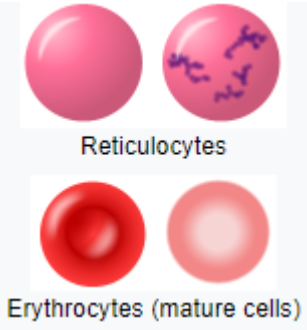
2.1.6

Erythropoiesis

(See the image in 2.1.3 of Hematopoiesis)

In a healthy adult's body, it is estimated that around twenty-five trillion red blood cells exist at any given moment. These blood cells will last for approximately 120 days before being broken down by macrophages. If not continually replaced, the overall oxygen containing capacity of the blood would decrease. Thus, to keep the blood population around 25 trillion, over two million new red blood cells enter the bloodstream each second to replace those that are lost! This process of producing new red blood cells is called **erythropoiesis** and occurs within the red bone marrow of the skeleton.

Erythrocytes (or Red Blood Cells) are unique in that they contain no nucleus or any organelles. During erythropoiesis, hemocytoblast stem cells ultimately differentiate into mature erythrocytes. Small signaling molecules known as **hematopoietic growth factors (HGF's)** stimulate the production and differentiation of the various types of blood cells. The HGF responsible for the production of red blood cells is known as **erythropoietin (EPO).** Upon sensing low blood oxygen levels, special cells in the kidneys release erythropoietin into the bloodstream where it travels to target cells within the red bone marrow. Erythropoietin stimulates hemocytoblasts to differentiate into cells known as **proerythroblasts.** Ultimately, several more intermediates will be produced via mitotic division before the cells reach the **reticulocyte** stage, which is the final stage before final maturation to an erythrocyte. By this point hemoglobin is contained within the cells, the nuclei are absent, and only a few ribosomes remain in the cytoplasm. Upon staining a reticulocyte, these remaining ribosomes give the appearance of a sort of net-like or reticular network which explains the origin of the name reticulocyte.



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Reticulocytes have a reticular (mesh - like) organization of ribosomes that can be seen with certain microscopic staining techniques. Reticulocytes are found in the blood for about a day after leaving the bone marrow and then they mature into a fully formed red blood cell and cannot be distinguished as a reticulocyte anymore.

The reticulocytes are released into the blood where they differentiate to become mature erythrocytes about 24 hours later. It is interesting to note that in certain conditions which require accelerated erythrocyte production, the number of reticulocytes in the blood increases. A measurement of the number of reticulocytes in the circulation can give an

indication of how strong the recent erythropoietic stimulus has been. A measurement of reticulocytes can also be used to test for cheating in athletes, as some choose to inject erythropoietin into their bodies (ie., Lance Armstrong). Interestingly, during the 7-year window that Lance Armstrong won every Tour de France (1999-2005), 87% of the top-10 finishers (61 of 70) were confirmed as using erythropoietin.

Erythropoiesis requires dietary intake of iron, folic acid, and vitamin B12. Any sort of deficiency related to these required dietary elements can cause a condition known as **anemia.** Anemia results when the bloodstream is unable to properly distribute oxygen throughout the circulatory system to the cells of the human body.

If a vitamin deficiency results in the decreased production of red blood cells, then the oxygen carrying capacity of blood is certainly diminished. Vitamin B12 deficiency may sometimes be called **pernicious anemia.** Vitamin B12 absorption requires a molecule synthesized by the stomach called intrinsic factor. Individuals with certain types of stomach issues may also develop anemia (more specifically, pernicious anemia) because they do not release intrinsic factor and therefore cannot absorb Vitamin B12, even though they eat plenty of it. Additionally, individuals practicing vegan or vegetarian diets need to be especially aware of their B12 intakes as they are at a much higher risk to develop B12 deficiencies (natural B12 is found in fish, eggs, meat, and milk). Supplemental B12 is readily available, but the key word is supplemental, thus these diets must add-in the supplement.

Anemia may also be caused by severe hemorrhaging (called hemorrhagic anemia), conditions that result in defective hemoglobin production (sickle cell anemia is one example), or any condition that causes excessive destruction of red blood cells (also called hemolytic anemia).