Dopaminergic (co-mediator) modulation of release of histamine and SRS-A in the calf

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Mast cells of ruminants contain dopamine (Falk, Nystedt, Rosengren & Stenflo, 1964; Aviado & Sadavongvivad, 1970), which is released from sensitized tissue by antigen (Eyre, 1971a). Lung, especially pulmonary vasculature, is an important anaphylactic shock organ in the calf (Eyre, 1971b; Eyre, Lewis & Wells, 1973), whose pulmonary blood vessels possess dopamine receptors which may participate in anaphylaxis. A role for pulmonary dopamine in cattle has not been established.

During studies of adrenergic modulation of anaphylaxis, it seemed important to investigate possible modulatory effects of dopamine.

Calves were sensitized to horse plasma as previously described (Eyre *et al.*, 1973). Blood was collected and the granulocyte fraction separated (Holrodye & Eyre, 1975). Calves were killed with pentobarbitone and lungs removed and 'chopped' (Eyre, 1971a; Burka & Eyre, 1974). Aliquots of washed granulocytes or chopped lung were incubated at 37°C with antigen in buffered saline. Supernates were assayed for histamine and SRS-A (Eyre, 1971a; Burka & Eyre, 1974). Concentration ranges of dopamine, or dopamine plus antagonist were added to the mixture prior to antigen and incubation. Modulation of histamine or SRS-A release was expressed as a percentage of that released by antigen alone. Appropriate corrections were made for 'spontaneous' mediator release in the absence of antigen.

Dopamine (10^{-7} to 10^{-6} M) significantly potentiated antigen-induced release of histamine and SRS-A from lung ($P < 0.05$). Dopamine (10^{-6} to 10^{-3} M) did not alter histamine release from leucocytes. In the presence of spiperone (10^{-7} to 10^{-5} M), the potentiating effect of dopamine (10^{-6} M) on SRS-A release was abolished. By contrast, spiperone (10^{-7} to 10^{-5}M) did not affect the dopamine-enhanced release of histamine. Phentolamine or propranolol (10^{-8} to 10^{-5}M) did not antagonize the enhancing properties of dopamine.

Other work in this laboratory has shown unusual adrenergic modulation of SRS-A release from calf lung and of histamine release from leucocytes. In leucocytes, adrenergic modulation is biphasic: a potentiatory phase (β-adrenoceptor mediated) and an inhibitory phase (α-adrenoceptor mediated). Dopaminergic receptors may be absent in leucocytes and dopamine does not stimulate α- or β-adrenoceptors at concentrations tested.

In lung by contrast, our previous work has shown that both α- and β-adrenoceptor stimulation inhibited histamine and SRS-A release from calf lung.

Dopamine consistently *enhances* anaphylactic mediator release and when liberated with other mediators from local mast cells, dopamine may reinforce the release of the other mediators by positive feedback. Dopamine itself has very low activity on pulmonary smooth muscle in calves and therefore should not be described as a true mediator. Dopamine may be regarded as a 'co-mediator' of pulmonary anaphylaxis. As far as can be ascertained this situation has not been described previously.

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