TABLE 1

EFFECT OF CHOLINERGIC BLOCKERS ON SURVIVAL TIME IN IRRADIATED MICE

Drug	Concentration $\times 10^{-3}$ M	ST_{50}* and range in days	Slope and range	Total mortality	
				Day	Percentage
Saline	—	9.1 (8.4– 9.9)	1.21 (1.14–1.29)	13	90
	0.45	9.1 (8.4– 9.9)	1.21 (1.14–1.29)	12	100
Atropine	0.90	9.1 (8.4– 9.9)	1.21 (1.14–1.29)	12	100
	1.35	9.1 (8.4– 9.9)	1.21 (1.14–1.29)	14	100
Saline	—	7.0 (6.4– 7.7)	1.25 (1.16–1.33)	10	100
	0.45	10.2 (9.6–10.9)	1.15 (1.10–1.20)	11	100
MK-02	0.90	10.7 (9.8–11.6)	1.22 (1.14–1.29)	13	90
	1.35	10.7 (9.8–11.6)	1.22 (1.14–1.29)	16	90
Saline	—	7.0 (6.5– 7.6)	1.20 (1.13–1.27)	10	100
	0.45	8.3 (7.6– 8.9)	1.20 (1.13–1.27)	12	100
Win-2299	0.90	10.3 (10.0–10.6)	1.07 (1.04–1.09)	12	100
	1.35	8.2 (7.6– 8.9)	1.20 (1.13–1.27)	12	100
Saline	—	5.3 (4.7– 6.0)	1.32 (1.21–1.44)	10	100
	0.45	8.3 (7.4– 9.3)	1.29 (1.18–1.40)	13	100
Bentyl	0.90	8.7 (7.9– 9.5)	1.24 (1.16–1.33)	12	95
	1.35	6.1 (5.1– 7.2)	1.50 (1.30–1.70)	11	100

* ST_{50} = day on which 50% of animals are alive. Values are at odds of 19/20.

might be useful in the preliminary phase of the syndrome.

There is no general agreement concerning the part played by the cholinergic branch of the autonomic nervous system in the radiation syndrome. Burnett, Burke, and Upton (*4*) showed that cogeners of acetylcholine protected C_{57} strain mice from the lethal effects of x-irradiation and that atropine could negate such protectant action. On the other hand, Larkin (*1*) reported that atropine increased survival time in CF1 strain mice, although it did not affect the total mortality caused by such irradiation. The results herein reported show that atropine does not increase survival time in x-irradiated CF1 strain mice. Other related synthetic drugs, however (MK-02, Win-2299, and Bentyl), which have been shown to have equivalent *in vitro* antispasmodic potency and to be less toxic than atropine (*5–7*) do increase survival time but have no effect on total mortality. We have no explanation for the ineffectiveness of atropine, because *in vivo* this drug should have been as active as the other antispasmodics employed.

Analysis of the mechanism(s) involved in the so-called protectant effect of antispasmodic drugs must be based upon present knowledge of the actions of ionizing radiation on the animal organism. Quastler *et al.* (*8*) have shown that the early deaths from ionizing radiation in mice are due to intestinal damage. Conard (*9*) showed that drugs that inhibit acetylcholine inhibit x-ray response, and drugs that augment the action of acetylcholine also augment the x-ray response. Burn *et al.* (*10*) have observed that loops of intestine obtained from x-irradiated rats are more sensitive to acetylcholine 1–2 days postirradiation. There is also a concomitant fall in the "pseudo" but not in the "true" cholinesterase content of the intestine at the same time. Upon the basis of these reports it seems probable that the increase in survival time may be the result of peripheral cholinergic blockade decreasing intestinal actitvity and thus decreasing intestinal trauma that might result from active propulsive movements of the intestinal contents. Although intestinal relaxation by the antispasmodics might decrease intestinal damage, these drugs would not affect the bacterial and hemorrhagic phases of the radiation syndrome and thus would not decrease the mortality caused by these factors. The results herein presented, with the exception of those with atropine, would tend to support such a hypothesis and would indicate that the approach to radiation injury therapeutics should be a multiple one designed to combat successive phases of the radiation syndrome.

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