Unit 1 Lecture 1

THE CARDIOVASCULAR SYSTEM

Think of the cardiovascular system (CVS) as a series of tubes filled with fluid (blood) and connected to a pump (heart). The major function of the CVS is to transport materials between all parts of the body. Those substances include nutrients, gases, and water. Pressure gradients in the heart propel blood through the system continuously. The blood picks up oxygen in the lungs and nutrients from the gastrointestinal system and delivers them to cells while simultaneously removing wastes for excretion. Hormones are transported via the blood to target cells. Immune cells and antibodies in the blood help protect the body from foreign invasion.

BLOOD

FUNCTION OF BLOOD

Blood transports gases and nutrients throughout the body and transports wastes (carbon dioxide and heat) to the lungs, kidneys and skin for elimination from the body thus regulating water content of cells and body temperature. Circulating blood helps maintain homeostasis in all body fluids. Blood regulates pH via acid-base buffering system. Blood protects against blood loss by its ability to form clots. Lastly many blood constituents protect the body against disease.

Blood is divided into two components: plasma and formed elements. Plasma contains water, proteins (albumin, globulin, and fibrinogen), electrolytes, nutrients, gases, enzymes, wastes. There are a number of types of albumins found in the plasma. They are formed in the liver and contribute to colloid osmotic pressure and act as carriers for various substances. Globulins (which are formed in the liver) transport iron, lipids, and fat-soluble vitamins throughout the body. Fibrinogen, formed in the liver, forms fibrin threads necessary in blood clotting. Antibodies are produced by plasma cells and help in fighting viruses and bacteria and other foreign invaders. The formed elements include erythrocytes (red blood cells), leukocytes (white blood cells) and thrombocytes or platelets.

The process of forming blood cells is called hemopoiesis. Hematopoietic growth factors (erythropoietin, cytokines such as colony stimulating factors and interleukins, and thrombopoietin) stimulate proliferation of various cell types. A hemocytoblast (hemopoietic stem cell) differentiates into other cell types in the bone marrow. Rubriblasts form erythrocytes. Monoblasts form monocytes. Lymphoblasts form lymphocytes. Megakaryocytes form platelets. Myeloblasts develop into progranulocytes which differentiate into basophils, neutrophils and eosinophils.

Red Blood Cells (Erythrocytes)

Erythrocytes are biconcave disc whose function is to carry oxygen to the cells and tissues of the body. Red blood cells are produced in red bone marrow. Late in their formation, the nucleus is discharged from the reticulocyte as are other organelles. The life span of an RBC is about 120 days and number produced each day equals the number destroyed. The number of RBC is about two million cells produced per second.

Red cells contain hemoglobin, a protein that carries oxygen. Normal hemoglobulin levels are: (infant 14-20 g/100 ml of blood), female (12-16), male (13.5-18), Hematocrit (3x hemoglobin) is the percentage of red blood cells of the total blood volume. Red cell counts are important values the physician looks at in maintaining homeostasis in the patient.

Events in hormonal control

When the kidney (mainly) and liver experience oxygen deficiency (hypoxia) they release the hormone erythropoietin. Erythropoietin travels to bone marrow and stimulates increased production of RBC. As more RBC are released into bloodstream, O_2 carrying capacity increases taking more O_2 to the liver and kidneys causing a decrease in release of erythropoietin. Dietary factors affecting RBC production include vitamin B_{12}, and folic acid which affects DNA synthesis, and iron.

Red Blood Cell Disorders

Deficiencies in the amount of Red blood cells decrease the amount of oxygen that is transported in the blood. These disorders are called anemia. Anemia is caused by an accelerated blood loss, decreased red blood cell production or inadequate production of erythropoietin. Causes of accelerated blood loss are bleeding (cells are normal, but low in number) or cells rupture at an abnormally high rate due to hereditary (membrane defects, enzyme defects, or abnormal hemoglobin, i.e. sickle-cell disease) or acquired problems (parasitic infections, drugs, or autoimmune reactions). Defective RBC or hemoglobin synthesis in the bone marrow is due to inadequate dietary intake of nutrients, iron deficiency, folic acid deficiency, and vitamin B_{12} deficiency. Drugs or radiation can also shut down RBC production. Too many RBC produced is called polycythemia. Polycythemia increases the thickness or viscosity of blood, thus causing a strain on the heart.

White Blood Cells (Leukocytes)

The white blood cells are also known as Leukocytes. There are two types: granulocytes (granules in cytoplasm) and agranulocytes (no granules in cytoplasm). Granulocytes can be further subdivided into neutrophils (PMN whose function is to phagocytize bacteria and fungi and release cytokines), eosinophils (associated with allergic reaction and parasitic worm

infestations), and basophils (release histamine that promotes inflammation). There are two types of agranulocytes: Monocytes (phagocytize bacteria, dead tissue) and Lymphocytes (form antibodies, destroy foreign material directly). WBC life span varies from less than one day to years depending on cell type. A differential count provides the percentages of WBC in the blood. A normal differential will contain 54-62% PMN, 1-3% Eosinophils, <1% Basophils, 25-33% Lymphocytes, and 3-9% Monocytes. Leukocytosis refers to a WBC count of >10,000/mm whereas leucopenia is defined as a WBC count of <5,000/mm.

Platelets
Thrombocytes or platelets function in control of blood loss by forming a platelet plug. The normal platelet count is 130-360,000/µl. Platelet activation starts the clotting process.

Hemostasis
Hemostasis refers to the stoppage of bleeding. The steps of hemostasis are:

- Vascular spasm whereby the ends of blood vessels contract by themselves to stop bleeding.
- Platelet plug formation in which the platelets adhere or stick to ends of injured blood vessels and to each other.
- Coagulation follows two pathways (extrinsic and intrinsic) that end up in the same place with the formation of prothrombinase (stage 1). From this point a common pathway, stage 2, (the conversion of prothrombin into thrombin) is followed. Stage 3 is the conversion of soluble fibrinogen into insoluble fibrin. As one can see from the diagram, calcium plays an integral role in the coagulation process. Another vital component needed in clotting is vitamin K. Vitamin K is produced in the large intestine by bacteria.
- Finally there is Clot retraction, the tightening of the fibrin clot.

Hemostatic control mechanisms are regulated by both positive and negative feedback mechanisms. As the clot is being formed, each step activates the formation of a new factor. Once the damage has been repaired a negative feedback system is activated to destroy and remove the clot (fibrinolytic system). This negative feedback also prevents intravascular clotting.

Anticoagulants prevent coagulation within the circulatory system. When a clot (thrombus) does form in a blood vessel breaks away, an embolism results. A pulmonary embolism lodges in the lung and can be fatal if not treated immediately. The body produces two anticoagulants: heparin and antithrombin III.

Blood grouping (typing)

Blood groups are determined by the presence or absence of antigens (agglutinogens) on the cell membrane. There are four groups A, B, AB and O

which are determined by the expression of genes a person inherits. A person with Type AB is considered the universal recipient because cells lack antibodies to types A & B blood. People with Type O blood are called the universal donors because their blood lacks antigens for type A, B, and AB. There are a number of other antigens present in the blood of an individual. Thus, it is extremely important that when that person requires a blood transfusion, that that blood being received be cross-matched to determine it's compatibility with the recipient's blood. This is done to prevent a transfusion reaction.

Another group of antigens, named after the rhesus monkey, is the Rh group. If an Rh-negative woman and an RH-positive man conceive a child, there is the possibility of subsequent children developing a disease called Erythroblastosis fetalis or hemolytic disease of the newborn (HDN) in those subsequent conceptions. Note: this does not affect the first conception. RhoGAM is given during the pregnancy and immediately after birth to prevent the development of antibodies that would affect the next conceived fetus.