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Factors affecting the rate of sebum excretion in man

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Synopsis—The local and systemic factors controlling human SEBACEOUS ACTIVITY are reviewed. ANDROGENS clearly stimulate sebum production, but our knowledge of the SEBOTROPHIC effect of other HORMONES in man is limited. The SEBORRHOEA of ACNE remains a mystery, and current concepts, such as cutaneous androgen synthesis, are briefly discussed. Neurological lesions occasionally cause seborrhoea and the evidence concerning nervous control of the sebaceous glands is summarized. LAEVODOPA reduces the seborrhoea of Parkinson, but a small study has shown no affect in acne vulgaris. Some anti-androgen and cholesterol blockers inhibit SEBUM excretion when given systemically, but they are much less effective topically. Sebum excretion is affected by SKIN temperature, but probably not by sweat secretion, though sweat may make the skin look more oily. The hypothesis, born in 1927 and buried in 1958 that the amount of LIPID on the skin affects the rate of sebum production by a feed back mechanism is exhumed in the light of a recent demonstration that a surface feed back mechanism exists in animals.

Introduction

Despite, or perhaps because of, the fact that the human sebaceous glands have been studied by dermatologists for many years, the factors controlling sebaceous activity are debatable. Our understanding has been hampered chiefly by the difficulty of devising an accurate quantitative method for the estimation of the rate of sebum secretion by the gland. The relatively large quantity of sebum stored in the follicular reservoir, and the

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slow turnover rate of the gland (1) make it difficult to distinguish between the rate of secretion by the holocrine process which occurs deep in the gland, and the rate of excretion of preformed sebum to the skin surface. Technical problems of estimating sebum chemically, volumetrically or gravimetrically have added to the difficulties, and many published observations are of doubtful validity because the assay methods employed have since been shown to be inaccurate. Most recent work has been performed using the method of Strauss and Pochi (2) which measures the rate of sebum excretion at the surface, but this does not invariably correspond to the true rate of secretion by the glands (3), and for this reason I shall refer to the sebum excretion rate (SER) rather than the sebum secretion rate.

Systemic factors

Endocrine

Most clinical and experimental evidence points to the endocrine system as the main factor controlling the activity of the sebaceous glands, but the relative importance of the individual hormones is less clear. It would appear from the literature on this subject (4, 5) that androgens provide a profound stimulus to sebum production, while oestrogens have the opposite effect. The effect of quite large doses of oestrogen is however overcome by small doses of androgen.

Our knowledge of the role of the other hormones is limited. Clinicians are aware that many endocrine diseases affect the oiliness of the skin, but there have been few quantitative studies. Acromegalics commonly complain of hyperhidrosis and seborrhoea, and we have recently shown that the SER is high in untreated acromegaly, but decreases after pituitary ablation (6). Unexpectedly the correlation between SER and plasma growth hormone levels was not significant, and this implies that some other factor was responsible for the initial seborrhoea. Little is known of the sebotrophic activity of the other pituitary hormones in man. Adrenocorticotrophic hormone in pharmacological doses sometimes causes acne, but it has not been shown that this type of acne is associated with seborrhoea, nor is it known if the same effect occurs in adrenalectomized patients. Strauss and Kligman (7) using a relatively insensitive histological technique found that ACTH may cause sebaceous gland hyperplasia in pre-pubertal males and post-pubertal females, but there was no effect in adult males. Gonadotrophins are without effect on the sebaceous gland in castrated males (8). The

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effect of the other pituitary hormones on the sebaceous gland has not been investigated in man.

Adrenal androgens probably play an important part in stimulating sebaceous activity in the female. Pochi, Strauss and Mescon (9) showed that dehydroepiandrosterone, the major adrenal androgen, has a powerful sebotrophic effect which will overcome the suppression induced by oestrogens. In the same publication they reported that in three women with Cushing's disease, the SER was increased above normal in only one patient, but decreased after adrenalectomy in every case. In a man with hypoadrenalism the SER was below normal, but increased after hydrocortisone replacement therapy. They concluded that dehydroepiandrosterone acts directly, whereas glucocorticoids probably act in a permissive capacity, physiological amounts being necessary for the gland to respond to androgenic stimulation. Pochi and Strauss (10) have also shown that prednisone in a dosage of 20 mg daily has no effect on the SER in normal men, but produces a variable suppression in normal women and a marked suppression of sebum excretion in castrated men. They explained these observations by the fact that prednisone suppresses adrenal androgen production but has no effect on testicular androgens.

Patients with myxoedema classically have a coarse dry skin, and we have confirmed that the SER is low in this condition (11).

The effect of progesterone is controversial. Several studies have shown that oral contraceptives decrease the SER, but the effect has been attributed to the oestrogen content of the preparations (12–14). Zeligman and Hubener (15) and Smith (16) found that progesterone increased sebaceous activity, whereas Jarrett (17) and Strauss and Kligman (18) found the hormone had no effect in physiological doses.

There have been very few quantitative studies of sebaceous activity in the endocrinopathies, and our knowledge of the interaction of several different hormones on the glands under physiological conditions is even more scanty. The commonly observed exacerbation of acne during the premenstrual phase has been attributed to increased sebum production, possibly in response to the increase in circulating progesterone. Kalz and Scott (19) using an insensitive osmic acid technique found that some women had an increased SER during the second half of the menstrual cycle, but Strauss and Kligman (18) using a more refined method found no fluctuations attributable to menstrual rhythm.

The effect of pregnancy on the sebaceous gland is also debatable. Theoretical considerations would suggest that the SER would pro-

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gressively decrease as a result of the large quantities of oestrogen formed in pregnancy. Brun and Ritz (20) using a semiquantitative method found as expected that a group of pregnant women excreted less sebum than a control group of non-pregnant women. Burton, Cunliffe, Millar and Shuster (21) however using a more accurate method with serial estimations in a group of women during and after pregnancy found no such decrease until after delivery had occurred. This would imply the formation of a powerful sebotrophic factor during pregnancy to counteract the effect of the oestrogen. This factor is unlikely to be of placental origin since women with multiple pregnancies (in which placental size is increased) do not have a greater SER than women with a single foetus (22).

Acne vulgaris

The commonest condition associated with seborrhoea is of course acne vulgaris. The severity of the acne is related to the SER, but seborrhoea cannot be the only causative factor since it persists into middle age, long after the acne lesions have cleared (23, 24). Acne can of course occur secondarily to endocrine disease, but the vast majority of acne patients are otherwise clinically normal. Surprisingly few reports of endocrinological studies in acne patients have been published, but the absence of virilization makes excessive systemic androgen production unlikely and normal plasma testosterone levels have been reported in acne patients (25, 26). The possibility of increased sensitivity of the sebaceous glands to normal androgen concentration cannot be dismissed, nor can the suggestion that one of the many androgens is strongly sebotrophic and weakly virilizing. The important new hypothesis that androgen may be synthesized in the skin will be discussed later. Strauss and Pochi (27) have reviewed recent advances in androgen metabolism in relation to the skin.

In this Symposium (28) Professor Ebling has already reviewed the animal studies implicating the pituitary gland in the control of sebaceous activity and the role of this gland in human seborrhoea cannot be ignored. Stafford, Cunliffe, Tubman and Hall (29) have shown that acne patients have a normal level of growth hormone which suppresses normally following glucose ingestion, but in the absence of quantitative data on the other pituitary hormones pontification would be premature.

It is a well-established tenet of dermatological faith that the ingestion of chocolate and fatty foods causes an exacerbation of acne. Like many

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faiths, this may be true for some individuals, but the supporting scientific evidence is tenuous. Serrati (30) claimed that both a high fat diet and a high carbohydrate diet increased the surface lipid in six subjects, but Cunliffe and Shuster, in a larger study, found no effect on the SER following the ingestion of large quantities of chocolate (31). Animal studies have shown that diet affects sebum composition, and recent work by Pochi, Downing and Strauss (32) has shown that prolonged starvation in man reduces the SER by about 40% and also changes the composition of sebum.

Neurological

Many workers have reported the presence of a plexus of nerve fibrils around the sebaceous glands (33–36), but there is surprisingly little evidence that these nerves, which are rich in cholinesterase (37), affect the function of the gland. Ikai (38) measured the SER after intracutaneous injection of epinephrine and acetylcholine and found this had no effect on sebum excretion. Ikai, Sugi and Nitta (39) also showed that unilateral stimulation of the cholinergic nerves provoked by a pressure reflex had no effect on the SER. It should be pointed out however that his experiments only measured short term responses to brief stimulation over a period of 20 min and since the glands take several days to respond to hormonal stimulation it is probable that the response to neuronal stimulation may be similarly delayed. Doupe and Sharpe (40) and Hodgson-Jones, MacKenna and Wheatley (41) were unable to detect any change in SER in a small number of patients after denervation, and Miescher and Schönberg (42), Kligman and Shelley (43) and Ikai (38) found no change in SER following emotional stimulation. These latter publications are again open to the criticism that the time allowed for the response was too short. In a longer study over 30 days, Lorenz, Graham and Wolf (44) found wide fluctuations in SER which they could not correlate with changes in emotional mood, but the monomolecular layer method they employed for sebum estimation depends more on the chemical composition than the actual quantity of sebum (45). Scott and Kalz (46) and Robin and Kepecs (47) claimed that fear increased lipid production, but these two studies are invalidated, since emotional sweating would affect the results obtained by the osmic acid method they employed. Against this negative experimental evidence must be weighed the many convincing case-reports of localized seborrhoea following a nerve-lesion which have appeared in the dermatological literature over the years (48-50).

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Burton, Cunliffe, Saunders and Shuster (51) have recently shown quantitatively that some patients with a unilateral facial nerve lesion have seborrhoea on the paralysed side, while others have decreased excretion on the affected side. This suggests that nerve lesions can affect the gland, although the effect may be indirect.

Serrati (30) using a crude quantitative method found generalized seborrhoea in a variety of diseases of the central nervous system, including epilepsy, pontine tumours and postencephalitic Parkinsonism. The presence of an increased SER in Parkinsonism of various types has since been confirmed by Kvorning (52) and Pochi, Strauss and Mescon (53). The cause of the suborrhoea is unknown, but the observation that it is bilateral, even in patients in whom the neurological signs are largely unilateral (54, 55) suggests that the lesion in the brain exerts its effect via a hormonal mechanism rather than directly via the autonomic nervous system. The intimate connections between the hypothalamus and the pituitary provide a likely efferent pathway for such a mechanism. Burton and Shuster (56) have shown that laevodopa which improves the neurological manifestations of Parkinsonism, also reduces the sebum excretion rate. The exciting hypothesis that laevodopa may exert an effect on sebum production by a central action on the hypothalamic releasing hormones which govern pituitary function, is supported by the demonstration that dopamine injected into the brain of rats may increase the concentration of releasing factors in the plasma of the hypophysial stalk (Kamberi, Mical and Porter (57, 58). It remains to be seen whether laevodopa will affect seborrhoea due to causes other than Parkinsonism, but we have found the drug has no effect on the seborrhoea of acne vulgaris (59).

Drugs

The effect of hormone preparations has been discussed above.

Antiandrogens are substances which prevent androgens from expressing their activity at target sites. Several antiandrogens other than oestrogen have now been developed and Strauss and Pochi (60) have reviewed our knowledge of their effect on the human sebaceous gland. Cyproterone acetate (61), 17 methyl-β-testosterone (62, 63) and chlormadinone acetate (60) all decrease the SER when given systematically. The side-effects of these drugs limits their systemic use for the treatment of seborrhoea, at least in the male (64). An important point which has emerged from animal studies is that androgens vary in their potency depending on the

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particular end-organ used in the bioassay system (65, 66). Conclusions about the activity of androgens or androgens on the sebaceous glands cannot therefore be extrapolated from data from other bioassay systems such as levator ani or preputial gland.

Another pharmacological approach has been the use of anti-cholesterol agents, since cholesterol makes a large contribution to sebum. Strauss, Pochi and Whitman (67) showed that eicosa 5,8,11,14-tetraynoic acid which blocks the pathway of cholesterol synthesis between acetate and mevalonic acid, caused a substantial decrease in SER when given systemically. Side-effects observed during long-term administration of the drug to animals have prohibited its further systemic use in man. Other anticholesterol agents such as aluminium nicotinate and clofibrate have been without effect (68).

Tetrayclines have a beneficial effect in acne vulgaris but do not affect the SER (69, 70).

Laevodopa has been discussed above.

Local factors

Cutaneous androgen synthesis

Much attention is currently being paid to local variations in skin metabolism. It has long been known that there is considerable variation in sebaceous activity in different parts of the body, the SER being greatest on the forehead, face, neck and upper chest (71). A potentially important development is the finding of Milne and his co-workers (72, 73) that there is considerable variation in the level of activity of the enzyme hydroxysteroid dehydrogenase in different areas of skin, the activity being greatest where the sebaceous glands are largest. The role of this enzyme is speculative, but it is thought to be implicated in steroid metabolic interconversions (74). In view of the important recent studies showing that the skin can synthesize and interconvert adrogens (75–78) this enzyme may conceivably regulate sebaceous gland development by an action on local androgen metabolism.

Sweating

Generations of dermatologists have recognized the clinical association between sweating and oiliness of the skin. Herrmann and co-workers (79, 80) and Prose, Baer and Herrmann (81) found a good quantitative correlation between the rate of sweating and the SER in different parts of the body. Their conclusion that sweating increases the SER was apparently sup-

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ported by their demonstration that sweat and sebum when mixed will emulsify (82), and their finding that the surface lipid was reduced by atropinization of the skin. On repeating this experiment however, Kligman and Shelley (43) obtained the opposite result, surface lipid being decreased on the sweating skin compared with the atropinized skin. Ikai, Sugi and Nitta (83) have since shown in a series of experiments that the SER is independent of the rate of sweating, though the sweat rate will of course affect the skin temperature (*vide infra*). It seems likely that the appearance of oiliness of the skin is influenced by the rate of sweating. Kligman *et al* (43) showed that sebum accumulates as small droplets at the follicular orifices on a dry skin, and Jones, Spencer and Sanchez (84) showed that sebum will spread rapidly over a wet surface. Thus a wave of sweating may suddenly cause the skin to appear oily without actually affecting the quantity of sebum excreted.

Skin temperature

Several authors albeit using relatively crude techniques have demonstrated that large changes in environmental temperature may affect the rate of sebum excretion (83, 85, 86), Cunliffe, Burton and Shuster (87) using a more refined technique have shown that a change of skin temperature of 1°C over the physiological range may cause a change in SER of the order of 10%. This effect is probably due to changes in sebum viscosity rather than changes in the rate of sebum production by the gland.

Feedback control by surface lipids

Schur and Goldfarb (88) first suggested that the amount of sebum on the skin surface might influence the rate of sebum production by the gland. This theory was based on the observation that after defatting the skin of an individual with ether, the amount of lipid recoverable from the surface at any given time, whether days, weeks or months after the defatting is relatively constant. The theory, supported and elaborated by Emanuel (71) and Butcher and Parnell (89, 90), suggested that when a given thickness of sebum was reached, depending on the viscosity of the sebum, the back pressure on the gland would counteract the excretory force of the gland and sebum production would cease. The gland would thus function periodically in proportion to the amount of sebum lost from the surface. Kligman *et al* (43) refuted this theory following an experimental appraisal of sebaceous gland function in 'sebaceous athletes'. They found, using direct vision and the osmic acid 'pore print' method, that despite the application

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of pressure to the skin surface using air, mineral oil and a glass slide, the glands continued to excrete sebum to the surface. They concluded that the glands function continuously irrespective of the amount of sebum on the surface. It should be pointed out however that their experiment showed only that the gland does not shut down completely when pressure is applied. They produced no evidence that the excretion rate is not modified by the surface lipid. Kvorning (91) had previously claimed that the application of 20% cholesterol in olive oil to the skin surface did suppress sebum excretion to some extent. Kligman *et al* (43) also confirmed the finding of Schur *et al* (88) and Herrmann *et al* (79) that the amount of surface lipid collected over several short time intervals greatly exceeds the amount which would be collected at a single removal at the end of the same total length of time. They attributed this phenomenon to the fact that sebum can penetrate the intercellular spaces of the stratum corneum. The more frequently the sebum in the 'capillary reservoir' of the stratum corneum is removed, the greater the amount of sebum which will be attracted from the follicular orifice by a 'wick' effect. This explanation of course blunts their attack on the feedback theory as their postulated mechanism is itself a type of feedback control. Archibald and Shuster (92, 93) have recently reopened this controversy by their demonstration that in rats the frequency of defatting of the skin by ether-dipping affects the SER. Despite a clinical impression that sebum reaccumulates more rapidly if the hair is washed more frequently, we have been unable to confirm this quantitatively in limited experiments in man with repeated ether washing (94). We have also investigated the relationship between sebum viscosity and SER but found no correlation between the two measurements (95). Nevertheless in view of its important cosmetic implications we feel that the feedback theory should not be too lightly dismissed.

Chalones

A similar feedback concept for epidermal growth was postulated by Pinkus (96) to explain the fact that removal of the stratum corneum by scotch tape stripping stimulates a burst of mitotic activity in the basal layer of the epidermis. The mysterious chalone has since been discovered and its role in the control of epidermal regeneration is currently under investigation at many centres; Bullough and Laurence (97) have claimed that another chalone may control mitotic activity in the sebaceous gland. Little attention has yet been paid to mitotic rates in relation to human

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sebum excretion, but if the sebaceous gland chalone, like the epidermal adrenalin-chalone complex, exhibits a 24 h rhythmicity this might explain the circadian variation in sebum excretion rate reported by Burton, Cunliffe and Shuster (98).

Pilo-erection

Despite *ex cathedra* statements to the contrary in vintage text-books it is doubtful whether contraction of the pilo-erector muscles has any effect on the S.E.R. in man. Kligman *et al* (43) found no visible sebum droplets at the follicular orifices following the induction of pilo-erection with intradermal epinephrine, and they have pointed out that the muscles associated with the larger sebaceous follicles are often vestigial.

Topical drugs

We now have a number of rational leads in the search for a topical agent to suppress sebaceous activity, but the results to date have been disappointing.

The antiandrogens have not yet been fully evaluated. Strauss, Kligman and Pochi (99) found that oestrogen applied topically to one side of the forehead was without effect unless it was used in a concentration sufficient to cause systemic side-effects and sebaceous suppression on the untreated side of the forehead. 1% cyproterone acetate in an oil in water emulsion caused a variable decrease in the SER (100), but 10% cyproterone acetate in dimethylsulphoxide apparently had no effect (101), and 17 methyl-β-testosterone had only a slight effect topically (62).

Topical anticholesterol agents are also under investigation, but no significant breakthrough has yet been reported. Tetraynoic acid appeared to cause a small but significant reduction in SER (102, 103), but aluminium nicotinate was without effect (104).

Scott *et al* (46) claimed that sulphur decreased the SER, but Kligman *et al* (43) using a variety of topical sulphur preparations could not confirm this. There is little evidence that other topical acne remedies such as benzoyl peroxide, resorcinol, retinoic acid, etc., affect the SER, but Powell (105) found a decrease in SER in four patients after the use of 2-naphthol paste.

Bereston (106) made the interesting observation that selenium sulphide shampoos increase sebum excretion, and Goldschmidt and Kligman (107) have confirmed this experimentally.

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Radiation

There is little doubt that X rays in adequate dosage will reduce the SER, but the dangers of radiation dermatitis and induction of neoplasm have restricted their use in recent years to desperate cases of acne vulgaris which have responded to no other therapy.

It is doubtful whether ultra-violet radiation, which also benefits acne vulgaris, affects the SER. Prose *et al* (81) found that a weekly erythema dose of uvr did not appreciably decrease the lipid layer on the skin surface.

Conclusion

The field of human sebaceous physiology has been relatively untilled in the past, but the last few years have produced a resurgence of interest and we appear to be due for a cultural revolution. This review, possibly exhausting but not exhaustive, has I hope given some idea of the harvest waiting to be reaped by modern investigative techniques. Apart from its important cosmetic implications the sebaceous gland probably has much to teach us of cutaneous metabolism and the way in which hormonal and other mechanisms regulate cellular division.

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DISCUSSION

MR. R. J. CHUDZIKOWSKI: You have touched briefly upon dietary factors. Two of such factors are bromides and chocolate. According to the press the latter seems to have been exonerated recently. This leaves bromides. Could you please comment?

THE LECTURER: There is no doubt that the bromides will produce a skin rash which is very similar to acne, though it is not exactly identical. I know of no data concerning the sebum excretion rate, so whether this is mediated by an increase in sebaceous gland activity or not, I do not know. The effect of chocolate is more controversial. All I can say is that the only quantitative study I know of, carried out by Dr. Cunliffe (108), showed that the ingestion of large quantities of chocolate over a period of about six weeks did not affect the sebum excretion rate. However, I think most dermatologists have come across patients who will swear that chocolate brings them out in spots, but again there is very little scientific evidence and many scientists have tended to play down the dietary factors.

MR. N. J. VAN ABBE: 1. I would have thought that sebum was not a Newtonian fluid, and expressing the viscosity in poises might be a measurement of the wrong parameter. Have you considered other ways of looking at it?

2. I can find no reference in the paper to any thoughts you have on the significance of the fauna and flora of the sebaceous gland; do you rule out any association between micro-organisms for instance and acne?

3. I was struck, during Mr. Barry's presentation (109) by the possibility that the histochemical changes he was showing reflected changes in chalone availability. I wonder if Mr. Barry looked for and has seen any circadian rhythm in the histochemistry of the sebaceous gland and its surrounding area?

THE LECTURER: May I deal with the first two points? I think the possibility that the sebum may not be a Newtonian fluid is a very real one; I did this work in col-

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(108) Cunliffe, W. J. and Shuster, S.—personal communication (1970).
(109) Barry, D. H., Robinson, W. E., Hunter, B. and Davies, R. E. Quantitative enzyme histochemistry of mouse skin: preliminary studies with cosmetics, Presented at Symposium on 'Appendages of the Skin,' Eastbourne, Sussex—9th March 1971.

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laboration with Dr. Roscoe (110); he suggested a number of experiments which I attempted to perform to try to throw some light on this problem. I cannot go into the physics of it now, but the results that I obtained suggested that sebum probably is a Newtonian fluid. We had hoped that it might not be Newtonian because gel formation might have provided an explanation for the blockage of the small duct of the sebaceous gland. We were interested in establishing whether increased viscosity of the sebum might block the ducts and cause acne. In fact, we found no evidence for this, the viscosity was the same in control, and in acne, subjects.

With regard to the flora, I think it is very likely that an organism such as Corynebacterium acnei may play a part in causing acne. I did not deal with this because my brief was to discuss the factors affecting the rate of sebum excretion. I think it doubtful that bacteria affect the rate of sebum production, but they probably affect its chemical composition and free fatty acid production, and so on.

MR. D. H. BARRY: An experiment is in progress at Huntingdon at this moment to investigate, histochemically, the presence or absence of a metabolic cycle. The initial aim is to examine the non-specific esterase in the sebaceous gland in order to determine if it is connected with the hair growth cycle. The epidermal and dermal activity will, however, be assessed for the enzyme systems discussed in our paper (109).

PROF. F. J. G. EBLING: I am extremely interested in the demonstration that sebum production is raised in acromegaly. The result is in keeping with the view that the activity of the sebaceous glands can be affected by pituitary hormones. I am also interested in your comments about the role of the thyroid gland. In rats, thyroxine significantly adds to the action of testosterone in increasing sebum production. So, apparently, does a regime of propylthiouracil, which inhibits the thyroid; thus our own results are a little difficult to interpret.

MRS. H. BUTLER: You mentioned that the rate of sebum excretion may not be a measure of the production of spots and pimples—would it be out of place to ask what is a pimple or spot?

It seems that the type of spot seen when over-excretion of sebum is taking place is different from the type which appears after the skin has been degreased, and is irritated and dry.

Are the spots not caused because the sebum is not flowing freely over the skin?

THE LECTURER: A 'spot' is a lay expression and can mean just whatever the person using the term wants it to mean, but acne vulgaris is a clearly circumscribed dermatological disease, which all dermatologists would recognize, and all agree on the diagnosis. It is really a spectrum of spots, not just a single spot, starting with the simple comedone or blackhead, going on to small inflammatory circular papules, some of which then go on to form pus in the centre, so that you can get a little pustular spot. You can see all these lesions in different stages in a patient with acne, and these then resolve, leaving pitted scars in some cases. All sorts of other dermatological pathological processes can give rise to 'spots' and there is no time to discuss all the other different varieties, but I think basically, a small inflammatory papule or pustule of the pilo-sebaceous follicle would be what most people mean by an acne spot.

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(110) Burton, J. L. and Roscoe, R.—unpublished data.

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MRS. BUTLER: If sebum is being excreted properly it should come out and flow over the skin and in the spot there seems to be a covering which must be an unusual growth of dermal cells, and a slowing down of the mitotic rate.

THE LECTURER: There is a hypothesis current that the acne spot may be related to a blockage of the sebaceous duct so that the products of the sebaceous gland are dammed back, the duct then bursts and liberates inflammatory material into the dermis. There is some histological evidence for this idea, and particularly in view of the fact that the sebum in acne patients has been shown to have higher concentration than normal of free fatty acids, which are inflammatory, it seems likely that this may be a mechanism. Comedones certainly would appear to provide one mechanism by which the follicle could be blocked, although most dermatologists are not convinced that every comedone forms an acné spot and certainly some acne spots do seem to arise in areas which have not previously been the site of a comedone. Thus although people think that there is a blockage, the site of the blockage and its relation to comedones is rather obscure.

MRS. BUTLER: It seems a shame that at the age of about 20, women must degrease the skin to make it beautiful and yet spend the rest of their life adding creams to beautify it.

THE LECTURER: I think this is quite true. We try to console our acne patients by telling them that when they are 60 they will have a beautiful skin, but of course this is not strictly true; they may still have the pits of the acne scars if they had a severe acne.

MR. M. K. SHEPHERD: As sebum increases significantly during pregnancy, why does the facial skin become free from spots in many cases?

THE LECTURER: I do not think it necessarily is true that it usually gets better. I have asked a lot of my patients about this and it seems that half of them seem to notice that their skin gets less spotty and half of them think the contrary. I believe there is such a flurry of metabolic and endocrine activity in pregnancy that different women are affected in different ways. There is another factor in the production of spots besides the sebum excretion rate, so that even if the sebum excretion rate were increased in every woman, which is doubtful, there may still be another variable factor, such as bacterial flora which could or could not produce the skin spots.

DR. C. PROTTEY: In view of what we have heard this morning about the obvious endocrine control of sebum flow and bearing in mind Kligman's ideas on the use or the non-use of sebum, would someone care to comment on the use of sebum in the human?

PROF. F. J. G. EBLING: The most important thing about sebum is that children get on very well with only a little of it—the sebaceous gland is only rudimentary before puberty. On the other hand, at puberty, sebaceous secretion becomes greatly increased in both men and women, due to stimulation of the gland by androgens. I cannot help thinking that sebum must have had an important function in our evolution, though perhaps cultural features have completely masked its significance. Does it in some way make the skin more sexually attractive, by improving its texture or

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perhaps its smell? In a number of mammals, sex attractant substances are produced by cutaneous glands. To take only one example, the inguinal apocrine glands of the rabbit not only produce a sex attractant, but they are stimulated by testosterone. If isotopically labelled testosterone is given to rabbits, labelled metabolites can be recovered from the inguinal glandular secretion.

THE LECTURER: I think Professor Ebling's idea of pheromones in humans is not as far-fetched as it might sound. They may have a subliminal effect. Recently it has been observed, for example, that the menstrual rhythm of women who are living together in an institution tends to become synchronous; this has been investigated and other possible factors, social factors, a.s.o., have been excluded. It does seem that there is some subliminal effect which tends to affect the endocrine secretions, and the women themselves are often unaware that their periods are in step until this is brought to their attention.

DR. J. HOLMBERG: Have you made any qualitative measurements on sebum excretion when the excretion rate changes?

THE LECTURER: No. Other people have, though, and this is an expanding field. People are now measuring the biochemical composition of sebum in a variety of physiological and pathological conditions. For example, Dr. Cunliffe has recently found a circadian rhythm in the biochemical composition of sebum excreted at different times of the day. I think this is obviously very important and more work needs to be done.

DR. J. HOLMBERG: We have measured the secretion of hair fat of the sebum on the scalp, and have found differences in the composition of the sebum between individuals.

THE LECTURER: I think this is likely to be very important in acne, and possibly in other diseases, too.

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