alone. This has been due in part to the toxicity and lack of palatability of high methionine rations. Uninoculated nutritional controls fed high methionine rations lose about 40% of their body weight during the test period and deaths in these groups are not infrequent. However, restricted food intake experiments have shown that the protective effect of excess methionine is not directly related to starvation.

Summary. 1. A decreased susceptibility to Lansing poliomyelitis, characterized by prolonged incubation and survival times, has been observed in mice fed excess methionine. To obtain this effect fully, a continuous period of high methionine intake was necessary prior to inoculation. 2. The addition of excess methionine to low tryptophan rations containing 6-methyl tryptophan resulted in a more marked protection against Lansing infection in mice than when the same amounts of methionine or 6-methyl tryptophan were fed alone.

1. Clark, P. F., *Ann. Rev. Microbiol.*, 1950, v4, 343.
2. Jones, J. H., Foster, C., Kenle, W., and Alexander, D., *Arch. Biochem.*, 1946, v11, 481.
3. Davies, W. L., Pond, W. L., Smith, S. C., Rasmussen, A. F., Jr., Elvehjem, C. A., and Clark, P. F., *J. Bact.*, 1952, v64, 571.
4. Rasmussen, A. F., Jr., Clark, P. F., Smith, S. C., and Elvehjem, C. A., *Bact. Proc.*, 1951, 93.
5. Newell, G. W., and Carman, W. W., *Fed. Proc.*, 1950, v9, 209.
6. Reiner, L., Misani, F., and Weiss, P., *Arch. Biochem.*, 1950, v25, 447.
7. Gershoff, S. N., and Elvehjem, C. A., *J. Nutrition*, 1951, v45, 451.
8. Ainslie, J. D., *J. Exp. Med.*, 1952, v95, 9.

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Studies on Irradiated Animals, III. Effect of Saline on Radiation-Induced Mortality and Weight Changes.* (19918)

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In pharmacological studies it is customary to dissolve chemicals to be injected in saline solution, and also to use saline as control. However, in pharmacological studies on irradiated animals saline solutions may not be inert since the "acute radiation syndrome" includes disturbances of the salt-water metabolism(1). Saline injections might, therefore, alter the course of radiation death. In order to clarify the effect of physiological sodium chloride injections on irradiated animals, the investigations reported in this paper have been undertaken.

Materials and methods. Swiss, male white mice of the Institute strain, 22 g ± 15% of body weight, were used. Irradiation was done as described previously(2,3). The radiation factors were: 200 kv, 15 ma, .25 Cu ± 1.0 mm Al filtration. HVL = .8 mm Cu. X-ray doses of 410 and 385/air, representing the LD_{60} 14 days and $LD_{30}/14$ days were given. Saline was administered daily in amounts of .3 cc of a 0.9% NaCl solution either intramuscularly or intraperitoneally, starting immediately after exposure, for an over-all period of 14 days (with the exception of Sundays) or for 6 consecutive days.† For graphic presentation of results the mortality rate of saline-injected animals is compared with that of the non-medicated irradiation control group. The figures in parentheses indicate the number of animals in the different groups.

Results. 1. *Effect of intramuscular saline injection in its relationship to the time of saline administration.* Fig. 1 summarizes pertinent results obtained in this study. As indicated in Fig. 1, saline injection slowed the death rate at the end of the first week for 2 or 3 days. If injection of saline was continued over the 14-day period (curve B), then a

*The opinions or assertions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

† The animals were kept during the 28-day observation period in air conditioned quarters at 75°F.

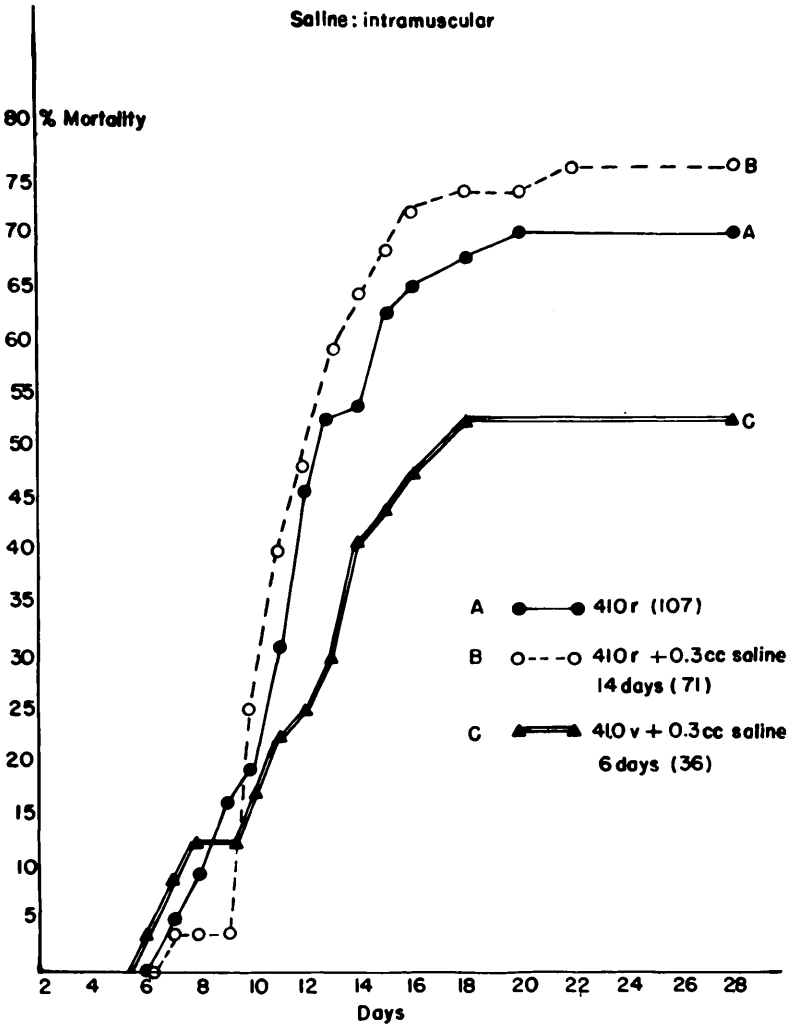

FIG. 1. Influence of length of inj. time on radiation-induced mortality: The graph demonstrates that reducing the over-all inj. time of saline from 14 to 6 days produces a statistically significant decrease in mortality.

steep increase of mortality took placed around the 11th day and the mortality curve of animals treated in this manner showed a slight, even though statistically not significant, increase. The mortality curve of animals receiving saline injections for 6 days only (curve C) indicated a statistically‡ significant decrease. (Comparison of curves B and C: $P < .01$ for the 16th day using the χ^2 method.) The delay in the development of mortality in saline-treated animals is also noticed in those animals exposed to the lower radiation dose as demonstrated in Fig. 2. There is also a slight, but not significant, decrease in the mortality rate of the saline-treated animals.

2. *Comparison of intramuscular vs. intraperitoneal injections.* In both instances administration of saline took place over a 14-day period and was administered to mice exposed to the X-ray dose of 410 r. There was no significant difference between the 2 mortality curves. But attention should be called to the fact that a delay of death for a period of 3

‡ We are indebted to Dr. E. A. Jerome for the statistical analyses.

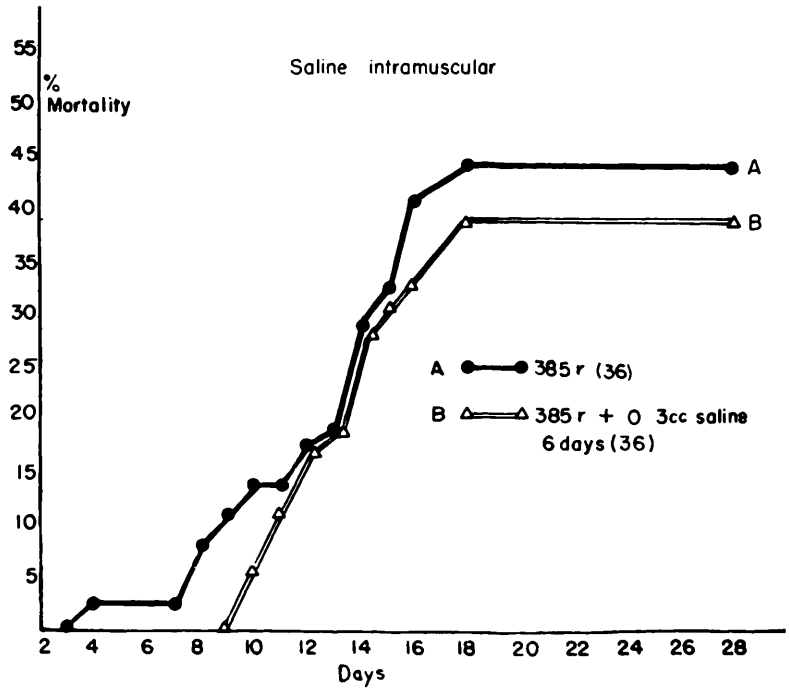

FIG. 2. Effect of 6-day inj. of saline on a lower X-ray mortality: At this level of X-ray mortality, saline inj. produces only slight delay in the development of mortality.

days at the end of the first week was also noticed in the intraperitoneal group.

3. *Influence of saline injections on radiation-induced weight changes.* The influence of saline injections demonstrated in the study of mortality is reflected in a similar manner in the weight curves of the animals as shown in Fig. 3.

Discussion. The results obtained in this study clearly indicate that saline cannot be considered as an inert agent in pharmacological studies on irradiated animals. This has to be kept in mind if and when the effect of a certain chemical dissolved in saline is used for a study of its effect on radiation-induced mortality.

Attention is called to the fact that saline administration *subsequent* to the exposure to lethal X-ray doses may under certain conditions change the mortality rate.

Furthermore, it appears noteworthy that the pharmacologically induced change of radiation mortality is reflected in the weight curve of the animals. As indicated in Fig. 3, weight gain in mice after saline administration for 6 days, which resulted in a significant reduction in mortality, was more speedy in this than in the non-medicated irradiated group or in the irradiated group of mice receiving saline over the 14-day period, which procedure slightly increased mortality. This observation is in line with our previous findings concerning the correlation between weight changes and percentage mortality as produced by varying X-ray doses(3).

Summary. 1. Daily injections of .3 cc of .9% NaCl solution into mice of 22 g $\pm$ 15% body weight subsequent to the exposure to X-ray doses representing the $LD_{60}/14$ days and $LD_{30}/14$ days for periods of 14 and 6 days respectively caused a delay in the development of the mortality produced by these X-ray doses. 2. While the 14-day administration of saline produced a slight but statistically not significant increase of the X-ray-induced mortality rate, the 6-day administration resulted in a statistically significant decrease of the mortality rate in mice exposed to the $LD_{60}/14$ days. 3. The saline-induced change of X-ray mortality was also reflected

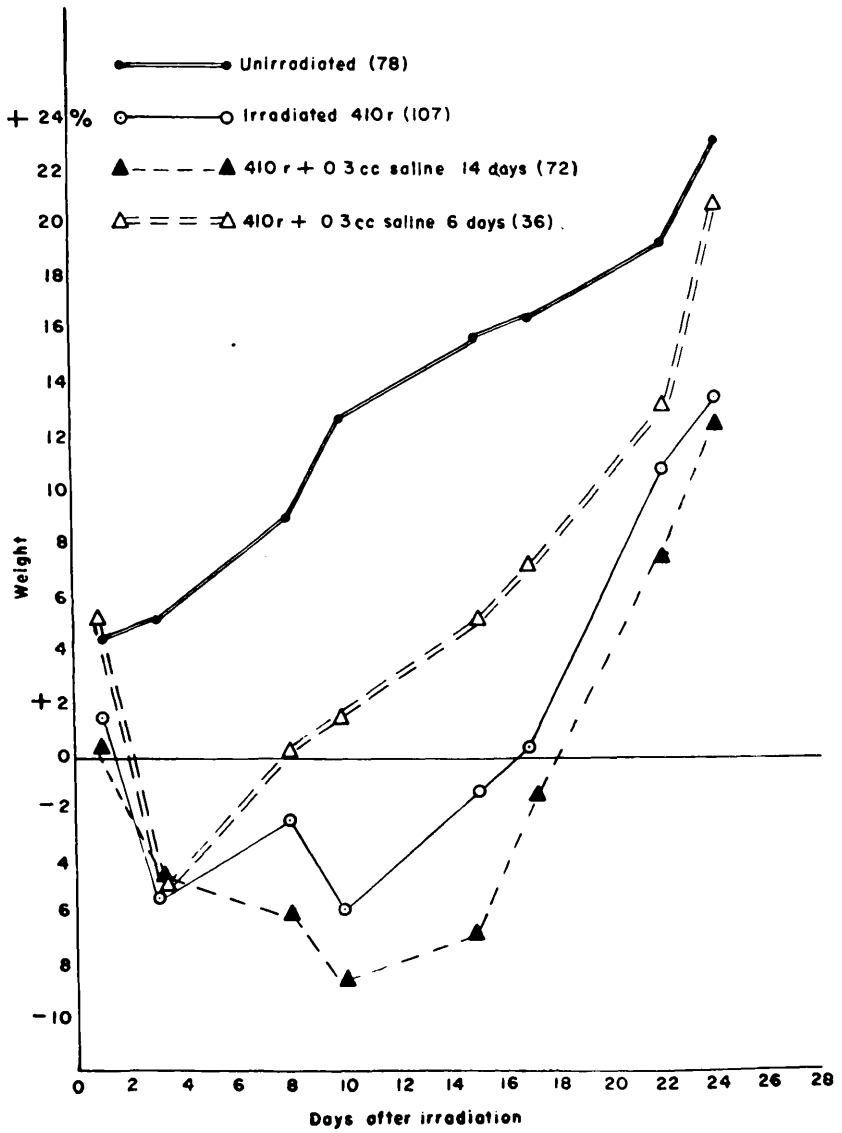

FIG. 3. Influence of intramusc. saline inj. on radiation-induced wt changes: In general the wt curves reflect the changes produced by 6-day saline administration on mortality. The wt gain in mice is more speedy in the group receiving saline for 6 days than in either the non-medicated irradiated group or the irradiated group of mice receiving saline for 14 days.

in the weight curve of the animals.

1. Ellinger, F., *Naval Med. Research Inst.*, Lecture and Review Series No. 51-6, 1951.

2. Morgan, J. E., Chambers, F. W., Jr., *Naval Med. Res. Inst. Rep.* NM 006 012.04, No. 43, 1952.

3. *Naval Med. Res. Inst. Rep.* NM 006 012.04, No. 44, 1952.

Received September 30, 1952. P.S.E.B.M., 1952, v81.