Antiserum titrations were carried out in the presence of four 50 per cent units of complement. The complement titrations were carried out using optimally sensitized cells². In this particular system, it was found that complement had from twenty-five to thirty 50 per cent cytolytic units per ml. All the components of this system were checked for anti-complementary activity in the sheep cell haemolytic system and were not found to be anticomplementary in the concentrations used.

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Protective Effect of orally administered S, β -Aminoethylisothiuronium.Br.HBr against X-radiation Death in Mice

S, β -Aminoethylisothiuronium.Br.HBr (AET) is of known value in mice, and given parenterally in an appropriate dose will convert a $LD_{100/30}$ dose of whole-body X-radiation to essentially a $LD_{0/30}$ (ref. 1). The oral administration of AET prior to X-radiation is said to be effective (ref. 2 and Doherty, D. G., personal communication), but no definite results have yet been published. Oral cysteamine has been reported to be effective in both mice and rats with a longer duration of action than intraperitoneal injection³, but this has been disputed⁴.

The outstanding advantage of the oral use of any chemical is, of course, ease of administration. The purpose of this communication is to present data on the oral administration of AET to mice, its toxicity, its value and its duration of action.

Young adult female mice, Walter Reed-Bagg strain, weighing 22–26 gm. were used in this work. The AET used was dissolved in a phosphate buffer of pH 7.2. The pH was then adjusted to 7–7.5 by the addition of the necessary amount of concentrated sodium hydroxide. The final concentration of AET was always about 100 mgm./c.c. based on the weight of the di-bromide salt. All solutions were prepared just before using.

Experimental animals were given 1,500 mgm./kgm. AET by gastric catheter (volume about 0.3 c.c.) while controls were given the same amount of the buffer solution alone.

At various times after AET administration exposure to 770 r. of whole-body X-radiation was carried out. Each exposure group consisted of experimental and control animals, totalling 20–30 mice. After exposure each group was housed in the same large cage, with standard laboratory food and water always available. Mortality and body-weight of the survivors were determined daily for 30 days.

The source of X-ray was a 250 Maxitron, operating at 250 kVp., 30 m.amp. Inherent filtration was equal to 3.2 mm. beryllium and half-value layer of

1.0 mm. aluminium and 1.0 mm. copper was added. The dose was measured in air in the appropriate mid-position of the animals with a Victoreen chamber. The rate of X-radiation was about 30 r./min. and the target source distance was 70 cm.

Toxicity analysis revealed that doses of AET of 1,200 mgm./kgm. or less were non-lethal to these mice. At 1,500 mgm./kgm. there was a 20 per cent mortality in the next 24 hr. Such a result was also noted in the treated X-radiated animals; however, all such deaths were discarded from the experimental groups reported. At doses of 1,800 mgm./kgm. or greater there was 100 per cent mortality in 48 hr.

Fig. 1 presents the results of this experiment. A total of seven groups of control mice showed a remarkably similar 30-day mortality. For purposes of statistical comparison the control groups were averaged together.

Fig. 1

AET by mouth exerts a significant protective effect at 2, 3 and 5 hr. after ingestion, but this is lost at 16 and 24 hr. Chi-square analysis of the 2 hr., 3 hr. (combined) and 5 hr. (combined) gives a $P > 0.001$ when compared with the control $LD_{50/30}$ in a total of 70 mice. The protection achieved is not so dramatic as when AET is given parenterally.

The loss of body-weight following X-radiation was similar in all groups for the first week. Thereafter, the controls continued to lose weight and eventually died, while the AET-treated mice began to regain weight and by 30 days had generally exceeded their pre-X-radiation body-weight.

AET is as effective at 5 hr. as at 2 hr. after ingestion. Duration of the protective action is unknown, but it is not apparent at 16 hr. Nor is the earliest time for protection following oral administration known from this experiment, except that it exerts its effect at least within 2 hr. Other reports indicate that protective action is apparent within a few minutes of ingestion for AET³ and cysteamine⁴.

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