# Radioactive Iodine Treatment for Hyperthyroidism

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## INTRODUCTION

Radioactive Iodine-131 therapy is one of the modalities of hyperthyroidism treatment. This kind of therapy has been practiced for about 50 years and have been noted to be effective, safe, and relatively economical.[1,2,3]

Beta radiation of Iodine-131 causes the ablation of thyroid follicle cells, thus stopping excessive production of thyroid hormone. Thyroid ablation shows its effect progressively and can be clinically observed after 8 to 12 weeks.[12] The effect can be accelerated or slowed down by administering higher or lower doses. A precaution regarding predicted side effects of radiation, such as possible carcinogenesis, leukemogenesis, and impacts on genes and fertility have not been proven.[1,4,5,6,7]

Hyperthyroidism as a side effect is considered as a problem. There is no age limit for this therapy, yet most experts choose not to administer this therapy to children or young adults for fear of long term effects.[2,8]

A controversy remains regarding the effect of radioiodine on ophthalmopathy. Some experts say that it aggravates ophthalmopathy, while others state that it has no effects on the disease.[9,10]

### Indications and Contraindications of Iodine-131 Treatment for Hyperthyroidism

Lately, there has been a tendency to use radioactive iodine as the treatment of choice for hyperthyroidism, especially in the United States.[2,3,5]

According to some experts, the indications of Iodine-131 therapy are:

- Relapsing hyperthyroidism after long-term anti-thyroid treatment
- Severe thyroid heart disease
- Side effects of anti-thyroid drugs
- Relapse following thyroidectomy

Radioactive iodine is contraindicated for pregnant and lactating women.[2,5,11,12,13]

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## TREATMENT STRATEGY AND PROTOCOL

The preparations before giving Iodine-131 therapy are:[1,8,11,12,14]

- Patients must cease the consumption of any drug or food containing high levels of iodine at least 1 week prior to therapy.
  Examples of iodine-containing food: iodized salt, milk and dairy products, egg, seafood, agar, etc
  Examples of iodine-containing drugs: PTU, nitrate, thyroxin, steroid, isoniazid, penicillin, etc.
- Patients must cease the consumption of anti-thyroid drugs at least 5 days prior to therapy.[1,8,12,14]
- On the day of the treatment, patients must fast, and are permitted to eat one hour following given Iodine-131.

The goal of radioactive iodine treatment for hyperthyroidism is to reach euthyroidism as quickly as possible and to reach hypothyroidism as low and as late as possible.[5,6,11] This condition is not always achieved due to many factors involved. Some experts believe that it is better to give high doses of Iodine-131 because the patient will become euthyroid quickly and also to anticipate early onset of hypothyroidism.[7,14]

This opinion is not approved by other experts, because it would be the same as treating one disease by replacing it with another. This group suggested stepwise treatment in small doses.

Although the incidence of hypothyroidism is lower in this kind of treatment, but the patient will suffer hyperthyroidism longer and may need repeated therapy.[3]

Every center has its own treatment protocol, depending on their strategy. There are a lot of ways to determine the dose of Iodine-131. The commonly given dose ranges between 5-15 mCi.[1,2,5]

One of the way to determine Iodine-131 dose is by using the following formula:[11,12]

$$\text{Dose } (\mu\text{Ci}) = \frac{\text{weight of the thyroid gland (g)} \times \text{dose } \mu\text{Ci/gr} \times 100}{\text{24 hours uptake \%}}$$

The choice of dose depends greatly on the clinical condition, the size of the thyroid gland and thyroidal iodine uptake.[2,5,14] Other influencing factors are iodine level in food and in anti-thyroid drugs. The weight of the thyroid gland is determined using thyroid scan with planimetry or ultrasound.

Besides the groups that prefer a high dose or low dose, there is another group that favors a medium dose. A low dose of Iodine-131 is approximately 50-80 μCi/gram, a medium dose 100 μCi/gram, and a high dose 150- 200 μCi/gram .[11,15]

High doses can be administered in a single dose or in divided doses. In divided doses, the second dose is given 8 days following the initial dose, in accordance with iodine half-life (8 days). In severe hyperthyroidism, treatment can be continued following radiation with anti-thyroid agents or beta blocker drugs whilst waiting for further radiation effect.[1]

If hyperthyroidism persists, a second radioiodine treatment can be administered in the same dose or larger dose 6 months following the first administration.[5]

A report stated that approximately 80-90% patients became euthyroid with one dose of treatment, 10-20% needed a second dose, and very few needed a third dose.[2]

Thyroid function (FT4 and TSH) must be monitored every 1-2 months until the patient becomes euthyroid. Afterwards, monitoring should be maintained and might be performed more frequency in order to quickly detect hypothyroidism.[4]

### The Effect of Iodine-131 on The Thyroid

Iodine-131 is given orally in a water solution. The solution is absorbed into the blood vessels and concentrated in the thyroid gland. There, it undergoes oxidation and organification by thyroid follicles.[2,18] Radioactive Iodine-131 radiates beta and gamma rays, the former being the one destroying the thyroid cells. The radiated thyroid cells will then undergo inflammation and necrosis.[2] Acute post radiation thyroiditis commonly occurs 2 weeks following radiation and should ameliorate in 2-4 weeks. The histological changes consists of cell swelling, thyroid follicles damage, necrosis, and leukocyte infiltration.[8] Symptoms include local inflammation, pain, and tenderness.[2,5,8,12]

Other than local inflammation, systemic symptoms can also occur as a result of the release of thyroid hormones in large quantities. This happens due to thyroid follicle damage and may, albeit rarely, cause thyroid crisis.[2,5]

Treatment effect will show itself as a decrease in thyroid size 4-6 weeks following radiation, accompanied by improvement in thyroid functions (decrease of T4 and T3) after 6-8 weeks and disappearance of hyperthyroidism symptoms after 10-12 weeks.[1,2]

Atrophy and fibrosis of the glands may occur for years until the cells die. Before they die, the cells still function in secreting thyroid hormones. This process explains the slow progression of hypothyroidism in 10 to 15 years, or even later, following treatment.[8,11]

Precautions After Radioactive Iodine Treatment:[4,5,6,7,11]

- pregnancy should be avoided for six months following treatment
- close contact with pregnant women, babies, and children should be avoided for at least 2 days after treatment.

## SIDE EFFECTS

### Hypothyroidism

Rather than calling it a side effect, hypothyroidism can be considered more as the inevitable effect of radioactive treatment. In the last 2 decades, the prevalence of hypothyroidism following Iodine-131 treatment has been escalating, accompanied by earlier appearing hypothyroidism, possibly due to the use of larger doses of Iodine-131.[2]

The onset of hypothyroidism depends on the administered dose. In addition, there are some risk factors that influence post iodine treatment hypothyroidism: the presence of anti-thyroid antibody, the administration of anti-thyroid agents, and the size of the thyroid gland.[2,17]

Patients with higher anti-thyroid antibody levels have higher a incidence of hypothyroidism than those with lower levels of anti-thyroid antibody.[15,17,18] Patients that have not received anti-thyroid agents prior to radioiodine treatment have a higher incidence of hypothyroidism than those who had received anti-thyroid agents.[15,17]

Anti-thyroid treatment should be terminated at least 3 to 4 days prior to Iodine-131 treatment, because it disturbs the organification process, and therefore reduces the radiation effect.[2,5]

Anti-thyroid agents administered immediately following radioiodine may reduce the incidence of hypothyroidism, but on the other hand may increase the risk of persistent hyperthyroidism.[2,5]

Transient hypothyroidism may occur 2-3 weeks after radiation due to temporary thyroid destruction, but this will eventually ameliorate. If the condition does not

improve in 2 months, then it is likely that permanent hypothyroidism has remained.[2]

Hypothyroidism commonly occurs 6 months following radiation.[4,5,14] Permanent hypothyroidism remains in about 50-80% patients.[1]

For small dose therapy, the mean onset of hypothyroidism in the first year is 10 to 20%, and for the following year it is 2-4% per year.[5,15] The incidence of hypothyroidism in 1 year following high dose therapy is 50%, while following small dose the incidence of hypothyroidism is 50% after 25 years.[5]

The incidence of hypothyroidism 5 years after radiation is approximately 30%, after 10 years it is about 40%, and even reaches 70%.[8]

### Malignancies

A lot of large-scale researches on Iodine-131 radiation effect with periods of more than 15-20 years did not reveal any evidence on increased incidence of thyroid carcinoma , leukemia, or lymphoma.[6,7,8,16,19] Small scale researches reported no significant increase in malignancy. An increase in the incidence of gastric carcinoma and breast cancer after 10 years have been reported, but the results were not significant.[5]

An increased incidence rate of thyroid carcinoma following the atomic bomb and nuclear accidents has been reported, but not in correlation with radioiodine treatment. This may be due to a difference in dosage, i.e. the dose administered in thyroid treatment is very low.[7]

### Genetic Abnormality

There is very few report on genetic abnormalities resulting from Iodine-131 treatment.[16] Several researches have reported that there was no proof supporting the occurrence of genetic abnormalities in children whose mothers underwent Iodine-131 treatment.[1,5,16]

A study conducted at the time of the atomic bomb in Hiroshima and Nagasaki involving 70,000 pregnancies reported no significant genetic disorders from the offspring.[7]

The rate of radiation-induced genetic abnormality is theoretically estimated to be about 0.005%, but this prediction is not supported by existing researches.[5]

Woeber (2000) stated that treatment using Iodine-131 did not cause an increase in teratogenesis.[4]

### Aggravation of Ophthalmopathy

The relation between radioiodine treatment for hyperthyroidism and aggravation of Graves' ophthalmopathy is still a controversy. Some experts state that the treatment does not aggravate ophthalmopathy, yet most have an opposing opinion.[9,10] Aggravation of ophthalmopathy is caused by thyroid antigen release and increased thyrotropin receptor antibody caused by thyroid damage.[9,10]

Bartalene et al (1998) stated that the aggravation of ophthalmopathy can be avoided by administering 0.4 – 0.5 mg/kg bodyweight of glucocorticoids immediately following radiation for one month, and then tapering it off and discontinuing it after 3 months.[8,9]

Wiersinga stated that prednisone should be administered if there are risk factors like smoking, high levels of triiodothyronin prior to treatment, or high levels of thyrotropin receptor antibody following treatment.[10]

## CONCLUSIONS

Radioactive iodine has been used to treat hyperthyroidism for about 50 years, and have been said to be effective, safe, and relatively economical.[1,2,3]

There is no age limit for this therapy, but it is better to avoid giving it to children and young adults.

Iodine-131 treatment has not been proven to cause thyroid carcinoma, leukemia, or genetic disorders. The effect of the treatment towards aggravation of ophthalmopathy is still a controversy.

The onset of hypothyroidism remains a problem. This depends on the administered dose, the administration of anti-thyroid drugs prior to treatment, and anti-thyroid antibody titer.

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