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Antagonistic effects of two anaesthetics on hypotonic haemolysis

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Many general and local anaesthetics are known to protect erythrocytes against hypotonic lysis, often at concentrations similar to those causing reversible nerve block. For this reason the erythrocyte has in the past been regarded as a good model for the study of the mechanism by which anaesthetics produce their effect. This striking correspondence is consistent with, although it does not prove, the theory that the primary action of anaesthetics is to increase the fluidity of membrane lipids (Seeman, 1972; Strichartz, 1976).

Seeman, in an earlier paper (Seeman, 1966) presented dose-response curves showing the effect on haemolysis of a number of local anaesthetics, including lignocaine. Rather high lignocaine concentrations (above 10^{-2}M) were needed to reduce haemolysis, and it was remarked that the protection in this case might be due to the increased tonicity of the test medium. That this may indeed be the explanation is suggested by a more recent finding (Sheetz & Singer, 1974) that a steady *increase* in haemolysis occurs between 10^{-3} and 10^{-2}M lignocaine. This steady increase is to be distinguished from the steep rise to 100% haemolysis observed at high, 'lytic' concentrations of many anaesthetics (Seeman, 1972).

The experiments reported here were performed as described by Seeman (1966) except that Tris buffer was used instead of phosphate buffer. They were designed to determine whether the haemolysis promoting effects of lignocaine, if confirmed, occurred at concentrations causing local anaesthesia, and if they could be antagonised by an anaesthetic known to decrease haemolysis at nerve-blocking concentrations. Figure 1 shows that lignocaine increasingly promotes haemolysis over the range 1–10 mM. The figures quoted for local anaesthetic concentrations of lignocaine (Strichartz, 1976) fall towards the bottom of this range, or below it, but they did not include figures for total nerve block.

Benzyl alcohol is known to decrease hypotonic haemolysis at local anaesthetic concentrations, and increase it only at much higher concentrations producing lysis even under isotonic conditions. The protective effect is explained by the expansion and fluidization of the membrane (Seeman, 1972). Figure 1 demonstrates that benzyl alcohol readily antagonises the effect of lignocaine; the effect of lignocaine (5 mM) on haemolysis can be balanced by benzyl alcohol (20 mM).

These results suggest that anaesthetics, at concentrations similar to those causing nerve block, do not necessarily protect erythrocytes but may, on the contrary, have antagonistic effects on haemolysis in hypotonic solution.

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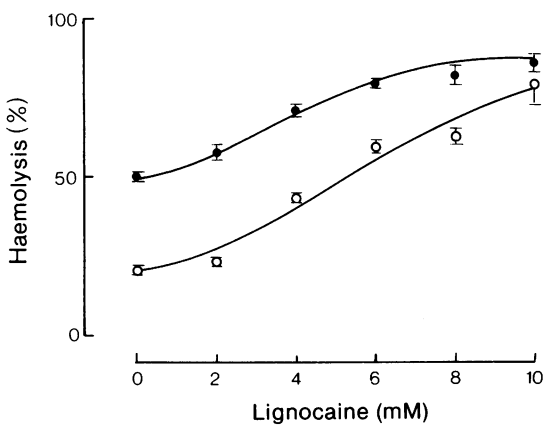

Figure 1 The effects of lignocaine on hypotonic haemolysis in the absence (●) and presence (○) of 20 mM benzyl alcohol.

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