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EFFECTS OF HISTAMINE RECEPTOR ANTAGONISTS ON HISTAMINE-INDUCED RESPONSES IN HUMAN SKIN

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The effects of intradermally administered histamine H_1- and H_2-receptor antagonists on the cutaneous responses—redness, weal, flare and itch—induced by intradermal injection of histamine were studied in man. Wheal and redness were studied after blockade of the axon reflex by local infiltration with lidocaine. All responses were significantly inhibited by the H_1-receptor antagonist mepyramine. The H_2-antagonists cimetidine and metiamide reduced flare and itch significantly but not to the same extent as mepyramine and not in a clearly dose-related manner. The extent of wheal and redness was not significantly reduced by cimetidine. No further reduction of flare, itch or wheal was obtained by adding metiamide or cimetidine to mepyramine. After blockade of the axon reflex with lidocaine the histamine-induced wheals turned white at the centre. This blanching was more prominent when histamine was injected, in combination with cimetidine. Substituting mepyramine for cimetidine resulted in small wheals with an intense red colour. It is concluded that, apart from being engaged in the direct vasodilatory response to histamine, H_2-receptors do not seem to be involved in the other cutaneous responses to histamine studied.

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DISCUSSION

Q: Did you work with Dimaprit or any other histamine H_2-receptor agonist? I ask because we have used it and observed not only redness but also wheal and flare.

A: We had wanted to complete our investigation by studying the effects of some of these new H_2-receptor agonists, but we did not obtain permission to use them in humans. However, we tried the old drug betazole (Histalog) which has been used for gastric secretion studies for many years. I don't know how specific this drug is as an H_2-agonist, but it is known to stimulate gastric secretion without producing other histamine effects. Using low doses of betazole in the intradermal injections we obtained a redness but not the typical triple response. We thought this confirmed our results with inhibitors.

Zachariae (Aarhus). Q: Could not the decrease in the redness be ascribed to the edema of the wheal?

A: Wheal and redness were studied after blocking the axon-mediated flare reaction by local anaesthesia. Although the decrease in the redness appearing after cimetidine might seem subtle, our experiments were made in a double-blind fashion and I am quite convinced of our results.

Q: Could you be certain that your patients were certainly not atopics? Secondly, could atopics have different reactivity in and outside skin lesions and compared with normals? A: We have not injected histamine in skin lesions. We know from the studies of Georg Rajka that the itch duration is longer in atopics than in controls. Our own experience indicates that although the itch duration is longer in atopics, they do not show an increased flare reaction. I cannot exclude that some of our subjects could be classified as atopics.

Dobson (Buffalo) Some years ago we injected histamine into uninvolved surfaces of patients with atopic dermatitis and noticed greater wheals on flexural sites than on extensors, whereas this was not seen in normals.

Q: Have you any data that some antihistaminics are better than others? Hydroxizine is very effective in some cases of urticaria.

A: I cannot state that one antihistamine is better than another, but in this connection I might mention that some years ago we compared the effects of a Swedish antihistaminic drug, *N*-hydroxy-ethylpromethazine (Aprobit), which is a quaternary phenothiazine, with the tertiary derivative promethazine. We found that oral administration of Aprobit did not inhibit the cutaneous histamine responses (Acta Allergologica *29:* 462, 1974). It turned out later, that previous experiments had been performed after i.v. injection in animals.