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SUMMARY

Perchlorate discharge test (PDT) was performed in 48 patients with hyperthyroidism previously treated with radioactive iodine (^{131}I) and at different stages regarding thyroid function. It was noted that all euthyroid patients (22) treated with RAI and followed up to 30 months had a negative PDT; the same was observed for patients with hyperthyroidism (5) but still on the hyperthyroid range. However hyperthyroid patients in remission (4) and euthyroid patients (14) recently treated (1-3 months) had a positive PDT. A positive test was also found in 3 patients whom were hypothyroid 14-20 months after RAI therapy. An enzymatic damage to the peroxidase system induced by the radiation, and partially reversible with time, was postulated in order to explain the outcome of the PDT in these groups of patients.

In view of an early thyroid uptake (two hours) relatively higher than that of twenty-four hours in some of our patients treated with radioactive iodine we decided to use the perchlorate test, as a means of ascertaining the integrity of the enzymatic systems responsible for the organification of iodine in this class of patients.

This study was carried out in 48 hyperthyroid patients treated with radioactive iodine (I^{131}) who, when the perchlorate test was performed, could be classified on clinical and laboratory grounds as follows: Group A, 22 euthyroid patients treated five to thirty months previously; Group B, 5 hyperthyroid patients treated two to three months previously; Group C, 14 euthyroid patients treated one and a half to three months previously; Group D, 4 patients with hyperthyroidism in remission, treated one and a half to five months previously; and Group E, 3 hyperthyroid patients treated fourteen to twenty months previously. None of these patients were receiving any drugs at the time of the study or during the months preceding it.

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The perchlorate test was performed as follows: the patient received an intravenous tracer dose of I^{131} (or I^{132}), and the thyroid radioactivity was measured one hour later; immediately afterward 2 gm. of potassium perchlorate was administered by mouth. Radioactivity over the neck was measured every fifteen minutes during the next hour.

The thyroid count after the administration of perchlorate was expressed as the percentage of the initial value. After one hour the counts were sufficiently high to minimize the experimental error. In some patients I^{132} was given, specially when the thyroid background (because of I^{131} previously given) was still very high. In these cases a pulse-height analyzer was used.

The control group was composed of 20 normal subjects and 20 hyperthyroid untreated patients on whom the perchlorate test was performed. The mean value of the lowest percentage observed in the normal group was 97.2 per cent ± 3.6, and that of the hyperthyroid group was 98.5 per cent ± 4.3. On that basis, a drop in the thyroid radioactivity in excess of 10 per cent was considered a positive test.

The test when positive was repeated at intervals of fifteen to twenty-five days whenever possible.

TABLE 1

Results of the Perchlorate Test in Hyperthyroid Patients Treated with I^{131}.

GROUP	CLINICAL & LABORATORY DIAGNOSIS AT TIME OF PERCHLORATE TEST	Nº OF CASES	PERCHLORATE TEST		MEAN TIME ELAPSED SINCE I^{131} RADIOIODINE DOSE
			POSITIVE	NEGATIVE	
			nº of cases	nº of cases	mo.
A	Euthyroidism	22	0	22	15.5
B	Hyperthyroidism	5	0	5	2.4
C	Euthyroidism	14	14	0	2.1
D	Hyperthyroidism in remission	4	4	0	2.5
E	Hypothyroidism	3	3	0	17.3

RESULTS

Table 1 summarizes the results and the mean time elapsed after the administration of the dose of radioactive iodine. As indicated, the test in Groups A and B was negative. All the patients of Groups C, D and E had positive tests.

When the test was repeated, Groups C and D showed a progressively smaller drop in the thyroid radioactivity, with a higher rate in Group D and a lower one in Group C. The 3 patients of Group E were still positive at the end of the observation period (six and a half months).

Figure 1 shows the chronologic evolution of the perchlorate test in a patient of Group C.

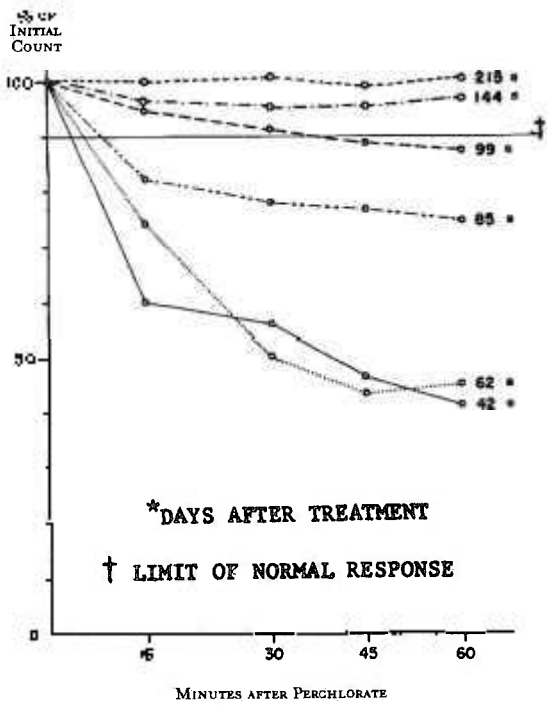

Figure 1. Chronologic Evolution of the Perchlorate Test in a Thirty-Year-Old Male Patient of Group C.

DISCUSSION

The results of this study confirmed on a wider scale those of Kirkland[1] and led us to postulate, in the immediate follow-up period (half a month to five months) after treatment with radioactive iodine, the existence of a defect of the biosynthesis step responsible for the iodide organification, both in the subjects who rapidly reach the euthyroid state (Group C) and in those still presenting clinical and laboratory evidence of thyrotoxicosis (Group D).

In the follow-up period of the I^{131}-treated subjects the enzymatic damage was sufficiently widespread to be detected by the perchlorate test and must have been responsible, at least in part, for the lowered hormonal production.

At a later time, the enzymatic defect must regress, since it becomes less and less detectable through the perchlorate test (Fig. 1). Finally, it becomes negative, and the patient's hormonal production is adequate (Groups A and C).

From this evidence, it seems reasonable to assume that the damage either could be partially reversible or could be compensated for by an increase in the number of follicular cells in which reproductive capacity is preserved.

TABLE 2

Perchlorate Test and Tanned Red-Cell Agglutination Test in Hyperthyroid Patients Treated with I^{131}.

GROUP	CLINICAL & LABORATORY DIAGNOSIS AT TIME OF PERCHLORATE TEST	Nº OF CASES	PERCHLORATE TEST		TANNED RED-CELL TEST	
			POSITIVE nº of cases	NEGATIVE nº of cases	POSITIVE nº of cases	NEGATIVE nº of cases
A	Euthyroidism	22	0	22	5	17
B	Hyperthyroidism	5	0	5	2	3
C	Euthyroidism	14	14	0	5	9
D	Hyperthyroidism in remission	4	4	0	0	4
E	Hypothyroidism	3	3	0	2	1

In the hypothyroid patients treated more than a year before the test (Group E) the positive results repeatedly obtained by the perchlorate test during the period of observation suggest that the damage was sufficiently strong to induce an irreversible process resulting in a biosynthetic defect incompatible with an adequate hormonal production. In cases in which subsequent tests remain positive it is tempting to postulate a reproductive incapacity.

The hypothesis that positive results on the perchlorate tests would be associated with an autoimmune mechanism, as might be suggested by the high incidence of positive tests in Hashimoto's thyroiditis (as reported by Doniach and Hudson,[2] Morgans and Trotter[3] and Murray and McGirr[4]) and after I^{131} treatment (as demonstrated by O'Gorman et al.[5]), does not seem very probable in view of the insignificant distribution of the tanned redcell agglutination tests in our groups of patients, as shown in Table 2.

We are continuing to investigate the incidence and the outcome of the perchlorate test, hoping that such a technic will lead us to a more appropriate prediction of the subsequent evolution of the I^{131}-treated patients and also to a better interpretation of the chronologically progressive incidence of hypothyroidism in this class of patients.

RESUMO

O teste do perclorato foi realizado em 48 pacientes com hipertireoidismo previamente tratados com iodo radioativo em diferentes estádios de função tireoidiana.

Todos os pacientes com eutireoidismo já há 30 meses e aqueles cujo hipertireoidismo estava estacionário tiveram teste de perclorato negativo.

Testes de perclorato positivos foram encontrados nas seguintes eventualidades:

a) Pacientes com hipertireoidismo em remissão;
b) Pacientes que tinham sido levados ao eutireoidismo recentemente (1 a 3 meses);
c) Pacientes com hipotireoidismo.

Aventa-se uma alteração enzimática no sistema peroxidase induzida pelo radioiodo e parcialmente reversível para explicar as alterações no teste do perclorato.

RÉSUMÉ

Le teste du perchlorat a été realizé em 48 patients, avec hypertireoidisme, qui avaient été d'avance traités avec de l'iode radioative en différents niveaux de fonction tiréoidienne.

Tous les patients qui étaient en eutireoidisme, il y avait déjà 30 mois, et ceux dont le hypertireoidisme était stationnaire, ont en le teste de perchlorat negative.

Des testes de perchlorat positives ont été trouvés dans les eventualités suivantes:

a) Des patients avec hypertireoidisme en remission;
b) Des patients qui sont devenus eutireoidiens récemment;
c) Des patients avec hypotireoidisme.

On peut admettre l'hypothèse d'une alteration enzimatique dans le sistéme peroxidase induite par le radioiode e partiellement reversible pour faire comprendre les altérations dans le teste du perchlorat.

REFERENCES

1. Kirkland, R.H. Impaired organic binding of radioiodine by thyroid following radioiodine treatment of hyperthyroidism. J. Clin. Endocrinol. & Metab. **14** : 565-571, 1954.
2. Doniach, D., and Hudson, R.V. Lymphadenoid goitre (Hashimoto's disease): diagnostic and biochemical aspects. Brit. M.J. **1** : 672-678, 1957.
3. Morgans, M.E., and Trotter, W.R. Defective organic binding of iodine by thyroid in Hashimoto's thyroiditis. Lancet **1** : 553-555, 1957.
4. Murray, I.P.C., and McGirr, E.M. Radioactive iodine studies in diagnosis of Hashimoto's thyroiditis. Brit. M.J. **1** : 838-841, 1960.
5. O'Gorman, P., Staffurth, J.S., and Ballentyne, M.R. Antibody response to thyroid irradiation. J. Clin. Endocrinol. & Metab. **24** : 1072-1075, 1964.