HEMATOPOIETIC & LYMPHATIC SYSTEM

-HAYAT BATCH-

SUBJECT : Anatomy

LEC NO. : Lec-3

DONE BY : Saja Afaneh

وَقُل رَّبِّ زِدْنِي عِلْمًا

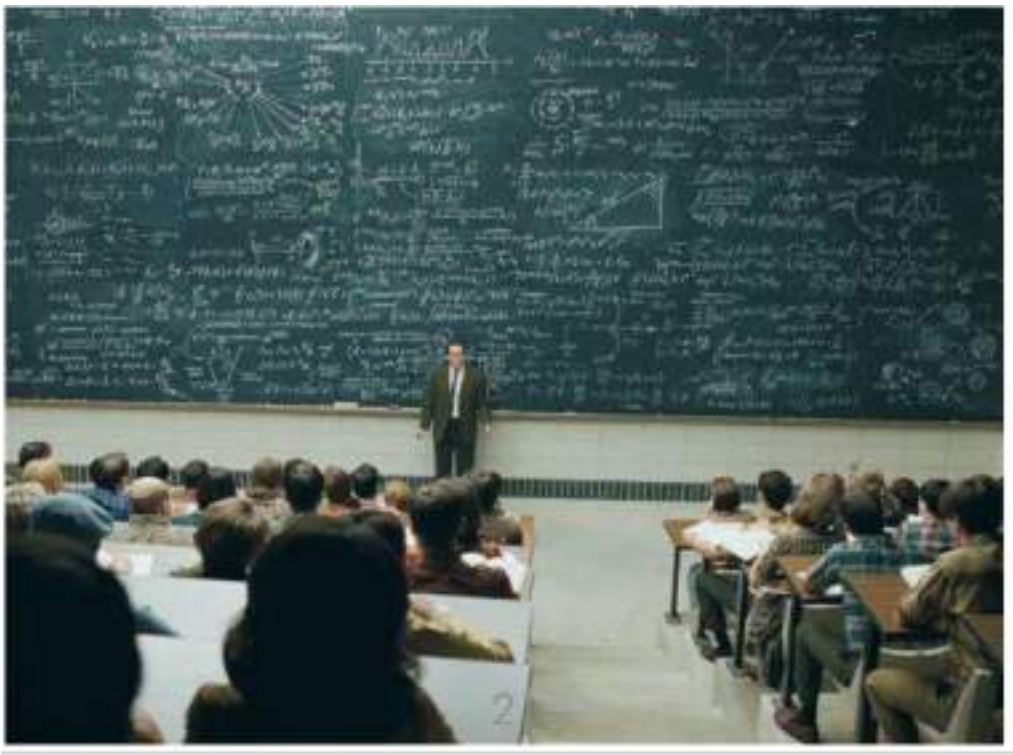
Hemopoiesis

The topic is soooo easy

The following is the Summary of the lecture on the board

JUST CONCENTRATE

Otherwise, you will not understand it



يعطيكم العافية حياة ❤️❤️استعنت بتفريغ المحاضرة بسلايدات الدكتور محمد فتحي ا وحطيتلكم المهم منهم وما تعملو ***skip*** عليهم بس لو تقرأوهم بتركيز لأنه الدكتور زياد كتير بحكي وما بكون هذا الحكي بالسلايدات وأي اشي ما بتفهمو على الدكتور زياد بإمكانكم ترجعو لشرح الدكتور محمد لأنه شرحه سفاح 🔥حتى لو السلايدات مختلفة بس المحتوى واحد 👌🏻

اللون الازرق كلام الدكتور

اللون الزهرى كلام اضافي

Hemopoiesis

تصنيع الدم

- Because of the short life span of blood cells, they must be replaced by stem cells found in HEMATOPOEITIC ORGANS

Hematopoiesis or the formation of blood cells is needed. Why? Because that the lifespan of red blood cells is around 120 days and for the other white blood cells that is between hours to days and then all blood cells will die

and this is why it is important for the blood animals to be replaced and it's actually replaced by stem cells that are found in the hematopoeitic organs at different levels of development of the human being.

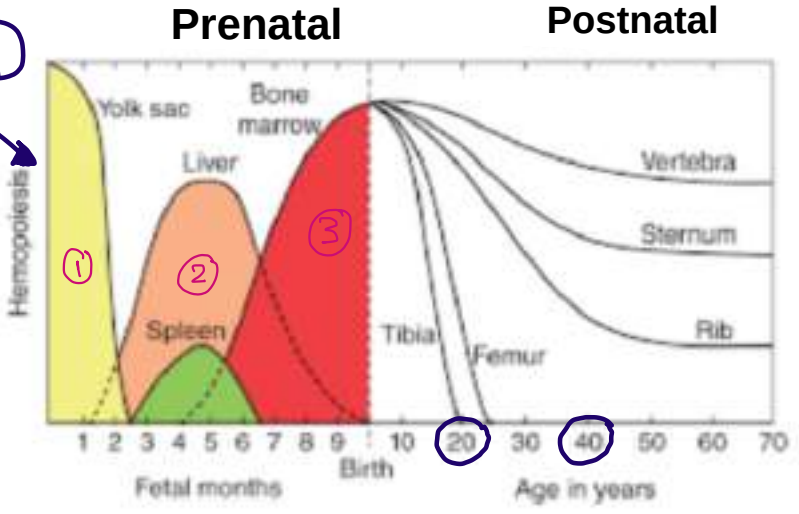
- In early development, blood cells arise from the mesoderm in the yolk sac

.Yolk sac: A sac that provides early nourishment to developing embryos with essential nutrients during the initial stages of development.

- Later, the liver and spleen take over

after a few weeks from eight weeks on during intraterineal life the liver here and the spleen will take over in the formation of

قبل الولادة Prenatal | بعد الولادة Postnatal



- Late in pregnancy, bone marrow takes over and becomes the main source of blood elements

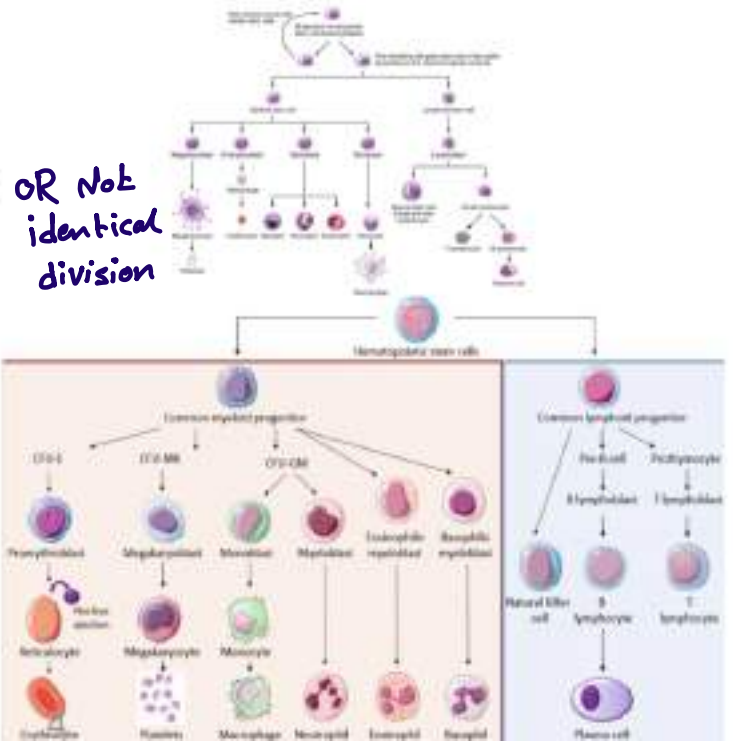
Where are the places in the bone marrow that take the function of blood formation?

In the early stages up to 20 years in the tibia in the bone marrow of the tibia and femur and then including there the other elements

but after that after 20 years يعني بعد اربعين سنة the flat bones or the bone marrow on the flat bones mainly the vertebrae and the sternum and the ribs will take over in blood formation.

Stem Cells

- They are pluripotent cells
- Capable of asymmetrical division and self-renewal
- Some daughter cells become irreversibly differentiated cells
- Other cells remain as stem cells
- Pluripotent cells proliferate and form two cell lineages:
  - Myeloid cells
  - Lymphoid cells



there are stem cells found in the bone marrow that are taking the function of formation of different blood cells

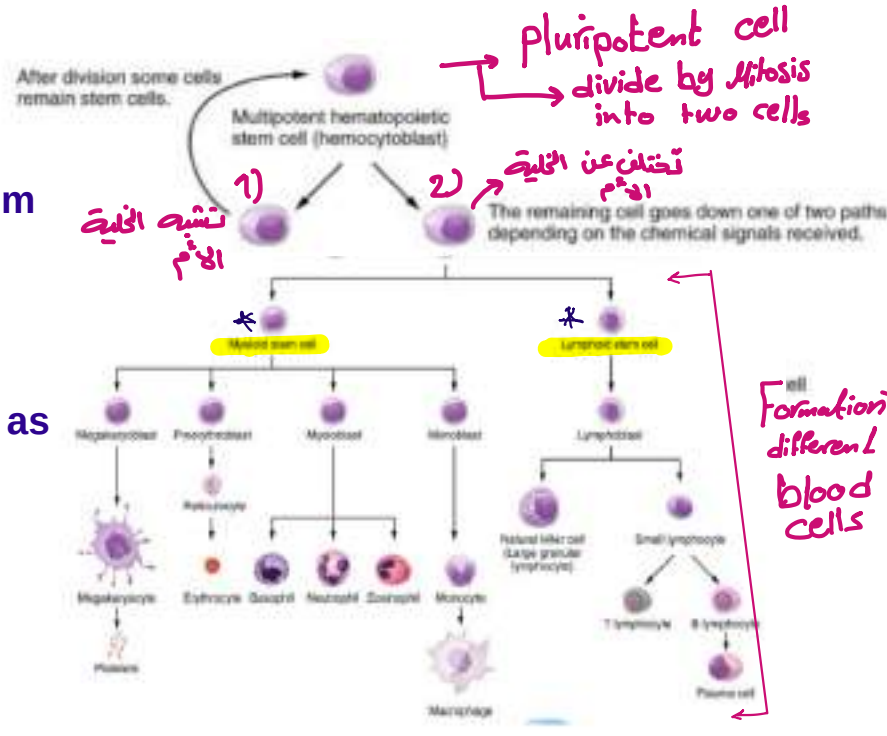
Pluripotent cell: means that we have one cell in the bone marrow that is capable to form many types of other cells, namely here is the blood cells.

The first stem cell in the bone marrow is not identifiable. We cannot identify to say this is the first cell in the blood formation line. What we know is that this cell can actively divide by mitosis, giving me many cells.

the pluripotent cell will divide into two cells:

1)One is identical to the mother cells and gives me the reserve for more stem cells.

2)The other cell is different from this cell. It will not go back as a reserve or as a mother cell, but it can continue in other path.



Stem Cells

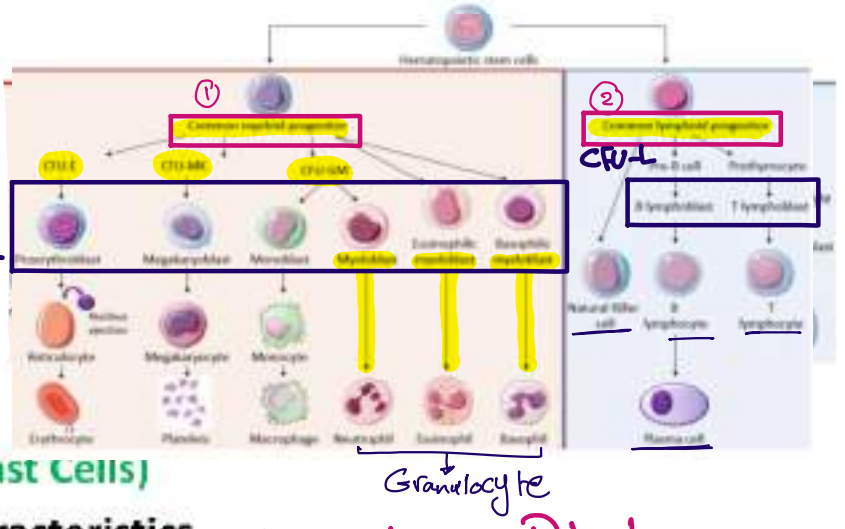
- Stem cells give rise to daughter cells with restricted potentials called Progeniator Cells ① + ②
- Four groups are formed:

  CFU-E

  CFU-meg

  CFU-GM

  CFU-L
- All these progenitor cells in (CFUs) produce Precursor (Blast cells)
- They have morphological characteristics
- They differentiate into the mature cells



immature = Blasts
mature = cytes

* هيدا خلونا متفقين أنه ال stem cell (pluripotent cell) إذا
Lymphoid ← بنسميها B,T Lymphocyte كانت رح تتكوّن
myeloid ← أما إذا رح تتكوّن الباقي من خلايا الدم
والهم أسماء أخرى
CFU-L = Lymphoid (colony forming unit Lymphocytes)
CFU-S = myeloid (colony forming unit spleen)

* ورح تتحول بهاي الطريقة

stem cell ← progeniator cell ← Blast cell or precursor cell ← mature cells

CFU-E: Colony-Forming Unit - Erythroid, responsible for the formation of erythroid cells (red blood cells).

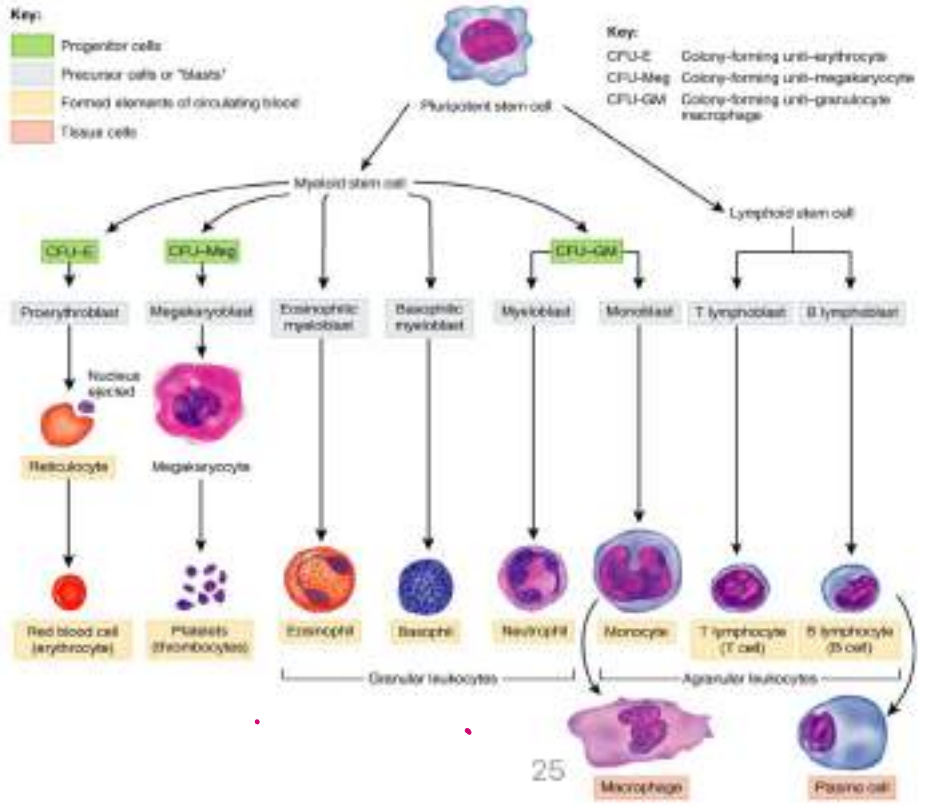
- **CFU-meg: Colony-Forming Unit - Megakaryocyte, involved in the formation of megakaryocytes, which eventually produce platelets.**

- **CFU-GM: Colony-Forming Unit - Granulocyte-Monocyte, contributes to the development of granulocytes (neutrophils, eosinophils, and basophils) and monocytes.**

- **CFU-L: Colony-Forming Unit - Lymphocyte, plays a role in the formation of lymphocytes, essential components of the immune system.**

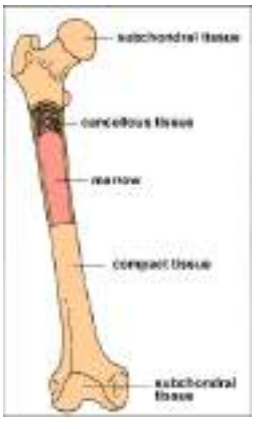
هاي الصورة بتوضح الفكرة اكتر ورح نحكي تفاصيلها تحت أكتر وهلا ارجعو شوفوها.

Summary of Blood cells formation

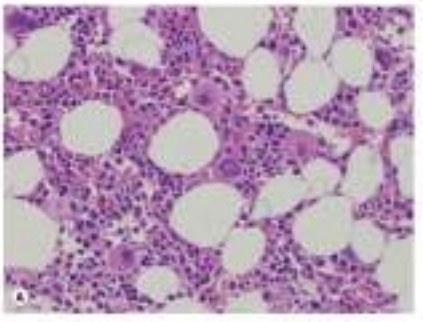


ترتيب الدكتور للسلايدات شوي معجق بس خليكم مركزين لأنه بعد ال **bone marrow** حنرجع نحكي عن خطوات تكون خلايا الدم بالتفصيل .

Bone Marrow



- Bone marrow is found in medullary canals of long bones and cavities of cancellous bone (العادي)
- Yellow bone marrow
- Red bone marrow



Stroma made of reticular cells and fibers

Hematopoietic cords or islands of cells

Sunusoidal capillaries

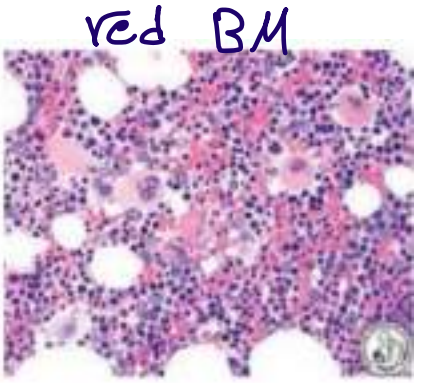
Matrix:

Collagen type I, Proteoglycan, Fibronectin, macrophages and Laminin binds to integrins

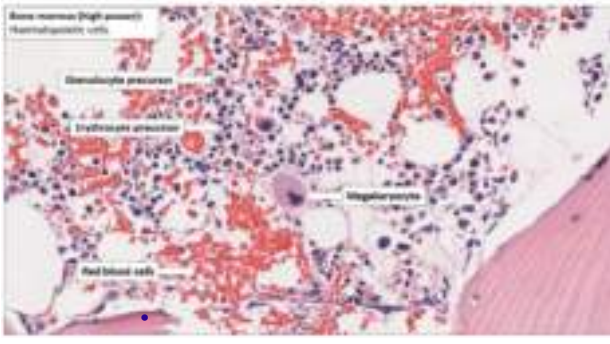
↳ protein

هذا الجدول جبته من سلايدات الدكتور محمد فتحي كتير مهم تدرسو

	Yellow inactive type	Red active type
Color	Is yellow in color due to its high content of fat cells.	Is red in color due to its high content of HB (in RBCs).
Site	Forms most of marrow in adults & is present in diaphysis of long bones. لما تجيب عظمة من عند اللحام وتكسرها بطلع منها مادة هاي هي النخاع yellow inactive type	– In fetus: most of the marrow is of the red type. – In adults, is present in: epiphyses of long bones, diploes of flat bones, vertebrae, sternum & ribs.
Functions	– Storage of fats. – In time of need as in haemorrhage, it can change into active red type. - serves as a Reserve for red Bone M	-Production of blood cells. -Destruction of old RBCs. -Storage of iron in macrophages.
Stem cell	present and can transform into Red Bone Marrow	present.



- **Higher magnification of this red BM it contain all type of stem cells, precursor cells, and blast cells of different blood elements.**
- **Mature types of different blood elements may also be present in the bone marrow**



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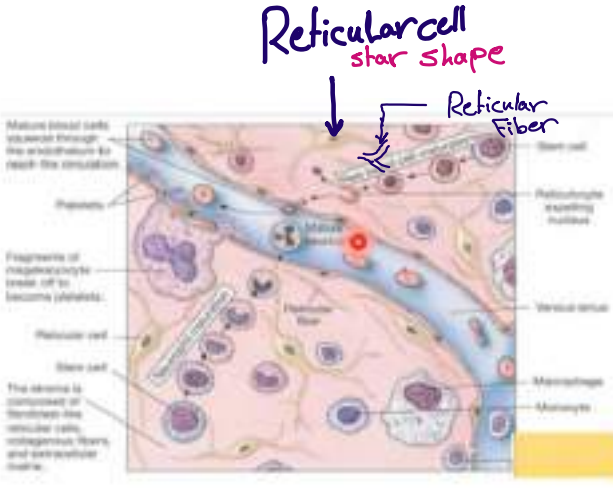
Bone Marrow Components:

- ***Contains various stem cells, precursor cells, and blast cells.***
- ***Reticular cells and fibers form stroma And this form is called folding or spallata.***
  - ***Capillaries allow mature blood cells to enter circulation.***
  - ***Matrix (الارضية) has glycosaminoglycans and blood elements.***
  - ***Macrophages handle apoptotic cells.***
  - ***Support from collagen fibers, laminin fibers, and other lymphatic matrix components.***

الشبكة اللي تحتوي فيها different elements of BM



هسا خلونا نرجع نكمل كيف ال ***stem cell*** بتكون خليتين وخلينا نركز اكتر على الخلية التانية اللي بتختلف عن الام واللي بتكونلنا ال ***lymphoied and***

Changes during Erythropoiesis

The following are the changes that occur in the blast cell until RB formation:

- Cell decreases in size
- Nucleus decreases in size
- Decrease basophilia
- Increase acidophilia
- Condensation and then expulsion of the nucleus
- Cell organelles gradually disappear

هيك بيصير كمية Hb بالسيتوبلازم أكتر بعني خلية RBC بتقدر تحمل كمية O_2 أكبر

↑ Hb → ↑ redness

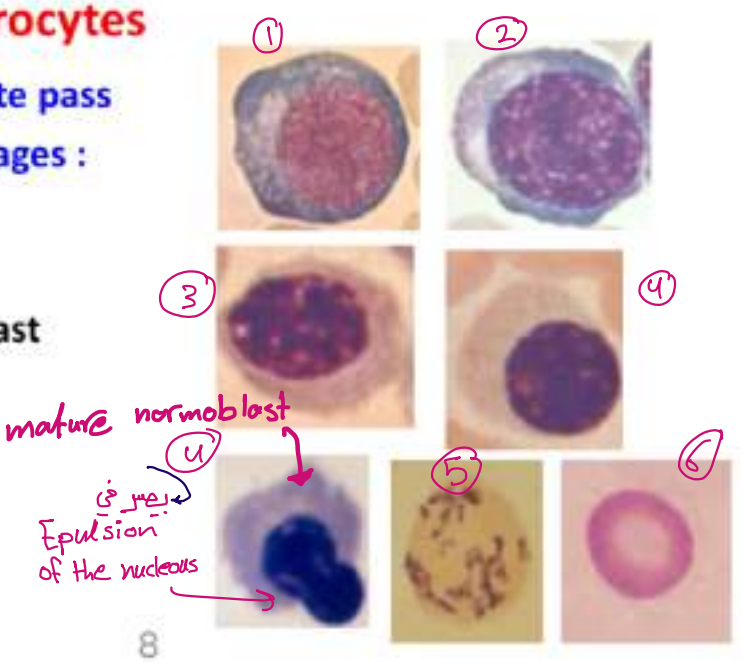
طردها

لا تنسو انه ال *myeloid progenitor* رح تكون *CFU-E* وبعدها رح تتحول إلى *precursor* اللي رح نسميها *proerythroblast* *(Blastcell)* وآخر اشي رح تنتهي بال *erythrocytes*

Maturation of Erythrocytes

Maturation of erythrocyte pass through the following stages :

1. Proerythroblast
2. Basophilic erythroblast
3. Polychromatic erythroblast
4. Normoblast
5. Reticulocyte
6. Mature erythrocyte



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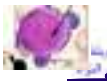
هدول السلايدات جبتهم من سلايدات الكتور محمد فتحي اقرأوهم بتركيز عشان تقدرو تفهمو الخطوات لأنه الدكتور زياد شرحهم من ضمن حكيه ✅

1- Proerythroblasts:



الخلايا بتكون كبيرة بحجم النواة وبتصغر مع تعقيد السيتوبلازم

- About 17µm
- Basophilic cytoplasm (due to ribosomes & polysomes) with perinuclear halo and sometimes bulge forming ear shaped process. Large centrally located pale nucleus with 2 nucleoli.

لأنخ حجم النواة كبير فبتبقع السيتوبلازم للخارج

4- Normoblasts:

- Smaller (8µm)
- Cytoplasm is acidophilic because it is rich with Hb.
- The nucleus is small and deeply stained and it is found near the cell membrane (eccentric) ready to come out.

2- Basophil erythroblasts:

- Smaller (14 µm)
- Deeply basophilic cytoplasm.
- Smaller nucleus with NO nucleoli seen.

5- Reticulocytes:

- Immature RBCs
- Slightly larger than normal RBCs
- Cytoplasm still retains some polyribosomes which appear as spots or threads.
- Normally their percentage not exceeding 1-3% of the total erythrocytes.
- Can be demonstrated with Brilliant cresyl blue dye.
- Significance of reticulocytes: Increased percentage of reticulocytes in the peripheral blood means increased erythropoietic activity (e.g. haemorrage, hemolysis).

3- Polychromatophil erythroblasts:

ألوان متعددة

- Smaller (11µm)
- The cytoplasm is polychromatophilic = it has many colors, because it takes both the blue color due to the polyribosomes as well as the red color of Hb which is synthesized by polyribosomes (RER)
- Nucleus is small and deeply stained.

6- Erythrocytes:

- Biconcave discs (7.5µm) circulating in peripheral blood.
- Cytoplasm full of Hb and no nucleus.

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هسا هيك عرفنا كيف بتتكون ال RBC هسابدنا نشوف كيف بتتكون ال White Blood cells ولا تنسو انهم بتكونو من ال myeloid progenitoro

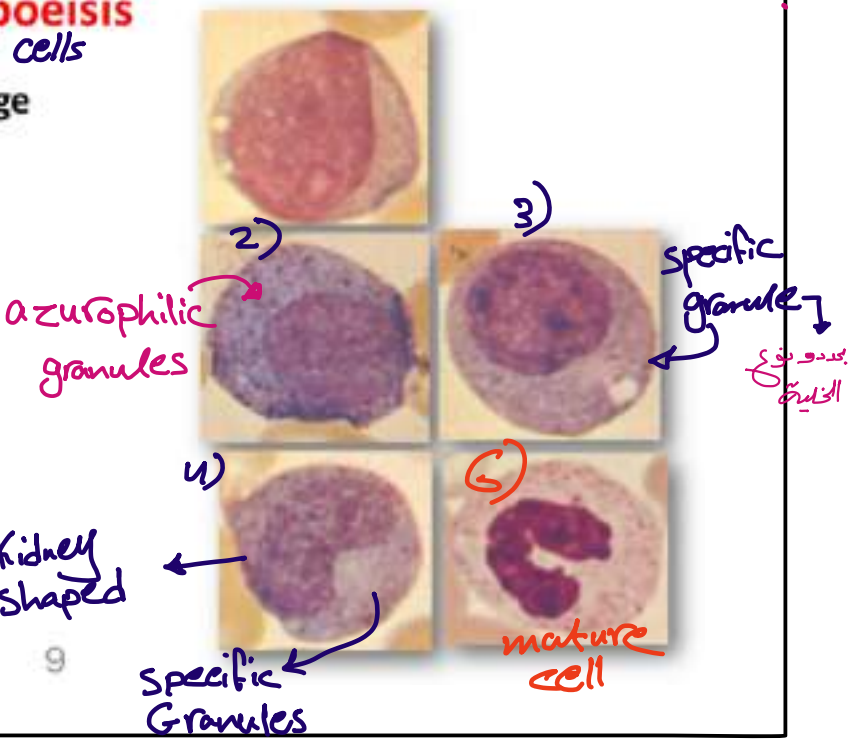
Changes during Granulopoeisis

Formation White Blood cells

1. Myeloblst: first recognizable stage
2. Promyelocyte
3. Myelocyte
4. Metamyelocyte
5. Band cell
6. Mature cell

Esinophil
Basophil
neutrophil

(بمعنى أنه صار فيها ابتعاج وصارت تأثرها صعبين) Kidney Shaped



1) **Myeloblasts**, which are **precursor cells**, show similarities to proerythroblasts in the RBC. They are large with a large nucleus and multiple nucleoli. The cytoplasm more or less is clear at this stage. وما ننسى انه هاي الخلايا رح يصيرلها **differentiate into neutrophils, basophils, and other types,**

2) **Promyelocyte** : **Basophilic cytoplasm that contains non-specific azurophilic granules.**

① they are Lysosomes
② they are Large in size
③ لونهم قرمزي

3- **Myelocytes:** Smaller in size. The nucleus has a deep indentation and assumes an eccentric position within the cell. • The cytoplasm contains both types of granules: specific and non-specific. So, there will be three types of myelocytes:

*Neutrophilic myelocytes: with specific neutrophilic granules.

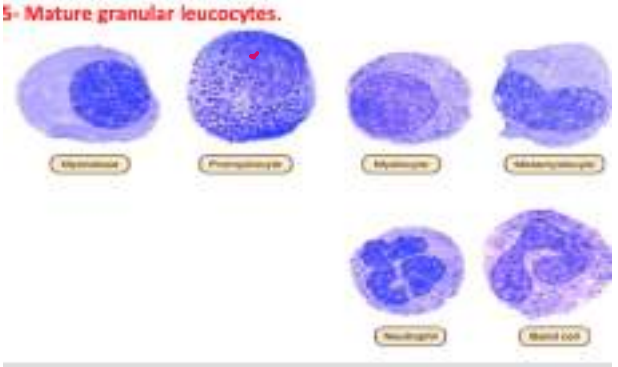
*Eosinophilic myelocytes: with specific acidophilic granules.

*Basophilic myelocytes: with specific basophilic granules. At this stage, myelocytes lose their capacity for mitosis and they change to metamyelocytes.

4- **Metamyelocytes:** Smaller cells with more specific granules and less developed organelles. Nucleus becomes kidney-shaped with more condensed chromatin. Neutrophilic metamyelocytes pass through an intermediate stage where the nucleus becomes curved rod (band cells), then, they pass to mature neutrophils with segmented nucleus.

*Neutrophilic only → Band cells

5- Mature granular leucocytes.



للتذكير

By E.M: they contain Granules : Three types:

Specific:
*Neutrophilic granules: consist 80% of granules. They are small, membrane bounded and contain alkaline phosphatase, collagenase and lactoferrin (bacteriostatic).

Non-specific:
*Azurophilic (AZ) granules: consist 20% of granules. They are large. They are primary lysosomes which contain: hydrolytic enzymes, proteolytic and lipolytic enzymes, peroxidase and bactericidal basic protein. (type of cell membrane ump)

*Tertiary granules: contain glycoprotein as well as gelatinase enzyme

gelatin membrane

Neutrophils

الغالبية العظمى

Vast majority of granulocytes are neutrophils

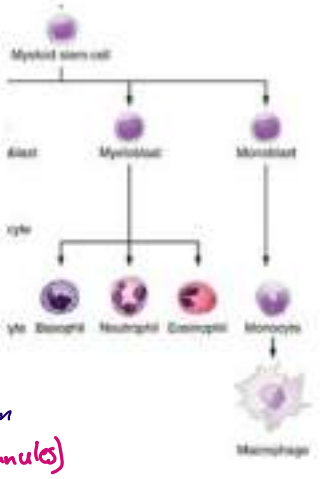
Developing and mature neutrophils are found in:

- Granulopoietic component in bone marrow (immature neutrophils)
- Stored as mature neutrophil in bone marrow
- Circulating neutrophils (mature)
- Marginating neutrophils adhering to the endothelium of venules and small veins → in the inflammation

Diapedesis: neutrophils move to the connective tissue (from circulation)

Monocyte Maturation

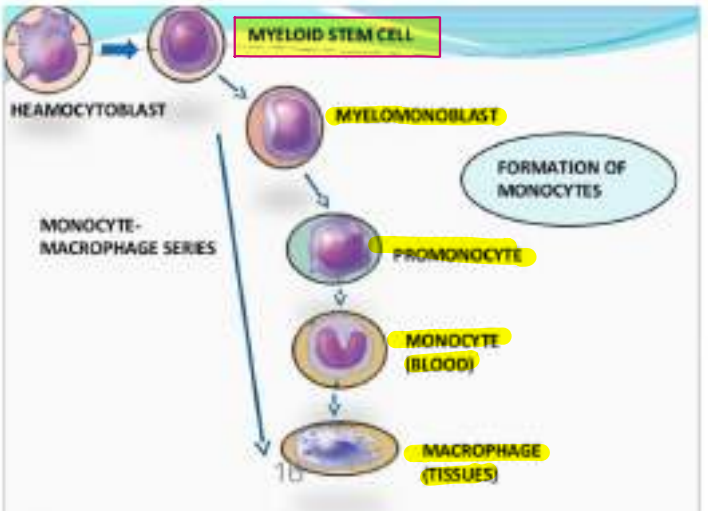
- (1) Monoblast is the first recognizable cell in monocyte lineage (تتحول)
- It is more like myeloblast
- (2) Promonocyte with basophilic cytoplasm and intended nucleus. It has lacy chromatin and few nucleoli
- It divides twice before it differentiates into (3) monocyte (immature)
- It is characterized by abundant RER and Golgi with azurophilic granules (why?)



* Because when they leave to the connective tissue (رح يتحولوا إلى) Macrophages → تنتج organells (bacteria) → فيحتاج إلى Lysosomal enzyem (Cazurophilic granules) from RER and Golgi.

- They leave to the circulation for few hours and then to connective tissue to become Macrophage

رسمة خارجية للتوضيح



Lymphocyte Formation

- Lymphoblast is the first recognizable cell in the lymphocyte series
- They have few nucleoli and less dense chromatin
- It is capable of dividing 2-3 times
- It differentiates into prolymphocyte
- It is smaller in size with dense chromatin and invisible nucleoli
- None of these cells carry any surface antigens
- In bone marrow and thymus (الغدة الزعترية), they synthesize surface receptors and become B and T lymphocytes

صورة خارجية للتوضيح

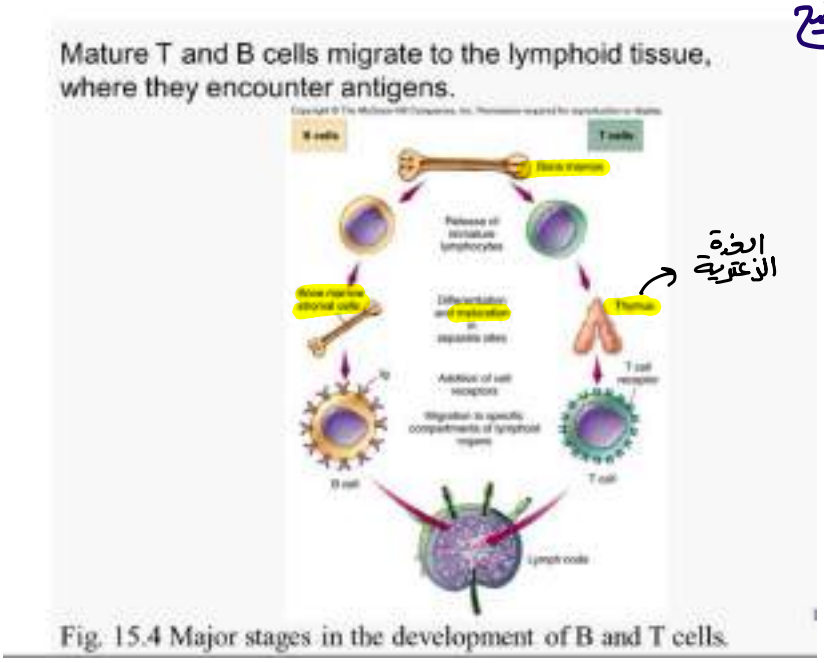
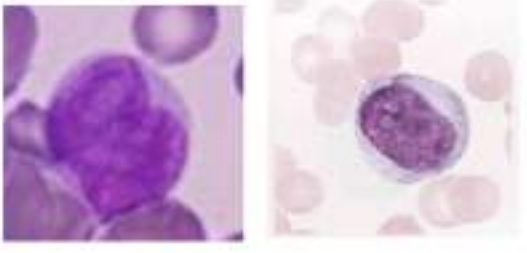
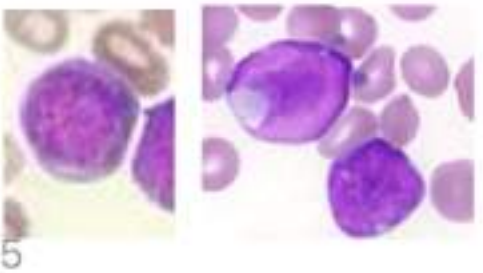


Fig. 15.4 Major stages in the development of B and T cells.

- Monoblast

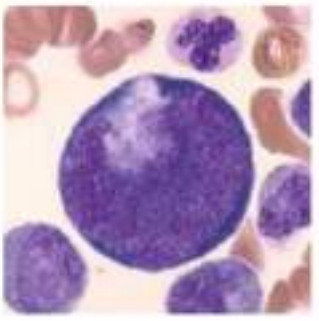


- Lymphoblast



Platelet Formation

- Megakaryoblast in bone marrow is large 25-50 µm in diameter with an ovoid to kidney-shaped nucleus with numerous small nucleoli
- This cell goes endomitosis several times resulting in a highly polypoid nucleus.
- It has homogeneous and intense basophilic cytoplasm
- It differentiates into Megakaryocyte, which is three times larger than the ancestor cell



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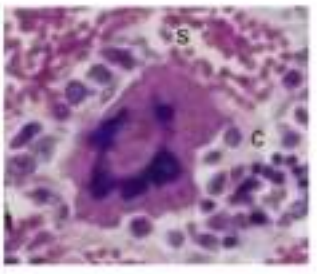
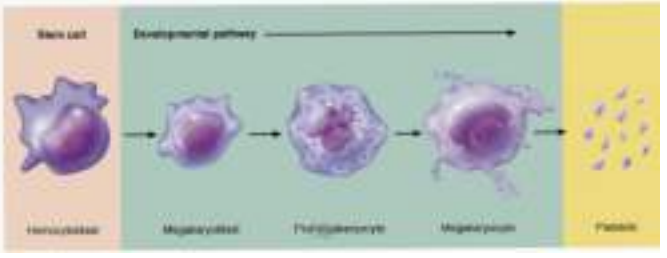
endomitosis. . But it is endo, what does it mean? This means that the nucleus or the chromatin or the chromosomes, they are divided inside the cell many times, and becomes highly haploid or polypoid nucleus.

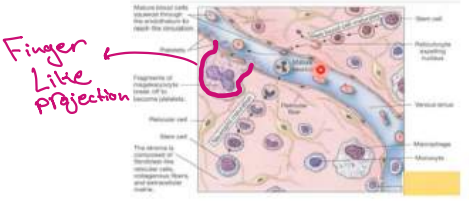
Megakaryocyte

- It has coarse chromatin, a multilobulated nucleus, and invisible nucleoli
- They show all organelles involved in protein synthesis
- They form proplatelets (long cytoplasmic processes)
- The elongation of proplatelets depends on the sliding microtubules
- Platelets are pinched off from the end of the proplatelet
- The remnant of megakaryocytes show apoptosis and removed by macrophages

Finger Like projection





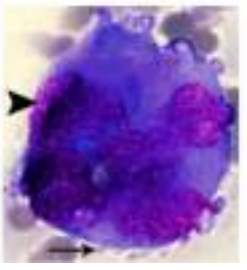


وهيك بتكون خلصت محاضرتنا لليوم ✅ باقي السلايدات حكا الدكتور *just for help you* 👌 وبتنمى تكون استفدتو

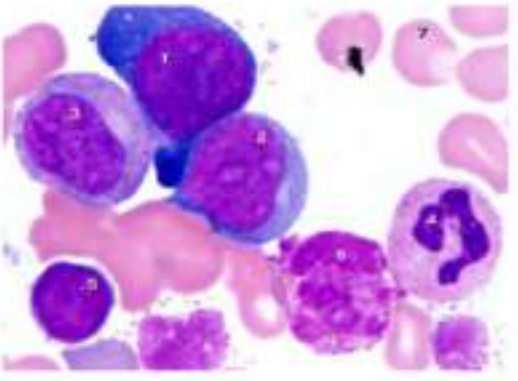
ولا تنسونا من دعائكم ❤️

- Megakaryoblast

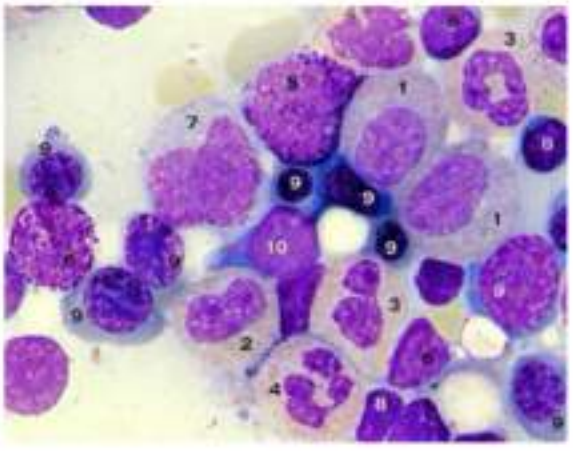
- Megakaryocyte



1. Proerthroblast: More basophilic cytoplasm, nucleoli long curved comma shaped
2. Myeloblast: less basophilic cytoplasm, round nucleoli
3. Myelocyte

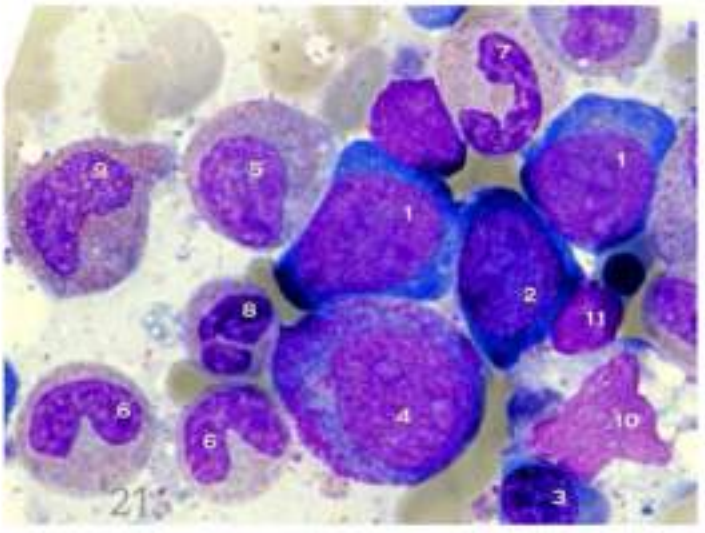


1. Myelocyte
2. Metamyelocyte
3. Band
4. Mature nutrophil
5. Basophilic myelocyte
6. Basophil
7. Monocyte



NORMAL BONE MARROW

1 = Proerythroblast
2 = Basophilic erythroblast
3 = Polychromatic erythroblast
4 = Promyelocyte
5 = Myelocyte
6 = Early band neutrophil
7 =Late band neutrophil
8 = Segmented neutrophil
9 = Band eosinophil
10 = Monocyte
11 = Small lymphocyte.b



NORMAL BONE MARROW

- A myeloblast (#1) is the earliest recognizable cell in the myeloid series. It has scant agranular to sparsely granular cytoplasm and large nucleus with fine chromatin and one to three prominent nucleoli. The quality of chromatin is the most important morphologic feature to identify a myeloblast.
- A promyelocyte (#2) is the next morphologic stage in myeloid maturation where cells accumulate more cytoplasm and azurophilic granules and the nucleus

  becomes smaller and show coarser

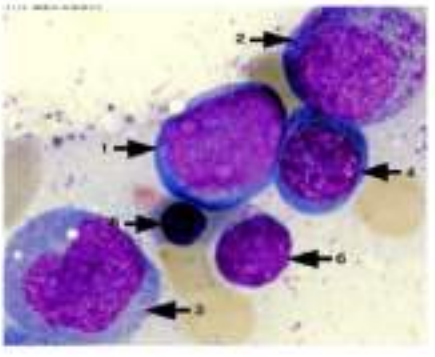
  chromatin with small to distinct nucleoli.

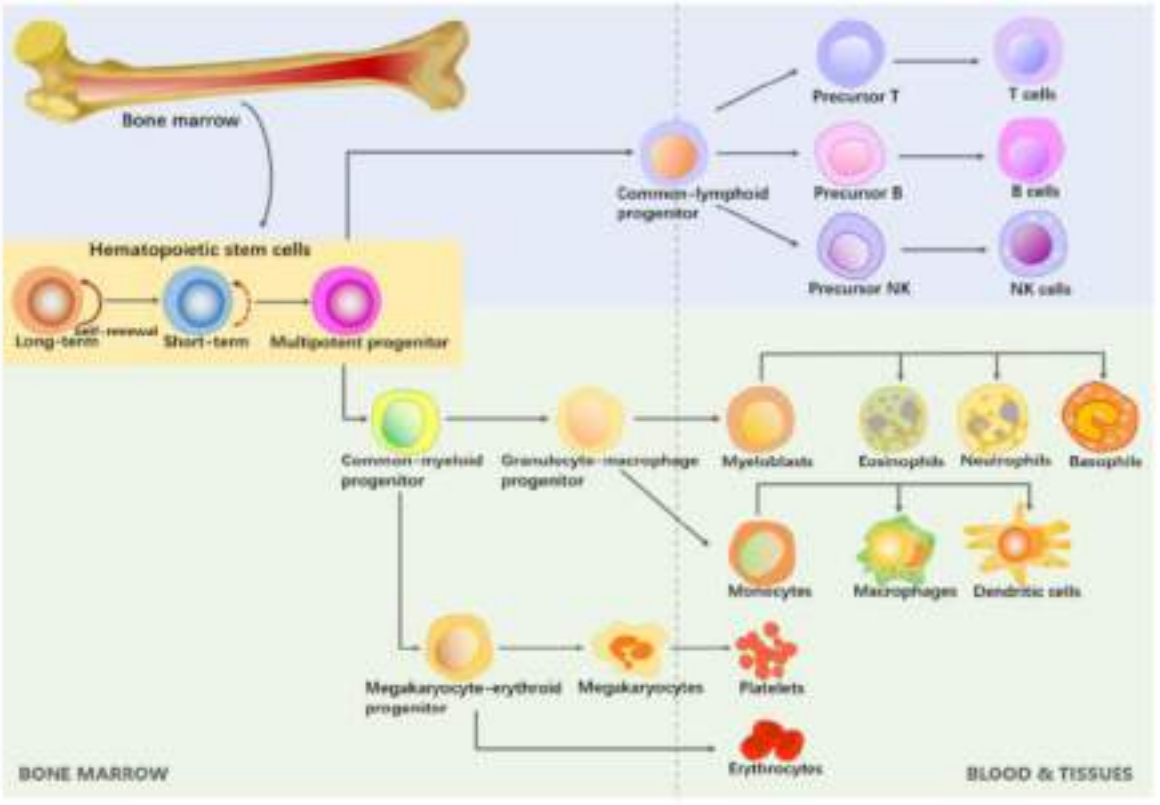
  A monocytes (#3) is shown with abundant

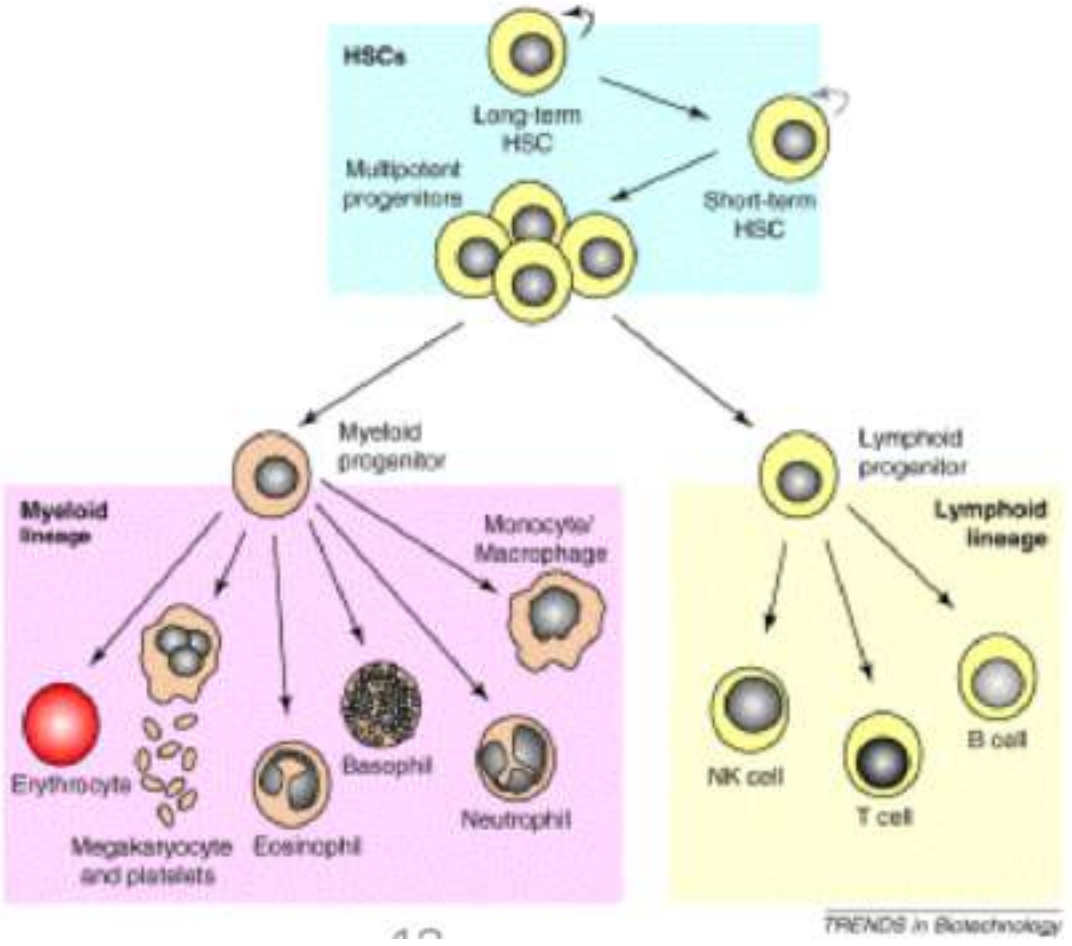
  cytoplasm and finer and fewer granules

  than a promyelocytes and no prominent

  nucleoli.




Bone marrow
Hematopoietic stem cells
Long-term
Self-renewal
Short-term
Multipotent progenitor
Common-lymphoid progenitor
Precursor T
T cells
Precursor B
B cells
Precursor NK
NK cells
Common-myeloid progenitor
Granulocyte-macrophage progenitor
Myeloblasts
Eosinophils
Neutrophils
Basophils
Monocytes
Macrophages
Dendritic cells
Megakaryocyte-erythroid progenitor
Megakaryocytes
Platelets
Erythrocytes
BONE MARROW
BLOOD & TISSUES


HSCs
Long-term HSC
Multipotent progenitors
Short-term HSC
Myeloid progenitor
Lymphoid progenitor
Myeloid lineage
Monocyte/ Macrophage
Erythrocyte
Megakaryocyte and platelets
Eosinophil
Basophil
Neutrophil
Lymphoid lineage
NK cell
T cell
B cell
TRENDS in Biotechnology