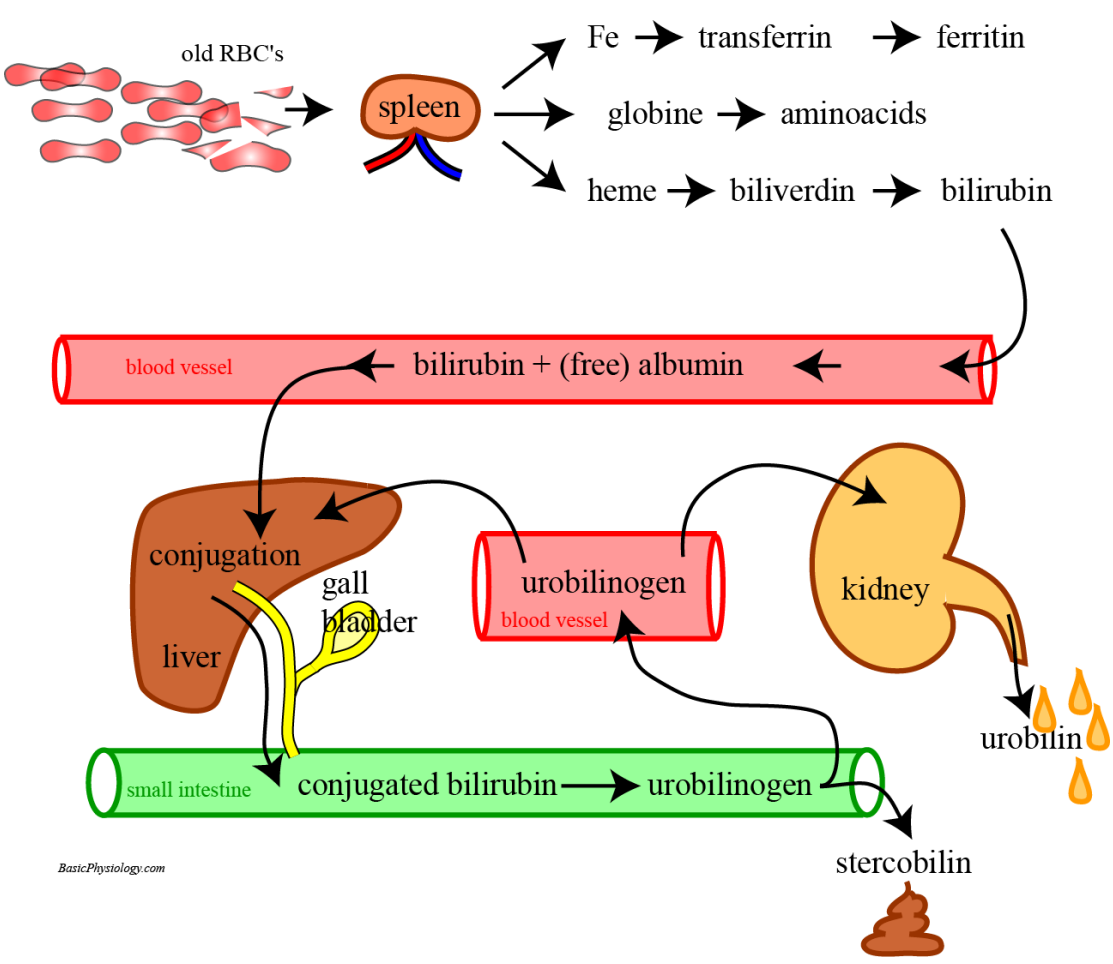
D.2.3. The Destruction of Erythrocytes

A. What happens to the 'old' RBC's?

1. Remember that the RBC's (erythrocytes) have no nucleus, no endoplasmic reticulum and no mitochondria. In other words, they are seriously limited in their life span!	2. There is however some glucose oxidation in the RBC's which produces ATP. This ATP is necessary: 1. To keep the membrane **flexible** 2. To make active membrane **transport** possible 3. To keep **Fe** in **ferrous** format (Fe^{2+}). Otherwise the iron will become **ferri**-format (Fe^{3+}), which will cause the hemoglobin to become **methemoglobin** (which is not suitable for oxygen binding).
3. **The RBC test:** All RBC's (7-10 micron wide) will, at one moment or another, flow through the **spleen**. But the spleen consists of the narrowest **capillaries** (3 micron) in the body!	4. If the membrane of an old RBC is no longer flexible enough, it will break (=**hemolysis**) and the life of this RBC is then terminated!
5. There is enough glucose and ATP to keep the RBC membrane flexible for about 120 days!	6. In the old Olympics, the Greeks already were able to remove the spleen in young athletes. Without a spleen, the RBC's will live longer and there will then be more (and older) RBC's in the circulation, thereby increasing the oxygen transportation.
7. (*I find it actually mind boggling that they already performed such aggressive surgery in those days; without anesthesia, sterilization etc.!)*	8. But eventually the RBC's will still die. But now, without a spleen, they don't break in the spleen but elsewhere in the body; in the capillaries of the brain, the heart or in the muscles. This will, in time, lead to a decrease in the quality of these organs. These young athletes typically **died too young!**

B. Destruction process of the RBC's:

1. In the spleen, the components of the old destroyed RBC's are **recycled**. That's nice!	2. The iron (Fe) is stored and saved as ferritin (in all kinds of cells in the body): Fe => Transferrin => Ferritin. *(link: D.2.2. Erythrocytes Production; panel G)*
3. The **globin** is broken down into amino acids, which can be used for building new proteins.	4. The **heme** is processed in a very special manner, which is really the topic of this panel.
5. The heme is converted, while still in the spleen, first into **biliverdin,** which is then converted into **bilirubin**.	6. This bilirubin then appears in the **blood** and is bound to the transport protein in the blood: **albumin**.



7. This bilirubin is called "**free**" or "**indirect**" bilirubin (historically, they have different names for this compound!).	8. This free (or indirect) bilirubin is then transported by the blood to the **liver,** where it is **conjugated**.
9. This bilirubin is now called "**conjugated**" or "**direct**" bilirubin. Whatever the name, this type of bilirubin is then secreted into the **bile**.	10. The bile flows into the **intestine**, where the bilirubin is converted, by the intestinal bacteria, into **urobilinogen**.
11. This urobilinogen is absorbed by the blood and either: a) goes back to the **liver** (to go back to the bile, to make a loop) b) or excreted by the kidney (as **urobilin**) c) or excreted via the stool (as **stercobilin**).	12. **Important**; the stercobilin gives the stool its characteristic **brown** color. If you don't have stercobilin, then the stool becomes pale like **clay**. This is an important **symptom** to discover diseases of the gall bladder or the bile duct!

C. Jaundice:

1. Why is this story about bilirubin so important? In one word: **jaundice** (yellow color of the skin and the whites of the eye). Medical name: **icterus**.	2. When someone turns "**yellow**", that means that something is **wrong** with the bilirubin processing. This is a very useful signal because it reveals that there is something pathological going on somewhere in the body. It works like a **marker**. There are three types of jaundice:
3. **Hemolytic jaundice**: In this disease, too much RBC's are being destroyed which increases the "free" bilirubin. This can be due to poisoning, a defect in the RBC, mismatched transfusion etc.	4. **Hepatocellular jaundice**: When the liver cells are diseased (such as in hepatitis), then they will be unable to conjugate the bilirubin. That will also increase the indirect (or free) bilirubin.
5. **Obstructive jaundice**: This occurs when the bile in the liver	6. Because it is possible, in the lab, to **differentiate** between the conjugated and

does not reach the intestine due to obstruction of the bile ducts (gallstones!) or to cholestasis (= no bile flow). This will lead to an increase in the conjugated bilirubin in the blood.	the free bilirubin in the blood, it is possible to have an idea of the location or the type of the disease. That is why the **jaundice** story is so useful in medicine to make a diagnosis.

D. Physiological responses to loss of erythrocytes:

1. In the case of a significant blood loss in the body, the following will occur: a. venous (and arterial) **constriction** b. **fluid shift** in the capillaries c. **increased production** of erythrocytes.	2. Vessel constriction is induced by the **sympathetic** nervous system when the blood pressure is too low. Since most of the blood is located in the veins (reservoir function), **venous constriction** will be most helpful but arterial construction will also occur. (*Link: B.7.1. Cardiac Shock.)*
3. **Fluid shift in the capillaries:** You may remember the **Starling exchange** system (*B.5.3. The Capillaries*). There, the difference between the local blood pressure and the oncotic pressure determined how much water was perfused from the capillaries into the tissues.	4. If the blood pressure is **higher** than normal, then more fluid (plasma) will **flow into** the tissues.
5. But if the blood pressure is lower than normal, then more fluid will flow ("**shift**") back into the capillaries. This will help increase the blood pressure. This will also decrease the **hematocrit** (which can be measured).	6. **Increased RBC production**: This is induced by an increase in **erythropoietin**, but that will take days to weeks to reach normal values (the hematocrit will then gradually increase) and requires folic acid, vitamin B12 and iron.