The fibrin plates are incubated on a horizontal shelf at 37° C for 18 h and the diameter of the zone of fibrinolysis measured with calipers. Fibrin clots in the tubes are observed in a water-bath until lysis is complete. Inhibition by ε-amino-caproic acid is demonstrated both by incorporating this in the fibrin plate and alternatively by adding it to the fractions after adding the 'Triton' and before putting these on the fibrin plates or in the clotting mixtures. The final concentration of amino-caproic acid in these mixtures was 0·001 per cent w/v.

We have obtained similar results using purified *O* somatic antigen of *Shigella dysenteriae* as an endotoxin. Further biochemical methods are now being used to provide a more quantitative basis for these observations.

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Function of High-level Melanocytes

THE concept that high-level melanocytes (Langerhans cells) are effete, except in a melanogenic sense, has required modification since our previously reported demonstration of adenosine triphosphatase (ATPase) and non-specific esterase activity in these cells[1], and it has been postulated by Jarrett[2,3] that material elaborated by high-level melanocytes may influence the mode of keratinization of the epidermis. In a more detailed discussion by Jarrett and Spearman[4] it is suggested that the effect on keratinization might be achieved by augmenting the catabolic processes in the transitional zone of the epidermis, thus influencing the rate and degree of cytoplasmic dissolution occurring during keratinization and consequently altering the type of horny layer produced. This involves either the transfer of lysosomes from the high-level dendritic cells to the epidermal cells[4], a cytocrine[5] transfer similar to the distribution of melanin granules in the basal layer of the epidermis, or alternatively the inclusion of the dendritic cells in the lytic process. If this incorporation of supplementary hydrolases into granular layer cytolysis is to be regarded as the mechanism by which high-level melanocytes modify epidermal keratinization, then it is mandatory that these high-level cells should contain considerable concentrations of these enzymes.

While it is clear that not all hydrolytic enzymes are lysosomal[6–8] there is compelling evidence[9] that lysosomal hydrolases are the main agents in the catabolism of regressing tissues. Moreover, many of the enzymes considered to be lysosome-linked exhibit marked activity in the transitional zone[10–12].

Following the proposal of the lysosome concept by De Duve *et al.*[6] much work has devolved on the question of establishing adequate cytochemical criteria for the demonstration of lysosomes. At the present time this question rests primarily on the demonstration of acid phosphatase activity in a particulate distribution within the cell and the failure of the particles to stain following treatment of sections with the detergent 'Triton X 100'[13–17].

The Gomori technique for acid phosphatase[18] was applied to formal–calcium fixed human and mouse-tail skin. I was able to demonstrate an even distribution of lysosomal staining in the epidermis, which became indistinct just below the granular layer. No localized concentrations of particulate staining which could correspond to the high-level melanocytes were detected. I, therefore, did not obtain evidence by this method of the presence of high concentrations of lysosomes in epidermal ATPase positive dendritic cells.

It is, however, possible, by the use of a pararosaniline technique[19] using 'Naphthol *AS-BI*' phosphate as substrate, to demonstrate such concentrations of acid phosphatase in occasional cells in the epidermis which may correspond with the distribution of high-level dendritic cells. However, proof of this is lacking and the staining appears to be diffuse, unaffected by 'Triton', and confined to the cytoplasm immediately surrounding the nucleus.

Thus, although it cannot be excluded, the evidence available at present does not support a scheme based on the addition of lysosomal enzymes to the cytolytic process in the transitional zone. Nevertheless, this does not affect the basic hypothesis concerning the regulation of granular layer cytolysis, for which there is some evidence[4,20].

It is suggested that regulation of cytolysis may be brought about by mechanisms which either increase the fragility[21] of keratinocyte lysosomes or directly cause damage to the lysosomal membrane. This would allow a far greater scope for a regulatory system. The possible implications of such a scheme are at present under investigation.

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