HT in PRP, but when 5-HT was incubated in human PRP for 1 min or longer, the inhibitory effect of ADP was increased. The mechanism by which ADP inhibits 5-HT uptake is not fully understood, but since it occurs at submicromolar concentrations of ADP, it may be of considerable physiological significance.

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A further action of sodium cromoglycate

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At the last meeting of the British Pharmacological Society at Chelsea College we described a model of reflex bronchoconstriction in the anaesthetized dog (Richards & Jackson, 1976). The activity of sodium cromoglycate (DSCG) has now been investigated using this model.

Beagle dogs of either sex and weighing 9–12 kg were used in this study. The dogs were initially sedated with thiopentone sodium (5–10 mg/kg i.v.) and then anaesthetized with chloralose (80 mg/kg i.v.). The dogs were respired at constant pressure with a Bird Mk. VII ventilator and airways resistance (R) and dynamic lung compliance (Cdyn) measured continuously. Bronchoconstriction was produced by allowing the dogs to inhale 4 breaths of a histamine aerosol of 10 μm mean particle size through a tracheal cannula. The concentration of histamine solution from which the aerosol was generated was selected so that a change in R of 10–20 cm H_2O l^{-1} s^{-1} was produced. The concentrations used were 0.0625%–0.25%. The reflex component of the induced bronchoconstriction was determined by bilateral vagal cooling.

Histamine challenges were given every 30 min, and when 4 consistent reflex bronchoconstrictions had been produced the effects of 4 breaths of an aerosol of DSCG of 10 μm mean particle size, generated from either 1% or 2% solutions, on this bronchoconstriction were investigated. (The DSCG was given 10 min prior to the next histamine challenge.) The results of this study are shown in Figure 1.

After 1% DSCG there was some reduction in the

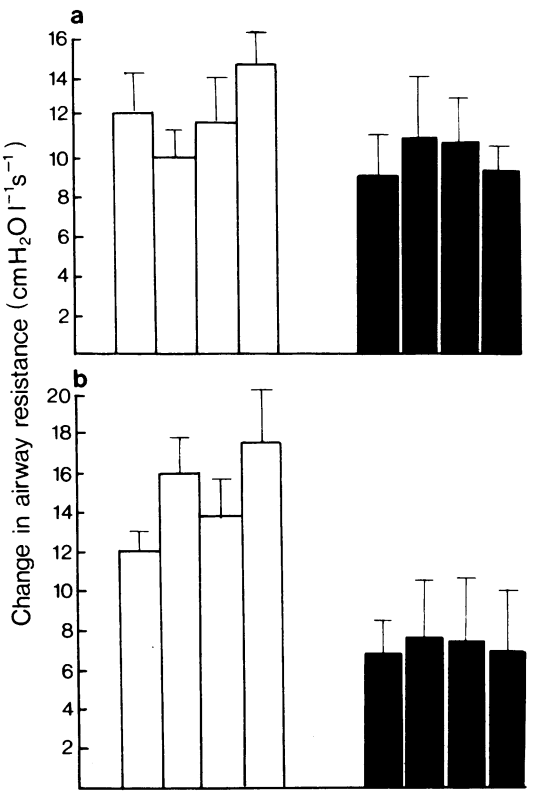

Figure 1 Changes in airway resistance produced by inhalation of 4 breaths of histamine aerosol of 10 μm mean particle size. The open histograms are control values and the closed histograms are the responses after inhalation of 4 breaths of an aerosol of DSCG of 10 μm mean particle size generated from a 1% solution (a) and a 2% solution (b). (Results are from 6 and 4 dogs respectively. Bars are s.e. mean.)

response to histamine, although this was not statistically significant (Fig. 1A). Two per cent DSCG produced a significant reduction ($P < 0.05$) in the induced bronchoconstriction which lasted for at least 2 h (Figure 1b). When DSCG (50 μg/kg) was given intravenously during a sustained reflex bronchoconstriction, complete reversal of the constriction was seen. The ability of the efferent autonomic nerves to produce a bronchoconstriction was checked throughout the experiment by direct electrical stimulation of the vagus nerves in the neck. DSCG, whether given by aerosol or intravenously did not inhibit the bronchoconstriction produced by direct electrical stimulation.

DSCG is not a bronchodilator or an antagonist of histamine or acetylcholine (Cox, Beach, Blair, Clarke, King, Lee, Loveday, Moss, Orr, Ritchie & Sheard, 1970) and it does not penetrate the central nervous system to any degree (personal communication from Dr B. Clarke, Dept. Metabolic Studies, Fisons Ltd.). We concluded, therefore, that DSCG reduced the bronchoconstriction to histamine aerosol, in our experiments, probably by desensitizing the lung irritant receptors which are thought to be responsible for the initiation of the reflex bronchoconstriction to histamine aerosol (Sellick & Widdicombe, 1971).

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The effects of corticosteroids on the responses of the anococcygeus and gastrocnemius muscles to nerve stimulation in the pithed rat

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Corticosteroids have been used to treat myasthenia gravis (Seybold & Drachman, 1974). The mechanism by which corticosteroids improve neuromuscular functioning in myasthenia is unknown but could be an immunosuppressive action on an auto-immune mechanism, which may cause this disease (Simpson, 1960). Since corticosteroids also have diverse effects on cardiac and smooth muscle (Thorp & Cobbin, 1967; Gibson & Pollock, 1975), this study considered the possibility that corticosteroids might have actions in striated muscle unconnected with an immune defect.

This study sought to determine whether corticosteroids could modify the responses of the rat gastrocnemius muscle to nerve stimulation. For comparison, the responses of a smooth muscle were also investigated. The smooth muscle chosen was the anococcygeus because its responses to agonists *in vitro* were enhanced by treatment of rats with corticosteroids (Gibson & Pollock, 1975). The responsiveness of these two muscles was investigated using the pithed rat preparation, in which a movable electrode was introduced into the spinal canal (Gillespie, MacLaren & Pollock, 1970). This technique permitted electrical stimulation of the spinal motor outflows to the gastrocnemius and anococcygeus in the same rat.

Male Wistar rats were treated with corticosterone (20 mg kg^{-1} day^{-1}, i.p. for 5 days) or prednisolone (20 mg kg^{-1} day^{-1}, i.p. for 4 days) or either saline or ethyl oleate as a control. The effects of reserpine (1 mg/kg, i.p. 20 h before pithing), which releases ACTH and therefore raises blood corticosteroid levels, were also investigated both in intact and in adrenalectomized rats. The rats were anaesthetized with trichloroethylene, respired artificially and pithed by the method of Gillespie, MacLaren & Pollock (1970). The spinal motor outflows were stimulated with supramaximal voltage using a Palmer stimulator. Responses of the muscles were recorded isometrically with Grass strain gauges and a Devices pen recorder. When the responses of the anococcygeus muscle were recorded, the rats received pancuronium bromide (2 mg/kg i.v.) to prevent interference by the contractions of the voluntary muscles.

Corticosterone and prednisolone increased the force of contraction of the single twitch and tetanic responses of the gastrocnemius muscle but the ratio of the tensions developed during these two responses was unchanged from control values. The corticosteroids impaired the ability of the gastrocnemius muscle to maintain a tetanus. Reserpine also increased the tension developed by the gastrocnemius muscle. This effect was absent in adrenalectomised rats. Corticosterone also increased the responses of the anococcygeus muscle to electrical stimulation. This

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