

The acidic milieu of the horny layer: new findings on the physiology and pathophysiology of skin pH.

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The acidic pH of the horny layer, measurable on the skin surface, has long been regarded as a result of exocrine secretion of the skin glands. The 'acid mantle' was thought to regulate the bacterial skin flora and to be sensitive primarily to skin cleansing procedures. In recent years, an increasing number of investigations have been published on the changes in, and constituents and functions of, the pH of the deeper layers of the stratum corneum, as well as on the influence of physiological and pathological factors. A central role for the acidic milieu as a regulating factor in stratum corneum homeostasis is now emerging. This has relevance to the integrity of the barrier function, from normal maturation of the stratum corneum lipids through to desquamation. Changes in the pH and the organic factors influencing it appear to play a role, not only in the pathogenesis, prevention and treatment of irritant contact dermatitis, but also of atopic dermatitis and ichthyosis and in wound healing. On the basis of these findings, a broader concept, exceeding the superficial 'acid mantle' theory, has been formulated.

Assessment of epidermal barrier function by photoacoustic spectrometry in relation to its importance in the pathogenesis of atopic dermatitis.

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With the use of the photoacoustic spectrometry system, in which a mixture of lipid- and water-soluble dyes is applied to the skin and then irradiated with light from a xenon lamp (425 nm and 550 nm), we measured photoacoustic signals of both dyes within the stratum corneum and their disappearance rate through the stratum corneum. The signal intensity was higher and dyes penetrated faster in clinically normal skin of patients with atopic dermatitis (AD) compared with healthy subjects, indicating an impairment of the in vivo cutaneous permeability barrier function against both lipophilic and hydrophilic chemicals. Furthermore, penetration rates of the hydrophilic dyes tended to increase in proportion to the severity of AD and significantly correlated with serum IgE levels in the severe AD group. Thus, abnormal barrier functions of clinically normal skin in AD may predispose inflammatory processes evoked by irritants and allergens, especially their water-soluble elements.

Electron microscopic observations of stratum corneum intercellular lipids in normal and atopic dogs.

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The barrier function of mammalian skin is maintained by intercellular stratum corneum lipids. In human patients with atopic dermatitis, an abnormal lipid barrier results in dry skin and increased transepidermal water loss. At this time, it is not known if a defective lipid barrier is present in atopic dogs. Normal and atopic canine skin were postfixed in ruthenium tetroxide and studied using transmission electron microscopy to determine structural differences within stratum corneum lipids. Intercellular lipid lamellae were graded on a semiquantitative scale. The deposition of stratum corneum lipid lamellae in atopic canine skin appeared markedly heterogeneous compared with that seen in normal canine skin. When present, the lamellae often exhibited an abnormal structure. The continuity and thickness of the intercellular lipid lamellae were significantly less in nonlesional atopic than in normal canine skin. These preliminary observations suggest that the epidermal lipid barrier is defective in atopic canine skin. Additional studies are needed to further characterize the biochemical defect and to possibly correct it with nutritional and/or pharmacologic intervention.

The activity of fatty acid synthase of epidermal keratinocytes is regulated in the lower stratum spinosum and the stratum basale by local inflammation rather than by circulating hormones.

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The epidermal keratinocytes produce and secrete lipids to maintain the water barrier of the epidermis. To clarify the regulation of epidermal lipid synthesis, we investigated the hormonal effect on the activity of fatty acid synthase (FAS) of the keratinocytes, and the expression of FAS in the human skin. In cultured keratinocytes, the FAS activity, assayed by measuring the oxidation of NADPH, was slightly increased by hydrocortisone or testosterone, but not influenced by thyroid hormone, estrogen, progesterone or insulin. In immunohistochemical study of normal human epidermis, FAS was expressed strongly in the stratum granulosum and moderately in the uppermost layer of the stratum spinosum (SS), suggesting that fatty acid synthesis may increase during normal epidermal differentiation. In inflammatory disorders, such as psoriasis, lichen planus, and atopic dermatitis, FAS was also expressed in the lower SS and the stratum basale (SB), resulting in strong staining in the whole layers of the epidermis. Remarkable increase

of FAS expression was only observed in the lower SS and the SB. Therefore, the activity of FAS in the epidermis may be regulated in the lower SS and the SB by local inflammation rather than by circulating hormones. In other components of the skin, FAS was strongly expressed not only in adipose tissue and sebaceous glands, which are known as active sites of lipid synthesis, but also in sweat glands, suggesting that the sweat glands can synthesize abundant fatty acids *de novo*.