Experiments have also been carried out with caffeine which causes augmentation of the twitch but does not antagonise the anticholinesterase effects and also with the local anaesthetic lignocaine which reverses and prevents the anticholinesterase effects but produces only slight twitch augmentation . It is suggested, therefore, that the acetylcholine antagonists being studied possess both caffeine-like and local anaesthetic activity.

REFERENCES

BRIMBLECOMBE, R. W. & EVERETT, S. D. (1969a). Actions of a cholinergic antagonist on mammalian skeletal muscle. *Br. J. Pharmac.*, **36**, 172–173P.

BRIMBLECOMBE, R. W. & EVERETT, S. D. (1969b). Interactions between sarin and the cholinergic antagonist PMCG in fast and slow skeletal muscle of the cat. *J. Physiol., Lond.*, **203**, 19–20P.

BRIMBLECOMBE, R. W. & EVERETT, S. D. (1970a). Actions of some cholineigic antagonists on fast-twitch and slow-twitch skeletal muscle of the cat. *Br. J. Pharmac.*, **40**, 45–56.

BRIMBLECOMBE, R. W. & EVERETT, S. D. (1970b). Actions of sarin on fast-twitch and slow-twitch skeletal muscles of the cat and protective action by anticholinergic drugs. *Br. J. Pharmac.*, **40**, 57–67.

BULLER, A. J. & LEWIS, D. M. (1965a). The rate of tension development in isometric tetanic contractions of mammalian fast and slow skeletal muscle. *J. Physiol., Lond.*, **176**, 337–354.

BULLER, A. J. & LEWIS, D. M. (1965b). Further observations on the differentiation of skeletal muscles in the kitten hind limb. *J. Physiol., Lond.*, **176**, 355–370.

Antagonism by burimamide of inhibitions induced by histamine in plexus-containing longitudinal muscle preparations from guinea-pig ileum

N. AMBACHE, S. W. KILLICK* and M. ABOO ZAR

Medical Research Council, Department of Physiology, Royal College of Surgeons of England, Lincoln's Inn Fields, London, WC2A 3PN

In plexus-containing longitudinal muscle preparations, in which histamine-contraction has been largely eliminated by H_1-receptor blockade with mepyramine, histamine produces a second effect, namely a dose-related inhibition of the neurogenic atropine-resistant tetanic spasms elicited by field stimulation (Ambache & Zar, 1970). Since Black, Duncan, Durant, Ganellin & Parson (1972) introduced 4-methyl histamine and burimamide [N-methyl-N'-(4-(4(5)-imidazolyl)-butyl)thiourea] as selective agonist and antagonist, respectively, for H_2-receptors, these compounds have now been tested.

Atropine, 10^{-7} g/ml, and mepyramine, $1–10\times10^{-7}$ g/ml, were present throughout. Tetanic spasms were elicited every 1 min by trains of ten 0·2 ms pulses (50 Hz).

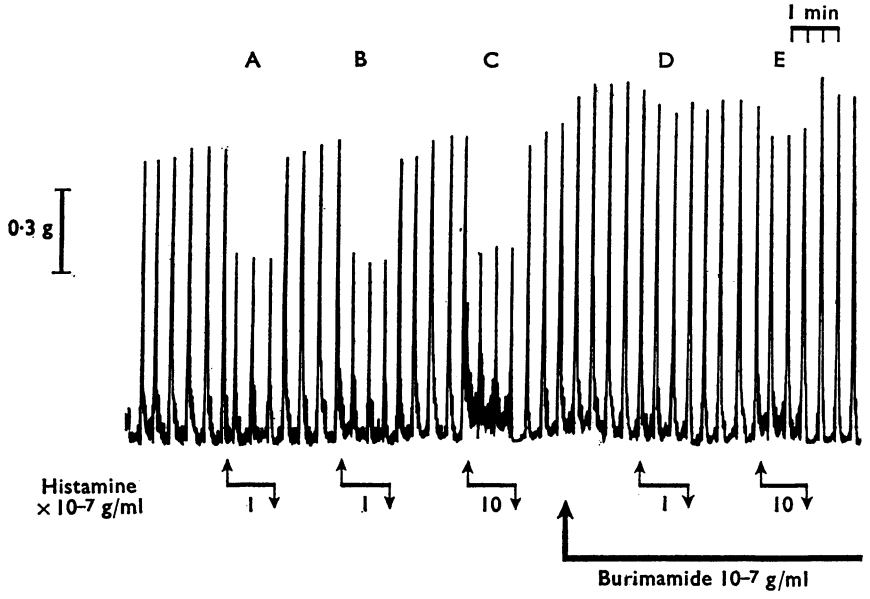

FIG. 1. Antagonism of histamine induced inhibitions by burimamide.

Fig. 1 illustrates the antagonism of histamine-inhibition by burimamide. Repeatable maximal inhibitions of tetanic spasms were obtained at A and B with histamine, 10^{-7} g/ml, administered for 3 min; at C, the degree of inhibition was no greater with 10^{-6} g/ml, but this comparatively large dose of histamine partially overcame the mepyramine block and produced a slight contraction concurrently with the inhibition. After the introduction of burimamide, 10^{-7} g/ml, the inhibitory effect of histamine, 10^{-7} g/ml, was totally blocked at D (within 4 min); and that of histamine, 10^{-6} g/ml, was greatly reduced, at E. The burimamide effect was reversible but persisted for at least 1 h after its removal.

The inhibitory effect of histamine could not be obtained with 4-methyl histamine, $1–500 \times 10^{-7}$ g/ml, suggesting that the receptors mediating histamine-inhibition resemble H_2-receptors in their susceptibility to burimamide blockade but differ in being insensitive to 4-methyl histamine.

The atropine-resistant tetanic spasms are also known to be inhibited by 5-hydroxytryptamine, even in the presence of methysergide (Ambache, Verney & Zar, 1970); unlike histamine-inhibitions, the inhibitions induced by 5-HT were unaffected by burimamide.

We thank Dr. J. W. Black, Smith, Kline & French Ltd., for burimamide and 4-methyl histamine.

REFERENCES

AMBACHE, N., VERNEY, J. & ZAR, M. ABOO (1970). Evidence for the release of two atropine-resistant spasmogens from Auerbach's plexus. *J. Physiol., Lond.*, **207**, 761–782.

AMBACHE, N. & ZAR, M. ABOO (1970). An inhibitory action of histamine on the guinea-pig ileum. *Br J. Pharmac.*, **38**, 229–240.

BLACK, J. W., DUNCAN, W. A. M., DURANT, C. J., GANELLIN, C. R. & PARSONS, E. M. (1972). Definition and antagonism of histamine H_2-receptors. *Nature, Lond.*, **236**, 385–390.

The cardiovascular actions of prostaglandins C_1 and C_2 in the cat (T)

R. L. JONES*, KATHLEEN A. KANE and A. UNGAR

Department of Pharmacology, University of Edinburgh, 1 George Square, Edinburgh EH8 9JZ

Vascular histamine receptors in the rabbit (T)

J. W. BLACK, D. A. A. OWEN and M. E. PARSONS*

The Research Institute, Smith Kline and French Laboratories Ltd., Welwyn Garden City, Hertfordshire

DEMONSTRATIONS

A 'working' model of the haemoglobin molecule as a receptor for 2,3-diphosphoglycerate

C. R. BEDELL, P. J. GOODFORD, F. E. NORRINGTON and S. WILKINSON

The Wellcome Foundation, Beckenham, Kent

Haemoglobin combines reversibly with oxygen:

$$Hb + 4O_2 \rightleftharpoons Hb(O_2)_4$$

and exhibits a characteristic sigmoidal dissociation curve (A, Fig. 1), which differs from the monotonic curve predicted by simple chemical theory, B (Douglas, Haldane & Haldane, 1912). The shape of curve A allows haemoglobin, fully saturated with oxygen, to deliver some 25% of its oxygen to a tissue at a partial pressure of 40 mg/Hg. Moreover, there is still a large reserve of oxygen bound to haemoglobin, which can be released if the partial pressure falls lower.