Evans[3] formula, on the basis of a thyroid weight of 50 g. (The table gives estimates of the dose per 12 or 24-hour interval and of the total dose). The total dose is estimated to be 9950 roentgens for the first administration of 9.1 millicuries, and 5500 roentgens for the second administration of 3 millicuries. It should be noted that the total dose in roentgens following the second administration (3 millicuries) agrees with the simplified formula of Hertz and Roberts,[2] roentgens eqivalent

$$= 117{,}000 \times \frac{\text{millicuries } I^{131}}{\text{grams thyroid}}$$

It is too early to evaluate the result of the treatment. Though the patient has improved somewhat and has gained weight, no decided reduction of the BMR occurred in the first 2 months following the first dose, and it seems probable that further treatment will be required.

Summary. Information is given of the urinary excretion of radioactive iodine following administration of relatively large doses in a patient with severe hyperthyroidism. Administration of stable iodine (in Lugol's solution) after the urinary excretion of I^{131} had reached a low level resulted in a pronounced increase in this excretion, which lasted some 48 hours after discontinuing Lugol's solution. This increase in excretion of I^{131} was not observed following administration of Lugol's solution in one case of carcinoma of the thyroid with metastasis. Retention of 85% of the I^{131} by the thyroid agrees with other figures on the retention of I^{130} by the hyperplastic thyroid, when iodine has been withheld for a period of over 4 weeks prior to radioactive iodine.‡

‡ A third dose of 9 millicuries of I^{131} was given the same patient in January, 1947. Loss of iodine in the first 2 days was high (50%). Use of Lugol's solution again resulted in increased excretion of radioactive iodine. The metabolic rate had returned to normal when the patient was next seen in March, 1947.

Two additional cases have since been treated with doses of 9 millicuries of I^{131} (estimated 50 grams thyroid tissue). Excretion was much the same as that following the second dose of iodine for patient No. 1. Use of Lugol's solution resulted in increased excretion of radioactive iodine in both of these cases.

Dr. C. J. Watson, Director of the Department of Internal Medicine, University of Minnesota Hospitals, made the arrangements for the treatment of the patient, and we are obliged to him for the opportunity to carry out these measurements and for valuable advice.

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The Development of *Fundulus heteroclitus* Embryos in Solutions of Metrazol.

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Speidel[1] has attempted to ascertain the specific effect of metrazol on the nervous system by immersing frog tadpoles in aqueous solutions of it and by studying, by direct microscopic and ciné-photomicrographic methods, the outgrowth of living nerve fibers in the tadpoles' tails. Using a 2% solution for approximately 20 minutes, Speidel found that the growing nerve endings degenerated during the period of immersion, but recovered and subsequently regenerated when the tadpoles were returned to pond-water.

The present communication reports the results of studying the development of cer-

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1 Speidel, C. C., *Proc. Am. Philos. Soc.*, 1940, **83**, 349.

tain aspects of gross behavior in whole embryos (*Fundulus heteroclitus*) which were immersed in solutions of metrazol at different stages of development and which remained in them for varying periods of time. The investigation was undertaken with the possibility in mind that subjecting embryos to treatment at various stages of development might produce alterations of structure and function in the central nervous system which could be correlated with the particular fiber-tracts being laid down during the period of treatment.

Over 500 eggs of *Fundulus heteroclitus* were treated with aqueous solutions of metrazol (Pentamethylentetrazol, Bilhuber-Knoll Corporation). Solutions, made in distilled water, were used in strengths of either 0.1% or 2%. The embryos were introduced into the solutions at stages varying between 6 and 34 (Oppenheimer[2]), and remained in them for periods varying from a few hours to 14 days. In some cases they remained in the solutions until fixation; in others they were transferred to tap- or sea-water. Some embryos were dechorionated before treatment, others were left in their chorions throughout; still others were dechorionated during the course of treatment or recovery. All embryos were observed at least twice daily; those which survived treatment were preserved and are being prepared for histological study.

The gross effects, which were more drastic in dechorionated embryos than in those with chorions intact, varied also in degree according to the age of the embryos, the strength of the solutions used and the duration of the experiments. In some cases recovery occurred after the embryos were transferred to tap- or sea-water.

None of the embryos treated with 2% metrazol solution before gastrulation developed normally; some of those treated at pregastrular stages with 0.1% solution reached stage 32, the stage of hatching, and completed the major part of their early development. Embryos treated subsequent to gastrulation but before the establishment of circulation developed for as long as 14 days in the 0.1% solution; of comparable embryos treated with 2% solution, only 2 (both left in their chorions during treatment and transferred from metrazol after 2½ days), reached stage 31

There was a marked effect on the circulation of embryos treated between stages 23 and 32; the rate of the heartbeat became markedly slowed, and a large vesicle, filled with static blood, formed just distal to the sinus venosus. In addition, the tonic relationships of the longitudinal body musculature were often affected in embryos treated at these stages. Many of the embryos treated between stages 23 and 26 exhibited sharp localized contractures of the trunk musculature. In addition, many embryos treated between stages 23 and 32, whether or not such localized contractures were present, exhibited various degrees of kyphosis or lordosis which involved sometimes trunk, sometimes tail, sometimes both. Embryos treated between stages 27 and 32 in some cases also showed abnormalities in the action of the mouth and opercular apparatus, which were held open without performing the usual rhythmic movements.

Embryos treated subsequent to stage 32 did not exhibit the same tonic abnormalities which characterized the group just described and were not kyphotic or lordotic. They sometimes, however, in contrast, exhibited sharp lateral contractions and held their tails bent to left or right. Their mouths were almost invariably stretched wide open and exhibited no rhythmic movements. Righting reflexes were lost in these embryos during the period of treatment.

Whether the effect of the drug on the reactions of the embryos acts through the nervous system or directly on the muscular system, and whether or not the drug has resulted in morphological changes within the nervous system that do not produce functional changes in behavior, can be ascertained only after histological examination of the embryos is completed. It is clear, however, that subjecting whole embryos to the action of the drug provides a further method for study of the development of structural and functional relations in the embryonic central nervous system.

[2] Oppenheimer, J. M., *Anat. Rec.*, 1937, **68**, 1.