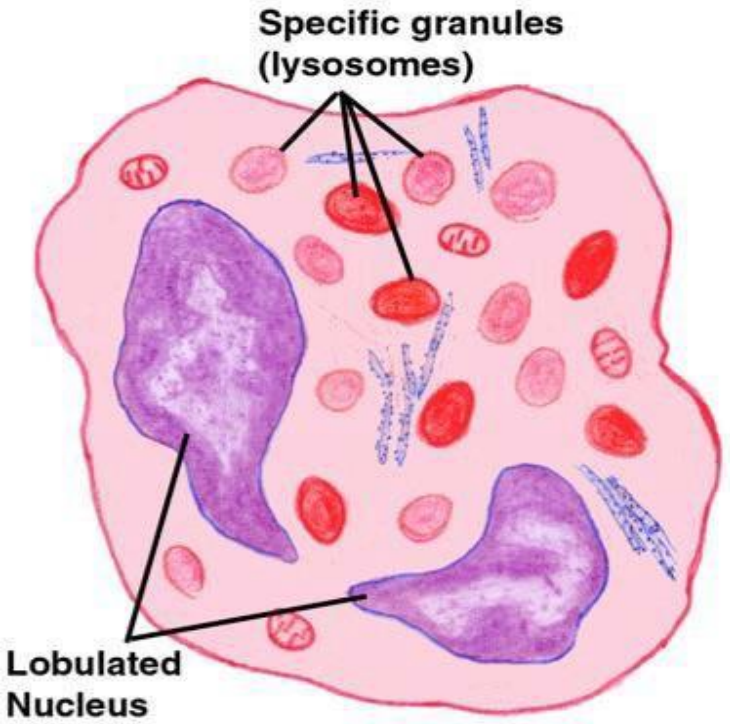


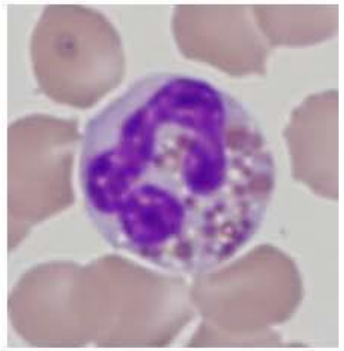
Granulocytes - Eosinophils

- Size 10-15 μm
- Contain coarse red round cytoplasmic granules in most species, rod shaped in cats. Some parrots have pale blue granules
- Multi-lobed nucleus (polymorphonuclear)
- Life-span is 6-12h in blood & 2-3 days in tissues if not stimulated
- Eosinophil function
  - Major role in controlling parasitic infestation
  - Possible roles against bacterial and viral infections
  - Role in allergic responses

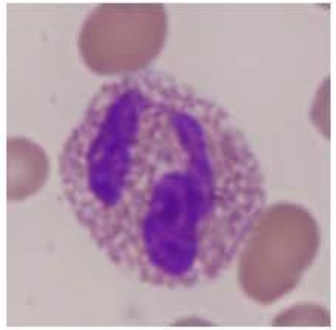


Eosinophils

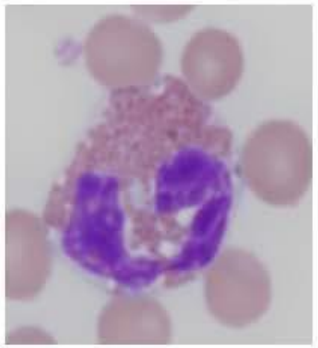
Dog



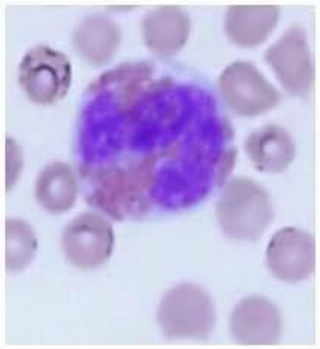
Cat



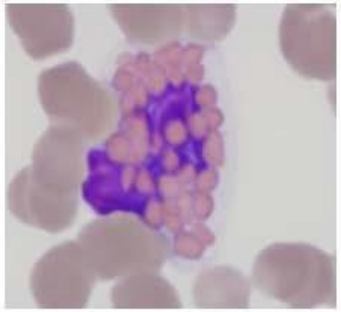
Cow

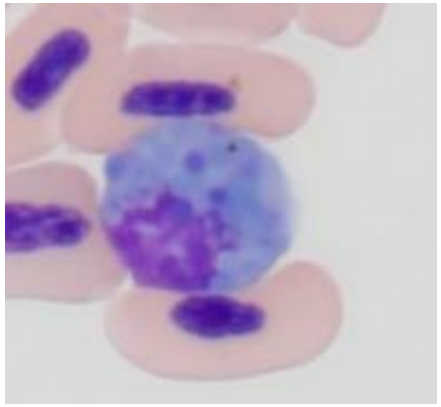


Sheep



Horse

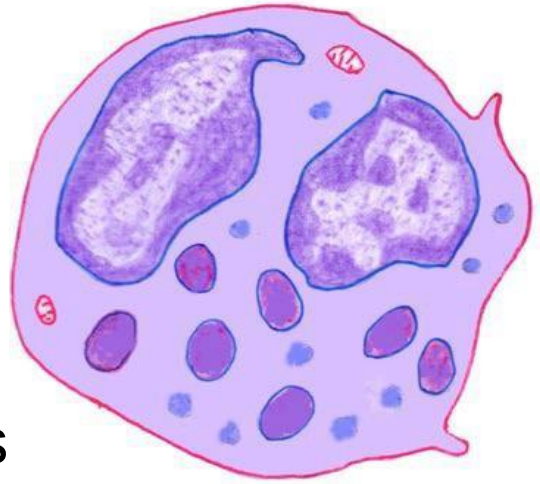




African Grey Parrot

Granulocytes - Basophils

- Basophil size 10-12 μm
- Segmented nucleus in mammals, round nucleus in birds and reptiles
- Coarse round dark purple cytoplasmic granules contain histamine, heparin, serotonin, hyaluronic acid, hydrolytic enzymes, chemotactic factors. Lavender oval granules in cats
- Produced in bone marrow in adults

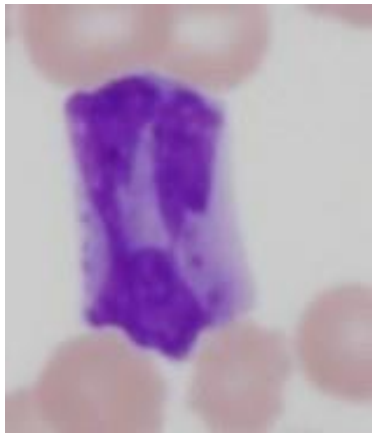


Functions:

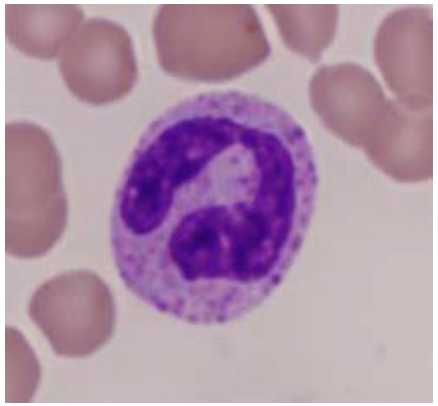
- Major role in allergic and inflammatory actions
- Surface receptors for IgE
- Limited phagocytic and bactericidal activity
- Predominant source of IL-4 and IL-13 in allergic disease

Granulocytes - Basophils

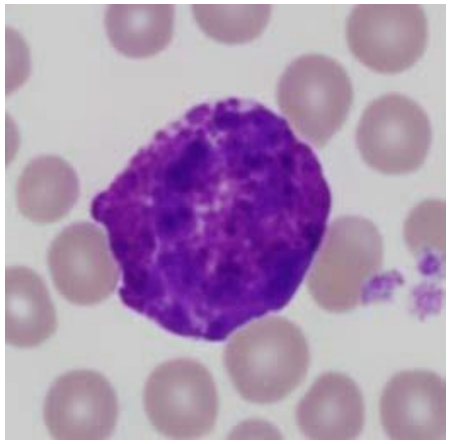
Dog



Cat

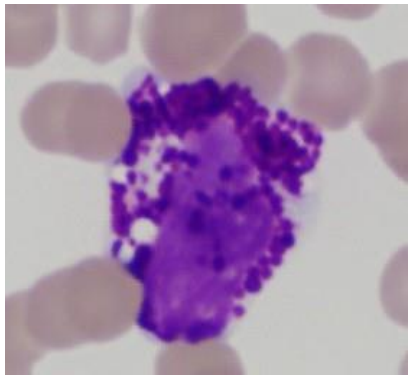


Cow



Sheep

Horse



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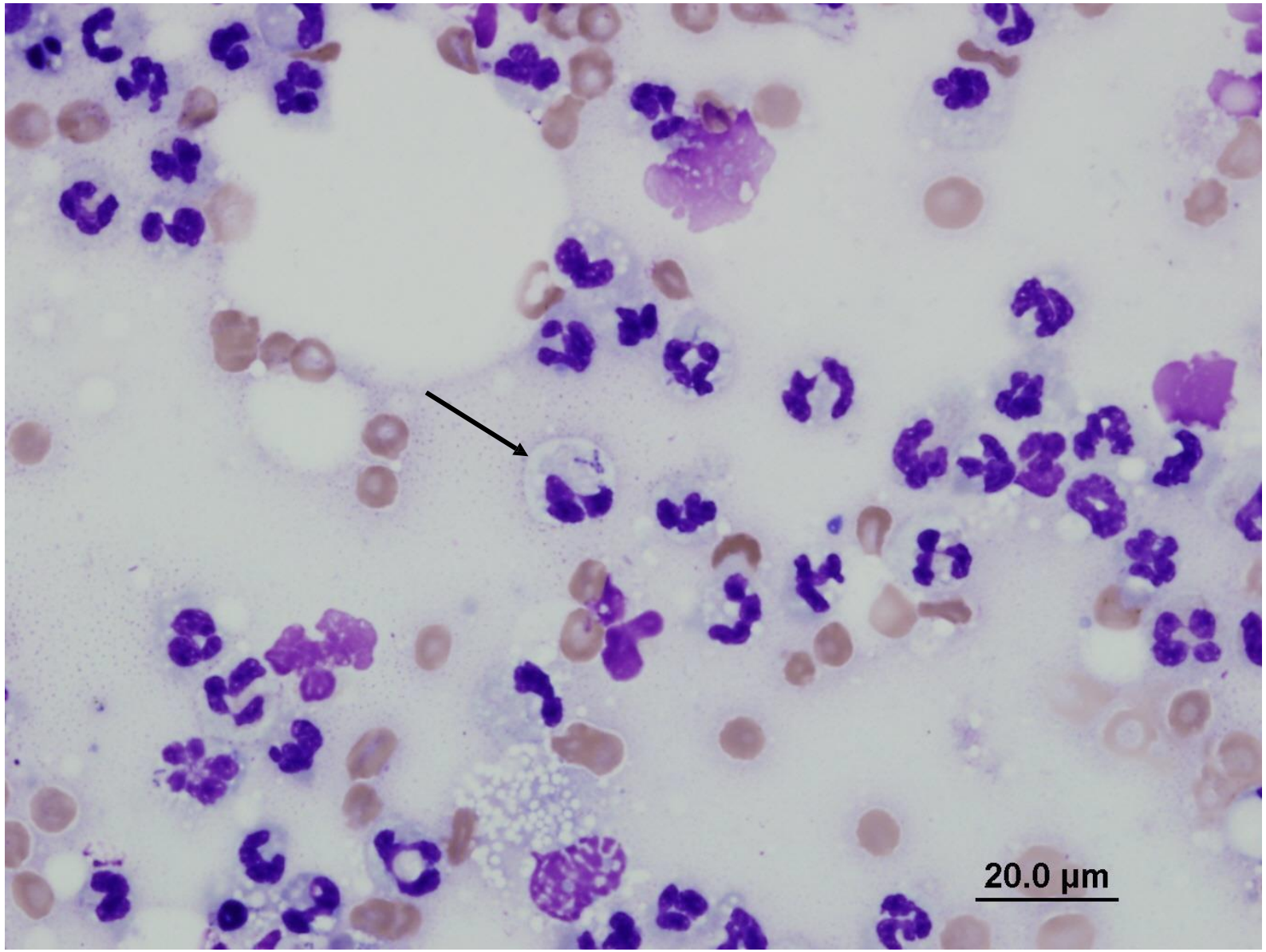
Quick Quiz - What is this cell?



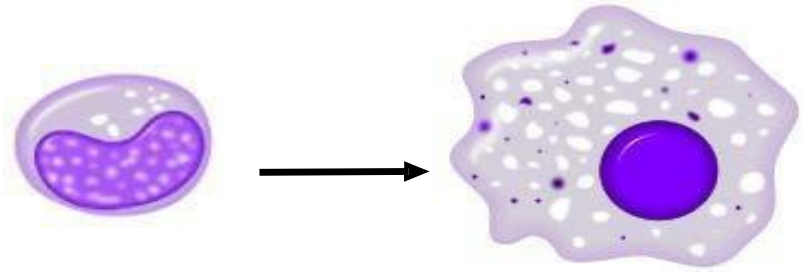
Tissue Leukocytes – Histiocytes

Macrophages:

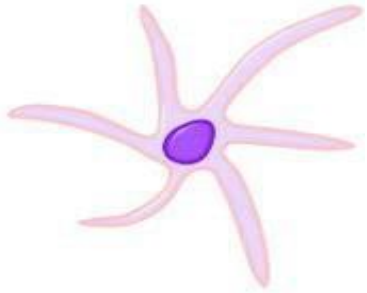
- Highly phagocytic - ingest and kill microbes
- Clearance of damaged dying cells
- Antigen presenting cells (APC) – initiate immune response
- Produce cytokines – signalling and amplification of immune response

Dendritic cells:

- Arise from common dendritic cell precursor. Two forms - classical DC and plasmacytoid DC
- APC - activate T cells
- Present in tissues that are in contact with the external environment (skin, intestines)



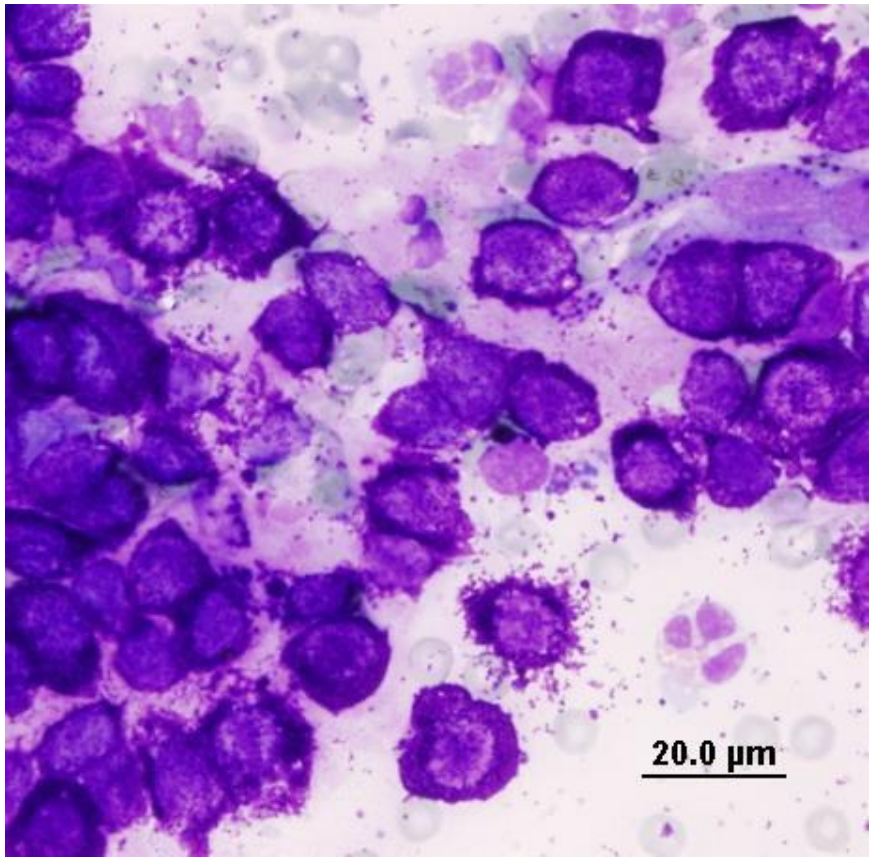
monocyte macrophage



dendritic cell

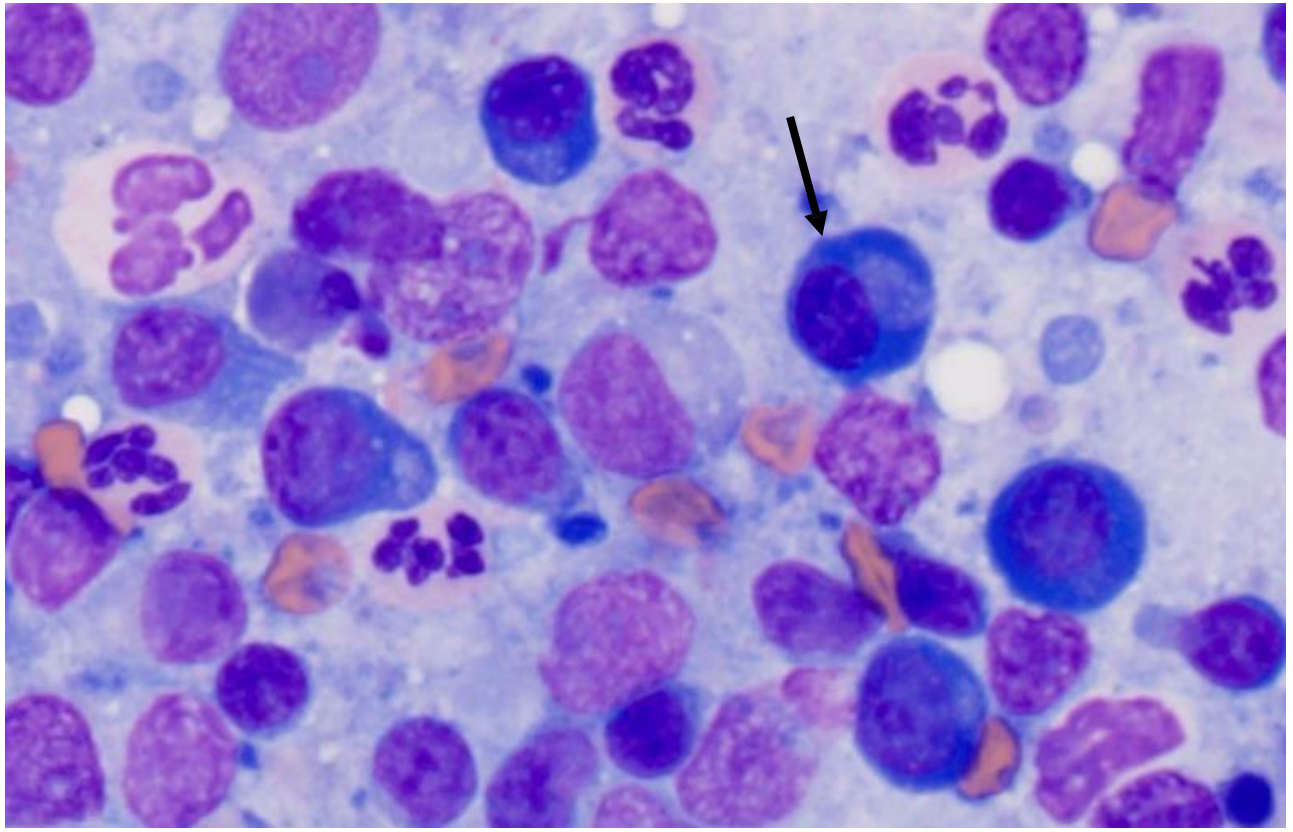
Tissue Leukocytes – Mast Cells

- Round cells with eccentric round nuclei containing abundant purple granules
- Contain histamine, heparin, serotonin, hyaluronic acid, hydrolytic enzymes, chemotactic factors (similar to basophils)
- Attract eosinophils to tissue
- Not usually found in blood – can be seen in blood with neoplasia (mast cell tumours) and in low numbers in dogs with marked inflammation e.g. pancreatitis.

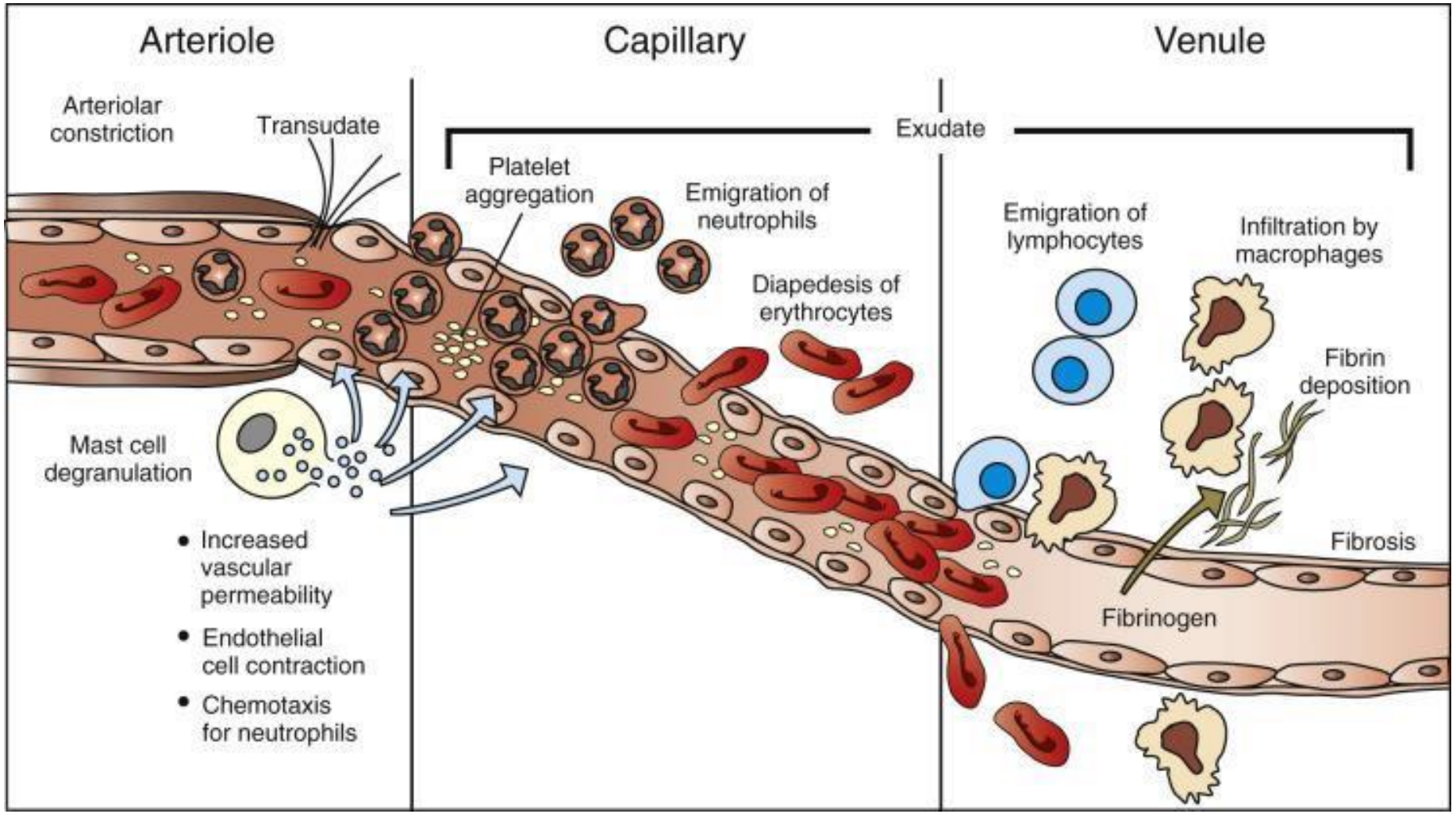


Tissue Leukocytes – Plasma Cells

- Round cells with eccentric round nuclei and abundant deep blue cytoplasm with a prominent golgi zone
- Differentiate from B lymphocytes
- Produce antibodies
- Not usually seen in blood (but you can see similar looking “activated” lymphocytes

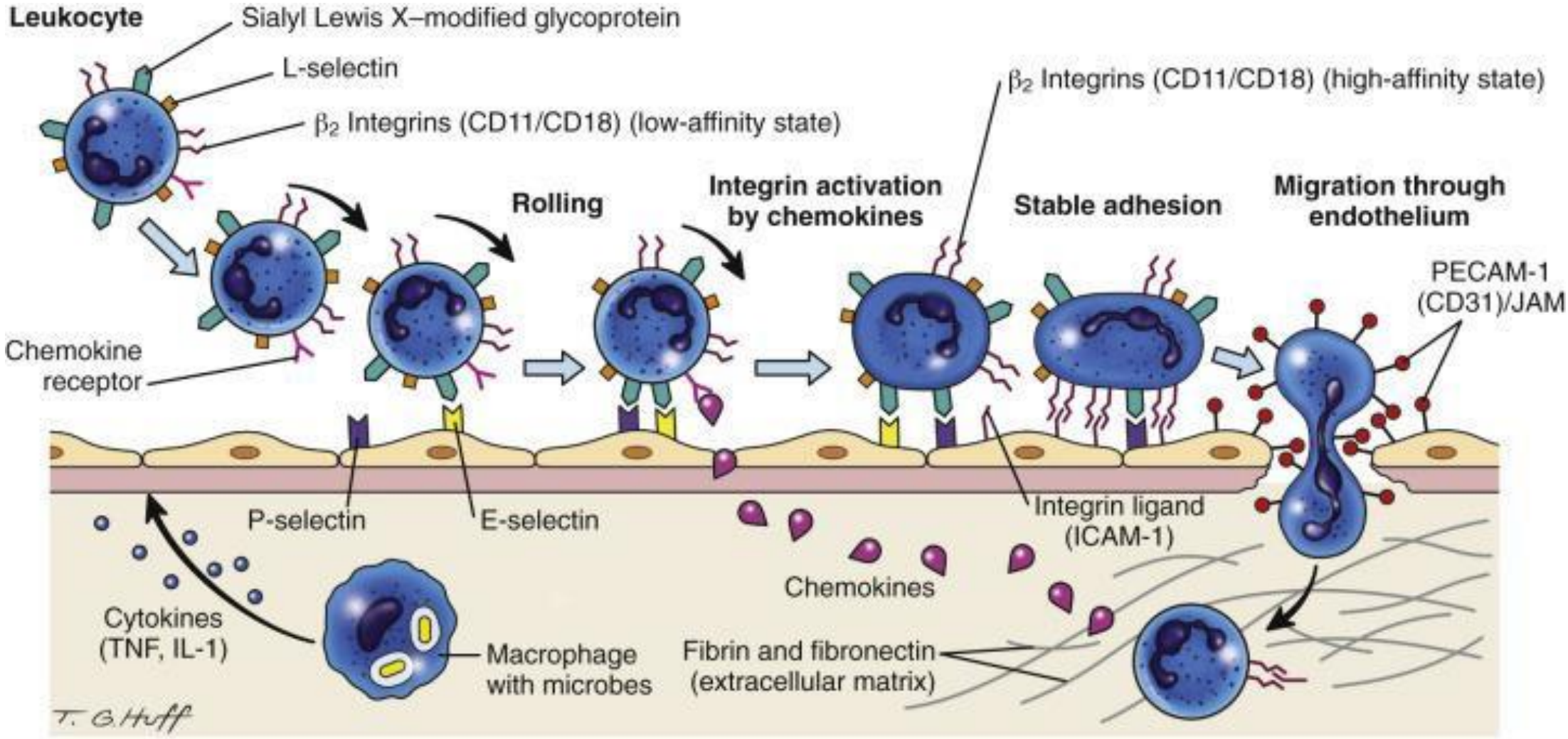


Blood movement into tissues



Pathologic basis of veterinary disease. Ed JF Zachary and M.D McGavin. Elsevier Mosby 2017

Leukocyte migration into tissues

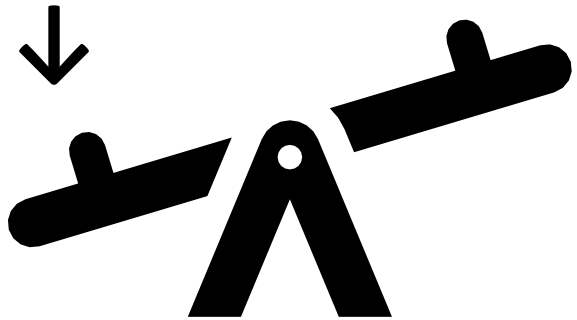


Pathologic basis of veterinary disease. Ed JF Zachary and M.D McGavin. Elsevier Mosby 2017

What causes a change in blood numbers

Factors causing ↓ RBC in blood

- Decreased production e.g. bone marrow disease
- Loss of RBC – haemorrhage or haemolysis



Factors causing ↓ WBC in blood

- Decreased production e.g., bone marrow disease
- Redistribution e.g., into tissues with acute inflammation

Factors causing ↓ Platelets in blood

- Decreased production e.g., bone marrow disease
- Redistribution e.g., spleen

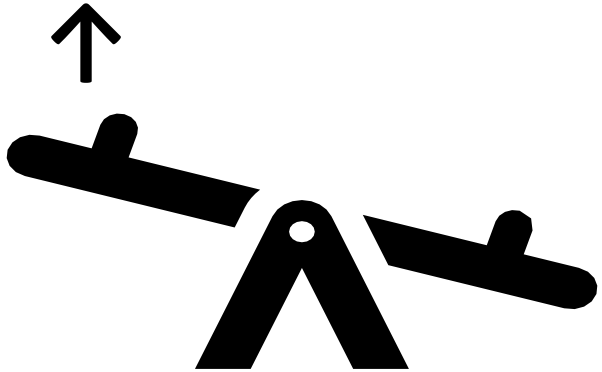
Factors causing ↓ Plasma components in blood

- Reduced plasma volume - loss of water e.g., dehydration due vomiting, diarrhoea (causes ↑Hct ↑ TP)
- Loss of proteins leading to ↓ TP
- Loss of electrolytes ↓ Na, Cl, K e.g., diarrhoea

What causes a change in blood cell numbers

Factors causing ↑ RBC in blood

- Increased production e.g. response to hypoxia
- Reduced water in blood e.g. dehydration



Factors causing ↑ WBC in blood

- Increased production e.g. inflammation
- Redistribution e.g. excitement or stress

Factors causes ↑ Platelets in blood

- Increased production e.g. inflammation
- Redistribution e.g. splenic contraction

Factors causing ↑ Plasma components in blood

- Plasma volume expansion with heart disease
- Gain of electrolytes e.g. salt poisoning
- Increased production of immunoglobulin e.g. inflammation

Quick Quiz….

What changes are expected with dehydration?

A. Increased blood volume

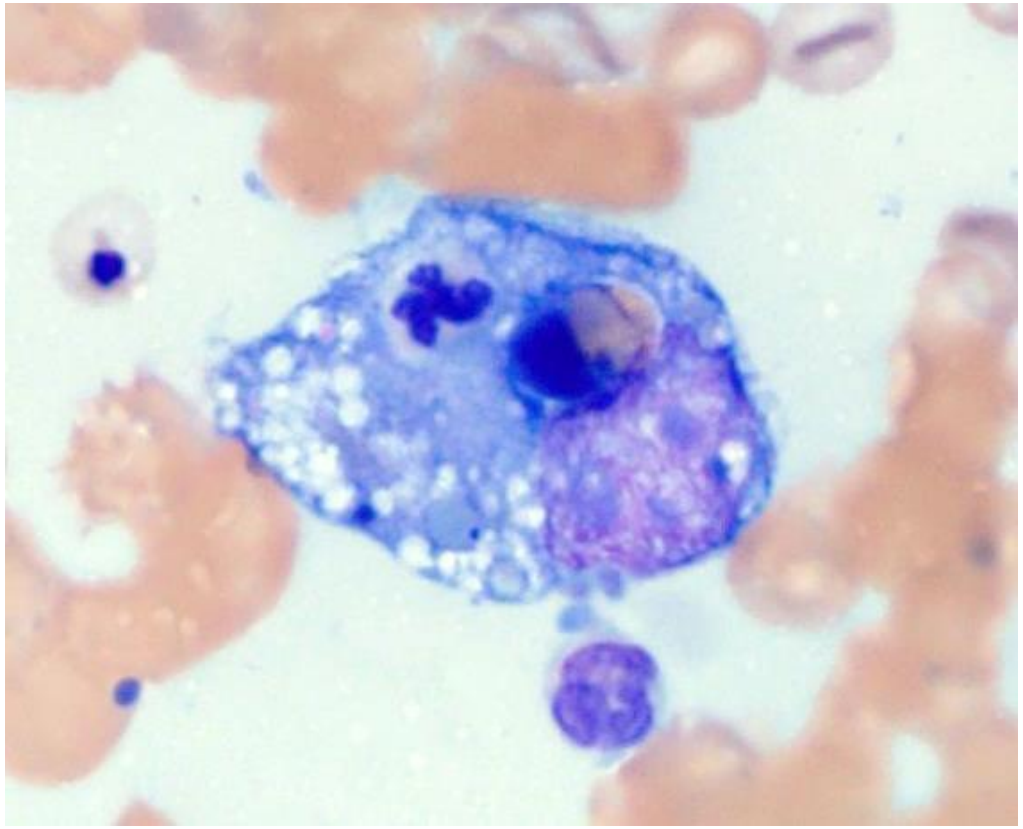
B. Increased Hct and TP

C. Decreased blood volume

D. Decreased Hct and TP

Where do leukocytes go when they die?

- 2-3 x 10^{11} new cells are produced and die each day
- Nucleated cells undergo apoptosis (programmed cell death)
- Removal - phagocytosis by macrophages in spleen, liver, bone marrow, tissue



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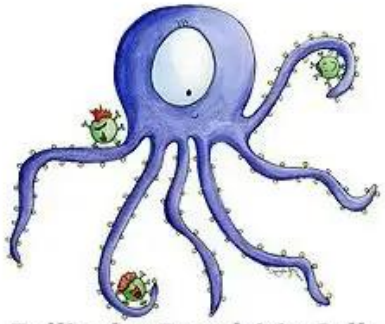
Questions?

NK Cell

Cytotoxic T Cell

Helper T Cell



Follicular Dendritic Cell

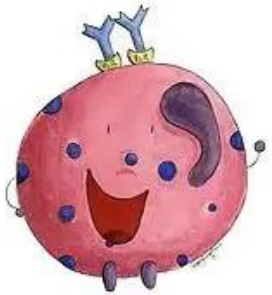
Macrophage

Treg

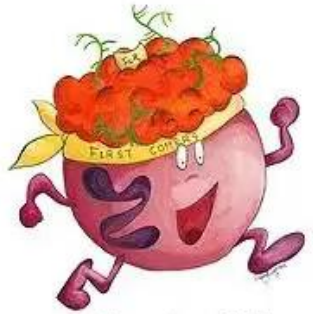
B Cell

Plasma Cell

Mast Cell



Basophil



Neutrophil

Eosinophil