cyclophosphamide suppressed the antibody production whereas oxisuran and prednisolone slightly enhanced the humoral response.

In conclusion, using two different antigens in the mouse we have produced a model that is capable of detecting drugs that modulate either limb of the immune system. This model may be of use in the discovery of new immunomodulator agents.

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Histamine H_1 antagonists and histamine release from human lung *in vitro*

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Lichtenstein & Gillespie (1975) reported that histamine H_1 antagonists inhibited antigenic histamine release from human leucocytes at low concentrations whereas at higher concentrations they caused histamine release in the absence of antigen. We have examined the activity of representatives of the five major classes of antihistamines (Douglas, 1970) in passively sensitized human lung *in vitro*.

Surgical specimens of human lung were chopped finely, divided into replicates of approximately 200 mg and sensitized for 18 h at room temperature and 1 h at 37°C in 2 ml of Tyrode's solution containing 0.2 ml of serum from an allergic donor. In experiments on the inhibition of antigen induced histamine release, antihistamines (10^{-10}–10^{-3}g/ml) were added 30 s before antigen (1/1000 dilution of anti-IgE – Miles Yeda) and the tissue incubated for 15 min. To assess histamine released by antihistamines alone, antigen was omitted. Histamine release was expressed as a percentage of the total histamine content of each lung sample.

Mepyramine, an ethylenediamine, inhibited antigen induced histamine release only at the highest concentrations used, 10^{-4} and 10^{-3} g/ml. It did not release histamine. Similarly, the alkylamine derivative chlorpheniramine, was a weak inhibitor of antigen induced histamine release and only caused release of small amounts of histamine at 10^{-4} and 10^{-3} g/ml. Diphenhydramine and cyclizine, ethanolamine and piperazine derivatives respectively, were approximately equiactive. Both inhibited antigen induced histamine release by approximately 50% at 10^{-6} g/ml and caused histamine release at higher concentrations. The most active antihistamine tested was the phenothiazine derivative, promethazine, which inhibited antigen induced histamine release by 70% at 1×10^{-6} g/ml. Above this concentration promethazine caused histamine release both in the presence and absence of antigen.

Because of the pharmacological relationships between phenothiazine antihistamines and central nervous depressant drugs, other compounds used primarily for their central effects were tested. The phenothiazine major tranquillizers, chlorpromazine and trimeprazine, and the tricyclic antidepressant, amitriptyline, were marginally more active than promethazine both in inhibiting antigen induced histamine release and releasing histamine. The monoamine oxidase inhibitor, phenelzine, was approximately equiactive with promethazine. The results obtained with these compounds correlate quite closely with similar results obtained using human leucocytes (Lichtenstein & Gillespie, 1975). It is concluded that the ability of these drugs to inhibit antigen induced histamine release is not due to their interaction with classical histamine H_1 receptors. An investigation of their mechanism of action is proceeding.

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