diagnosing pheochromocytoma. Although, on average, semiquantitative indicies are highly discriminant, the overlap between values observed in normal and abnormal adrenal medullae make them of little additional use in clinical practice.

CONCLUSION

We found that the adrenal medulla is more often visualized after injection of 74 MBq ^{131}I-MIBG and that adequate interpretation of a MIBG scan should take into account that 56% and 73% of normal glands are seen at 24 and 48 hr postinjection, respectively. Since 1989, the optimal visual score for diagnosing pheochromocytoma is 3 or more. Thus, only an intense uptake should be considered to be positive. We could not find any factor related to the patient recruitment and the scanning protocol to explain this change. Therefore, we strongly suspect that the increase in SA of labeled MIBG during recent years is the probable explanation of the higher proportion of normal adrenal medullae displaying visible uptake.

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Changes in Radioiodine Turnover in Patients with Autonomous Thyroid Adenoma Treated with Percutaneous Ethanol Injection

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In 24 patients with autonomous thyroid adenoma, we studied the hormonal pattern (free thyroxine, free triiodothyronine and thyroid stimulating hormone) and markers of radioiodine turnover before and after nodule ablation with percutaneous ethanol injection. **Methods:** The hormonal pattern was studied before treatment and at various intervals after nodule ablation. Changes in radioiodine turnover were studied measuring ^{131}I protein-bound iodine and the biologic half-life of radioiodine in the thyroid (calculated from thyroid uptake at 24 and 48 hr) before and after ethanol treatment. **Results:** The hormonal pattern was normalized by treatment in all patients and remained normal for the follow-up period. Before treatment, protein-bound ^{131}I was elevated in all patients but 4; after treatment, it normalized in 15 patients with the disappearance of the adenoma on scintigraphy. In the remaining 9 patients with only partial nodule destruction on scintigraphy, protein-bound ^{131}I remained elevated although markedly reduced. Biologic half-life was shortened in 18 of 24 patients before treatment; after treatment, it was normal in 18 of 24 patients (13 of 15 with complete nodule ablation and 5 of 9 with partial ablation). **Conclusion:** Ethanol treatment normalized the hormonal pattern in all patients. Measures of radioiodine turnover were better markers of residual disease in that they normalized in almost all patients with complete nodule ablation, whereas they remained abnormal in a high proportion of patients with incomplete ablation. Thyroid hormones remained normal over a follow-up period of 3–7 yr in all patients.

Key Words: autonomous thyroid adenoma; percutaneous ethanol injection; ethanol injection

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Percutaneous ethanol injection for the treatment of the autonomous thyroid adenoma was proposed by our group in 1990 (*1*). Subsequent reports by us and others (*2–10*) have confirmed the efficacy of this treatment, which is now an accepted method of nodule ablation (*11*). The results of treatment were judged on the basis of changes in the hormonal pattern, particularly changes in thyroid stimulating hormone (TSH) levels, and on qualitative changes in the scintigraphic appearance of the thyroid gland. In this article, we report changes induced by ethanol treatment on radioiodine turnover in a group of patients with autonomous thyroid adenoma.

MATERIALS AND METHODS

Since 1989, we have treated with percutaneous ethanol injection more than 200 patients with autonomous thyroid adenoma. The main clinical and hormonal results have been published (*1,2,7*). This article includes a subset of 24 patients in whom, in addition to the usual scintigraphic study with pertechnetate, we performed a study with radioiodine (^{131}I), including an uptake curve up to 48 hr, the determination of ^{131}I protein-bound iodine at 48 hr, and scintigraphy at 24 hr. The patients studied were treated in the early years of ethanol use for nodule ablation, when a study with radioiodine was associated with pertechnetate to be certain that the nodules were not of the trapping-only type (*12*) and to collect parameters of dose calculation for treatment with ^{131}I in the event the patient eventually preferred it to ethanol ablation. More recently, we ceased using ^{131}I for diagnosis and used ^{123}I for dosimetry calculations (*13*). Among the patients who had the basal ^{131}I study, 24 had a repeat study after the treatment of the nodule with percutaneous ethanol injection to investigate the changes in radioiodine turnover induced by treatment. Demographic data, hormone levels and parameters of radioiodine turnover at baseline are reported in Table 1, Figure 1 and Table 2. All patients had suppressed serum TSH concentrations (<0.1 mU/liter). According to the hormonal data, 15 were toxic (hormone levels above the normal range) and 9 were nontoxic (hormone levels still normal). Thyroid uptake measurements were performed 6, 24 and 48 hr after oral administration of 1.85 MBq ^{131}I using a probe connected with a scaler having a window centered on the 364-keV photopeak of the radionuclide. Scintigraphy was performed at 24 hr with a rectilinear scanner. The biologic half-life of iodine in the thyroid was calculated from the uptake measurements at 24 and 48 hr; mean normal value is 65 days (*14*) and it was shortened when lower than 20 days (*15*). Protein-bound ^{131}I was measured at 48 hr counting 4 ml of plasma after removal of the free iodine by an ion-exchange resin. Results were given as a percent of administered activity per liter of plasma (normal values < 0.3% dose per liter of plasma). Free thyroid hormones in serum (normal range 7.7–19.3 pmol/liter for FT4 and 4.0–8.6 pmol/liter for FT3) were assayed by radioimmunoassay according to Romelli et al. (*16*). Serum TSH was assayed by a sensitive immunoradiometric assay; the results are given in units of the 80/558 reference preparation of the World Health Organization (normal range 0.4–4.5 mU/liter). The thyrotropin releasing hormone (TRH) test, done in 17 patients before treatment and in 22 after treatment, was performed by the intravenous injection of 200 μg of the peptide. Blood for TSH measurement was taken before injection and 20 and 30 min after. Normal peak levels of TSH after TRH range between 3 and 20 mU/liter.

Nodule volume was measured by ultrasonography using the formula for ellipsoids. Ethanol was injected into the nodules by the

TABLE 1
Demographic Data, Nodule Volume and Treatment Modalities in 24 Patients with Autonomous Thyroid Adenoma Treated with Percutaneous Ethanol Injection

Patient no.	Age (yr)	Sex	Nodule volume (ml)*		Cycles of treatment	Injected ethanol (ml)†	Follow-up (mo)
			Before treatment	After treatment			
1	57	M	11 + 3	1.3 + 0.5	1	6 + 2	86
2	48	F	14	0.9	1	11	78
3	70	F	14	1.5	1	12	72
4	28	F	17	1.2	1	13	70
5	62	F	14	2.4	2	11 + 9	69
6	68	M	28	2.5	1	44	67
7	23	F	9	3.1	1	17	66
8	54	M	33	3.0	1	40	65
9	59	M	23	1.3	2	17 + 7	64
10	58	F	6	1.5	1	14	64
11	61	F	23	1.3	2	14 + 20	63
12	51	M	34	3.2	1	42	62
13	54	F	5	1.4	1	8	54
14	32	F	10	1.5	1	22	53
15	54	M	33	2.7	1	36	53
16	59	M	17 + 21	1.1 + 10	1	26 + 4	65
17	49	F	25	4.5	1	36	64
18	54	F	14	1.6	1	19	63
19	45	F	23	2.0	1	30	63
20	65	F	27	3.0	1	26	62
21	40	M	66	10.0	1	142	60
22	41	F	8	2.0	2	14 + 4	59
23	64	F	8	3.0	1	9	54
24	39	F	11	7.2	1	13	36
Mean ± s.d.	51.4 ± 12.4		20.7 ± 13.7	3.1 ± 2.6		27.8 ± 26.8	63.0 ± 9.5

*Patients 1 and 16 had two nodules.
†For Patients 1 and 16, the amount of ethanol injected in each nodule is reported. Patients 5, 9, 11 and 22 had two treatment cycles in a single nodule.

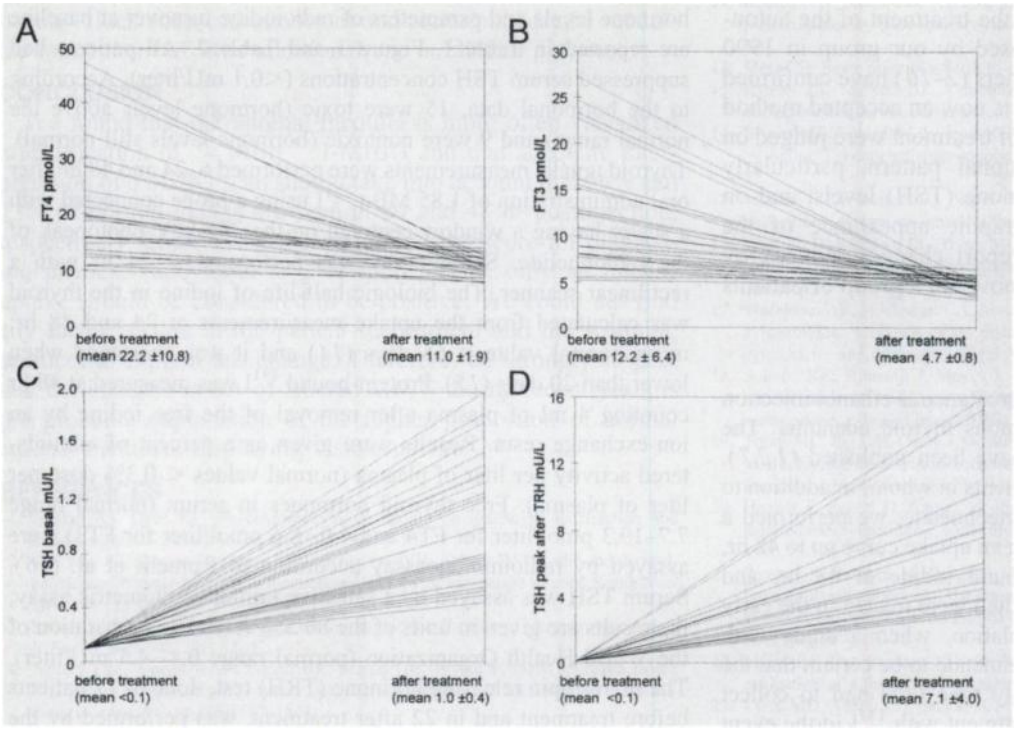

FIGURE 1. Serum hormone levels before and after ethanol treatment in the 24 patients studied. Individual data and mean values ± s.d. are shown. (A) FT4. (B) FT3. (C) TSH basal. (D) TSH peaks after TRH for only the 16 patients who had a TRH test both before and after ethanol treatment.

percutaneous route under ultrasound guidance as previously described (*2,7*). The total amount of ethanol injected was divided into 2–12 injections (mean 6) made at 4- to 7-day intervals. The post-treatment ^{131}I radioiodine study was performed after resumption of TSH secretion and completion of nodule shrinkage, generally at least 6 mo after the end of treatment. The hormone values reported in Figure 1 are those recorded at the time of the radioiodine studies. The follow-up period after treatment is 3–7 yr. All patients gave informed consent to the treatment and scintigraphic studies.

RESULTS

The results of ethanol treatment on nodule volume, FT4 and FT3 serum levels, TSH levels before and after TRH stimulation

TABLE 2
Parameters of Radioiodine Turnover Before and After Treatment with Percutaneous Ethanol Injection in 24 Patients with Autonomous Thyroid Adenoma

Patient no.	Before treatment					After treatment				
	% Thyroid uptake			Biologic half-life	Protein-bound ^{131}I %/	% Thyroid uptake			Biologic half-life	Protein-bound ^{131}I %/
	6 hr	24 hr	48 hr	(d)	liter plasma	6 hr	24 hr	48 hr	(d)	liter plasma
1	15.0	25.0	20.0	3.1	0.18	10.2	14.4	13.4	9.6	0.09
2	27.0	35.0	27.0	2.7	2.3	30.7	45.4	44.5	34.6	0.14
3	16.5	28.5	30.5	∞	0.24	23.0	38.4	40.7	∞	0.15
4	35.0	47.0	47.0	∞	0.20	23.1	38.6	42.4	∞	0.16
5	27.0	43.0	43.0	∞	0.25	9.1	15.5	15.5	∞	0.15
6	21.3	35.5	29.0	3.4	1.1	20.1	30.8	27.7	6.5	0.28
7	28.0	42.4	37.6	5.8	1.2	19.6	27.0	30.5	∞	0.13
8	26.8	34.1	30.3	5.9	0.9	20.1	27.0	27.0	∞	0.31
9	48.3	44.4	37.4	4.0	4.4	32.3	43.0	42.3	42.2	0.65
10	21.5	27.7	27.9	∞	0.66	39.1	49.4	48.7	48.5	0.24
11	56.2	66.9	66.0	51.1	1.6	24.4	38.9	40.6	∞	0.32
12	27.0	39.0	35.0	6.4	1.3	30.1	41.8	45.0	∞	0.19
13	26.5	36.4	34.2	11.1	0.5	19.3	29.1	28.6	40.0	0.14
14	29.6	38.0	36.2	14.3	0.55	23.2	31.3	31.2	216.5	0.23
15	41.1	44.6	43.8	38.3	0.97	14.4	28.0	27.8	96.7	0.18
16	33.2	43.4	33.0	2.5	3.2	11.2	22.2	22.5	∞	1.2
17	16.5	22.1	18.7	4.1	1.54	11.2	17.9	19.0	∞	0.58
18	34.0	49.0	44.0	6.4	0.52	17.0	25.9	25.0	19.6	0.48
19	51.0	55.7	52.4	11.3	2.0	20.6	29.6	27.4	9.0	1.5
20	31.6	38.5	36.1	10.8		24.9	38.3	38.8	∞	0.35
21	30.1	56.0	36.1	1.6	3.2	22.2	35.8	26.1	2.2	0.54
22	12.3	19.6	15.5	2.9	1.5	14.4	19.0	15.1	3.0	0.59
23	29.9	42.3	39.9	11.8	2.1	24.1	42.4	46.6	∞	0.45
24	47.8	53.4	43.9	3.5	6.5	34.5	40.7	41.4	∞	2.5
mean ± s.d.	30.5 ± 11.5	40.3 ± 11.3	36.0 ± 11.0		1.6 ± 1.5	21.6 ± 7.8	32.1 ± 9.8	31.9 ± 10.7		0.48 ± 0.5

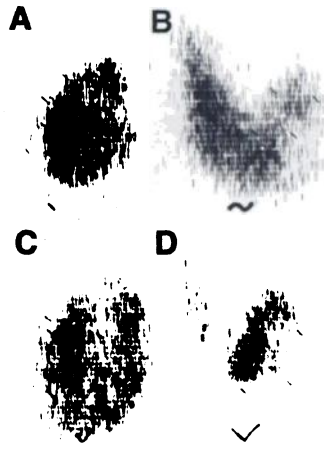

FIGURE 2. Thyroid scintigraphy before (left) and after (right) ethanol injection in two patients with autonomous thyroid adenoma. (A,B) Complete nodule ablation (Patient 12). (C, D) Partial nodule ablation (Patient 21).

and parameters of radioiodine turnover (biologic half-life and protein-bound ^{131}I) are reported in Table 1, Figure 1 and Table 2. Marked reduction in nodule volume occurred in all cases. FT4 and FT3 serum concentrations were normalized in all cases when previously elevated. TSH levels, undetectable and unresponsive to TRH before treatment, became both normal and normally responsive after therapy. On the basis of scintigraphic appearance after treatment, the patients were categorized as completely cured (Patients 1–15), when the nodule was no longer visible or was replaced by a cold area within the reactivated normal tissue, or partially cured (Patients 16–24), when the nodule or parts of it were still visible above the partially reactivated normal tissue (Fig. 2). This is a scintigraphic distinction, because the hormonal pattern was not different in the two categories of patients. Parameters of radioiodine turnover were markedly changed by treatment. In all but 4 patients, protein-bound ^{131}I before treatment was elevated and it was essentially normalized after treatment in all completely cured patients except 1 (Patient 9) in whom it was markedly reduced. In partially cured patients, protien bound ^{131}I remained above the normal range, although it was greatly reduced in most patients. Biologic half-life before treatment was shortened in 18 of 24 patients and after treatment it was normalized in 18 of 24. Of the 6 patients with short biologic half-life after treatment, 4 were partially cured and 2 were completely cured on the basis of scintigraphy appearance.

DISCUSSION

Results of ablation by ethanol of the hyperfunctioning nodules have been evaluated on the basis of changes in hormonal pattern, qualitative inspection of changes in scintigraphy and demonstration of reduction in nodule volume after treatment (*1–10*). In the small series presented here, we included parameters of radioiodine turnover. Although our study had several technical limitations due to the fact that the data were derived from diagnostic studies, the results are of interest. One drawback was the fact that the biologic half-life was obtained from only two points of uptake measurement (24 and 48 hr). Since hyperfunctioning nodules generally have rapid iodine turnover, the phenomenon of dismission was easily demonstrated under these conditions of uptake measurement. The results of our study clearly showed the shortened half-life before treatment and the correction after treatment in the majority of patients especially those with complete nodule ablation. In patients with partial ablation, radioiodine half-life remained frequently short due to the presence of different degrees of residual autonomous tissue. Another technical limitation was the fact that uptake was measured with a probe seeing the entire thyroid gland. This was of little importance in uptake measurements before treatment when radioactivity was confined to nodular tissue, and in cases of complete ablation, when radioactivity was almost entirely in the reactivated normal tissue. In cases of partial ablation, uptake measure reflected a combination of radioiodine content in residue of the nodule and in partially reactivated normal tissue. For these patients, the best technical approach would be an uptake study with a gamma camera, which allows separation of the uptake values of the two parts of the thyroid gland (nodule and extranodular tissue). We have used this method in recent cases (*13*). Values of protein bound ^{131}I likewise reflected the degree of nodule destruction—normalized in almost all patients with complete inactivation and abnormal, although reduced, in patients with partial inactivation. Parameters of radioiodine turnover appeared to be more sensitive indices of residual disease than the hormonal values. Once a nodule was sufficiently damaged to allow resumption of TSH secretion, the levels of circulating thyroid hormones became normal and no difference was demonstrable between complete and partial ablation. TSH levels showed wide overlap in the two groups of patients as well, although a significant mean difference in both basal and TRH-stimulated TSH levels was demonstrated between patients with complete and partial nodule ablation (*7*).

Studies of radioiodine turnover after nodule ablation with ^{131}I therapy would be of interest because after successful radioiodine treatment residual nodule function can be demonstrated in a large proportion of patients in post-treatment scintigraphic studies (*17–22*). A discussion of the relative benefits of the three therapeutic methods of nodule ablation (surgery, radioiodine and ethanol) was beyond the scope of this article. We have reviewed this topic elsewhere (*23*). Ethanol treatment was cheaper than surgery and more expensive than radioiodine. The main advantage of ethanol over radioiodine was the virtual absence of post-treatment hypothyroidism (*7,23*), whereas the prevalence of postradioiodine hypothyroidism was 12% (151 of 1293 published cases) (*23*). The main disadvantage of the ethanol treatment was the difficulty of sufficiently inactivating big nodules (over 40 ml in volume). However, if the nodule was damaged sufficiently to decrease hormone production to an extent that allowed resumption of TSH secretion, the results remained stable for several years. In the patients we have treated to date, no cases of resuppression of TSH have been seen, even among patients with nodules still partially visible on post-treatment scintigraphies. This phenomenon was probably similar to what happens with radioiodine treatment, which leaves a consistent proportion of nodules still visible (*17–22*). The absence of post-treatment hypothyroidism with ethanol was due to the complete sparing of extranodular tissue that in contrast can be partially damaged during radioiodine treatment (*13,24*).

CONCLUSION

Parameters of radioiodine turnover are sensitive markers of inactivation of hyperfunctioning thyroid nodules by percutaneous ethanol injection. They reflect the presence of residual disease more accurately than the measurement of TSH and free thyroid hormones in serum.

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Fluorine-18-FDG PET Imaging Is Negative in Bronchioloalveolar Lung Carcinoma

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The goals of our study were to establish PET accuracy with ^{18}F-fluorodeoxyglucose (FDG) in finding localized formations of bronchioloalveolar lung carcinoma (BAC) and to investigate the correlation between FDG uptake and the degree of cell differentiation in adenocarcinoma of the lung. **Materials:** Twenty-nine patients with 30 adenocarcinomas of the lung (7 bronchioloalveolar lung carcinomas, 9 well differentiated, 2 well-moderately differentiated, 11 moderately differentiated and 1 poorly differentiated) were studied. All patients underwent thoracotomies within 4 wk after the FDG PET study. For qualitative analysis, the degree of FDG activity in the tumors was visually scored using a five-point grading system: 0 = same to background activity, 1 = less than mediastinal blood-pool activity, 2 = same to mediastinal blood-pool activity, 3 = slightly greater than mediastinal blood-pool activity and 4 = substantially greater than mediastinal blood-pool activity. Foci of activity with Grades 2–4 were considered tumors. For semiquantitative analysis, standardized uptake values (SUV) were calculated. **Results:** In 7 BACs, 4 lesions (57%) showed negative results on FDG PET, while in 23 non-BACs, only 1 lesion (4%), which was a well-differentiated adenocarcinoma showed a negative result. BACs' mean visual score (1.43 ± 1.27) was significantly lower than that of non-BACs (3.17 ± 1.03) ($p = 0.001$). The BACs' mean SUV (1.36 ± 0.821) was significantly lower than that of well-differentiated adenocarcinomas (2.92 ± 1.28) ($p = 0.014$); the mean SUV of well-differentiated adenocarcinomas was significantly lower than that of moderately differentiated adenocarcinomas (4.63 ± 1.86) ($p = 0.031$). No significant differences were apparent in average size among these three histologic types. **Conclusion:** A correlation was observed between FDG uptake and the degree of cell differentiation in adenocarcinoma of the lung. FDG PET may show negative results for BAC.

Key Words: PET; fluorine-18-fluorodeoxyglucose; bronchioloalveolar lung carcinoma

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PET with ^{18}F-fluorodeoxyglucose (FDG) may play a valuable role in delineating viable tumor tissue due to FDG PET's ability to detect a tumor's increased glucose metabolism. It is known that malignant tumors tend to show higher metabolic demands than normal tissues. Recent articles have indicated FDG PET's value in diagnosing human lung cancer (*1–7*). FDG PET has a sensitivity and specificity of 93% and 88%, respectively, for detecting malignancy in indeterminate solitary pulmonary nodules (*7*). However, wide variations in glucose consumption exist among individuals depending on the type of neoplasm. In cases of malignant lung neoplasms, few negative results of malignancy have been reported using FDG PET (*4,5,8*). Negative results have occurred in patients with bronchioloalveolar lung carcinomas (BACs) (*4,8*). BAC is a form of peripheral lung adenocarcinoma growing as a single layer of malignant cells along the walls of terminal airways (*9*). It is known that the tumor growth rate for BACs is lower than that for non-BAC

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