Table 1 Chemotactic activity of prostaglandin E_1 (1 μg/ml)

Fresh solution		*Solution after 12 h*	
Random migration	*Directed migration*	*Random migration*	*Directed migration*
62.0 ± 3.5	61.7 ± 5.2	49.8 ± 0.7	96.8 ± 15.2*
17.3 ± 2.3	17.4 ± 0.7	27.4 ± 1.0	47.0 ± 1.1*
29.9 ± 2.8	33.9 ± 7.1	65.9 ± 6.1	182.8 ± 28.6*
125.9 ± 12.0	119.5 ± 16.4	17.4 ± 1.9	30.5 ± 2.0*
73.9 ± 1.3	73.5 ± 1.2	34.4 ± 1.4	45.8 ± 5.8

Results given as number of cells per high power field, each figure being the mean ± s.d. of three chambers. For the measurement of random migration PGE_1 was placed in both compartments of the Boyden chambers; for directed migration (chemotaxis) it was present in the lower chamber only.
* $P < 0.05$

an increased emigration of leucocytes (Søndergaard & Wolf-Jürgensen, 1972; Arora, Lahiri & Sanyal, 1970).

We have therefore studied the effect of solutions of prostaglandin E_1 on the directed migration of rat polymorphonuclear leucocytes using the Boyden chamber technique described previously (Walker, Smith, Ford-Hutchinson & Billimoria, 1975). The results (Table 1) show that when a 1 μg/ml solution of Prostaglandin E_1 in a suitable aqueous medium, e.g. Medium 199 or Hanks, is tested immediately no chemotactic activity is detectable. When the aqueous solution has been allowed to stand either at $-20°$ or at room temperature for 24 h then chemotactic activity appears. It is concluded that the material responsible for this activity is not prostaglandin E_1 itself but some product formed by chemical changes in the aqueous media.

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References

ARORA, S., LAHIRI, P.K. & SANYAL, R.K. (1970). The role of prostaglandin E_1 in inflammatory process in the rat. *Int. Arch. Allergy*, **39**, 186-191.

HIGGS, G.A., McCALL, E. & YOULTEN, L.J.F. (1975). A chemotactic role for prostaglandins released from polymorphonuclear leucocytes during phagocytosis. *Br. J. Pharmac.*, **53**, 539-546.

KALEY, G. & WEINER, R. (1971). Prostaglandin E_1; a potential mediator of the inflammatory response. *Ann. N.Y. Acad. Sci.*, **180**, 338-350.

McCALL, E. & YOULTEN, L.J.F. (1973). Prostaglandin E_1 synthesis by phagocytosing rabbit polymorphonuclear leucocytes; its inhibition by indomethacin and its role in chemotaxis. *J. Physiol., Lond.*, **234**, 98-100P.

McCALL, E. & YOULTEN, L.J.F. (1974). The effect of indomethacin and depletion of complement on cell migration and prostaglandin levels in carrageenin-induced air bleb inflammation. *Br. J. Pharmac.*, **52**, 452P.

SØNDERGAARD, J. & WOLF-JÜRGENSEN, P. (1972). Cellular exudate of human cutaneous inflammation induced by prostaglandin E_1 and $F_{2\alpha}$ *Acta Derm., (Stockholm)*, **52**, 361-364.

TURNER, S.R., CAMPBELL, J.A. & LYNN, W.S. (1975). Polymorphonuclear leukocyte chemotaxis toward oxidized lipid components of cell membranes. *J. exp. Med.*, **141**, 1437-1441.

WALKER, J.R., SMITH, M.J.H., FORD-HUTCHINSON, A.W. & BILLIMORIA, F.J. (1975). Mode of action of an anti-inflammatory fraction from normal human plasma. *Nature, Lond.*, **254**, 444-446.

Inhibition of phagocytosis by mepacrine

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When human or horse plasma containing leucocytes is passed through a column of glass wool, most of the granulocytes, monocytes and platelets are trapped but most of the lymphocytes are not. The number of cells sticking can be measured by counting the cells in the plasma before and after it has passed through the column. In conditions which will be described, 43.0 ± 4.6% (mean ± s.e. mean, $n = 10$) of the leucocytes applied are recovered. When mepacrine hydrochloride is added to the plasma, fewer cells stick. Concentrations

below 10^{-4} M have little effect: with 10^{-3} M in plasma 63.0 ± 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.

References

BAKER, D.J., TRIST, D.G. & WEATHERALL, M. (1975). *J. Physiol., Lond.*, (Demonstration to Physiological Society November 1975).

DUNHAM, P.B., GOLDSTEIN, I.M. & WEISSMANN, G. (1974). *J. cell Biol.*, **63**, 215-226.

ØDEGAARD, A. (1975). *Acta path. microbiol. scand.* Sect. C., **83**, 59-73.

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).