Effect of Treatment with Radioactive Iodine and Iodine-Deficient Diet on Development and Maintenance of Renal Hypertension in Rats

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The antithyroid drug, propylthiouracil, is an effective antihypertensive agent against hypertension induced in rats by renal "ischemia,"1,2 administration of desoxycorticosterone acetate,3 regeneration of adrenal gland4 and administration of hypertonic NaCl solution as the sole drinking fluid.5 Whether the effectiveness of propylthiouracil in this regard is the result of suppression of thyroxine production, or whether it is due to some secondary action of the drug, such as decreased vascular reactivity or cardiac output, is unknown. An aim of this investigation was to determine whether hypothyroidism, induced by radiothyroidectomy, also prevented the development and maintenance of renal hypertension. A further aim was to establish the extent of thyroid depression necessary to prevent hypertension. In addition, the effect of administration of an iodine deficient diet on development and maintenance of renal hypertension was studied.

Methods and Results

Male albino rats, 2 or 3 per cage, were kept in a room maintained at 26 ± 1 C. and illuminated from 8 AM to 6 PM. In all experiments, food and fluids were given ad libitum. The food and fluid used were ground Purina laboratory chow and distilled water, unless otherwise designated. Kidney encapsulation was performed by the method of Abrams and Sohini, using ether as an anesthetic.

Blood pressures of unanesthetized animals were measured, utilizing the microphonic manometer technic,7 modified as described earlier.8 Cooling tests, as described in detail previously,9 were used as one criterion of thyroid function, since rats rendered hypothyroid with propylthiouracil have been shown to cool 55 per cent faster than controls when restrained and subjected to air at 5 C.10 Colonic temperature was recorded at 1-minute intervals, using thermocouple and recording potentiometer. Each rat was removed from cold and rewarmed when its colonic temperature reached 26 C. Since the decrement of colonic temperature with time closely approximates linearity,8,11 colonic cooling rate (CCR) was used to compare responses of the different groups to cold.

Thyroid function was also assessed by measurement of uptake and release of radioactive iodine in rats injected with a tracer dose (\(1 \mu C\)) of carrier-free radioactive iodine (Na \(I_1^31\)). Twenty-four hours later, radioactivity of the thyroid gland was counted by holding the neck of the unanesthetized rat over a well-type scintillation counter and counting for one-half minute intervals until successive counts agreed within 5 per cent. Loss of radioactivity was followed at approximately 8-hour intervals thereafter until 48 hours postinjection. The uptake and release of radioactive iodine was expressed as percentage of injected dose and is corrected for radioactive decay of the isotope.

When rats were sacrificed, heart, kidneys, testes, prostate, seminal vesicles, adrenals and thyroid gland were removed, trimmed of excess fat and connective tissue and weighed on a Roller-Smith torsion balance. The thick connective tissue capsule, covering the surface of the latex encapsulated kidney, was removed prior to weighing each kidney.

Statistical analyses of the data in each experiment were performed, using the "t" test for the 95 per cent confidence limit.12 Other techniques pertinent to each of the 4 separate experiments will be described below:

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Supported by Grant No. H-3503 from the National Heart Institute, National Institutes of Health, Bethesda, Md.

Received for publication March 2, 1960.

Circulation Research, Volume VIII, July 1960
Figure 1
A. Mean systolic blood pressures of encapsulated rats (•) and encapsulated rats treated with 850 µC of radioactive iodine at the end of the second week of the experiment (▲) are graphed throughout the experiment; ± 1 standard error is set off at each mean. B. Mean body weights of the 2 groups throughout the experiment.

Effects of Treatment with Radioactive Iodine and Iodine Deficient Diet on Development of Renal Hypertension

Experiment 1: Treatment with Radioactive Iodine

Blood pressures and body weights of 10 Holtzman rats were measured once during a 1-week control period and weekly thereafter for 24 weeks, with exceptions of weeks 11, 12 and 17. Kidneys of all rats were bilaterally encapsulated with latex envelopes at the end of the control period. Five rats, randomly chosen, were injected intraperitoneally with 850 µC of carrier-free radioactive iodine (Na I131) 2 weeks after kidney encapsulation. Blood pressure and body weight measurements were then continued for 24 weeks.

At the end of the twenty-fourth week, all rats were subjected to a cooling test as described above. Colonic cooling rate (CCR) was calculated for each rat and was not corrected for the small differences in body weight among rat groups, since CCR is only slightly influenced by body weight in excess of 320 Gm.13 Body weights of the rats at the time of the cooling test were greater than 320 Gm.

One week after the cooling test, all rats were injected intraperitoneally with a tracer dose (1 µC) of radioactive iodine. Uptake and release by the thyroid gland were measured, as described above.

One week later, all rats were sacrificed by ether. At sacrifice, the organs mentioned above were removed and weighed. A length of trachea, including thyroid gland, was removed and fixed in 10 per cent formalin. These tissues were then prepared for histologic examination and were stained with hematoxylin-eosin and Masson's trichrome stains.14

Administration of 850 µC of radioactive iodine to rats 2 weeks after kidney encapsulation, prevented development of the elevated blood pressure usually accompanying kidney encapsulation (fig. 1A). The blood pressure of encapsulated, control rats became elevated within 6 to 8 weeks after kidney encapsulation. The blood pressure of the treated group rose in a fashion similar to that of untreated controls until the fourth week after treatment with radioactive iodine. At this time, a sharp fall in blood pressure occurred to levels of approximately 140 to 145 mm Hg. This blood pressure range was maintained throughout the remainder of the experiment.

Treatment with radioactive iodine decreased growth rate slightly (fig. 1B). The effect of this treatment on growth, however, was much less severe than has been observed for propylthiouracil, used previously.1 2

The uptake of a tracer dose of radioactive iodine 24 hours after injection by thyroid gland of kidney-encapsulated, I131-treated rats was approximately half that of untreated, kidney-encapsulated rats (table 1, experiment 1). Release of radioactive iodine was more rapid in treated than in untreated rats. This more rapid rate may represent the loss from thyroid of uncombined iodine rather than thyroid hormone, although there is no data to support this hypothesis, since protein-bound iodine determinations were not made. Gross sandwich-type radioautographs of the thyroid glands of 3 radioiodine-treated rats, chosen at random, were made on Kodak No-Screen film and compared with a nontreated control. All rats had been given 1 µC of radioactive iodine intraperitoneally 24 hours before sacrifice. The
thyroid glands of only 1 treated rat contained a very slight amount of radioactivity, as compared with the nontreated control. Thyroid glands of the other 2 rats contained no observable radioactivity (fig. 2).

These results suggest that a small amount of functioning thyroid tissue remained in some of the I¹³¹-treated rats. However, other evidence exists that these rats were hypothyroid. In table 2, experiment 1, it may be observed that rats treated with radioactive iodine showed lower \( p = .08 \) initial colonic temperature in air at 25 C. prior to cold exposure and significantly \( p < .01 \) increased colonic cooling rate after exposure to cold air (5 C.). The CCR of radioactive iodine-treated rats was 42 per cent faster than controls. The lower resting colonic temperature and increased CCR are characteristic of hypothyroidism in rats.¹⁰

Histologic sections of the thyroid glands of rats treated with high doses of radioactive iodine show complete disorganization of normal architecture. Although it is evident that the disorganization at the interior is greater than that at the periphery, even the cells on the outer aspects of the glandular structure contain nuclei which are predominantly pycnotic and the cytoplasm, when the cellular membrane is intact, appears densely staining (eosinophilic) and exhibits a minimum of organizational detail. Few colloid-containing follicles are noticeable. The periphery, as well as the interior, contains many phagocytes. At inner aspects of the gland, the cells are largely disrupted, the cytoplasmic membrane presenting a ragged appearance. The greater effect of treatment within the thyroid gland than at its periphery can be predicted from the data and equations of Feller et al.¹⁵ and Loevinger et al.¹⁶ These show that an average radiation dose of a lobe of thyroid tissue with a lobular mass (sphere) of 10.6 mg. and a radius of 1.36 mm. is 81 per cent of the center dose, while the surface dose is 41 per cent. Figure 3 (top and bottom) illustrates the microscopic appearance of typical normal and treated rat thyroid glands.

**Figure 2**

Radioautographs of 1 encapsulated control (upper left) rat, and 3 I¹³¹-treated encapsulated rats used in experiment 1. Only 1 of the I¹³¹-treated rats (rat #56 upper right) appeared to have picked up sufficient I¹³¹ to record a trace on the film. Rats were sacrificed 24 hours after administration of a tracer dose of radioactive iodine.

-Treatment with radioactive iodine prevented hypertrophy of the heart accompanying renal hypertension (table 3, experiment 1). In addition, kidney weight was also reduced. Ratios of other organs weighed were similar to those of control encapsulated rats.

**Experiment 2: Treatment with Radioactive Iodine and with Iodine-Deficient Diet**

Blood pressures of 15 Wistar rats were measured twice during a 1-week control period. Then the kidneys of all rats were bilaterally encapsulated with latex envelopes. The rats were then divided at random into 3 groups, with 5 rats per group. Group 1 was injected intraperitoneally with 550 \( \mu \)C. of carrier-free radioactive iodine 1 week after kidney encapsulation. Group 2 was given an iodine-deficient diet* immediately after kidney

*Iodine-deficient diet: Nutritional Biochemicals Corp., Cleveland, Ohio.
Table 1

<table>
<thead>
<tr>
<th>Experimental group</th>
<th>No. of rats</th>
<th>Mean body weight (Gm.)</th>
<th>Radioactive iodine uptake and release (% injected dose)</th>
</tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td>24 hours</td>
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<tr>
<td>Control-encap.</td>
<td>10</td>
<td>455</td>
<td>11.0±1.1*</td>
</tr>
<tr>
<td>Experiment I131-encap.</td>
<td>5</td>
<td>423</td>
<td>5.8±0.5†</td>
</tr>
<tr>
<td>Experiment I131-encap.</td>
<td>4</td>
<td>437</td>
<td>6.6±0.5</td>
</tr>
</tbody>
</table>

*± 1 standard error.
†Difference from control-encapsulated rats highly significant (P<01).

Table 2

<table>
<thead>
<tr>
<th>Experimental group</th>
<th>No. of rats</th>
<th>Mean body weight (Gm.)</th>
<th>Initial colonic temp. (C.)</th>
<th>P.*</th>
<th>Colonic cooling rate (C./hour)</th>
<th>P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experiment 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control-encap.</td>
<td>5</td>
<td>464</td>
<td>38.2±0.2†</td>
<td>.08</td>
<td>2.99±0.37</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>I131-encap.</td>
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<td>431</td>
<td>37.7±0.1</td>
<td></td>
<td>4.23±0.26</td>
<td>.95</td>
</tr>
<tr>
<td>Experiment 2</td>
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<td></td>
</tr>
<tr>
<td>Control-encap.</td>
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<td>352</td>
<td>38.1±0.3</td>
<td>.66</td>
<td>2.67±0.41</td>
<td>&lt;.01</td>
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<tr>
<td>Iodine-deficient</td>
<td>5</td>
<td>362</td>
<td>38.3±0.2</td>
<td>.04</td>
<td>2.89±0.32</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Diet-encap.</td>
<td>5</td>
<td>340</td>
<td>37.4±0.3</td>
<td></td>
<td>5.10±0.38</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Experiment 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control-encap.</td>
<td>5</td>
<td>333</td>
<td>37.8±0.3</td>
<td>.18</td>
<td>3.08±0.42</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>I131-encap.</td>
<td>5</td>
<td>361</td>
<td>37.1±0.2</td>
<td></td>
<td>5.26±0.48</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

*Probability value.
†± 1 standard error of mean.

encapsulation, while group 3 served as encapsulated controls. All rats were given double distilled water ad libitum and groups 1 and 3 were given ground Purina laboratory chow as food. Blood pressures and body weights were then measured weekly for 17 weeks. At the end of the experiment, all rats were subjected to a cooling test as described above to assess thyroid function.

Treatment of kidney-encapsulated rats with 850 μC. of radioactive iodine prevented elevation of blood pressure usually accompanying encapsulation (fig. 4A). The results of this experiment are in excellent agreement with those of experiment 1. In contrast is the effect of the iodine-deficient diet. This treatment failed to prevent development of the elevated blood pressure.

Growth rate of rats given either radioactive iodine or iodine-deficient diet was similar to that of encapsulated control rats (fig. 4B). A decrease in body weight of control encapsulated rats occurred during the fourth to sixth weeks for unknown reasons. Thereafter, these rats gained weight, and body weights of all groups were similar. The difference in growth rates between these rats and the rats in experiment 1 can be attributed to strain difference. Holtzman rats grow to a larger size than Wistar rats.
Colonic cooling rates and initial colonic temperatures of these rats are given in table 2, experiment 2. The results of these studies indicate that rats treated with radioactive iodine cooled 9.1 per cent faster than control rats when subjected to cold air. The I\textsuperscript{131}-treated rats also cooled significantly faster than the iodine-deficient group. Cooling rate of the latter group was similar to that of controls. Initial colonic temperatures of control and iodine-deficient rats were similar, while that of I\textsuperscript{131}-treated rats was decreased below that of either control or iodine-deficient groups. The results indicate that I\textsuperscript{131} treatment depressed thyroid function, while treatment with an iodine-deficient diet for 14 weeks did not.

Effects of Treatment with Radioactive Iodine and Iodine-Deficient Diet on Maintenance of Renal Hypertension

Experiment 3: Treatment with Radioactive Iodine

Ten Wistar rats weighing 340 to 365 Gm. were used. Kidneys of these rats had been encapsulated 17 weeks prior to beginning the experiment and individual blood pressures were at least 35 mm. Hg above usual range of normal (140 mm. Hg). During a 4-week control period, blood pressure and body weights were measured weekly. At the end of the fourth week, 850 \textmu C. of carrier-free radioactive iodine was injected intraperitoneally into 5 of 10 rats chosen at random. Blood pressures and body weights were then measured weekly for 17 weeks after administration of radioactive iodine.

At the end of the 18th week of the experiment, all rats were subjected to a cooling test as described in experiment 1. At the end of the twentieth week of the experiment, a tracer dose of radioactive iodine (1 \textmu C.) was injected intraperitoneally into each rat to assess the amount of functioning thyroid tissue remaining. Both uptake and release of radioactive iodine from thyroid glands of all rats were measured.

Oxygen consumption measurements were made individually on all rats. The apparatus and method (open circuit) used was that of Adolph,\textsuperscript{17} with the chamber immersed in a water bath maintained at 25 ± 0.5 C. The rats used were not fasted prior to measurement of oxygen consumption. Hence, these were not "basal" metabolic rates and are designated as "resting metabolic rates."

One week after completion of oxygen consumption measurements, all rats were sacrificed. The organs described above were removed and weighed.

Figure 3

Photomicrographs of the thyroid tissue of an encapsulated rat used in experiment 1 (top) and an experimental animal (bottom) given 850 \textmu C. radioactive iodine 22 weeks earlier. Magnification X 480. Note the disorganization of the normal architecture of the treated rats.

Histologic sections of trachea, including thyroid gland, were prepared and stained with hematoxylin-eosin and trichrome stains.

Treatment with high doses of radioactive iodine after hypertension had been established for 17 weeks lowered blood pressure on the average, although there was some overlap when blood pressures were compared with untreated controls (fig. 5A). This overlap is apparent during weeks 10, 11, 12, 16 and 17.

As in previous studies, I\textsuperscript{131} treatment appeared to have little influence on growth (fig. 5B). The treated rats actually grew at a faster rate than controls. Other evidence, cited below, indicates that these rats were hypothy-
Table 3

Organ Weight to Body Weight Ratios of Certain Organs of Rats in Experiments One, Three and Four

<table>
<thead>
<tr>
<th>Experimental group</th>
<th>No. of rats</th>
<th>Mean body weight (Gm.)</th>
<th>Oxygen cons. (cc./min./Kg.)</th>
<th>Colonie temp. (°C.)</th>
<th>Organ weight/body weight ratio (mg./100 Gm. BW)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Heart</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Kidneys</td>
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<td>Encap.-control</td>
<td>5</td>
<td>456</td>
<td>454.1±36.01</td>
<td>37.0±0.6</td>
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<tr>
<td>Eiicap.-f-131</td>
<td>5</td>
<td>455</td>
<td>943.1±100.9</td>
<td>56.5±3.9</td>
<td></td>
</tr>
<tr>
<td>Treatment (850 μC.)</td>
<td></td>
<td></td>
<td>688.5±6.5</td>
<td>±2.0</td>
<td></td>
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<td></td>
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<td></td>
<td></td>
<td>±6.5</td>
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<td></td>
<td>±11.7</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>±11.4</td>
<td></td>
</tr>
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<td>Experiment 3</td>
<td></td>
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</tr>
<tr>
<td>Encap.-control</td>
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<td>388</td>
<td>292.3±5.6</td>
<td>707.6±7.7</td>
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<tr>
<td>Eiicap.+I131</td>
<td>5</td>
<td>411</td>
<td>39.7±6.3</td>
<td>773.4±11.4</td>
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</tr>
<tr>
<td>Treatment (850 μC.)</td>
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<td>11.4±5.6</td>
<td>±9.0</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>±1.4</td>
<td></td>
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<td>±9.7</td>
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<td>±17.4</td>
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<td></td>
<td></td>
<td>±12.7</td>
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<tr>
<td>Experiment 4</td>
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<tr>
<td>Encap.-control</td>
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<td>440</td>
<td>32.0±5.6</td>
<td>826.2±15.7</td>
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<tr>
<td>Eiicap.+I131</td>
<td>5</td>
<td>425</td>
<td>12.7±5.6</td>
<td>699.4±34.5</td>
<td></td>
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<tr>
<td>Treatment (850 μC.)</td>
<td></td>
<td></td>
<td>39.0±1.5</td>
<td>±12.0</td>
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<td>±4.5</td>
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<tr>
<td>Deficient diet</td>
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</table>

*Significant difference (P<.05).
†±1 standard error of mean.
‡Highly significant difference (P<.01).

It is curious that in experiments 1, 2 and 3, hypothyroidism produced by I131 administration was not accompanied by a decreased growth rate. The CCR of the I131-treated rats subjected to cold was about 71 per cent faster than that of control rats (table 2, experiment 3). These results, as well as the decreased initial colonie temperature, suggest that thyroid gland was hypofunctional, but fail to establish how much thyroxine the remaining thyroid tissue was able to produce.

Mean resting oxygen consumption of I131-treated rats is compared with that of control rats in table 3, experiment 3. Resting oxygen consumption of I131-treated rats was about 62 per cent of that of control encapsulated rats. This also indicates that I131-treated rats were hypothyroid.

The organ weight to body ratios of organs removed at sacrifice are given in table 3. No significant differences were observed.

Experiments 1 and 3 were performed concurrently, hence radioactive iodine uptake of all rats in each experiment were measured at the same time. The radioactive iodine uptake of all control encapsulated rats have been grouped together since the data of the 2 individual groups did not differ statistically one from the other. Table 1 gives results of these experiments for the rats of experiment 3. The radioactive iodine uptake of the thyroid glands of treated rats was 60 per cent that of untreated control rats 24 hours after injection of a tracer dose of I131. The thyroid glands of control rats discharged 26 per cent of their initial 24-hour uptake within 48 hours after injection, while treated rats discharged 44 per cent within the same period of time. These results are similar to those seen in rats used in experiment 1.

Histologic sections of the thyroid glands of these rats are typical of those seen in experiment 1 (fig. 3 top and bottom). Distortion of normal cellular architecture is a prominent feature. Grossly, the thyroid glands of the treated rats were very small and difficult to dissect intact.
Experiment 4: Treatment with Iodine Deficient Diet

Ten Holtzman rats, weighing 460 to 500 Gm., were used. Kidneys of these rats had been encapsulated 20 weeks prior to the beginning of the experiment and blood pressures were significantly elevated. During a 1-week control period, blood pressure and body weight were measured. Iodine deficient diet* was then given to 5 rats chosen at random. The remaining 5 rats received the diet supplemented with iodine (1 mg./Kg. food as potassium iodide). Double distilled water was used as drinking fluid. Blood pressure and body weight of each rat were then measured weekly for 15 weeks. During weeks 15 and 16, 500 I.U. estrone/day in oil was administered subcutaneously to rats given an iodine-deficient diet. Control rats received oil without the drug. The drug was discontinued after 2 weeks of treatment because of the large weight loss accompanying administration.

At the end of the eighteenth week of the experiment, all rats were sacrificed by guillotine decapitation. The necks of the rats had been shaved of hair one day before to prevent contamination of collected blood by hair. Blood was collected in chemically clean beakers without anticoagulant, centrifuged and serum removed. Serum sodium and potassium concentrations were determined by flame photometry (Baird Model DB4) and calcium concentration by the method of Bachra et al.18 Adrenal cholesterol concentration of the left adrenal of each rat was determined by the method of Knobil et al.,18 but using the phosphoric acid-ferric chloride color reagent described by Rosenthal et al.20

At sacrifice, the organs mentioned above were removed and weighed.

Iodine deficiency did not influence the elevated blood pressure of established hypertensive rats (fig. 6A). Treatment with high doses of estrone caused a slight, but not significant, fall in blood pressure. Iodine deficiency had no effect on body weight (fig. 6B), while administration of estrone was accompanied by a rapid decrease.

At sacrifice, a significantly decreased kidney weight ratio, testis weight ratio and prostate weight ratio were observed in treated rats (table 3, experiment 4). On the other hand, iodine-deficient diet increased adrenal, thyroid and thymus weight ratios. Serum calcium, sodium and potassium levels were not significantly influenced by the treatment.

*Iodine-deficient diet: Nutritional Biochemicals Corp., Cleveland, Ohio.

Discussion

Administration of high doses of radioactive iodine prevents development of renal hypertension in rats whose kidneys are bilaterally encapsulated with latex envelopes. Treatment with an iodine-deficient diet is much less effective.

Rats treated with high doses of radioactive iodine were hypothyroid by all the criteria used to test them, i.e., lowered resting colonic temperature, increased colonic cooling rate, decreased uptake of radioactive iodine 24 hours after injection of a tracer dose, and decreased resting oxygen consumption. In addition, histologic sections of the radioactive iodine-treated thyroid gland revealed a complete distortion of normal architecture. Hence, the hypothyroidism produced in this fashion was as
effective in preventing blood pressure rise in encapsulated rats as was treatment with propylthiouracil used in earlier studies.\textsuperscript{1, 2} Radioactive iodine treatment was not accompanied by 2 of the prominent side effects observed with propylthiouracil in that growth rate appeared normal and testicular size was not affected. Propylthiouracil treatment decreases growth rate in young rats, causes weight loss in adult rats, and increases testicular size in either young or adult rats.\textsuperscript{1, 2}

Treatment with high doses of radioactive iodine during development of hypertension prevented the cardiac hypertrophy usually accompanying hypertension. Renal size was also reduced. When the same treatment was given to established hypertensive rats, the elevated blood pressure level was reduced and a suggested decrease in heart weight occurred. However, variability of blood pressure levels was large in the treated group. Reasons for the greater variability are not apparent.

The lack of effect of iodine-deficient diet in preventing blood pressure rise in experiment 2 may be due to the fact that these animals were not hypothyroid, as judged from resting colonic temperature and CCR (table 2, experiment 2). Both measurements were well within the normal range. These facts are interesting in view of the 5-fold increase in size of the thyroid gland observed at autopsy (table 3, experiment 4).

There seems little doubt, on the other hand, that iodine-deficient diet had only slight influence on the blood pressure of established hypertensive rats. (fig. 6) Estrone was administered to these rats in an attempt to increase thyroid clearance of iodine.\textsuperscript{21} Studies have also been reported in which estrogen administration prevented the expected rise in metabolic rate after thyroxine administration.\textsuperscript{22, 23} Presumably these actions of estrone might enhance the effectiveness of the iodine-deficient diet. The dose was chosen to correspond with that used acutely by Feldman.\textsuperscript{21} On a more chronic basis, this dose proved to be too high and caused severe weight loss. Treatment was discontinued after 2 weeks. During the time of administration, only slight reduction of blood pressure occurred. However, estrogens...
in much lower doses have been reported to reduce the blood pressure of rats rendered hypertensive by desoxycorticosterone-acetate administration.24

Rats with established hypertension given iodine-deficient diet not only failed to show a fall in blood pressure but also failed to show a significant change in heart weight or kidney weight. On the other hand, thyroid weight increased approximately 5-fold, while testis weight decreased approximately 35 per cent with a concomitant decrease in prostate weight by approximately 50 per cent. These latter findings probably reflect the depressor effect on gonads of treatment with estrone.

The exact extent to which thyroid function must be reduced before an antihypertensive effect manifests itself cannot be stated. The data of experiment 3, in which resting oxygen consumption (−38 per cent) and radioactive iodine uptake (−40 per cent) were measured on the same rats permit the guess that a 40 per cent reduction may be necessary.

The success of effective antithyroid treatments against development of renal hypertension in rats suggests that a critical analysis of thyroid function during development of hypertension should be made. Studies in the dog suggest an increase in thyroid activity occurs during development of renal hypertension.25

Recent studies have implicated hypersecretion of the parathyroid glands in the development of hypertension in rats under certain conditions.26 It is unlikely that the antihypertensive effect of high doses of radioactive iodine may be due to hypoparathyroidism, since the parathyroid gland appeared normal histologically and the rats never develop tetany. In addition, the more detailed experiments of Parrott et al.27 have shown doses of radioactive iodine, similar to that used here, are without influence on serum calcium level or on histologic appearance of the parathyroid glands in rats.

Summary

Treatment of kidney encapsulated rats with 850 μC. of radioactive iodine effectively prevented both the characteristic rise of blood pressure to hypertensive levels and cardiac hypertrophy. Iodine-deficient diet was ineffective under these conditions. Once hypertension was established, treatment with 850 μC. radioactive iodine lowered blood pressure toward normal levels although a significant decrease in heart weight was not observed. The iodine-deficient diet was also ineffective under these conditions. It is felt that hypothyroidism produced by administration of high doses of radioactive iodine is as effective in preventing blood pressure rise as that observed with propylthiouracil treatment. The antihypertensive effect of these antithyroid treatments appears to be the direct result of inhibition of secretion of thyroid hormone.

Acknowledgment

The late Dr. E. Braun-Menendez kindly suggested experiment 1 to us. Mrs. W. Pickels and Mrs. G. Hindman rendered valuable help.

Summario in Interlingua

In rattos con incapsulate renes, le tractamento con 850 μC de iodo radioactive preveniva tanto le caracteristic augmento del tension de sanguine a nivellos hypertensive como etiam le disveloppainento tie hipertrophia cardiac. Dietas a carentia de iodo non esseva efficace sub iste conditiones. Si hypertension essova jam presente, le tractamento con 850 μC de iodo radioactive reduciva le tension de sanguine verso nivellos normal, sed significative reductiones del pesos cardiac non esseva notate. Dietas a carentia de iodo esseva inefficace etiam sub iste conditiones. Es opinate que hypothyroidismo proclucitc per le administration de alte doses de iodo radioactive es tanto efficace in le prevention de augmentos del tension de sanguine como le hypothyroidismo inducite per tractamento con propylthiouracil. Il pare que le effecto antihyper- tensione del duo mesuras antithyroidic resulta directemente de un inhibition del secretion de hormon thyroido.

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Circ Res. 1960;8:749-758
doi: 10.1161/01.RES.8.4.749

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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