THE MAMMALIAN EPIDERMIS AND ITS DERIVATIVES

THE twelfth symposium of the Zoological Society of London, held on March 7, 1963, on "The Mammalian Epidermis and its Derivatives" showed the present growth of interest in the skin both in the scope of its papers and in the large number of participants.

Prof. M. Abercrombie took the chair for the morning session. The opening paper by Prof. W. S. Bullough and E. B. Laurence on "The Production of Epidermal Cells" was presented by Prof. Bullough, who outlined evidence that the diurnal rhythm in epidermal mitotic activity was inversely dependent on changes in the rate of adrenaline secretion. Adrenaline inhibition was felt primarily in the antephase when it prevented the onset of mitosis. The inhibitory effect was, however, relaxed after epidermal wounding, and was not felt in active hair bulbs, so it seemed evident therefore that there must be some co-factor without which adrenaline cannot act. Experiments were described from which it was argued that the high mitotic activity which results from wounding is due to the withdrawal from the wound area of some epidermis-specific mitotic inhibitor. For such a substance the name of 'chalone' was proposed. Prof. Bullough announced that such a chalone had been extracted from epidermis; it could be destroyed by boiling, was non-dialysable, and was precipitated at concentrations of between 60 and 80 per cent alcohol; thus it was possible that it is a moderate-sized protein. The separate and combined actions of epidermal chalone and adrenaline had been analysed and they could provide explanations for the mitotic reactions of epidermis during the diurnal cycle, after wounding, and *in vitro*. Prof. Bullough concluded this challenging announcement by surveying the successive phases of the epidermal mitotic cycle and discussing at what point the cell differentiated either for mitosis or for keratin synthesis. He suggested that the determining factor might be the position of the cell within the epidermis, and that this might be related to a concentration gradient of the chalone–adrenaline complex across the epidermal layer.

During the past ten years considerable advances have been made in the knowledge of metabolic processes of the epidermis and, according to Dr. C. N. D. Cruickshank, they could be attributed mainly to the development of three types of technique; namely, microvolumetric, radio-isotope, and fluorometric enzyme assay. Observations from each of these sources now made it clear that the Embden-Meyerhof pathway, the tricarboxylic acid cycle and the hexose monophosphate shunt all operate in skin. In its carbohydrate metabolism, however, the skin appeared to be different from many tissues in that, even in the presence of high oxygen tensions, considerable amounts of lactic acid were produced, although this substance might also be readily metabolized in the absence of any other substrate. High rates of endogenous respiration might be maintained for relatively long periods; it seemed likely that during this period the substrate was phospholipid although a certain amount of glycogen and some protein catabolosis occurred. Dr. Cruickshank concluded by mentioning some work on sulphate metabolism in relation to the synthesis of epidermal mucopolysaccharides. It had been shown that vitamin A increased the incorporation of sulphate into mucopolysaccharides and altered the amount of sulphate thus incorporated into the individual mucopolysaccharide. Chondroitin sulphate *a*, *b* and *c*, keratosulphate and heparin had been demonstrated in epidermis and in addition a substance yet unknown, but possibly a mucopolysaccharide precursor, had been discovered; this last substance was particularly responsive to the presence of vitamin *A*.

The ultra-structure of the epidermis, as observed in the electron microscope, was described by Dr. A. Charles. He discussed the nature of the dermo-epidermal junction and of the basement membrane, doubting that it was a membrane in the normal sense since dermal cells could readily migrate through it. There was evidence that the tonofibrils could be regarded as forming a continuous network throughout the epidermis, being attached at both ends to the desmosomes, at which localized and specialized regions the cells also adhered. In this way the elastic structural properties of α-keratin, of which the tonofibrils probably consisted, could be effectively utilized to give strength and extensibility to the epidermis. Dr. Charles described the observable changes during cornification. It seemed reasonable to believe that the non-fibrillar cytoplasm was precipitated on to the poorly staining tonofibrils in the form of densely staining keratohyalin. This increased progressively in amount, and became less densely stained as it became fully compacted in the newly formed horny cell. At the same time changes in the nucleus, in the tonofibrils, in the cell membranes and in the desmosomes were seen. From these observations it was concluded that, by and large, the older theories of cornification were more satisfactory than the newer ones of Mercer and of Brody. Considerable discussion was provoked by these statements.

Keratinization from the point of view of the histochemist was discussed by Dr. A. Jarrett. In his view keratinization was an active, vital process involving numerous enzyme systems. Over most of the body of mammals keratin had a basket-weave pattern due to elimination of nearly all the epidermal cell contents with keratinization limited to the cell periphery. Thus a sort of pliable lattice network was formed. On the palms and the soles, on the other hand, the whole cell with the exception of the nucleus became involved in keratinization. In scale keratin and in certain pathological types of mammalian keratinization even the cell nuclei were carried up in a relatively intact state into the horny layer. Dr. Jarrett suggested that the greater the energy potential of the granular layer the greater the proportion of the epidermal cell removed during keratin formation. In the basket-weave type most of the cell was removed, but in plantar keratin the energy system was lower and consequently more of the cell became keratinized. In parakeratosis, in which epidermal nuclei were retained, no granular layer was present and therefore virtually none of the cell constituents was removed. Under such conditions a 'scale-like' keratin very similar to the tail-scale keratin of rodents was produced. The different types of keratin could be easily detected by fluorescence microscopy. It was possible to alter parakeratotic keratin to the basket-weave type.

Dr. R. I. C. Spearman continued by discussing the evolution of the mammalian keratinized structures. He pointed out that keratinized epidermal scales in lizards closely resembled those of rodent tails and neither type was preceded by a granular layer. He considered that the evolution of a granular layer began in the hair follicles, which developed at the scale imbrication. The granular layer then extended into the adjacent epidermis and finally became continuous over the whole body surface; thus the stratum corneum was altered from the scale type

of reptiles to the flexible type of mammals. The evidence available did not support the view that hairs were directly homologous with reptilian prototrichs; the hair follicles were probably entirely new structures which arose in the epidermis adjacent to reptilian-like scales and not derived from any part of them. In addition to such primary follicles secondary follicles forming the underfur were later evolved, with a consequent increase in the extent of the granular layer. The close association of the hair follicles with a flexible type of stratum corneum was seen in certain aquatic species where hairs were reduced in number and a parakeratotic layer occurred. The pathological appearance of parakeratosis in mammalian epidermis might be considered a reversion to this more primitive type.

Dr. J. Cohen described his experiments on the transplantation of the end bulb of the vibrissa follicle in the rat. Such a transplant produced a succession of whiskers when implanted into spleen or ear but regressed in the thigh. The dermal papilla, still surrounded by its matrix, produced a succession of whiskers when implanted into ear skin; the follicles of such implants were either of donor or host type, or both; this was considered to depend on the origin of the follicular cells. The matrix, when transplanted to ear skin, occasionally produced a short length of whisker shaft, but usually keratinized without further growth, with a scatter of its melanocytes. The dermal papilla alone produced no whisker and was not 'visible' at biopsy after more than two weeks; before this it became invested in local epidermis and it was presumed that it initiated hair growth of local type. Dermal papillæ might produce whiskers or scales when transplanted to the tail. It was presumed that whiskers were produced from 'dirty' papillæ, that is, papillæ with adherent epidermal cells.

The cyclic activity of hair follicles was discussed by Dr. F. J. Ebling and Dr. E. Johnson. Dr. Johnson opened by describing the waves of hair growth throughout life in a colony of albino rats. Hair first erupted from dorsal follicles at 5 days of age and from ventral at 10 days. Hair replacement, with almost simultaneous eruption ventrally and dorsally, first occurred at 35–42 days; in subsequent activity there was an increasing lag in eruption in the back and head regions, so that a wave pattern was produced and indeed the waves came to overlap. A number of experimental treatments, for example, hypophysectomy, adrenalectomy, gonadectomy, and administration of thyroxine, advanced the start of follicular activity, and a number of others, for example, œstradiol, testosterone, ACTH, and thiouracil, retarded it. All these effects were more marked in the dorsal region than in the ventral. Œstradiol also reduced the rate of growth of hair during the active phase and thus hair length was increased by ovariectomy or hypophysectomy. Thyroxine also slightly increased hair length in the female but not in the male. No other hormonal treatments affected hair length. Experiments on the plucking of hair to some extent supported the idea that a rhythm inherent within the follicle was due to the build-up and release of an inhibitor, since the maximum advancement of activity was secured by plucking the hair towards the end of the previous phase of growth, when any inhibitor would be at its highest concentration. But the inhibitor hypothesis would not explain why plucking early in activity did not prolong the period of growth but on the contrary induced premature transformation to the resting stage, nor why plucking just before the onset of activity actually delayed it.

Dr. Ebling continued by describing their experiments on skin grafts. In grafts rotated through 180° on the flank or in transposed flaps of skin, hair follicles continued in their original rhythms, inducing the requisite vascularization during activity. But when homografts were exchanged between rats having an age difference of three weeks, follicular activity in some circumstances came into line with that of the host. Similarly, a cross-effect on follicular activity could be clearly shown in parabiotically joined rats of the same or different ages. Thus it appeared that there were transmissible systemic factors influencing hair growth. Dr. Ebling and Dr. Johnson concluded that both an inherent rhythm, possibly involving a build up of inhibitor, and some systemic timing factor contributed to the control of follicular activity. Experimental evidence was against the idea that the wave of activity was propagated. The apparent self-wise behaviour of follicles in autografts could be reconciled with the idea of systemic timing factors by supposing that after the first wave, the reaction time of dorsal follicles became longer than that of ventral ones. There was preliminary evidence to suggest that changes took place in the dermis at the critical time. When the events of the first wave were determined, about twelve days before eruption of hair, there was little difference between the amounts of collagen in dorsal and ventral skin. But, by the second wave, though it had increased in both regions, the dorsal skin contained much more collagen. Perhaps, therefore, differences in timing between dorsal and ventral follicles developed as a result of changes in the dermis. Such differences could also explain the differential effect of hormonal treatments; hormones might act by modifying this dermal environment.

The full report of the symposium will be published as a memoir of the Zoological Society. F. J. EBLING

GROUND-WATER: GEOLOGICAL AND ENGINEERING ASPECTS

UNDER this general title a symposium of communications was presented on February 27, at the Institution of Civil Engineers, in the course of a meeting organized jointly by the Institution of Water Engineers and the Geological Society of London. It was attended by nearly 600 people widely representative of the various interests which were associated with the meeting. Six communications were presented.

The meeting originated from a proposal, made early in 1962 by Prof. S. E. Hollingworth (University College, London), during his presidency of the Geological Society, that a joint meeting be held by the Society and the Institution, for the discussion of certain matters of immediate interest to both bodies, relating to the geological and engineering aspects of ground-water.

The symposium was divided into two sessions: at the first, the chair was taken by Prof. O. M. B. Bulman, president of the Geological Society, and during its course five communications were presented. At the second, Mr. N.A.F. Rowntree, president of the Institution of Water Engineers, took the chair for the presentation of the sixth communication.

In the introductory communication, "Geology in Relation to Ground-water", Dr. S. Buchan (assistant director, Geological Survey of Great Britain, London, S.W.7), paid tribute to the pioneers, William Smith, William Whitaker, and Oscar Meinzer, who realized, respectively, the need for the stratigraphical classification of rocks, the systematic gathering of statistics relating to bore-hole yields and water-levels, and the application of the principles of hydrology to ground-water.

Buchan summed up the types of field data and tests which are needed in ground-water investigations, and the methods of analysing and applying the statistics obtained from actual observations. He referred to the attempts which have been made to draw up a 'water balance' from