Basophils in peripheral blood

Thesis

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By

Suzan Samir Habib

(M.B.,B.Ch.)

Under supervision of

Prof.Dr. WAGEEH NAGUIB IBRAHIM

Professor of Clinical Pathology

Ain Shams University

Dr. NEVINE KASSEM

Lecturer of Clinical Pathology

Ain Shams University

Ain Shams University

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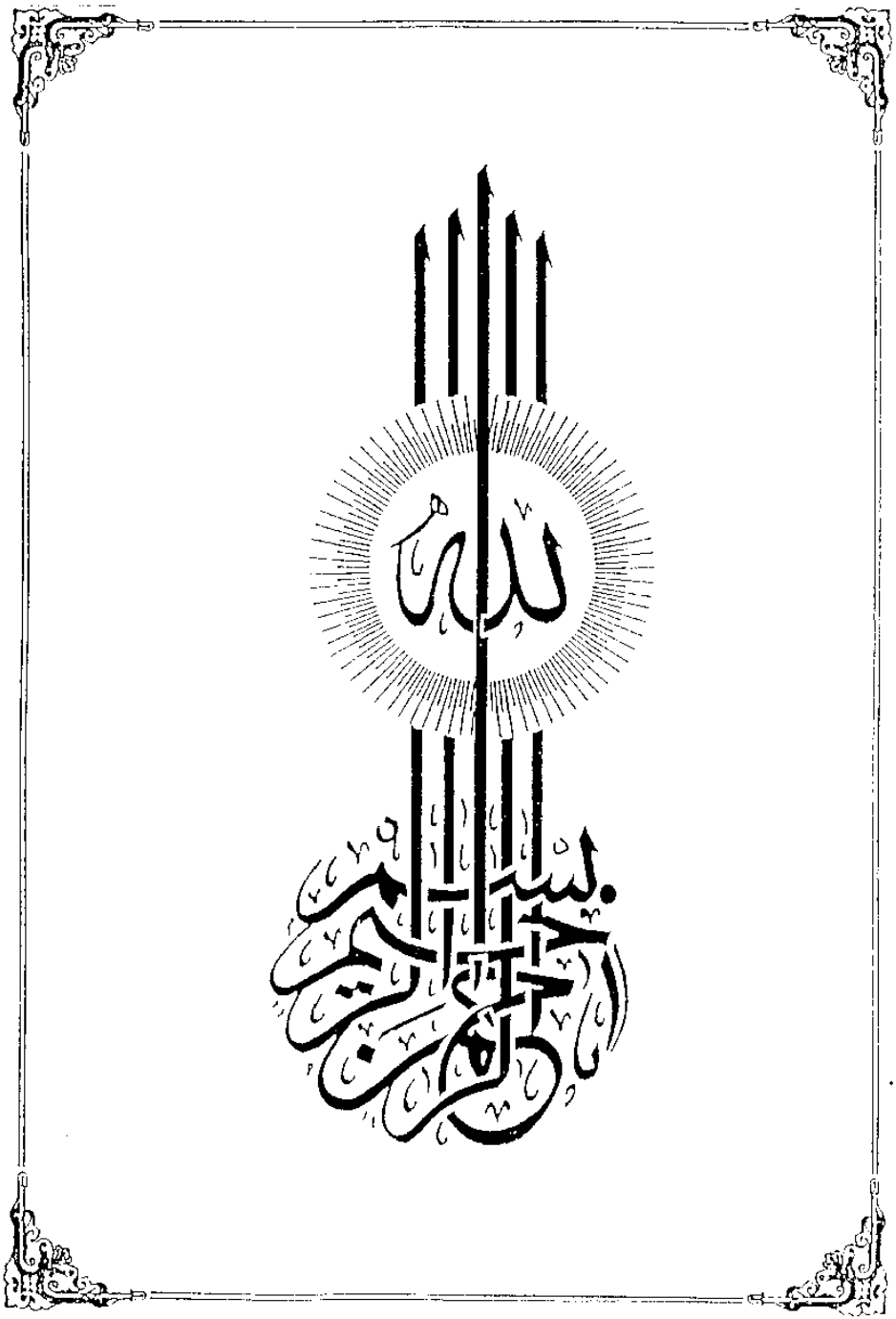

ABBREVIATION LIST

BAF-T	Human T lymphocyte-derived basophil activating factor.
CLC	Charcot-Leyden crystal.
CML	Chronic myeloid leukemia.
5-HT	5-hydroxy tryptamine.
ICH	Isocapnic hyperventilation.
LPR	Late phase reaction.
MBP	Major basic protein.
MD	Myeloproliferative disorders.
NCF	Neutrophil chemotactic factor.
PAF	Platelet activating factor.
PGS	Prostaglandins.
PMSC	Pluripotent myeloid stem cell.
SRS-A	Slow reacting substance of anaphylaxis.
THSC	Totipotent hematopoietic stem cell.

INTRODUCTION AND AIM OF WORK

The basophil is the rarest of peripheral blood leucocytes. It is distinguished by its large coarse dark basophilic granules that usually, fill the cytoplasm and often obscure the nucleus.

Its appearnce has long been associated with a variety of myeloproliferative disorders. Recently, the appearance of excess basophils in the bone marrow aspirates has been believed to be of diagnostic significance in lymphoproliferative and preleukemic syndromes.

Although the exact relationship between human basophils and mast cells, which normally reside in the connective tissue is not fully known, they both have receptors for IgE, IgG and complement.

Basophils sensitized by cytophilic antibody release mediators, including histamine and various peptides, on contact with specific antigen,giving rise to some of the symptoms of immediate hypersensitivity.

AIM OF WORK

To review the role of basophils and mast cells in various hematological disorders and also their role in hypersensitivity reactions.

CHAPTER I

ORIGIN AND DEVELOPMENT OF BASOPHILS

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Cells of the blood (erythrocytes,platelets,neutrophils,lymphocytes,monocytes,eosinophils,and basophils) are constantly lost and destroyed, and to maintain homeostasis each system must have the capacity for self renewal . Thus , in these systems , renewal involves division of immature cells coupled with diffrentiation and maturation (Post and Hoffman, I968) .

Self renewal systems must contain stem cells. A stem cell can be defined as one in which the progeny (daughter cells) of cell division are identical in appearance and potential to the mother cell i.e. the capacity of self-renewal and differentiation (Laytha et al.,I962) .

STRUCTURE OF THE HAEMOPOIETIC STEM CELL COMPARTEMENT :

The structure of the haemopoietic stem cell compartment has been defined , at least partially , by functional in vivo and in vitro assays and by studies of human disease .
The most definitive data have been derived from functional studies in the mouse,beginning in I96I with Till and McCulloch's studies of spleen colony formation(Till and McCulloch I96I) .

However,based primarily upon morphologic studies of human bone marrow in health and in disease,a fairly accurate picture of the interrelation of stem cell was inferred many years ago by investigators such as Downy who agreed with Maximow's interpretation that there is a cell capable of giving rise to all blood cells,and that this cell,in turn, gives rise to stem cells with separate pluripotentiality for the lymphoid and myeloid systems,and that these,in turn, produce stem cells of more restricted potentiality . (Downy,I938 ; Maximow,I924) .

A model of stem cell compartment :

The model presented in figure I is based on the reasonably firm data which are available .
The earliest cell is totipotent for all blood cells, the totipotent hematopoietic stem cell(THSC) .
Differentiating daughters of the THSC are slightly more restricted in potential differentiation,one pathway giving rise to the lymphoid system and the other to the myeloid system, the pluripotent myeloid stem cell (PMSC) .

The PMSC in turn gives rise to at least 4 separate lines of cellular differentiation : neutrophilic-monocytic, eosinophilic , erythrocytic , and megakaryocytic lines .

In all probabilities there is at least a fifth line for basophils and perhaps a sixth line for mast cells .

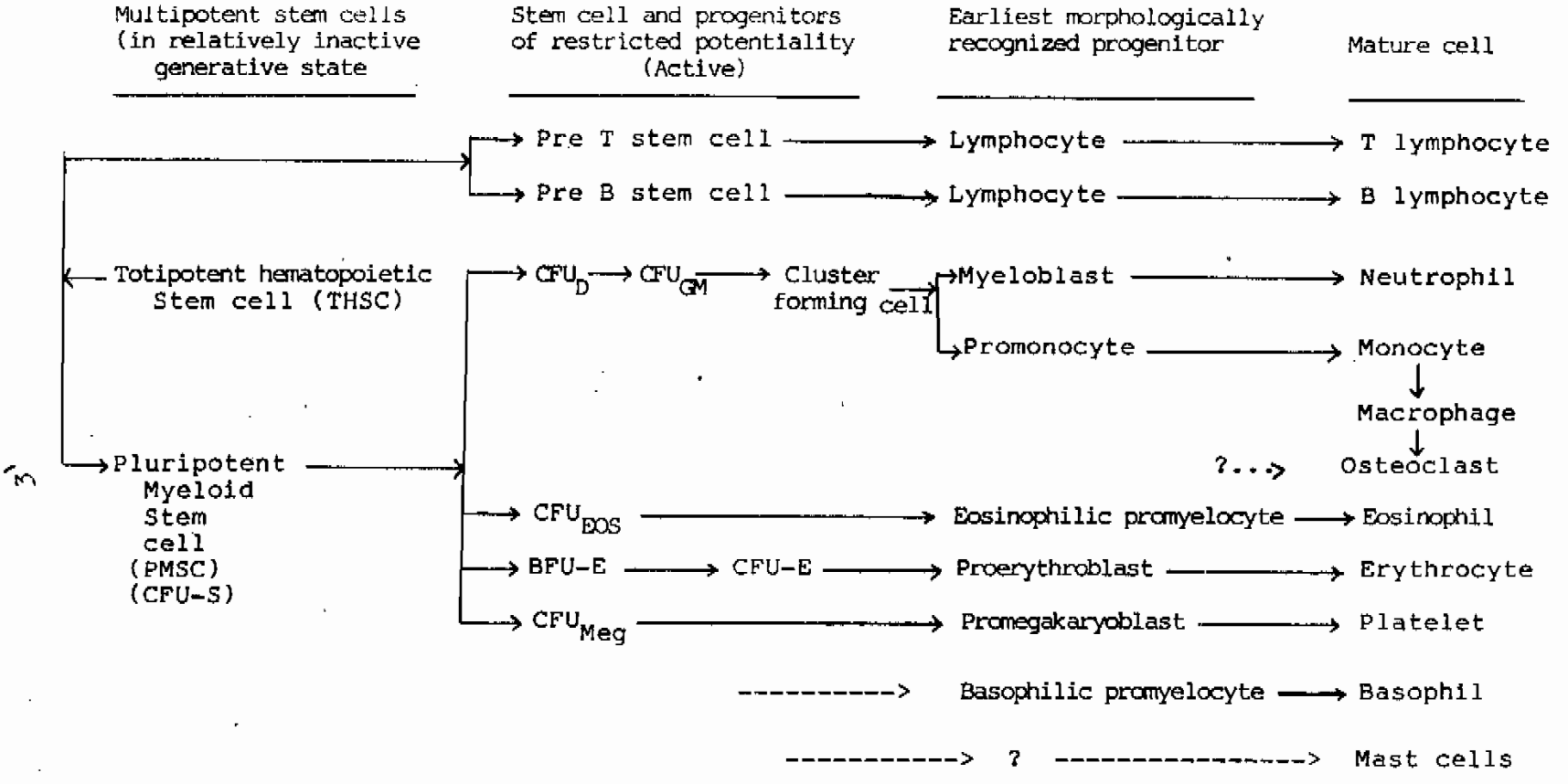

Fig. (1): Hierarchy of the hematopoietic stem cell and progenitor systems. BFU, burst forming unit; CFU, colony-forming unit; D, diffusion chamber; E, erythroid; Eos, eosinophil; MEG, megakaryocyte; NM, neutrophil, monocyte; S, stem cell. (Williams, I972).

EVIDENCE FOR A COMMON BASOPHIL - EOSINOPHIL PROGENITOR :

Charcot Leyden Crystal (CLC) are characteristically associated with diseases involving tissue or blood eosinophilia and considered to be a hall mark of eosinophil involvement in the tissue reactions of asthma , myeloid leukemia , and allergic and parasitic diseases (Benson and Boss , I977) .

In I965 , Archer and Blackwood reported that CLC could be prepared from human basophils .
Ackerman , Weil , and Gleich (I982) reexamined this question and showed that basophils obtained from the peripheral blood of normal individuals form CLC and that basophils contain a protein that is immunochemically indistinguishable from eosinophil CLC protein .

Major Basic Protein in human basophils :

The large specific granule of human eosinophil contains a number of low molecular weight ; highly basic proteins that have been purified to homogeneity , including the major basic protein (MBP) .
MBP has been regarded as a unique eosinophil protein and its release both in vitro and in vivo ,has been used as a specific marker for eosinophil localization,degranulation and function (Butterworth et al.,I979;Ackerman et al.,I98I; Wassom et al.,I98I;and Filley et al.,I982) .

Because it was demonstrated that the CLC protein , was also present in and crystallized from human basophils ,it was postulated that MBP might also be a constituent of the blood basophil (Ackerman et al.,I982) .
So, Ackerman et al.(I983) found that MBP was detected by immunofluoresence and radioimmuno assays in cells obtained from a patient with basophil leukemia and in purified basophils.

So, it is concluded that basophils contain a protein that is immunochemically indistinguishable from eosinophil granule MBP (Ackerman et al., I983) .

Heterogeneity of human peripheral blood eosinophil-type colonies :

It was reported that a proportion of previously designated human eosinophil "Eo-type" colonies in methylcellulose contain basophils and histamine (Denburg et al., I983) .
In a more recent study,individual Eo-type colonies have been analyzed by cell morphology as well as by biochemical assays for histamine,CLC,and eosinophil granule MBP.
Clonal origin of Eo-type colonies was confirmed by G6PD isoenzyme analysis. Morphological observations of such colonies revealed the existence of two distinct colony types :
(I) Eo-type containing I00 % basophils , and
(2) Eo-type containing mixture of basophils and eosinophils,

including cells with mixed basophil eosinophil granulation. Histamine was not detected in pure,mature peripheral blood eosinophils .9

Immunofluorescent studies demonstrated bright staining for CLC and MBP in 95% ± 3 % of cells in Eo-type colonies but only 5 % ± 4 % of cells in neutrophil-macrophage (GM-type) colonies.Radioimmunoassay for MBP was positive in 5/9 Eo-type and 0/IO GM-type colonies .

These and previous findings point out the morphological and biochemical heterogeneity of peripheral blood Eo-type colonies ,and provide direct evidence of a common,circulating basophil-eosinophil progenitor(Denberg et al.,I985) .

HUMAN BASOPHIL

The human basophil is the least common blood granulocyte, with a prevalence of 0.5 percent of total leukocytes ,and 0.3 percent of nucleated marrow cells (Juhlin ,I963) . It is characterized by spherical or ovoid granules,which stain dark violet or purple with giemsa (Klein ,I982) .

Morphology of human basophil :

Basophils have bilobed nuclei with a dense chromatin pattern and no nucleoli (Altman , I98I) . Ultrastructurally,human basophils contain round or oval cytoplasmic granules surrounded by a membrane and containing

a substructure of dense particles(figure 2),less dense matrix,and,occasionally membrane whorls (Zucker-Franklin,I967)

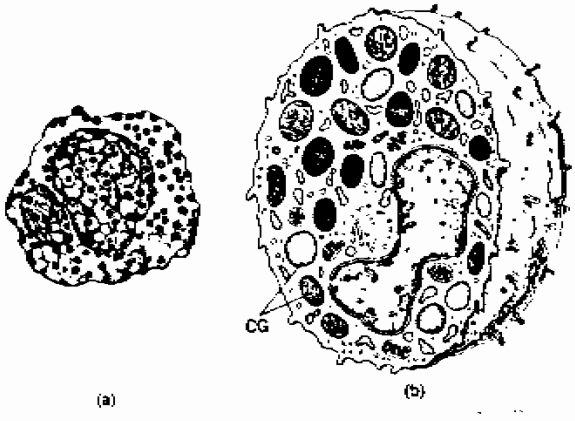

Figure 2. Human basophil, as seen with (a) a light microscope and (b) electron microscope. CG, crystalloid granule.
(Klein, I982).

A second minor population of small uniform granules is characteristically located close to the nucleus .
The cytoplasm of mature human basophils also contains glycogen particles and small membrane-bound vesicles .
(Hastie , I974) .

Contents of basophilic granules :

The cytoplasmic granules of basophils contain sulfated glycosaminoglycans that stain metachromatically with basic dyes under appropriate conditions. This substance is predominantly chondroitin sulfates. The function of these substances is unknown (Porter and Mitchell , I972) .

The basophilic granules contain large amount of hitamine about I.I to 2.I pg/cell (mean I.6 pg/cell) .
(Ishizaka et al. , I972) .

Basophils also generate many other mediatora that can influence the course of inflammatory processes .
These substances are either preformed and granule-associated (glycosaminoglycans,histamine,eosinophil-chemotactic factors) or are produced during activation of the cell , such as leukotrienes(slow reacting substance of anaphylaxis) and other metabolites of arachidonic acid .
(Galli and Dvorak , I979) .

Basophils also possess neutral proteases that may have a role in inflammatory processes, such as the granule-associated trypsin and chemotrypsin-like enzymes,and a plasma membrane plasminogen activator in guina pig(Galli and Dvorak , I979) and the basophil kallikrein of anaphylaxis in humans (Newball et al., I979) .