NEUTROPHIL CHEMOTAXIS

IN

BRONCHIAL ASTHMA

THESIS

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BY

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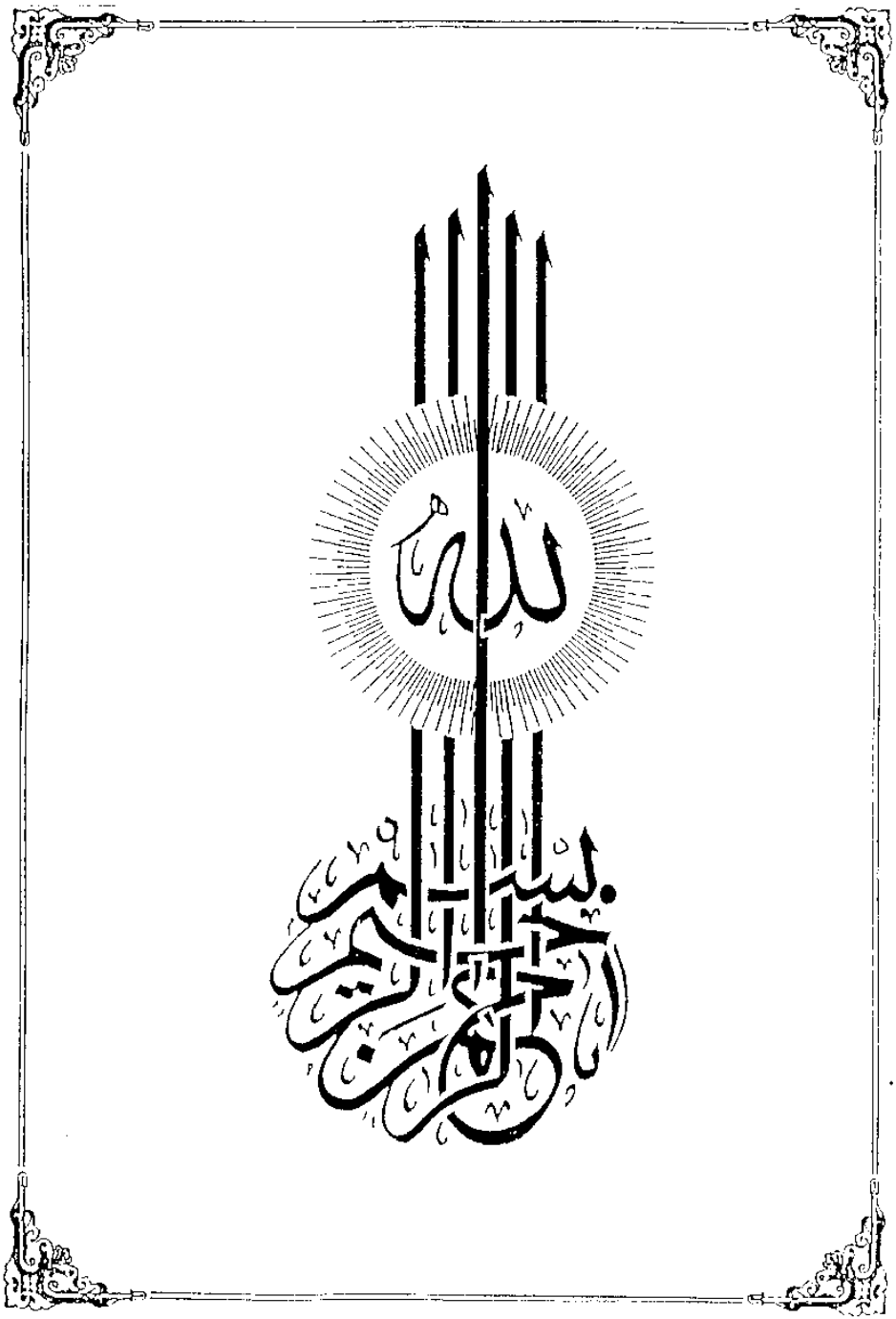

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ABBREVIATIONS

A.C.E.P.C.	Acetyl glyceryl ether phosphoryl choline
A.M.P.	Adenosine monophosphate
A.T.P.	Adenosine triphosphate
A.C.T.H.	Adreno corticotrophic hormone
AM_s	Alveolar macrophages
B.H.R.	Bronchial hyperreactivity
B.R.	Bronchial reactivity
C.D.I.	Cell directed inhibitor
C.H.S.	Chediak-Higashi Syndrome
C.F.A.	Chemotactic factor inactivator
C.G.P.	Circulating granulocyte pool
C.S.A.	Colony stimulating activity
C.C.F.	Crystal-induced chemotactic factor
D.S.C.G.	Disodium cromoglycate
E.C.F.-A	Eosinophil chemotactic factors of anaphylaxis
E.I.A.	Exercise induced asthma
$F.E.V_1$.	Forced expiratory volume in the first second.
F.M.L.P.	Formyl-methionyl-leuco-peptide
$H.P.E.T.E_s$.	Hydroxy peroxy-eicosatetraenoic acid
Ig.	Immunoglobulin
L.P.R.	Late phase reactions
L.I.F.	Leucocyte inhibitory factor
LT_s.	Leukotrienes
L.D.C.F.	Lymphocytes derived chemotactic factor
M.G.P.	Marginated granulocyte pool
M.C.G.	Mast cell granule
N.C.A.	Neutrophil chemctactic activity
N.C.F.	Neutrophil chemotactic factor
N.S.A.I.	Non steroidal anti-inflammatory
P.A.F.	Platelet activating factor
P.A.N.	Polyarteritis nodosa
P.N.L.	Polymorphonuclear leucocytes
PG_s.	Prostaglandins
S.R.S.-A.	Slow reacting substances of anaphylaxis
S.L.E.	Systemic lupus erythematosis
T.X.	Thromboxane
T.B.G.P.	Total blood granulocyte pool

INTRODUCTION & AIM OF THE WORK

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Bronchial Asthma is multifactorial disease i.e. Heriditary Factor, Disturbed immune mechanism, Infection, Hormonal Disturbance, Psychogenic factors etc...

There is much enecdotal evidence which suggests that infection plays some part in pathogenesis of asthma.
Three aspects are considered.

1- The inception of hyperreactivity
2- It's persistence
3- It's liability to be provoked, leading to acute attacks of asthma.

It is about the last of these three aspects that most is known.

There is now good evidence that infection by viruses, particularly rhino-viruses, can provoke episodes of Asthma. Although the mechanisms whereby viral infection provoke Asthma are obscure, it seems clear that host factors play an important role. Much less is known about the part played by bacterial infection [Clark, T.J.H., 1977].

There is an evidence that acute respiratory infection occuring during early life in a child with an inherited predisposition, might

be the factor responsible for the inception of Asthma.

- It is well known that Asthma is characterised by both Bronchial and Systemic hyperresponsiveness.

The effect of the previous two opposing factors, infection and hyperresponsiveness on Neutrophil chemotaxis will be studied.

Chemotaxis or the directional migration of leucocytes in response to a diffusion gradient of chemical attractants is a subject that has been suddenly found respectability after many years of doubt and nonacceptance by the scientific community. Chemotaxis is one of the important mechanisms in immune reactions. It involves different types of cells, neutrophils, basophils, eosinophils, lymphocyte, and monocyte.

Neutrophil chemotaxis plays a basic role in defending the body against infection. Defects in the generation of chemotactic factors, the regulation of these mediators or the responsiveness of neutrophils to these factors may be translated clinically into recurrent, persistent and often life threatening infection episodes [Peter and Ward, 1974].

The Aim of this work is to find whether there is any neutrophil chemotactic activity in different asthmatic patients or not and to study the neutrophil chemotaxis in Asthmatic patients compared to control.

REVIEW OF LITERATURE

PHYSIOLOGICAL ASPECT OF NEUTROPHIL GRANYLOCYTES

Neutrophil Production:

The granulocytes are formed in the bone marrow by a series of mitotic divisions that occurs in the immature cells of intermediate morphologic maturity i.e. myeloblasts, promyelocytes and myelocytes.

Beyond the myelocyte stage, the cells are no longer capable of division, but only of maturation giving rise to metamyelocyte, band form and lastly to segmented neutrophil. [Cline, 1975].

The stem cell has been defined as a dividing cell with dual capabilities of self renewal and differentiating into more mature haematologic cells. It may be either pluripotent and capable of giving rise to cells of several haemopoietic lines or unipotent with maturation capabilities along a single line. [Goldman, 1981].

Under normal steady-state, the stem cell compartment of an animal or man is assumed to be constant in size. Two mechanisms for achieving this constancy are present, the first mechanism is that under a differentiating stimulus, a stem cell could divide

asymmetrically, one off spring remaining within the stem cell compartment, while the other leaves and progeny. These progeny mature along one or more haemopoietic cell line depending upon the nature of the stimulus. The second mechanism is that the stem cell leaves a compartement under differentiating stimulus and is replaced by the progeny of another stem cell [Cline, 1975].

Contraversy exists regarding the cell of origin for the three granulocytic cell lines i.e. neutroplil, eosinophil and basophil. The traditional view is that a primitive granule-containing precursor cell, the promyelocyte is common to all the three cell lines, the modern view of granulocyte development, based on leucocyte fine structure and cytochemical reactions, is that once progenitor cells mature sufficiently to have cytoplasmic granules, they are already committed to one of the three pathways of differentiation. Other evidence also suggests that the earliest azurophilic granules are cytochemically distinct for each cell line and persist in the more mature cells of that line. [Bainton and Farquhar, 1968].

Control Of Granulopoiesis:

A colony stimulating activity [C.S.A.] can be demonstrated in serum [Cline et al.; 1974], the most important sources of C.S.A. in humans are the peripheral monocytes [Gold and Cline,1974].

One potent stimulus for the release of C.S.A. by macrophages is endotoxin from gram negative bacteria, thus the macrophages may be the key to the activation of body defence in the presence of infections. [Gold and Cline, 1974].

The rate of release of neutrophil from marrow appears to be influenced by humoral factor which has been demonstrated. This plasma granulocyte releasing factor mobilizes cell from the marrow granulocyte storage pool to the circulating blood pool. Hormones as A.C.T.H. and hydrocortisone and bacterial products can stimulate mobilization of granulocyte from bone marrow [Leavell and Thorup; 1976].

Neutrophil Kinetics:

The total mass of marrow granulocytes can be divided into an early mitotic pool in which cell division growth and maturation take place ending at the myelocyte, a subsequent maturation pool that ends with mature neutrophil and storage pool of mature neutrophils residing in the marrow. These pools all overlap to some extent. In normal circumstances neutrophils are released into blood at rate of 16×10^8 cell/kg. body wt/day. [Goldman, 1981].