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.