Absorbed Dose to the Human Adrenals from Iodomethylnorcholesterol (I-131) "NP-59": Concise Communication

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During the past 2 years, adrenal uptake percentage values were measured in more than 40 patients, using an external counting technique. They suggest that the absorbed dose to the adrenals is significantly less than the 150 rads/mCi previously estimated using concentration values from animal adrenals.

The measured combined uptake percentage for both adrenals ranged from 0.15% to 0.52% in 21 patients without evidence of adrenal disease, with a mean of 0.33% ± 0.1%; also from 0.22% to 1.5% in 22 patients with Cushing's disease, with a mean uptake of 0.78% ± 0.35%. The absorbed dose to the adrenals was estimated to be 25 rads/mCi for patients without evidence of adrenal disease, and 57 rads/mCi for patients with Cushing's disease. Both values are calculated for the respective mean uptake percentages by using the MIRD formalism.

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Because of its more rapid uptake and greater target-to-background ratio (*1,2*), 6β-[^{131}I]-iodomethyl-19-norcholesterol (NP-59) provides better human adrenal images than 19-[^{131}I]-iodocholesterol (NM-145) and is now the agent of choice for both adrenal uptake percentage and imaging studies.

Since the clinical availability of NP-59 in 1975, adrenal uptake percentages have been systematically obtained with it in all patients undergoing adrenal imaging at our medical center. This communication presents revised absorbed-dose estimates to the human adrenals calculated using externally measured uptake values from 21 studies performed on five normal volunteers and on 16 patients with no evidence of adrenal disease and from 22 studies performed on patients with Cushing's disease.

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MATERIALS AND METHODS

The Np-59 was prepared and administered as described by Freitas et al. (*6*). Adrenal uptake percentages were calculated on all patients using the method of Koral and Sarkar (*7*), with individual depth corrections applied to each gland (*6*). One millicurie of NP-59 is the usual administered activity.

The absorbed dose to the adrenal glands from activity measured in the glands with the above technique was calculated using the following equation (*9*):

$$\tilde{D}(AD \leftarrow AD) = \tilde{A}_{AD} S(AD \leftarrow AD), \qquad (1)$$

where $\tilde{D}(AD \leftarrow AD)$, in rads, is the mean absorbed dose to the adrenal glands; $S(AD \leftarrow AD)$, in rads/μCi-hr, is the absorbed dose per unit cumulated activity to the adrenal glands from activity concentrated in the adrenals; $\tilde{A}_{AD}$, in μCi-hr, is the cumulated activity in the adrenal glands and is given

TABLE 1. CALCULATED ABSORBED DOSES TO ADRENAL GLANDS

	Average* ± 1 s.d. (rads/mCi)	Range* (rads/mCi)
Patients without adrenal disease	25 ± 7.2	12 – 39
Patients with Cushing's disease	57 ± 25	17 – 160

* Includes a 1.4 rads/mCi contributed from activity in the total body irradiating the adrenals (*10*).

by the following equation, modified from Smith et al. (*9*):

$$\tilde{A}_{AD} = [1.443 \sum_{j=1}^{j=n-1} A_j(O)T_{jeff} + 1.443A_N(O)T_{Neff}(1 - e^{-0.693t^*/T_{Neff}}) + 1.443A_N(t^*)T][1 - Tup/T_{Neff}], \quad (2)$$

where $A_j(O)$, in microcuries, is the initial activity in the adrenal glands for the *jth* component, and T_{jeff}, in hours, is the effective half-life of the *jth* component; $A_N(O)$, in microcuries, is the initial activity in the adrenal glands for the longest-lived component of the disappearance curve; T_{Neff}, in hours, is the effective half-life of the longest-lived component of the disappearance curve; t*, in hours, is the time from dose administration, to the time when the last datum point on the disappearance curve was determined; $A_N(t^*)$, in microcuries, is the activity calculated in the adrenal glands, using the above method, at time t*; T, in hours, is the physical half-life of the radionuclide; and T_{up}, in hours, is the effective half-life of the uptake curve.

Using the sequential human adrenal uptake data of Koral et al. (*7*), a T_{Neff} of 6 days was calculated and used to describe the elimination of NP-59 from the adrenal glands to time t*, which was 8 days. For times after t*, a T_{Neff}, equal to the physical half-life of I-131, was assumed to be 8 days. T_{up} was calculated to be .92 days. S was obtained from Reference *8* as .031 rad/μCi-hour.

Values for $A_N(O)$ were obtained using linear regression analysis and extrapolation to time t = 0.

Values for $A_N(t^*)$ were obtained from calculated adrenal uptake percentages assuming a T_{Neff} of 6 days.

Inserting the values for $A_j(O)$, T_{jeff}, T_{Neff}, t*, T, and T_{up} into Eq. (1), we get:

$$\tilde{D}(AD \leftarrow AD) = 3.3\ A_N(O) + 7.3\ A_N(t^*) \quad (3)$$

RESULTS

The uptake percentage values obtained in "normal" patients averaged 0.33% ± 0.1%, with a range of 0.15-0.51%. For patients with Cushing's syndrome—due either to ACTH excess or adenoma—the average uptake percentage was 0.78% ± 0.35%, with a range of 0.22-1.5%.

Table 1 lists the calculated absorbed doses for these externally measured uptake percentages values. The average absorbed dose to the normal adrenal glands is 25 rads/mCi, with a range from approximately 12-39 rads/mCi. The average absorbed dose to the adrenals of the Cushing's patients is 57 (range 17-155) rads/mCi.

DISCUSSION

The absorbed dose to the adrenals from NP-59 was initially calculated (*3*) using concentration data from animal tissues (*1*). The resulting adrenal uptake percentages, normalized to man, were 1% or greater. The absorbed dose to the human adrenals using these values was 150 rads per administered millicurie and is about five times that from NM-145 (*4,5*). More recently (*10*), an absorbed dose to the human adrenals of 150 rads/mCi was again calculated using adrenal tissue concentration data from three patients with diagnosed adrenal disease.

Over the past several years we have measured adrenal uptake percentage values in patients with and without adrenal disease. The external counting technique used (*7*) has an expected uptake error, due to statistics, of ± 7% (1% s.d.) and an additional error of ± 1% for each millimeter of uncertainty in depth determination. The observed average uptake values for both categories of patients, using this technique, were lower than those used in the initial calculation of adrenal absorbed dose. For patients with normal adrenal functions, the average absorbed dose ± one standard deviation was 1/5 to 1/13 of the published 150 rads/mCi. For patients with a final diagnosis of Cushing's disease, the calculated absorbed dose to the adrenals was 20-50% of the published value. However, the upper range of absorbed dose for these patients, calculated using our series of uptake values, yielded an absorbed dose of approximately 160 rads/mCi administered. Therefore, for patients with adrenal disease it may be proper to asssume, conservatively, that 150 rads/mCi is the absorbed dose to the human adrenal.

When applying published absorbed-dose values calculated for radiopharmaceuticals used in nuclear medicine, one must bear in mind that these absorbed doses were not calculated for the individual patient but for a phantom designed to represent a

class of individuals (e.g., "standard man"). Moreover, the tracer distribution and retention data are obtained, at least initially, from animal experiments. In the case of NP-59, our clinically measured adrenal uptakes indicated that the uptake values used in the initial absorbed-dose calculations resulted in a potential overestimation of the adrenal absorbed dose, especially for those patients with normal adrenal function.

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