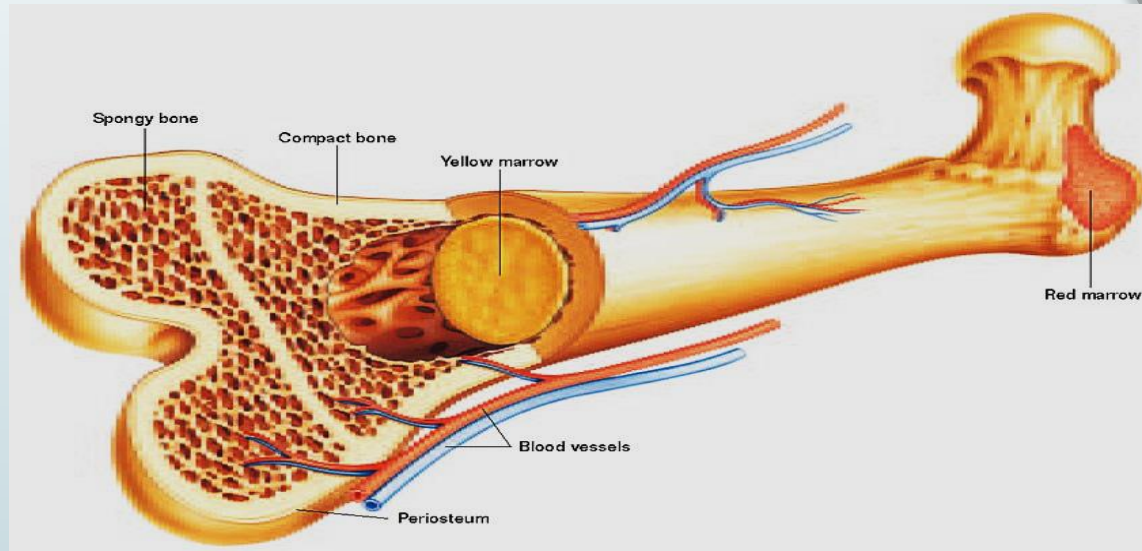


BONE MARROW



BY

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Bone marrow

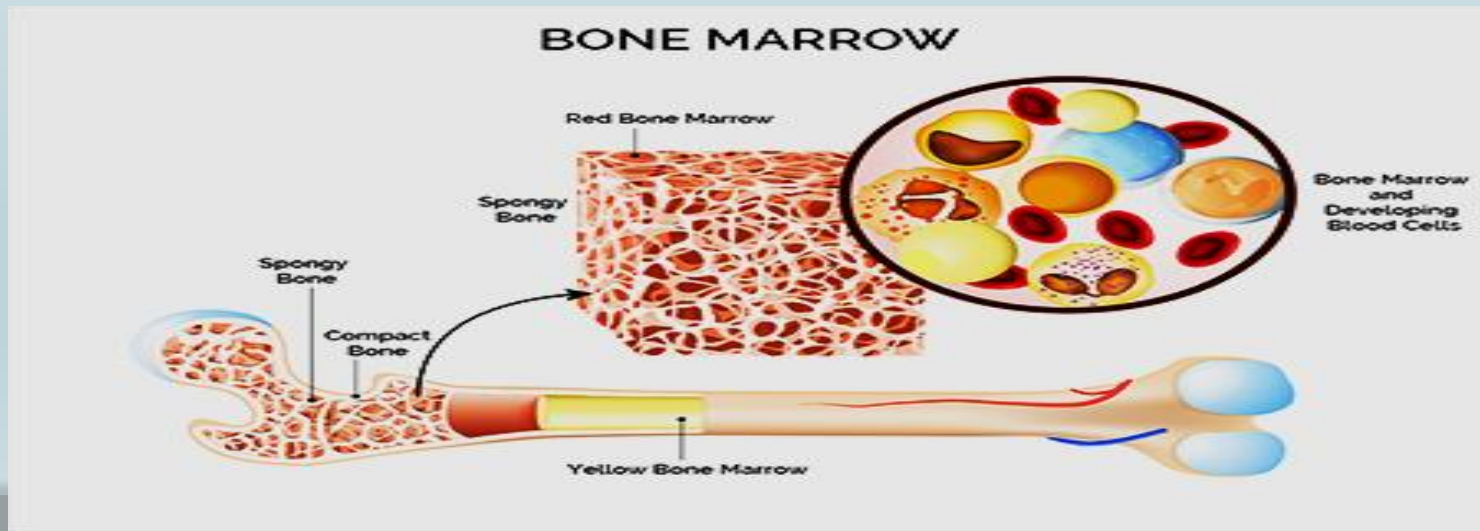
- ❖ **Bone marrow** is a spongy highly vascular connective tissue that fills the center of bones in your body.
- ❖ Serve as the primary site of new blood cells production or **hematopoiesis**.
- ❖ It is where **stem cells** produce red and white blood cells and platelets. Without bone marrow, you couldn't move oxygen through your body or fight infections, and blood wouldn't clot.

It is composed of :

1. Stem cells (hematopoietic).
 2. Marrow adipose tissue.
 3. Supportive stromal cells.
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- ❖ In adult humans, bone marrow is primarily located in the axial bones **ribs, vertebrae, sternum, and bones of the pelvis**.
 - ❖ Bone marrow comprises approximately **5%** of total body mass in healthy adult humans.

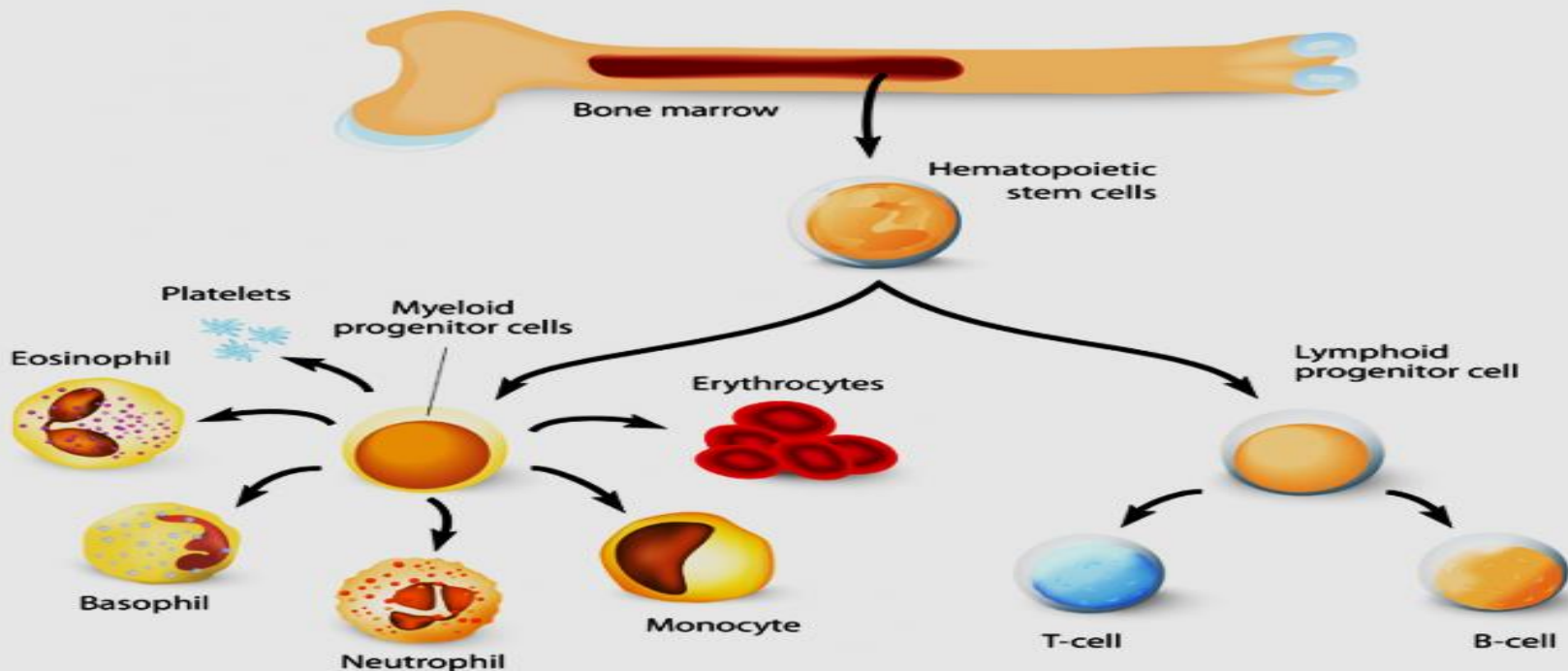
Structure

- ❖ In humans, marrow is characterized as **"red"** or **"yellow"** marrow, respectively depending on the prevalence of **hematopoietic (stem cells) vs fat cells**.
- ❖ A newborn baby's bones exclusively contain haematopoietically active **"red"** marrow, and there is a progressive conversion towards **"yellow"** marrow with age.
- ❖ **Yellow** bone marrow stores **fat and nutrients** for **red** bone marrow to use and to maintain body functions.
- ❖ In conditions of **chronic hypoxia**, the body can convert **yellow** marrow back to **red** marrow to **increase blood cell production**.



Hematopoietic components

- ❖ At the cellular level, the main functional component of bone marrow includes the **progenitor cells** which are destined to mature into **blood and lymphoid cells**.
- ❖ Marrow contains **hematopoietic stem cells** which give rise to the three classes of blood cells that are found in circulation: white blood cells (**leukocytes**), red blood cells (**erythrocytes**), and platelets (**thrombocytes**).



Stroma

- ❖ Stromal cells may be **indirectly** involved in hematopoiesis, providing suitable-environment that influences the function and differentiation of hematopoietic cells.

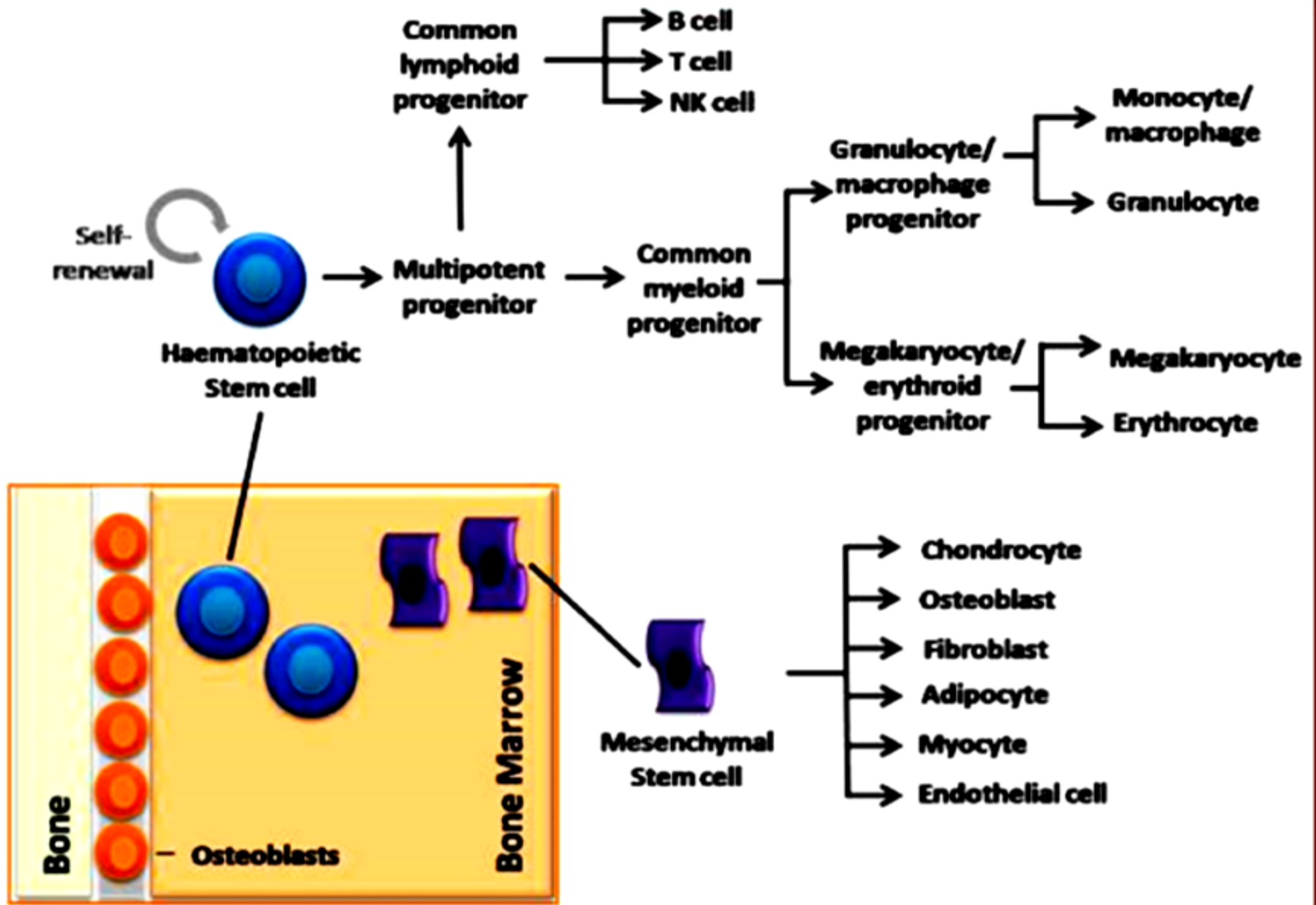
For example : They generate **colony stimulating factors**, which have a significant effect on hematopoiesis.

- ❖ Cell types that constitute the **bone marrow stroma**

Stroma

Mesenchymal stem cells

- ❖ The bone marrow stroma contains mesenchymal stem cells (**MSCs**), also known as marrow stromal cells.
- ❖ These are **multi-potent stem cells** that can differentiate into a variety of cell types.
- ❖ MSCs have been shown to differentiate, **in vitro** or **in vivo**, into **chondrocytes**, **myocytes**, **beta-pancreatic islets cells**, **fibroblasts** (formation of connective tissue), **Adipocytes** (fat cells), **Osteoblasts** (synthesize bone), **Osteoclasts** (resorb bone) and **Endothelial cells**, which form the sinusoids.



Cellular constitution of the red bone marrow parenchyma

Bone marrow barrier

- ❖ The **blood vessels** of the bone marrow constitute a barrier, inhibiting immature blood cells from leaving the marrow.
- ❖ Only **mature blood cells** contain the membrane proteins, such as **glycophorin**, that is required to attach to and pass the blood vessel endothelium.

Lymphatic role

- ❖ The **red bone marrow** is a key element of the lymphatic system, being one of the **primary lymphoid organs** that generate lymphocytes from **hematopoietic stem cells**.
- ❖ The **bone marrow** and **thymus** constitute the primary lymphoid tissues involved in the **production** and **maturation** of lymphocytes respectively.

Bone marrow diseases

1. Aplastic anemia

- ❖ This serious blood disorder arises when damage, such as from **autoimmune disorders** or **exposure to toxins**, sustained to the stem cells in bone marrow causes it to create fewer number of all types of blood cells.
- ❖ As a result, your blood supply won't meet your body's demands and you may be easily fatigued, shortness of breath, weakness, bleeding tendency and immunity suppression.

2. Leukemia

- ❖ Leukemia originates in the bone marrow. This blood cancer accelerates production of abnormal **white blood cells**, which replace healthy bone marrow cells, interfering with other blood cell production.
- ❖ The abnormal white blood cells also are **unable to fight infections**.
- ❖ There are two main types:
acute leukemia, which progresses rapidly, **chronic leukemia**, which develops more slowly.

Bone marrow tests

There is screen test that can determine if your bone marrow and blood cell counts are healthy.

One test is the complete blood count (**CBC**):

- ❖ It measures the number of red blood cells ,white blood cells and platelets in your blood.
- ❖ If blood cell counts generally fall within the normal ranges for age & gender, It means normally functioning bone marrow .

- ❖ If your **red** or **white blood cell** or **platelets** count is out of normal ranges, your doctor may want to test your bone marrow tissue directly for disease.
- ❖ There are **two main** methods of collecting bone marrow for further testing, often performed together:
 1. **Bone marrow aspiration** : A needle is inserted into the bone and a small sample of liquid marrow is extracted for examination.
 2. **Bone marrow biopsy** : A specialized bone marrow biopsy needle is inserted to remove a solid piece of bone marrow for examination.

Bone marrow transplantation

- Severely damaged bone marrow may require replacement via bone marrow transplantation.
- Bone marrow transplant (BMT) is a special therapy for patients with diseases such as leukemia, aplastic anemia, immune deficiency disorders, and some solid tumor cancers
- A bone marrow transplant involves taking (stem cells), filtering those cells, and giving them back to the patient .

Different types of bone marrow transplants

➤ Autologous bone marrow transplant

The donor is the patient himself. Stem cells are taken from the patient by a process of collecting peripheral blood stem cells → frozen → then given back to the patient .

➤ Allogeneic bone marrow transplant

The donor shares the same genetic type as the patient. Stem cells are taken from a genetically matched donor, usually a brother or sister.

Unrelated bone marrow transplants

- ❖ The genetically matched marrow or stem cells are from an unrelated donor. Unrelated donors are found through national bone marrow registries.

Umbilical cord blood transplant

- ❖ Stem cells are taken from an umbilical cord immediately after delivery of an infant. These stem cells reproduce into mature, functioning blood cells quicker and more effectively than do stem cells taken from the bone marrow of another child or adult. The stem cells are tested, typed, counted, and frozen until they are needed for a transplant.

How are a donor and recipient matched?

- ① Matching involves the human leukocyte antigen (HLA) .
- ① There are at least 100 HLA antigens; however, it is believed that there are a few major antigens that determine whether a donor and recipient match.
- ① The more antigens that match, the better the engraftment of donated marrow. **Engraftment** of the stem cells happens when the donated cells make their way to the marrow and begin making new blood cells.
- ① Most of the genes that "code" for the human immune system are on one chromosome. **Since** we only have two of each chromosome, one we received from each of our parents, a full sibling of a patient in need of a transplant has **a 1 in 4 chance** of having gotten the same set of chromosomes and being a "full match" for transplantation.

How are the stem cells collected?

➤ Peripheral blood stem cells

Peripheral blood stem cells (PBSCs) are collected by **apheresis**

This is a process in which the donor is connected to a **special cell separation machine** via a needle inserted in arm veins. Blood is taken from one vein and is circulated through the machine which removes the stem cells and returns the remaining blood and plasma back to the donor through another needle inserted into the opposite arm. Several sessions may be needed to collect enough stem cells .

How are the stem cells collected?

➤ Bone marrow harvest

-Bone marrow **harvesting** involves collecting stem cells with a needle placed into the soft center of the bone (the marrow).

-Most common sites used for bone marrow harvesting are located in the **hip bones** and the **sternum**.

-The procedure takes place in the **operating room**. The donor will be anesthetized during the harvest and will not feel the needle.

-**In recovery**, the donor may experience some pain in the areas where the needle was inserted.

Complications & side effects following BMT

1-Infections

- Infections are likely in the patient with severe bone marrow suppression. **Bacterial infections** are the most common.
- Viral and fungal infections can be life-threatening.
- Any infection can cause an extended hospital stay, prevent or delay engraftment, and/or cause permanent organ damage.
- Antibiotics, antifungal, and antiviral medicines are often given to try to prevent serious infection in the immunosuppressed patient.

2-Pain

- Pain related to **mouth sores** and **gastrointestinal irritation** is common.

3-Low platelets and low red blood cells

-Thrombocytopenia (low platelets) and anemia (low red blood cells), as a result of a non-functioning bone marrow, can be dangerous and even life-threatening.

-Low platelets can cause dangerous bleeding in the lungs, gastrointestinal (GI) tract, and brain.

4-Fluid overload

-Fluid overload is a complication that can **lead to pneumonia, liver damage, and high blood pressure.**

-The main reason for fluid overload is because **the kidneys** cannot keep up with the large amount of fluid being given in the form of intravenous (IV) medicines, nutrition, and blood products.

The kidneys may also be damaged from disease, infection, chemotherapy, radiation, or antibiotics.

5-Respiratory distress

-Respiratory status is an important function that may be compromised during transplant.

-Infection, inflammation of the airway, fluid overload, graft-versus-host disease, and bleeding are all potential life-threatening complications that may happen in the lungs and pulmonary system.

6-Organ damage

-The **liver** and **heart** are important organs that may be damaged during the transplantation process. Temporary or permanent damage to the liver and heart may be caused **by infection, graft-versus-host disease, high doses of chemotherapy and radiation, or fluid overload.**

7-Graft failure

-May happen as a result of infection, recurrent disease, or if the stem cell count of the donated marrow was insufficient to cause engraftment.

8-Graft-versus-host disease

Graft-versus-host disease (**GVHD**) can be a serious and life-threatening complication of a bone marrow transplant.

GVHD occurs when the **donor's immune** system **reacts against the recipient's tissue**.

-As opposed to an organ transplant where the patient's immune system will attempt to reject only the transplanted organ, **in GVHD** the new or transplanted immune system can attack the entire patient and all of his organs.

-This is because the new cells do not recognize the tissues and organs of the recipient's body as self.

-Over time and with the help of medicines to suppress the new immune system, it will begin to accept its new body and stop attacking it.

-The most common sites for **GVHD** are GI tract, liver, skin, heart and lungs.

Thank You