inhibition of cholinesterase with di-isopropylfluorophosphonate (dyflos, DFP, 20 μg/ml for 1 hr) also inhibited the potentiation. It is interesting to note that physostigmine and dyflos have by far the highest lipid solubility and this may be related to their ability to inhibit this potentiation.

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The influence of hypoxia upon toxicity of a nucleotoxic agent, mustine hydrochloride

SIR,—Although many radioprotective substances also provide protection against nucleotoxic agents (Scarborough & Thomas, 1962), this is not so for 5-hydroxytryptamine (5-HT) which is a powerful chemical radioprotector (Uroić, Rabadjija & Supek, 1964) but enhances the toxicity of a typical representative of radiomimetic poisons—mustine hydrochloride (nitrogen mustard).

Tissue hypoxia provides protection against ionizing radiation (Brues & Patt, 1953). According to van den Brenk & Haas (1961) 5-HT exerts its radioprotective effect in terms of pharmacologically-induced hypoxia. If this is true then hypoxia alone should not protect against mustine hydrochloride. To test this assumption we have examined the influence of acute hypoxia upon the chronic toxicity of mustine hydrochloride in rats. Hypoxia was produced by administering 55 mg/kg of hydroxylamine hydrochloride intraperitoneally. This dose does not change the toxicity of mustine, but exerts a strong methaemoglobinaemia (40–50%) with consequent anaemic hypoxia.

Two groups of 34 albino rats were injected intravenously with mustine hydrochloride (0·8 mg/kg). The first group received saline and the second group hydroxylamine hydrochloride (55 mg/kg) intraperitoneally 30 min before mustine. The survival of rats was observed every 12 hr during 30 days. The mortality (%) and the mean survival time (days $\pm$s.e.m.) were: 64·7 and 13·7 $\pm$ 2·09 for the saline group and 30·3 and 22·4 $\pm$ 2·04 for the group treated with hydroxylamine hydrochloride.

A decrease in mortality rate (χ^2-test; $P < 0.01$) and increase in mean survival itme (t-test; $P < 0.01$) was observed. It is evident that hypoxia in our experimental conditions significantly reduces the toxicity of mustine hydrochloride.

The present finding does not seem to be consistent with the hypothesis that 5-HT exerts its radioprotective action by means of cellular hypoxia.

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