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Iodine-131-MIBG Scintigraphy in Adults: Interpretation Revisited?

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Iodine-131-metaiodobenzylguanidine (MIBG) scintigraphy is a reliable method used to diagnose pheochromocytoma. Although the adrenal medulla usually is not visualized, faint uptake can be observed in 16% of the patients 48–72 hr after injection of 18.5–37 MBq ^{131}I-MIBG. We recently observed an increase in the frequency of visualization of the adrenal medulla in patients injected with 74 MBq ^{131}I-MIBG. Therefore, we retrospectively evaluated the pattern of uptake and potential changes between 1984 and 1994. **Methods:** Scintigraphic data from 103 patients referred for suspected pheochromocytoma were reviewed randomly. Data from 19 patients with medullary thyroid carcinoma were analyzed separately. Patients were injected with 74 MBq ^{131}I-MIBG and imaged at 24 hr postinjection, 48 hr postinjection, or both. Adrenal uptake was scored visually as 0 (no visible uptake) and 1 (uptake just visible) to 4 (most intense activity in the picture). Semiquantitative indicies were evaluated for discriminating between normal adrenal medullae and pheochromocytomas. Twenty-seven pheochromocytomas were surgically proven in 25 patients. **Results:** A visual score ≥3 was noted in 81% and 90% of the pheochromocytomas at 24 hr and 48 hr postinjection, respectively. From 1984 to 1988, 16% and 31% of adrenal medullae were seen at 24 and 48 hr postinjection, respectively, whereas from 1989 to 1994, 56% and 73% were visualized at 24 and 48 hr postinjection, respectively. Before 1989, the best cutoff criterion to identify a pheochromocytoma, determined from receiver operating characteristic curve analysis, was a score ≥1 at 24 hr and ≥3 at 48 hr postinjection, with a sensitivity and specificity of 92% and 84% at 24 hr and 92% and 99% at 48 hr postinjection. From 1989, the best cutoff was a score ≥3 at both imaging sessions, with a sensitivity and specificity of 82% and 100% at 24 hr and 100% and 97% at 48 hr postinjection. Among the semiquantitative indicies, the adrenal-to-liver and adrenal-to-heart ratios were the best discriminators between normal and pathological adrenals. They were, however, of little use because of the overlap between normal adrenal medullae and pheochromocytomas. **Conclusion:** The high rate of visualization of the normal adrenal medulla in this study was related to the larger-than-usual injected dose (74 MBq). Over recent years, however, this rate has been increasing, possibly because of the increased specific activity of ^{131}I-MIBG. Adequate interpretation should take into account that a faint or definite uptake may be visible in more than 50% of normal adrenal medullae.

Key Words: iodine-131-metaiobenzylguanidine; adrenal medulla; pheochromocytoma

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Although rare, pheochromocytoma is a potentially life-threatening tumor that usually can be managed with minimal morbidity provided that it is diagnosed early (*1*). Since its introduction in 1980, metaiodobenzylguanidine (MIBG) labeled with ^{131}I has proven to be a safe, noninvasive and efficient localization procedure. This is particularly true for tumors arising from extra-adrenal sites or exhibiting malignant metastatic disease and for postoperative tumor recurrence (*2–7*).

MIBG is an analog of the endogenous neurotransmitter norepinephrine, and two mechanisms of uptake have been described. The first is an energy- and sodium-dependent specific uptake mechanism (known as Type I); in addition, there is some degree of nonspecific diffusion (known as Type II). After entering neuroendocrine cells, MIBG is concentrated in the intracellular hormone storage vesicles by an energy-dependent, tetrebenazine-sensitive process similar to the cell membrane specific uptake mechanism (*8*). Uptake can be found in a variety of normal tissues, such as the adrenals, and the sympathetic innervation of the salivary glands and myocardium. Consistent with the neuroadrenergic uptake mechanism, there is a good correlation between the uptake of radioactivity and the amount of neurosecretory granules (*9*). The normal distribution of this agent was first described in detail by Nakajo et al. (*10*) in 1983. They found that, after injection of 18.5 MBq, normal adrenal medullae were observed only in 2% of patients at 24 hr and in 16% of patients at 48 hr postinjection, whereas pheochromocytomas had an intense focal area of uptake between 24 and 72 hr postinjection. Other researchers (*3, 4*) found that the adrenal medulla usually was not depicted using this dosage, whereas uptake could be delineated more frequently with higher doses.

Examining the ^{131}I-MIBG distribution pattern over recent years, we had the impression that the adrenal medulla was more often visualized, although the prevalence of pheochromocytoma was stable (i.e., 2–3/yr) and the injected radioactivity

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remained unchanged (74 MBq). We conducted a retrospective study to determine whether the visualization rate of the adrenal medulla really is higher now than previously. In addition, we tried to analyze the factors that might have influenced the uptake of ^{131}I-MIBG by the normal adrenal medulla.

MATERIALS AND METHODS

Patients

This retrospective study was based on data from 103 patients (57 women, 46 men; age range 15–88 yr) referred to our department between January 1984 and December 1994 for suspicion of pheochromocytoma based on a history of paroxysmal or severe hypertension or episodic spells (e.g., flushing, headache, sweating).

Patients were instructed by their physician to withdraw drugs known to potentially interfere with MIBG uptake (*11*); in particular, sympathicomimetics, labetalol, alpha-blocking agents and reserpine were strictly avoided. Twenty-seven pheochromocytomas were surgically proven in 25 patients. Patients were classified as normal if no tumor was found at completion of the workup, including biochemistry and additional localization procedures (transmission CT, MRI or both), and this was confirmed by a negative follow-up course.

In addition, 19 patients with histology-proven medullary thyroid carcinoma (MTC) in whom MIBG scintigraphy was performed for screening of pheochromocytoma or for assessment of tumor recurrence were analyzed separately. They comprised 12 sporadic and 7 familial MTC. One patient was part of a kindred with the multiple endocrine neoplasia syndrome, Type 2 (MEN-2), in which 2 cases of pheochromocytoma had been recorded previously in other hospitals. This patient had repeated measurements of urinary catecholamines within normal limits between 1984 and 1996. Ten patients, including 5 familial cases, had multifocal disease, and 9 patients, including 3 familial cases, had metastases at the time of diagnosis. In none of the 19 patients was a definite diagnosis of pheochromocytoma made during a median follow-up period of 8 yr (range 3–13 yr).

Scanning Protocol

Patient preparation included thyroid blockade by the administration of Lugol's solution (40 mg iodide per day) beginning 2 days before the tracer injection until 3 days afterward. Scans were obtained 24 hr ($n = 101$) or 48 hr ($n = 94$) after slow intravenous injection of 74 MBq ^{131}I-MIBG. Over the 10-yr period, ^{131}I-MIBG was obtained from three different radiopharmaceutical companies (IRE, Fleurus, Belgium; Amersham Belgium; and Mallinckrodt, Inc., Petten, Holland). Although the specifications (i.e., the specific activity [SA] and radiopharmaceutical purity) of the tracer supplied were not recorded on an individual basis, they could be derived from catalog information. From 1984 to 1986, the doses were obtained from IRE (SA: 18–55 MBq/mg). The doses were obtained from Amersham in 1987 and 1988 (SA: 37–74 MBq/mg) and in 1989 and 1990 (SA: 185 MBq/mg). In 1990 until mid-1992, doses were obtained from IRE (SA: 148 MBq/mg). Finally, during the last months of 1992 until 1994, the doses were purchased from Mallinckrodt (SA: ≥370 MBq/mg). The radiopharmaceutical purity stated by the manufacturers was always in excess of 95% at the calibration date. In a few instances, ^{131}I-MIBG was tested for the presence of free iodide at injection, which was never greater than 1%. Most generally, ^{131}I-MIBG was injected on the day of dispatching and kept at 4°C between dispatching and injection.

Images were acquired using a large-field-of-view gamma camera equipped with a high-energy, general-purpose collimator (General Electric Starport 400 AC/T, General Electric, Hölte, Denmark [$n = 39$], or Elscint 410, Elscint, Haïfa, Israel [$n = 64$]). Overlapping anterior and posterior views of the head, thorax, abdomen and pelvis were obtained. Images of at least 200 kcounts or 20 min were acquired. A similar protocol was followed in the MTC group, in which 18 patients were scanned at 24 and 48 hr postinjection, respectively; 10 were imaged using the General Electric camera.

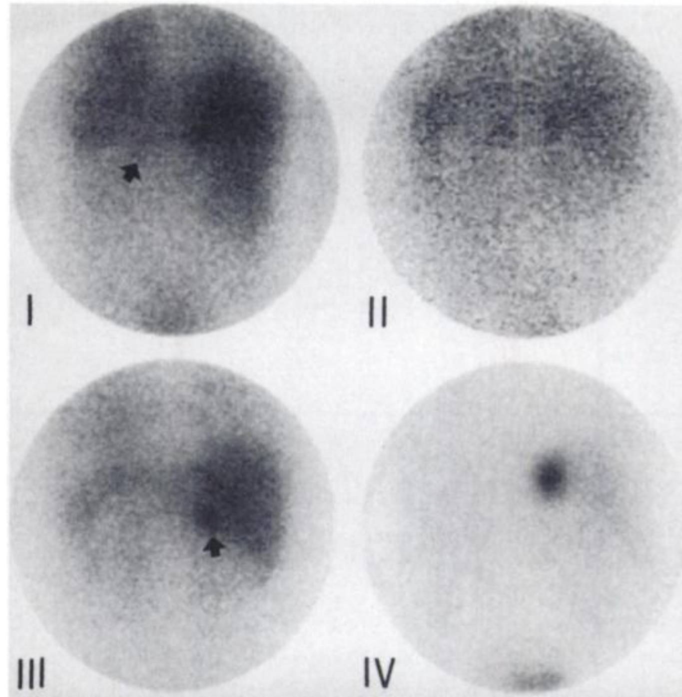

FIGURE 1. Ann Arbor visual scale used to grade the adrenal ^{131}I-MIBG uptake intensity. Grade 1 (I) = uptake just visible; Grade 2 (II) = uptake clearly visible; Grade 3 (III) = prominent uptake and Grade 4 (IV) = hottest spot in the picture. Grade 0 is assigned when no uptake can be distinguished from the background (not illustrated). Examples of Grades 1 and 2 were obtained from patients without pheochromocytoma. Examples of Grades 3 and 4 were obtained from patients with histology-proved pheochromocytoma.

Data Analysis

Visual Analysis. All scans were reviewed on screen in random order over a 1-mo period by an observer who did not know the experimental conditions. A total of 176 and 167 normal adrenals could be analyzed at 24 and 48 hr postinjection, respectively. In MTC patients, no pheochromocytoma was identified, so 38 adrenals could be considered normal. The intensity of adrenal uptake was graded according to the Ann Arbor visual scale (*10*), in which Grade 0 = no uptake; Grade 1 = uptake just visible; Grade 2 = uptake clearly visible; Grade 3 = prominent uptake and Grade 4 = hottest spot in the picture. Figure 1 shows the range of intensities used to grade the adrenal ^{131}I-MIBG uptake.

Semiquantitative Evaluation. To better discriminate between normal and abnormal adrenals, we calculated semiquantitative indicies using adrenal-to-liver, heart, lung and background (i.e., mediastinum) ratios of activity normalized per pixel and for acquisition time, at 24 and 48 hr postinjection. Note that such indicies are partly biased by the fact that only those adrenals that could be delineated from the surrounding background were quantitated.

Statistical Analysis. Sensitivity and specificity values were calculated in the usual fashion, taking surgical demonstration of pheochromocytoma as the reference for true-positives and negative workup and clinical follow-up as reference for true-negative results. Receiver operating characteristic (ROC) curves were used to derive the best cutoff criteria for the visual analysis of adrenal uptake (*12,13*). The areas under the curves were compared using dedicated software (INDROC-IBM-PC version). A Z value of ≥1.96 was considered significant.

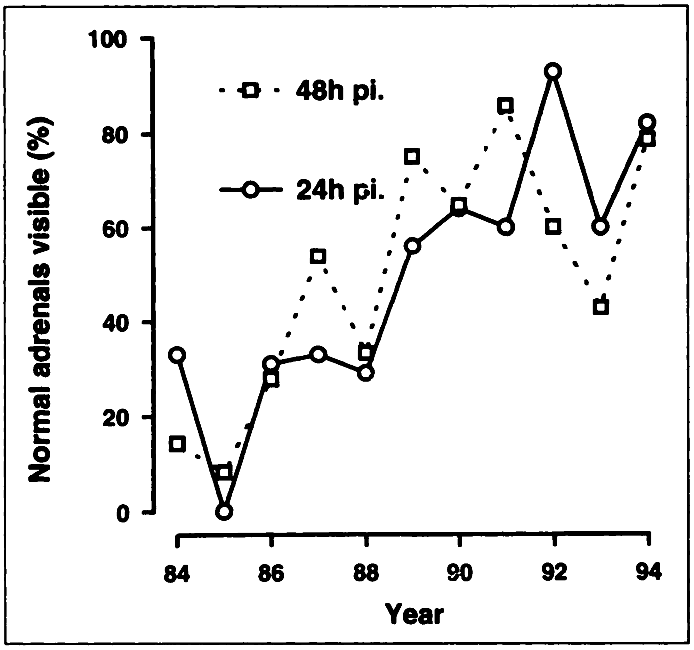

FIGURE 2. Proportion of adrenal medullae visualized at 24 and 48 hr postinjection as a function of time since 1984.

For comparison of the frequency of adrenal visualization, mean visual scores, semiquantitative indicies and the factors that might interfere with the uptake of the radiopharmaceutical, we used Student's t-test and Fisher's test as appropriate. Significance was set at the 0.05 level.

RESULTS

Visual Analysis

Among the 27 glands for which a final diagnosis of pheochromocytoma was established, 25 were clearly visualized (score 2–4), and 2 were either faintly or not detected (score 0–1) at 24 and 48 hr postinjection. Overall, 36% and 52% of normal adrenals were visualized at 24 and 48 hr postinjection, respectively. Figure 2 shows the proportion of normal adrenals visualized at 24 and 48 hr postinjection as a function of time since 1984. There was a clear increase over the years, with a change between 1987 and 1989. Therefore, the 10-yr period was divided into two periods, one from 1984 to 1988 and another from 1989 to 1994. Approximately the same number of patients were studied in these two periods. For the subsequent analysis, each period was subdivided into two groups of patients according to the result observed at 48 hr postinjection. Indeed, in all but two cases, when a particular adrenal medulla was visualized at 24 hr postinjection, the finding was confirmed at 48 hr postinjection. Finally, four groups of patients were identified: Group 1, from 1984 to 1988, visible adrenal medullae (n = 14; 11 bilaterally); Group 2, from 1989 to 1994, visible adrenal medullae (n = 33; 25 bilaterally); Group 3, from 1984 to 1988, adrenal medullae not visualized (n = 25) and Group 4, from 1989 to 1994, adrenal medullae not visualized (n = 6). Table 1 summarizes the frequency of visualization of the normal adrenal medulla at 24 and 48 hr postinjection for the two periods. The difference between the frequency observed in the two periods was statistically significant ($p < 0.0001$).

The adrenal medulla was visualized more often in MTC patients (i.e., 71% at 24 hr and 70% at 48 hr postinjection). In this group, no difference was noted between the two time periods (Table 2) This held true in both the familial and sporadic groups. No statistically significant difference was observed between patients with sporadic and familial MTC. Overall, at either 24 or 48 hr, 13 of 14 adrenal medullae were visible in the familial group compared with 18 of 24 in patients with sporadic MTC. When combining the patients suspected of having pheochromocytoma and patients with MTC, the frequency of visualization of normal adrenal medullae at 24 and 48 hr was still significantly different between the two time periods (19% versus 61% at 24 hr and 34% versus 73% at 48 hr; $p < 0.0001$ for both comparisons).

ROC Curve Analysis

ROC curves used to determine the best cutoff for the visual criteria to localize pheochromocytoma are shown in Figure 3. The areas under the curves from data at 24 and 48 hr postinjection, during both periods, were highly similar (a Z value was not significant for all comparisons). This suggests

TABLE 1
Frequency of Visualization of the Adrenal Medulla at 24 and 48 Hr Postinjection in Patients Referred for Suspicion of Pheochromocytoma During Both Test Periods

	24 hr postinjection			48 hr postinjection		
Period	n	VS ≥ 1	Mean VS	n	VS ≥ 1	Mean VS
1984–1988	89	16%	0.2	87	31%	0.4
1989–1994	87	56%*	0.7	80	73%*	1.1

*$p < 0.0001$ versus 1984–1988.
VS = Ann Arbor visual scale.

TABLE 2
Frequency of Visualization of the Adrenal Medulla at 24 and 48 Hr Postinjection in Patients with Medullary Thyroid Carcinoma During Both Test Periods

	24 hr postinjection			48 hr postinjection		
Period	n	VS ≥ 1	Mean VS	n	VS ≥ 1	Mean VS
1984–1988	10	50%	0.7	10	60%	1.5
1989–1994	24	79%	1.2	20	75%	1.4

All comparisons were nonsignificant.
VS = Ann Arbor visual scale.

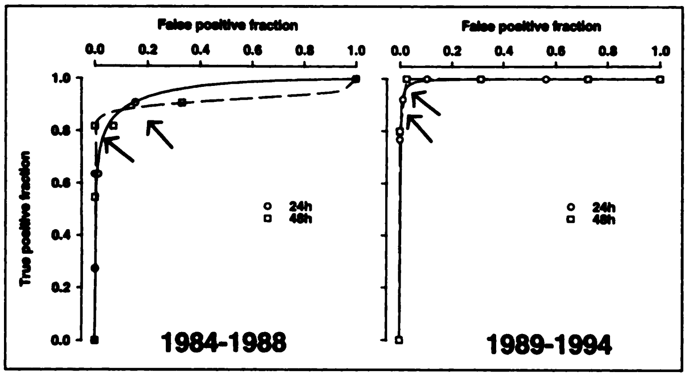

FIGURE 3. Receiver operating characteristic curves showing the best cutoff for visual criteria for identification of pheochromocytoma at 24 and 48 hr postinjection for both tests periods. Arrows point toward the best cutoff criterion for each curve.

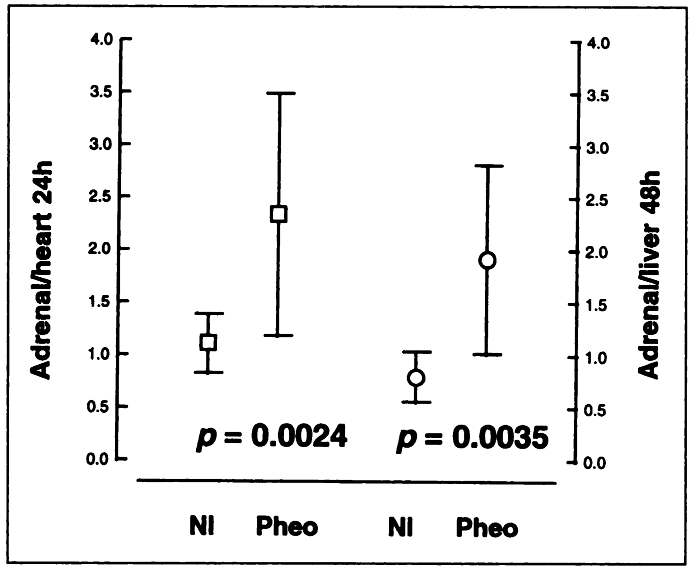

FIGURE 4. Values of the best semiquantitative indices (adrenal-to-heart and adrenal-to-liver) used to discriminate between normal and abnormal adrenal medullae.

that the overall diagnostic performance of the test has not changed over the years. However, the criteria leading to the best diagnostic performance varied as indicated by the arrows in Figure 3: Before 1989, the best cutoff score was ≥1 at 24 hr postinjection and ≥3 at 48 hr postinjection, with a sensitivity and a specificity of 92% and 99%, respectively, at 48 hr postinjection. From 1989, the best cutoff score was ≥3 at both scanning times, with a sensitivity and a specificity of 100% and 97%, respectively, at 48 hr postinjection.

Semiquantitative Analysis

Table 3 shows the results of the four semiquantitative indicies that were computed (adrenal and liver, adrenal and heart, adrenal and lung, adrenal and background). The indicies were calculated with a view to possible prospective use. Therefore, only results from the 1989–1994 period are shown. The best indicies to discriminate between normal and abnormal adrenal medullae were the adrenal-to-heart ratio at 24 hr postinjection (2.3 ± 1.1 versus 1.1 ± 0.2; p = 0.002) and the adrenal-to-liver ratio at 48 hr postinjection (2.0 ± 0.9 versus 0.8 ± 0.2; p = 0.003). Although differences between normal and abnormal adrenals were statistically significant, the overlap between the semiquantitative values made them of little additional use to visual scoring (Fig. 4).

Factors Influencing Iodine-131-MIBG Uptake in Normal Adrenal Medullae

As shown in Table 4, the distribution of patients taking drugs that could interfere with MIBG uptake was relatively homogeneous. No statistically significant difference was found between the different groups. Also, no relationship was found between the visualization of normal adrenals and age, gender, renal function and camera used.

There seemed to be a relationship between the frequency of visualization of the adrenal medulla and the specific activity of the tracer. It is, however, impossible to establish a mathematical parallelism between these parameters because the specific activity of each individual injected dose is not known.

DISCUSSION

Results of this study indicate that normal adrenals imaged with 74 MBq ^{131}I-MIBG were more often visualized than reported in the literature with dosages that were most often 50%–75% less and that the frequency of adrenal visualization increased with time (56% and 73% at 24 and 48 hr postinjection, respectively, during the period 1989 to 1994). Currently, only prominent uptake (visual score ≥3) at either 24 or 48 hr postinjection indicates a high probability of pheochromocytoma.

Previous research has shown that the normal distribution of MIBG labeled with ^{131}I includes infrequent (2% at 24 hr postinjection and 16% at 48 hr postinjection) or no visible uptake of normal adrenals (*3,4,10*). These reports, however, referred to studies performed with 18.5–37 MBq ^{131}I-MIBG. The fact that even before 1989, normal adrenal medullae were more often seen is most probably related to the greater activity injected (74 MBq). This is related to the general phenomenon known as "the more you give, the more you see." Brown et al. (*14*) reported clear visualization of a normal adrenal medulla, resulting in an incorrect diagnosis of bilateral pheochromocytoma. The patient was imaged after injection of 74 MBq ^{131}I-MIBG. Similarly, Morais et al. (*15*) mentioned that a greater activity injected accounted for the increase in sensitivity. A patient with pheochromocytoma was injected and imaged

TABLE 3
Semiquantitative Indices at 24 and 48 Hr Postinjection for Normal and Abnormal Adrenal Medullae from 1989 to 1994

	24 hr postinjection			48 hr postinjection		
Index	Normal	Pheo.	p	Normal	Pheo.	p
Adrenal/Liver	0.7 ± 0.2	1.6 ± 0.9	0.007	0.8 ± 0.2	2.0 ± 0.9	0.003†
Adrenal/Heart	1.1 ± 0.2	2.3 ± 1.1	0.002*	1.2 ± 0.3	3.6 ± 3.0	0.028
Adrenal/Lung	1.3 ± 0.4	2.4 ± 1.4	0.012	1.3 ± 0.4	4.1 ± 4.3	0.068
Adrenal/BG	1.6 ± 0.5	3.1 ± 2.1	0.021	1.6 ± 0.4	5.3 ± 6.1	0.089

*Best discriminator.
†Best discriminator.
BG = background (i.e., mediastinum); pheo. = pheochromocytoma.

TABLE 4
Characteristics of Patients Without Pheochromocytoma With Visible or Nonvisible Adrenal Medullae During the Two Test Periods

Variable	AM visible		AM not visible	
	1984–1988	1989–1994	1984–1988	1989–1994
No. of patients	14	33	25	6
Age (mean ± s.d., yr)	45 ± 20	50 ± 16	55 ± 14	51 ± 16
Gender	8 F, 6 M	19 F, 14 M	12 F, 13 M	3 F, 3 M
Abnormal serum creatinine*	0	0	0	0
Drugs				
T_3C	1	0	0	0
Beta blockers	1	1	1	0
Calcium channel blockers	2	6	2	0

*Number of patients with values above 1.3 mg/dl.
AM = adrenal medullae; T_3C = tricyclic antidepressant.

at 1-wk intervals, respectively, with 18.5 and 37 MBq ^{131}I-MIBG; the tumor was successfully detected only with the higher activity. A greater injected activity results in a greater dose per kilogram of body weight. This explains why the adrenal medullae of dogs or monkeys studied with the same dosage used in humans (17.5 MBq, which is 5–10 times more on a MBq/kg basis) are generally well imaged (*16*). Finally, in confirmation of previous data (*5,10*) in the frequency of visualization of the normal adrenal medulla with ^{131}I-MIBG was higher at 48 than 24 hr postinjection.

In our department, the injected activity (74 MBq) has remained unchanged since 1984. This can explain the initial higher rate of visualization of the adrenal medullae but not the increasing visualization with time. How can we explain an increased visualization rate of normal adrenals with time? Among the different factors that might interfere with the distribution of MIBG, drug intake, which can reduce the uptake and impaired renal function, leading to a reduction of MIBG clearance and increased uptake, are the most frequently reported (*17–20*). No relationship was found between these factors and the visualization of the normal adrenal medulla or with the age, gender and the camera used. It has been reported that calcium channel blockers, such as nifedipine, improve MIBG retention in the adrenals (*21*). In our population, most of the patients taking such drugs were classified in the group "visible adrenal medullae, 1989–1994" (Table 4), but no statistically significant trend was observed when compared with the other groups. The increased frequency of patients on calcium blockers who displayed visible adrenals is probably related to the fact that this family of drugs has, in recent years, gained popularity in the treatment of hypertension. Although intake of calcium blockers cannot be ruled out as a determinant of increased uptake in adrenal medullae, it might be considered as a possible cofactor because only one patient in six with a visible adrenal was treated with this type of drug. An increased SA of the MIBG during the last years is strongly suspected as the explanation for the more frequent visualization.

Over the past 10 yr, we have used commercially available MIBG from three different companies. The SA ranged from 10 to 55 MBq/mg in 1984 as compared with 100–300+ MBq/mg in the past 4 or 5 yr. However, because the information about each dose was not kept in our files or was not available at the time of dispatch, it is impossible in retrospect to establish an objective (e.g., linear) relationship between the scan pattern and the specific activity of the MIBG used. Nevertheless, this finding is in accordance with experimental evidence that the uptake of ^{131}I-MIBG in the adrenal medulla of mice is greater when the SA is higher (*22*). This is true in absolute terms as well as when the uptake is expressed as a adrenal-to-liver ratio. With increased SA, or at low MIBG concentration, there is increased uptake in organs in which the high-affinity, specific uptake-I mechanism is predominant, such as the adrenal medulla. In another study performed in humans, adrenal medullae imaged with ^{123}I-MIBG at an SA of 320 MBq/mg were most often visualized at 48 hr, whereas no uptake could be detected in the same patients with ^{131}I-MIBG at a lower SA (i.e., <100 MBq/mg) (*23*). In this comparison, however, the different physical properties of the isotopes, especially the higher photon yield and better spatial resolution with ^{123}I, also must be considered. In the same article, the uptake of ^{131}I-MIBG also was clearly visible when a therapeutic dose was given to one of the patients. In that case, the total amount of radioactivity, the higher SA (1.16 GBq/mg) and imaging delayed at 6 days postinjection all could have contributed to the visualization of normal glands.

The increased specific activities of commercially available ^{131}I-MIBG can be explained by the improvement in radiolabeling methods, as reviewed by Wafelman et al. (*24*). In the early years of ^{131}I-MIBG, radiolabeling was performed using the halogen exchange method, which did not allow for high SA with an acceptable yield (*25*). The development of copper(I)-assisted or copper(II)-catalyzed methods, which have been adopted by several companies, permitted one to increase the specificity by a factor of 3–10. Other approaches, such as the "no carrier added" method devised by Vaidyanathan and Zalutski (*26*), result in the formation of ^{131}I-MIBG with an extremely high SA (in the order of 0.1–1.0 TBq/mg) that can be used for therapy but are not necessary for diagnostic scanning (*27*).

The change in the pattern of adrenal visualization was not observed in the MTC group: the frequency of visualization of normal adrenals has been higher since 1984 and did not change over time. The majority (*12*) of the MTC patients are sporadic MTC, and none of the patients of the familial group has developed a pheochromocytoma. Accordingly, the higher rate of visualization of the adrenals in the first period could not be related to the presence of asymptomatic pheochromocytoma. It cannot be ruled out that some of these patients might have adrenomedullary hyperplasia. This, however, is unlikely because: (a) only one patient was part of a well-characterized MEN-2 kindred, (b) urinary catecholamines were consistently within normal limits and (c) none of the patients developed a pheochromocytoma over a median follow-up period of 8 yr. The only difference between the MTC group and the normal group is that most of the MTC patients had high calcitonin levels at the time of evaluation.

In addition, the results of our study have again confirmed the excellent sensitivity and specificity of MIBG scanning in 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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