ADVANCES IN

BIOLOGY OF SKIN

Vol. IV

Edited by

WILLIAM MONTAGNA

RICHARD A. ELLIS

and

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The Sebaceous Glands

Proceedings of the Brown University Symposium on the Biology of Skin, 1962

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INTRODUCTION

MOST of the material contained in this book was presented in a symposium held at Brown University on 27 and 28 January 1962. The contributions by Miles (Chapter IV) and Hyman and Guiducci (Chapter V), though not presented in the symposium, are nonetheless essential for the continuity of the subject matter. The plan of this book is similar to that of the previous volumes. It begins with a consideration of the developmental sequences of sebaceous glands in man; progresses to structural and functional attributes, and then devotes considerable space to the newer findings in the analysis of skin surface lipids and their synthesis. A great many half-truths have been published on the control of sebaceous glands by hormones, and it is gratifying to be able at last to sift out truth from fiction. The last two chapters of the book, by Ebling (Chapter XIII), and Strauss and Pochi (Chapter XIV), give us, for the first time, a completely up-to-date analysis of our knowledge of the hormonal control of sebaceous glands in experimental animals and in man.

Many of the observations presented here have not been published before. For the sake of orientation, balance and completeness, however, much material, even when well known, has had to be included. The succinct summary by Ellis and Henrikson (Chapter VI) on the ultrastructure of the sebaceous glands of man is completely new, whereas the general review of the structure (Chapters II and III) contains mostly older material.

For those who must find significance in organ systems, whether this is apparent or not, the book may seem somewhat disappointing. Surely, sebum must have a function, perhaps one that is even indispensable to the well-being of the organism. There are broad hints of its function in almost every chapter of this book. It has been suggested that sebum acts as an emulsifier, emolient, lubricant, and as a protective substance against the growth of microorganisms. Kligman (Chapter VII), however, dismisses sebum as a relatively inconsequential substance, and perhaps he is right. Who knows, however, if sebum may not have some other, more important functions? Thus, we must hold in abeyance our verdict as to the ultimate value of sebum to the total organism.

Enormous changes take place in sebaceous glands from their inception in the fetus to the early postnatal periods, late childhood, prepuberal, and postpuberal; the long, normal adult period, the declining sexual years, climacterium and senescence. No one doubts that changes must characterize each of these epochs, but neither morphological, physical, nor chemical data are available.

The omission of a discussion of *acne* is deliberate. The literature that pertains to the management of this widespread contributor to man's afflictions is vast and largely trivial. It is discouraging to contemplate that even the most advanced progress made on the biology of sebaceous glands makes little direct contribution to our understanding of acne. This is not to say that such practical knowledge will not spring from this and other work, but for the present we are at a loss. Thus, we have not ignored the problems of acne; we have omitted them in order not to confuse the major aims of this volume.

To prove that much of this work is still in progress, we have had to revise some manuscripts several times, as their authors discovered new things. We predict that during the brief time that it takes to publish the book there will be a substantial amount of additional information. This, however, reflects the vigor with which some of these problems are being investigated.

As do the previous volumes in this series, this book probably asks more questions than it answers. Gaps in details, however, are being filled rapidly and we anticipate that soon the biology of the sebaceous glands of man will be understood and that the clinical problems that result from their dysfunction may become controllable.

The symposium, "Sebaceous Glands", was aided by financial contributions from: Burroughs–Wellcome & Co., Inc.; Chesebrough–Pond's, Inc.; Colgate–Palmolive Company; Desitin Chemical Company; Dome Chemicals, Inc.; E. I. du Pont de Nemours & Co.; The Gillette Co.; Johnson & Johnson; Lever Brothers Company; Procter & Gamble Co.; Revlon, Inc.; Schering Foundation; The Squibb Institute for Medical Research; The Upjohn Company; Warner–Lambert Research Institute; and Westwood Pharmaceuticals. We thank all of the companies for their support of this and other symposia. Our students at Brown University have been very helpful, and Mrs. Elaine T. Grenier has contributed much energy, imagination, and skill to the organization of the symposium and to the preparation of the manuscripts.

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CHAPTER I

THE DEVELOPMENT OF SEBACEOUS GLANDS IN MAN

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I. INTRODUCTION

SINCE the differentiation of sebaceous glands is intimately related to the differentiation of hair follicles and epidermis, the development of these structures will be briefly described.

Horstmann (1957), Pinkus (1958), and Montagna (1962) have already given satisfactory and adequate accounts of the embryology and the anatomy of the hair follicle and the sebaceous gland. Therefore, these details and others found elsewhere will not be repeated (Serri *et al.*, 1961, 1962; Serri, 1962). The descriptions in this paper are based on skin from a large number of fetuses of all ages from various sites of the body. These specimens were treated with well-established histochemical methods as well as with the stains routinely used in our laboratory.

II. DEVELOPMENT OF THE EPIDERMIS

On about the third week of fetal life the epidermis consists of a single layer of undifferentiated cells which are filled with glycogen (Fig. 1). On the fourth week the epidermis is composed of an outer layer of cells, the *periderm* or *epitrichial layer*, and a basal layer or *stratum germinativum*. All cutaneous structures subsequently develop from the stratum germinativum. At the beginning of the tenth to twelfth week of fetal life the basal layer proliferates a *stratum intermedium* (Fig. 2). At approximately the thirteenth to sixteenth week the stratum intermedium becomes stratified and forms a spinous layer. The cells of the outer layer, the periderm, which also become stratified, are often globular in shape, later becoming flattened, polygonal and polymorphic with oval nuclei and vacuoles in the cytoplasm. The vernix caseosa which appears on the skin surface toward the fourth to fifth month is composed

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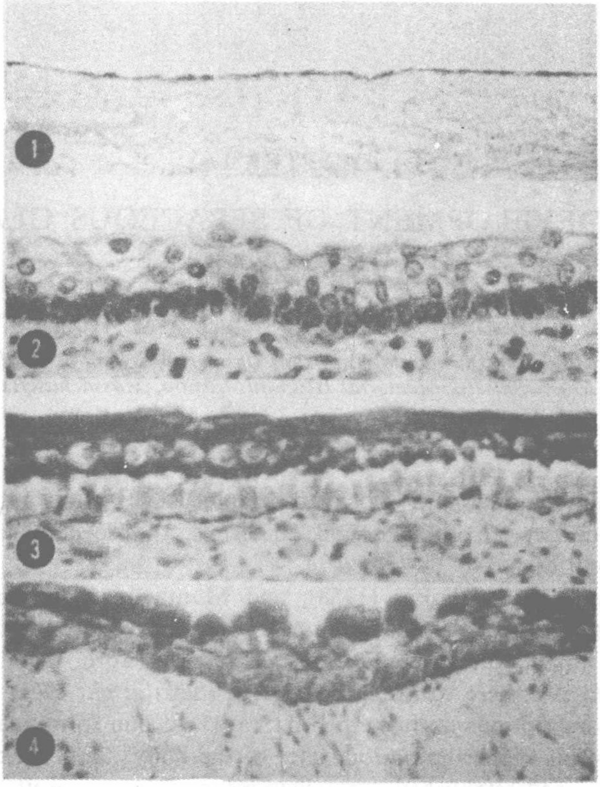

FIG. 1
Skin of the thorax in a 4-week-old fetus. The periderm alone is well visualized. In occasional areas the germinative layer appears to be developing. The presence of glycogen is illustrated throughout the epidermis. (Periodic acid Schiff. × 100.)

FIG. 2
Skin of the hand in an 11-week-old fetus. The epidermis is made up of basal cells, cuboidal in shape, and of a periderm 2 to 3 layers thick. Cells of the stratum intermedium are appearing above the basal layer. (Toluidin blue. × 800.)

FIG. 3
Skin of the finger in a 16-week-old fetus. The epidermis now consists of three layers. The basal cell layer in contrast to the other layers is almost entirely free of glycogen. The mucopolysaccharides of the basement membrane are well visualized. (Periodic acid Schiff. × 100.)

FIG. 4
Skin of the hand in an 11-week-old fetus. Illustrated are the globular cells of the outer periderm and the earliest stages in the formation of a hair follicle. The cells of the basal layer are columnar, deeply staining, the orientation is downward, and there is beginning an aggregation of cells of the mesenchyme at this site. Glycogen is still present in basal cells. (Periodic acid Schiff. × 440.)

of the residue of these periderm cells (which later will be replaced by the cells of the horny layer), shed lanugo hairs, sebum, formed in the newly differentiated sebaceous glands, and probably other debris.

The cells of the stratum intermedium, rich in glycogen, are oval and smaller than the mother cells of the germinative layer. When they begin to show stainable cytoplasmic fibrils, they are referred to as cells of the stratum spinosum.

The cells of the germinative layer in the early stages are cuboidal, large, compactly arranged and have a distinct nucleus (Fig. 2). Soon they become cylindrical and glycogen-free. The nucleus, usually located in the distal portion of the cell, stains intensely. The basal membrane is clearly evident (Fig. 3).

The development of the epidermis and that of its appendages is dyschronous in the various surfaces of the body. Differentiation takes place from the ninth to tenth week, first in the eyebrows, lips, chin and nose where the earliest hair germs appear. The process is slower on the back, abdomen, and limbs.

III. DEVELOPMENT OF THE HAIR FOLLICLE

The earliest development of hair follicles occurs as early as 9 weeks and is manifested as a palisade of cells at various points in the basal layer. These cell aggregates are always accompanied by the alignment and concentration of the subjacent mesenchymal cells (Fig. 4), which are very rich in alkaline phosphatase (Fig. 5). Later, an accumulation of deeply basophilic nuclei in the basal layer forms a slight projection of the epidermis into the dermis (Fig. 6). This swelling is free of glycogen and is separated from the dermis by a distinct basal membrane which is PAS positive and diastase resistant. The number of mesenchymal cells and fibroblasts beneath the hair germ increases, forming the anlage of the hair papilla; this will subsequently increase in size and in its content of alkaline phosphatase (Figs. 7, 8). Meanwhile, the hair germ becomes larger by a proliferation of its own cells and no longer at the expense of the basal cells of the epidermis (Figs. 9, 10). The elongation of the presumptive follicle into the mesenchyme takes an oblique direction, its movement apparently directed by the cluster of mesenchymal cells which accumulate beneath it and around it (Fig. 11). The outermost cells of this peg are columnar and compact with a radial arrangement, the inner cells tend to be arranged longitudinally and are less regularly aligned. As the hair peg develops further, its advancing extremity becomes bulbous and gradually grows around and envelops the mass of mesodermal cells at its base establishing a true papilla (Fig. 12). When the hair follicle has attained the bulbous "hair peg" stage, two epithelial swellings of columnar cells appear on the posterior wall. The lower hemispherical, larger one, rich in glycogen, is the bulge to which the arrector pilorum

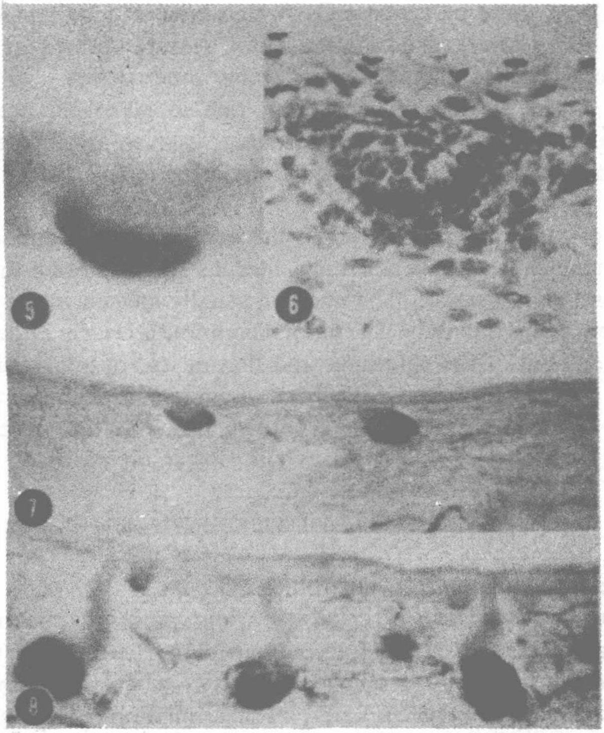

FIG. 5
Skin of the face in an 11-week-old fetus. Concentration of alkaline phosphatase in mesodermal cells beneath an early hair germ. (Alkaline phosphatase. × 440.)

FIG. 6
Skin of the scalp in a 16-week-old fetus illustrating a further stage in the development of a hair germ. Note the aggregation of columnar hyperchromatic cells with downward orientation, and the crowding of cells in the dermis beneath the developing hair germ. (Toluidin blue. × 800.)

FIG. 7
Skin of the back in a 13-week-old fetus. A concentration of alkaline phosphatase is noted in the anlage of the papilla of young developing hair germs which are remote from any demonstrable blood supply. (Alkaline phosphatase. × 100.)

FIG. 8
Skin of the forehead in a 12-week-old fetus illustrating the heavy concentration of alkaline phosphatase in the papillae of the developing hair germs. (Alkaline phosphatase. × 100.)

muscle will later become attached. During fetal life the bulge becomes even larger; at the end of fetal life, however, the bulge is very small. The upper swelling, usually smaller than the bulge, but at times more evident in the early stages of development (Figs. 13, 14), is the anlage of the sebaceous

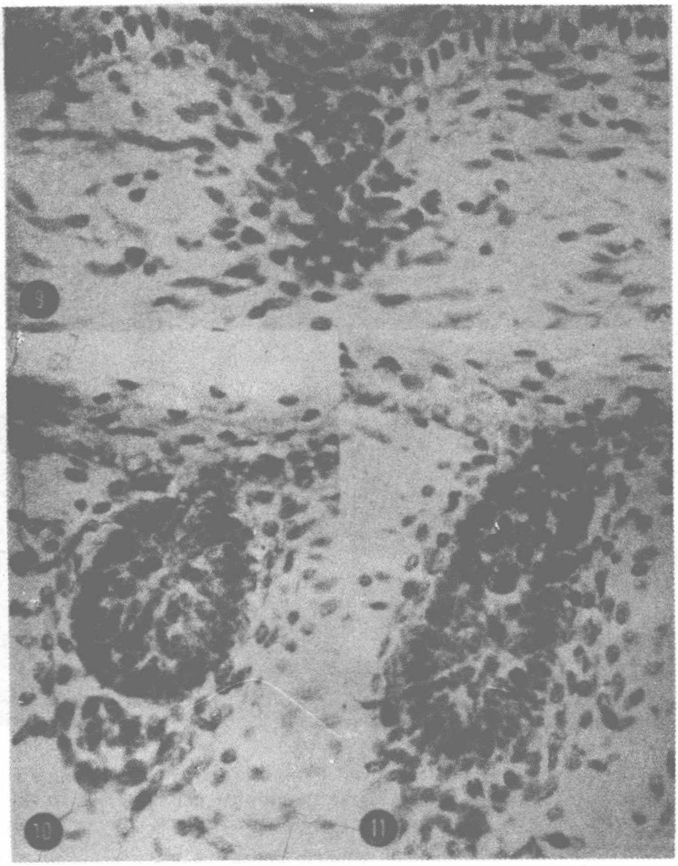

FIG. 9
Skin of the face in a 16-week-old fetus. The early development of a hair germ and the concentration of the surrounding mesenchymal cells is illustrated. (Toluidin blue. × 800.)

FIG. 10
Skin of the scalp in a 16-week-old fetus, illustrating the further development of the hair germ. Note the beginning development of the papilla and the concentration of the surrounding mesenchymal cells. (Toluidin blue. × 800.)

FIG. 11
Skin of the scalp in a 16-week-old fetus. Further extension downward into the dermis of the growing follicle. Note the upward growth of the inner cells of the peg into the epidermis, Mitoses are present. (Toluidin blue. × 800.)