# EOSINOPHILS IN RELATION TO SKIN DISEASES

THESIS

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BY


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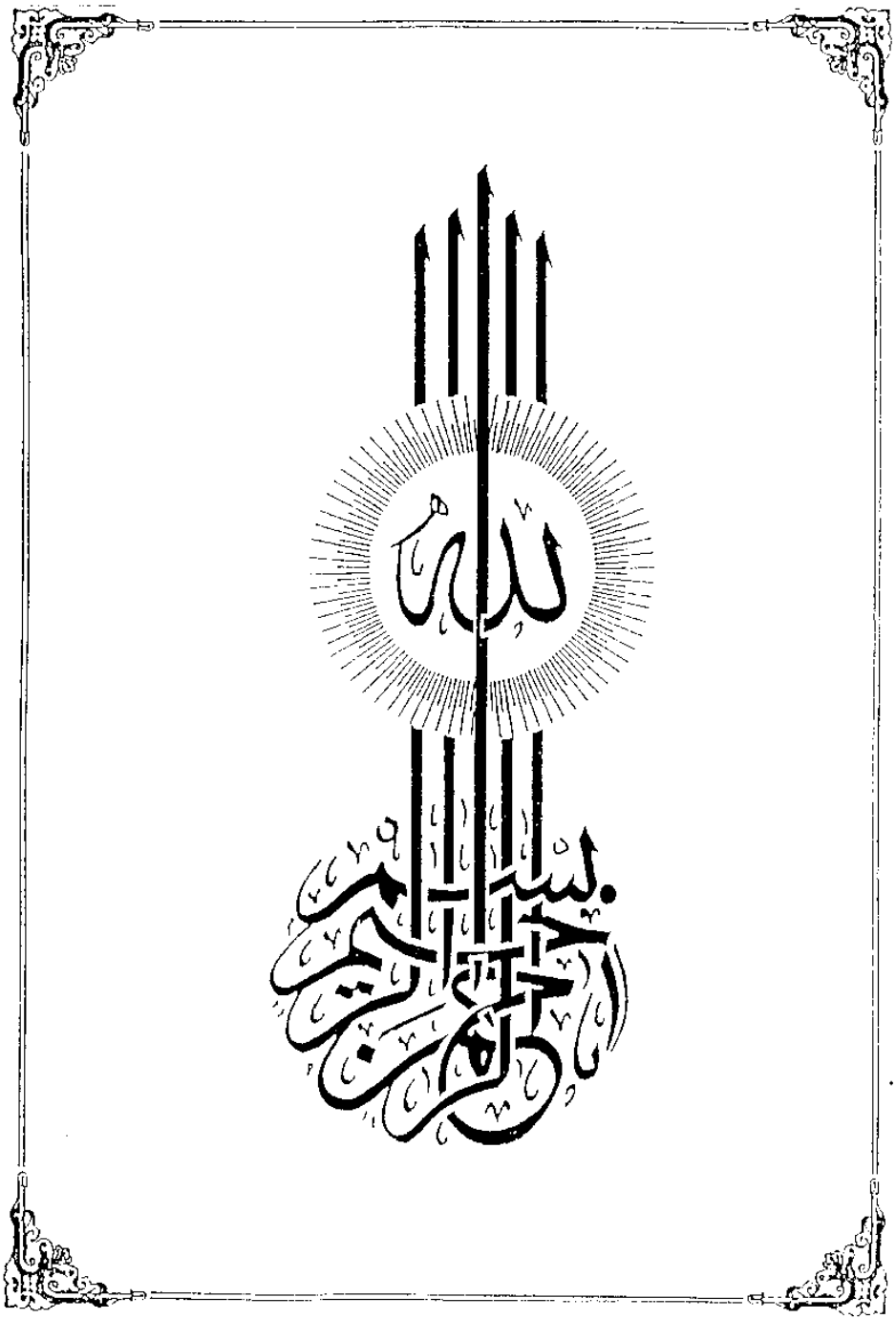

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# INTRODUCTION

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Eosinophils are present in many skin diseases. They are produced in the bone marrow and after distribution through the blood, they migrate into tissue sites where they carry out their functions (Tai and Spry, 1976).

The eosinophilia is a consequence of both increased eosinophil production in the bone marrow (Strykman et al., 1968) and prolonged eosinophil survival in the blood (Dale et al., 1976) and these factors can also affect the structure and properties of blood eosinophils.

The eosinophil leukocyte appears to participate in disease processes that include allergy, metazoan parasitic infestations, some neoplasms, a few vasculitides and certain skin diseases (Bass, 1979).

Certain skin diseases are associated with peripheral blood eosinophilia such as: hypereosinophilic syndrome (Hardy and Anderson, 1968), eosinophilic pustular folliculitis (Ofuji et al., 1970),

atopic dermatitis, dermatitis herpetiformis, urticaria or angiodema, bullous pemphigoid, ichthyosis, pemphigus, exfoliative dermatitis, herps gestationis, pityriasis rosea, papular urticaria, psoriasis, contact dermatitis, lichen planus, urticaria pigmentosa, erythema annulare centrifugum, erythema nodosum, toxic epicermal necrolysis (Otteson and Cohen, 1978), Wells' syndrome (Wells' and Smith), and Kimura's disease (Moesner et al., 1981).

Other skin diseases show local tissue eosinophilia without peripheral blood eosinophilia: persistent insect bites (Allen, 1948) and the inflammatory infiltrate occasionally seen surrounding parasitic larvae (Woodruff, 1979).

This essay includes a detailed review on the skin diseases associated with eosinophils which are present in large numbers in the blood and skin and have a role in the aetiology and pathology of such diseases.

# REVIEW
# of
# LITRATURE

## Histology of Eosinophils

Leukocytes or white blood corpuscles are frequently found in connective tissue. In general, they migrate across the capillary and venule walls from the blood. There is a continuous movement of leukocytes from blood to connective tissue, and this process increases greatly during inflammation. Eosinophils are 1-4% of leukocytes normal blood (Junqueira and Corneiro, 1980), the endoplasmic reticulum, mitochondria, and Golgi apparatus are poorly developed.

The eosinophil has a diameter 12 um to 17 um (Berretty and Cormane, 1978).

The main morphologic characteristic of eosinophils is the nucleus. It is usually composed of two lobes which may or may not be connected with a strand of nuclear material (Berretty and Cormane, 1978 and Zucker-Franklin, 1978).
Coarse clumps of chromatin are not so densly packed in the nucleus of eosinophils as they are in the neutrophils; hence eosinophil nuclei do not stain so deeply as neutrophils (Ham and Cormack, 1979).

The cytoplasm of eosinophils is somewhat irregular in outline because of occasional pseudopodia and is

characteristically packed with large refractile granules (Gleich, 1977) that in well stained blood films are coloured red or orange. In poorly stained films their colour may near towards pink or a muddy blue. Even in poorly stained preparations they can be distinguished from the granules of neutrophils because they are more numerous (Berretty and Cormne, 1978 and Ham and Cormack, 1979).

The granules of cytoplasm are lysosomes containing acid phosphatase, cathepsin, and ribonuclease but not lysozyme (Junqueira and Carnerio, 1980).

## Ultrastructure of Eosinophils

Gleich, (1977) reported that the distinguishing feature of eosinophil under the light microscope is the dense eosinophilic granulation which may completely fill the cytoplasm. When viewed under the electron microscope the eosinophil granule is seen as a membrane bound cytoplasmic organelle with distinctive internal structure. In most cases, the eosinophil granule has an electron dense core (internum) and a less dense matrix (externum). The internum is relatively resistent to mechanical trauma and osmotic lysis. It consists of phospholipids and unsaturated fatty acids. The externum is rich in acid phosphatase (Junqueira and Carneiro, 1980).
The core occurs in a variety of sizes and shapes (Gleich, 1977). When eosinophils are stained for peroxidase activity, there is a reversal of usual pattern of a granule staining; in this case the matrix is electron-dense and the core is less dense (Zucker-Franklin, 1978). This finding is consistent with the view that eosinophil peroxidase is localised in the matrix because the electron-dense product from the peroxidase reaction deposits in the granule matrix. When the core of the granule is examined under high magnification, it appears to be a periodicity in both the longitudinal and cross sectional dimensions (Miller et al., 1966).

This regular structure, entitled the name crystalloid for the core of the eosinophil granule and some authors have suggested that the charcot-leyden crystal is derived from the core (El-Hashimi, 1971).

The core structure of human eosinophil granules is poorly soluble in physiologic media (Zucker-Franklin, 1978).

In addition to the typical eosinophil granules noted above, another type of granule has been described in human eosinophils (Parmley and Spicer, 1974). This granule is membrane bound. It is smaller in diameter than the crystalloid-containing granules and is enriched in acid phosphatase and arylsulfatase. In contrast, the large granules contain little if any arylsulfatase and very little acid phosphatase (Glich, 1977).

Finally a third cytoplasmic organelle is detected in eosinophils (Solley et al., 1976). As viewed by electron microscopy, these organelles are larger than the crystalloid containing granules and often as an enclosing membrane which cannot be readily seen (Gleich, 1977). Occasionally the electron-dense material composing the organelle appears to have spread in a centrifugal pattern creating a sunburst appearance. These inclusions do not possess the characteristic crystalline core

of mature granule and they are strongly osmiophilic, i.e., they appear equally dense regardless of whether or not the cells are treated with uranyl acetate and lead citrate. In these studies it was not possible to determine whether these inclusions possessed peroxidase activity because the electron density was the same in the reacted and unreacted preparations (Solley et al., 1976).

During phagocytosis, eosinophil degranulation, which resembles that of neutrophils, involves membrane fusion and discharge of granule content into the phagosome (Zucker-Franklin and Hirsch, 1964). The cytoplasm has more vesicles, ribosomes, profiles of rough endoplasmic reticulum, and mitochondria than that of neutrophils. These findings are in accord with evidence that eosinophils are metabolically more active than the neutrophils (Baehner and Johnston, 1971 and Klebanoff et al., 1977) and that they have a longer life span (Dale et al., 1976). An often ignored cytoplasmic structure of eosinophils is a profile of endoplasmic reticulum, which may assume cuplike, ring, or dumb-bell-shaped conformations (Zucker-Franklin, 1978). These structures have been called "microgranules" and have been found in eosinophils of about 20 different species of mamals. The biochemical makeup and function of microgranules have not yet been elucidated, but there

appear to be increased numbers of these structures in some patients with eosinophilia (Ward et al., 1972 and Schaefer et al., 1973).

The nucleus of eosinophils resembles that of neutrophils: the heterochromatin has peripheral distribution and the nucleolus is smaller or absent.

In about 80% of normal blood eosinophils, the nucleus is bilobed. Hypersegmentation occurs with vitamin $B_{12}$ and/or folate deficiency, and following treatment with antifolates.

Under such circumstances, the eosinophil nuclei are hypersegmented and the cells could be mistaken for neutrophils when poorly stained (Zucker-Franklin, 1978).

## Physiology of Eosinophils

Kay (1976) reported that the number of eosinophils increases during the course of allergic and parasitic diseases as well as certain skin diseases and some neoplasms.

The eosinophils have ameboid movement and are capable of phagocytosing, though they phagocytose in a slower but more selective way than the neutrophils. It was experimentally observed that the eosinophil does not phagocytose isolated bovine serum albumin (antigen) or its antibody (specific gamma-globulin). However, the eosinophil phagocytoses the complex of this antigen with its antibody. It is a function of the eosinophil to perform selective phagocytosis of antigen-antibody complexes (Junqueria and Carneiro, 1980).

In the same way as the neutrophil, the eosinophil exhibits the phenomenon of granule coalesence with the phagosomes, at which time the respective membrane fuse. In the eosinophil after fusion, it can be observed that only the network or externum of the granule appears to fulfil the function of destroying the engulfed material since the internum remains intact within the vacuole for a long time. Consequently, hydrolytic