utilized for the synthesis of non-essential amino acids by the intact young rat. The possibility that urea can be utilized in anabolic processes in the eviscerate rat should be considered.

The possibility that urea can be metabolized in the eviscerate rat weakens one point of evidence that urea synthesis occurs only in the liver. The earlier studies(1) on nephrectomized-hepatectomized animals have shown that the blood and tissue urea did not change during the times that these observations were made. The assumption that urea could not be metabolized therefore required the conclusion that no extra-hepatic synthesis of urea could have occurred since the concentration in the body fluids remained unchanged. However, if urea can be metabolized, it is hypothetically possible for extra-hepatic urea synthesis to coexist with an equal or higher rate of urea metabolism without increasing the concentration of urea in the body. As an analogy, it was first assumed that gluconeogenesis occurs only in the liver because the blood glucose falls following hepatectomy. It has now been clearly established that glucose can be formed in the kidney, but that this extra-hepatic gluconeogenesis is masked by a higher rate of glucose utilization(11). Evidence has been reported by Graham, Houchin and Turner(12) that the active mammary gland of the goat can synthesize urea.

Summary. Male rats of the Sprague-Dawley strain were eviscerated at a weight of 250 g and were given intravenous infusions of solutions of glucose, insulin and 0.9% sodium chloride for periods up to 48 hours. Comparisons were made of the total carcass plus urinary urea in 26 control rats taken immediately following evisceration, 24 rats which were killed 24 hours following evisceration and 16 rats which were killed 48 hours following evisceration. The average total carcass urea of the 24-hour rats was lower than that of the controls, and the average value for the 48-hour group was still lower. From the statistical standpoint, it is highly probable that there was some extra-renal loss of urea following evisceration. These results are indirect evidence for the occurrence of urea catabolism. The results are in agreement with observations on other species in showing that there is no rise in the urea concentration of the body in the absence of the liver.

10. Rose, W. C., Smith, L. C., Wormack, M., and Shane, M., *J. Biol. Chem.*, 1949, v181, 307.

11. Reinecke, R. M., *Am. J. Physiol.*, 1943, v140, 276.

12. Graham, W. R., Houchin, O. B., and Turner, C. W., *J. Biol. Chem.*, 1937, v120, 29.

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Increased Tolerance of Mice to Lethal X-Radiation as a Result of Previous Sublethal Exposures.* (17619)

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The pathogenesis of acute radiation illness is poorly understood. The discovery of factors that may influence the survival after exposure to doses of radiation in the lethal range will help considerably in the understanding of the mechanisms that produce this illness. The release of heparin and histamine in irradiated animals has been reported(1,2,3). This suggests an anaphylactoid response. In fact a similarity between hypersensitive states and

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

1. Allen, J. G., *et al., University of Chicago Metallurgical Laboratory*, Nov., 1946.

2. Cronkite, E. P., *Am. J. Path.*, 1947, v23, 891.

3. Ellinger, F., *Science*, 1946, v104, 502.

TABLE I.
Tabulation of Comparative Mortality and Weight Data on 3 Groups of Mice (100 mice each) Showing That Mice Previously Exposed to Fractional Sublethal Doses of X-ray Radiation Have an Increased Tolerance to a Subsequent Lethal Dose of X-ray Radiation.

Group	Comparative groups of mice	28-day mortality %	Days after exposure for max. wt loss	Wt loss or gain in % of original wt	Avg survival time, days
1. Irrad. control	703 r	41	14	—14.4	14.3
2. " "	144 r × 3	0	14*	— 1.6	
3. " "	144 r × 3, 703 r	26	14.5	—13	15.1

0.05 P_{diff} 0.02.
* Fourteen days after the last sublethal exposure.

the toxicity of ionizing radiation has been suggested(4,5).

The natural course of acute radiation illness induced by total body exposure to ionizing radiation suggests that sensitization phenomena may participate in provoking the exacerbation in the severity of the illness that terminates the latent period(6,7,8). Of great interest is the report of Raper in which the LD_{50} of total surface beta radiation was increased by a previous sublethal cutaneous exposure to beta rays(9). With these facts in mind it was decided to try to alter the lethality of total body x-ray exposure on mice by previous fractional exposure to sublethal total body x-ray radiation.

Materials and Methods. White, Swiss, female mice raised at this Institute by brother-sister matings were used exclusively. Mice were obtained from stock at 30 days of age, observed for 2 weeks and then irradiated by the angular beam of a 1,000 KV, 3 ma, GE Industrial X-ray machine(10,11). The experiment utilized 3 groups of mice. Group 1 received no preliminary radiation. Groups 2 and 3 were irradiated according to the following schedule: A sublethal dose of 144 r was given at weekly intervals for 3 weeks. Thirty days after the third weekly dose Groups 1 and 3 were given a lethal range dose of 703 r simultaneously. All x-ray radiation was delivered at the rate of 31.2 r/min. Animals were checked 2 times per day and deaths recorded. Other studies, except weighing, which was done as a group without handling, were omitted so that extraneous factors such as handling and bleeding would not influence mortality. All mice were given Purina Mouse Chow and water *ad lib.*

Results. In Group 1, the controls, the first deaths occurred on the ninth day after the exposure to 703 r. Most of the deaths occurred between the ninth and the twenty-first days. The twenty-eighth day mortality was 41%. In Group 2, the mice that received only the 3 initial sublethal exposures of 144 r each there were no deaths. These animals appeared healthy at all times. However, there was a slight weight loss following each initial sublethal exposure in Groups 2 and 3. This was practically regained by the time each subsequent exposure was given and all weight loss was regained at the end of the 30 day rest period. Group 3 which received 144 r at weekly intervals for three weeks and then 703 r had an ultimate 28 day mortality of 26%. The probability that the difference in mortality between Groups 1 and 3 is due to chance was calculated by Chi square and found to be between 0.02 and 0.05 (Table I).

Comments. It is difficult to understand the mechanism by which previous sublethal ex-

4. Rolleston, H., *Quart. J. Med.*, 1930, v23, 101.
5. Lewis, T., Shaw and Sons, Ltd., London, 1927.
6. LeRoy, George, *J. A. M. A.*, 1947, v134, 1143.
7. Cronkite, E. P., Naval Medical Research Institute, Project 007-039, Rep. No. 10, Mar., 1948.
8. Ellinger, F., *Radiology*, 1945, v44, 125.
9. Raper, J. K., *Radiology*, 1947, v49, 314.
10. Chapman, W. H., Sipe, C. R., Eltzholtz, D. C., Cronkite, E. P., Lawrence, G. H., and Chambers, F. W., Jr., Naval Medical Research Institute Project NM 007-039, Rep. No. 14, 12 Aug., 1948.
11. Tullis, J. L., Tessmer, C. F., Cronkite, E. P., and Chambers, F. W., Jr., Naval Medical Research Institute Project NM 007-039, Rep. No. 3, Dec., 1947.
12. Selye, H., *J. Clin. Endocrinol.*, 1946, v6, 117.

posures presumably increase resistance to radiation. It may be that the non-specific resistance to stress as defined by Selye(12) is increased. Perhaps specific resistance to the products of cellular destruction is increased comparable to the increased resistance of rabbits to bacterial toxins produced by previous x-irradiation as described by Bisgard(13). The results reported here for total body x-irradiation are similar to those reported by Raper(9) for total body surface Beta radiation of mice.

Summary and Conclusion. 1. It has been demonstrated with a fair degree of certainty ($0.05 > P_{diff} > 0.02$) that three weekly exposures of 144 r followed by a 30 day rest period increases the resistance of mice to a subsequent lethal dose of x-radiation.

2. It is concluded that no adequate explanation for this phenomenon of increased tolerance to x-ray radiation is available at the present time.

13. Bisgard, J. P., Hunt, H. B., and Dickinson, R. H., *Radiology*, 1944, v43, 330.

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Phytotoxic Properties of Spinal Fluids from Paresis, Tabes and Neuro-Syphilis. (17620)

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The author has been studying the pharmacological properties of bloods from various psychoses for many years(1,2). The findings established clearly that sera from patients with organic and functional psychoses when tested by the author's standardized phyto-pharmacological methods, exhibited marked toxic effects on the root-growth of *Lupinus albus* seedlings grown in plant physiological solutions. The sera from purely psychoneurotic patients were not phytotoxic. More recently, the writer has begun a phyto-pharmacological examination of normal and pathological spinal fluids by exactly the same methods as those employed for examination of blood sera. In the present paper are reported the findings with the spinal fluids from a series of cases with general paresis and a series of non-psychotic patients suffering from Tabes Dorsalis and other cases of neuro-syphilis.

The methods employed have been described(3,4,5). The effect of spinal fluids dissolved in Shive's plant physiological solution(6), was studied quantitatively on the root-growth of *Lupinus albus* seedlings for 24 hours under standardized ecological conditions. By the index of growth is meant the ratio of the root-growth in a solution of the unknown drug to the growth of control seedlings in normal physiological solutions.

$$\text{Index of growth} = \frac{X}{N} \times 100$$

It was found that 1% solutions of normal spinal fluids exert practically no phytotoxic effect on the root-growth. A 2% solution of spinal fluid gives an average index of growth of 92%, the readings ranging from 80% to 100%. Table I shows the results obtained with a series of 16 cases of paresis, 10 cases of tabes and 14 cases of other neuro-syphilitic patients. It will be seen that all of the paretic spinal fluids yielded readings far be-

1. Macht, D. I., and Macht, M. B., *J. Lab. and Clin. Med.*, 1941, v26, 597.

2. Macht, D. I., *Southern Med. J.*, in press.

3. Macht, D. I., and Livingston, M., *J. Gen. Physiol.*, 1922, v4, 573.

4. Pels, I. R., and Macht, D. I., *Arch. Dermat. and Syph.*, 1931, v23, 601.

5. Macht, D. I., and Grumbein, M. L., *Arch. Internat. de pharmacodyn et de therap.*, 1938, v60, 95.

6. Shive, J. W., *Physiol. Researches*, 1915, v1, 327.