# NEUTROPHIL CHEMOTAXIS

# IN

# RHEUMATOID ARTHRITS

THESIS
SUBMITED IN PARTIAL FULFILMENT
FOR THE MASTER DEGREE OF
GENERAL MEDICINE

B Y

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( MB.B.CH )



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# N E U T R O P H I L  C H E M O T A X I S

# I N

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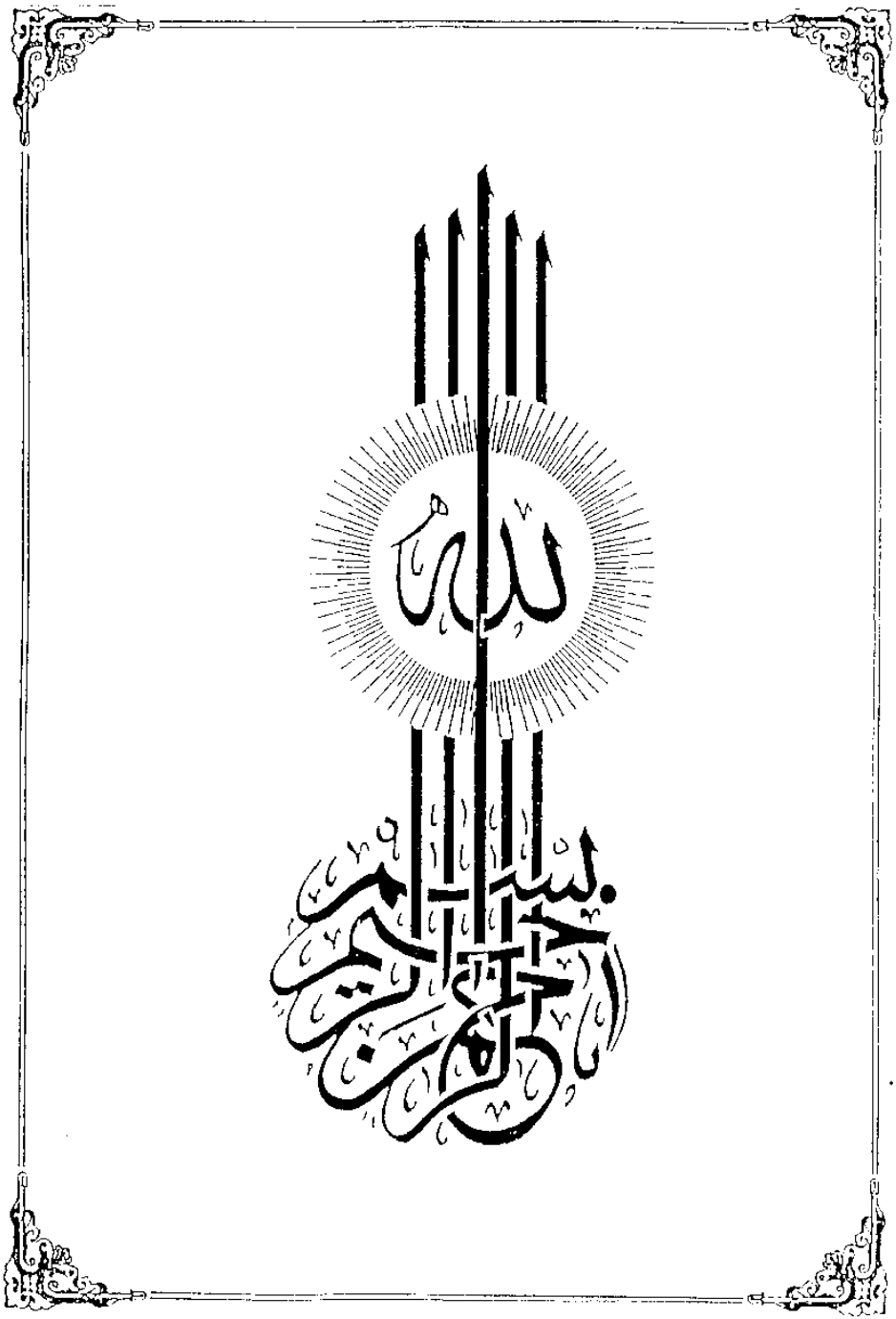

## A C K N W L E D G E M E N T

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# C O N T E N T S

# A B B R E U I A T I O N S

| | | |
|---|---|---|
| ANF | = | Anti-nuclear factor. |
| ACTH | = | Adreno-cortico-trofin hormone. |
| CDI | = | Cell directed inhibitor. |
| CFI | = | Chemotactic factor inactivator. |
| CSA | = | Colony stimulating activity. |
| ESR | = | Erythrocyte sedementation rate. |
| PNL | = | Polymorpho-nuclear leucocyte. |
| RA | = | Rheumatoid arthritis. |
| RF | = | Rheumatoid factor. |

# Introduction & Aim Of The Work

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## INTRODUCTION AND AIM OF WORK

It is a well known fact that immune disturbances are the playing role in the etiology of rheumatoid arthritis.

Many investigators described different immune defects e.g. Hannestad, (1968), Mcsweanetal. (1967) and many others have found abnormalities in humoral immunity and panayi. (1983), panush (1982) and many others have found abnormalities in cellular immunity in RA.

Infection is a frequant cause of death in patients with RA. Udin et al, (1970) found that the observed incidince of death from infection was about ten times higher than expected in males and about seven times higher than expected in females. The reasons for these increased rates of infection are not clear.

Chemataxis 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 inovlves different types of cells,

neutrophils, basophils, esino - phils, lymphocytes and monocytes.

Neutrophil chemotaxis plays a basic role in defending the body against infection. Defects in the generation of chematactic factors. the regulation of these mediators or the responsiveness of neutrophils to these factors may be translated clinically into recurrent, persistant and often life threatening infection episodes (Peter and Word, 1974).

The aim of this work is to study the chemotactic activity of neutrophils in patients with RA.

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# Review Of Literature

# CHAPTER [1]

# PHYSIOLOGICAL ASPECTS OF NEUTROPHIL GRONNULOCYTES

## Neutrophil Production:

The granulocytes in animal and man are produced in bone marrow, where in normal individual, there is an orderly progression of division and maturation from the earliest cell, stem cell, successivelly through the virous cell types to the mature polymorphonuclear leucocyles (PNL) (Perry, 1970).

The stem cells that are the progenitor of the myeloblasts are not identified by morphologic criteria, but for expermental evidence presumed to exist (Cline, 1975). The stem cell has been defined as a dividing cell with dual capabilities of self renewal and differentiating into more mature hoematologic cells. It may be either pluripotent and capable of giving rise to cells of several hoemopoietic lines or unipotent with maturation capilities along a single line (Goldman, 1981).

Under normal state the stem cell compartement of an animal or man is assumed to be constant in size. Two mechanisms for achiving this constancy are present, the first mechanism is that under a differentiating stimulus a stem cell could divide asymetrically or symetrically, one offspring remaining within the stem cell compartment, while the other leaves and provides progeny. These progeny mature along one or more hoemopoietic cell line depending on the nature of 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).

In addition to stem cell compartement, which is self replicating, there is also a large differential proliferating pool consisting of the myeloblasts and promyelocytes. There are large and small myelocytes and these two types of cells represent subdivisions of the main pool, the large cells representing a dividing pool supplying cells to the small cell maturation pool. It is not known whether all of these small myelocytes then go onot divide or to mature and enter the next compartement. It is belived that granulocyle production is expanded by an increase in number of myelocyte devisions and a short of the generation time (Perry, 1970).

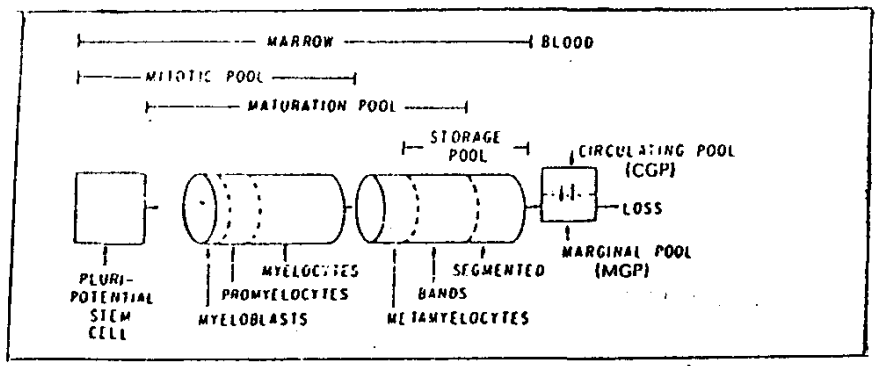
Beyand the myelocyte stage, the cells are not longer of division but only maturation, giving rise to metamyelocyte, band form and lastly to segmented neutrophil (Cline, 1975).

Contraversy exists regarding the cell of orgin for the three granulocytic cell line e.g. neutrophil, esinophil and basophil. The tradional view is that a primitive granule-containing precurser cell, the promyelocyte is common to all the three cell lines, the modern view of gronulocyte development, based on leucocyte line structure and cytochemical reactions, is that once progenitor cells mature sufficiently to have cytoplasmic granules, they already commited to one of the three pathways of differentiation. Other evidence also suggests that the earliest azurophil granules are cytochemically distinct for each cell line and presist in the more mature cells of that line (Bainton and Farquhar ; 1968).

## Control Of Granulopoiesis

A colony stimulating activity ( C.S.A. ) can be demonistrated in serum (Cline et al ; 1974). The most important sorces of C.S.A. in humans are the prepheral monocytes. (Gold and Cline, 1974). One potent stimulus for the release of C.S.A. by macrophages is endotoxin from grame negative bacteria thus the macrophage may be the key to the activation of body defence in the presence of infections. Studies of human serum and urine shown that most of C.S.A. resides in glycoprotein with molecular weight 45,500,0 that migrate electrophoritically as an alpha glubulin ( Gold and Cline, 1974). Whether this colony stimulating glycoprotein is a granulopoitin remain undecided at present time.

It is proposed that mature granulocytes contain and propably produce specific feed back inhibitor, granulocytic chalone, which inhibits cell proliferation through its regulating action on DNA and cell devision (Rytomo, 1973 and Perry, 1970).




A MODEL OF NEUTROPHIL GRANULOCYTE KINETICS IN NORMAL HUMAN SUBJECTS. CGP = CIRCULATING GRANULOCYTE POOL. MGP = MARGINATED GRANULOCYTE POOL.

( Fig. 1 )