

incubated in the presence or absence of glucose in close time relation to the histamine release. In the anaerobic experiments antimycin A was used to block the oxidative phosphorylation. After preincubation with antimycin A, glucose and A23187, calcium was added to the cell suspension. There was a marked reduction in the ATP content during the same period, when histamine release occurred. In other anaerobic experiments oligomycin was added to the cells during

the preincubation period together with antimycin A, glucose and A23187. By incubation with calcium the ATP content of the mast cells was reduced during the histamine release. The observations are consistent with the view that energy requiring processes are involved in A23187 induced histamine release from mast cells, although part of ATP reduction in the aerobic experiments may be due to an uncoupling effect of Ca^{++} on the oxidative phosphorylation.

The effect of histamine antagonists on antigen-induced contractions of sensitized human bronchus *in vitro*

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The nature and mechanisms of the participation of histamine in bronchial asthma are unclear despite its long history. The object of this work was to identify the relative importance of histamine in allergic bronchospasm in a passively sensitized human bronchial muscle preparation.

Human bronchus, 2-3 mm in diameter, dissected free of macroscopically normal tissue removed for carcinoma, was passively sensitized in undiluted serum from patients with house dust mite allergy. Sensitized bronchi were cut into spiral strips and suspended in 10 ml organ baths under a load of 250 mg, perfused with Krebs at 37°C and gassed with 95% O₂ and 5% CO₂. Changes in muscle length were recorded electronically with an isotonic transducer and recorded on moving paper. When the muscle tone was steady responses to a maximum dose of acetylcholine chloride (200 µg/ml for 3 min) and to a series of doses of histamine acid phosphate (5, 20, 80 µg/ml for 5 min) were obtained for each preparation. This was repeated after half the tissues had been treated with the inhibitor being tested, the remainder being parallel controls. Finally, all the tissues were challenged with freeze-dried house dust mite antigen (*D. Pteronyssius* 10 µg/ml). These responses were expressed as a percentage of the maximum acetylcholine response (MAR) recorded prior to challenge to enable comparison between tissues. In two series of experiments the effect of the H₁ receptor antagonist mepyramine (25 µg/ml), and the H₂ receptor antagonist metiamide (10 µg/ml) were

studied on the dose response curve to histamine and response to antigen challenge. The effect of metiamide on a submaximal challenge (0.1 µg/ml *D. Pteronyssius* antigen) was also studied.

Dose related bronchial muscle contraction occurred in response to histamine but in the presence of mepyramine dose related relaxation occurred which was subsequently abolished by metiamide.

Antigen challenge caused contraction of the muscle in all cases. Mepyramine significantly reduced this response from 117.3 ± 6.2 in controls to $89.2 \pm 8.3\%$ MAR ($P < 0.005$, $n = 53$). Metiamide alone increased the response to histamine when compared with parallel controls, but it has no significant effect on the maximum antigen challenge response which was 124.0 ± 10.0 in controls and $114.6 \pm 10.3\%$ MAR in metiamide treated tissues ($P > 0.05$, $n = 21$). It did, however, cause a significant increase in the submaximal antigen challenge response from 81.2 ± 7.1 in controls to $116.4 \pm 21.1\%$ MAR ($P < 0.02$, $n = 42$). The challenge response in the presence of the two antagonists together, $109.3 \pm 5.1\%$ MAR, was not significantly different from the parallel control experiments, $107.9 \pm 6.2\%$ MAR ($P > 0.05$, $n = 38$).

The results of the experiments indicate that both H₁ and H₂ receptors occur in human bronchus and that both participate in allergic bronchospasm, H₁ receptors stimulating and H₂ receptors inhibiting muscle tone. Their effects, however, appear to cancel each other out, which suggests that if histamine plays any role in asthmatic bronchospasm, it is more likely to be via an indirect (DeKock, Nadel, Zwi, Colebatch & Olsen, 1966) rather than a direct action.

Reference

DeKOCK, M.A., NADEL, J.A., ZWI, S., COLEBATCH, H.J.H. & OLSEN, C.R. (1966). *J. appl. Physiol.*, **21**, 185-192.