

Physiology Undergraduate League of Students

PHGY 313

01/08/2025

Lecture #: 1
Professor: Dr. Blank

Blood Overview

Learning Aims

Knowledge of

- Principles of blood cells and associated signaling pathways
- Important regulatory proteins in blood cell function and differentiation and how they regulate these cells
- Methodologies of blood cell analysis
- Molecular mechanisms leading to common blood pathologies

Conceptual Understanding

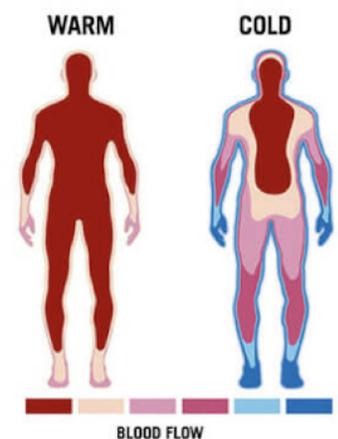
- Integration of knowledge (context of blood physiology)
- Comprehension of underlying hypotheses
- Critical assessment of scientific data/literature

Human Genome by Functions

- Dealing with mostly signaling molecules, cytokines, growth factors, receptors (cells need to be able to respond to signaling molecules), transcription factors (important in regulation of different genes). Human genome by function percentages:
 - Receptors = 6.3%
 - Transcription factors = 12.0%
 - Signaling molecules = 5.6%

Why Study Blood?

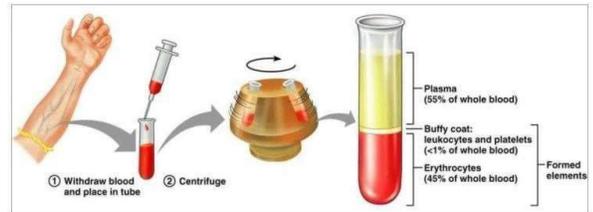
- Removal of waste products – urea, CO₂, lactic acid
- Urea: from the degradation of amino acids
 - Ammonia: converted into urea and transported by the blood to the liver then eventually excreted from the body through the kidney
 - CO₂: consequence of oxygen consumption and cellular metabolism
 - Lactic acid: mostly from muscle metabolism, exercise
- Transport of signaling molecules
 - Hormones and cytokines
- Innate and adaptive immune response
- Blood clotting and wound repair
- Thermoregulation
 - Expanding and contracting blood vessels depending on temperature outside



- Blood restriction in extremities in severe cold to avoid losing much heat since blood is centralized to important organs (sensation of numbness)
 - ie. if it's cold outside your blood will warm your core organs first
- Frostbite – if blood constriction in extremities is too severe, we can lose our limbs

Blood Components

- > 100 billion blood cells produced/day
- Increase ~5-10 fold due to injury or infection
- Healthy adult can donate 500mL of blood
- The average person carries ~5L of blood in total
 - We can centrifuge blood to visualize its layers
- **Plasma:** 55% of whole blood, non-cellular part of the blood; yellow
- **Buffy coat:** <1% of whole blood, leukocytes, and platelets; middle layer.
 - This layer increases during chronic myeloid leukemia (CML), as there is an increase in white blood cells (shown in diagram (right))
- **Erythrocytes (RBCs):** 45% of whole blood



Question: what is the minimal time interval between whole blood donations in Quebec?

Answer: 56 days for males and 84 days for females

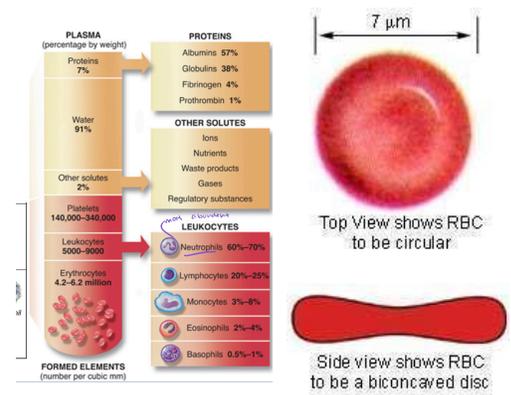
- There are certain restrictions for donating blood like pregnancy, tick bites, cold, sore throat, travel

Normal Hematological Parameters

- Hematocrit: percentage of RBCs in the blood
 - Not clear why females and males have different numbers
 - Females: ~37-46%
 - Males: ~42-52%
- Hemoglobin
 - Female: 12.3-15.7 g/dL
 - Male: 14.0 -17.4 g/dL
 - Normal: ~12-14 g/dL
 - Anemic: 8-9 g/dL
- Blood is made up of different cells:
 - Plasma (percentage by weight)
 - 91% water
 - 7% dissolved proteins (albumins, globulins, fibrinogen, prothrombin)

Parameter	SI Units (Canada)	Traditional Units (USA)
Red Blood Cells		
Erythrocytes (RBC) (MCC 2012)		
Female	4.0 – 5.2 X 10 ¹² /L	4.0 – 5.2 X 10 ⁶ /mm ³
Male	4.4 – 5.7 X 10 ¹² /L	4.4 – 5.7 X 10 ⁶ /mm ³
Reticulocyte Count (MCC 2012)	20-84 X 10 ⁹ /L	0.5 – 2.5%
Hematocrit (MCC 2012)		
Female	0.370 – 0.480	37 – 48%
Male	0.420 – 0.520	42 – 52%
Hemoglobin		
Female	123 – 157 g/L	12.3 – 15.7 g/dL
Male	140 – 174 g/L	14.0 – 17.4 g/dL
Erythrocyte Sedimentation Rate (ESR Westergren) (MCC 2012)		
Female	< 10 mm/h	< 10 mm/h
Male	< 6 mm/h	< 6 mm/h
White Blood Cells (WBC)		
White Blood Cell Count	4.0 – 10.0 X 10 ⁹ /L	4.0 – 10.0 X 10 ³ /mm ³
WBC Differential (MCC 2012)		
Segmented Neutrophils	2 – 7 X 10 ⁹ /L	45 – 75%
Lymphocytes	1.5 – 3.4 X 10 ⁹ /L	16 – 46%
Monocytes	0.14 – 0.86 X 10 ⁹ /L	4 – 11%
Band neutrophils	< 0.7 X 10 ⁹ /L	0 – 5%
Eosinophils	< 0.45 X 10 ⁹ /L	0 – 5%
Basophils	< 0.10 X 10 ⁹ /L	0 – 3%
Coagulation		
Bleeding Time (Ivy) (MCC 2012)	< 9 min	< 9 min
Clothing Time	5 – 15 min	5 – 15 min
Fibrinogen	5.1 – 11.8 µmol/L	175 – 400 mg/dL
International Normalized Ratio (INR) (MCC 2012)		
	0.9 – 1.2	0.9 – 1.2
Plasminogen	75 – 140 %	75 – 140 %
Platelet Count (Thrombocytes) (MCC 2012)	130 – 400 X 10 ⁹ /L	130 – 400 X 10 ³ /mm ³
Prothrombin Time (PT) (MCC 2012)	10 – 13 sec	10 – 13 sec
Partial Thromboplastin Time (PTT) (MCC 2012)	28 – 38 sec	28 – 38 sec
Thrombin Time	14 – 16 sec	14 – 16 sec

- Albumins are the most abundant
- 2% other solutes (ions, nutrients, waste products like lactic acid and urea, gases, regulatory substances)
- Platelets
 - Important for wound repair
 - Leukocytes (neutrophils 60-70%, lymphocytes 20-25%, monocytes 3-6%, eosinophils 2-4%, basophils 0.5-1%)
- Erythrocytes



Blood Components

- Red blood cells (Erythrocytes) ~ $5 \times 10^6 / \text{mm}^3$
 - Most abundant and can be made readily visible by many different stains
 - Oxygen transport (main function)
 - Contain hemoglobin (~65-70% of entire mature RBC)
 - Lack nuclei and most organelles
- Platelets (Thrombocytes) ~ $2.5 \times 10^5 / \text{mm}^3$
 - Blood clotting, coagulation
 - Cell fragments – originating from fragmentation of megakaryocytes
 - 2-3µm in diameter (very small); lack nuclei and most organelles
- White blood cells (Leukocytes) ~ $7 \times 10^3 / \text{mm}^3$
 - Immune and inflammatory response
 - Granulocytes
 - Lymphocytes
 - Different and distinguished based on lobes and cytosolic granules
 - Restricted in number

Cell Types, Characteristics, Size, Life Spans and Functions

Cell Type	Characteristic	Size	Life Span	Function
Erythrocyte	biconcave shape	7 µm	120 days	oxygen transport
Platelet	cell fragments	2-3 µm	7-8 days	blood clotting
Lymphocyte	large round nucleus, no granules	10 µm	5-90 hours (inactive) 24-48 hours (activated)	See below

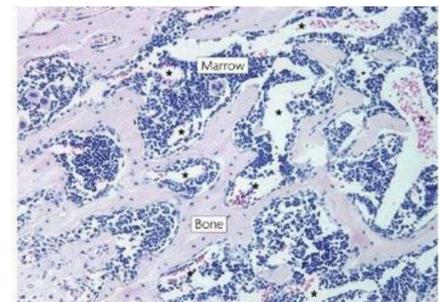
Monocyte	Horseshoe-shaped nucleus, Cytosolic granules	10-25 μm	3 days	host defense, immune surveillance (precursor of tissue macrophage)
Neutrophil	Multi-lobed nucleus, Large number of cytosolic granules	10 μm	5-90 hours (inactive) 24-48 hours (activated)	Host Defence
Eosinophil	Nucleus with 2 lobes, Cytosolic granules	10 μm	8-18 hours	host defense against parasites, allergies
Basophil	Nucleus with 2-3 lobes, Cytosolic granules (lower number)	10 μm	60-70 hours	inflammation and allergy

- T Lymphocyte
 - Variable lifespan depending on type of immunity
 - Function: cellular immunity
- B Lymphocyte
 - Variable lifespan (longer for memory cells, e.g. smallpox specific B cells can last up to 50 years)
 - Function: antibody defenses (precursor of plasma cells)

Note: Nucleus is a good marker for differentiation.

Bone Marrow

- Components
 - Hematopoietic cells (primary site of RBC production)
 - Osteoblasts (make new bone)
 - Osteoclasts (break down bone)
 - Vascular endothelial cells
 - Mesenchymal stem cells
 - Sympathetic neurons
 - Adipocytes (fat cells in bone marrow!)
- A 30-year-old has ~30% bone fat of growing bone marrow, spaces created fill up with adipose tissue
 - Increases through life (older people have more adipose tissue, younger people have less).
 - Fat cells have been shown to be important (They may have important functions including cytokine production, energy metabolism and RBC maturation)

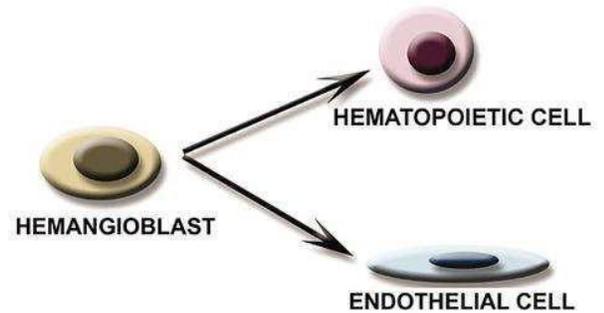


Question: Bone marrow fat comprises what percentage of the total fat in healthy adults?

Answer: 10%

Blood Development

- During embryogenesis embryo is divided into:
 - **Endoderm:** gut, liver, lungs
 - **Mesoderm:** skeleton, muscle, kidney, heart, blood
 - **Ectoderm:** skin, nervous system
- The mesoderm is the middle layer of the embryo that gives rise to the hematopoietic system
- Endothelial and hematopoietic cells share a common precursor: hemangioblasts
 - Hemangioblasts are mesodermal progenitors that give rise to blood and vascular endothelium

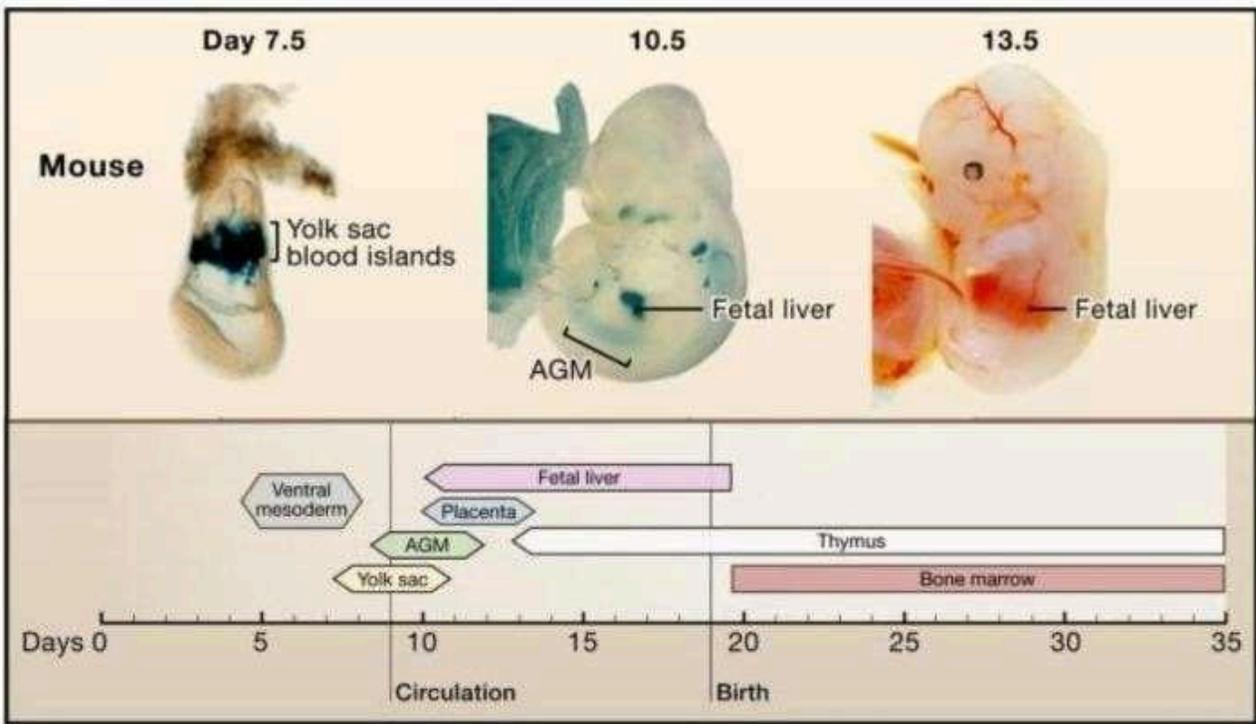


Embryogenesis

- Illustrated are the different organs important for blood cell synthesis in different developmental stages

Yolk sac → blood islands → other organs at day 10 (AGM; aorta-gonad-mesonephros) → placenta only harbors, but does not make blood cells → fetal liver

- After 13.5 days, the thymus and bone marrow take over
- Blood development in mice illustration: gestation time is not the same as humans (9 months vs about 20 days in mice)
 - You see pictures (below) of a mouse at day 7.5 and 10.5 and 13.5 and at different times you have blood cells derived coming from different parts that are developed from the embryo and come from the mesoderm. The first part is going to be the membrane around the embryo, the yolk sac, the AGM (which also produces RBCs at the early stages of development) and the placenta (it is not clear if it is producing or just harboring these RBCs).
- In terms of T0 cells the thymus takes over and after 20 days you can see that the bone marrow is the major producer



Hematopoiesis

- Liver and spleen take over the yolk sac, and then bone marrow, in the last months of gestation
 - blood development occurs in different locations during fetal development
- Bone marrow makes up a large portion of long bones (major site in later pregnancy)
- Hematopoiesis in the bone marrow
 - More in the spongy than long bone
 - Different levels of hematopoiesis along the bone
 - *Note:* similar in humans but different timespan

Sites of hematopoiesis

Fetus	0-2 months	yolk sac
	2-7 months	liver, spleen
	5-9 months	bone marrow
Infants	bone marrow (practically all bones)	
Adults	bone marrow: vertebra, ribs, sternum, skull, sacrum and pelvis, proximal ends of femur	

Hierarchy Organization

Long-term hematopoietic stem cells (LT-HSC) → short-term hematopoietic stem cells (ST-HSC) → progenitor cells → myeloid or lymphoid → specific blood cells that can become more and more mature

- **LT-HSC** → can self renew, eternally repopulate
- **SH-HSC** → repopulate cells in the short term

