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Publication Date

1954-05-01

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UCRL-2604
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Contract No. W-7405-eng-48

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May 24, 1954

Berkeley, California

ACCUMULATION OF ASTATINE-211 BY THE THYROID GLAND IN MAN*

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ABSTRACT

The accumulation of At²¹¹ by the thyroid gland in patients with thyroid disorders has been demonstrated; it appears to be relatively higher than in experimental rats. There may be a correlation between At²¹¹ uptake and stable iodine in thyroid tissue. There was no discernible accumulation of At²¹¹ in metastases of papillary adenocarcinoma in cervical lymph nodes.

* This work was performed under the auspices of the U.S. Atomic Energy Commission.

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INTRODUCTION

Astatine-211, which is the last member of the halogen group of elements, has been found to be accumulated by the thyroid glands of experimental animals to a degree similar to that of iodine-131.^{1,2,3,4} Since the average energy of the alpha particles arising from the disintegration of At²¹¹ is 6.8 Mev and the range in tissue is but 70 microns, the degree of specific ionization produced is much greater than by beta particles from I¹³¹. The maximum energy of I¹³¹ beta particles is 0.6 Mev and the range is 2,000 microns.

These extensive studies with At²¹¹ have been undertaken because the short range and high specific ionization of the alpha particles of At²¹¹ (as compared to the much longer range and more weakly ionizing beta particles from I¹³¹) may have clinical applications in treatment of thyroid disorders, in particular hyperthyroidism.

For several years this laboratory has been engaged in a study of the rate and degree of accumulation of both I¹³¹ and At²¹¹ in the thyroid gland and in other tissues and organs of experimental animals. The acute and chronic effects of relatively large amounts of these two radiohalogens have also been investigated.^{2,3,4} Results indicated that it would be safe to attempt tracer studies with At²¹¹ in patients who were to be subjected to surgical thyroidectomy.

METHODS

The At²¹¹ was prepared by a modification of the procedure described by Garrison, et al.⁵ Each patient received 50 microcuries of At²¹¹ in a solution of 25 cc of water at intervals which ranged from 13-1/4 to 22 hours prior to surgery. Food was withheld for at least two hours

prior to and after the oral administration of the solution of At^{211} .

The patients selected in this group were all more than 30 years of age, and in the majority, either a complete thyroidectomy was performed or a remaining lobe of the thyroid gland was removed.

In all, there were eight patients in the series. One had a papillary adenocarcinoma of the thyroid gland with metastases to the cervical lymph nodes. Following the removal of this surgical specimen it was immediately weighed and a weighed portion was taken for routine hospital pathological studies, while the remainder was brought to this laboratory for the assay of its At^{211} content as well as the total iodine content. Before the specimen was subjected to physical and chemical processing, a small representative portion was removed by the use of the dissecting microscope. This specimen was then fixed in 10% neutral formalin, subjected to routine paraffin impregnation and clearing techniques, and finally stained with hematoxin and eosin. Since the decay scheme of At^{211} is associated with the emission of 80-kev x-rays,⁶ it was possible to make a relatively accurate measurement of the At^{211} content of the wet sample employing a sodium iodide--thallium iodide activated crystal scintillation counter.

Two patients had previously received I^{131} , which made this type of determination essentially impossible owing to the presence of gamma rays from I^{131} . The stable iodine content in these studies was determined in a carbon tetrachloride solution by means of a spectrophotometer rather than by titration employing dilute solutions of sodium thiosulfate used in earlier experiments.⁷ The At^{211} was quantitatively isolated from the specimens by a procedure to be reported elsewhere.⁸

RESULTS

The results of the experiments are shown in Table I. A number of observations may be made. The accumulation of At^{211} by the thyroid gland appears to be relatively higher than has been observed in some of the previously reported experiments, which employed laboratory animals.² Admittedly, the number of patients is too limited to draw conclusions of a statistical nature, but there certainly does appear to be a trend of a relatively higher uptake. It should be noted that in three patients only one lobe of the thyroid gland was available for assay. Moreover, histologically, the thyroid tissue obtained from most of these patients was obviously quite abnormal. A very low uptake of At^{211} was noted in a patient who had had a very unusual series of therapeutic attempts to control his disease and at one stage had received both thyroxin and Lugol's Solution. In the one patient from whom an entire relatively normal thyroid gland was available, the total uptake was approximately 17% of the administered dose. There appears to be a correlation of the amount of At^{211} accumulated per gram of tissue with the stable-iodine content per gram of tissue. In general, when there was a relatively high total iodine content, the astatine content was increased. Finally, it should be noted that in the patient with a metastatic papillary adenocarcinoma there was no demonstrable accumulation of At^{211} in the cervical lymph nodes, which contained essentially nothing but neoplastic tissue showing no tendency towards the formation of either follicles or colloid.

Table I

The Uptake of Orally Administered Astatine-211 (Eka-Iodine) by the Human Thyroid Gland in Various Disorders of that Organ

Name	Age	Sex	Thyroid Sample	Diagnosis	Time hours	% At ²¹¹ in sample	Conc. At ²¹¹ %/g wet tissue	Mg I ₂ in sample	Mg I ₂ /g wet tissue
I.H.	~40	F	Left lobe	Grossly normal	15	5.95	0.54	32	2.94
			Right lobe	" "	18	11.85	1.19	30.1	3.01
			Cervical lymph node	Papillary adenocarcinoma	18	<0.01	<0.001	-	-
C.A.	41	F	Right lobe	Nontoxic metaplasia	13 1/4	2.85	0.27	5.19	0.49
E.B.	31	F	Whole gland	Nontoxic nodular goiter with cyst formation	16 1/4	6.75	0.55	6.34	0.53
D.M.	35	F	Whole gland	Toxic goiter (Lugolized)	15	6.66	0.21	13.42	0.43
H.	52	M	Right lobe	Graves' Disease (Thyroxine, Lugolized)	18	0.172	0.017	5.8	0.58
T.A.	43	F	Left lobe	Nontoxic nodular goiter	14	6.55	0.26	-	-
C.W.	56	M	Left lobe	Grossly normal	13 1/2	4.90	0.39	3.78	0.50
			Right lobe	Nontoxic nodular goiter	13 1/2	2.56	0.024	7.12	0.07
R.C.	68	M	Whole gland	Nontoxic nodular goiter	22	4.61	0.021	28.5	0.13

DISCUSSION

With the exception of the one patient who had received thyroxin, there was a quite good correlation between accumulation of At^{211} per gram of thyroid tissue and the amount of stable iodine present. Correlation between the histological findings in thyroid tissue from the eight patients and the measures of stable iodine present per gram and of uptake of At^{211} is difficult. The interpretation of the apparent relatively greater concentration of At^{211} by human thyroid tissue as contrasted to animal studies is hard to establish. If this apparent effect can still be demonstrated involving a larger number of patients, then consideration must be given to the factors such as total iodine intake and the possible existence of the species difference. The At^{211} uptake studies in the monkey are too limited to be of any value in attempting to make any comparison with humans presented in this paper.²

The evaluation of the potential use of At^{211} for the therapy of human thyrotoxicosis must of necessity await much more information, derived both from further studies with experimental animals and from more extensive human uptake studies.

The chemical properties of astatine are considerably different from those of iodine in many respects.⁹ An indication of the biochemical differences between astatine and iodine has been presented in another paper. The effect of pretreatment with propyl thiouracil resulted in the enhancement of the accumulation of At^{211} in the thyroid gland in the rat by a factor of nearly 20, while there was, at the same time, a decrease in accumulation of iodine-131.¹⁰ With these considerations in mind, there is a very remote possibility that certain types of

neoplasms in the thyroid gland may more effectively accumulate At^{211} than I^{131} . This concept is purely hypothetical and is based upon the probability that At^- may be oxidized to At^0 more readily than I^- may be oxidized to I_2 . It should be emphasized that this phase of the discussion is purely speculative in nature, and the very questionable validity of this theory can be tested only by doing tracer studies on many patients suffering from various types of neoplasms of the thyroid gland.

SUMMARY

1. The accumulation of At^{211} by the thyroid gland in patients suffering from various disorders of that organ has been demonstrated.
2. The accumulation of At^{211} by the thyroid glands of these patients appears to be relatively higher than has been observed in experiments employing rats.
3. There may be a correlation between the uptake of At^{211} and stable iodine in thyroid tissue.
4. One patient with papillary adenocarcinoma showed no discernible accumulation of At^{211} in metastases present in cervical lymph nodes.

ACKNOWLEDGMENTS

The production of At²¹¹ was the responsibility of Mr. G. Bernard Rossi and the staff of the 60-inch cyclotron at this laboratory. The continued interest and encouragement by Robert S. Stone, M.D., Professor of Radiology; Earl R. Miller, M.D., Professor of Radiology, and members of the Staff of the Division of Radiology; Theodore L. Althausen, M.D., Professor of Medicine; Morris E. Dailey, M.D., Assistant Professor of Medicine; H. Glenn Bell, M.D., Professor of Surgery; Henry H. Searls, M.D., Associate Professor of Surgery; and the surgical staff at the University of California School of Medicine made the experiments with human subjects possible. The assistance and cooperation of members of the Division of Pathology were most helpful. William A. Reilly, M.D., Clinical Professor of Pediatrics, University of California School of Medicine, and Director of the Isotope Unit at the Veterans Administration Hospital at Fort Miley, made their facilities available for one of the human studies.

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