I. **OVERVIEW**

- Function: Transportation of water soluble particles, and "Water Reservoir".

  * Transport of gases, nutrients, electrolytes, hormones, metabolites.

  * Never leaves the circulatory system. Leaves heart via **ARTERIES** which branch into a smaller diameter until they become **CAPILLARIES** (high surface area; simple squamousal epithelium = **DIFFUSION SURFACE**), which then converge to become larger diameter **VEINS**, which lead back to heart.

**Arteries**: carry blood away from the heart  
**Veins**: carry blood towards the heart  
**Capillaries**: exchange nutrients & wastes with surrounding tissues  
**Oxygenated Blood**: high O2 levels, low CO2 levels. Always RED in images and models.  
**Deoxygenated Blood**: low O2 levels, high CO2 levels. Always BLUE on images and models.  
**Systemic Circuit**: takes blood to body’s cells to deliver nutrients, pick up wastes  
**Pulmonary Circuit**: Takes blood to the lungs to become oxygenated
A) FUNCTIONS - all related to “distribution of substances” (see below)

1) DISTRIBUTION

Distribution is so important. We refer to the entire organ system, including the heart and blood vessels, the Circulatory System.

The term "circulate" means "to move around". What is circulated?

1. CIRCULATION: The heart is a pump that keeps the blood moving to where it needs to go.
   i. Go pick up nutrients.

   DIGESTION: Breaking particles down.

   ABSORPTION: Bringing particles into the bloodstream.

   RESPIRATION: transporting gases between cells and the external environment
   ii. Nutrient-filled blood to the somatic cells.
   iii. Wastes to the disposal sites.

2. O2 & NUTRIENTS sent to somatic cells. Also, other stuff, such as:

   HORMONES - regulate the activity of the cells.

3. WASTES are sent to the elimination sites (lungs, kidneys & skin)

   EXCRETION: removing wastes from the body.

   You have 3 main excretory organs: lungs, kidneys and the skin.
- Vasodilation and Vasoconstriction – changing the width of a blood vessel in order to control blood flow.

* More detail in Blood Vessel Chapter

* dilate: open a tube, make it wider.

* constrict: close a tube, make it narrower.

We will see that the body has several ways to regulate blood flow, and therefore distribution of nutrients. One way: active cells release chemicals causing vasodilation.
2) REGULATION (HOMEOSTASIS)
   1. Body temperature
      * water absorbs heat well
   2. pH
      * using buffers (esp. Bicarbonate) – more detail near end of semester
   3. Fluid volume
      * Rule of thumb: if water leaves the bloodstream and isn’t returned, it is going to be lost from the body via evaporation, etc.
      * To prevent this, an osmotic pressure INTO the blood vessels is maintained by keeping a relatively HIGH concentration of electrolytes and proteins, especially albumin, in the bloodstream.

- A drop fluid volume in tissues (dehydration) can be caused by an increase [salt & protein] in vessel = water moves into vessel through osmosis.

- Kwashiorkor – swelling of abdomen of starving children - opposite case. Low protein diet after weaning (high carb diet) leads to too low protein level in blood. We believe this switches the osmotic gradient, causing water to pool up in the interstitium (Ascites “Ah –Sy- Tees”). First signs = swelling of hands, feet.

3) PROTECTION
   1. Hemostasis: Blood clotting--prevent blood loss
   2. Immunity: Protect against infection--antibodies & WBCs
II. Histology

A) Overview
- Blood is a fluid connective tissue
  * 2 parts: cells + matrix
    1) FORMED ELEMENTS - cells (some are “non-living”) – detail in later section
      a. ERYTHROCYTES (Red Blood Cells or RBCs) - O2 transport
      *45% of whole blood
      b. LEUKOCYTES (White Blood Cells or WBCs) - immune system role
      c. THROMBOCYTES (Platelets) -- Cell fragments, stop Bleeding (HEMOSTASIS).
      WBCs + platelets < 1% whole blood.
  2) PLASMA - non-living fluid MATRIX – detail in later section
      *55% of whole blood
      *contains dissolved fibrous proteins
      *Ground Substance = SERUM
      Serum + Protein = PLASMA

* We can separate the individual parts and measure their abundance:

**CENTRIFUGE:** due to different masses & densities of components, can separate by spinning, using a machine called a centrifuge.

In males, at sea level:

Plasma on top (lightest) – should be around 55%

Buffy Coat – leukocytes and platelets, less than 1%

Erythrocytes on bottom (heaviest) – should be around 45%

There is a LOT of variation in these percentages!!

**HEMATOCRIT:** measure the percent RBCs

B) PLASMA details
- 90% H2O plus > 100 different dissolved solutes.
  *nutrients, gases, hormones, wastes, products of cellular activity (proteins, etc.), ions, blood proteins (albumin, clotting proteins, globulins)

*PLASMA PROTEIN - most abundant solute (~ 8% of plasma).
  **Most are produced by liver. NOT taken up by the cells - too big to pass across cell membrane.
  **ALBUMIN = most common type BY FAR. Albumin is a buffer, carrier protein, and the major controller of BLOOD OSMOTIC PRESSURE (see earlier “Regulation” section of notes).
  ** Alpha & Beta globular proteins are made in the liver, and make up hemoglobin & myoglobin.
  ** Nitrogenous” means “nitrogen containing”. Nitrogenous wastes are a product of cellular metabolism.

Important related terms:

**Plasma levels:** the amount of a substance (glucose, sodium, etc.) in the plasma (serum + protein).

**Serum levels:** the amount of a substance in the serum (we've removed the proteins).

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Plasma Constituents:

<table>
<thead>
<tr>
<th>Water: 90% of plasma volume</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solutes:</strong></td>
</tr>
<tr>
<td><strong>A. Proteins</strong></td>
</tr>
<tr>
<td>1. Albumin: 60% of all plasma proteins.</td>
</tr>
<tr>
<td>2. Globulins:</td>
</tr>
<tr>
<td>*Alpha &amp; Beta: liver, transport.</td>
</tr>
<tr>
<td>*Beta: antibodies</td>
</tr>
<tr>
<td><strong>C. Cloting. Some = liver.</strong></td>
</tr>
<tr>
<td><strong>4. Others: Cloting, Enzymes, Hormones, etc.</strong></td>
</tr>
<tr>
<td><strong>B. Non-protein Nitrogenous:</strong></td>
</tr>
<tr>
<td>1. Urea, Lactic Acid, Creatinine, etc.</td>
</tr>
<tr>
<td><strong>C. Nutrients: glucose, vitamins, A.A.s, etc.</strong></td>
</tr>
<tr>
<td><strong>D. Electrolytes: Na, Cl, K, Ca, H, etc.</strong></td>
</tr>
<tr>
<td><strong>E. Respiratory Gases: O2 &amp; CO2</strong></td>
</tr>
</tbody>
</table>
C) FORMED ELEMENTS details

- Includes the living cells (Erythrocytes & Leukocytes), and Thrombocytes (or Platelets), which are cell fragments.

- Continual renewal & removal from blood; only survive in blood a few days.

  * Do not divide. Instead, formed from PRECURSOR CELLS found in the marrow, etc. through a process called HEMATOPOIESIS (“blood forming”).

  * ALL blood cells start out as the same PRECURSOR CELL = HEMOCYTOBLAST.

Pathways of hematopoiesis:

(we will go into the details you need to know when we talk about each individual blood cell later)

Which path to maturity the cell takes depend on which hormone is applied.
1) ERYTHROCYTES (RBCs)
- Carry gases in blood (O2 & CO2)

1. STRUCTURE
- Small, biconcave disks, annucleate, no organelles.

  * = basically a “bag” of HEMOGLOBIN (= protein used for gas transport).
  ** Why no organelles?--no mitochondria = ANAEROBIC RESPIRATION ONLY!!--don’t use up the O2 they are carrying! But, that means they cannot repair themselves; short-lived, only about 100-120 days in the bloodstream.

* Shape is important!!!!
  ** Small size and biconcave = increase SA to carry gases (both O2 & CO2).

Move through capillary single-file. As they pass through the narrow capillaries, they “twist” slightly; therefore, O2 is dropped, which then diffuses into the tissues.

** To maintain shape, a net of fibrous proteins inside maintain shape while giving it ability to change shape.

- VISCOSITY - blood “thickness” - how many RBCs are present = major contributor. Males have higher viscosity than females = more skeletal muscle tissue = higher O2 demands.

2. FUNCTION - COMPLETE dedication to GAS TRANSPORT:
  take O2 from the lungs to the tissues for cellular respiration; take gas waste of cellular respiration (CO2) to lungs for removal from body.

  * O2 & CO2 bind to hemoglobin on RBC; this binding is reversible, depending on the shape of the RBC & the [ ] gradient of the gases!

See later discussion on Sickle Cell Anemia

More detail in the Respiratory chapter
Shuster's A&P2 Note Series
- HEMOGLOBIN MOLECULE

*heme group contains iron, which binds weakly to oxygen gas (it is a good carrier).

Formation of ferrous oxide FeO2. FeO2 also releases its oxygen easily, making it a good carrier molecule, as hemoglobin can release the oxygen at the tissues.

*NOTE: oxygen, in the presence of oxygen gas is red, as ferrous oxide is red in color.

It has 2 alpha globulins, & 2 beta globulins. Each globin has 1 heme group.

*Therefore, each hemoglobin has 4 heme groups and can carry 4 oxygens; each RBC has 250 million hemoglobin molecules; therefore, each RBC can carry 1 billion molecules of O2!

3. PRODUCTION & DISPOSAL OF ERYTHROCYTES, & IRON METABOLISM

- RECALL: all blood cells formed through HEMATOPOIESIS, and arise from the same stem cell called a hemocytoblast (a “pluripotent stem cell”)

*RBCs formed in red bone marrow of axial skeleton & girdles, & proximal epiphyses of humerus & femur.

* Which adult cell is form is determined by which hormone is applied to the precursor cells. If body needs more of a specific cell, more of the hormone is produced.

- Regulation is important; too many RBCs = blood is too viscous. Too few = HYPOXIA (tissue deprivation).

* ERYTHROPOIESIS: Form RBC.

If kidney or liver become hypoxic, kidney cells begin to produce hormone ERYTHROPOIETIN (EPO).

** Hormone that begins formation of precursor cell into RBC.

** Can occur if lowered # RBC due to hemorrhage, low availability of O2 (high altitude or pneumonia), or an increased O2 demand (exercise).

- Immature RBC increases # ribosomes (to make hemoglobin). RBC accumulates hemoglobin. When full, it ejects nucleus & organelles.

Compare this image to image of “Pathways of hematopoesis” seen earlier

- SKIP DETAILS, except for the following:

(i) Know the name “Normoblast”. It is the cell that ejects the nucleus and other organelles. A lot in the blood often indicates anemia and hypoxia (see later discussion of “Disorders”).
is a strong oxidizing agent! Must be careful when breaking down old cells:

**Destruction of RBCs:**

Only last 100 – 120 days
(remember: do not have nuclei or other organelles!).

- Old RBCs transported to liver and spleen.
- RBCs broken down into their 2 basic components:
  (i) Cell fragments
  (ii) Hemoglobin

- Hemoglobin then degraded into:
  (i) Globin – re-use the amino acids.
  (ii) Heme

- Heme contains iron, so it must be further processed:
  (i) Iron is stored in ferritin in liver (see previous section), and re-used.
  (ii) In liver, heme is converted into bilirubin.

**Bilirubin:** yellow pigment, formed from breakdown of heme.

It is one of the few things that is excreted in feces (see later Digestion chapter). It gives feces its typical color.

**Jaundice:** Yellowing of the skin due to a build-up of bilirubin.
4. Clinical Conditions (not all are pathologies):

(i) ANEMIAS - blood w/ low O2 capacity

Anything lowering the blood’s ability to carry oxygen, LOTS of different types:

- Problems with production of RBs
- Problems with production of Hb
- Problems with removal of either
- Problems with blood loss
- Hb doesn’t work
- Something else is interfering with delivery

- Examples:
  (a) Low # RBC: many, including:
    - Hemorrhagic (blood loss)
    - Aplastic (drugs, toxins, radiation inhibit hematopoietic tissues)
    - Hemolytic (blood cells explode, for any number of reasons)

  (b) Low “functioning” hemoglobin content - many types, including:
    - Dietary (low fat/protein intake)
    - Pernicious (low vitamin b12)
    - Sickle Cell (genetic)

*Special case of a genetic problem: Sickle cell anemia*

Sickle cell anemia is a genetic disease, with a mutation in the hemoglobin gene. The abnormal hemoglobin causes a change in the shape of the red blood cells, giving many of the red blood cells in the bloodstream a "sickle" shape. First of all, the sickle cells cannot carry as much oxygen, as the change in shape lowers their surface area. Also, the sickle cells tend to become sticky and stick to each other, forming small clots within the capillaries.

When the patient cells begin to sickle and form clots, they undergo what is called a sickle cell crisis, with severe edema and tissue damage to their vital organs. It is extremely painful, and deadly if not controlled.

For most genetic diseases, the patient must have two copies of the mutated gene: one from mom, and one from dad.

"Carriers" have one mutation, but the other gene is normal. The term for having a different gene from each parent is "heterozygote". For most genetic diseases, the person must have 2 bad copies; one from each parent. Carriers usually do not have the disease, but can pass it to their children if their mate also has the mutation. Most children will not have the disease...most will also be carriers.

Don’t worry about the details!
It turns out that in some parts of the world, being a carrier for the sickle cell trait is actually beneficial, as it protects people against a common deadly disease … Malaria: A parasite that is transmitted by mosquitos.

Often here in the United States, we don't understand just how bad malaria is. Even today, with modern advancements in treatment, it is still a huge killer in some regions. In 2010 there are about 250 million malaria cases worldwide and close to 1 million deaths. Most were in West Africa, the place of origin of most African-Americans, who are the descendants of slaves.

Malaria is a parasite that travels to the blood on red blood cells. It turns out that this parasite doesn't travel well and sickle cells. People who are carriers for this trait have some sickle cells in their bloodstream, enough to make it difficult for the parasite to travel, but not enough for them to ever go into crisis. So in areas with a lot of malaria, carriers for the sickle cell trait have quite an advantage.

Know for exam:
- Genetic mutation in Hb gene.
- Change in shape of RBC = holds less O2. The person goes into "crisis". Very painful, life threatening.
- 1/450 African Americans births in U.S. are affected (carriers or have the disease)
- Seems as originally was protection against malaria in tropics

(ii) POLYCYTHEMIA - excess # RBCs - symptom of other disorders

(a) POLYCYTHEMIA VERA - hematocrit of over 80%; novel mutation in bone marrow.

(b) 2<sup>nd</sup> POLYCYTHEMIA - higher # RBC due to less O2 in environment (e.g.: people in higher altitudes).

People who live at higher altitudes have a higher hematocrit as an adaption to living in an environment with less O2.

This is why athletes like to train at higher elevations! When they come back to a lower elevation to compete, they have a higher hematocrit, and their blood has a greater ability to carry oxygen to their tissues.

“Blood doping” - Injecting EPO (erythropoietin) has the same effect.