Atypical adrenergic modulation of allergic histamine release from bovine leucocytes

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Histamine is released from sensitized mast cells and leucocytes of several species, following exposure to specific antigen. Modulation of this release by adrenoceptor stimulants has been studied principally in two systems: isolated human leucocytes (Bourne, Lichtenstein, Melmon, Henney, Weinstein & Shearer, 1974), and chopped lung of man, guinea pig and monkey (see Assem, 1974). In both systems, β-adrenoceptor stimulation elevates intracellular cyclic AMP concentrations and inhibits histamine release. Stimulation of α-adrenoceptors enhances histamine release from chopped lung, but is without effect on isolated human leucocytes. A study of the adrenergic modulation of allergic histamine release from bovine leucocytes revealed radical differences from the systems described above.

As previously described (Holroyde & Eyre, 1975), granulocytes were isolated (94% purity) from venous blood of 6 week old Jersey and Guernsey calves which had been sensitized to horse plasma. Aliquots of the granulocyte fraction (approximately 18×10^6 leukocytes) were incubated at 37°C for 30 min in Tris buffer (Holroyde & Eyre, 1975) together with sufficient horse plasma to release 40–60% of the total available histamine. Adrenoceptor agonists (10^{-6}–10^{-3}M) were added to the incubate 2 min before the horse plasma; adrenoceptor antagonists were added 2 min before the agonists. Histamine release was determined fluorometrically.

Isoprenaline ($n=6$) potentiated histamine release at 10^{-6} M and 10^{-5} M ($P<0.05$), but inhibited at higher concentrations ($P<0.01$). In the presence of 10^{-5} M propranolol, the potentiation was reversed to significant inhibition. In the presence of 10^{-5} M phentolamine, the potentiatory phase was significantly enhanced and the inhibitory phase somewhat reduced. Phenylephrine (10^{-6}–10^{-3} M) produced only inhibition of histamine release. These results indicate the presence of both α- and β-adrenoceptors on bovine granulocytes. Stimulation of α-adrenoceptors causes inhibition of histamine release, whereas β-stimulation causes potentiation. This is the exact opposite of the situation in all other species so far described.

Adrenaline, which inhibits the release of most mediators of allergy in all species examined, significantly potentiated the release of histamine in this study (10^{-8}–10^{-3} M, $n=5$).

It is clear that the bovine granulocyte is regulated by adrenoceptors in a manner radically different from any other comparable immunological system so far described.

References

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An investigation of histamine aerosol induced reflex bronchoconstriction in the anaesthetized dog

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The role of the vagus nerve in histamine-induced bronchoconstriction in anaesthetized dogs appears variable. Some workers claim that histamine induced bronchoconstriction is entirely reflex (Gold, Kessler & Yu, 1972; Nadel, 1974), while others have attributed a significant proportion of the bronchoconstriction to the direct action of histamine on bronchial smooth muscle (Krell, Chakrin & Wardell, in press). The purpose of this communication is to try to offer some explanation for these differing views.

Using anaesthetized beagle dogs we have measured changes in airways resistance (R_L) and dynamic lung compliance (Cdyn) after administration of histamine aerosol. The dogs were respired at constant pressure with a Bird Mk. VII ventilator. The reflex component of histamine induced bronchoconstriction was determined by bilateral vagal cooling.

A comparison was made between the effects on R_L and Cdyn of 4 breaths of 2 aerosols of different particle sizes in 11 dogs anaesthetized with pentobarbitone sodium (30 mg/kg i.v. followed by 0.1 mg kg^{-1} min^{-1}). Using a Bird micro-nebulizer, which produced particles of 0.5 μm mean diameter, relatively small increases in R_L were produced (e.g. 4 inhalations of an aerosol generated from a 0.5% w/v solution histamine produced increases in R_L of