Normal Adrenal Asymmetry: Explanation and Interpretation

John E. Freitas, James H. Thrall, Dennis P. Swanson, Ayman Rifai, and William H. Beierwaltes

University of Michigan Medical Center, Ann Arbor, Michigan

Although adrenal imaging with 19-iodocholesterol provided much useful diagnostic information, spatial resolution was less than ideal. With the greater target-to-background ratios afforded by NP-59, differences between the right and left adrenal glands—in terms of position, configuration, and depth-related activity—can now be defined. Analysis of the scintigrams of 21 individuals with no evidence of adrenal disease has allowed us to characterize the normal degree of adrenal asymmetry. Appreciation of this asymmetry is necessary if the potential for greater diagnostic accuracy afforded by NP-59 is to be realized.

J Nucl Med 19: 149–153, 1978

The imaging of human adrenal glands has been clinically possible since 1971, when Beierwaltes et al. (*1*) reported their initial experience with [^{131}I] 19-iodocholesterol in the evaluation of adrenal diseases. From 1971 to the present, several thousand adrenal scintigrams have been performed using 19-iodocholesterol, and numerous articles have been published on various aspects of adrenal scintigraphy. Although much useful diagnostic information is obtainable, the anatomic resolution achievable with 19-iodocholesterol has been less than ideal. The detection and interpretation of abnormalities such as the negative defect (e.g., pheochromocytoma), mild adrenal displacement, and adrenal-gland asymmetry have been difficult at best; false-negative and false-positive interpretations have occurred. In recognition of these problems, the search for improved imaging radiopharmaceuticals for the adrenals continued and led to the development of 6β-iodomethyl-19-norcholesterol (NP-59) (*2*). In experimental animals, NP-59 shows a more rapid adrenal uptake with a five-fold greater target-to-background ratio than was obtainable with 19-iodocholesterol (*3*). Adrenal scintigraphy can be performed with NP-59 in the majority of patients 2 to 5 days post injection.

Since early 1975, we have performed more than 150 adrenal scintigrams on patients with known or suspected adrenal disease and on a number of normal volunteers using this new agent. Of the first 150 scintigrams, 21 studies have been performed on five normal volunteers and on 16 patients in whom subsequent study (urinary and plasma chemistries, venography, arteriography) revealed no evidence of adrenal disease. We report here some new observations on the interpretation of the normal adrenal scintigram.

MATERIALS AND METHODS

The adrenal images of 21 individuals with no evidence of adrenal disease were reviewed. The NP-59

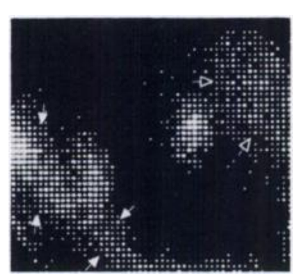

FIG. 1. Computer-processed posterior view at 4 days. Closed arrows-bowel activity; open arrows = liver activity.

Received May 4, 1977; revision accepted Aug. 3, 1977.

For reprints contact: William H. Beierwaltes, Nuclear Medicine Div., University of Michigan Medical Center, Ann Arbor, MI 48109.

used for these studies was prepared by the procedure of Basmadjian (*4*) with certain minor modifications. Quality-control procedures ensuring radiochemical and radionuclidic purity, sterility, and apyrogenicity were performed before injection. All patients received 1–2 mCi of NP-59 intravenously and adrenal images were obtained on at least two occasions within 2–8 days. To decrease free I-131 uptake by the thyroid gland, each patient was pretreated with 3 drops of Lugol's iodine twice a day by mouth, commencing 48 hr before radionuclide administration and continuing 10 days post injection.

Posterior and left lateral views were obtained with the patient prone, using a gamma camera interfaced to a mini-computer. Anterior views were also obtained in selected patients. Some images obtained 2–4 days post injection displayed activity remaining in the liver, spleen, and bowel, which interfered with assessment of relative adrenal activity and the delineation of the superolateral margin of the right adrenal gland (Fig. 1). In such cases, repeat scintigraphy was performed after a 24- to 48-hr delay and laxatives were administered to some patients to remove bowel radioactivity.

All images were displayed on a precalibrated 64 × 64 computer matrix and recorded on Polaroid film. Adrenal depth as displayed on the lateral view was determined with the aid of a radioactive line source placed over the spine from the T-10 to the L-2 level. The adrenal uptake percentage of the NP-59 was determined by the method of Koral and Sarkar (*5*).

FIG. 2. Computer-processed posterior view. Superior border of right adrenal gland is 2 cm higher than that of the left adrenal. Left adrenal is elongated, whereas the right is more circular in outline.

FIG. 3. Computer-processed posterior scintigram. Right adrenal shadow indicates greater activity than the left.

FIG. 4. Computer-processed left lateral view. Overlapping right and left adrenal shadows (closed arrows) appear to be oriented obliquely with respect to surface marker (open arrows).

RESULTS

On the posterior view, the right adrenal gland was located in most cases slightly above the level of the left adrenal gland (Fig. 2). In 18 of 21 subjects, the superior border of the right adrenal gland was 1–2 cm higher than the superior border of the left adrenal. In three subjects, the superior borders of the two glands were at the same level. In no case was the left adrenal gland seen to be higher than the right.

The shapes of the right and left adrenal glands also differed. The vertical span of the left adrenal image was greater than its width in 95% of cases giving it an oval or oblong outline. By contrast, the normal right adrenal appeared to be circular or truncated in 66% of the cases (Fig. 2).

In 66% of the posterior scintigrams the activity of the right adrenal gland appeared greater than in the left (Fig. 3). The explanation for this apparent asymmetry was determined by correlating the standard posterior image with lateral and anterior images. On the lateral view, the right and left adrenal images partially overlap. Their combined image appeared most frequently as a band of activity sloping upward and toward the back (Fig. 4). The length of this band, projected vertically, equaled the distance on the posterior view from the inferior border of the left to the superior border of the right adrenal in all cases. Thus we find that in many individuals the left adrenal is not only lower but also more anteriorly located than the right adrenal (Fig. 5). This difference in depth between left and right adrenal glands was substantiated by a reversal of the right-left posterior-view asymmetry when anterior views were obtained (Fig. 6).

The significance of the right-to-left difference in depth was further demonstrated by the calculation of the adrenal uptake percentages. In the past a single depth has been assumed for the two adrenal glands (*6*). When a single depth was assumed in our series, a variation in uptake percentage of up to 37% was noted between the left and right adrenal glands (Table 1). When the uptake percentages were recalculated using individual depth corrections for left and right adrenal glands, the maximum variation noted was 20% (Table 2). The individual depths were determined by establishing the relative cephalocaudal positions of the respective superior and inferior borders on the posterior view, and then calculating the position of the center of activity of each adrenal gland as displayed on the lateral view (Fig. 7).

The range in percentages of uptake per gland in this series was 0.07–0.26%, with a mean uptake of 0.16%. The range of the right-to-left uptake percentages ratio was 0.91--1.20 (Table 2).

DISCUSSION

Adrenal imaging has been shown to be of value in the diagnosis of adrenal disease (*7–10*). The scope of adrenal imaging has gradually expanded over the past several years for cortical and medullary disease. Proper scintigraphic interpretation requires an appreciation of the variation between the normal right and left adrenal glands.

Although the difference in height between the

TABLE 1. UPTAKE PERCENTAGES WITH SINGLE DEPTH ASSUMED

	Posterior view		Lateral view	Posterior view
Patient No.	L % uptake	R % uptake	Matrix points	R/L uptake ratio
1	0.23	0.29	28.5	1.26
2	0.22	0.21	26	0.95
3	0.19	0.22	19	1.15
4	0.14	0.19	21.5	1.35
5	0.07	0.08	18.5	1.14
6	0.11	0.15	15.5	1.36
7	0.14	0.18	20	1.28
8	0.11	0.13	20	1.18
9	0.13	0.17	18.5	1.30
10	0.10	0.11	18	1.01
11	0.18	0.24	18.5	1.33
12	0.23	0.23	20	1.00
13	0.15	0.17	27	1.13
14	0.16	0.21	19	1.31
15	0.20	0.21	20	1.05
16	0.07	0.08	16.5	1.14
17	0.15	0.16	20	1.06
18	0.14	0.15	14	1.07
19	0.11	0.12	19	1.09
20	0.16	0.22	27.5	1.37
21	0.18	0.24	15	1.33

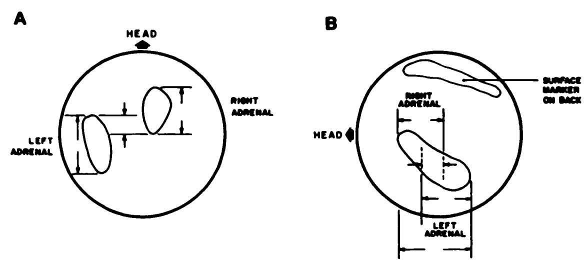

FIG. 5. (A) Posterior view demonstrating cephalocaudal relationships of right and left adrenal glands. Superior and inferior borders of each gland are marked by horizontal bars. (B) Left lateral view showing combined adrenal image divided into right and left adrenal components. Horizontal bars in (A) are now shown as vertical bars in (B).

TABLE 2. UPTAKE PERCENTAGES WITH INDIVIDUAL ADRENAL DEPTH CORRECTIONS

	Posterior view (Corrected for depth)		Lateral view (Matrix points)		Posterior view
Patient No.	L % uptake	R % uptake	L depth	R depth	R/L uptake ratio
1	0.25	0.26	31	26	1.04
2	0.22	0.21	26	26	0.95
3	0.20	0.21	21	17	1.05
4	0.15	0.18	24	19	1.20
5	0.07	0.08	20	17	1.14
6	0.12	0.14	18	13	1.16
7	0.15	0.17	22	18	1.13
8	0.12	0.12	22	18	1.00
9	0.15	0.15	21	16	1.00
10	0.10	0.10	19	17	1.00
11	0.20	0.22	21	16	1.10
12	0.23	0.23	20	20	1.00
13	0.16	0.16	29	25	1.00
14	0.17	0.20	20	18	1.17
15	0.21	0.21	20	20	1.00
16	0.07	0.08	18	15	1.14
17	0.15	0.16	20	20	1.06
18	0.14	0.14	15	13	1.00
19	0.12	0.11	20	18	0.91
20	0.18	0.20	30	25	1.11
21	0.20	0.22	17	13	1.10

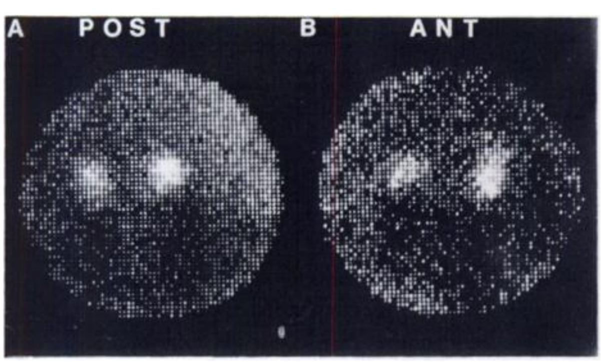

FIG. 6. (A) Computer-processed posterior view. Right adrenal activity appears greater than left adrenal activity. (B) Computer-processed anterior view of same patient. Left adrenal activity now seems greater than that on the right.

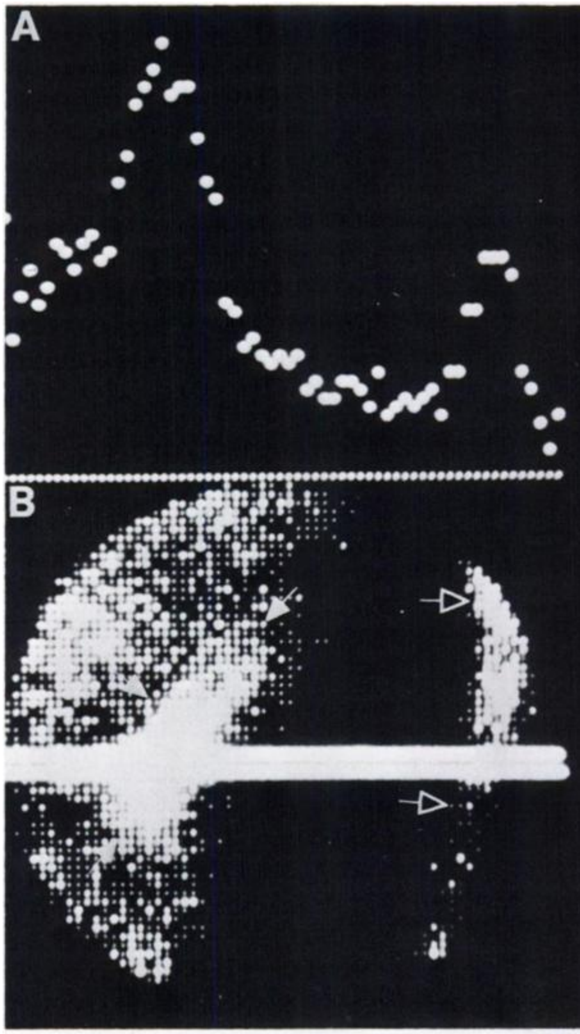

FIG. 7. (A) Activity histogram of x-axis profile defined by cursors in (B). (B) Left lateral view as in Fig. 4, showing source of profile in (A). Closed arrows = combined adrenal image. Open arrows = surface marker.

right and left adrenal glands was recognized with 19-iodocholesterol, the subtle differences in adrenal shape and the depth-related asymmetry were not. Both of these findings bear directly on adrenal scintigraphic interpretation. Specifically, if the shorter length of the right adrenal is not recognized as normal, it may be attributed incorrectly to a space-occupying "cold" lesion of the lower pole, such as a pheochromocytoma or an adrenal carcinoma.

Likewise, there are several potential pitfalls if one fails to recognize the normal depth-related asymmetry of activity between the right and left adrenal images as seen on the standard posterior view. Patients with normal adrenal glands may be incorrectly labeled as having evidence of adrenal disease because of this asymmetry. Moreover, the same depth considerations apply to patients with aldosteronism, adrenal androgenism, and Cushing's disease. Scintigrams in some have been incorrectly interpreted in the past as showing a right adrenal adenoma because of the failure to appreciate the degree of adrenal asymmetry that a scintigram can show on the basis of depth variation alone. Conversely, patients with left adrenal adenomas could potentially show a false symmetry. The poor ability of adrenal scintigraphy to lateralize aldosteronomas, as reported in one series, may have this basis (*11*).

Correlation between anterior and lateral views should clarify the appearance of the posterior view in most cases. Because of the posterior location of the adrenal glands and the resultant greater photon attenuation that occurs on the anterior view, the degree of depth-related asymmetry will appear more prominent on the posterior view than on the anterior view. In some instances, liver activity masks the right adrenal activity, but this can be corrected by the computer-assisted background subtraction.

Review of angiographic and pathologic literature supports the observations of differing adrenal position, shape, and depth. In describing the position, shape, and size of the adrenal glands, Kahn (*12*) states: "Apart from their proximity to the upper poles of the kidneys and their weight (5–7 grams each) there is little similarity in the gross relationship and morphology of the right and left adrenal glands." Kahn also noted that the left adrenal gland is usually lower than the right and more medially located. Soffer (*13*) described the variable shapes of the left and right adrenal glands, noting that the right adrenal was roughly triangular, whereas the left adrenal was more crescentic or elongated. He also commented upon the application of the left adrenal gland to the anteromedial aspect of the left kidney, whereas the right adrenal has a looser attachment to the superior pole of the right kidney. These differences in their relationships to the kidneys account for the differences in the position, shape, and depth appreciated scintigraphically.

With NP-59, there is potential for greater accuracy in the detection of various adrenal diseases because of the greater target-to-background ratio afforded by this new agent. The results of the current study indicate that there are significant differences in scintigraphic appearance between the right and left adrenal glands. Correct interpretation of adrenal scintigrams requires an appreciation of these differences and a correlation of information derived from the anterior and lateral views as well as the standard posterior views. The clinical role of the adrenal uptake percentage remains to be established. Because of the differences in adrenal depth, however, it is clear that individual depth corrections must be applied to each gland for accurate uptake determinations.

ACKNOWLEDGMENTS

This investigation was supported by Grant No. CA-09015-02, awarded by the National Cancer Institute, DHEW, by a contract with E.R.D.A. #EY-76-S-02-2031, and by the Nuclear Medicine Research Fund.

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