Chapter 1

Skin under the microscope:
the organization, kinetics and
dimensions of skin

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A histological tyranny has subverted dermatologists and skin biologists and impeded a better understanding of how the skin behaves either at rest or after challenge in some way. The conventional histological section represents a tiny part of the entire integuement seen in two dimensions and at one point in time. This inability to view anything other than a fragment of skin 'frozen in time' is not the only problem with the conventional histological section. What is seen down the microscope has been chemically assaulted by fixation, dehydration, wax impregnation and staining as well as having been physically battered by the sectioning technique. It seems unlikely that anything but the grossest changes will be evident. To gain insight into interrelationships within skin and to obtain information concerning skin function we need to use a variety of other techniques. It is my intention in this chapter to encourage readers to appreciate and even surmount the constraints implicit in the histological approach. There are constraints of space and time.

SPATIAL CONSTRAINTS

A major limitation to an understanding of the nature of normal or diseased organs by examining their histological structure is that with few exceptions, organs are not homogenous structures, and it is unlikely that the sample obtained will accurately represent the whole part of interest. This problem is compounded in the histological study of disease as it is uncommon for a disease process to affect an organ uniformly, regardless of whether infection, trauma, neoplasia or metabolic inadequacy is the cause. The problem is particularly pronounced with skin, as it is an amalgam of closely intertwined tissues. To illustrate the difficulties that arise because of undue emphasis on the histological approach, I will cite examples based at both ends of the dimensional spectrum.

It has always been of interest to me that nuclear fragments are hardly ever seen in the granular cell layer of the epidermis, despite the fact that all keratinocytes destined to become corneocytes lose their nuclei. Fragments are occasionally seen by electron microscopy, but hardly ever by light microscopy. Presumably this odd apparent absence of an event that we know must take place is due both to the short-lived nature of the event and the difficulties of identifying nuclear fragments in a flattened granular cell that also
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contains basophilic granules of keratohyalin.

Apoptosis is the process of programmed intratissue cell death. It seems likely that this process plays some role in the population dynamics of the epidermis but because apoptotic bodies have been difficult to identify in the normal epidermis it has been difficult to believe that it is physiologically important. Perhaps this is analogous to the invisibility of nuclear fragments, and is the result of the relatively small size of apoptotic bodies and their relative infrequency.

Identification of the hyphal elements of dermatophyte fungus within the stratum corneum of a biopsy from a lesion of ringworm may be very difficult, even with special stains, because of the sparseness of the microorganism. It is universally recognized that there are more efficient methods of diagnosis of ringworm than by biopsy. Microscopic examination of scraped-off scale in KOH or of skin surface biopsy and PAS staining are much more likely to yield positive results (Figure 1.1) Similar considerations apply to the identification of sparsely distributed structures more deeply embedded within the skin, and we need techniques analogous to skin surface biopsy to detect them.

Figure 1.1 Skin surface biopsy from ringworm lesion stained with periodic acid Schiff reagent to show hyphal forms of ringworm. With this technique it is quite easy to see the infecting microorganisms within the stratum corneum.

We can improve our chances of detecting a rare event or a sparsely distributed structure in a number of ways. The simplest is to increase the number of samples examined by taking 'step sections' in which the tissue is examined by looking at sections mounted at regular intervals throughout the sample or by serially sectioning the