Eicosanoid Levels in Human Skin

To the Editor:

It is with great interest I read the paper by Fogh et al [1]. These authors presented very fine analytical results on eicosanoids in keratome biopsy specimens of normal human epidermis and of different psoriatic lesions. However, the amounts of eicosanoid found in these specimens are called "levels" by the authors, and these "levels" are believed to represent in vivo concentrations. I shall like to argue that these "levels" instead may represent ex vivo biosynthetic capacity, and that the true in vivo concentrations in fact may be much lower. Prostaglandins, for instance, are only formed in very small amounts in normal human beings, e.g., the total diurnal production of E-type prostaglandins has been estimated to be 46–333 μg/24 h on the basis of measuring excretion of urinary metabolites [2]. Within the field of prostaglandin research, it has for a long time been argued that "tissue levels" of non-catabolized prostaglandins cannot be readily measured due to very rapid production of prostaglandins during tissue sampling [3,4]. This production is mainly caused by a rapid release of arachidonic acid, and even immediate freezing of the tissue samples in liquid nitrogen may not avoid the problem [3].

In order to strengthen my argument I shall make some calculations on the results of Fogh et al [1]. They claim that the level of PGE_2 in normal human epidermis is 27.1 ng/g wet weight [1]. This value is obtained in biopsies measuring 0.2 mm in thickness. The surface area of an average man is approximately 1.85 m^2, indicating that the amount of PGE_2 in the total epidermis of 0.2 mm thickness should be:

$$27.1\ ng/g \times 1.85 \times 10^4\ cm^2 \times 0.02\ cm \times 1\ g/cm^3 = 10\ \mu g\ PGE_2.$$

This may of course appear to be a low amount, but if 27.1 ng/g represents a steady-state level of PGE_2, one has to consider the half-life of PGE_2 in the epidermis in order to compare the epidermal "levels" with total body production. Prostaglandins are very rapidly catabolized in the tissues and intravenously injected PGE_2 has a half-life of less than 30 sec [2]. I do not know the half-life of PGE_2 in epidermis, but I find it difficult to believe that it should be more than around 10 min. If 10 min is the value, it means that the total epidermal production of PGE_2 would be 5 μg/10 min and thus 720 μg/24 h. If this figure is compared with the estimated total body production of PGE_2 of 46–333 μg/24 h [2], one can easily see that one of these figures must be wrong. Of course my value for the half-life is a guess and may be too small. Anyhow, I shall suggest that the major part of the amounts of PGE_2 (and the other eicosanoids) measured by Fogh et al [1] are artefactural, produced during the sampling of the tissue specimens. The shift between cyclooxygenase products and lipoxygenase products seen in psoriasis [1] may very likely involve infiltration of neutrophils into the involved epidermal areas as suggested by the authors.

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REPLY

In our study we focused on the potential significance of eicosanoids as mediators of the inflammatory processes of acute guttate and chronic plaque psoriasis. Prostaglandin E_2 (PGE_2), leukotriene B_4 (LTB_4), 12- and 15-hydroxy-eicosatetraenoic acid (HETE) were determined in keratomed strips of normal and involved psoriatic skin according to the methods published previously [1,2]. The concentrations of eicosanoids we found are in full accordance with the values determined by both Hammarström et al in the original paper [1] and later by Duell et al [2] by use of similar sampling techniques. We are well aware that the analysis of eicosanoids in tissues may lead to errors due to ex vivo catabolism/transformation due to rapid release of arachidonic acid. However, the assumptions and calculations made by Harald S. Hansen have to be questioned. The half-life of eicosanoids in the skin may as well be longer than assumed by Dr. Hansen and it may be different in inflamed skin. Furthermore, it is impossible to compare levels measured in tissues with an *estimated* daily production (based upon excretion of metabolites and information on recovery of metabolites from their precursors; Dr. Hansen's reference [2]). Therefore, we think that the concentrations of eicosanoids measured in the skin may reflect in vivo production and may not simply be an artifact produced during the sampling of the tissue.

After this study had been published, we have in detail investigated the capacity of lesional skin of psoriasis to transform arachidonic acid ex vivo [3]. In this study we found that at 4°C there was no change in eicosanoids even at incubation times up to 45 min. This observation suggests that in our hands there is no ex vivo transformation of eicosanoids.

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