LETTERS TO THE EDITOR

Are Endothelial Cells Stimulated by Autoantibodies in Scleroderma?

Sir,

In their article on endothelial cell (EC) renewal in the skin of patients affected by Progressive Systemic Sclerosis (PSS) (8), Kazandjian et al., while confirming previous findings of increased [^{3}H]thymidine labelling (5), suggested that such acceleration of EC turnover may "take place in order to replace damaged EC".

In fact, a number of observations, such as the disappearance of endothelia with fibrinoid necrosis, the absence of EC within the thickened intima and the duplication of basement membrane (7), the nuclear granular degeneration with swelling of mitochondria and large cytoplasmic vacuoles (6), a circulating cytotoxic EC-specific factor (7), indicate that in PSS, EC are destroyed.

However, Kazandjian et al. found no difference in the labelling index of EC between indurated and normal skin and no relation with the duration of the disease. Their findings therefore imply that the acceleration of the EC turnover is a primary event and not a phenomenon that follows an exaggerated cellular death.

In fact, Fleishmayer (4) regards it as such in his pathogenetic hypothesis of PSS: a specific antigen would invade EC, activating both cellular and humoral immunity. T cells would release lymphokines that may be responsible for stimulating collagen synthesis by fibroblasts and may play a role in the increase of [^{3}H]thymidine labelling of EC. Destruction of EC is a lymphocytic–cytotoxic effect or may be secondary to immunocomplexes and eventually lead to the plasmacellular synthesis of a variety of non-specific antibodies, including perhaps those directed to the cell membrane and the nucleus of fibroblasts, which have been recently shown in culture (2).

The factors that incite EC proliferation are still far from being known (5). A lymphocyte (T cell?) mediator inducing angiogenesis has been described during the Graft-vs-Host reaction (14), which has been considered as a potential model for scleroderma (10), but the increase in EC [^{3}H]thymidine labelling occurs even in the absence of infiltrates (5) and neo-vascularization has never been regarded as a sclerodermal feature.

We believe that other findings should be taken into account to explain EC proliferation.

ANA directed to EC or dermal arterioles has been found in scleroderma, including morphea and mixed connective tissue disease, and lacking only in the inactive stages (3, 12, 13). These antibodies appear to be carried further by circulating lymphoid cells from which they can be eluted in acid pH and proved to react in vitro even to normal EC (3). Moreover, they do not bind complement, which suggests that they may have stimulating properties rather than pernicious ones.

Autoantibodies that may stimulate cell proliferation and/or activity have been described in Graves's disease (1) and postulated in other conditions, in schizophrenia (9) for example.

ANA released in response to a specific antigen to EC may well represent the factor that promotes the intimal proliferation of cells concentrically arranged and narrowing the vascular lumen, which are described as the main feature of the widespread vascular pathology affecting most organs in PSS (11).

Local ischaemia and lymphocyte recruitment would ensue, the latter leading to further degenerative phenomena as in Fleishmayer's hypothesis.

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Exanthema fixum Due to Ultraviolet Radiation—Once More

Sir,

In a comment (1) to my short report Exanthema fixum Due to Ultraviolet Radiation (3) dr. Commens calls attention to a case of fixed eruption produced by UVA reported by Emmet 1975 (2). In his conclusion Emmett says: "Neither sharp margins nor localized hyperpigmentation, which are both common features of fixed drug eruption, were seen in this patient" (2). Our patient did show these clinical signs.

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