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Reply

The methods of synthesis of 6-iodomethylcholesterol reported by Scott et al. (*1*) were obvious, insignificant modifications (if any) that had been discussed by Kojima et al. and myself at the presentation of our respective findings at the 1975 Annual Meeting of the Society in Philadelphia.

Neither Kojima et al. (*2*) nor our group at Michigan (*3*) accepted the claim that the NMR scans proved unequivocally the purity of 6-iodomethylcholesterol we had discovered. Before and after our publications (*3,4*), we were working on different ways of identifying impurities and toward new synthetic methods for 6-iodomethylcholesterol that is now established.

There is no doubt in our minds that ^{13}C Nuclear Magnetic Resonance is probably the ultimate tool in establishing the purity of a compound, but at the time we isolated the 6-iodomethylcholesterol, we felt that the sample we had was pure enough to obtain an NMR, a mass spectrum, a melting point, and chromatographic data that warranted its identification and publication.

It is always pleasant to know that other researchers have continued to confirm the pioneering findings at Michigan and have worked diligently to improve our simple synthetic procedures to obtain purer end products.

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Gonadal Radiation Dose and its Genetic Significance in Radiation Therapy of Hyperthyroidism

In their recent paper (*1*) concerning radiation dose to the gonads resulting from the therapeutic dose of ^{131}I in hyperthyroidism, Robertson and Gorman have estimated the ovarian dose as 0.2 rad/mCi administered. They assumed a thyroidal uptake of 80% of the dose and average values for urinary excretion and release rate of thyroidal hormone of 7.2%/hr and 0.18%/hr, respectively.

We have used thermoluminescent dosimeters of LiF and Ca/Dy sulfate, attached to copper intrauterine contraceptive devices, to measure directly the dose to the uterus in a series of patients with Graves' disease. The dose-meters were inserted just before the administration of ^{131}I and were retrieved 1 month later. This method measures only the gamma-radiation dose to the uterus and neglects that resulting from beta particles.

The mean result obtained from our first seven observations was 0.145 (±0.10) rad/mCi administered.

The mean thyroidal uptake in our patients was 74 ± 7%. To compare our results with the calculations of Robertson and Gorman, we assume a gamma dose to the ovaries equal to the dose to the uterus. Furthermore, one must subtract the self irradiation by beta particles from the calculated dose, for this was not measured in our in vivo dosimetry. This component is 0.086 rad/mCi, and the calculated gamma dose to the ovaries is therefore 0/204 − 0.086 = 0.118 rad/mCi. This value is in fair agreement with our measured results, and we feel that our in vivo findings support the validity of the assumptions made by Robertson and Gorman in their calculations.

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REFERENCE

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Reply

We appreciate the comments by Philippon and Briere relating their measurements of the uterine dose to our calculations of the ovarian dose. Further measurements of this nature as a cross check on radiation dose calculations are to be encouraged.

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Chromatography of ^{99m}Tc Labeled Radiopharmaceuticals

The article by Colombetti, et al. (*1*) confirms our own findings with the MAC-1 kit in the testing of water soluble radiopharmaceuticals. The MAC-1 kit indicates high values

for reduced unbound technetium which do not correlate with our clinical findings.

The explanation given for this phenomena by Colombetti, et al. is interesting but according to the manufacturer's directions the strips are supposed to be run individually in their own separate solvent and it is difficult to understand how the acetic acid in the acetone solvent would affect the material running in the saline solvent. A possible explanation for the higher values of reduced unbound technetium indicated in the MAC-1 kit is the transfer of technetium from the relatively unstable Tc-Pyrophosphate to the cellulose contained in the paper of the MAC-1 kit. The stronger chelates of Tc DTPA and Osteoscan do not show as great a disparity between the Michrom and MAC systems. This is consistent with findings on Sephadex column (*2*).

The method we employ entails the use of short, slim ITLC-SG strips (5 mm × 75 mm) which are developed in normal saline to determine reduced technetium, and acetone to determine free TcO_4 in water soluble radiopharmaceuticals. Strips of Whatman #1 (7.5 mm × 75 mm) developed in 85% methanol can also be used to determine free TcO_4^- in Tc-Pyrophosphate but produces artifacts when used to analyze Tc DTPA. All systems run very rapidly but still give enough separation to determine relative amounts of free Tc and reduced Tc by scanning on a radiochromatogram scanner which consists of a NaI crystal collimated with a 3 mm sliting lead plate attached to a 3 decade ratemeter and graphed on a TI dual channel recorder. Alternatively, readings may be made by cutting the strip into 1-cm segments and individually counting each section of the chromatogram. For visual determination of the origin, the solvent front progress during development, and final location of solvent front we have found it convenient to place a small dot with an ordinary black felt tipped pen about 1 cm from the bottom of the chromatogram next to the area intended for the application of the sample. Different color patterns will develop in the different solvents allowing quick determination of which solvent system has been used.

The ITLC-SG in normal saline system can also be used for the rapid determination of free Tc in water insoluble radiopharmaceuticals such as Tc MAA and Tc sulfur colloid. The use of these two systems does not involve any extensive preparation and can be rapidly instituted in any Nuclear Medicine Department.

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2. RICHARDS P, STEIGMAN J: Chemistry of Technetium as it is Applied to Radiopharmaceuticals. Presented at the International Symposium on Radiopharmaceuticals, Atlanta, Georgia, Feb. 12–15, 1974

Reply

We appreciate the interest shown by Kuperus and Lyons in our paper, and recognize that in our explanations for the apparent high content of reduced technetium in phosphorous-based compounds, two facts are combined that are not related. Initially, the explanation of the artifacts produced during the chromatographic testing of these compounds was similar to that of Kuperus and Lyons, however, after reviewing our data, we changed our opinion. Indeed, Tables 1 and 2 (1) show that for all the chromatographic systems mentioned, the content of reduced technetium in labeled phosphorous compounds is larger than expected; nevertheless, the largest content of apparently reduced technetium was found with the MAC kit. These unusually high values for reduced technetium in pyrophosphates, and to some extent in diphosphonate (Osteoscan), cannot be attributed only to the higher instability of these compounds, since both MICHROM and MAC are fast resolving systems providing little time for chemical reactions to take place. This is confirmed by the fact that a much slower system, ITLC, showed the lowest content of reduced species of technetium (Table 1) (*1*). Further tests carried out in our laboratory under different conditions, (including oxygen-free atmosphere in the development chamber, and the use of other nonpolar or low polarity mobil phases) did not improve the testing results.

This is a complex problem, in which instability of these compounds is only a part of it, and that other factors involved create these artifacts. Most probably, the finding of a more suitable combination of stationary and mobil phases will permit one to obtain chromatograms indicating the true state of technetium in these compounds. These chromatograms may also show a closer correlation with the clinical findings.

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Increased Salivary Gland Uptake of ^{67}Ga-Citrate 36 Months After Radiation Therapy

A recent article (*1*) in the *Journal of Nuclear Medicine* discussed the uptake of gallium within the salivary glands after radiation therapy for Hodgkin's Disease. The authors did not indicate how many (if any) of their chronic clinical period cases (2–5 years) were positive. Since the publication of this article we have seen a case of increased activity within the salivary glands in a patient who was 36 months after radiation therapy for Hodgkin's Disease (Fig. 1). This patient was unable to complete his therapy because of consistently low leucocyte and platelet counts secondary to chemotherapy. He therefore received a total target dose of only 2,000 rads to a mantle port in an elapsed time of 3 weeks.

The findings that within the salivary glands gallium uptake may be present for a long period after radiation ther-