

BLOOD

of Burstami /

a tissue consisting of a variety of cells suspended in a fluid medium called plasma



Main function → a vehicle for the transport of
gases nutrients metabolic waste products cells
& hormones throughout the body



PLASMA → essentially aqueous solution of inorganic salts which is constantly exchanged with extracellular fluid of body tissues

Plasma also contains → Plasma Proteins of 3 main types.

albumins
globulins
fibrinogen

} collectively exert a colloid osmotic pressure within the circulatory system which helps to regulate the exchange of aqueous solutions between plasma & ECF

Albumins → constitute the bulk of plasma proteins

bind insoluble metabolites such as fatty acids & serve as transport proteins

Globulins → includes the antibodies of immune system transport lipids

Fibrinogen → soluble protein which polymerises to form the insoluble protein fibrin during blood clotting

Blood cell types → 3 major classes

- Red blood cells (RBCs) (erythrocytes)
- white blood cells (WBCs) (leucocytes)
- platelets (thrombocytes)

All are formed in the bone marrow
in a process known as haemopoiesis

Erythrocytes involved in transport of O_2 & CO_2
function exclusively within the vascular system

Leucocytes important part of defence & immune system
act mainly OUTSIDE blood vessels
in the TISSUES

platelets play a vital role in the control of bleeding (haemostasis) by a) plugging the defects in blood vessels b) activating the blood clotting cascade

Methods used to study blood & bone marrow

→ to make a smear on a glass slide

After fixation stained by a Polychromatic stain ↴
Giemsa
Wright
Leishman

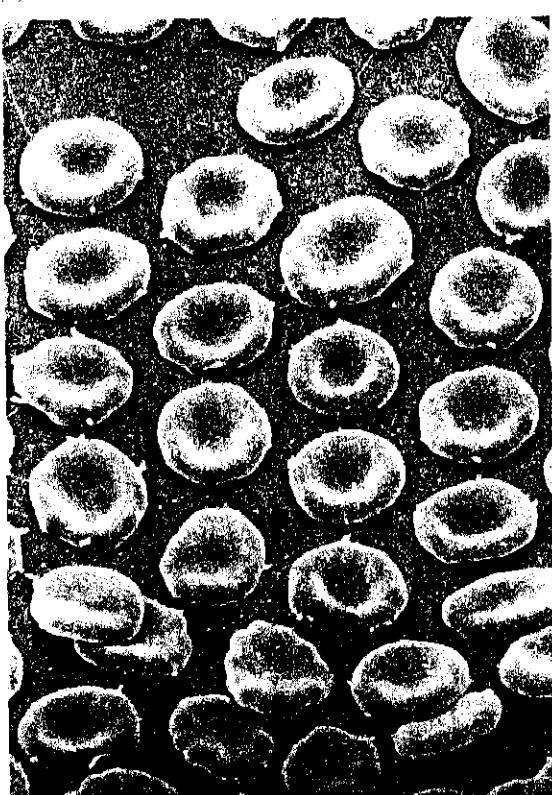
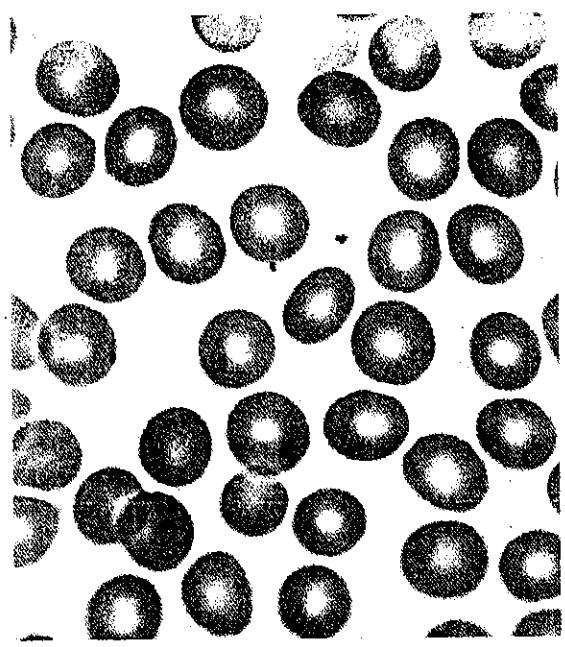
(4) distinctive staining characteristics (according to the affinity of the various cellular organelles to the different stains employed)

(a) Basophilia (deep blue): affinity for the basic dye methylene blue → characteristic of DNA in nucleus & RNA in the cytoplasm e.g. ribosomes

(b) azurophilia (purple) → affinity for azur dyes, typical of lysosomes (azurophilic granules in leucocytes)

(c) eosinophilia (pink) → affinity for acidic dye (eosin)
particular feature for hemoglobin within erythrocytes

(d) neutrophilia (salmon Pink/lilac) : characteristic of the specific cytoplasmic granules of neutrophil leucocytes (the dye is not of neutral pH)



Erythrocytes

Giemsa stain
Scanning EM
③

RBC are pink biconcave discs that are 7-8 μm in diameter.

Pink (eosinophilia/acidophilia) is due to their high content of hemoglobin which is a basic protein.

The pale staining of the central region is a result of its biconcave disc shape provides 20-30% greater surface area than a sphere relative to cell volume → thus significantly enhancing gas exchange.

This shape along with the fluidity of the plasma membrane allows erythrocytes to deform readily & thus erythrocytes (average diameter 7.2 μm) are able to pass through the smallest capillaries (3-4 μm in diameter).

Erythrocytes are enclosed by a typical cell membrane → During differentiation in the bone marrow, vast quantities of the iron-containing respiratory pigment haemoglobin are synthesized → Before release into the blood circulation, the erythrocyte nucleus is extruded and by maturity all cytoplasmic organelles degenerate.

The fully differentiated erythrocyte consists merely of an outer plasma membrane enclosing haemoglobin and the limited number of enzymes necessary for maintenance of plasma membrane integrity & gas transport functions.

Immediately beneath the plasma membrane is a MESHWORK of proteins forming a cytoskeleton → responsible in part for the biconcave shape of erythrocytes.

Number of erythrocytes in ♂ 4,500,000 - 6,000,000 / cu. mm
in ♀ 3,800,000 - 5,000,000 / cu. mm
Lifespan = 120 days → without organelles → erythrocytes are unable to replace necessary enzyme & membrane proteins

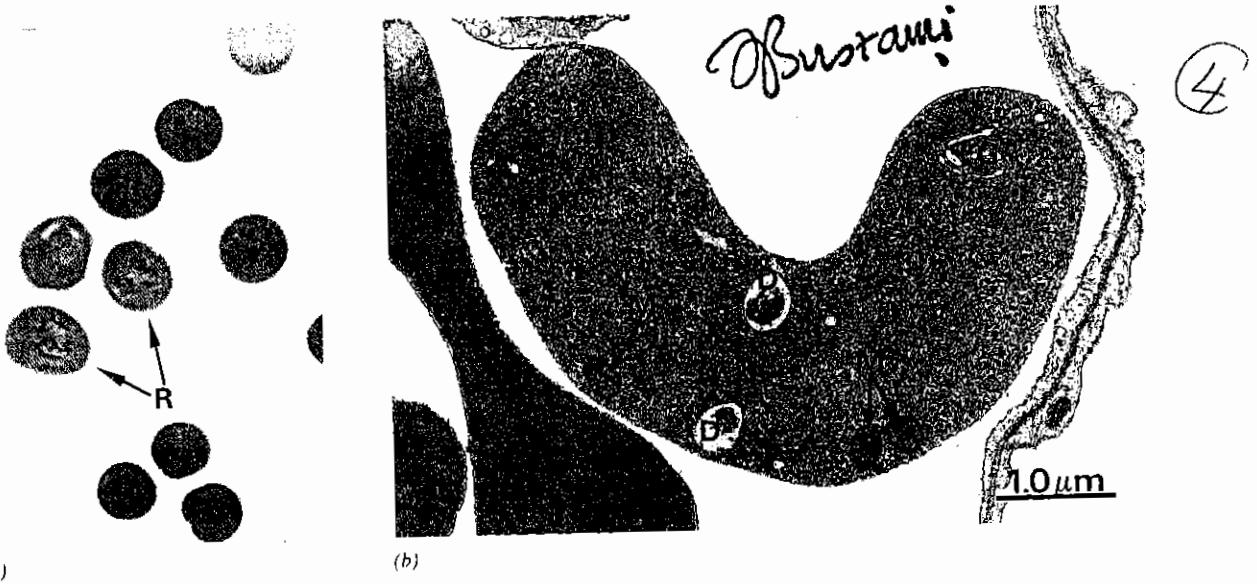


Fig. 3.3 Reticulocytes (a) Cresyl blue/eosin $\times 1200$ (b) EM $\times 16\,000$

Reticulocytes are the immature form in which erythrocytes are released into the circulation from the bone marrow

They still contain sufficient { mitochondria } to complete cytoskeleton & ribosomes } & the remaining 20% Golgi of hemoglobin synthesis

Final maturation into erythrocytes occurs within 24 - 48 hours of release

The rate of release of reticulocytes into the circulation generally equals the rate of removal of spent erythrocytes by the spleen & liver \rightarrow Reticulocytes constitute slightly less than 1% of circulating red blood cells

In routinely stained blood smears \rightarrow Reticulocytes cannot be easily distinguished from mature erythrocytes.

When fresh blood is incubated with basic dye \rightarrow brilliant cresyl blue \rightarrow a blue-stained Reticular precipitate is formed in the reticulocytes due to the interaction of the dye with ribosomal RNA remnants \rightarrow the technique is called supravital staining.

Reticulocytosis

Abnormalities of Erythrocytes

Obscurans ⑤

A change from the normal size shape or staining properties of erythrocytes are important indicator of disease. However, some of these abnormalities may be found in healthy individuals.

Anisocytosis → abnormal VARIATIONS in the SIZE)

of the red cells which may be Macrocytes (larger than normal) or microcytes (smaller than normal)

Poikilocytosis → abnormal shape of RBCs

the cells may show blunt Pointed Projections from their surface.
Crenation of red cell → if normal cells are placed in a hypertonic solution → water is abstracted from the cells leaving it shrunken & bearing numerous projections from its surface

One of the most severe changes in shape occurs during Sickling of RBCs in Sickle cell anaemia

Where the erythrocytes take on the form of crescents.

Hypochromia → denotes a decrease in the intensity of staining → indicates a decreased amount of haemoglobin
→ frequently accompanies microcytosis
→ hypochromic microcytic anaemia

Howell-Jolly bodies → nuclear fragments left over from the nucleated precursors of the red cell

An increase in the number of Reticulocytes is considered an abnormality but the cell itself is not an abnormal erythrocyte

White blood cells

(6)

5 types of leucocyte are normally present in the circulation → depending on their nuclear shape & cytoplasmic granules. of course

Granulocytes

- * Neutrophils
- * eosinophils
- * basophils

Mononuclear leucocytes

- * lymphocytes
- * monocytes

Granulocytes

so named → their prominent cytoplasmic granules

each cell → type-specific granules $\begin{smallmatrix} N \\ E \\ B \end{smallmatrix}$

single multilobed nucleus (old concept → multinuclear)

Polymorphonuclear leucocyte (Polymorph) ? the multilobed nucleus may assume many morphological shapes !!
mostly used to refer to neutrophils !!

Lymphocytes & monocytes → have Non-lobulated nuclei

Agranulocytes (old term !!) (Mononuclear !!)

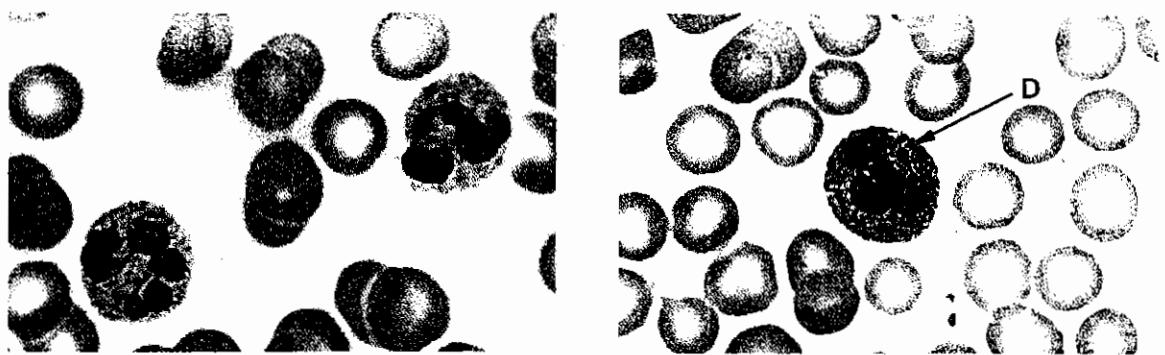
< they are not devoid of cytoplasmic granules >

Recall → lymphocytes play a key role in all immune responses → in contrast to the other leucocytes their activity is always directed against specific foreign agents

Neutrophils & monocytes

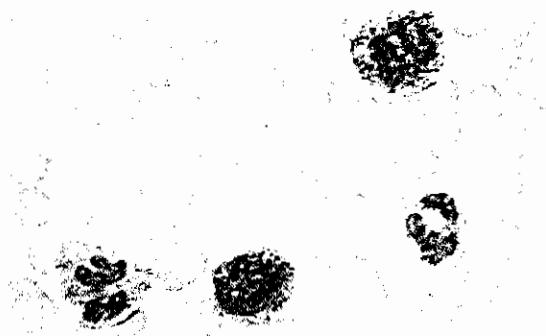
→ highly phagocytic & engulf microorganisms, cell debris → in a Non-specific manner

All the leucocytes perform their functions in the tissues & merely use the blood as a vehicle for transit between sites of formation → storage → activity



(a)

(b)



(c)

(d)

of sustans

Fig. 3.4 Neutrophils (a) Giemsa $\times 1200$ (b) Giemsa $\times 1200$
 (c) Histochemical method for alkaline phosphatase $\times 800$ (d) Giemsa $\times 2400$

Neutrophils → the most common type of leucocyte in blood & constitute (40-75%) of circulating leucocytes

→ characterized by the shape of the nucleus which contains (small lobes) connected by thin filaments

When mature → there are usually 5 lobes connected by fine strands of nuclear material. In less mature neutrophils the nucleus is less lobulated.

→ **Neutrophil of ♀** → the condensed quiescent X-chromosome or Barr body exists in the form of a small drumstick-shaped appendage of the nuclear lobes → visible in about 3% of neutrophils in Peripheral blood.

→ **Cytoplasm** contains

2 types of granules:

- The most numerous are the specific granules (barely visible by light microscopy) which are small and take on a pinkish colour. These granules contain Lysozyme an enzyme Phagocytin is present and also has bactericidal activity

The Azurophilic granules are less numerous
Somewhat larger and stain a reddish purple. (8) A
They are modified large lysosomes and contain
the usual lysosomal hydrolases and a number of
bactericidal agents including myeloperoxidase →
this can be demonstrated by the peroxidase stain and is
used as a marker for the Primary (Azurophilic) granules
and for identification of leukaemia arising in neutrophil
precursors

Functions of Neutrophils

Being highly motile & phagocytic → their principle function is in the Acute inflammatory response to tissue damage where they ingest & destroy damaged tissue & invading bacteria



Opsonins

Neutrophils in the circulation are attracted by the presence of organisms, particularly bacteria → This process is mediated by chemotactic factors (chemotaxins) released from damaged tissue & generated by the interaction of antibodies with antigens on the surface of micro-organisms.



The COATING of organisms with antibodies & complement greatly enhances neutrophilic phagocytic activity → opsonisation ←

organisms which do not generate chemotaxins or become opsonised → are relatively resistant to Neutrophil Phagocytosis & are thus highly pathogenic

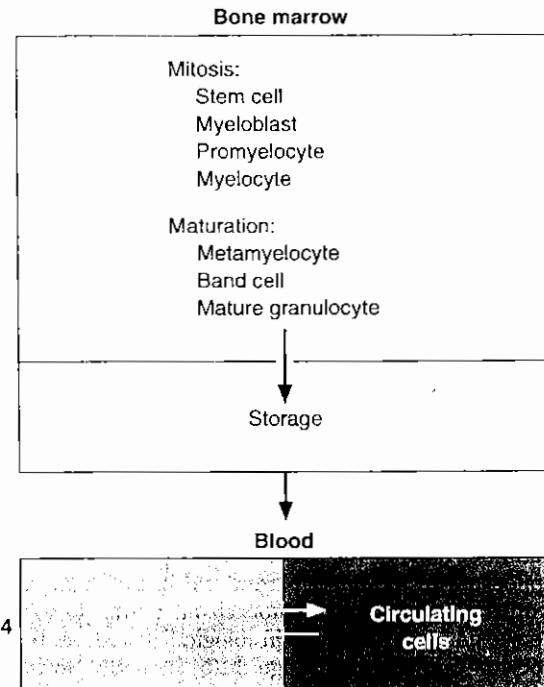
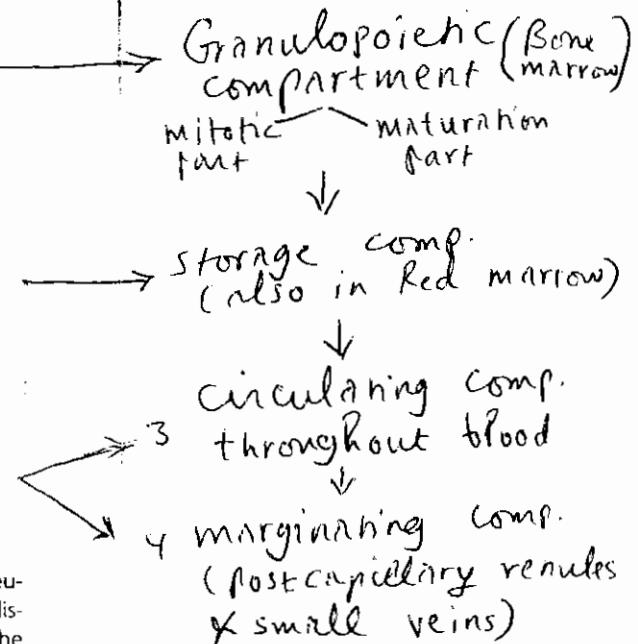


Figure 13-10. Functional compartments of neutrophils. Neutrophils exist in at least four anatomically and functionally distinct compartments, the sizes of which are proportional to the number of cells. (1) Granulopoietic compartment subdivided into a mitotic part and a maturation part. (2) Storage (reserve) compartment, also in red marrow, acts as a buffer system, capable of releasing large numbers of mature neutrophils on demand. (3) Circulating compartment throughout the blood. (4) Marginating compartment, in which cells temporarily do not circulate, but rather adhere via selectins to vascular endothelial cells of postcapillary venules, particularly in the lungs. The marginating and circulating compartments are of about equal size, and there is a constant interchange of cells between them. The half-life of a neutrophil in these two compartments is less than 10 hours. The granulopoietic and storage compartments together include cells in the first 11 days of their existence and are about 10 times larger than the circulating and marginating compartments.

Neutrophilia

!!
8/B



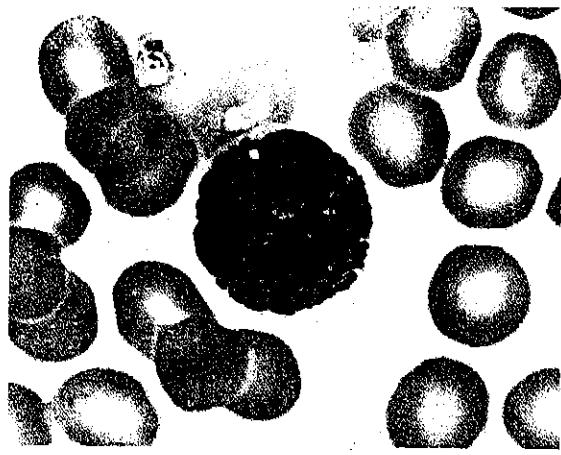
Obstruction

Neutrophilia (increase in the number of neutrophils in the circulation) → DOES NOT necessarily imply an increase in neutrophil production

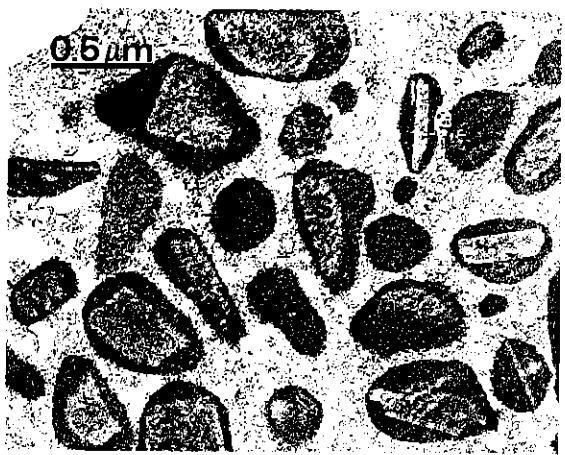
intense muscular activity administration of epinephrine → produce APPARENT neutrophilia!!
 → Causes neutrophils in the marginating compartment to move into the circulating compartment

glucocorticoids → increase the mitotic activity of neutrophil precursors in the marrow → increase blood count of neutrophils

Neutrophilia that occurs during bacterial infections
 increase production of neutrophils of these cells in bone marrow
 (+) short duration
 Band cells, neutrophilic metamyelocytes & even myelocytes may appear in blood stream



(a)



(b)

Fig. 3.6 Eosinophils (a) Giemsa $\times 1600$ (b) Human EM $\times 25\,000$
 (c) Mouse EM $\times 20\,000$ (opposite) (d) Rat EM $\times 25\,000$ (opposite)

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Eosinophils: account for $1-6\%$ of leucocytes in circulating blood \rightarrow their numbers exhibit a marked diurnal variation, being greatest in the morning \leftarrow and least in the afternoon.



- The eosinophil (12-17 μm) in diameter, is larger than the neutrophil → easily recognized by its large specific granules which are stained bright red & eosin
- most cells have bilobed nucleus (often partly obscured by cytoplasmic granules)



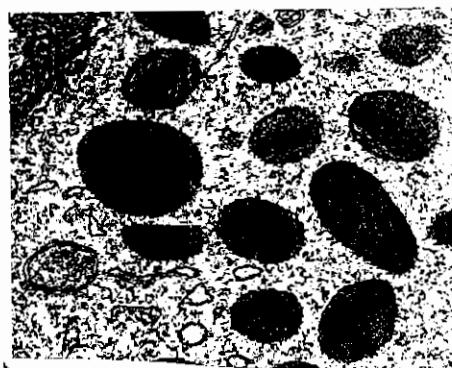
The granules are membrane-bound and shows an internal structure that has been called a crystallloid or internus (In Man it assumes various forms and is translucent, including histaminase)

The eosinophils granules are lysosomes and contain the usual lysosomal enzymes \rightarrow They show a higher content of peroxidase than do the azurophilic granules of neutrophils & lack lysozyme & phagocytin

Eosinophils are Phagocytic cells But less bactericidal than neutrophils, however they have a particular phagocytic affinity for antigen- antibody complex

All eosinophils have receptors for IgE (important in the destruction of parasites) \rightarrow this is Not present on neutrophils

(10)



Eosinophils undergo (chemotaxis) in response to (histamine) & eosinophil chemotactic factor of anaphylaxis (ECF-A) released from basophils & mast cell.

Eosinophils → ameliorate some aspects of hypersensitivity reactions ?? → they neutralize histamine & produce a factor → eosinophil-derived inhibitor which inhibits mast cell degranulation

Eosinophilia → ↑ No. of circulating eosinophils are found in ① many types of parasitic disease (defence against parasites is one of their principle functions) ② in some allergic disease e.g. hay fever & asthma → their role here ??

From bone marrow → circulation (3-8 hours) → enters skin, pulmonary mucosa, GI mucosa → local secretion

Fate & lifespan → unknown !!



Fig. 3.7 Basophils (a) Giemsa $\times 1500$ (b) EM $\times 10\,500$

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Basophils

- least common leucocyte
- constitutes less than 1% of leucocytes in circulating blood.
- lifespan \rightarrow unknown (few days !!)
- $\approx 14-16 \mu\text{m}$ in diameter (intermediate between N&E)
- bilobed nucleus obscured by large densely basophilic (deep blue) specific granules which are larger but fewer in number than those of eosinophils \rightarrow granules are metachromatic !! they contain Proteoglycans. The granules contains heparin, histamine, eosinophil chemotactic factor of anaphylaxis (ECFA)

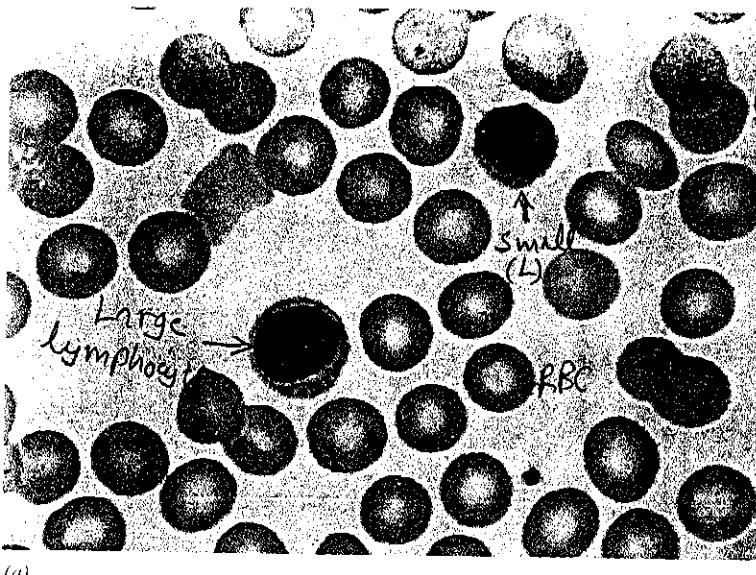
Basophil & mast cells \rightarrow have membrane receptors highly specific for the Fc segment of IgE

① which is produced by plasma cells in response to a variety of allergens

② Exposure to allergen results in antigen forming bridges between adjacent IgE molecules which triggers rapid exocytosis of granules (degranulation)

The release of histamine \downarrow other mediators is responsible for the so called \rightarrow immediate hypersensitivity (anaphylactoid) reaction characteristic of allergic rhinitis (hay fever) some forms of asthma urticaria anaphylactic shock

Basophils \rightarrow account for up to 15% of infiltrating cells in allergic dermatitis & skin allograft rejection \rightarrow cutaneous basophil hypersensitivity



(d)

Lymphocytes

(12)

- ① the smallest cells in the white cell series (slightly larger than erythrocytes)
- ② the second most common leucocyte in circulating blood & make up 20-25% of the differential white cell count
- ③ increased numbers are commonly seen in viral infections

Observations:

- ④ Characterised by large round densely stained nucleus & a relatively small amount of basophilic non-granular cytoplasm
- ⑤ The amount of cytoplasm depends upon state of activity of the lymphocyte → In circulating blood there is predominance of Small inactive lymphocytes (6-9 μm in diameter) - Large lymphocytes (9-15 μm) make up about 3% of lymphocytes in peripheral blood → Represent activated B lymphocytes en route to the tissues where they will become antibody-secreting plasma cells, they also include natural killer cells

In the large lymphocyte → the cytoplasm is readily visible ↓ but in the small lymphocyte the cytoplasm is almost too sparse to be seen (contain few mitochondria, rudimentary Golgi apparatus, minimal endoplasmic reticulum but large No. of ribosomes → account for basophilia (blue cytoplasm))

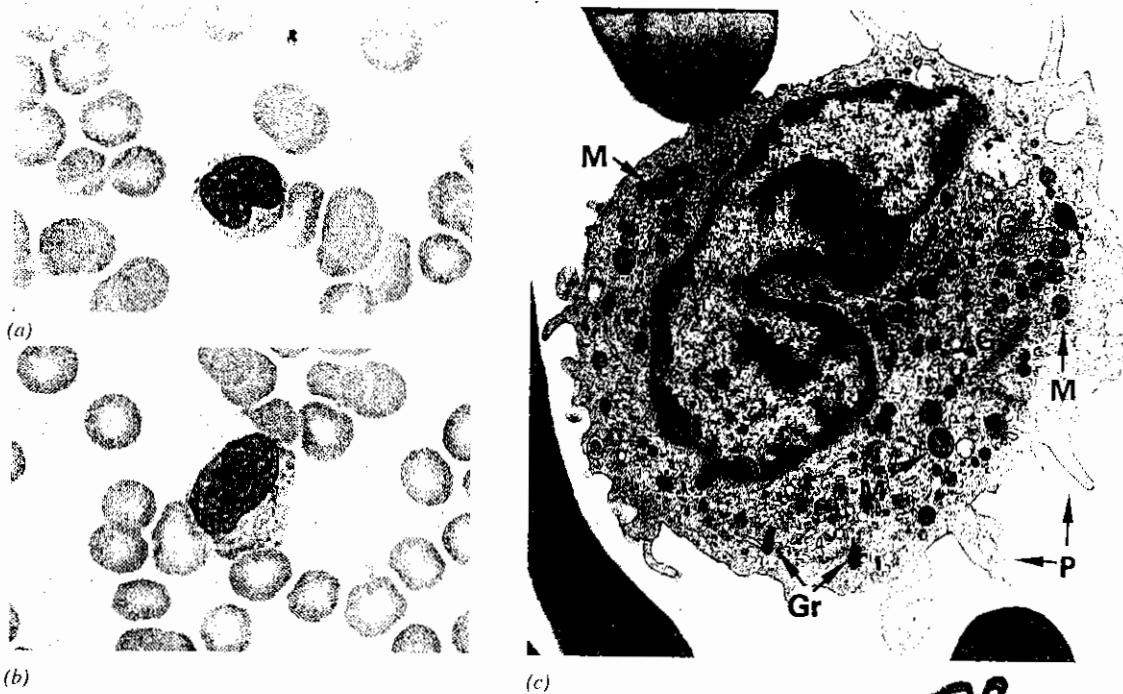


Fig. 3.9 Monocytes (a) Giemsa $\times 1000$ (b) Giemsa $\times 1000$ (c) EM $\times 20\,000$

Observe:

Monocytes → the **LARGEST** of white cells (up to 20 μm in diameter)
 → constitute 2 - 10% of Leucocyte in peripheral blood
 → highly motile & phagocytic

Precursor of MACROPHAGES found in peripheral tissues & lymphoid organs

nucleus → large eccentric stained less intensely than that of other leucocytes often with deep indentation + 2-3 nucleoli

cytoplasm → stain pale greyish-blue
 contains small pink-purple lysosomal granules
 → at EM → primary lysosomes similar to azurophilic granules of neutrophils (contain acid phosphatase & peroxidase)

Monocytes-macrophage system → monocytes migrate to peripheral tissues where they assume the role of macrophages → This has led to the concept of a single functional unit (precursors in bone marrow → circulating monocytes → tissue macrophages)

Included in this system are → Kupffer cells of liver, microglia of CNS, Langerhans cells of the skin, Antigen-presenting cells of lymphoid organs (APC), osteoclasts of bone

The system does not include: vascular endothelial cells or reticular cells & fibroblasts of lymphoid organs which may exhibit some phagocytic activity

Multinucleate giant cells → may form by fusion of macrophages or nuclear reduplication (14)

Monocyte function ↗ little function in circulating blood

they migrate into the tissues & differentiate into macrophages in response to

- presence of necrotic material (necrotaxis)
- invading microorganisms (Chemotaxis)
- inflammation

Observe:

- have great capacity for phagocytosis
- large content of hydrolytic enzymes

form an integral part of immunological mechanisms e.g. Antigen presentation
(final destruction of antigen)



Lymphocyte activation results in the production of factors which enhance macrophage phagocytic activity

Hemo Poiesis " " Haemato Poiesis

(15)

Prenatally

- ① Mesoblastic phase → in mesoderm of yolk sac
(2nd - 6th) weeks of pregnancy
- ② Hepatic phase → within liver & spleen also
In the second trimester play a role
- ③ myeloid phase (in bone marrow)
begins in the 3rd trimester

Post-natally

occurs almost exclusively in bone marrow :-
 Red bone marrow :-
 sternum, Ribs, Pelvis
 Proximal ends of femur
 Vertebral

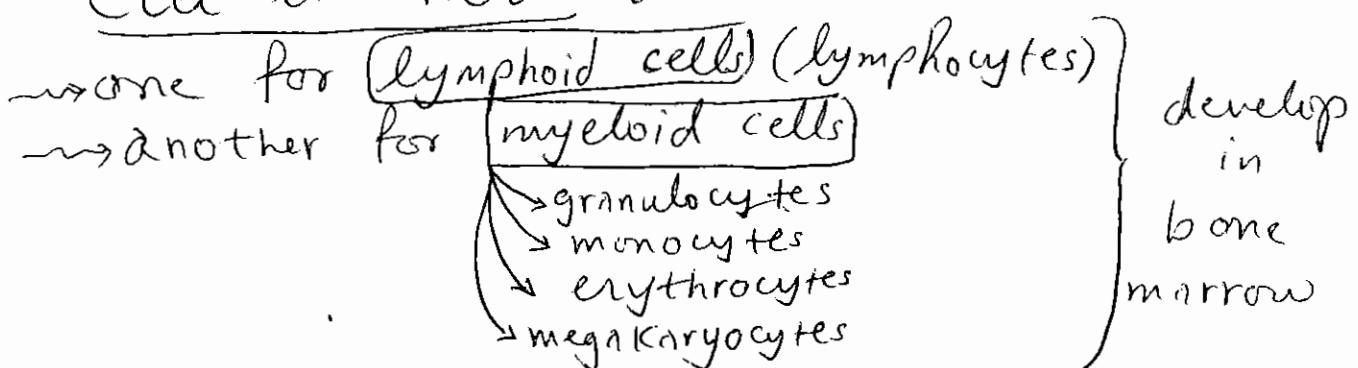
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Pluri Potent Hemopoietic Stem cells

It is believed that ALL BLOOD CELLS arise from a single type of stem cell in the bone marrow called a PLURIPOTENT STEM CELL

it can produce ALL BLOOD CELL TYPES

Proliferate & form TWO MAJOR CELL LINEAGES :



Early in their development lymphoid cells migrate from the bone marrow to thymus or to the lymph nodes, spleen and other lymphoid structures where they proliferate & differentiate.

Progenitor & Precursor cells

(16) A

The (Pluripotent Stem cells) give rise to daughter cells with restricted potentials called :

Progenitor cells or colony-forming units → CFUs

(CFUs)

④ types

* { Since they give rise to colonies of ONLY ONE CELL TYPE when cultured or injected into spleen

- A) Erythroid lineage of CFU- erythrocytes (CFU-E)
- B) Thrombocytic >> >> CFU-megakaryocyte (CFU-Meg)
- C) Granulocyte-monocyte lineage of CFU - granulocyte-monocytes (CFU-GM)
- D) lymphoid lineage of CFU-lymphocytes of all types (CFU-L)

ALL ④ Progenitor/CFUs Produce  PRECURSOR, cells
or Blasts,
"Offspring"

morphologic characteristics begins to differentiate suggesting the mature cell types they will become

STEM CELLS

PROGENITOR CELLS

Cannot be morphologically distinguished & resemble LARGE LYMPHOCYTE

- * Rate of cell division  slow in stem cells
Rapid in progenitor cells
- * Progenitor cells → can divide & produce both Progenitor cells, Precursor cells
- * Precursor cells → produce only mature blood cells

(16)B

Table 13-1. Changes in properties of hematopoietic cells during differentiation.

Stem Cells	Progenitor Cells	Precursor Cells (Blasts)	Mature Cells
Potentiality		Mitotic activity	Typical morphologic characteristics
Self-renewing capacity	Influence of growth factors		Differentiated functional activity

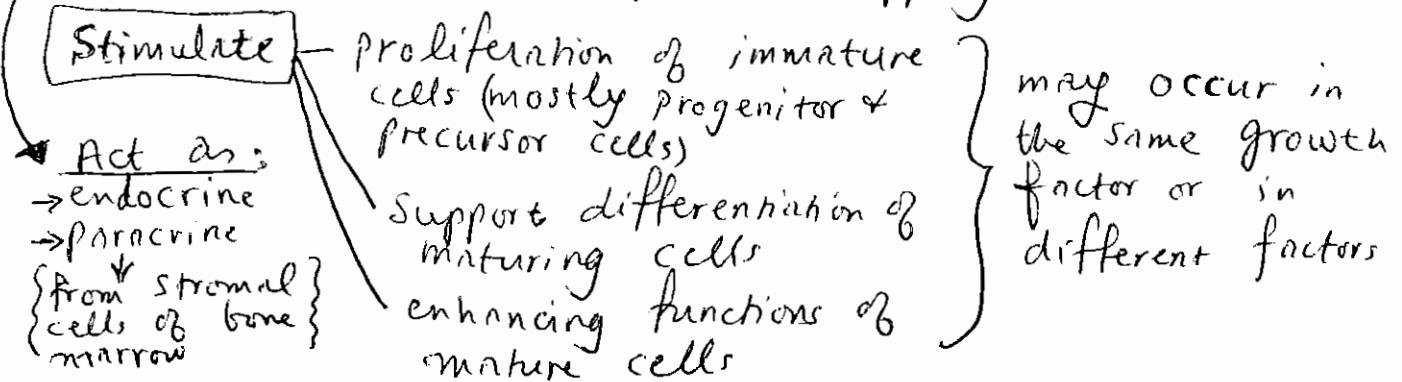
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Table 13-2. Main characteristics of five hemopoietic growth factors (colony-stimulating factors, CSF).

Name	Human Gene Location and Producing Cells	Main Biologic Activity
Granulocyte (G-CSF)	Chromosome 17 macrophages Endothelium fibroblasts	Stimulates formation (<i>in vitro</i> and <i>in vivo</i>) of granulocytes. Enhances metabolism of granulocytes. Stimulates malignant (leukemic) cells.
Granulocyte + macrophage (GM-CSF)	Chromosome 5 T lymphocytes Endothelium fibroblasts	Stimulates <i>in vitro</i> and <i>in vivo</i> production of granulocytes and macrophages.
Macrophage (M-CSF)	Chromosome 5 macrophages Endothelium fibroblasts	Stimulates formation of macrophages <i>in vitro</i> . Increases antitumor activity of macrophages.
Interleukin 3 (IL-3)	Chromosome 5 T lymphocytes	Stimulates <i>in vivo</i> and <i>in vitro</i> production of all myeloid cells.
Erythropoietin (EPO)	Chromosome 7 renal interstitial cells (outer cortex)	Stimulates red blood cell formation <i>in vivo</i> and <i>in vitro</i> .

Haemopoietic growth factors (colony stimulating factors)

are proteins with complex overlapping functions → they

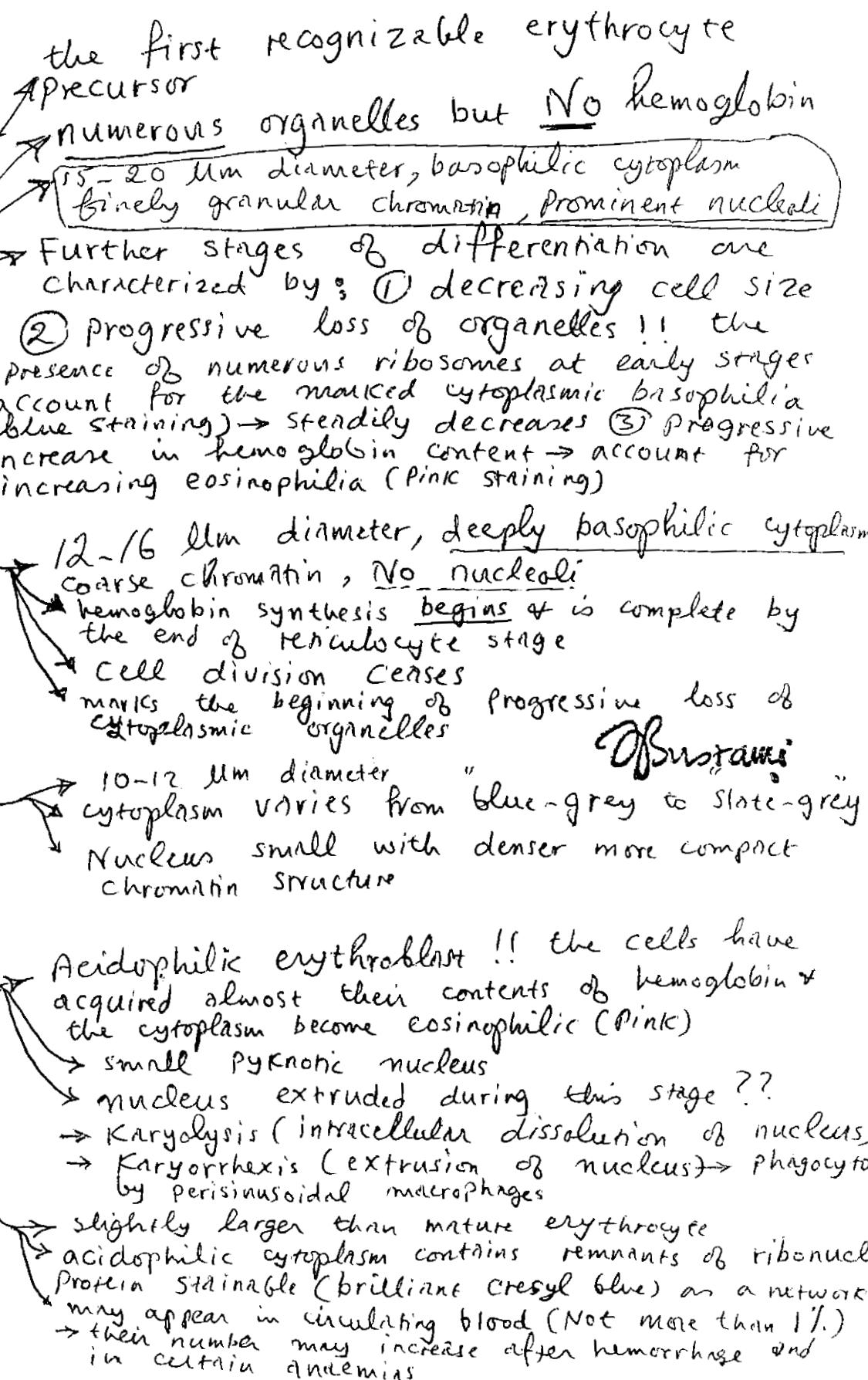


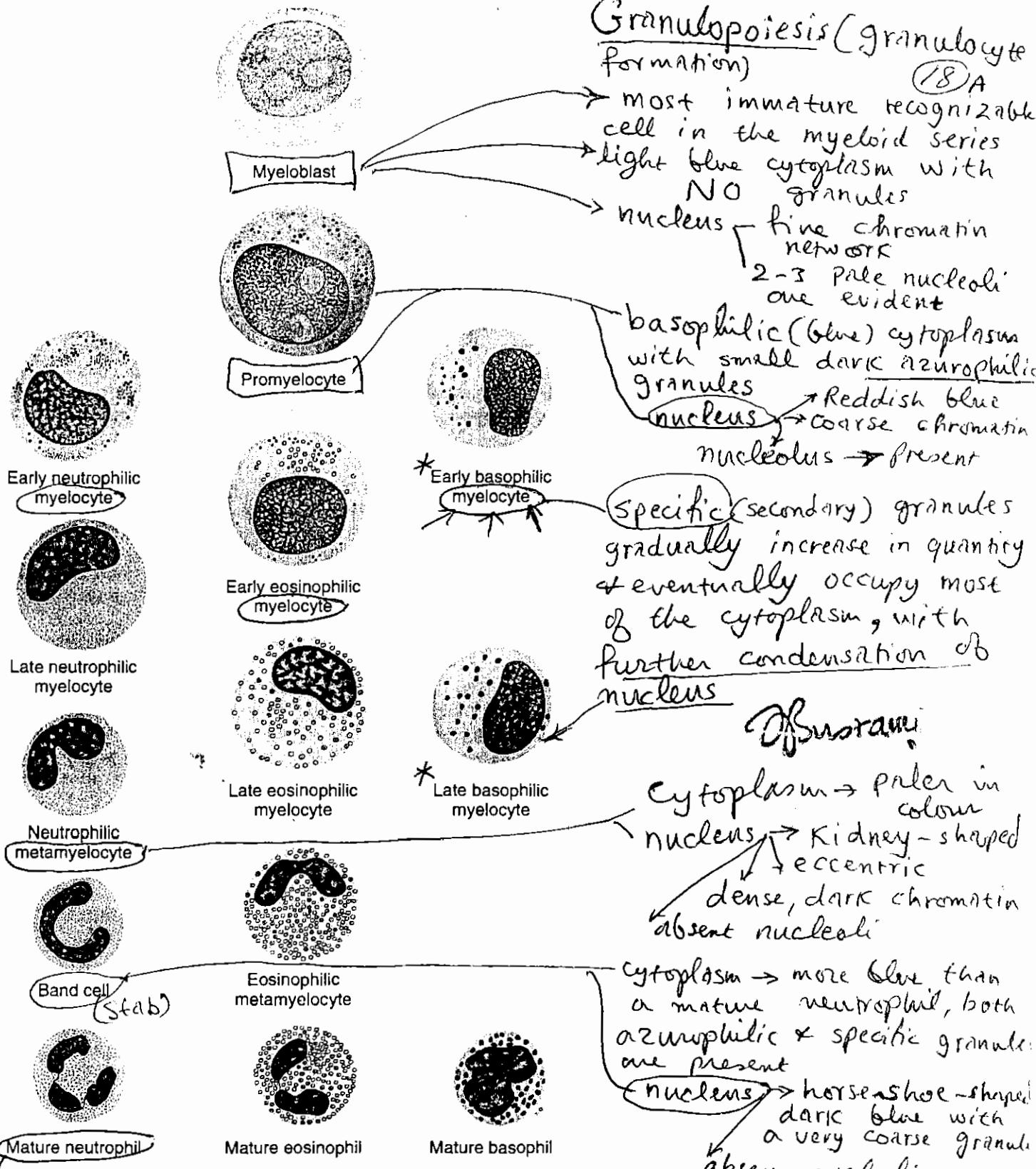
Potential therapeutic uses of growth factors

- * After chemotherapy or irradiation → low blood count
- * increasing the efficiency of marrow transplants by stimulating cell proliferation
- Erythropoietin → activates cells of the erythrocytic series
- Thrombopoietin → stimulates platelets production
- Steel factor (stem cell factor) → produced by stromal cells of bone marrow & acts on multipotent pluripotential cells

Erythropoiesis (Red cell formation)

- from stem cell to erythrocyte takes about **1 week**
- rate is controlled by the hormone (erythropoietin) **17**
secreted by the Kidney & by the availability of iron folic acid & Vit. B₁₂ & protein precursors





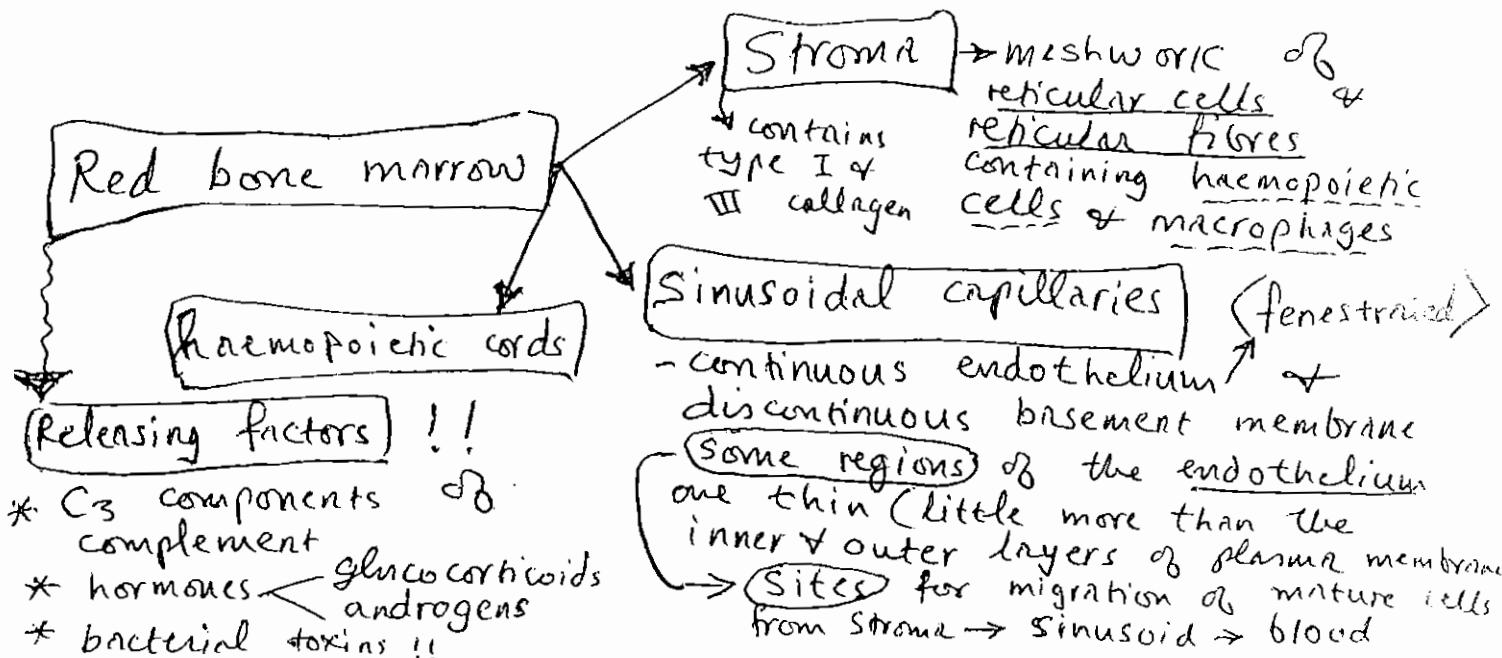
- Enters the blood stream :-
- ① Some appears to CIRCULATE
 - ② Others become adherent to endothelial cells of small vessels (Marginated pool)

* Entering the circulating pool in response to exercise & stress

* Bone marrow → contains a huge pool of stored neutrophils which can be rapidly mobilized should the need arise. ▶ corticosteroids increase the rate of release from the bone marrow

Recall:
Azurophilic granules
Primary granules !!
Large lysosomes

The appearance of large numbers of immature neutrophils (band cells) in the blood is called a shift to the left and is clinically significant, usually indicating bacterial infection.



Recall → There are two types of **bone marrow** Red
Yellow

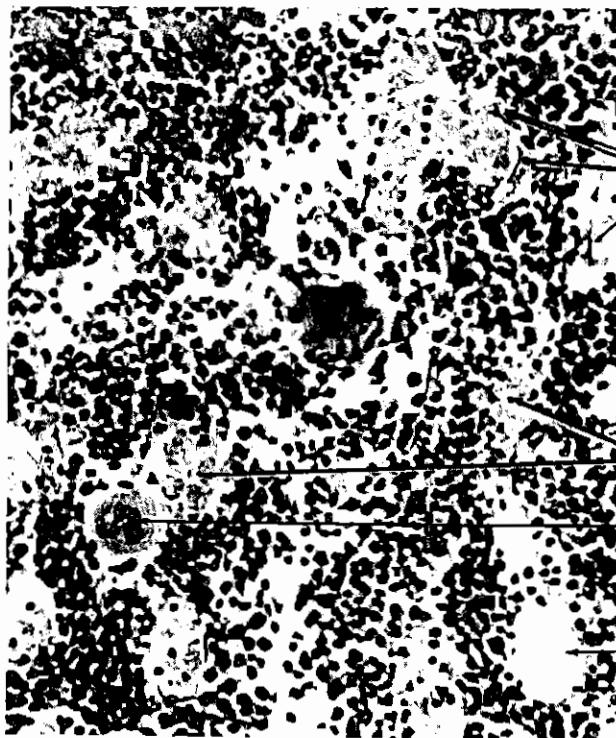
- Red bone marrow → abundance of blood & hemopoietic cells
- Yellow bone marrow → filled with adipocytes
- In the newborn → ALL BONE MARROW IS RED & active in blood cell production

As the child grows, most of the marrow changes gradually to the yellow variety

Under certain conditions { severe bleeding } hypoxia yellow marrow reverts to Red

Reticular cells of bone marrow → also called adventitial cells → produce steel factor (stem cell factor) that promote hemopoiesis through a paracrine effect

Offspring



(19)

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Figure 7-1
Section of red marrow (low power).

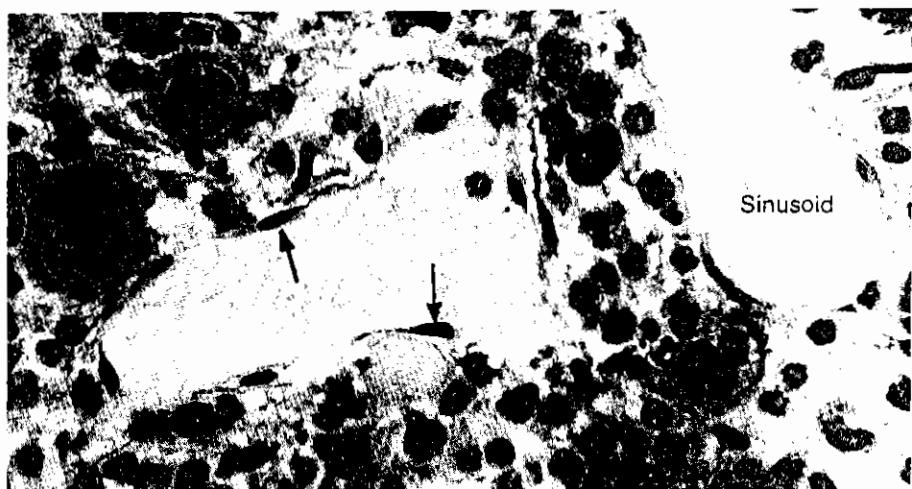
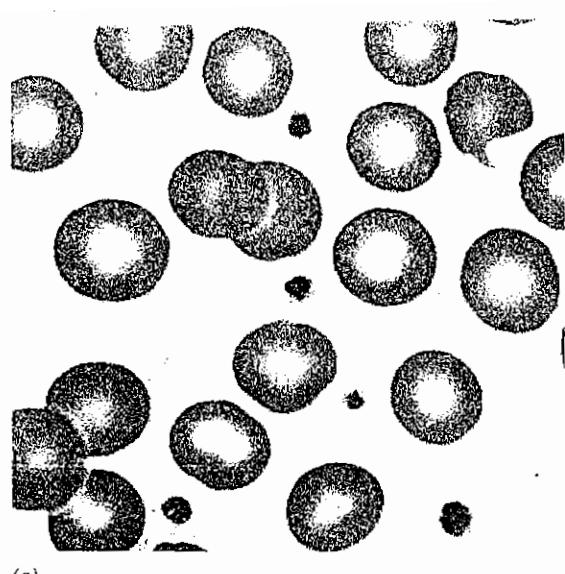


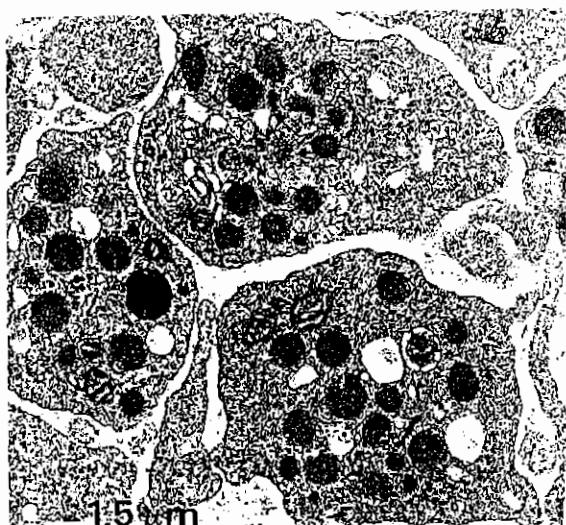
Figure 7-2
Sinusoids in red marrow (mouse), seen after experimental depletion of hematopoietic cells.
Arrows indicate nuclei of fenestrated endothelial cells that line the sinusoids.

Functions of the Red bone marrow:

- ① Production of blood cells
- ② destruction of red blood cells (along with spleen & liver → removal of aged & defective erythrocytes from the circulation).
- ③ plays a central role in the immune system, being
 - ⓐ the site of B lymphocyte differentiation (the mammalian equivalent of the bursa of Fabricius of birds)
 - ⓑ containing large numbers of antibody-secreting plasma cells



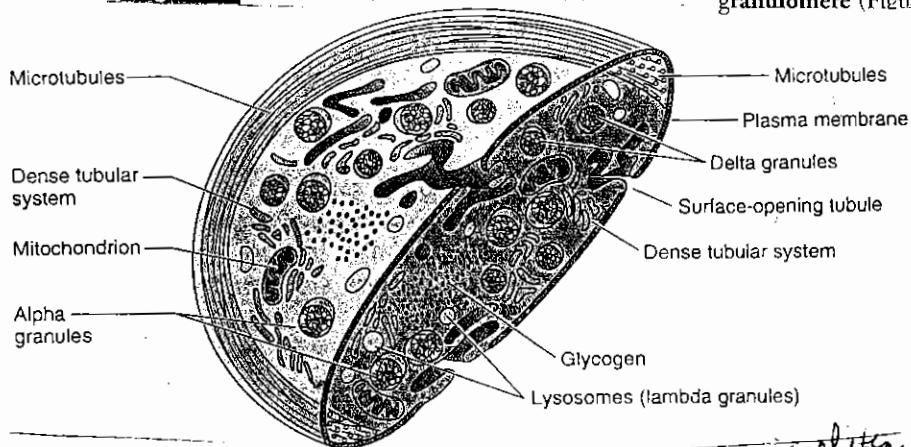
(a)



(20)

Fig. 3.10 Platelets (a) Giemsa $\times 1600$ (b) EM $\times 18\,000$

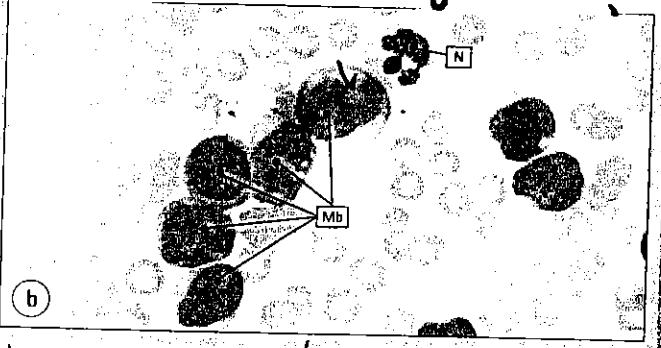
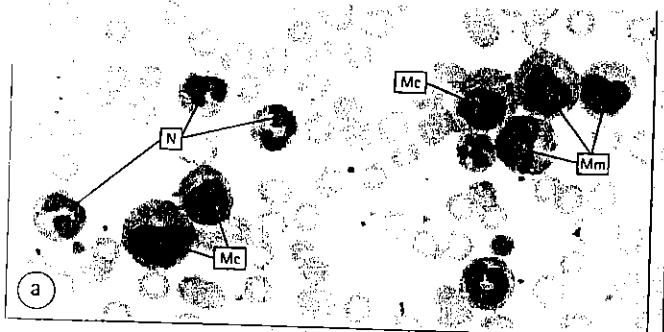
In stained blood smears, platelets often appear in clumps. Each platelet has a lightly stained peripheral zone, the **hyalomere**, and a central zone containing darker-staining granules, called the **granulomere** (Figure 12-13).



- Number : 150.000 - 400.000 / ~~megaloblast~~
- Shape : biconcave discs 1.5 - 3.5 μm
- In blood film : Not clearly seen
(smear) Often partially clumped together
- Cytoplasm → Purple granular (numerous organelles)
hyalomere more must conspicuous organelles → electron dense granules
- Granules → alpha (largest) contains : fibrinogen, factors VII
platelet factor 4 → regulate vascular permeability
- Dense (delta) lysosomes → Serotonin (absorbed from plasma)
lysosomes → lysosomal enzymes → aid clot resorption
- Dense tubular System (DTS) → beneath cell membrane : marginal band of contractile protein actin & myosin → microtubules & microfilaments
- Functions : Hemostasis
 - 1) Form plugs to occlude sites of vascular damage by adhering to collagen tissue at margin of wound
 - 2) Promote clot formation by providing surface for coagulation of protein complexes → thrombin formation

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→ Blood film ← Obustami



Blood film from a Patient with Chronic granulocytic leukemia → increased number of MATURE WBCs mainly neutrophils (N) as well as PRECURSORS mainly myelocyte (Mc)
meta myelocyte (Mm) } escaped from bone marrow into blood

Blood film from a Patient with an Acute granulocytic leukemia

the malignant cells are immature granulocyte precursors mainly myeloblast (Mb)
 very few mature neutrophil (N) are being formed (arrow → nucleus)



WHITE BLOOD CELL ABNORMALITIES

Increased numbers of white cells appear in the peripheral blood in a variety of disorders and provide a useful clue to underlying disease. For example, while in both cases the white cells are qualitatively normal, there is:

- a considerable and sustained increase of circulating neutrophils in bacterial infections
- an increase of circulating eosinophils in parasitic infestations and some allergies

(Leukemia) → malignant proliferation of white cell precursors in the bone marrow

Vast number of white cells & their precursors → many of which spill over into the blood

Classification → According to the cell line involved (ie granulocytic, monocytic, lymphocytic) + degree of malignancy

In Chronic leukemia

cells are partly or completely differentiated
 e.g. myelocytes, metamyelocytes
 band cells & neutrophils → disease → slowly progressive

In acute leukemia

the proliferating cells are undifferentiated precursors cells
 e.g. myeloblasts in acute granulocytic leukemia & lymphoblasts in acute lymphocytic leukemia.
 → rapidly progressive