Histopathological Study of Acne Vulgaris

Thesis submitted for partial fulfillment of M.D. Degree in Dermatology and Venereology

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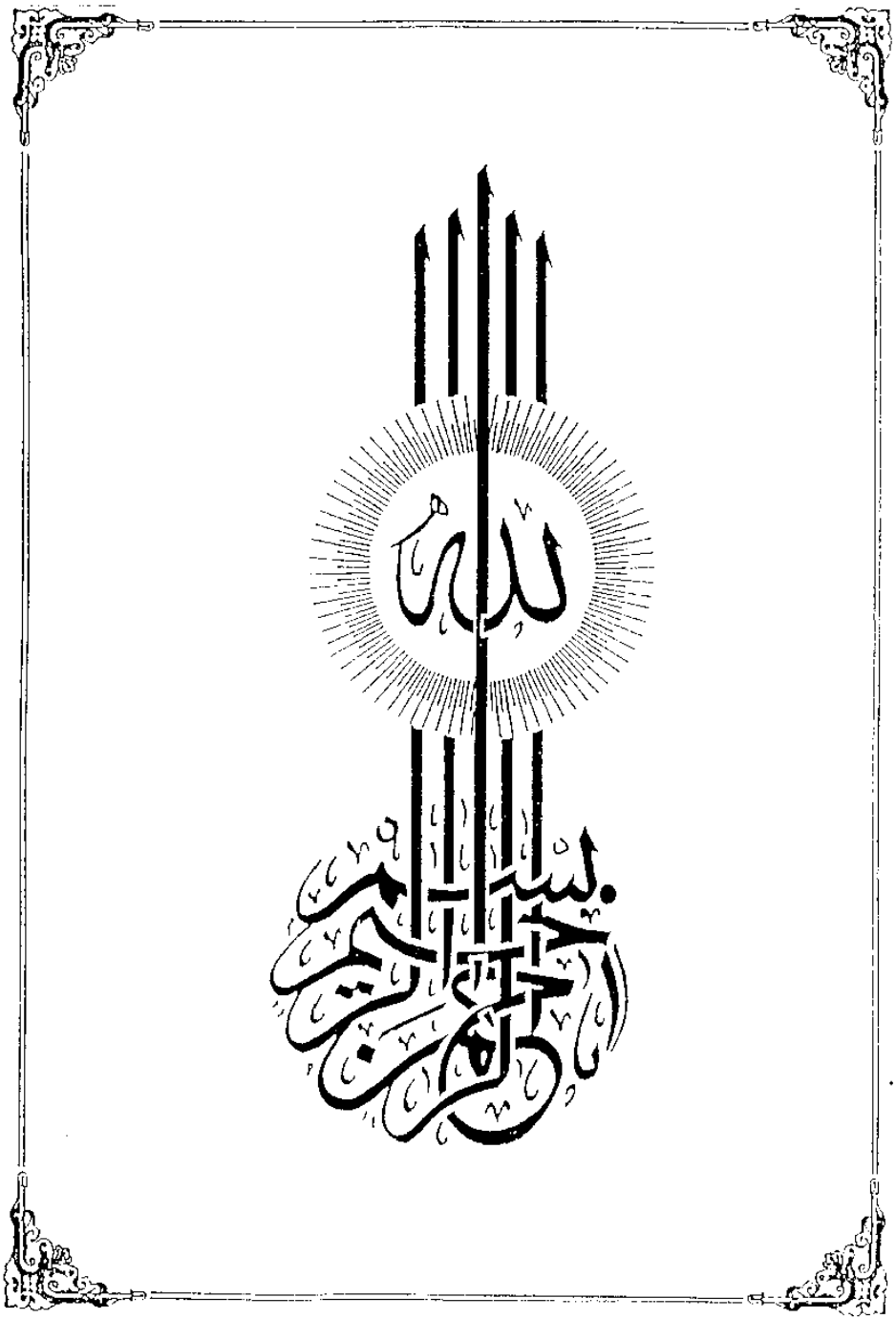

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Acne vulgaris is considered as one of the most common and wide-spread diseases that attracted the attention of many workers. This very common malady, however, lacks an accurate and decisive explanation of its true nature and in spite of its very high incidence, its exact pathogenesis is not yet precisely known.

Many current theories have been put forward to explain some factors of etiological significance in acne vulgaris, but none could provide a comprehensive explanation.

These theories included the roles of hormones, sebum, bacteria and more recently the immunological factors. They also clarified the integrated roles of these factors and therefore we are not so far from understanding the exact pathogenesis of acne vulgaris.

The aim of this work is to clarify some aspects of acne pathogenesis, based mainly on histopathological and immunological studies.

With the exception of the more recent ultrastructural observations in acne vulgaris, histopathological studies of the disease have been done a long time ago and from thence, they have been a matter of acceptance through successive decades until recently. Some of the previously described histopathological findings, however, were not adequately explained. the present work through the histopathological studies of serial sections of different acne lesions aims to investigate the pathologic changes occurring in the formation of these lesions and also to re-evaluate the pathological changes previously described.

Much interest, on the other hand, has been aroused on the study of the immunological aspects of acne vulgaris on the assumption that an immune process may be implicated. The present work has also been extended to include immunological and bacteriological studies in an attempt to explain some observations in the histopathological study.

REVIEW OF LITERATURE

I. SEBACEOUS GLANDS

Acne is a multifactorial disease, many factors have been implicated to be causally related to its pathogenesis. Sebum, hormones, bacteria and abnormal follicular keratinization of the sebaceous duct have been intensively studied. Data, however, revealed no more than a highly possible contribution and still the exact pathogenesis has to be determined. Since the process of acne is played out in the pilosebaceous apparatus, it is important to study the sebaceous glands as regards their evolutional development, structure and function so as to clarify some aspects in the pathogenesis of acne.

The human sebaceous gland and its product sebum, has been intensively investigated. A great deal is known about the embryology, biochemistry, anatomy and physiology of this unique structure. Acne has not been the only stimulus for this exceptional effort (Cunliffe, 1972).

1. Relationship between sebaceous glands and acne.

There is no evidence that acne is a disease of the sebaceous glands even though during the inflammatory stage glandular units sometimes become secondarily involved by being entrapped within active lesions (Strauss, **et al.**, 1974). However, several factors, admittedly circumstantial but nonetheless compelling, link the sebaceous glands and acne:

1.1. Acne sometimes occurs at birth or in the neonatal period at a time when the sebaceous glands are still enlarged from their fetal stage of development. Sebaceous glands later become small and remain largely atrophic during childhood when acne is ordinarily absent. During puberty the sebaceous glands again enlarge and as a result acne can develop (Strauss and Pochi, 1963). The alterations in sebum that have been seen during the early pubertal period (Ramasastry **et al.**, 1970) in studies of facial sebum were detected between the ages of 8 and 12. They consisted of an increase in wax esters and squalene, which are of sebaceous origin, and a decrease in cholesterol and cholesteroi esters, which are mainly epidermal in origin (Boughton **et al.**, 1957 and Ramasastry **et al.**, 1970). This does not reflect a change in sebum composition but rather an increase in sebum synthesis which result in a reapportionment of the epidermal and sebaceous contributions to the surface lipid film. Acne sometimes

begins at this time, but major inflammatory acne usually begins somewhat later after the sebaceous glands have undergone a greater degree of enlargement which is manifested by increased sebum production, as measured by gravimetric assay.

1.2 Patients with acne generally produce higher than normal amounts of sebum (Pochi & Strauss, 1974) although there is considerable overlap in values so that some patients with acne have sebum values that are well within the normal range (Pochi & Strauss, 1964). On the other hand, some individuals including teen-agers, with high sebum production values do not have acne, despite their statistically high-risk rating. This is one of the most compelling reasons for considering other factors in the pathogenesis of the disease.

1.3 Sebum is an irritant, and the free fatty acids produce more irritation than any other fraction in sebum (Ray & Kellum, 1971). When the various fatty acids of sebum are applied to the skin, those with chain lengths of C_{10} and C_{12} produce the most inflammation. The relation between these observations and the inflammatory response was also studied by Kligman & Katz (1968) who demonstrated the comedogenic potential of the various fatty acids when applied to the inner surface of a rabbit ear.

1.4 The causal relationship between sebum and acne is further suggested by the effects produced by certain therapeutic agents. The ones that significantly decrease the amount of sebum likewise ameliorate acne; for example, estrogens (Jarrett, 1955), superficial X-ray (Strauss & Kligman, 1959a). Another class of widely accepted therapeutic agents, the broad-spectrum antibiotics, inhibits the breakdown of triglycerides to free fatty acids without, however, reducing the total amount of sebum (Freinkel **et al.**, 1965).

Finally, it is necessary to achieve perspective concerning the sebaceous glands as targets for disease process. The prominent fact is that with the exception of nevoid growths or rare neoplasms no disorder originates in the sebaceous gland. Acne is certainly not a disease of the sebaceous gland (nor is rosacea). Its products are indispensible but the gland undergoes

atrophy during comedo formation or is destroyed by inflammation. The sebaceous gland is a rugged, rather resistant structure which can be caught up in other cutaneous disorders but is not in itself the primary seat of aberration (Plewig & Kligman, 1975).

It is concluded, therefore, that in the pathogenesis of acne, sebum is not only an important factor but probably an essential one. If so, a satisfactory animal model is important to study the relationship between sebum and acne, (Strauss **et al.**, 1974). From comparative studies of animal sebum, Nicolaides **et al.** (1968) found that triglycerides, the source of fatty acids in human sebum, were absent. In addition to this biochemical difference, there is a structural one; other mammals lack structures comparable to sebaceous follicles; the sites of acne lesions in man. Studies with animal models commonly substitute such specialized glands as the ventral gland of gerbils, the preputial gland of rats and the costovertebral gland of hamsters. However, there is evidence that these glands do not always respond to hormonal stimulation like human sebaceous glands.

2. Development of the pilosebaceous apparatus

The differentiation of sebaceous glands is intimately related to the differentiation of hair follicles and epidermis. Hortsmann (1957) and Pinkus (1958) provided satisfactory and adequate accounts of the embryology and anatomy of the hair follicle and the sebaceous gland.

The epidermis develops from the surface ectoderm on about the third week of fetal life and consists of one layer of undifferentiated cells. By four weeks, it has an inner layer of cuboidal cells and an outer layer of slightly flatter cells.

The earliest development of the hair follicles occurs at about 9 weeks in the regions of eyebrows, upper lip and chin (Pinkus, 1958). The first sign of a hair follicle is a crowding of nuclei in the basal layer of the epidermis, the so-called primitive hair germ or pre-germ stage. The pre-germ passes rapidly into the hair germ stage; the basal cells become high, the nuclei become elongated and the structure starts to grow downward into