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LETTERS TO THE EDITOR

We are pleased to receive Letters to the Editor on appropriate subjects. These letters should be submitted in typewritten form, double-spaced, and are not to exceed 2½ pages. When appropriate, we will solicit comments from the original authors. All Letters to the Editor are subject to editing and possible abridgment.

Fd DEFICIENCY AND MOLECULAR SIZE OF SCLEROMYXEDEMA MONOCLONAL IMMUNOGLOBULINS

To the Editor:

Recently [1], Fd deficiency of the monoclonal IgG-lambda immunoglobulin has been observed in a patient with scleromyxedema. The molecular weight of this paraprotein was 110,000 daltons. This stimulated us to perform similar investigations in 2 cases. After purification of the monoclonal immunoglobulins (both IgG_1-lambda) by isoelectric focusing [2] these were subjected to immunoelectrophoresis with anti-Fd and anti-Fab antisera (Behringwerke, Marburg, F.R.G.) and analytical ultracentrifugation. No Fd deficiency could be detected by immunoelectrophoresis, the molecular weight of monomeric immunoglobulins calculated from ultracentrifugation was approximately 160,000 daltons. These results are in accordance with amino acid analysis of the monoclonal immunoglobulin of an early described case with papular mucinosis, which did not show substantial differences from normal IgG [3]. The described Fd deficiency appears to be exceptional and may not explain the obscure skin abnormalities.

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REPLY

We do not consider the Fd defect to be the cause of scleromyxedema although in the case reported by us demonstrated such a defect. As it is different from 2 cases reported by Kovary et al and further it possesses a different monoclonal immunoglobulin (their 2 cases demonstrate existence of monoclonal immunoglobulin at IgG_1 position while our case had monoclonal immunoglobulin at slow position), no comparison between them is possible but we would like to point out several problematic points in methods.

1. It seems that Fd can not always be separated by the purification of immunoglobulins through isoelectric focusing. It is more desirable to examine the reactions of anti-Fd, anti-Fab and anti-Fc against immunoglobulin after purification as well as the determining molecular weight using column chromatography.

2. In their 2 cases existence of stereostructural abnormality may be assumed even if normal IgG_1 and molecular weight are identical; thus it seems necessary to examine reactions with anti-Fd, anti-Fab and anti-Fc against monoclonal immunoglobulin treated with mercaptoethanol after purification.

3. Reactions with anti-Fd, anti-Fab and anti-Fc should also be examined after postpurified monoclonal immunoglobulin has been decomposed by papain.

Since we do not know the details of their methodology, it is difficult to comment further on the differences between these patients.

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SUBSTANCE P

To the Editor:

Drs. Hägermark, Hökfelt, and Pernow (J Invest Dermatol 71:233–235, 1978) describe the induction of flare and itch by intradermal injection of Substance P (SP) in human skin. While these authors state that SP evoked flare, wheal, and itching at the injection site, nowhere do they describe any systemic effects of such intradermal injections. We recently injected 0.05 ml of SP intradermally into the forearms of 7 normal volunteers who had provided informed consent in concentrations ranging from 6.2×10^{-7} M to 2×10^{-9} M and were surprised by the systemic reactions we observed in all subjects. At the lowest concentrations we employed, generalized flushing was noted within 5 min of injection, and this flushing persisted for about 10 min. At higher concentrations, this generalized flushing was accompanied by extraordinary injection of the conjunctivae and sclerae, tachycardia, diaphoresis, and was followed within 10 min by generalized vasoconstriction which lasted another 10–20 min. Two subjects experienced mild wheezing and tightness in their chests, as well as uncomfortable abdominal sensations. Unfortunately, because of the unexpected nature of these systemic reactions, monitoring of cardiopulmonary status was neglected. All subjects recovered fully within 30 min and none required special medical attention or cardiovascular drugs such as epinephrine. However, all who received the highest concentration of SP employed, described their reaction as being among the most unpleasant they had experienced. Considering the exceedingly small dosages employed intradermally, one must be impressed by the potency of SP as a vasodilating agent. In light of such potent effects, inadvertant intravenous introduction of such concentrations of SP could prove fatal. We, therefore, caution other investigators who have read Hägermark et al's article to exercise extreme caution in injecting human subjects with SP.

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REPLY

Drs. Bernstein and Hamill describe systemic reactions with flushing, tachycardia, and other symptoms of vasodilation after intradermal injection of Substance P (SP). We are as surprised as they to learn about this, since we in no case observed any sign whatsoever of systemic effects after the SP injections although we gave as much as 10^{-5} M. However, we did not inject more than 0.02 ml and always in the upper arms, while Drs. Bernstein and Hamill gave 0.05 ml and in the forearms. Similar reactions as those described by them have previously been found to occur in humans during intravenous infusion of SP [1]. During infusion of 65 to 366 ng/min (5×10^{-11}–2.8×10^{-10} moles/min) the subjects described feelings of warmth and sometimes experienced temporal pulsations. At the same time a bright red flush was clearly seen in the head and neck and in isolated spots on other parts of the body [1]. Within seconds after stopping the infusions the reactions disappeared, which contrasts in a remarkable way from the observation of Drs. Bernstein and Hamill that the flushing persisted for about 10 min. They used SP from Sigma, while the SP used in our studies was synthesized by Prof. K. Folkers, Austin, Texas.

It should be added that we always perform the initial experiments