REGENERATION OF HUMAN THYROID AFTER SO-CALLED TOTAL THYROIDECTOMY*

JOHN V. GOODE, M.D., ARTHUR GROLLMAN PH.D., M.D., AND ALLEN F. REID, PH.D.

DALLAS, TEXAS

FROM THE DEPARTMENT OF SURGERY, SOUTHWESTERN MEDICAL SCHOOL OF THE UNIVERSITY OF TEXAS, DALLAS

THE EXTENT TO WHICH the thyroid gland should be removed in conditions in which thyroidectomy is indicated, and the fate of the residual thyroid tissue left at operation, have long been the subjects of controversy. When the disease process is a diffuse one, as in Graves' disease and in struma lymphomatosa, the surgeon must decide whether to leave behind diseased thyroid tissue or to attempt to carry out a complete thyroidectomy. Occasionally, when multiple small adenomas or multiple areas of hyperinvolution distort the entire thyroid, no normal tissue can be recognized,[3] so again the question arises: should all of the thyroid tissue be removed, or should evidently diseased thyroid be left behind?

Since the operation of thyroidectomy for hyperthyroidism improves a patient chiefly by reducing the hypermetabolism found in the disease,[3] it stands to reason that the more hyperfunctioning thyroid tissue removed, the greater the reduction of the hypermetabolism and the greater the improvement of the patient. Conversely, the larger the amount of hyperplastic thyroid allowed to remain in the neck, the more certain there will be persistence of symptoms, and the more likely the development of recurrent hyperthyroidism.[7,8] For these reasons, and because it seemed illogical to leave in the neck diseased thyroid tissue, our thyroidectomy operation has become more and more radical until, for certain patients, we have carried out as nearly a complete thyroidectomy as was possible. This paper is in no sense an argument for a routine total or complete thyroidectomy, but rather a report on the careful follow-up of 77 cases that for one reason or another were chosen for as nearly a total thyroidectomy as could be carried out (Table I).

In order to determine if removal of the entire thyroid gland caused any changes in the chemical composition of the blood, 13 patients were studied. As shown in Tables II and III, these showed very little variation from normal except for a slight increase in the blood cholesterol values in some instances. The body weights were not excessive. None of the patients received more than 2 gr. of desiccated thyroid daily; however, the basal metabolic rates were low normal. There was only one patient in whom proptosis of the eyes seemed more pronounced postoperatively than before operation. However, all these patients were protected from developing clinical evidence of myxedema by the administration of 1 or 2 gr. of desiccated thyroid daily. This may have contributed to the prevention of exhaustion atrophy of the residual thyroid tissue.

In addition, 34 patients were given 50 microcuries of radioactive iodine (I^{131}) and examined after 48 hours with the Geiger-Müller counter.[6,9] Examinations were made within a few weeks after oper-

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ation to check the radical nature of the operation. Similar tests were made at one or two years postoperatively to observe the regeneration of thyroid tissue in these thyroidectomized patients. All of the patients receiving the very radical thyroidectomy showed practically no uptake of radioactive iodine within the first few weeks following operation, as shown in Tables IV to VII, inclusive. This indicates that the operation had removed practically all of the thyroid gland, since the normal gland with the technic employed will store from 20 to 30 per cent of the administered iodine. As these patients were examined with repeated Geiger-Müller counter tests, it became evident that they followed one of two patterns: either there was a progressive increase in the capacity for storing radio-

TABLE I.—*Classification of Patients Undergoing a "Total" Thyroidectomy.*

Nodular toxic goiter	14
Graves' disease	26
Nodular non-toxic goiter	23
Hashimoto's disease	7
Carcinoma	7
Total	77

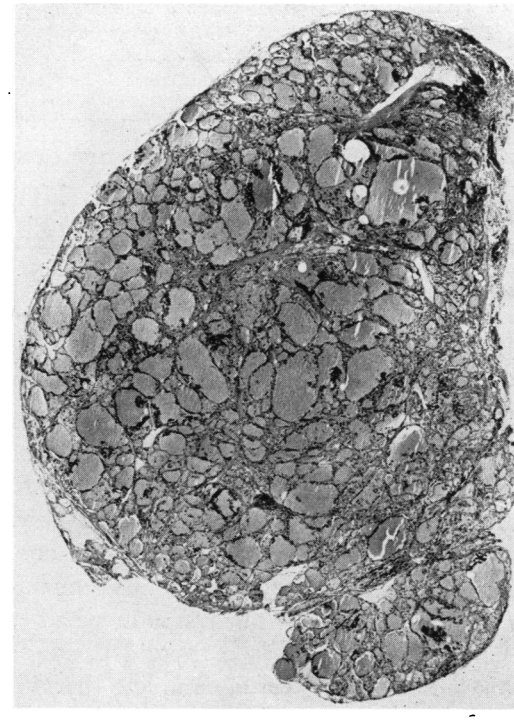

FIG. 1.—A microphotograph of an accessory thyroid nodule removed from a patient suffering from Graves' disease and prepared with 300 mg. of propylthiouracil daily for 16 weeks followed by 15 drops of Lugol's solution for four weeks.

TABLE II.—*Postoperative Laboratory Findings in the Toxic Goiter Group.*

Patient	Sex	Age	Weight lbs.	BMR %	Hgb. Gm. %	WBC x 1000	Lymphs. %	Cholesterol mg. %	Blood Ca. mg. %	Free HCl
M.B.	M	50	182	−22	15	11.8	51	165	10	..
W.D.	F	63	119	− 6	12	4.4	43	360	11	28
M.C.	F	40	139	−10	14	10.6	53	210	10	11
L.M.	F	38	201	−13	13	7.3	31	282	9	15
C.R.	F	41	134	−10	13	5.6	40	168	10	16
C.Y.	F	34	122	− 4	17	6.3	47	222	11	8

TABLE III.—*Postoperative Laboratory Findings in the Non-toxic Goiter Group.*

Patient	Sex	Age	Weight lbs.	BMR %	Hgb. Gm. %	WBC x 1000	Lymphs. %	Cholesterol mg. %	Blood Ca. mg. %	Free HCl
E.E.	F	57	110	+ 7	14	4.2	40	150	10	13
V.F.	F	60	147	−23	13	6.4	29	205	11	0
L.H.	M	48	198	− 7	14	7.1	35	197	10	38
W.M.	F	44	147	− 9	15	6.0	48	258	10	0
G.S.	F	44	148	+11	14	7.7	51	204	10	10
F.S.	F	39	135	+ 2	17	8.7	29	250	11	15
J.W.	F	40	148	−11	13	9.5	47	314	10	12

TABLE IV.—*The Uptake of Radioactive Iodine in 14 Patients with Graves' Disease at Varying Periods Following Radical Thyroidectomy.*

Patient	Sex	Age	Date of Operation	Date of Measurement	Per Cent Uptake
M.B.	M	50	12/16/46	5/29/48	5.9
				7/7/50	6.6
M.C.	F	40	10/16/46	5/30/48	6.3
				6/30/50	6.0
I.P.	F	42	4/29/49	7/13/50	2.2
O.P.	F	23	7/12/49	8/31/49	0.2
				7/31/50	4.3
T.R.	F	30	12/27/48	2/ 7/49	0.26
				6/30/50	3.1
C.R.	F	41	6/ 4/45	5/14/48	4.3
				3/21/51	9.94
G.S.	M	31	9/29/48	10/ 4/48	0.01
				10/18/48	0.63
				6/16/50	1.5
C.S.	F	23	6/18/48	6/25/48	0.4
				6/16/50	0.18
				3/16/51	13.0
J.S.	M	32	10/6/46	5/14/48	0.3
V.W.	F	40	4/11/47	5/30/48	1.1
				6/30/50	3.8
C.Y.	F	34	7/24/48	11/ 3/50	4.0
L.R.	M	37	1/19/43	4/25/49	0.06
				4/29/49	3.0
K.N.	M	38	10/20/48	10/25/48	0
				9/ 1/49	7.0
M.D.	F	47	3/22/50	3/ 9/51	1.17

active iodine, indicating an increasing amount of functioning thyroid tissue in the neck, or there was no increase or even a decrease in the capacity for storing iodine. All 14 of the patients falling into the first, or thyroid-regenerating, group had been diagnosed both clinically and pathologically as having Graves' disease. The group that failed to show regeneration of thyroid tissue comprised the nodular non-toxic goiters with areas of hyperinvolution, adenomas (both toxic and non-toxic), and instances of struma lymphomatosa of Hashimoto.[5] The fact that our patients received desiccated thyroid would tend to cause a reduction in the uptake of radioactive iodine but could not completely block the iodine uptake.[9]

The 14 patients with Graves' disease showed no symptoms of persistent or recurrent hyperthyroidism; however, within one year of operation, about half of them had developed the ability to store from 5 to 10 per cent of the administered iodine. This represents approximately 25 to 30 per cent of the normal iodine uptake. These readings were obtained only in the operative region and not over the mediastinum. The other half of the patients with Graves' disease showed a more gradual but definitely increasing ability to store iodine. Subsequent to one year following operation, the iodine uptake remained at 25 to 30 per cent of normal, so that it was possible in some cases to eliminate the use or reduce the dose of desiccated thyroid to half a grain a day without evidence of hypothyroidism.

TABLE V.—*The Uptake of Radioactive Iodine in Seven Patients with Nodular Toxic Goiter at Varying Periods Following Radical Thyroidectomy.*

Patient	Sex	Age	Date of Operation	Date of Measurement	Per Cent Uptake
J.B.	F	38	10/26/49	11/ 3/49	0.06
				7/13/50	0.05
H.E.	F	49	6/19/48	6/23/48	1.1
S.H.	F	41	11/12/49	1/25/50	0
Z.Y.	F	36	10/31/45	7/24/50	0.06
W.C.	F	63	6/ 8/46	5/14/48	0.6
				12/14/50	0.26
W.B.	F	20	9/28/48	10/ 5/48	0.3
				8/17/50	0.24
L.M.	F	38	6/ 4/46	5/14/48	0.8
				7/13/50	0.32

There were 20 patients who received the same radical operation, but in whom the pathologic diagnosis was not Graves' disease. This group included seven patients with toxic adenoma, five with struma lymphomatosa of Hashimoto, and eight with nodular non-toxic goiter due to hyperinvolution of parts of the thyroid gland. As in the previously mentioned group, immediately after operation the radioactive iodine uptake was zero or a fraction of one per cent, but in sharp contrast to the patients with Graves' disease, this group failed to regenerate thyroid tissue. Geiger-Müller counter studies made as long as five and six years after operation showed a decreasing capacity for the storage of radioactive iodine.

From a clinical standpoint, the results in these patients were entirely satisfactory.

There were no deaths, no instance of injury to the recurrent laryngeal nerve, and no instance of permanent parathyroid insufficiency. Several patients showed circumoral numbness, stiffness of the hands and feet and a positive Chvostek's sign. These disappeared within a few days, during which period 4 Gm. of calcium gluconate powder were administered three or four times a day. In two patients, both of whom had developed a hematoma in the wound, the parathyroid injury was more severe. These were given 10 cc. of 5 per cent calcium chloride intravenously for the immediate control of cramps in the hands and feet. At the same time they were given 1 cc. of parathormone intramuscularly and calcium gluconate by mouth. After this the urine was tested with Sulkowitz reagent and whenever the test was negative, 1 cc. of dihydrotachysterol (Hytakerol®) was given by mouth. Whenever the test was cloudy no Hytakerol was given. Two patients were sent home on this regimen; both reported that within eight weeks they required no more dihydrotachysterol or calcium gluconate, and had no symptoms of parathyroid insufficiency.

TABLE VI.—*The Uptake of Radioactive Iodine in Eight Patients with Nodular Non-toxic Goiter at Varying Periods Following Radical Thyroidectomy.*

Patient	Sex	Age	Date of Operation	Date of Measurement	Per Cent Uptake
E.E.	F	50	5/20/46	5/14/48	0.3
				6/30/50	0.5
W.R.	F	61	1/14/47	9/18/50	0.29
U.H.	F	50	1/31/44	10/23/50	0.27
L.C.*	M	42	6/11/48	7/14/48	0.1
				8/17/50	1.7
V.F.*	F	60	5/12/49	5/27/49	0.06
				7/10/50	0.1
L.C.*	M	48	10/15/48	10/19/48	0
				10/18/49	0.06
				6/16/50	0.3
J.H.*	F	64	5/11/48	5/17/48	1.1
W.M.*	F	47	8/26/44	5/30/48	0.2
				12/21/50	0.15

* Lymphoid goiter.

DISCUSSION

This study indicates that even in the most radical thyroidectomy one does not remove all the thyroid tissue. Either tiny bits of the thyroid gland or thyroid rests remain, and these by hypertrophy and hyperplasia, as suggested by Halsted,[4] may become capable of taking over the function of the ablated thyroid gland. It is a source of relief to the surgeon to realize that within one year after the most radical thyroidectomy most patients with Graves' disease were able to store about 20 per cent as much iodine as a normal gland could store. In support of the above-mentioned suggestion that hyperplasia of thyroid rests may account for this increasing capacity for iodine storage, the following observation may be cited. Occasionally after the preoperative use of propylthiouracil one may find at operation tiny pinkish nodules of thyroid tissue near the thyroid gland but quite separate from it. A typical example of these nodules, which are several millimeters in diameter and on section show a structure identical with the hyperplastic thyroid gland, is shown in Figure 1. Both the appearance of the tissue section as well as the location of the nodules in the neck indicate that they represent accessory thyroid tissue. Histologically there is nothing to suggest that these structures could be considered papillary thyroid tissue in cervical lymph nodes. Since such nodules have been

TABLE VII.—*The Uptake of Radioactive Iodine in Five Patients with Hashimoto's Disease (Struma Lymphomatosa) at Varying Periods Following Radical Thyroidectomy.*

Patient	Sex	Age	Date of Operation	Date of Measurement	Per Cent Uptake
V.A.	F	37	8/24/49	8/31/49	2.3
				7/ 7/50	0.06
G.S.	F	44	4/19/47	5/14/48	0.03
				12/21/50	0.03
J.W.	F	40	7/25/45	5/30/48	0.2
				7/14/50	0
J.S.	F	35	7/27/49	7/21/50	0.08
V.Mc.	F	51	8/ 4/42	3/25/50	0

found only in cases receiving propylthiouracil therapy, it is probable that these nodules represent thyroid rests that have been rendered visible by the hyperplasia induced by the propylthiouracil.

It is interesting that when this very radical thyroidectomy was carried out on a normally functioning thyroid gland which contained either nodules of hyperinvolution or adenomas, there was no regeneration of thyroid tissue. This was true even if the adenomas were associated with clinical signs of toxicity, thus supporting the view of Cope *et al.*,[2] who found that the hyperfunctioning tissue in toxic adenomas was found in the adenoma and not in the surrounding tissues. For this reason, and because the patients with struma lymphomatosa not only failed to show regeneration but actually showed a tendency to store less iodine as they were followed, it seems safe to suggest that for goiters other than that of Graves' disease a conservative thyroidectomy is indicated.

SUMMARY

1. In operating for Graves' disease, a surgeon need not fear removing too much of the thyroid, because in such cases about one-fifth the normal iodine uptake can be expected within a year even after the most radical thyroidectomy.

2. Following operation for goiters of other types, this tendency for regeneration is not noted; therefore, a more conservative operation is adequate. This is especially true for Hashimoto's struma lymphomatosa, where progressive atrophy is to be expected.

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