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.

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

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Vascular histamine receptors in the rabbit (T)

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DEMONSTRATIONS

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

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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.

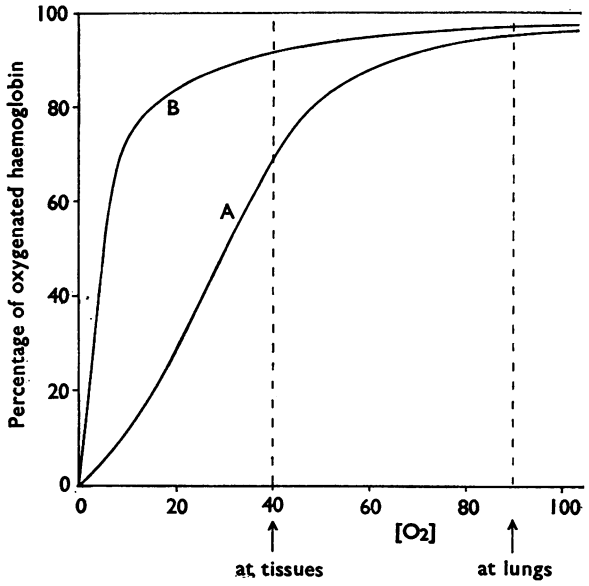

FIG. 1. Abscissa, partial pressure of oxygen in mm Hg. Ordinate, percentage of protein in the oxy form. Haemoglobin dissociation in the presence of 2,3-diphosphoglycerate is described by the sigmoid A (Benesch & Benesch, 1970), and shows cooperation between the subunits. Curve B is a rectangular hyperbola theoretically predicted by Michaelis–Menton kinetics.

The shape of curve A is due to the fact that the conformation of the four protein subunits in haemoglobin changes slightly on taking up and releasing oxygen (Perutz, 1968). The position of the curve is also regulated by the naturally occurring small molecule 2,3-diphosphoglycerate (DPG) which can bind to a specific site on the haemoglobin when it is in the deoxy conformation, and hence tends to stabilize that conformation (Benesch & Benesch, 1970). The DPG binding site consists of amino and imidazole groups arranged to complement the shape and charge of the DPG molecule when the protein is in the deoxy form (Arnone, 1972). However, in oxyhaemoglobin the shape of the site changes so that it can no longer admit DPG.

The combination of DPG with haemoglobin may be analogous to a drug-receptor interaction, and models have been built to study this interaction at the molecular level. The large model can be positioned in either the oxy or deoxy conformation, but this quaternary change is accompanied by alterations of tertiary structure within the protein, which cannot be shown. Two smaller non-working models have therefore been built to display the DPG interaction site more accurately in its oxy and deoxy forms.

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Some persistent effects of the pre- and neonatal administration of psychotropic drugs on noradrenaline metabolism in discrete areas of rat brain

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Werboff & Gottlieb (1963) have described behavioural abnormalities in the offspring of rats treated with psychotropic drugs during pregnancy. In view of the probable asso-