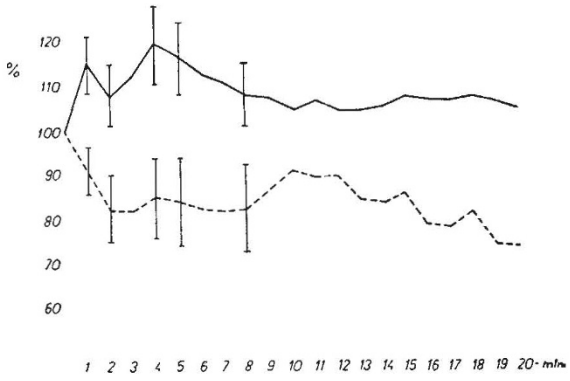

Fig. 1. Comparison of the changes in oxygen consumption of control (– – – –) and irradiated (——) rats. Standard error level is given by vertical lines

minute (50 r.), at the fourth minute it reaches the maximum (200 r.) and in the tenth minute it approaches the values before irradiation, but is still higher than in control animals.

The difference in oxygen consumption in twenty irradiated and twenty control animals during the period from the first to the eighth minute of irradiation is statistically significant ($P > 0{\cdot}01$).

We have found in the literature two reports on changes in respiratory metabolism during irradiation. In both cases the oxygen consumption was increased at higher doses of radiation than those we have used. In the first case, the rate of oxygen consumption was raised after a dose of 1,000 r. in monkeys. In the second case, oxygen consumption of rats and mice was increased during irradiation with a dose-rate of 100 r./min. Our results are in accord with these; significant changes were found after the relatively low dose of 50 r.

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Prophylactic Effects of Amine Oxides in Radiation Injury in Mice

In 1957, Haley *et al.*[1] found that quinoxaline-1,4-di-N-oxide reduced X-radiation mortality in mice by 50 per cent. Two mechanisms were involved, reduction of bacteræmia[1] and interaction with X-ray-produced oxidizing radicals[2]. Comparisons have been made of other N-oxides (Table 1) using groups of 20 *CF*-1 mice and the same radiation conditions as before[1]. The 250 mgm./kgm. oral dose of drugs was given 24 hr. prior to irradiation with 550 r. The two quinoxaline derivatives significantly increased the ST_{50} day but had less effect on total survival than quinoxaline-1,4-di-N-oxide. Erythromycin N-oxide significantly reduced the ST_{50} day and total survival while its anhydro derivative was equivalent to quinoxaline-1,4-di-N-oxide as a radiation prophylactic. All the above compounds are readily absorbed,

Table 1. Orally Administered Amine Oxides and Survival after X-Irradiation

Treatment	ST_{50}* and range Days	Slope and range	Total mortality Per cent	Day
Saline control	9·4 (8·4–10·5)	1·29 (1·19–1·40)	100	14
2 : 3-Dimethyl-quinoxaline-1,4-di-N-oxide	12·4 (10·1–15·2)	1·56 (1·32–1·84)	85	30
6-Chloro-2 : 3-dimethyl quinoxaline-1,4-di-N-oxide	13·4 (10·9–16·6)	1·60 (1·35–1·90)	80	30
Saline control	12·3 (10·6–14·3)	1·41 (1·26–1·59)	90	30
Erythromycin N-oxide	10·0 (9·0–11·2)	1·29 (1·19–1·40)	100	18
Anhydroerythromycin N-oxide	—	—	45	30

* ST_{50}, day upon which 50 per cent of animals are expected to be still alive. Confidence limits are calculated at $P = 0{\cdot}05$ (ref. 3). All drugs 250 mgm./kgm. orally 24 hr. pre-irradiation.

excreted slowly in the urine and exert antibiotic effects so the radiation bacteræmia could be reduced. On the other hand not all of them can interact with equal facility with the radiation-produced oxidizing radicals. Examination of the chemical structures involved indicated that an amine oxide either in an unsaturated ring, for example, quinoxaline or within one carbon atom of a double bond, for example, anhydroerythromycin is necessary if oxidizing radicals are to be prevented from exerting their deleterious effects. In the dimethyl-substituted quinoxaline compounds difficulties in oxidizing the methyl groups are probably the reason for the decrease in protectant activity even though Francis *et al.*[4] showed that hydroxylation in the 2 position occurs *in vivo*. With erythromycin N-oxide, the double bond is lacking and the compound can be oxidized only with difficulty even *in vitro*[5]. Thus, it would appear that amine oxides with the above chemical structures can reduce mortality from ionizing radiation when administered orally 24 hr. prior to exposure.

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