trend in the epidemiology of poliomyelitis is comparable to the epizoology of lymphocytic choriomeningitis in mice. Mouse encephalomyelitis is also being explored along these lines.

Summary and conclusions. Freshly isolated strains of lymphocytic choriomeningitis virus induced inapparent infection and immunity in infant mice. A mouse-adapted strain, however, caused obvious signs of infection and a high mortality rate among infant mice. Adult mice were fully susceptible to both freshly isolated and mouse-adapted virus. These findings are in keeping with the epizoology of the disease in naturally infected mouse colonies.

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Changes in Adrenal and Pituitary Concentrations of I^{131} and P^{32} Following Thyroidectomy.* (19037)

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It has been reported that an increased concentration of radioiodine I^{131} occurs in the pituitary and the adrenals of rats subjected to prolonged propylthiouracil treatment(1). This study was undertaken to determine whether a similar response occurs in total thyroidectomy, and by the uptake of radiophosphorus P^{32} to determine if the rate of phosphate utilization is altered in those organs.

Methods and procedure. Twenty young male albino rats weighing between 60 and 100 g were randomly divided into an experimental (Group I) and a control group (Group II). The experimental group was thyroidectomized and maintained with the control animals on regular laboratory Rockland rat ration for a period of 70 days following thyroidectomy. Twenty fully mature male albino rats weighing between 250 and 300 g were similarly divided into an experimental (Group III) and a control group (Group IV). The experimental group was thyroidectomized and maintained with the control animals under identical food, water and housing conditions as the younger rats of Groups I and II, for the same period of time. Three hours before sacrifice, a randomly selected one-half of each group (Groups I-IV) was injected intraperitoneally with 200 microcuries of radioactive iodine I^{131} in 2.5 ml of normal saline. The other half of each group of animals was injected intraperitoneally with 100 microcuries of radioactive phosphorus P^{32} in 2.5 ml of normal saline. At sacrifice the adrenals, pituitary, thymus, a portion of muscle and the thyroids of the control groups (Groups II and IV) were removed, weighed and the entire adrenals, pituitary, muscle sample, thyroid and a weighed portion of thymus dissolved in 5 ml of concentrated HNO_3. The acid, after the tissue was digested, was then diluted with distilled water to a measured volume of 50 ml and dip-counted, by a method previously described(2). Aliquots of the injected solutions of I^{131} and P^{32} were prepared and dip-counted in an identical manner as the tissue specimens. All assays were expressed as the percentage of injected activity after allowing for the respective dilutions for assay. To determine the relative ability of a tissue to concentrate radiophosphorus or radioiodine, the percentage of the administered isotope found in an organ was divided by that organ's percentage of body weight. Where only a portion of muscle was assayed, the activity was determined on the basis of one gram and the percentage of body weight of one

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1. Boatman, J. B., and Moses, C., *Endocrinology*, 1951, v48, 413.

2. Boatman, J. B., Sunder, J. H., and Moses, C., *Fed. Proc.*, 1951, v10, 16.

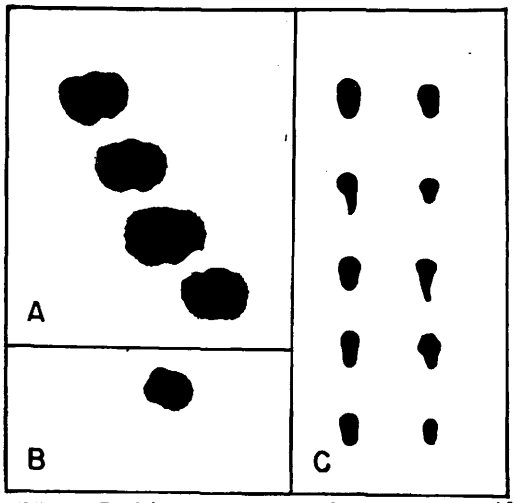

FIG. 1. Positive radioautographs of the thyroid area from: A. normal; B. unilaterally thyroidectomized; C. bilaterally thyroidectomized rats. Excised thyroid area placed directly on double black paper covered no-screen x-ray film for 3 days under light pressure.

gram was used. These ratios were termed the concentration ratios.

The completeness of thyroidectomy was determined by comparing radioautographs including the thyroid area of thyroidectomized animals from this study with radioautographs from non-operated albino rats of the same age and sex similarly treated with radioiodine I^{131} (Fig. 1) adapted from the method of Reinhardt(3).

Results. Young rats. There was observed a profound inhibition of rate of body weight increase 2 weeks following thyroidectomy (Fig. 2). This was seen to inhibit growth to approximately 5 g increase of body weight in 45 days, compared to the control rats which showed an increase of 80 g in the same time interval. The I^{131} concentration ratio was significantly increased in the pituitary (+2650%) of the thyroidectomized rats over the levels found in the control animals, while the differences found in the thymus and adrenal were also significantly higher than those of the control group (Table I). The P^{32} concentration ratios were significantly depressed in the pituitary and adrenals of the thyroidectomized rats compared to the levels in the control animals. Muscle P^{32} concentration ratios were also significantly depressed. An increased pituitary percentage of body weight and a decreased thymus percent body weight was also observed in the thyroidectomized animals.

Adult rats. Little change in body weight of the experimental and control groups was observed (Fig. 2). The concentration ratio of I^{131} was again significantly increased in the pituitary (+250%) in the thyroidectomized animals over the levels found in the control animals. It was found that the thyroidectomized rats showed no significant differences in the concentration ratios of P^{32} compared to the control animals. The adrenals and thymus showed a significantly smaller percentage of body weight in the thyroidectomized animals (Table I).

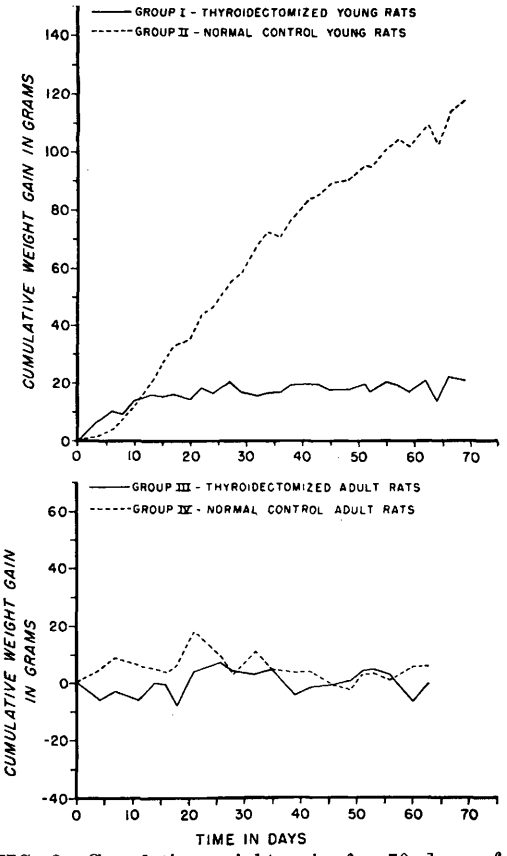

FIG. 2. Cumulative weight gain for 70 days of young (upper graph) and adult (lower graph) male albino rats compared to normal control animals.

3. Reinhardt, W. O., PROC. SOC. EXP. BIOL. AND MED. 1942, v50, 81.

TABLE I. Mean Organ % of Body Wt, I^{131} and P^{32} Concentration Ratios in Thyroidectomized and Control Animals.

Group	Mean organ % of body weight: Pituitary	Adrenal	Thymus	Thyroid
I – thyroidect.	.012*	.027	.165†	
II – control	.005‡	.032	.235‡	.013
III – thyroidect.	.007	.020*	.078†	
IV – control	.007	.029	.100	.013

Group	Mean I^{131} concentration ratios $\left[\frac{\text{Organ's \% total activity}}{\text{Organ's \% body wt}}\right]$: Pituitary	Adrenal	Thymus	Muscle	Thyroid
I – thyroidect.	1.180*	.506†	.434*	.142	
II – control	.043	.264‡	.233	.129	52.161
III – thyroidect.	.537*	.235	.240	.109	
IV – control	.153	.131	.167	.047	37.064

Group	Mean P^{32} concentration ratios $\left[\frac{\text{Organ's \% total activity}}{\text{Organ's \% body wt}}\right]$: Pituitary	Adrenal	Thymus	Muscle	Thyroid
I – thyroidect.	3.741†	3.903*	8.605	.538†	
II – control	6.045	8.232	9.730	1.127	4.867
III – thyroidect.	4.873	5.262	5.236	.788	
IV – control	4.392	8.534	5.171	1.182	4.201

* Significantly different from control values to a probability $<.01$.
† " " " control values to a probability $<.05$.
‡ " " " Group IV control values to a probability $<.01$.

In a comparison between the normal groups of non-operated rats, the mature control animals showed a decreased concentration ratio of I^{131} in the adrenals, compared to the young control animals. The concentration ratios of P^{32} in the adult animals were not significantly different compared to levels seen in the young control animals. However, the older animals showed a significantly greater percentage of body weight in the pituitary and a lower percentage of body weight in the thymus, compared to the younger control animals (Table I).

Discussion and conclusions. It was observed that the effects of thyroidectomy were most noticeable in young rats, and were most pronounced upon the pituitary and the adrenals of these animals. Both the pituitary and adrenals of the young thyroidectomized rat had increased I^{131} concentration ratios and decreased P^{32} concentration ratios. The mature thyroidectomized animals exhibited a significantly increased pituitary I^{131} concentration ratio, but many of the other changes seen in the younger animals were absent or less pronounced.

Greenberg *et al.*(4) concluded that the observed relationships of increased P^{32} uptake in the organs of the hyperthyroid rats and the decreased P^{32} uptake in the organs of the hypothyroid rats, suggests that thyroid activity influences the rate of transfer of phosphorus across cell membranes. Such a conclusion does not offer explanation for the greatly increased iodine (I^{131}) content of the pituitary and adrenal glands of animals reported here.

Summary. 1. Seventy days after thyroidectomy the ability of various organs of young and adult male albino rats to concentrate radioiodine I^{131} and radiophosphorus P^{32} was determined and compared to control animals. 2. The pituitary and adrenals of the young rats showed a markedly increased 3-hour concentration of I^{131} and a decreased 3-hour concentration of P^{32}, significantly different from the control animals. 3. Mature animals exhibited an increased 3-hour concentration of I^{131} in the pituitary, with no significant

4. Greenberg, D. M., Frankel-Conrat, J., and Glendening, M. B., *Fed. Proc.*, 1947, v6, 1.

differences in the 3-hour concentration of P^{32} from levels seen in the control animals. 4. The deleterious effects of thyroidectomy in the young animals with a high rate of tissue phosphate utilization was evidenced by the sharply decreased P^{32} concentration in the organs of those animals. Explanation for the markedly increased I^{131} concentrations in pituitary and adrenal of young and adult thyroidectomized animals is not readily apparent.

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Dithiol Antagonism and Potentiation of Chemotherapeutic Agents. (19038)

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Ehrlich(1) formulated the hypothesis that arsenicals act on pathogenic microorganisms through receptors formed by "conjugated" -SH or -OH groups.† Since then the participation of -SH groups in the mechanism of chemotherapeutic action has been widely studied, particularly after Voegtlin, Dyer and Leonard(2) demonstrated the antagonistic action of monothiols on arsenicals. The literature on this subject and the more recent conception that arsenicals act as thiol-enzyme inhibitors, has been reviewed by Findlay(3), Barron(4), Waters and Stock(5), Peters(6), Stocken and Thompson(7). The last 3 authors were "led . . . to the realization that the more stable form of arsenic with the enzyme must be a ring form in which two sulphur atoms are combined with one arsenic, as follows: $\left.\begin{matrix} R\text{—}S \\ \\ R\text{—}S \end{matrix}\right\} > As\text{—}$"(6). This idea was confirmed in the successful use of dimercaptopropanol (BAL) as an antidote in lewisite, and more generally, in metal poisoning. We reported(8) that BAL interferes to a much greater extent with the therapeutic action of arsenoxide against *T. equiperdum* than with its toxic effect on the host.‡ The intensive reversal of the therapeutic effect could not be explained alone with the formation of an arsenoxo-BAL compound, since this compound, prepared and studied in various laboratories, maintains a definite therapeutic activity and toxicity(9-12). Searching for an explanation, we assumed that BAL determines the reversal of the therapeutic effect by acting

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1. Ehrlich, P., *Ber. dtsche Chem. Ges.*, 1909, v42, 17.

† Ehrlich was referring explicitly to the dithiol function: "dass vielleicht solche orthoständigen Hydroxyloder Sulphhydrylgruppen durch geeignete Bedingungen befähigt sein können, als Metallreceptoren zu fungieren". Note the analogy with the expression used by modern biochemists (Stocken and Thompson, *Biochem. J.*, 1946, v40, 529): "it seems probable that the arsenic has combined with two -SH groups closely placed in space on the same molecule, to form a ring".

2. Voegtlin, C., Dyer, H. A., and Leonard, C. S., *J. Pharmacol.*, 1925, v25, 297.

3. Findlay, G. M. *Recent advances in chemotherapy*, Vol. I. Churchill, London, 1950.

4. Barron, G. E. S., *Advances in Enzymology*, 1951, v11, 201. Interscience, New York.

5. Waters, L. L., and Stock, Ch., *Science*, 1945, v102, 601.

6. Peters, R. A., *Symp. Soc. Exp. Biol.* III. 36, Cambridge University Press, 1949.

7. Stocken, L. A., and Thompson, R. H. S., *Physiol. Rev.*, 1949, v29, 168.

8. Ercoli, N., and Wilson, W., *J. Pharmacol.*, 1948, v92, 121.

‡ This finds a certain analogy in observations made by Voegtlin on monothiols: "it is more difficult to counteract the toxic effect of As in the higher animals than that exerted on protozoa"(2).

9. Peters, R. A., and Stocken, L. A., *Bioch. J.*, 1947, v41, 53.

10. Friedheim, E. A. H., and Vogel, H. J., PROC. SOC. EXP. BIOL. AND MED., 1947, v64, 418.

11. Friedheim, E. A. H., and Berman, R. L., PROC. SOC. EXP. BIOL. AND MED., 1947, v65, 180.

12. Sawyers, J. L., Burrows, B., and Maren, H. T., PROC. SOC. EXP. BIOL. AND MED., 1949, v70, 194.