STUDIES IN DENERVATION

G.—SEBACEOUS SECRETION

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(RECEIVED 27TH OCTOBER, 1943)

THE need for inquiries into the physiological mechanisms underlying the secretion of sebum is indicated, not only by the lack of information concerning this function of the skin, but also by the fact that it has not as yet been determined how far perversions of secretion are the cause of various pathological conditions such as seborrhœic dermatitis. In these circumstances it seemed desirable to ascertain to what extent the sebaceous glands are under the control of the nervous system. The results of an investigation directed to this end will be reported in this paper, but it is first necessary to indicate the background of the study.

As is well known the sebaceous glands are holocrine in nature and the secretion is the end product of cellular disruption. On *a priori* grounds it would seem unlikely that these glands would be activated by nervous influences, but Boeke (1934) has described a plexus of nerves investing the glands. He considered it to be sympathetic in origin and excitator in function though he noted that the individual cells are not innervated. Moreover, many authors such as Stein (1926), Pachur (1931), and Serrati (1938) have reported that sebaceous secretion is disturbed in various affections of the central nervous system, most notably in chronic encephalitis lethargica. Details of unilateral disturbances of secretion are furnished by Serrati. This has led to the tacit assumption that the sebaceous glands are activated directly by nerves. In further support of this position are the observations of Arloing (1891) on the ear of the ass which lead him to believe that the sympathetic fibres exerted both an excitatory and an inhibitory action. Also frequently quoted is the case of supra-orbital neuralgia reported by Marschalko (1905) in which a seborrhœic condition existed in the area supplied by the nerve. Abel (1936) also appears to concur, for he states that sympathectomy abolishes sebaceous secretion. Contrary opinions indicating that the glands are not directly under nervous regulation are expressed in Starling's text book (1936) and by Goldsmith (1936). This would seem to be the view of the majority at the present time, but the literature does not reveal any reason for modifying the statement of Reid (1898) that "Nothing is definitely

known as to the existence or not of any action of the nervous system upon the sebaceous glands."

Method

The method used to assay the amount of sebaceous secretion is a modification of that employed by Serrati. The areas of skin under observation were wiped gently with cotton wool moistened with ether and then left exposed to the air for a time. They were then wiped thoroughly with grease free filter papers moistened with ether. The filter papers were dried in a vacuum chamber and weighed. The weight of the paper was subsequently obtained after extracting the grease with ether and drying. The difference of these weights indicated the amount of ether-soluble material which had been adsorbed on to the papers from the skin. The areas of skin on which the individual estimations were made varied from 200 to 300 sq. cm. and the results are expressed in the amount per 100 sq. cm. The limitations of the method were indicated by the following procedures. Measurements made immediately after the preliminary cleansing resulted in figures of 1.0 to 2.0 mg., while a comparison of the amount of sebum obtained from two symmetrical areas on the face of a normal subject after an interval of 1 hour showed a disparity of 2 mg. on one occasion and 3 mg. on another. It would appear, therefore, that differences of 3 mg. or less as estimated by this method are without significance and may be due to incomplete removal of the sebum from the skin or to other errors introduced in weighing or in extracting the fat from the filter papers.

The subjects are described in paper A and they had skin of normal appearance.

Results

The results are expressed in Table I.

TABLE I

Subject	Time	Areas under observation	
		Right face (sympathecto- mized)	Left face (normal)
S.S.	12 hr.	17 mg.	14 mg.
	1.5 hr.	11 mg.	12 mg.
S.B.	1 hr.	Right arm (denervated) 7 mg.	Left arm (normal). 6 mg.
M.V. (normal)	1 hr.	Face (subject cold)	Face (subject warm)
		15 mg.	13 mg.

* Working on behalf of the Medical Research Council.

Subject S.S., who had a right stellate ganglionectomy of 4 months duration exhibited no difference in sebaceous secretion on the two sides of the face as is shown by the equal values obtained from the normal and from the sympathectomized area after intervals of 1.5 and 12 hours. This indicates that sympathetic fibres are not requisite for the activity of the glands. Subject S.B., who had a complete lesion of the right brachial plexus of 5 months duration showed an equal secretion on the two arms. Therefore, sebaceous glands can function in the absence of all nerve fibres. Nevertheless, it seemed possible that the amount of sebum estimated in these two cases might represent a basal level of secretion and that the influence of nervous regulation might be only appreciable in certain circumstances. An effort was made to discover these circumstances by comparing the amount of secretion when the individual was cold and when warm. On one occasion a normal male volunteer was kept shivering for an hour with his legs in cold water, while on another, he was kept warm and gently sweating for an hour. The amounts of sebum collected from the face on these two occasions were approximately equal, indicating that the activity of the sebaceous glands is not modified by the thermal needs of the body. Thus no reason was found to qualify the conclusion that the sebaceous glands function independently of the peripheral nervous system.

Supplementary observations were made on two other processes occurring in the skin. The growth of hair was estimated by measuring the length of all the hairs in a given small area 10 days after shaving. In Fig. 1 is shown the distribution curves

FIG. 1.—Chart showing the lengths of 40–50 hairs 10 days after shaving on a denervated area on the medial side of the left leg compared to those on control areas. Key to symbols given on the face of the chart.

of the lengths of 40–50 hairs on a denervated and on control areas. Similar results were obtained on subject C.B. It is clear that loss of nerve supply does not affect hair growth.

It was considered that if denervation affected the cells of the epidermis this might be disclosed by microscopic examination. Available for this pur-

pose was the leg of subject S.H. which was amputated because of an irreparable lesion of the sciatic nerve of 18 months duration. Skin from a denervated area on the lateral aspect was compared to that from a normally innervated area on the medial aspect of the leg. Microscopic examination of hæmatoxylin stained preparations revealed no abnormality in any of the constituents of the skin and in particular cellular metaplasia in the epidermis appeared to have been progressing in a normal fashion in both areas.

Comment

It was indicated in the introduction that little progress has been made in our knowledge concerning sebaceous secretion. This, however, only applies to the nervous factor in its regulation. Definite advances have been made by Emanuel (1938) and by Serrati (1938) in delineating the course of secretion under normal conditions. Their findings indicate that when the sebaceous material is removed from the skin it is replaced by the action of the glands, at first rapidly and then more slowly, so that at the end of 1 hour approximately 50 per cent. is replaced, but the original amount is not replaced for 3 hours or longer. This has been interpreted by both authors to mean that sebaceous secretion ceases when a layer of sebum of normal thickness is reformed. Emanuel considered that an inhibitory influence was exerted on the glands by the pressure of the sebaceous layer, while Serrati invoked the mediation of nerves. However, their findings are equally well explained by the assumption that sebaceous material is being constantly extruded from the glands and is at the same time being reabsorbed through the skin; it being known by analogy to lanoline that such absorption can occur. The thickness of the layer and its site of formation would therefore be determined by the relative rates of production and absorption. With the passage of time the layer of sebaceous material would become more diffusely spread over the surface of the skin leading to an increasing rate of absorption. At some point this would equal the rate of secretion and make it appear as though secretion had ceased. Thus it is possible to conceive that sebaceous secretion is simply a manifestation of the growth of the cells of the glands and as such would not be influenced directly by the nervous system. In agreement with this concept is the finding that hair-growth and the metaplasia of the cells of the epidermis is similarly unaffected by deprivation of direct nervous influences.

It might be considered that the results recorded here demonstrating an equal replacement of sebaceous material on denervated and on normal areas could be explained by a co-existing defect in secretion and absorption, the latter being determined either by an abnormality of the skin or of the secretion. This, however, is unlikely because it was shown in subject S.S. that not only was the final balance between secretion and absorption the

same on the two sides, but that the rate of replacement as judged by the amount present at the end of 1.5 hrs. was also the same.

On the basis of the present concept of sebaceous secretion it may be assumed that the physical state of the skin would influence the relative amounts of sebaceous material being formed and being absorbed. Thus, before assessing the significance of the unilateral disturbance demonstrated by Serrati in cases of hemiplegia it would be necessary to know if alterations in temperature or blood flow were present in the extremities. The abundant secretion encountered in cases of encephalitis lethargica is of great interest because the present results would indicate that it is due to some disturbance of hormonal regulation. Obviously, before such a suggestion can be entertained it will be necessary to show that in these individuals as in normal subjects the sebaceous secretion is independent of the peripheral nervous system.

Summary

Sebaceous secretion has been estimated in a subject with a sympathectomy and in a subject with a lesion of the brachial plexus.

No evidence was found that the activity of the sebaceous glands is directly under the control of the nervous system.

By analogy with the growth of hairs and of the epidermis it was concluded that sebaceous secretion is the result of a continuous growth process of the cells of the sebaceous glands.

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