

below 10^{-4} M have little effect: with 10^{-3} M in plasma $63.0 \pm 4.8\%$ ($n = 8$) of the cells are recovered.

Granulocytes which have been adsorbed on glass wool can be recovered by washing with ice-cold sodium citrate buffer. Such cells have been resuspended in a physiological salt solution and maintained at 37°C in order to measure their potassium content and turnover (Baker, Trist & Weatherall, 1975). When mepacrine (10^{-5} M to 10^{-3} M) is added, K^{+} entry to the cells is reduced and the total cell potassium diminishes. The EC_{50} for inhibition of potassium entry by mepacrine in these experiments is about 0.6 mM.

When yeast or latex particles are added to a suspension of granulocytes, phagocytosis occurs promptly, as can be shown by electron micrographs. Potassium entry is sometimes increased in the first 10-15 minutes. After 30 min or longer, it is reduced significantly below control values (Dunham, Goldstein & Weissmann, 1974). In the presence of mepacrine (10^{-5} to 10^{-4} M) potassium entry is reduced more rapidly than in the absence

of particles. Pseudopodia are not formed on the surface of the granulocytes, and phagocytosis is reduced or absent.

The mechanism by which mepacrine alters the stickiness of cells and prevents uptake of particles and of potassium is not known. Chloroquine acts similarly but is less potent. Chlorpromazine has been shown to inhibit K^{+} entry to mononuclear cells and to prevent phagocytosis by monocytes (Ødegaard, 1975). In our experiments it is comparable in potency to mepacrine in inhibiting K^{+} entry to polymorphs.

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Inhibition by antigen and by histamine antagonists of the uptake of histamine by isolated human leucocytes

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Antigen is known to release histamine from sensitized mast cells and basophil leucocytes, but its possible effect on the reverse process, i.e. the incorporation of histamine, has not been investigated. The work to be described deals with this point, using [^{14}C]-ring-labelled histamine (dihydrochloride or phosphate), and the effect of various histamine antagonists, exemplified by mepyramine (an H_1 -receptor antagonist, Ash & Schild, 1966), and metiamide, an H_2 -receptor antagonist (Black, Duncan, Emmett, Hesselbo, Parsons & Wyllie, 1973).

Two types of human leucocyte preparations were used. 1. Whole leucocyte population (WLP) from patients with allergic airways disease (asthma and rhinitis) due to *Aspergillus fumigatus* or the house-dust mite *Dermatophagoides pteronyssinus*, and from which histamine could be released with these antigens, and with anti-IgE. 2. Isolated blood lymphocytes from tuberculin-sensitive patients.

Incubation of WLP with either the specific antigen or anti-IgE inhibited the uptake of labelled histamine (ULH), the inhibition being related to antigen concentration and to incubation time, reaching a maximum in 30 min (which is slower than histamine release), and persisting after removing the antigen and washing the cells. Calcium lack, which inhibited histamine release, abolished the inhibition of ULH.

Mepyramine and metiamide equally inhibited ULH in absence of antigen, but metiamide seemed to have a greater adding effect on the antigen-induced inhibition of ULH (Figure 1).

Tuberculin-sensitized lymphocytes previously incubated with tuberculin for four days showed an increase in ULH, which was blocked by metiamide, and to a smaller extent by mepyramine, suggesting the presence of H_2 receptors on lymphocytes. This finding, together with the inhibition of ULH by WLP, though requiring an extension of control studies with drugs other than antihistamines, provide further support for the presence of histamine receptors on human blood leucocytes participating in different allergic reactions, as suggested by a number of authors including Lichtenstein and his collaborators (Plaut, Lichtenstein & Henney, 1973; Lichtenstein & Gillespie, 1973, 1975).

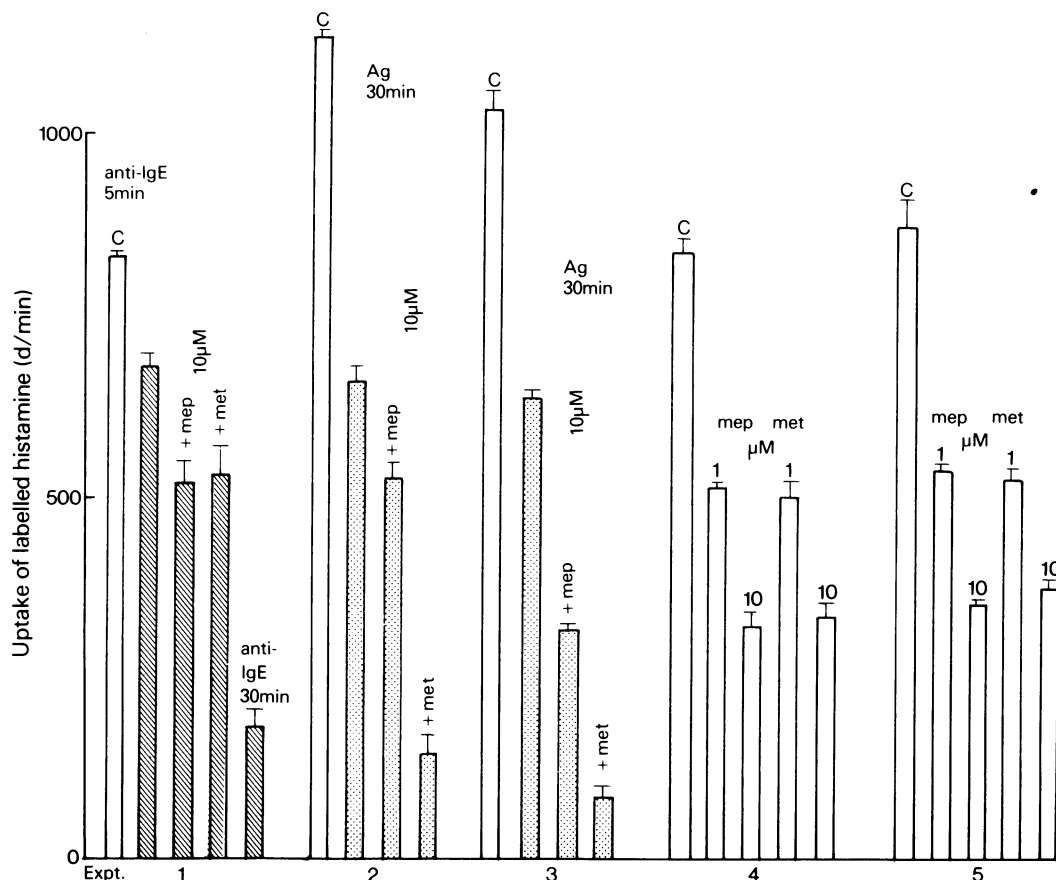


Figure 1 Inhibition of the uptake of labelled histamine by isolated human leucocytes, in five different experiments. Experiments 1, 2 and 3 show the inhibition by anti-IgE, and by the specific allergens, *Aspergillus fumigatus* and house-dust mite extracts, respectively in three different allergic patients, with and without the addition of the histamine antagonists, mepyramine (mep) metiamide (met), 5 min before the simultaneous addition of [14 C]-labelled histamine and the allergen. Experiments 4 and 5 show the effects of these two drugs in absence of the allergen (or anti-IgE) challenge (the drugs were added 5 min before the labelled histamine; the incubation with the latter was 30 min), in two of the three patients. C = control aliquots. The counts of labelled histamine shown represent a mean \pm s.e. mean of triplicate aliquots (10^7 cells each) for each treatment; all aliquots obtained from the same venous blood sample.

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