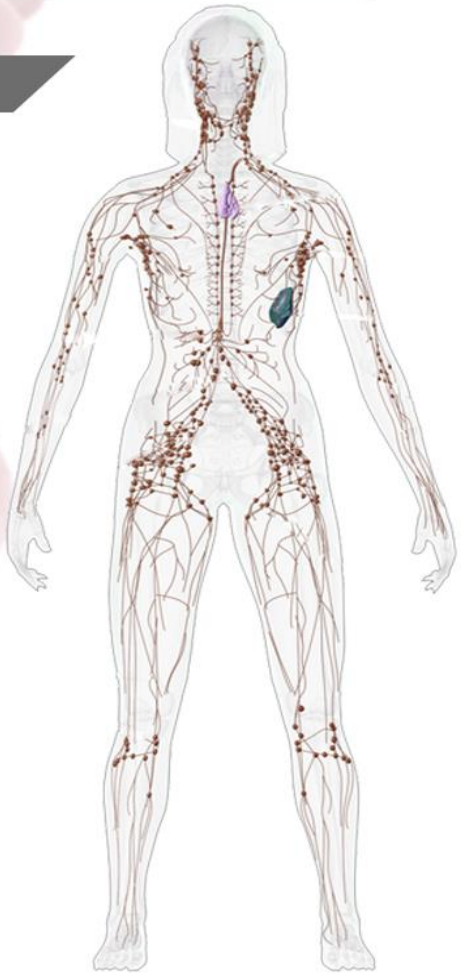
Sheet 3

Hematology and Lymphatic system

Subject | Pathology



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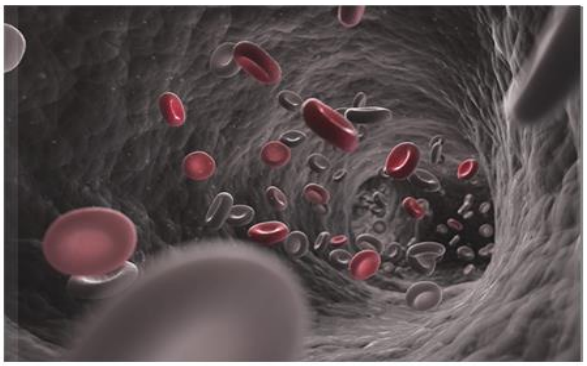


Anemia of Increased Blood Consumption:

Any type of anemia that is characterized by an increase in the peripheral blood consumption. These anemias usually have a high reticulocyte count compared to anemia of impaired bone marrow function, because the marrow is trying to compensate for the loss of RBCs. These anemias are divided into 2 major categories; anemia of blood loss (hemorrhage) and hemolysis.

Anemia of Blood Loss:

These anemias are either acute or chronic, however chronic will not be discussed as it is iron deficiency anemia. Acute is the result of a hemorrhage from external (gun shot, car crash) or internal sources (aortic aneurysm rupture). If blood loss is less than 20% (about 1L) of the total blood volume, normal patients can tolerate it without major problems. If blood loss exceeds 20%, the resulting threat is **hypovolemia**, not anemia. The symptoms of anemia show up 2-3 days after the hemorrhage, if the patient survives. During this period the erythropoietin levels will be high, as the body needs to make up for the RBCs lost. The anemia these patients suffer from is characterized by:

- Normocytic, normochromic RBCs
- Leukocytosis

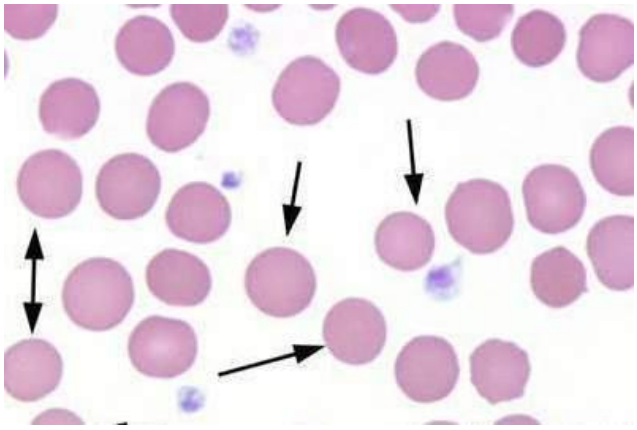
The reason we have leukocytosis is because of adrenaline and cortisol level spike during the shock of having an acute drop in BP. This causes the neutrophils in the marginal pool to detach from vessel walls and enter the circulation. After the patient recovers, they will have slightly macrocytic RBCs and thrombocytosis.

Hemolysis:

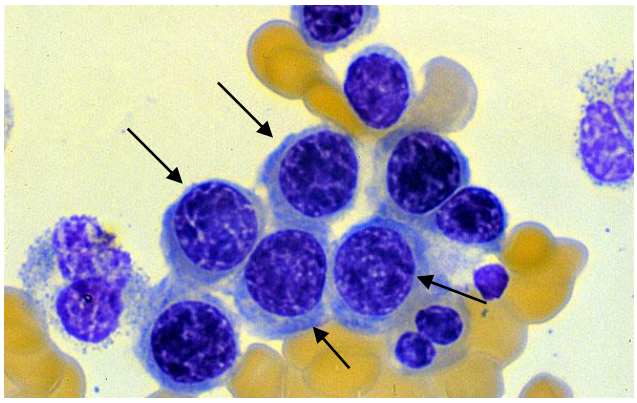
Anemia of premature destruction of RBCs, with increased reticulocytes and erythropoietin (EPO). Because these cells are being destroyed in the body, the products of Hb degradation are going to be high as well (bilirubin and iron). This does not mean there will be jaundice or hemochromatosis, only that the levels are higher than normal. Because of the high EPO levels, there will be erythroid precursor hyperplasia in the bone marrow. Hemolysis can either be intravascular or extravascular. Extravascular means RBC destruction in the **spleen** (some in liver), while intravascular is in the vessels themselves. Extravascular hemolysis:

- No free Hb in blood or urine
- Low haptoglobin (binds to free Hb)
- High lactate dehydrogenase (found intracellularly)
- Splenomegaly (macrophage hyperplasia)
- Jaundice with possible gallstones (high bilirubin due to RBC destruction)

Intravascular has the same symptoms, except they have hemoglobinuria and hemoglobinemia (free Hb in blood).



Spherocytosis usually indicates **extravascular** hemolysis.



These are erythroid precursor cells in the bone marrow, and normally they should not exceed 25% of the bone marrow. Here, they make up much more than 25%. This does not indicate extra- or intravascular hemolysis, only that there is increased blood consumption.

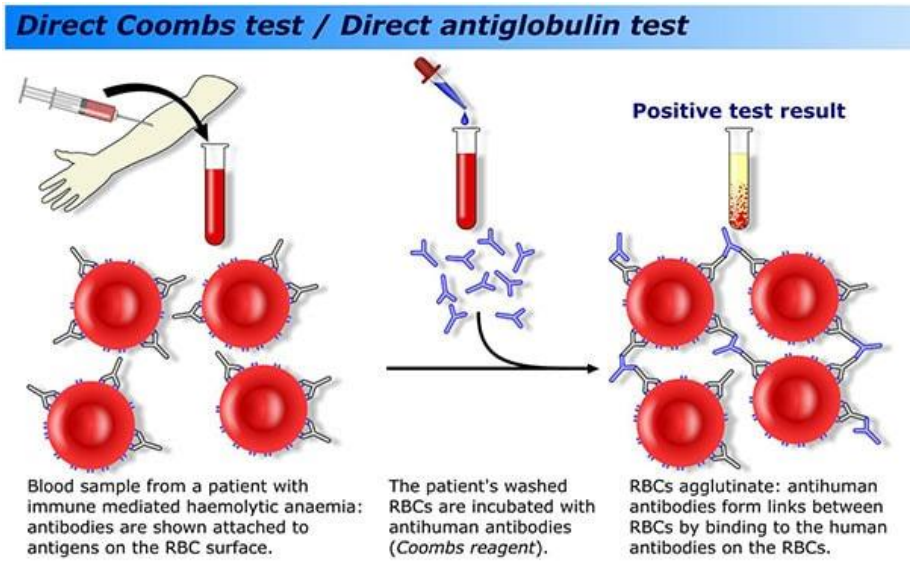
Immune Hemolytic Anemia:

Anemia as the result of an antibody binding to an RBC, causing its destruction. When antibodies bind to RBCs it causes macrophages in the spleen to recognize them as foreign and eat them. This type of anemia can be divided into 2 categories based on the **temperature** at which the antibodies bind. There are warm and cold antibodies. The warm antibodies bind to RBCs at a temperature around 37°C (core temperature) and cold antibodies bind to RBCs at around 34°C (peripheral temperature). So cold antibodies bind to RBCs in peripheral blood vessels, and warm antibodies bind to RBCs in core blood vessels. Warm antibodies are usually caused by **IgG** and cold antibodies are caused by **IgM**. Warm antibodies are usually idiopathic, but can be secondary to B cell neoplasms (B-CLL), autoimmune disorders (SLE), or some drugs (methyldopa). Cold antibodies can be acute (mycoplasma infection, infectious mononucleosis), or chronic (idiopathic, lymphoplasmacytic lymphoma).

Warm Antibodies	Cold Antibodies
IgG, rarely IgA	IgM
37°C	34°C
Mainly idiopathic (>60%), SLE, CLL, or drugs (methyldopa, penicillin)	Idiopathic, mycoplasma, infectious mononucleosis (EBV), lymphoplasmacytic lymphoma
Mild anemia	Mild anemia, Raynaud Phenomenon
Splenomegaly	Splenomegaly
No treatment	No treatment

Direct Coombs Test:

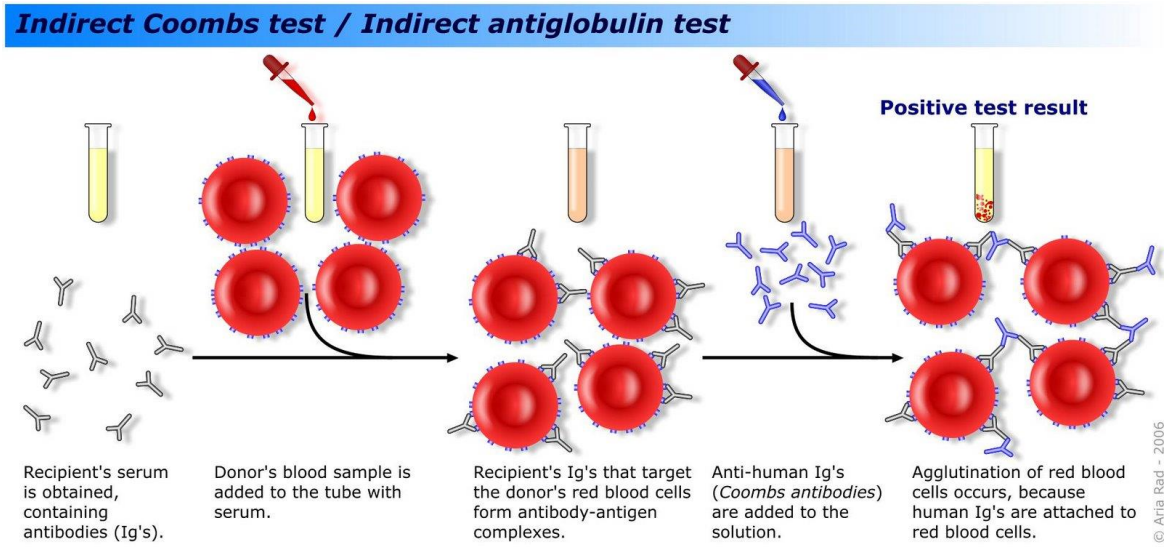
A test that sees whether there are antibodies bound to a **patient's blood**.



We add exogenous antibodies (Coombs reagent) whose antigen are endogenous antibodies bound to RBCs. If there are antibodies bound to RBCs, they will agglutinate, forming a clot (positive result).

Indirect Coombs Test:

A test that sees whether there are antibodies in the patient's **serum**.



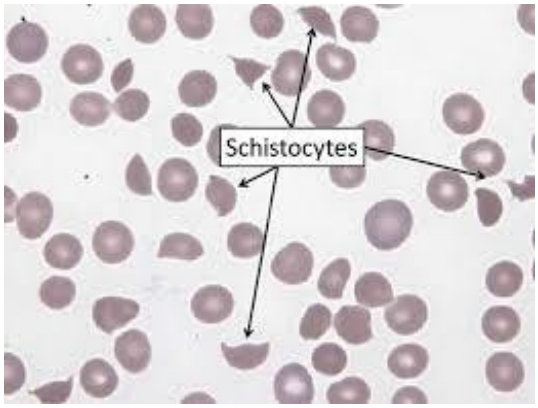
A patient's serum is taken (plasma without fibrinogen), and we add to it someone else's blood (so the patient's antibodies can bind), then we add Coombs reagent again to see if agglutination occurs.

Hemolytic Anemia Resulting from Mechanical Trauma:

Can be a result of repeated strenuous activity (marathon runners), but this is not a clinically significant anemia, mechanical cardiac valves (RBCs literally are torn open when they hit the valve), or microangiopathic hemolytic anemia (MAHA). MAHA is not a diagnosis, but it is a disease that is the result of a serious underlying disorder. MAHA can be caused by:

- Disseminated intravascular coagulation (DIC)
- Malignant hypertension
- Systemic lupus erythematosus (SLE)
- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS, E. coli O157:H7) *
- Disseminated cancer

In DIC, we have small strands of fibrinogen crisscrossing inside the small blood vessels, which tear RBCs when they hit them. TTP causes MAHA due to small clots that travel in the blood stream, which also tear RBCs when they hit them (the rest you don't need to know for now). Remember, in extravascular hemolysis we usually see spherocytosis, but in intravascular hemolysis we see schistocytosis, which are literally RBCs that have been torn because of a problem inside the blood vessels (in this case it is in the small vessels).



Infection (Malaria):

Plasmodium has part of its lifecycle inside the RBC, and they cause them to rupture in episodes (not chronic). P. Falciparum is the worst type of plasmodium as it has the ability to infect the brain, causing cerebral malaria. Hematin inside the RBCs spills into the blood, giving the liver, spleen, and bone marrow brown pigmentation. These patients also have massive splenomegaly, and occasionally hepatomegaly.