was 22.3 T.R.U./cc, so that a total of 158 T.R.U. hyaluronidase was excreted. There was no increase of the urinary protein excretion of 22 rats. During the control 18 hour period, 5.7 cc of urine were excreted, containing 1.33 mg protein per cc, or a total of 7.6 mg protein. During the comparable post-injection interval, the animals passed 5.5 cc of urine, that contained 1.33 mg protein per cc for a total of 7.3 mg protein.

Discussion: Meyer(7) has written that "intravenously injected enzyme is rapidly eliminated from the circulation". Seifter(8) found in rabbits a short sojourn of the injected hyaluronidase in the blood as assayed with the mucin-clot method. It was considerably longer when measured by the spreading technique. In the rabbit and the dog, large amounts of the hyaluronidase were excreted in the urine. In the albino rat, intravenously administered hyaluronidase disappeared rapidly from the blood. Approximately 2% of the enzyme was found in the urine in an active turbidity reducing form. The amount of hyaluronidase injected into the animal represented 12.5 mg protein. The absence of significant proteinuria was added evidence of the lack of renal excretion of the enzyme. The fate of the injected enzyme has not been elucidated completely. Hyaluronidase most probably is a small protein molecule(9) and may be lost by simple diffusion from the vascular bed. This diffusion may be increased by the specific action of the enzyme *in vivo*, in which fluid and proteins are actively passed through the capillary wall.(1,2) A small amount of the enzyme was lost in the urine, and an unknown amount was inactivated by the blood inhibitors. As yet, the remainder has not been traced.

The plasma inhibitors were diminished by the administration of hyaluronidase, suggesting a direct action of one on the other. Recovery to normal levels did not occur for 24-72 hours. The source of the newly formed inhibitors has not been found. Wattenberg and Glick(10) have suggested that the inhibitors may be formed in the blood stream itself, since the tissues of the body had no anti-hyaluronidase activity.

Summary: Following the intravenous administration of testicular hyaluronidase to albino rats, the following changes were noted:

1. The maximum concentration of the enzyme was attained within 5 minutes and diminished rapidly, so that at one hour it was no longer detected by turbidimetric methods.

2. Approximately 2% of the hyaluronidase appeared in the urine in an active form.

3. The plasma hyaluronidase inhibitor level was depressed for 8 hours and returned to normal within 24-72 hours.

4. No significant proteinuria resulted.

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Received November 15, 1949. P.S.E.B.M., 1950, v73.

Destructive Action of Astatine^{211} (Element 85) on the Thyroid Gland of the Rat.* (17572)

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The observation that astatine accumulates in the thyroid suggested that this new element might be of possible therapeutic application in hyperthyroidism as has already been demonstrated in the case of radioiodine.(1,2) As-

* This document is based on work performed under the auspices of the Atomic Energy Commission, Contract No. W-7405-eng-48-A.

tatine is not only radioactive with a half-life of 7.5 hours,(3) but unlike most of the artificial radio-elements, it emits alpha particles† rather than electrons and gamma rays. The radiobiological significance of the fact that astatine^{211} emits alpha particles is that each of these nuclear particles arising from the disintegration of an astatine nucleus will dissipate an initial kinetic energy of 6 Mev in about 50 μ of a soft tissue such as the thyroid. The beta rays from the 8-day radioiodine, I^{131}, possess a maximum energy of .6 Mev with a range of nearly 2,000 μ of tissue.

Methods. The At^{211} was produced by the bombardment of bismuth by 29 Mev alpha particles from the 60 inch cyclotron at the Crocker Laboratory. The astatine^{211} was distilled from the bismuth target and collected in 12 N HCl, which in turn was diluted and made isotonic by the addition of an appropriate quantity of sodium hydroxide. The procedures outlined above were derived from a report by Segre and his co-workers which describes the nuclear and chemical properties of astatine.(4) Preliminary thyroid uptake studies in the rat revealed that in a group of eight 200 g animals of both sexes that from 2% to 8% of the administered astatine^{211} was present in the thyroid at the end of 18 hours,(5) the necessary corrections for the decay of the astatine^{211} having been applied. These values are comparable to the results obtained in earlier studies in which guinea pigs were employed as the experimental animals.(1) More detailed studies on the distribution of astatine^{211} in other tissues are now in progress. Three 200 g white rats were selected to observe the radiobiological action of the alpha particle irradiation of the thyroid from the accumulated astatine^{211}. The astatine^{211} in an isotonic solution of NaCl was administered to two of the rats by intraperitoneal injection. They received 10 μc and 50 μc respectively. The third animal was used as a control. After 30 days the 3 animals

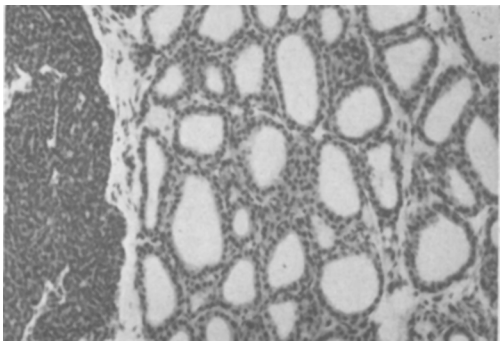

FIG. 1.
Photomicrographs of thyroid and parathyroid tissue of rats. H&E, × 140.
Normal control. (Bouin's fixation).

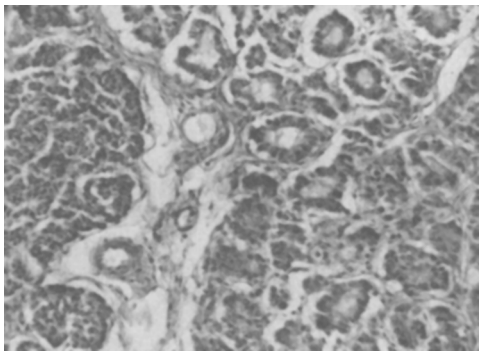

FIG. 2.
Thirty days after injection of 10 μc of At^{211}. (Alcohol fixation).

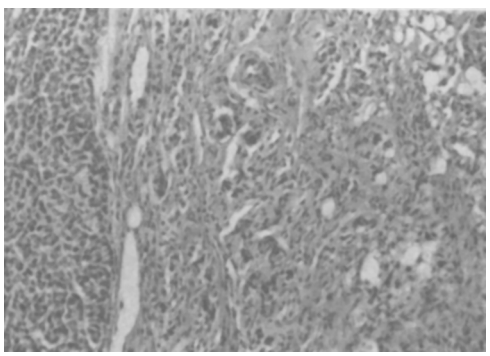

FIG. 3.
Thirty days after injection of 50 μc of At^{211}. (Alcohol fixation).

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2. Hamilton, J. G., *Radiology*, 1942, v39, 541.

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† In addition there are emitted x-rays of 80 Kev which makes possible *in vivo* thyroid uptake studies in man.(2)

4. Johnson, G. L., Leininger, R. F., and Segre, E., *J. Chem. Phys.*, 1949, v17, 1.

5. Unpublished data.

were sacrificed and the thyroids removed. The tissue was fixed, embedded in paraffin, and the sections stained with haematoxylin and eosin for histological study. The sections were cut in such a manner that from each of the 3 thyroids a portion of the parathyroid gland was included.

Results. Photomicrographs of the sections from the control, 10 μc, and 50 μc studies are shown in Fig. 1, 2 and 3 respectively. At the 10 microcurie dosage level it is apparent that there was a marked degree of injury to the thyroid follicles as evidenced by their diminished size, loss of colloid, and increase in size of the follicular epithelium, Fig. 2. The general thyroid architecture is distorted to such a degree that it would seem probable that in this instance the degree of radiation injury approached a level of being totally irreversible even if a recovery period of from six months to a year had been allowed. The adjacent parathyroid tissue did not reveal any observable changes that would suggest radiation injury to this organ. The thyroid tissue in the rat which received 50 microcuries of astatine^{211} is not recognizable as such. Here there is complete obliteration of the follicles, colloid, and follicular epithelium. The thyroid tissue has been replaced by fibrous tissue with some infiltration of lymphocytes and fat cells. In this instance it appears that a complete and irreversible destruction of the thyroid gland took place, as a result of an extreme degree of radiation injury. It is significant to note that there was no histological evidence of manifest radiation injury in the adjoining parathyroid tissue.

Summary. The results from this preliminary study demonstrate the capacity of astatine to induce an extreme degree of radiation injury of the thyroid gland in the rat without apparent involvement of the adjoining parathyroid gland.

Received November 14, 1949. P.S.E.B.M., 1950, v73.

Prevention of Procaine Convulsions by Presidon and Sodium Pentobarbital. (17573)

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While the use of procaine is extensive and relatively safe, an occasional subject is found sensitive to the drug. The toxic reactions to subcutaneous procaine are caused by stimulation of the central nervous system resulting in restlessness and tremors which may proceed to convulsions. There is also an initial period of respiratory stimulation followed by depression of the medullary centers resulting in dyspnea and respiratory collapse. The use of hypnotics in the prevention and treatment of toxic reactions to local anesthetics is based on animal studies which show that hypnotics, especially the barbiturates, depress the convulsive effects of local anesthetics.(1,2) Presidon (Pyrithyldione; 3,3-diethyl-2,4-dioxotetrahydropyridine) is a relatively short acting hypnotic with a wide margin of safety.(3,4) It was shown to inhibit the convulsions produced by caffeine,(3) picrotoxin and Metrazol.(4) It was found to be an effective hypnotic in human subjects.(5) We have extended the studies on the anticonvulsive properties of Presidon to the prevention of pro-

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