Anti-inflammatory activity was assessed using the carrageenin rat paw oedema test (Winter, Risley & Nuss, 1962); the substances under test being administered intraperitoneally (10 ml/kg dose vol.). Irritant activity was estimated by measuring the increase in paw volume following subplantar injection (0·1 ml/paw dose vol.) of the substances under test. The anti-inflammatory and irritant properties of sponge exudate were compared with those of a known irritant, carrageenin.

Examination of the dose-response curves revealed a good correlation between each type of activity for both carrageenin and sponge exudate over the range of concentrations investigated (0·0125–0·2%, carrageenin; 1·25–20%, sponge exudate). The correlation coefficients were 0·88 and 0·98 respectively. These results indicated that the two activities of sponge exudate were directly related.

Billingham (1968) showed that the anti-inflammatory potency of sponge exudate varied according to its time of collection. The irritant potency of exudate harvested 1, 2, 3, 4, 6 and 8 days following sponge implantation was evaluated and compared to the corresponding anti-inflammatory potency (10% concentration used for each determination). The two curves obtained did not significantly differ from parallelism, thus indicating a correlation.

It might be expected that there should be some correlation between the anti-inflammatory and irritant activities of counter-irritants with respect to time, and thus evaluation of these parameters was undertaken. It was found that maximum anti-inflammatory activity was almost always associated with maximum irritation in the case of both carrageenin (0·05%) and sponge exudate (10%). However, the anti-inflammatory activity tended to deviate as the irritation waned.

These results further support a counter-irritant mode of anti-inflammatory action for rat inflammatory exudate.

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The inhibition of allergic reactions by sympathomimetic amines and methylxanthines

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Sympathomimetic amines have been shown to be potent inhibitors of the antigen-induced histamine release from passively sensitized human lung (Assem & Schild, 1969). This inhibition was obtained with very low concentrations (5×10^{-12} to 5×10^{-9}M isoprenaline), and it was suggested that it might be due to the effect of the sympathomimetic compounds on β-adrenoceptors. The degree of inhibition of allergic reactions was influenced by several factors, for example, inhibition is greater with submaximal than with maximal antigen concentrations.

Further studies have shown that the sympathomimetic amines can inhibit the antigen-induced histamine release in both actively and passively sensitized guinea-pig lung; they seemed less effective in actively sensitized than in passively sensitized lung (Table 1).

TABLE 1. *Inhibition by isoprenaline of antigen-induced histamine release*

	Passively sensitized human lung			Passively sensitized guinea-pig lung			Actively sensitized guinea-pig lung		
Isoprenaline concentration (M)	No. of experiments	Histamine release (%)	% inhibition	No. of experiments	Histamine release (%)	% inhibition	No. of experiments	Histamine release (%)	% inhibition
	6	12–40		11	15–26		7	10–15	
10^{-9}			80–93			12–64			13–29
10^{-8}			85–100			80–95			45–65

Histamine release by antigen in terms of % tissue content.

Inhibition of histamine release expressed as $\frac{\text{uninhibited release} - \text{inhibited release}}{\text{uninhibited release} - \text{blank release}} \times 100$

The methylxanthines theophylline and caffeine were also found to be capable of inhibiting antigen-induced histamine release from passively sensitized human lung, and from both actively and passively sensitized guinea-pig lung, but they were less potent than the sympathomimetic amines and their dose response curves were irregular. Theophylline produced significant inhibition in a concentration range of 10^{-7} to 10^{-6}M.

The actions of sympathomimetic amines and methylxanthines may be related to their effect on the 3′,5′-cyclic adenosine monophosphate system.

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An amino-acid receptor in the guinea-pig ileum

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During an investigation of the quantity of histamine in different layers of human skin, aqueous extracts of an acetone powder of the stratum corneum were found to cause a histamine-like contraction of the guinea-pig ileum which, however, was not reduced by concentrations of mepyramine sufficient to abolish the response of the tissue to histamine (Lewis, Rosenthal & Trahan, 1959).

The products responsible for most of this activity were isolated by ion exchange chromatography and identified as the amino-acids L-serine and L-alanine. Usually these compounds contract the guinea-pig ileum at concentrations of 10–20 μg/ml, although a few preparations were almost completely insensitive. A large amount of L-serine is present in the stratum corneum (10 mg/g) and when assayed on the guinea-pig ileum this would be equivalent to a histamine concentration of 1 μg/g.