at a slower rate and at lower temperatures through the alternate use of sunlight and an improvised electric plate oven.

Because any difference in the environment will be reflected in the food and therefore the nutrition, this fact will continue to remain as a possible explanation for the differences between the lots from Hawaii and the Palau Islands.

At the height of reproductive activity, the albumen gland of the female conduit in these hermaphroditic animals may become so large that it actually exceeds the size of the liver or digestive gland. Because of the proteinaceous nature of albumen, the hypertrophy of this gland is almost certain to produce changes in the amino acid ratios.

A comparison of the values for Lot D with those of Dunn (*4*) indicates that arginine is nearly 2⅓ and lysine over 1⅓ times the amounts in whole egg. All other values, although appreciable and significant, fall below the values for whole egg. Similar analysis of cottonseed meal (*5*) shows that its value as a poultry and livestock feed is limited, as is almost universally the case with many other vegetable products, because of the deficiency of the very essential amino acid, lysine. The immediate inference is that this deficiency could be overcome through the addition of snail meal. Tests designed to determine both the effectiveness of this combination and the growth adequacy factors of snail meal alone are currently being set up through the use of controlled chick feeding experiments at the University of Arizona. It is expected that the results of these tests, along with additional amino acid assays, will be announced at an early date.

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Influence of Peripheral Cholinergic Blocking Drugs on Survival Time in X-Ray Irradiated Mice[1]

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In 1949 Larkin (*1*) reported that atropine increased the survival time in x-ray irradiated mice. It was difficult, however, to understand how a dose of 0.65 mg/kg of atropine could possibly produce sufficient cholinergic blockade to influence the survival time in irradiated animals. Furthermore, if such a small nontoxic dose of atropine could favorably influence irradiation survival time, doses two and three times that amount should prove even more beneficial, because they would have a tendency to increase the effective cholinergic blockade while still remaining in the nontoxic range. Other cholinergic blocking drugs less toxic than, and almost as potent as, atropine should also prove beneficial under the above conditions.

Male CF1 strain mice, weighing an average of 20 g each, were arranged in groups of 20 animals each. Except during irradiation, the animals were maintained in an air-conditioned room at 72° ± 5° F and were given a diet of Rockland pellets supplemented weekly with additional vitamins A and D. Beginning 1 day prior to irradiation and continuing until 90–100% of the animals had died (10–16 days), each animal received daily by intramuscular injection a constant volume of 0.1 ml of the following concentrations of peripheral cholinergic blocking drugs: Group I, 0.45×10^{-3} *M*; Group II, 0.90×10^{-3} *M*; Group III, 1.35×10^{-3} *M*. The controls received 0.9% saline. The drugs used were atropine, Merck MK-02 (tropine benzhydrylether methane sulfate); Win-2299 (1-methyl-3-piperidyl-methyl-phenyl-2-thienyl acetate); and Bentyl (1-cyclohexylhexahydrobenzoic acid, β-diethylaminoethyl ester). The injections were given in alternate thighs. The 550-r radiation dose was administered from above and below the mice with two 250 kvp Picker Industrial Units operating simultaneously. The technical factors were: 250 kvp; 15 ma; FOD 100 cm, filters, 0.21 mm Cu inherent, 0.5 mm Cu parabolic, and 1.0 mm Al; HVL 2.02; size of field —total body, r/min measured in air 17.2–18.4. Both units were calibrated prior to each experiment with a Victoreen thimble r-meter. The animals were restrained in a plastic cage similar to the one previously described for guinea pigs (*2*). The results obtained were analyzed statistically by the method of Litchfield (*3*).

The results obtained with the four drugs are given in Table 1. From the data it is evident that none of the drugs had a significant effect on total mortality. Furthermore, the response of the animals to the radiation dosage was remarkably constant over the 8 months during which the experiments were conducted. This is borne out by the total mortality figures, as well as by the slopes of the time-percentage effect curves. Statistical analysis of the reaction time ratios shows that all concentrations of MK-02, the 0.90×10^{-3} M concentration of Win-2299, and the 0.45 and 0.90×10^{-3} *M* concentrations of Bentyl significantly affected the survival time of the mice in a favorable manner. From a practical viewpoint, however, the over-all differences between the ST_{50} day and the day on which 90–100% of the mice were dead are so small that such medication cannot be considered highly benecial in counteracting over-all radiation injury, but it

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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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