

Chapter 19 Blood

Introduction

How does blood contribute to homeostasis? It contains most of the immune cells, but by itself doesn't do anything--it is a transport medium.

Arteries = Oxygenated blood that is going to the tissues
Veins = Deoxygenated blood that is going back to the heart

Exchanges are made
at the capillaries!

Functional components of the CV System

Digestive System: Nutrients are absorbed across the wall of the small intestine
Kidneys: Part of the circulatory path. Blood is filtered here!
Lungs: Where oxygenation occurs. Blood picks up oxygen here, and drops off CO₂

pH of blood is
7.35 to 7.45

Functions of Blood

All the functions of blood contribute to homeostasis.

Distribution: **Nutrients** (oxygen, glucose, fatty acids, vitamins, minerals, etc...)
Wastes to kidneys for excretion
CO₂ to lungs for excretion
Chemical messengers to target cells (Hormones)
Enzymes (Ex: Renin-AngII-Aldosterone pathway)

Regulation: **Temperature (thermoregulation)**. This is done via redistribution and shunting of blood flow depending on body needs
pH of body fluids: blood contains buffers...albumin is the main one
Volume of body fluids: maintaining blood volume, thus ECF volume and BP. If blood vessel is at the right volume, the ICF and ECF are good, too.
Composition of body fluids: fluid/solute exchanges are continuous between the ICF/ECF fluid compartments

Protection via: **Hemostasis** prevents blood loss to maintain ECF volume. This is done via blood clotting. The blood carries clotting proteins (fibrinogen becomes fibrin when clotting is necessary).
Leukocytes are the primary cellular component of the immune system. Basically, all the blood cells except erythrocytes and platelets are part of the immune system.

Composition of Whole Blood

Blood is a fluid connective tissue (matrix + cells)
The matrix of blood is plasma (matrix is ground substance + fibers)
Ground substance = serum
Fibers = fibrinogen

Fibrinogen is a fibrous protein that is dissolved in the plasma unless converted into fibrin during clotting.

The watery portion of whole blood is the plasma. The cellular portion is the hematocrit (WBC, RBC, platelets).

The major components of blood can be seen in a tube after centrifuge:

- Plasma makes up 55% of blood
- Buffy coat accounts for less than 0.1% and includes leukocytes and platelets
- Erythrocytes account for about 45%

Hematocrit refers to the percentage of blood that consists of formed elements. RBCs make up 99.9% of the formed elements, WBCs and platelets account for 0.1%. Men have a higher hematocrit due to more lean body mass, at about 46%. Women have a hematocrit of about 42%.

Characteristics of blood

- The amount of blood you have is equal to about 7% of body weight in kilograms.
- Blood is not neutral. It is slightly alkaline at 7.4pH. Note that though this is alkaline, it is NORMAL for the body, so anything above 7.4 is considered basic (causing alkilosis) and anything below 7.4 is considered acidic (acidosis).
- At a normal hematocrit of 40%, blood is 3-4x more viscous than water. The more cells you have the higher the viscosity of the blood. If hematocrit rises to 60%, then the relative viscosity increases to 8x that of water....sludgy!! This is why blood doping is sooo dangerous! The higher the hematocrit, the more viscous the blood gets, and the harder the heart has to work to pump the thicker blood. You can have heart failure and blood vessels can get clogged, causing tissue death.
- Note that plasma has a relative viscosity of about 1.8.

Plasma

Plasma is made up of about 92% water, and 8% solutes (both protein and non-protein). Most of the major proteins of plasma are produced in the liver (except for hormones and gamma globulins).

The major proteins are:

- Albumin: Most abundant protein in plasma (2/3 or 60%)
Carrier protein for lipophilic substances
Acts as a buffer to maintain pH
Contributes to osmotic pressure b/c it affects exchange between blood and interstitial fluid.
 - Globulins: Next most abundant (1/3 or 35%)
Alpha and Beta globulins act as transport proteins
Gamma globulins are antibodies... made by B-lymphocytes
Not produced in liver!
 - Cltng Protns: Fibrinogen makes up 4% of plasma proteins
 - Enzymes/Hs: Make up less than 1% of plasma proteins
- Non-protein solutes account for about 1% of plasma
- Nutrients & Waste Products

- Electrolytes (ions)
- Gases (O₂ and CO₂)

Plasma and Homeostatic Regulation

Plasma composition is kept pretty constant by the collective effort of the body's organs systems, which are under nervous and endocrine control.

- The urinary (renal) system deals with electrolytes, water, wastes
- The digestive system deals with nutrients/fuels
- The cardiovascular/respiratory system deals with O₂ and CO₂

Formed Elements

Erythrocytes: RBCs are not "true cells" because they do not have a nucleus and they have few organelles. The reason for this is that RBCs main goal is to transport oxygen. They are all formed from stem cells in the bone marrow.

RBCs = 99.9% of formed elements

They have a concave shape which makes them more efficient carriers of oxygen. They can fold like a taco to fit into the smallest capillaries. ç have 30% more surface area, which contributes to a better ratio of surface area to volume. Surface area is important for the exchange of O₂ and CO₂.

Hemoglobin: Hemoglobin is the iron-protein component in the red blood cells that carries oxygen to the tissues. It has a quaternary structure, made up of 2 alpha and 2 beta chains. In each one of these chains is a heme group. In the middle of the heme group is Fe...Fe binds to oxygen! When the oxygen carrying capacity of blood goes down it results in anemia.

The standard amount of hemoglobin is 14-18 g/dl for males, and 12-16 g/dl for females.

There are two types of hemoglobin...fetal and adult. Fetal hemoglobin has a stronger binding affinity for oxygen, so that the baby can steal oxygen from mom. Soon after birth the fetal hemoglobin is converted to adult hemoglobin.

Hb accounts for 97% of RBC volume (excluding water)...the rest is cytoskeleton

Hb transports 98.5% of the O₂ carried in the blood (bound to iron of heme group)

Hb transports 20% of the CO₂ carried in the blood (bound to globin)

RBC Turnover

Red blood cells don't last very long...they get pretty banged up in circulation and are unable to repair themselves so they generally live about 3 months. As they break down, they are pulled out of circulation by macrophages on the cellular level and the spleen, liver and bone marrow at the organ level. The AAs and Fe is recycled and put back into the bone marrow for the construction of new RBCs. Transferrin is the plasma protein that transports Fe in circulation.

A small amount of Hb is lost from hemolysis and is not recycled...it is lost in the urine. When you have too much Hb in the urine it is Hemoglobulinuria (red/brown urine color).

When you have RBCs in the urine it's Hematuria. This may be a sign of kidney damage.

The Heme Group does not go to the bone marrow for recycling...it is converted to bilirubin in the macrophage and is transported to the liver and incorporated into bile. Some goes to the digestive system to be secreted in the feces, and some goes out in the blood stream to the kidney and out in the urine.

Macrophages do not always get the RBCs before they die. About 10% of them undergo hemolysis in the blood plasma and get lost through the kidneys and aren't recycled. When you do a urinalysis you will see some Hb. If outside the normal range, then there is a problem.

If you have an abnormal accumulation of bilirubin then you have jaundice!

Hemotopoiesis is the formation of blood cells in the red bone marrow. The blood cell stem cell is the hemocytoblast...it produces RBCs, WBCs and platelets. The hemocytoblast is the most "pluripotent" stem cell. The "committed cell" is the one in the pathway that is now committed to making a specific type of cell. For the RBC that is the proerythroblast.

Red Blood Cell Formation = Erythropoiesis

All RBCs are produced in the red bone marrow from the proerythroblast, which is the committed cell. The pathway is:

Hemocytoblast to Myeloid stem cell to Proerythroblast to Reticulocyte to Erythrocyte

The RBC enters the blood stream as a reticulocyte (immature RBC). It then ejects the nucleus to become an erythrocyte...this takes about a day.

Hormonal regulation of erythropoiesis

Erythropoiesis is controlled by negative feedback. It goes like this: EPO (released by the kidney in response to low oxygen delivery to the kidney cells) stimulates the red bone marrow, which leads to enhanced erythropoiesis to increase the RBC count. This increases the oxygen-carrying ability of blood, which eventually puts the brakes on the feedback loop. The goal of the loop is to maintain a level hematocrit, or to adjust it if necessary due to altitude. Erythropoiesis requires AAs, Fe and B Vitamins. If you don't have enough B12, then you have pernicious anemia.

RBC Disorders

Anemia: Anemia is caused by any lack of Fe, AA or B12. This leads to insufficient oxygen carrying capacity, so it is important to note that anemia is not always based on a low RBC count. It can have several causes!

Causes for the kidney cells to be low on oxygen are:
altitude, anemia,
pulmonary disease.

Anemia caused by deficient numbers of RBCs

- Hemorrhage causes *hemorrhagic anemia*
- Premature cell death causes *hemolytic anemia*
- Dysfunctional red bone marrow causes *aplastic anemia*

Anemia caused by deficient Hb content

- Iron deficiency causes *Iron-deficiency anemia*
- Vit-B12 deficiency causes *Pernicious anemia*
 - This is caused by a lack of intrinsic factor, which is produced by the stomach
- *Athlete's anemia* is caused by acute high BV, which dilutes RBCs relative to the normal hematocrit volume, it is low because BV is high.

Anemia caused by abnormal Hb (usually genetic)

- *Sickle-cell anemia* is caused by a small genetic defect (an incorrect AA). With this disease, the Hb becomes rod-like and spiky, which leads to the RBC “sickling” and becoming crescent-shaped.

Polycythemia: This disease is caused by too many RBCs, which raises blood viscosity to dangerously high levels.

Hematocrit
above 60%
is risky!

Polycythemia Vera

- Up to 80% hematocrit
- Indicative of bone cancer. The tumor cells are functional in this case, and make RBCs uncontrollably.

Secondary Polycythemias

- Low O₂ availability causes excess EPO
- Red bone marrow is overstimulated by altitude or blood doping

Blood Grouping

There are 25-26 types of antigens found on the blood cell surface. Most don't cause any problems, but a few do. They are the Antigens Type A, B, Rh...these cause strong reactions. If a patient is getting a *complete transfusion*, then you may need to consider the other antigens, mainly because they are getting so many cells. Most of the time though...we only deal with the main antigens.

Blood typing is based on the presence and absence of A, B, Rh antigens on the RBC membrane. Recall that antigens are substances that trigger immune reactions...antibodies attack antigens!

A unique feature the A & B blood groups is the presence of preformed antibodies...most antibodies are acquired after exposure to an antigen (chicken pox, for example). Note that Rh-factor antibodies are not preformed. In order for someone to have Rh antibodies they first need exposure to Rh+ blood cells. Subsequent exposures would result in a strong immune reaction (ex: Rh- mother has second Rh+ baby...problems!!!)

The antigens for ABO/Rh blood groups elicit strong reactions:

- Agglutination and hemolysis
- Transfusion reaction (donor's RBCs are attacked by the recipient's plasma...remember plasma is where the antibodies live)
- The donor's plasma antibodies may agglutinate the recipient's RBCs, but the donor antibodies are so small in number, they become diluted and is not usually a problem)
- Agglutination is used to ID blood types!

Type A Blood: Has A antigens on the cell surface
 Has B antibodies in the plasma

Type B Blood: Has B antigens on the surface
 Has A antibodies in the plasma

Type AB Blood: Has A & B antigens on the cell surface
 Has no antibodies in the plasma

Type O Blood: Has no antigens on the surface
 Has A & B antibodies in the plasma

Only concerned with the antigens coming in!

Note that if you take out the plasma, you take out the antibodies...which can be important if doing a large transfusion of more than 1 liter...in this case the number of donor antibodies would not be diluted and ineffective...they could cause problems.

When blood typing, it is based on which antigens are present! In addition to the A, B antigens, a third antigen is added to determine the Rh-Factor. Recall that Rh antibodies are not preformed. If you are Rh-, then you might someday form Rh antibodies. You can do this by being pregnant with an Rh+ baby because the antigens can get across the barrier...causes problems with subsequent Rh+ baby.

If you are Rh+ then you will never form antibodies to Rh-Factor...and can receive blood that is either Rh+ or Rh-.

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