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COMPLICATIONS IN RADIOIODINE TREATMENT OF HYPERTHYROIDISM

by

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The complications resulting from radioiodine therapy in cases of hyperthyroidism fall into two groups; according to whether they occur within one month of treatment or later they may be referred to as initial and late complications, respectively. Initial complications are of two types, namely a local reaction with swelling and tenderness of the thyroid gland and an exacerbation of hyperthyroidism. Reactions of this type are extremely common but usually so mild as not to be noticed by the patient. Even slight swelling of the thyroid may however be fatal in cases of large goitres and compression of the trachea. Where there is marked hyperthyroidism or severe cardiac disease, exacerbation can be particularly serious. It seems likely that the initial reaction after ^{131}I treatment has sometimes been a cause of death (NELSON et coll. 1952, LARSSON 1955, LAMBERG et coll. 1959, WERNER 1962).

A large series of patients were followed up after ^{131}I treatment for hyper-

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thyroidism and the initial and late complications observed in this series are reported; the mortality from initial complications is evaluated. Part of this series, the 370 patients treated between 1951 and 1953, has been reported earlier (LARSSON 1955).

Material and Methods. The series consisted of 2 035 patients — all those cases of hyperthyroidism treated by radioiodine from 1951 to 1961. The patients to receive radiotherapy were selected in collaboration with surgeons or internists; about half the number had been referred from the goitre clinic of the Surgical Department of St. Erik's Hospital (Hj. Wijnbladh). The usual treatment was surgery for patients under 40 to 45 years of age, provided there were no contraindications. Older patients were given radiotherapy with ^{131}I. The mean age of the patients given radiotherapy was 62 years. Of the whole series, 541 had no palpable goitre, 811 had diffuse enlargement of the thyroid gland and 683 had nodular goitre.

The radioiodine dose was chosen according to the size of the thyroid gland — as judged by palpation and scintigraphy — and to the 24-hour uptake and effective half-life of the radioiodine in the gland. The intended radiation dose for the gland was 5 000 to 12 000 rad, the lower doses being given to younger patients who showed little if any thyroid enlargement. The highest doses were administered to patients with nodular goitre.

The patients were followed up regularly every 2 to 4 months during the year following treatment, and then every 6 to 12 months. If necessary, another dose of radioiodine was given, usually 3 to 8 months after the earlier treatment. Altogether 3 482 treatments were given to these 2 035 patients. All but 14 of the survivors were observed for at least 2 years after the first treatment; most of the 14 patients (0.5 %) who were not available for follow-up had left the country.

The monthly mortality rate was calculated in relation to the time when the last ^{131}I treatment was given. All the patients dying within one month after ^{131}I therapy were subjected to autopsy.

Results and Discussion

Out of 2 035 patients receiving 3 482 treatments 9 died within one month of treatment, giving a mortality of 0.3 %. Since the patients selected at this hospital for radioiodine therapy are usually among the older ones or have complicating diseases, some deaths from causes other than thyroid disease could be expected during the period in question.

The mortality in the first month of treatment was by chance the lowest

Table

Patients dying within 30 days of ^{131}I treatment for hyperthyroidism — all patients were autopsied

Year of death	Age	^{131}I Dose	Time in days between treatment and death	Cause of death
1956	63	First	8	Initial reaction
1954	70	First	12	Initial reaction
1955	67	Third	14	Initial reaction
1954	80	First	5	Cerebral hemorrhage
1954	63	First	29	Cerebral hemorrhage
1960	56	Second	8	Cardiac infarction
1961	61	First	17	Acute encephalomyelitis
1960	59	First	22	Carcinoma of pancreas
1959	67	Third	6	Carcinoma of gallbladder

monthly figure during the first 6 months after treatment, as may be seen from the data given below:

Period after last ^{131}I treatment:	⩽ 1	1—2	2—3	3—4	4—5	5—6 months
Number of deaths:	9	12	13	9	11	18

During the first 18 months on an average 9.5 patients died every month, which corresponds with the mortality during the first month. It is not possible from the above figures or from any similar collations to draw any conclusions as to the mortality from the initial reaction.

From the reports of the individual cases (see Table) it was found that of the 9 patients dying within one month of radioiodine therapy, three had died with signs that suggest an exacerbation after treatment as cause of death; they were classified as dying from the initial reaction; in three other patients the reaction to the treatment may have been a contributory cause of death; two died from cerebral haemorrhage and one from myocardial infarction; in a further three patients, the treatment can hardly have been a contributory cause of death since two died from abdominal carcinoma known before the ^{131}I treatment was begun and the third from acute encephalomyelitis.

Patients with large goitres, severe hyperthyroidism, or heart disease, are not treated as out-patients. It was noted, however, that the initial reactions, if present, always appeared within 7 days of treatment. A week in hospital is in most cases sufficient and if no deterioration is observed at this time, there seems to be little likelihood of severe reactions occurring later on. When

radioiodine treatment is followed by severe reactions — whether swelling of the gland or exacerbation of hyperthyroidism — the current routine treatment at this hospital consists of giving large doses of cortisone. This usually has a dramatic effect within an hour of the injection. The doses are 100 to 150 mg of cortisone acetate two or three times daily for 3 to 6 days; a longer period is seldom necessary. Since this management of the initial reactions was introduced, there has been no death ascribable to the early complications of therapy, that is, not in the 1 239 cases treated since 1956 (see Table).

Possible complications after a long interval are late hypothyroidism, recurrence of hyperthyroidism and hazards of radiation, such as induction of thyroid carcinoma and leukemia, and genetic damage.

The incidence of hypothyroidism occurring long after the ^{131}I treatment was studied in the first 796 cases treated from 1951 to 1956 (BELING & EINHORN 1961). Of these patients, 99.6 % were followed up for at least two years. Hypothyroidism within one year of treatment occurred in 7.5 %. Each year thereafter hypothyroidism developed in a further 3 % of the patients followed up so that the incidence after 7 years was about 27 %. The curve shows no tendency to level off during the follow-up period, and, to judge by its course, the incidence of hypothyroidism will rise further with time (DUNN & CHAPMAN 1964). Hypothyroidism is not a severe complication, being easy to control by thyroid substitution therapy. Nevertheless, this late hypothyroidism overtakes the patient very slowly and it is important to carry out periodic checks so that substitution therapy can be started when necessary. If such control cannot be performed, the patient should be informed about the symptoms of this common complication so that he may recognize them if they appear.

Because the thyroid function has a tendency to diminish even long after treatment, the incidence of recurrence of hyperthyroidism following radioiodine treatment is very low; it was only 0.4 % in the patients who were euthyroid for one year after ^{131}I treatment (BELING & EINHORN).

Progressive exophthalmus was observed in about 1 % of patients after ^{131}I treatment for hyperthyroidism.

There is no patient with thyroid carcinoma or leukemia in this series of about 2 000 patients observed for 2 to 13 years. It would seem from the present and earlier series that were followed up for up to 20 years (DUNN & CHAPMAN 1964) that morbidity from thyroid carcinoma and leukemia (POCHIN 1960, WERNER et coll. 1961) in adults receiving ^{131}I treatment for hyperthyroidism is of little significance. For some reason there were fewer thyroid tumors among adults receiving radioiodine therapy than might have been expected on the basis of chance. However, the younger the patients the

greater the risk, and, as the age at which the treatment is given decreases, the risk probably increases (SHELINE et coll. 1959, 1962, STARR et coll. 1964). It is well established that external roentgen irradiation of the thyroid gland in childhood increases the incidence of thyroid carcinoma (CLARK 1955, SIMPSON et coll. 1955, WINSHIP & ROSVOLL 1961), and there is no reason to believe that the radiation delivered by radioactive iodine differs in its biologic effect.

The observation time is at present too short for an assessment of the genetic risks, and so long as these are unknown, surgery should remain the method of choice in patients of fertile age with hyperthyroidism. If the radiation dose received by the gonads is put at 0.5 rad/mCi of ^{131}I administered (MEANS et coll. 1964), the gonadal dose in radioiodine treatment of hyperthyroidism with moderate enlargement of the thyroid gland is comparable with the dose given at two urographic examinations (LARSSON 1958). The gonadal dose at urethrocystography or hysterosalpingography (LARSSON 1958) is often higher than at ^{131}I treatment for hyperthyroidism. However, this does not justify radioiodine treatment for young patients as a routine method.

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SUMMARY

Early and late complications of the ^{131}I treatment of hyperthyroidism were examined in 2 035 patients, 99.5 % of whom were followed up for from 2 to 13 years. The initial reactions to the administration of ^{131}I and the treatments for them are discussed; the mortality is evaluated.

ZUSAMMENFASSUNG

Insgesamt wurden 2 035 Patienten auf die frühen und späten Folgen der ^{131}I Behandlung bei Überfunktion der Schilddrüse untersucht; 99,5 % der Patienten wurden auf 2 bis 13 Jahre nachuntersucht. Die unmittelbare Reaktion auf die Behandlung mit ^{131}I sowie die Behandlungsweise werden diskutiert und die Mortalität wird ausgewertet.

RÉSUMÉ

Les auteurs ont étudié les complications précoces et tardives du traitement par ^{131}I de l'hyperthyroïdie chez 2 035 malades, dont 99,5 % ont été suivis de 2 à 13 ans. Ils examinent les réactions initiales à l'administration de ^{131}I et leur traitement, et évaluent la mortalité.

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