Radioiodine Treatment of Paroxysmal Supraventricular Tachycardia in the Euthyroid Patient

By Eliot Corday, M.D., Herbert Gold, M.D., and Henry L. Jaffe, M.D.

Twenty-five euthyroid patients subject to recurrent paroxysmal supraventricular tachycardias, which were resistant to usual prophylactic therapy, were treated with radioactive iodine. In many of the patients, with follow-up ranging up to 6 years, there were no recurrences of the tachycardia subsequent to the isotope therapy. Two patients were considered refractory to this therapy.

In the euthyroid patient, rapid supraventricular tachycardias occur and are often resistant to prophylactic treatment with quinidine or pronestyl. In an attempt to evaluate the effect of radioactive iodine in cases of supraventricular tachycardia resistant to antiarrhythmic drugs, the authors treated 25 such patients with radioactive iodine and observed them for periods up to 6 years. In all instances prophylactic treatment with antiarrhythmic drugs had failed to prevent recurrent attacks. Twenty-two of these patients had arteriosclerotic heart disease and 3 had rheumatic heart disease. Many of the patients had recurrent attacks as often as 4 times a day. In many instances, during the paroxysm of tachycardia, the patient suffered severe anginal discomfort. All patients were considered euthyroid on the basis of clinical examination by 3 physicians and normal laboratory findings, including serum protein-bound iodine and radioactive iodine uptake.

The patients with arteriosclerotic heart disease were selected from private practice. In these patients, the clinical history and the resting electrocardiogram or Master 2-step test revealed indications of coronary artery disease. The 3 patients with rheumatic heart disease all had multivalvular disease. The electrocardiograms during the episodes of tachycardia revealed supraventricular rhythms.

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either paroxysmal atrial tachycardia, nodal tachycardia, or atrial fibrillation.

Classification of Results

The results of treatment with radioactive iodine were classified as good, fair, or poor. A result was considered good when no recurrences or very few paroxysms of tachycardia occurred following the period of treatment. A result was classified as fair when there were no or very few paroxysms for 12 months after the period of treatment following which time there were occasional recurrences. A poor result was one in which radioactive iodine failed to affect the frequency of paroxysms.

Methods and Material

Treatment. We prefer to give oral doses of 6 mc. (millicuries) of radioactive iodine at weekly intervals until the patient has received a total of 25 to 30 mc. We have chosen the small dose technic to avoid the danger of suddenly releasing large amounts of thyroxin into the blood stream from the gland. This could produce a temporary increase in metabolism which, in a severely ill cardiac patient, might be detrimental. It usually took 2 to 3 months following treatment for the radioactive iodine to reach maximum hypometabolic levels. This is considered the usual period of treatment. However, some patients required a further course of 1st treatment adequately to depress thyroid function. Although our purpose was to induce a state of only relative hypothyroidism, occasionally some of our patients developed clinical myxedema. Four of the 25 patients became myxedematous following 1st therapy. This was corrected by the administration of thyroid in doses varying from 6 mg. to 45 mg. a day. All of the patients were comfortable and had few or no complaints as a result of the reduced thyroid function.

Medical Management Following Radiation. During the period of treatment, which usually lasted

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ATTACKS

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Fig. 1 Top. Clinical course of case 1, euthyroid patient treated with radioactive iodine for recurrent attacks of atrial tachycardia. Note that there have been no recurrences of the tachycardia in the last 61 months. This is a good result.

Fig. 2 Bottom. Graph of case 2 showing clinical course following treatment with radioactive iodine for recurrent episodes of atrial tachycardia. Note that there was only 1 episode of tachycardia in a 46-month period and this was precipitated by a gastrectomy. This is a good result.

from 8 to 12 weeks, the patients were asked to curb their physical and emotional activities. Following the period of treatment, the patients were examined for signs of myxedema, such as coldness, lacrimation, joint pain, muscle pain, lethargy, weight gain, edema of eyelids, swelling of submaxillary glands, dry skin, and cardiac enlargement. As soon as any sign of myxedema occurred, the patient was given 6 mg. of thyroid daily in the morning. If the early signs of myxedema did not subside within 2 weeks, the same dosage of thyroid was administered 2 or 3 times a day.

Case Reports. Reports of cases showing good, fair, and poor results of treatment with radioactive iodine follow.

Case 1 (fig. 1). A 51-year-old man had severe coronary artery disease and paroxysms of nodal tachycardia that occurred once or twice a day. They usually awakened him from sleep in the early morning hours. During the tachycardia, he experienced severe precordial pain radiating down the left arm. The patient also stated that heavy physical exertion, such as walking quickly, caused
Fig. 3 Top. Clinical course of case 3. Prior to treatment with I\textsuperscript{131} this patient had recurrent episodes of atrial tachycardia every 2 weeks. Following treatment, she has had but 2 episodes in a 51-month period. This is a good result.

Fig. 4 Bottom. Clinical course of case 4 showing a fair result following treatment with radioactive iodine. Attacks were induced by overmedication with thyroid extract.

similar pain. The resting electrocardiogram was normal; however, nodal tachycardia with marked S-T segment depression occurred following exercise for the Master 2-step test. Roentgenograms of the chest demonstrated no cardiac enlargement. The basal metabolic rate was –4 per cent, protein-bound iodine was 4.2 meg. per 100 ml., and blood cholesterol was 272 mg. per cent. The 24-hour I\textsuperscript{131} uptake was 18 per cent. The patient was given 25 mc. of radioactive iodine in divided doses in a 4-week period. The attacks then lessened in frequency over a period of 3 months following the treatment with radioactive iodine. In the fourth month, the patient had only 1 further severe attack of nodal tachycardia, at which time the 24-hour I\textsuperscript{131} uptake was 14 per cent and the protein-bound iodine, 4.0 meg. per 100 ml. In the last 61 months, the patient has experienced no attacks of tachycardia. Recent basal metabolic rate was –4 per cent, protein-bound iodine, 3.2 meg. per 100 ml., blood cholesterol 310 mg. per cent; and 24-hour I\textsuperscript{131} uptake 30.6 per cent. The result was classified as good in this patient followed for 66 months.
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Case 2 (fig. 2). A 48-year-old woman suffered recurrent attacks of atrial tachycardia every second or third month, which lasted for 3 to 4 hours. These attacks were not relieved by carotid sinus massage or other maneuvers, but appeared to respond to intravenous Cedilanid 3 hours following its administration. The patient experienced severe precordial pain within a half hour following the onset of the attack of tachycardia, which radiated down the left arm and into the left side of the jaw. During the paroxysms she became dyspneic. Physical examination during a free interval showed the heart to be normal in size and no murmurs were present; the blood pressure was 118/80 mm. Hg. The skin was dry and there were no signs of thyrotoxicosis. X-ray examination of the chest showed no abnormalities. The Master 2-step test was positive. The basal metabolic rate was +1 per cent, protein-bound iodine was 4.6 mcg. per 100 ml.; and blood cholesterol was 227 mg. per cent. The 24-hour I\textsuperscript{131} uptake was 23 per cent. The patient was given Pronestyl and Quinidine, but these drugs failed to prevent recurrent episodes of tachycardia. She was then given 30 mc. of radioactive iodine in divided weekly doses. The paroxysms recurred 4 times over a 9-week period and then ceased. The 24-hour I\textsuperscript{131} uptake was 19 per cent. Eighteen months after treatment with radioactive iodine, her 24-hour I\textsuperscript{131} uptake was 32 per cent. Although she was asymptomatic, she was given another 3 mc. of radioactive iodine. At the twenty-first month after the original treatment, the 24-hour I\textsuperscript{131} uptake was 16 per cent. Twenty-four months after the treatment with radioactive iodine a carcinoma of the fundus of the stomach was removed by a gastrectomy. On the third postoperative day, a paroxysm of atrial tachycardia occurred which stopped 2 hours after Cedilanid was administered intravenously. The patient, however, did not experience any precordial distress during this paroxysm. For 22 months since this last attack there has been no recurrence. The 24-hour I\textsuperscript{131} uptake at the thirtieth month was 14 per cent and then at the forty-second month was 21 per cent. The protein-bound iodine was 4.2 mcg. per 100 ml. The results were classified as good in this patient followed for 46 months.

Case 3 (fig. 3). A 51-year-old woman complained of severe “racing spells” of the heart due to paroxysmal atrial tachycardia which occurred every second or third week. Shortly after the onset of these attacks she developed severe precordial pain radiating to the left arm, associated with choking sensations. Examination revealed a rather obese woman of 170 lb. with a dry skin and no evidence of thyrotoxicosis. The heart was normal in size and there were no murmurs. The resting electrocardiogram was normal. However, the Master 2-step test was considered positive. The basal metabolic rate was −5 per cent, protein-bound iodine was 4.1 mcg. per 100 ml., and blood cholesterol was 242 mg. per cent. The 24-hour I\textsuperscript{131} uptake was 34 per cent. She was given 30 mc. of radioactive iodine in divided weekly doses. The paroxysms of atrial tachycardia continued for a 13-week period and then ceased. Twelve months following treatment with radioactive iodine, she experienced an episode of palpitation and an electrocardiogram revealed supraventricular tachycardia. However, at this time she did not notice any chest discomfort except for rapid heart action. It was then discovered that the patient had been taking 180 mg. of thyroid daily on her own initiative in an attempt to reduce her weight and this drug was discontinued. Her 24-hour I\textsuperscript{131} uptake was 21 per cent. She was given another 8 mc. of radioactive iodine. No further episodes of tachycardia occurred until the twenty-seventh month following treatment, at which time she had a short paroxysm of tachycardia, but again did not experience any precordial pain. At this time she was taking 60 mg. of thyroid, self-prescribed. The 24-hour I\textsuperscript{131} uptake was 6 per cent. Therefore, she was not given any additional treatment with radioactive iodine. During a further 27-month period she has not developed any more episodes of tachycardia. Her basal metabolic rate at this time was −21 per cent; protein-bound iodine was 4.2 mcg. per 100 ml.; and blood cholesterol was 324 mg. per cent. The 24-hour I\textsuperscript{131} uptake was 13 per cent. The result was considered good in this patient followed for 54 months.

Case 4 (fig. 4). A woman 55 years of age had sustained several attacks of coronary thrombosis. In addition, attacks of paroxysmal atrial tachycardia occurred every 3 to 4 months. Prior to treatment with radioactive iodine, she was admitted to the hospital on 4 occasions in a 6-month period because of severe angina associated with the tachycardia. The patient was markedly obese. Her weight was 172 lb. The heart sounds were normal. Roentgenogram of the chest revealed a normal size heart and clear lung fields. The electrocardiogram showed an old myocardial infarction. The basal metabolic rate was −12 per cent, protein-bound iodine 3.8 mcg. per 100 ml.; and blood cholesterol was 210 mg. per cent. The 24-hour I\textsuperscript{131} uptake was 31 per cent. Because of the severe angina resulting from the recurrent attacks of tachycardia, which could not be controlled with antiarrhythmic drugs, the patient was given 32 mc. of radioactive iodine in divided weekly doses. She had 3 further attacks, 3, 20, and 54 days following treatment. Twelve months following the initial dose, her 24-hour I\textsuperscript{131} uptake was 22 per cent. She was then given another 11 mc. of radio-
active iodine. No further episodes of tachycardia occurred until the fifteenth month following treatment. The 24-hour I\textsuperscript{131} uptake at the 15th month was 20 per cent. The patient then developed evidence of hypothyroidism. She was therefore given 45 mg. of thyroid per day in divided doses for a 7-month period. Subsequently, in the eighteenth month she developed 1 paroxysm of tachycardia. In the nineteenth month she experienced a very severe episode of tachycardia, which was converted to sinus rhythm by intravenous Cedilanid. This attack was associated with severe precordial pain. Her 24-hour I\textsuperscript{131} uptake shortly after this episode was 11 per cent. Following the news of the death of her father, 22 months after the first treatment with radioactive iodine, she again experienced a severe episode of tachycardia and another episode 1 month later. During the next 21 months the dosage of thyroid was reduced from 45 to 6 mg. daily and she had no further episodes of tachycardia. Forty-two months after treatment, her basal metabolic rate was -24 per cent, protein-bound iodine was 3.6 mg. per 100 ml., and blood cholesterol was 260 mg. per cent. The 24-hour I\textsuperscript{131} uptake was 5.0 per cent. Because the patient had experienced 5 episodes of tachycardia in the 48 months following treatment with radioactive iodine, the result was classified as fair. The probable reason for the recurrences of the tachycardia was the ingestion of excessive thyroid medication.

**Case 5 (fig. 5).** A woman 61 years of age with rheumatic heart disease developed paroxysmal atrial fibrillation every third or fourth week. There was a rumbling diastolic apical murmur and other findings indicating mitral valvular disease. Clinically her appearance was that of hypothyroidism. The protein-bound iodine was 4.3 mg. per 100 ml., and the blood cholesterol was 210 mg. per cent. The 24-hour I\textsuperscript{131} uptake was 31 per cent. She was given 30 mc. of radioactive iodine in divided weekly doses. Following the period of administration of this treatment, no further episodes occurred for a 4-month period. At this time, because of marked improvement in her cardiac condition, hysterectomy could be done. Following this procedure, the patient developed a menopausal psychosis. The 24-hour I\textsuperscript{131} uptake at this time was 17 per cent, and the protein-bound iodine was 3.5 mg. per 100 ml. Paroxysms then recurred almost daily. An additional radioactive iodine treatment of 29 mc. was therefore given and the attacks continued. At the end of the fifteenth month the protein-bound iodine was 1.3 mg. per 100 ml., and the blood cholesterol was 288 mg. per cent. In this patient, the result was classified as poor. She was subsequently readmitted to the Cedars of Lebanon Hospital Clinic with subacute bacterial endocarditis and had chronic atrial fibrillation.

### RESULTS

A total of 25 patients were treated with radioactive iodine. Of these, 20 had a good result, 17 patients had no paroxysms of arrhythmia, and 3 had an occasional paroxysm following treatment with radioactive iodine. However, in these latter patients, the paroxysms were induced by surgery or the ingestion of excessive thyroid.

Three other patients had a fair result, viz., no recurrence of tachycardia after treatment for periods of 12 to 14 months, but following this period, they experienced occasional episodes of tachycardia, much reduced in number and severity. Because there was a decided improvement maintained for a 12 to 14-month period, the results in these 3 patients were classified as fair. One of the patients was subsequently found to require further treatment with radioactive iodine because of return of function of the thyroid gland.

The results in 2 patients were classified as poor. These patients were both psychotic and difficult to evaluate.

Two patients who had severe angina during their paroxysms of tachycardia continued to experience occasional episodes of tachycardia after treatment with I\textsuperscript{131} but no longer suffered anginal pain with these attacks. Pain no longer occurred in association with the tachycardia although the ventricular rate

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TREATMENT OF PAROXYSMAL TACHYCARDIA

was at least as rapid as it was in the paroxysms observed before treatment.

DISCUSSION

The mechanism of action of radioactive iodine in abating and reducing the number of attacks of paroxysmal tachycardia in euthyroid subjects is difficult to understand. Consideration was given to the possibility that relative hyperthyroidism might have been present in these patients, despite the absence of any clinical or laboratory evidence for thyroid hyperfunction. However, it is extremely improbable that all the patients in this series who obtained favorable results could have had masked hyperthyroidism.

The fundamental genesis of the exaggerated cardiovascular responses, manifested by tachycardia, increased pulse pressure, booming heart sounds, systolic murmurs, increased blood volume and decreased circulation time in hyperthyroidism is not fully understood. No constant or specific myocardial lesions are found in the hearts of patients who have died of thyrotoxicosis. In this condition, however, there is an apparent hypersensitivity to circulating epinephrine. Furthermore, it has been shown by Raab that the heart in hyperthyroidism contains more epinephrine than in the euthyroid state. It is well known that epinephrine increases the irritability of even the normal heart. It is possible, therefore, that at least some of the cardiovascular manifestations commonly observed in hyperthyroidism may be related to the effects of epinephrine. This would seem a plausible explanation for the frequent occurrence of such arrhythmias as atrial tachycardia and fibrillation in patients with hyperthyroidism. This hypothesis, however, cannot explain how the production of a hypothyroid state often abolishes these arrhythmias in euthyroid patients. It may, of course, be theorized that the epinephrine content of cardiac muscle in our series of euthyroid patients is more than normal, or that the heart in this condition is relatively sensitive to normal amounts of thyroid, but evidence to support such a theory is lacking. It is also possible that in euthyroid patients with arrhythmias the irritability of the cardiac muscle is such that it cannot tolerate normal levels of thyroid hormone.

Ullrick and Whitehorn have demonstrated that under the influence of thyroid hormone the basic atrial metabolism is more markedly increased than that of the ventricle. The finding of an unusual sensitivity of the atrium to the action of thyroid hormone offers a physiologic basis for the atrial tachycardias that are so characteristic of hyperthyroid heart disease. By treatment of the euthyroid patient with radioactive iodine we probably decrease the level of atrial metabolism and thus the excitability. The change in atrial metabolism probably prevents recurrence of the tachycardias. Freedberg stated "a significant number of euthyroid patients with persistent auricular fibrillation have demonstrated a reversal to normal sinus rhythm after the induction of hypothyroidism."

It is interesting that 2 of 3 patients who previously had precordial pain during the paroxysms, no longer had pain with recurrent attacks after treatment with radioactive iodine. It has been suggested that radioactive iodine, when administered for treatment of angina pectoris, lessens the work of the heart. However, in our 3 patients with recurrent paroxysms of tachycardia after \( I^{131} \) treatment, the heart rate was at least as fast as before treatment. Therefore, it seems doubtful that the work load of the heart was really reduced by the \( I^{131} \) during a pain-free episode of tachycardia. However, it is possible that in the hypothyroid state the metabolic requirements of the myocardium may be reduced. Thus, with lessened demand for coronary flow, myocardial ischemia and angina might be less likely to occur. This could account for the brilliant success of the treatment for angina pectoris by the induction of hypothyroidism.

Whatever may be the mechanism by which the reduction in thyroid function decreases the incidence of arrhythmias, it seems clear that the administration of \( I^{131} \) is a simple, convenient, and relatively safe method for producing hypothyroidism and preventing
supraventricular cardiac arrhythmias. The use of propylthiouracil for the same purpose was investigated by us in another group of euthyroid patients. Although this drug was often found effective in reducing the frequency of paroxysms of arrhythmia through depression of the thyroid function, it was considered to be less practical and less safe than I$^{131}$.

**Summary**

Twenty-five euthyroid patients with paroxysmal supraventricular tachycardias were treated with radioactive iodine in an attempt to prevent recurrence of the paroxysmal arrhythmias. The production of a relative degree of hypothyroidism appears to be necessary in order to abolish episodes of supraventricular tachycardias in previously euthyroid patients resistant to other forms of treatment. The mechanism by which such attacks are prevented by suppressing thyroid function is not clear and should be studied further. Of the 25 euthyroid patients treated, 20 obtained good results. In 3 patients, the results were considered fair. In the remaining 2 patients, both of whom were psychotic, the treatment failed. In euthyroid individuals with paroxysmal supraventricular tachycardias that do not respond to the usual measures, radioactive iodine is often an effective agent for prevention of further attacks.

**Addendum**

Since this study was submitted for publication 8 additional cases of tachycardia were successfully treated with I$^{131}$.

**Acknowledgment**

We would like to thank Mr. and Mrs. Philip Raisin, Mr. and Mrs. E. D. Mitchell, Mr. and Mrs. F. Kaufman, and Mr. Beldon Katleman, whose financial assistance made this study possible.

**Summario in Interlingua**

Vinti-cinque patientes euthyroide con paroxysmal tachycardias supraventricular esseva tractate con iodo radioactive in un effortio de preventir recurrentias del arrhythmia paroxysmal. Le production de un grado relative de hypothyroidismo pare esser necessari pro abolir episodios de tachycardia supraventricular in patientes previemente euthyroide qui se ha mostrare resistente a alte forms de tractamento. Le mechanismo per que le suppression del function thyroido resulta in le prevention de tal attacces non es clar e merit studios additional. Le resultados obtenite esseva bon in 20 del 25 patientes euthyroido tractate. In 3 patientes le resultados esseva considerate como “sufficiente.” In le remanente 2 patientes—ambes psychotic—le tractamento falleva. In euthyroide individuos con tachycardia supraventricular paroxysmal non respondente al mesuras usual, iodo radioactive es frequentemente un agente efficace in le prevention de attacces additional.

**REFERENCES**

Radioiodine Treatment of Paroxysmal Supraventricular Tachycardia in the Euthyroid Patient
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