members of the Division of Pathology was most helpful. Dr. William A. Reilly, of the Medical School, and Director of the Isotope Unit at the Veterans Administration Hospital at Fort Miley made available the use of their facilities for one of the human studies.

1. Hamilton, J. G., and Soley, M. H., *Proc. Nat. Acad. Sci.*, 1940, v26, 483.

2. Hamilton, J. G., Asling, C. W., Garrison, W. M., and Scott, K. G., *Univ. Calif. Pub. Pharmacol.*, 1953, v2, No. 21, 283.

3. Hamilton, J. G., Durbin, P. W., and Parrott, M. W., 1954, Am. Goiter Assn., submitted for publication.

4. ———, 2nd Radioisotope Conf., Oxford, England, accepted for publication.

5. Garrison, W. M., Gile, J. D., Maxwell, R. D., and Hamilton, J. G., *Anal. Chem.*, 1950, v23, 204.

6. Hollander, J. M., Perlman, I., and Seaborg, G. T., *Rev. Mod. Phys.*, 1953, v25, 469.

7. Hamilton, J. G., and Soley, M. H., *Am. J. Physiol.*, 1939, v127, 557.

8. Durbin, P. W., Hamilton, J. G., and Parrott, M. W., submitted for publication.

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

10. Durbin, P. W., Hamilton, J. G., and Parrott, M. W., submitted for publication.

Received May 25, 1954. P.S.E.B.M., 1954, v86.

Effect of Pretreatment with Propyl Thiouracil on Accumulation of Astatine^{211} by Thyroid Gland of the Rat.* (21101)

PATRICIA W. DURBIN, JOSEPH G. HAMILTON, AND MARSHALL W. PARROTT.
From the Division of Medical Physics, Experimental Radiology and Medicine, Crocker Laboratory, University of California, Berkeley and San Francisco.

It has long been known that a variety of chemical agents act as anti-thyroid drugs to reduce or almost completely prevent the introduction of iodine into tyrosine and subsequently the production of thyroid hormone (1,2). Propyl thiouracil and related anti-thyroid drugs have been used extensively in the treatment of human thyrotoxicosis(3,4). Astatine is the heaviest member of the halogen group, and certain of its chemical properties resemble those of iodine. There are, however, some rather significant dissimilarities(5). Although 18 radioactive isotopes of astatine have been identified, no stable isotopes of this element are known to exist(6). The particular radioisotope used in these and other studies is the 7.3 hour At^{211} which decays by the emission of alpha-particles and 80 Kev x-rays.†

The capacity of the thyroid gland to concentrate and retain At^{211} has been demonstrated in experimental animals and man (7-10). The present studies were undertaken in order to determine the possible effect of propyl thiouracil upon accumulation and retention of At^{211} by the thyroid gland of the rat and to compare this effect with that obtained using carrier-free I^{131}. It was also hoped that these experiments would help to shed some light on the mode of entry of astatine into the thyroid gland and on its chemical state in that organ.

Methods. The animals employed for these studies were 75-day-old female Sprague-Dawley rats weighing about 165 g, all received from the dealer at the same time and maintained for 3 weeks prior to the start of the experiment on tap water and a pelleted stock diet which is in general use throughout the University of California Radiation Laboratory.‡ Both food and water were given

* This work was performed under contract of the University of California under the U. S. Atomic Energy Commission.

† Sixty per cent of the At^{211} nuclei decays by K-capture to form Po^{211} with a 0.5 second half-life, and 40% decays by alpha-particle emission to form Bi^{207}.

‡ This diet is similar in composition to "Diet 14" developed by the University of California Institute of Experimental Biology and contains a fairly large amount of added iodide. To every 270 lb of feed is added 300 ml of an 0.45% solution of KI.

TABLE I. Effect of Administration of 0.1% Propyl Thiouracil in Drinking Water for 11 Days on Body Weight, Thyroid Weight and Thyroidal Uptake of Intravenously Administered At^{211} and I^{131} in the Female Sprague-Dawley Rat.*

	Propyl thiouracil water	P†	Tap water
Animal wt	156.4 ± 1.68 g	<.02	164.8 ± 2.88 g
Thyroid "	37.4 ± 1.31 mg	<.01	15.2 ± .61 mg
Thyroid uptake, % admin. At^{211}	3.82 ± .26	<.01	.23± .0025
Thyroid conc., % At^{211}/g wet tissue	105.4 ± 6.61	<.01	16.2 ± 1.8
Thyroid uptake, % admin. I^{131}	1.13 ± .16	<.01	7.28± 1.47
Thyroid conc., % I^{131}/g wet tissue	30.3 ± 4.5	<.01	445 ± 83.3

* Stand. error of mean $= \sqrt{\frac{\Sigma d^2}{n\,(n-1)}}$.

† For calculation of P see Fisher(12).

ad lib. Propyl thiouracil was administered to 20 rats in the drinking water at a concentration of 0.1% by weight for 11 days. On the 10th day, 10 of these rats were each given 5 μc of At^{211}§, and 10 were each given 6 μc of I^{131}. Both At^{211} and I^{131} were administered intravenously. Ten rats that had received no pretreatment served as controls. Five of these were each given 5 μc of At^{211} and 5 each received 6 μc of I^{131}. Twenty-one hours after the administration of the radiohalogens the rats were sacrificed with chloroform and the thyroids were dissected out and weighed. The At^{211} and I^{131} contents of the thyroid glands were measured with an NaI-Tll scintillating crystal gamma counter. It was possible to measure the At^{211} in this manner, since its radioactive decay is associated with an 80 Kev x-ray.

Results. The results of these experiments are shown in Table I. The single most impressive observation is the nearly 20-fold enhancement of the accumulation of At^{211} in the thyroid glands of the animals treated with propyl thiouracil. This is in distinct contrast to the diminution of the accumulation of I^{131} in the thyroid glands of the animals treated with this drug, a result that has been shown previously by Taurog *et al.*(1). In fact, the concentration of At^{211} by the thyroid glands of the treated animals is more than 3 times the concentration of I^{131} in this group.

It should be noted that the values for the uptake of both I^{131} and At^{211} in the thyroid glands of the control animals are somewhat low. This is presumably due to the presence of a relatively large amount of stable iodine in the diet employed. It has been shown that the administration of stable iodide decreases the accumulation of both I^{131} and At^{211} in the thyroid gland of the rat(8). The uptake of At^{211} in the treated rats is far greater than has been seen previously even when they had been maintained on a low iodine diet(8).

Discussion. These results were quite unexpected. A possible explanation for the tremendous increase in the thyroidal uptake of At^{211} following the administration of propyl thiouracil is presented here with the understanding that it is highly speculative.

The apparent action of propyl thiouracil and related anti-thyroid drugs is to prevent the synthesis of iodotyrosine and similar compounds(1). From the results of experiments described here it appears that the effect of propyl thiouracil on the accumulation of At^{211} by the thyroid gland is quite different from its effect on the uptake of I^{131}. The inorganic chemistry of astatine is complex and not too well understood and nothing is known about its biochemistry. Astatine has been shown to possess at least 4 valance states, At^-, At^0, AtO^- and a higher oxidized state(5). It is likely that in the thyroid gland there are enzymes capable of oxidizing At^0 to AtO^-, the lowest of the oxidized states, and will thus tend to rob the thyroid gland of its accumulated astatine. In the presence of propyl

§ The physical and chemical procedures for the preparation of At^{211} are given elsewhere(11).

thiouracil it may very well be that the oxidation of At^0 to AtO^- is prevented permitting the continued accumulation and retention of astatine in some type of loose organic binding.

Summary. A study has been made of the accumulation of I^{131} and At^{211} in normal and propyl thiouracil-treated rats. A very marked enhancement of the accumulation of At^{211} in the thyriod gland has been observed following administration of propyl thiouracil. This is in contrast to the diminution of the uptake of I^{131} by the thyroid glands of the rats receiving propyl thiouracil.

The authors wish to thank Dr. Warren M. Garrison for his continued interest in this work and his many helpful suggestions, Mr. G. B. Rossi and the crew of the 60-inch cyclotron who were responsible for the production of the astatine, and Mrs. Marilyn Williams for technical assistance.

1. Taurog, A., Chaikoff, I. L., and Feller, D. D., *J. Biol. Chem.,* 1947, v171, 189.

2. Astwood, E. B., *Ann. N. Y. Acad. Sci.,* 1949, v50, No. 5, 419.

3. Lahey, F. H., and Bartels, E. C., *Ann. Surg,* 1947, v125, 572.

4. McCullagh, E. P., *Ohio State Med. J.,* 1950, v46, 127.

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

6. Hollander, J. M., Perlman, I., and Seaborg, G. T., *Rev. Mod. Phys.,* 1953, v25, 469.

7. Hamilton, J. G., and Soley, M. H., *Proc. Nat. Acad. Sci.,* 1940, v26, 483.

8. Hamilton, J. G., Asling, C. W., Garrison, W. M., and Scott, K. G., *Univ. Calif. Pub. Pharmacol.,* 1953, v2, No. 21, 283.

9. Hamilton, J. G., Durbin, P. W., and Parrott, M. W., submitted for publication.

10. Shellabarger, C. J., and Godwin, J. T., 1954, Am. Goiter Assn., submitted for publication.

11. Durbin, P. W., Hamilton, J. G., and Parrott, M. W., submitted for publication.

12. Fisher, R. A., *Statistical Methods for Research Workers,* 1950, Oliver and Boyd, Edinburgh.

Received May 25, 1954. P.S.E.B.M., 1954, v86.

Localization of Antimony in Blood. (21102)

CARL TABB BAHNER.* (Introduced by G. A. Andrews.)

From the Medical Division, Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn., under contract with the U. S. Atomic Energy Commission.

This study is an outgrowth of an observation by Andrews and Hamilton of this laboratory. Rats to which they gave a single intravenous injection of fuadin labeled with Sb 122, 124 showed a relatively high concentration of the antimony in the erythrocytes. The concentration tended to be maximal in approximately 8 days. Earlier workers had noted high concentration of antimony in red cells following administration of tartar emetic and other antimonial drugs(1,2). Several alternative hypotheses, which might be offered to account for these observations, have been explored. The results obtained are consistent with the hypothesis that the antimony in the red cells is attached to the protein portion of the hemoglobin.

Methods. The labeled antimony catechol disulfonate complex (fuadin) for this work was prepared as follows: A quartz ampoule containing 75 mg of Sb_2O_3 was irradiated in the Oak Ridge pile 1 week or more. The ampoule was transferred to a holder behind a lead screen, the neck was broken off, and 0.5 ml of concentrated HCl was introduced by means of a pipette. The mixture was stirred 10 minutes by a slow stream of air bubbles from a capillary tube. A solution of 0.63 g of sodium catechol disulfonate† in a little water was added while stirring was continued. These quantities provided an excess of the complexing agent. The solution was washed into a graduated test tube, neutralized with 10% NaOH to pH 7, and was

* Carson-Newman College, Jefferson City, Tenn.

† We are indebted to Dr. C. M. Suter of Sterling-Winthrop Research Institute for supplying this compound.