preparation and on the sciatic nerve tibialis anterior muscle preparation were antagonized slightly by glucocorticoids. Our recent work demonstrates that (+)-tubocurarine also effects the choline carrier system in rat diaphragm in a way that is comparable, but not the same as that of the choline structural analogue hemicholinium-3. These experiments indicate that glucocorticoids have direct presynaptic as well as postsynaptic effects on neuromuscular transmission. It is conceivable that part of their beneficial effects in myasthenia gravis may be due to these direct effects.

References

ARTS, W.F. & OOSTERHUIS, H.J. (1975). Effect of prednisolone on neuromuscular blocking in mice *in vivo*. *Neurology (Minneap.)* **25**, 1088–1090.

ITO, Y., MILEDI, R., MOLENAAR, P.C., NEWSOM DAVIS, J., POLAK, R. & VINCENT, A. (1978). Neuromuscular transmission in myasthenia gravis and the significance of anti-acetylcholine receptor antibodies. In: *The biochemistry of myasthenia gravis and muscular dystrophy*. Ed. G.G. Lunt and R.M. Marchbanks, 89–110. London, Academic Press.

Effect of histamine upon core and tail skin temperature of the conscious restrained rat

C.D. BEDFORD, J.A. BERTRAM & I.D. MORRIS
(introduced by B. COX)
Department of Pharmacology, Materia Medica and Therapeutics, University of Manchester, Manchester M13 9PT

The hypothermic effect of systemically administered histamine in the rat is well established (Lomax & Green, 1975). However, the mechanism by which this is achieved has not been fully elucidated. The tail of the rat has been shown to be of major importance in thermoregulation (Rand, Burton & Ing 1965), thus dilation of the tail blood vessels will promote heat loss while constriction will conserve heat. Histamine induced hypothermia has been suggested to be related to peripheral vasodilation (Lomax & Green 1975) and it was of interest to determine what role the tail vessels played in this process.

Core and tail skin temperature was measured in male Sprague–Dawley rats (270–350 g) restrained at an ambient temperature of 17 ± 1°C (Cox, Kerwin & Lee, 1978). Histamine acid phosphate (B.D.H.) was administered i.p. dissolved in 0.9% NaCl. Control rats received acidified saline (pH 4). The results obtained 30 min later are presented in the Table as the change in temperature (°C) relative to the average of three consecutive readings taken immediately before drug administration. Histamine produced a dose related fall in core temperature over the range 1.8–28.9 mg/kg. The hypothermic effect of histamine (36.2 mg/kg) was not as great as that produced by 28.9 mg/kg ($P < 0.05$) or 14.5 mg/kg. Histamine also produced a fall in tail temperature that was dose related over the range 1.8–7.2 mg/kg, larger doses produced no further falls in temperature.

The results demonstrate that the fall in core temperature following histamine is not mediated by peripheral vasodilation and suggest that other thermoregulatory processes should be investigated.

Table 1

Temperature change °C at 30 min
(mean ± s.e. mean n = 5–9)

Treatment	*Core*	*Tail*
Saline	+0.1 ± 0.1	−0.26 ± 0.1
Histamine (free base mg/kg)		
1.8	−0.24 ± 0.15*	−0.77 ± 0.31
3.6	−0.28 ± 0.16	−1.25 ± 0.27*
7.2	−0.59 ± 0.09*	−1.60 ± 0.38*
14.5	−0.83 ± 0.20*	−1.50 ± 0.24*
28.9	−1.10 ± 0.12*	−1.49 ± 0.30*
36.2	−0.58 ± 0.12*	−1.48 ± 0.28*

* Significance of difference v saline ($P < 0.05$).
Mann Whitney 'U' test.

References

COX, B., KERWIN, R. & LEE, T.F. (1978). Dopamine receptors in the central thermoregulatory pathways of the rat. *J. Physiol. Lond.*, **282**, 471–483.

LOMAX, P. & GREEN, M.D. (1975). Histamine and temperature regulation in temperature regulation and drug action (eds. Lomax, P., Schönbaum, E. & Jacob, J.) Basel: Karger.

RAND, R.P., BURTON, A.C. & ING, T. (1965). The tail of the rat in temperature regulation and acclimatization. *Can. J. Physiol. Pharmac.*, **43**, 257–267.

Inhibition of effects of isoprenaline and adrenaline by *Haemophilus influenzae* vaccination

F.P. NIJKAMP, J.A.M. RAAIJMAKERS, A.J.M. SCHREURS & G.K. TERPSTRA

Rudolph Magnus Institute for Pharmacology, Utrecht, and the Department of Lung Diseases, Academic Hospital, Utrecht, The Netherlands

Szentivanyi (1968) postulated that the pathogenesis of atopy is due to malfunctioning of the β-adrenoceptors resulting in an imbalance of α and β-adrenoceptors. This postulate was based on experiments with *Bordetella pertussis*. However, for *B. pertussis* no causative relation with chronic asthmatic bronchitis has been shown. On the other hand *Haemophilus influenzae* can be isolated from the upper respiratory airways in normal individuals and also from the deeper airways in asthmatic patients (see Hirschmann & Everett, 1979). Therefore we studied the influence of *H. influenzae* on functioning of the β-adrenoceptors in vaccinated animals (500×10^6 killed cells 100 g body weight i.p. administered 4 days prior to the experiments).

Lungs from guinea-pigs sensitized to ovalbumin were isolated and perfused with Krebs solution at 10 ml/min and shocked by ovalbumin injection into the pulmonary artery. Cascade superfusion apparatus was prepared and release of thromboxane A_2 and prostaglandins were measured (Piper & Vane, 1969). Minimal ovalbumin doses needed to detect release of prostaglandins and thromboxanes were determined in *H. influenzae* vaccinated and control lungs.

The vaccinated animals responded to lower doses of ovalbumin (threshold doses 0.4 ± 0.1 vs 1.9 ± 0.5 µg ovalbumin, $P < 0.01$, $n = 8$–11). Correcting for differences in sensitivity, in lungs and tissues, by means of internal and external standards (arachidonic acid and PGE_2), did not alter the significance. A significant inhibition of prostaglandin release was demonstrated in control animals during 6×10^{-9} M isoprenaline into the pulmonary artery. However in *H. influenzae* vaccinated animals no significant inhibition could be achieved with isoprenaline (2×10^{-9} and 6×10^{-9} M).

To obtain equal contractions of the bioassay tissues before and during isoprenaline infusion, the dose of ovalbumin had to be increased with the following factors: 2×10^{-9} M isoprenaline 2.7 ± 0.6 (*H. influenzae*) vs. 5.8 ± 2.7 (controls, n.s.; 6×10^{-9} M isoprenaline 2.7 ± 0.3 vs. 8.7 ± 2.8, $P < 0.05$. Prostaglandin and thromboxane A_2 release induced by these doses of ovalbumin were reproducible. Release of prostaglandins by histamine and bradykinin and conversion of arachidonic acid in prostaglandins did not differ in vaccinated and control animals.

In a second series of experiments we investigated the effect of adrenaline on the eosinophilic blood count which is believed to be mediated through β-adrenoceptors. Adrenaline was administered to rats (2 mg/kg body weight s.c.) and mice (0.3 mg/kg body weight i.p.) and the eosinophilic response was investigated 30 min later. This effect was inhibited in vaccinated animals (50% increase in *H. influenzae* and 130% increase in controls, $P < 0.02$). Furthermore the response to several drugs in different groups of mice was tested. LD_{50} values to isoprenaline in *H. influenzae* vaccinated mice were increased (26.4 mg and 172 mg resp., $P < 0.05$). In contrast LD_{50} values to noradrenaline were decreased (10.7 mg and 3.2 mg resp., $P < 0.05$).

In different experimental set ups and in different species the effects on isoprenaline and adrenaline were attenuated. This suggests a decreased functioning of β-adrenoceptors in *H. influenzae* vaccinated animals.

This research was supported by a grant from the Dutch Asthma Foundation (NAF-300).

References

HIRSCHMANN, J.V. & EVERETT, E.D. (1979). Haemophilus influenzae infections in adults: Report of nine cases and a review of the literature. *Medicine*, **58**, 80–95.

PIPER, P.J. & VANE, J.R. (1969). Release of additional factors in anaphylaxis and its antagonism by anti-inflammatory drugs. *Nature, Lond.*, **223**, 29–35.

SZENTIVANYI, A. (1968). The beta adrenergic theory of the atopic abnormality in bronchial asthma. *J. Allergy*, **42**, 203–232.