Transport Specificity." For the external imaging of an active transport system, the model substance is radioiodide. Its initial movement into the thyroid reflects a transport event of great specificity and one that functions against an electrochemical gradient. It is possible that $[^{75}\text{Se}]$-selenomethionine may also be considered in the "active transport specificity" class, for it has been shown to undergo transport analogously to methionine (2).

The prototype gamma-emitting compound for Eckelman and Reba's class B-4 (Enzyme Inhibitor or Enzyme Substrate) was described in this journal some years ago. This was 3-iodoaminothioplatin (a reversible inhibitor of the enzyme dihydrofolate reductase) (3). At that time, the criteria established for demonstrating the action of a "gamma-emitting active-site-directed enzyme inhibitor" were as follows.

1. Binding occurs to the known sites of the enzyme (correct distribution).
2. Displacement from its in vivo site can be produced by an even more firmly bound inhibitor of the enzyme (for example, the compound methotrexate was used as the "displacing" material).
3. Stability of the inhibitor could be shown by its partial recovery (from the urine in this case) after displacement from the in vivo enzyme.

Incidentally, this displacement of radiolabeled ligands from their in vivo sites can be used as a further tool in defining metabolic activities and in terminating their actions as desired (4,5).

RICHARD P. SPENCER
University of Connecticut Health Center
Farmington, Connecticut

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REFERENCES


Why the High Background?

$[^{75}\text{Se}]$ L-selenomethionine—A Longterm Culprit

In a recent patient, a high level of background radioactivity, incorrectly attributed to I-131, almost resulted in erroneous values for the uptake of radioactive iodine by the thyroid (RAIU).

The error was avoided by recognizing that the anomalous gamma activity was that remaining from 250 $\mu$Ci of Se-75 that had been given 8 mo before as L-selenomethionine for a pancreas scan. Since the effective half-time for I-131 is so much shorter than for Se-75, our correction for decay of background activity would have introduced errors into the thyroid measurement. Recognition of the culprit enabled us to avoid the error.

When the body background was measured in our clinical facility before the thyroid test, a high level of activity with a peak near 364 keV was found. Contamination with I-131 was considered because of the presumed emission spectrum and the wide clinical application of this emitter. However, an iodine source could not be found. Therefore, total-body radioactivity was measured in our low-background, whole-body counting facility using a single 20- by 10-cm NaI(Tl) scintillation crystal, ½-meter-arc geometry and multichannel analysis. Figure 1 shows the spectra obtained from the patient and from calibrated small sources of Se-75 (0.5 $\mu$Ci) and I-131 (0.2 $\mu$Ci). The gamma spectrum observed for the patient is consistent with that of Se-75. The energy peak near the 364-keV of I-131 is obvious. The total body burden of Se-75 was estimated by summing the counting data over the energy interval 0.03-1.0 MeV, and turned out to be between 20 and 30 $\mu$Ci. A range is given for the body burden because an exact attenuation factor for photons emitted within the body is not known. A simple point-source calibration factor gives 20 $\mu$Ci. If the activity is uniformly distributed in the body, allowance for the photon attenuation would require that the estimate be increased 50%, giving a value of 30 $\mu$Ci. A qualitative measurement with a small collimated scintillation detector indicated that nearly uniform distribution in the body probably did exist, so 30 $\mu$Ci is our best estimate of the burden.
LETTERS TO THE EDITOR

Review of the previous hospital records revealed that the patient received 250 μCi of [35Se]L-selenomethionine for a pancreas scan in March 1977. The whole-body measurement was performed 244 days later. The percentage retention of [35Se]L-selenomethionine as a function of time was fitted by Lathrop et al. to a three-component exponential (1), namely

\[ R = 13e^{-1.2t} + 44e^{-0.011t} + 42e^{-0.00006t} \]

where \( R \) = percentage effective retention (includes radioactive decay), and \( t \) = time in days since administration.

At 244 days the calculated effective retention is 11%. Our reported value of 30 μCi gives 100 \( \times \) 30/250 = 12%, and is in good agreement with the reported function.

Although [35Se]L-selenomethionine is initially distributed mainly to the liver and pancreas, after about 3 mo it is fairly uniform throughout soft tissue and blood (1,2). The effective half-time for whole-body [35Se]L-selenomethionine retention several months after administration is about 80 days.

The patient with multiple diseases and several physicians may not be aware of the nature of each radiopharmaceutical that has been used. The clinician must remain alert to factors that may complicate a diagnostic test. These results indicate that [35Se]L-selenomethionine can be a problem for a relatively long time.

REFERENCES


Percentage Uptake of Treatment Activity of I-131 by Thyroid

In a recent Letter to the Editor (1), Dr. Bruno Schober made several important observations. The present communication is for the purpose of confirming the importance of the subjects noted.

For more than a decade our procedure for radio-iodine therapy of thyrotoxicosis has been:

1. Diagnostic I-123 or I-131 uptake at 4 and 24 hr in patients in whom radio-iodine therapy is planned in order to document the patient's handling of iodine and confirm that radio-iodine therapy is appropriate. This is characterized done with the capsule form of preparation.
2. Therapy is then administered in liquid form using approximately 1 mCi of radio-iodine. Twenty-four hours later the uptake of that dose is also measured.
3. With this data, an estimate of gland size in grams, an assumption of effective T/12 of 6 days, the calculation to determine the number of μCi to be administered to deliver 3500 rads is performed using Quimby's formula (2).

As a consequence of this routine we have, as Dr. Shober has noted, numerous patients in whom the uptake of the liquid treatment dose is substantially different from the uptake of the capsule diagnostic study. We also firmly believe that low dose radio-iodine therapy must be measured in nads and not in mCi (3,4). It can be demonstrated very easily that a 1 mCi dose of I-131, depending on gland size and uptake, may deliver thyroidal doses of greatly differing magnitudes.

GEORGE JACKSON
Harrisburg Hospital
Harrisburg, Pennsylvania

REFERENCES


Atropine Clearance from Human Plasma

There is a need to measure blood levels of atropine, owing to its increased use for a variety of clinical problems—including treatment of bradycardia in infants (1) and adults (2), prevention of exercise-induced asthma (3), and current investigation of the role of high-dose inhalation of atropine for refractory air-flow obstruction in chronic bronchitis and emphysema (4). Previous methods have lacked sufficient sensitivity to measure the low levels of atropine present in plasma after the usual therapeutic doses. In 1975, Fasth (5) described the first radioimmunoassay (RIA) for atropine using rabbit antiserum. In 1977, Wurzburger et al. (6) reported a more sensitive and specific RIA for atropine and showed clearance curves for dog plasma. The purpose of this letter is to report the application of RIA to the measurement of atropine in human plasma.

Using antiserum kindly provided by Dr. S. Spector*, we have measured the plasma clearance of atropine in four adult volunteers. The measurement is accomplished by a competitive RIA, using rabbit anti-atropine antibody. Treated atropine is used as the radioligand. Samples of plasma (100 μl) are incubated over-night at 4°C with 100 μl of antiserum and 100 μl of [3H] atropine in phosphate-buffered saline. The bound atropine is separated by precipitation with ammonium sulfate and measured by liquid scintillation counting. A standard curve is simultaneously obtained from known dilutions of atropine. Using this RIA method, atropine concentration can readily be measured over a range of 0.6-100 ng per milliliter of sample.

Results of clearance studies following a single 0.32-mg atropine dose are shown in Fig. 1. In Subjects 1, 2, and 3, a bolus i.v. injection was made, with rapid (<5 min) distribution into an apparent volume of distribution (Vd) of 150-160 liters. The clearance half-time (t 1/2) was 2½-3 hr with levels still measurable as long as 4 hr after administration of the dose. In Subject 4 the injection was absorbed over a 30-min period, indicating subcutaneous infiltration; once absorbed, the clearance parallels that following i.v. injection.

This sensitive radioimmunoassay of atropine in human plasma should aid the deriving of effective dose schedules and the mon-