METABOLIC BEHAVIOR AND RADIATION DOSIMETRY OF ^{99m}Tc-ALBUMIN IN PREGNANCY

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The use of tagged albumin for placental localization is already well established, and the advantages of short-lived isotopes have been stressed by Hibbard (*1,2*). According to Herbert *et al* (*3*) ^{99m}Tc fulfils most of the optimal criteria for isotopes used for scanning and other similar purposes. Stern *et al* (*4*) and Gwyther and Field (*5*) have described methods for preparing technetium-labeled human serum albumin, while its use for placental localization has been reported by McAfee *et al* (*6*), Larson and Nelp (*7*), Herbert (*8*) and others. Estimates of the radiation dose to maternal and fetal tissues based on data originally published for IHSA by Hibbard and Herbert (*9*) have been given by Smith (*10*) and Herbert (*2*).

The behavior of technetium-labeled albumin might be expected to follow the same pattern as that of IHSA with variations related to the differences in metabolism between the liberated free technetium and the iodine. However, the exact site and nature of the attachment of the technetium atom to the albumin is not known with certainty. Therefore, in an assessment of the metabolic behavior and radiation dosimetry of ^{99m}Tc-albumin, it is justifiable to use observations made with IHSA only to obtain a first approximation.

For this reason we have devised a series of experiments to study the distribution of radioactivity in the mother, the fetus and the secundines to assess both the advantages of technetium-labeled albumin for placental localization and the radiation doses received. We made no attempt to estimate the dose to the maternal thyroid gland because limitations on the quantity of ^{99m}Tc-albumin administered are likely to be imposed by fetal rather than maternal considerations.

METHOD OF MEASUREMENT

Our initial results were different from some published results, and after carefully reviewing methods of preparation, handling and storage of our material, we decided on a more extensive assessment. This included serial measurements of the radioactivity of maternal plasma, umbilical-cord plasma, liquor amnii and maternal and infant urinary excretion as well as external counting of the neonatal thyroid, stomach and other organs and measurement of protein-bound technetium in selected biological samples.

The subjects were volunteers with pregnancies of 32-weeks gestation or more. In many cases there were clinical indications for placental-localization studies, while other volunteers were obtained because the approximate time of delivery was known; this facilitated a reasonable temporal spread of the readings.

Because of the inaccessibility of the uterine contents, serial measurements in individual cases are impossible. Therefore it is necessary to obtain samples at the time of delivery in subjects with varying injection-to-delivery intervals and to construct a composite picture from these data.

An activity of 250 μCi was administered intravenously in a volume 0.5–2-ml albumin solution. No attempt was made to adjust the initial dose to the patient's weight nor to correct the readings for maternal weight or other variables. This was because (1) there is a lack of reliable data from which to make corrections, (2) many of the measurements are concerned with proportionate changes in concentrations with time and are unaffected by the initial compartment size and (3) the purpose of the investigation was to obtain an average radiation dose and since a large number of observations were made, we felt that a more representative assessment would be obtained without these corrections.

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PREPARATION OF ^{99m}Tc-ALBUMIN

Stern *et al* (*4*) have emphasized the importance of attention to detail, especially in the control of pH, to obtain a good yield and to avoid possible contamination with oxidation products of iron complexes. We followed the technique described by these workers with only minor modifications.

The completeness of protein binding was assessed by paper chromatography. The solvent used was 85% methanol, and the development time was 3 hr, during which the solvent face travels 20–25 cm. The paper was then scanned with a G-M tube with a slit collimator and the radioactivity recorded on a paper-strip recorder. Free pertechnetate did not exceed 0.3%.

COLLECTION AND ASSAY OF SAMPLES

Maternal blood samples were obtained by venepuncture and transferred to heparinized centrifuge tubes. They were usually taken synchronously with samples of liquor amnii and/or fetal cord blood, but additional samples were obtained at various other times to correlate with urinary excretion and to obtain a reasonably comprehensive clearance pattern.

Fetal blood samples were obtained in duplicate with a syringe from the umbilical cord vessels at the time of delivery and were treated in the same manner as the maternal samples. The simpler procedure of "milking" blood from the cut end of the cord was unsatisfactory because even slight contamination by maternal blood led to unreliable results.

Liquor amnii was usually obtained from subjects who had the membranes ruptured artificially to induce labor. Samples were obtained by hind-water rupture with a Drew-Smythe catheter. The initial flow was discarded, and only samples without maternal red-cell contamination—judged by naked eye inspection—were used. Samples were also obtained from some patients at the time of abdominal amniocentesis or Caesarean section.

Maternal urine was collected up to 48 hr from the time of injection. Total volumes were measured.

Infant urine was obtained in various ways. Initially, all soiled napkins including voided meconium were placed in plastic bags, and total radioactivity was measured. Subsequently urine samples were collected from male infants by attaching Paul's tubing to the penis or, in both males and females, by applying to the perineum a specially designed plastic bag with an opening surrounded by adhesive. The receptacles were attached within a few minutes of birth, and any infant who passed urine before this time was excluded from the series. In this way reliably complete specimens were obtained. It was soon discovered that many newborn infants failed to pass urine within the first 24 hr and that the total volumes generally fell short of the usually quoted amounts.

Aliquots (3 ml) of plasma, urine and liquor were counted and compared with standards prepared from the original ^{99m}Tc-albumin solution. A 2-in. NaI(Tl) well crystal with a sensitivity of 32,000 cps/μCi and a background of 8.5 cps was used.

Because of the closeness of the apparatus to the delivery unit, it was usually possible to count the specimens within a few minutes after they were obtained. All specimens expected to be of low specific activity, irrespective of the time at which they were obtained, were assayed as soon as possible. If the specimens were expected to have a high specific activity, they were collected and counted in batches each day.

Estimation of free technetium. The proportion of free and protein-bound ^{99m}Tc in specimens of liquor, fetal and maternal plasma were estimated as early as possible to avoid errors caused by denaturation during storage. After measuring the total activity, the sample was passed through a Dowex 1 $\times$ 2 (Cl) 50–100-mesh ion-exchange column to remove free isotope. The eluate was then assayed and the amount of free isotope calculated by subtraction.

EXTERNAL COUNTING

In vivo counting of the infants was carried out with a hand-held scintillation counter similar to that described by Herbert *et al* (*3*). This counter has a crystal 2.54 cm in diameter and 4 mm thick, shielded with 3 mm of lead but no collimator. The crystal-to-skin distance was 2 cm. A total of approximately 10,000 counts was registered on a portable scaler with counting times of 100–300 sec, but the duration of the count was often dictated more by problems of controlling the infant than by statistical requirements. However, reasonably reproducible results were obtained. Measurements were made in the delivery room within a few minutes of birth.

The counter was calibrated with a simple water phantom made from a polythene container 30 cm in circumference and 18 cm high. Bottles 15 cm in circumference and 7½ cm long were attached to this container to represent the neck and the thighs. A small polythene pot containing 2 ml of liquid simulated the thyroid and was attached to the front of the neck.

Early in the clinical investigation we found that the correction to be applied to the thyroid uptake for extrathyroidal activity was rather large, and the usual practice of subtracting a thigh count was not considered applicable. An estimate of the athyroid

TABLE 1. CALIBRATIONS OF PORTABLE COUNTER USED FOR MEASUREMENTS ON INFANTS

Sensitivity for 2 ml simulated thyroid at 2 cm distance	1,500 cps/μCi
Sensitivity for body surface counts, mean over trunk	135 cps/μCi/liter
Background	7 cps
Athyroid neck/thigh ratio	0.83

TABLE 2. CONCENTRATION OF ^{99m}Tc IN MATERNAL PLASMA AFTER INTRAVENOUS INJECTION OF ^{99m}Tc-ALBUMIN*

Time (hr after injection)	y_m (% dose/liter)	Standard error of mean
0.66	22.8	0.82
1.67	18.6	1.06
2.53	15.8	0.77
4.00	14.2	0.56
6.35	12.4	0.56
9.14	10.1	0.50
12.16	9.47	0.40
15.99	8.94	0.42
21.32	8.00	0.40
32.73†	6.20	0.57

* Means of groups of 20 results.
† 4 results only.

TABLE 3. RATIO OF FETAL/MATERNAL PLASMA CONCENTRATIONS AND FETAL PLASMA CONCENTRATIONS OF ^{99m}Tc FOLLOWING MATERNAL INTRAVENOUS INJECTION OF ^{99m}Tc-ALBUMIN*

	Fetal/maternal plasma		Fetal plasma	
Time (hr after injection)	Ratio	Standard error of mean	y_f (% dose/liter)	Standard error of mean
0.91	0.0247	0.0034	0.55	0.080
1.86	0.0383	0.0049	0.64	0.080
2.70	0.0432	0.0036	0.70	0.057
4.08	0.0437	0.0049	0.66	0.057
6.29	0.0374	0.0008	0.54	0.065
10.80	0.0398	0.0032	0.41	0.041
14.36	0.0433	0.0039	0.40	0.032
18.10	0.0365	0.0044	0.33	0.040
24.10	0.0514	0.0050	0.36	0.040
31.56†	0.0393	0.0116	0.24	0.100

* Means of groups of 10 results.
† 6 results only.

neck-to-thigh ratio was made by the method of Goolden and Mallard (*11*) from measurements obtained on the phantom.

Little variation was observed in counting rates at different sites on the trunk with the exception of the bladder region, and we concluded that the trunk could be represented by a homogeneous phantom to determine the total-body content. The counter was calibrated using this phantom containing a known specific activity with the sensitivity expressed as cps/μCi/kg (mean baby density being assumed as 1). The calibrations are given in Table 1.

RESULTS

Maternal plasma. Measurements were made on 184 samples of maternal plasma, and the standard error of counting was less than 2%. From these measurements a representative curve was made by forming the observations into groups of 20 and plotting the centers of gravity of the groups. The radioactivity of the samples was expressed as a percentage of dose per liter of plasma. The values for the means of the groups with their standard errors are shown in Table 2 and plotted semilogarithmically in Fig. 1.

The curve can be broken down into two exponential components showing a rapid initial clearance with a half-time of 2 hr and a slow phase with a half-time clearance of 35 hr. It can be represented by the equation

$$y_m = 13\, e^{-0.85t} + 12\, e^{-0.020t}\ \%/\text{liter}. \quad (1)$$

The curve of this equation is superimposed on the practical observations in Fig. 1.

Fetal plasma. Measurements were made on 98 samples of fetal plasma. These were expressed both as a ratio of the fetal-to-maternal plasma concentrations at the time of delivery and as a percentage of dose per liter of plasma. The standard counting error was less than 5% except in 11 low-activity samples where the standard error was between 5% and 20%. The results for two subjects were ignored because contamination was suspected, and the value deviated from the mean by more than 3 standard deviations.

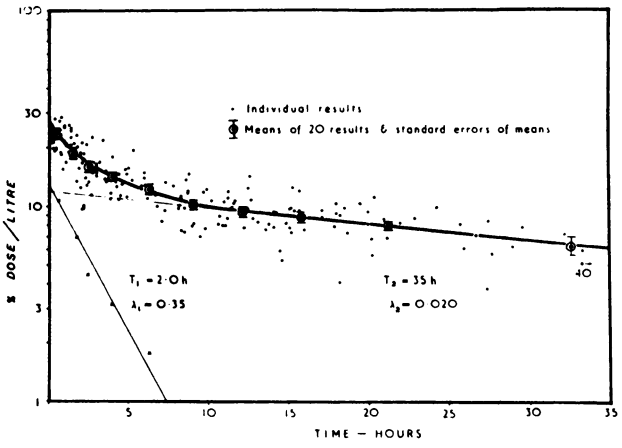

FIG. 1. Concentration of ^{99m}Tc in maternal plasma following intravenous injection of ^{99m}Tc-albumin.

Observations were formed into groups of 10 and the centers of gravity of these groups were calculated. The mean values and their standard errors are given in Table 3.

Transplacental passage of the isotope was evident a few minutes after maternal injection, and the activity of the fetal plasma rose to reach apparent equilibrium with the maternal plasma with a half-time of 0.63 hr (Fig. 2). Taking the mean of all the observations after 2½ hr gives an equilibrium ratio of 0.043. Thus the fetal plasma uptake curve can be represented by Eq. 2 below; the curve is shown superimposed on the observations in Fig. 3.

$$y_f = 0.043\ (1 - e^{-1.1t})$$
$$(13\, e^{-0.35t} + 12\, e^{-0.020t})\ \%/\text{liter}. \quad (2)$$

Liquor amnii. Measurements of the radioactivity of liquor amnii were made in 77 cases. Because of clinical problems involved in obtaining samples, the number of observations was limited and showed a wide scatter. The standard error of counting was less than 5% in all but nine, eight of which were less than 10%. Initially it was thought that some high readings might have resulted from unrecognized contamination by maternal plasma, but subsequent measurements on definitely uncontaminated specimens also showed unexpectedly high activity in many cases. The reasons for the wide divergence of readings are not entirely clear but will be discussed later. Both liquor uptake as percent of dose per liter and liquor-to-maternal plasma ratios were formed initially into groups of 10 (Table 4).

The scatter of the readings made reliable statistical analysis difficult and to obtain a representative curve for the liquor-to-maternal plasma ratios a number of assumptions had to be made. An equilibrium ratio of approximately 0.07 was assumed. It was recognized from the individual results that the ratio may in fact be falling after 15 hr but sufficient observations were not available to test this. The assumption of equilibrium might therefore result in a slight overestimate of radiation exposure (Fig. 4).

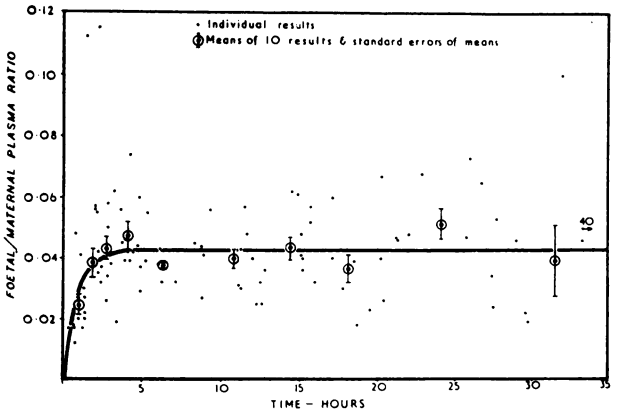

FIG. 2. Fetal-to-maternal plasma ratio of ^{99m}Tc after maternal intravenous injection of ^{99m}Tc-albumin.

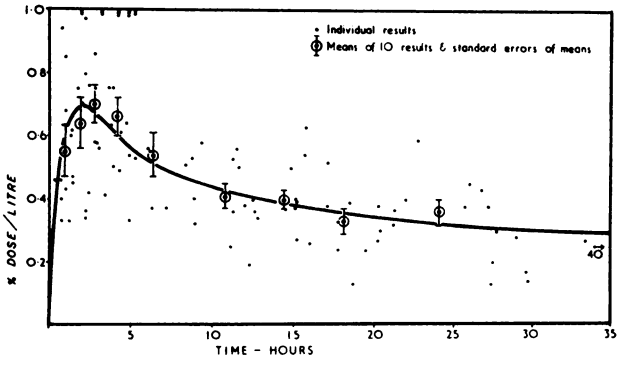

FIG. 3. Fetal plasma concentration of ^{99m}Tc after maternal intravenous injection of ^{99m}Tc-albumin.

TABLE 4. RATIO OF LIQUOR/MATERNAL PLASMA CONCENTRATIONS AND LIQUOR/AMNII CONCENTRATIONS OF ^{99m}Tc AFTER MATERNAL INTRAVENOUS INJECTION OF ^{99m}Tc-ALBUMIN*

Time (hr after injection)	Liquor/maternal plasma: Ratio	Liquor/maternal plasma: Standard error of mean	Liquor: y_a (% dose/liter)	Liquor: Standard error of mean
1.00	0.0021	0.0005	0.043	0.011
1.73	0.0058	0.0015	0.093	0.021
3.02	0.0242	0.0038	0.345	0.054
5.03	0.0302	0.0044	0.384	0.054
7.64‖	0.0628	0.0110	0.667	0.092
9.86	0.0708	0.0093	0.672	0.075
12.62‖	0.0732	0.0070	0.643	0.065
15.48†	0.0619	0.0070	0.501	0.063
39.00‡	0.0500	—	0.25	—

* Means of groups of 10 results.
† 8 results only.
‡ 1 result only.
‖ 9 results only.

TABLE 5. INFANT URINARY EXCRETION OF ^{99m}Tc AFTER MATERNAL INTRAVENOUS INJECTION OF ^{99m}Tc-ALBUMIN

Injection-delivery interval (hr)	Collection time (hr)	Volume of urine (ml)	Concentration (% dose/liter)	Total (% dose)
1.5	24	30	6.8	0.34
2.2	24	11	41.8	0.46
2.4	21	16	11.8	0.19
3.9	24	15	10.0	0.15
6.1	36	16.5	10.3	0.17
12.6	24	40	2.0	0.08
14.5	24	10	3.0	0.03
20.25	24	10	0.6	0.006

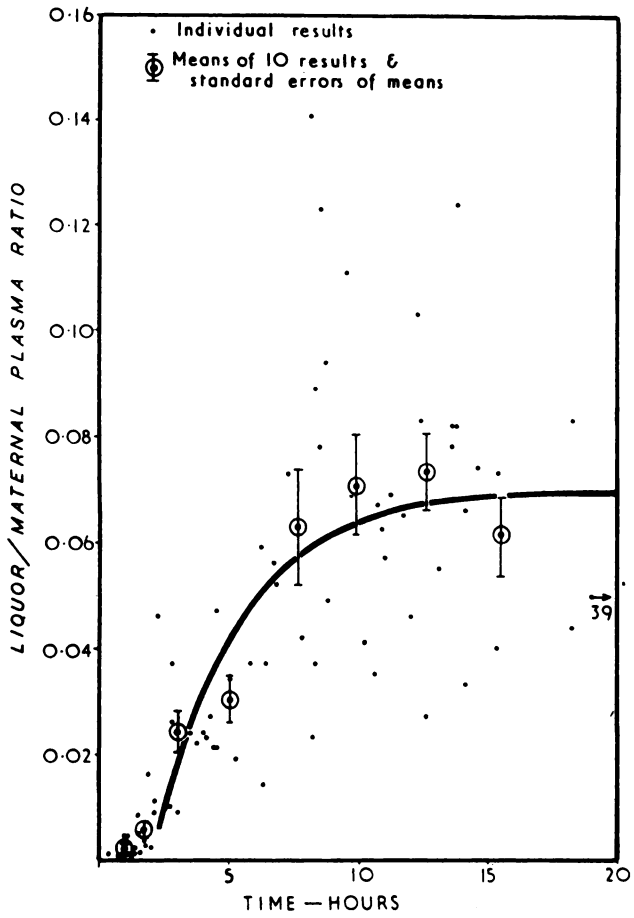

FIG. 4. Liquor amnii-to-maternal plasma ratio of ^{99m}Tc following maternal intravenous injection of ^{99m}Tc-albumin.

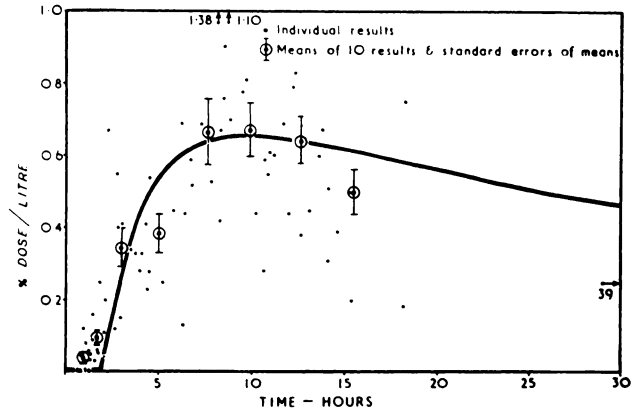

FIG. 5. Liquor amnii concentration of ^{99m}Tc after maternal intravenous injection of ^{99m}Tc-albumin.

In considering the liquor uptakes, the low initial values were ignored, and a delay of 2 hr was assumed. The half-time of uptake was then found to be 2.31 hr (Fig. 5) and an equation for the uptake curve was obtained as for the fetal plasma.

$$y_a = 0.07\,(1 - e^{-0.3(t-2)})$$

$$(13\,e^{-0.35t} + 12\,e^{-0.02t}). \quad (3)$$

This curve, together with the observed results, is shown in Fig. 5.

Free and protein-bound isotope in maternal and fetal plasma and liquor. The free technetium in 17 samples of maternal plasma ranged from 2% to 21.2%, the mean value being 13.6%. In fetal plasma the lowest content was 36%, but in four samples the counts on the eluates were less than background and 100% free isotope was assumed. The mean content was 78.4%. Little protein-bound isotope was detected in 14 samples of liquor amnii. the mean value being 8.2% with a range of 0% to 12%.

Infant urine. The results of the measurements on eight 24-hr samples obtained in bags are given in Table 5.

In cases where the infant was delivered within a few hours of maternal injection, relatively high excretion rates were encountered in spite of the fact that the total fetal plasma content was never likely to exceed 0.15% of the maternal administered dose.

The highest reading occurred in an infant delivered at a time when the fetal plasma concentration would be a maximum. This infant excreted a total of 0.46% of the dose in the 24 hr after delivery, at a concentration of 41.8% per liter, which was 60 times higher than the expected maximum plasma concentration.

Maternal urine. Excretion of ^{99m}Tc in the maternal urine occurred very soon after injection, and significant amounts could be detected in the bladder with an external counter after 20–40 min. The results of measurements in 71 cases are shown in Table 6.

Maternal feces. In six subjects samples of feces were collected for periods up to 48 hr after injection of ^{99m}Tc albumin. The activities were plotted semilogarithmically, and results given in Table 6 were taken from this graph.

Maternal whole-body content. This was estimated by subtraction of the total radioactivity excreted

TABLE 6. MATERNAL EXCRETION OF ^{99m}Tc FOLLOWING INTRAVENOUS INJECTION OF ^{99m}Tc-ALBUMIN

Time (hr after injection)	Urinary excretion: Number of results	Urinary excretion: Mean % dose	Urinary excretion: Standard error of mean	Fecal excretion (% dose)	Maternal whole-body content (% dose)
3	13	10.4	1.5	0	89.6
6	29	19.7	1.0	0	80.3
12	5	21.9	2.5	0.0051	78.1
24	18	31.9	1.9	0.0114	68.1
48	6	37.8	1.3	5.80	56.4

from the dose administered. Results are given in Table 6. The half-time clearance was 69 hr.

Fetal thyroid. Satisfactory measurements of thyroid uptake were obtained in 56 infants. The standard counting error was less than 10% in all but nine when it was between 10% and 30%. These were arranged in eight groups of seven results and are summarized in Table 7.

The grouped results were plotted on a semilogarithmic graph, and the equation for the best fitting curve obtained by dividing into exponential functions (Fig. 6) is

$$y_t = 0.013\, e^{-0.026t} + 0.020\, e^{-0.81t} - 0.033\, e^{-0.78t}. \quad (4)$$

This curve, plotted arithmetically and superimposed on the observed results, is shown in Fig. 7.

Neonatal total-body content. From measurements made at various sites on the trunks of 18 infants the mean specific activity was obtained and multiplied by the birth weight to derive total-body content. The standard error of counting was less than 2%.

Because there is only slight correlation with time and this is insignificant in relation to radioactive decay, it has been assumed that equilibrium is reached within 1 hr, the shortest interval at which a measurement was obtained. Then

Mean % dose/kg of infant = 0.47; s.e. 0.11

Mean % dose/whole infant = 1.55; s.e. 0.16

RADIATION EXPOSURE AND DOSIMETRY

The radiation exposures for the various organs and tissues, expressed as μCi-hr/100μCi, were calculated by integrating Eqs. 1–4 after allowing for radioactive decay. From these results the radiation doses were determined by conventional methods (*12*) (Table 8).

TABLE 7. FETAL THYROID UPTAKE OF ^{99m}Tc AFTER MATERNAL INJECTION OF ^{99m}Tc-ALBUMIN*

Time (hr after injection)	y_t (% uptake)	Standard error of mean
0.93	0.011	0.002
1.71	0.014	0.002
2.61	0.017	0.002
3.54	0.014	0.001
4.76	0.018	0.004
7.30	0.010	0.001
12.87	0.010	0.002
22.49	0.007	0.001

* Groups of 7 results.

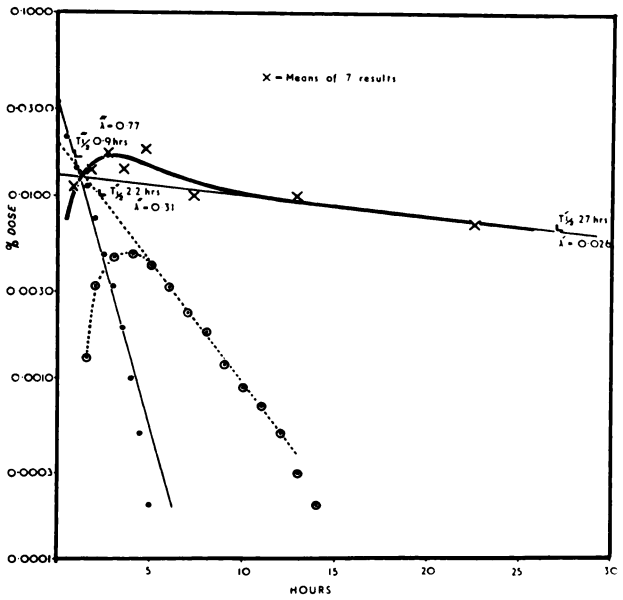

FIG. 6. Fetal thyroid content of ^{99m}Tc. Analysis of curve best fitting observed readings.

In these calculations the following assumptions are made:

1. For ^{99m}Tc the specific gamma-ray emission is 0.72 R/mCi-hr, there is 0.014-MeV of beta-like energy emitted per disintegration and the half-life is 6 hr (*10*).
2. Maternal weight is 60 kg, composition is uniform and distribution of the isotope is even throughout the maternal tissue.
3. The concentration of activity in the gonads is 0.8 of plasma concentration (*13*).
4. Fetal weight is 3.3 kg.
5. The fetal thyroid weighs 2 gm (*14*).
6. The fetus remains *in utero*.
7. Gamma radiation from the liquor is insignificant compared with maternal gamma radiation.

DISCUSSION

Although derived solely from studies on pregnant women, the data presented give a reasonable indication of the behavior of ^{99m}Tc-albumin in nonpregnant individuals, because transfer to the fetus is relatively slight. Because of its favorable radiation characteristics, ^{99m}Tc-albumin is being used increasingly as an alternative to IHSA for many investigations, especially in scanning procedures involving semiquantitative estimations. It is immediately evident from the present results that because of largely unknown factors which cause rapid and variable liberation of technetium from its carrier molecule, ^{99m}Tc-albumin cannot be used for studies of albumin metabolism.

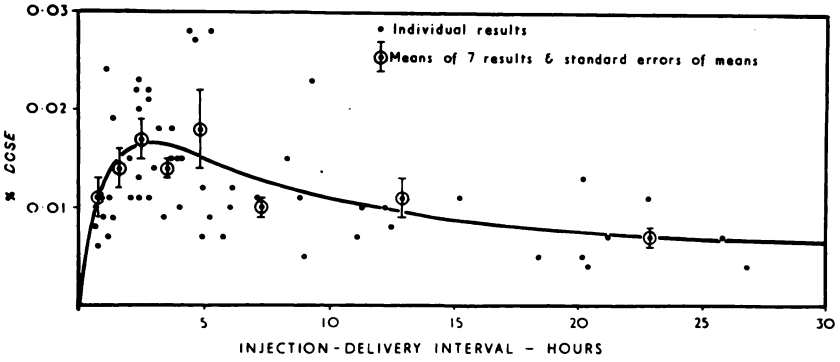

FIG. 7. Fetal thyroid content of ^{99m}Tc as percentage of initial dose.

Although the preparation injected in these studies appeared to be stable *in vitro* and contained virtually no free isotope, there was an initial phase of rapid breakdown *in vivo* which was reflected in the plasma clearance, excretion and fetal transfer studies.

The initial plasma clearance was 16% in the first hour and 51% in 6 hr; the latter clearance is similar to that found by McAfee *et al* (*6*). Thereafter there was a steady loss of 38% per day, approximately twice that found by McAfee *et al* (*6*). There was no evidence of sequestration or of excessive accumulation in the extravascular albumin pool since the ratio for plasma-to-extravascular albumin was calculated as 1.1-to-1, a figure similar to that reported for Europeans by Cohen and Schamroth (*15*).

TABLE 8. RADIATION DOSIMETRY OF ^{99m}Tc*

	Radiation exposure (μCi-hr/100 μCi)	Radiation dose				
		Maternal		Fetal		Total
		β (mrads)	γ (mR)	β (mrads)	γ (mR)	(mrems)
Maternal whole body	700	0.35	1.05	—	—	1.4
Maternal plasma	116/liter	3.46	1.05	—	—	4.5
Maternal gonads	—	2.77	1.05	—	—	3.8
Fetal whole body	13.4	—	1.05†	0.12	0.0026	1.2
Fetal plasma	4.2/liter	—	1.05	0.13	0.0026	1.2
Fetal gonads	—	—	1.05	0.10	0.0026	1.2
Fetal thyroid	0.10	—	1.05	1.49	0.2700	2.8
Liquor amnii	3.6/liter	—	—	—	—	—

* Estimated doses after intravenous injection of 100 μCi ^{99m}Tc-albumin.

† Calculated on the assumption that radioactivity is evenly distributed over the mother, fetus and liquor (g = 125 cm). This gives an overestimate because it does not take into account the fact that the fetus is contained in an almost non-radioactive enclosure.

The greater part of the loss from the albumin pool is accounted for by urinary excretion, and there was a remarkably consistent excretion from subject to subject, with a mean value of 32% in the first 24 hr.

This is at variance with the figure of 0.5% in 24 hr found by McAfee *et al* (*6*), and their figure is difficult to equate with their rapid plasma clearance. No other estimations are available, but it may be noted that Larson and Nelp (*7*), using the same method for preparing ^{99m}Tc-albumin as McAfee *et al* (*6*), drew attention to the high concentration of isotope in the bladder as shown in their scans.

A mean of 13.6% of the total plasma activity was due to free isotope, and it is doubtful whether this alone is sufficient to account for the high urinary excretion; this is of the same order as that found by Herbert *et al* (*3*), Nelp (*16*) and Andros *et al* (*17*) after administration of pertechnetate. Therefore this raises the question of whether there is a specific renal mechanism which liberates the isotope from the albumin. Fecal excretion was low during the period of study, with a maximum of 5.8% in 48 hr.

Transfer to the fetus and liquor amnii was greater than that found with IHSA, the fetal plasma equilibrium value of 4.3% of maternal plasma concentration being approximately twice that found by Hibbard and Herbert (*9*) in a previous investigation of IHSA. McAfee *et al* (*6*) in measurements on two infants only found a concentration of 2% at 1 and 4 hr after maternal injection. Larson and Nelp (*7*) found concentrations of 1.4–3.3% in the plasma of infants delivered 0.5–28 hr after maternal injection. The concentration of radioactivity in the liquor (final value—7% of maternal plasma concentration) was high compared with the IHSA investigations where no liquor radioactivity was detected. The technetium detected in the fetal plasma was principally free and that in the liquor almost totally so. This confirms previous observations that the passage of administered albumin across the placenta is slight.

The high concentration of isotope in the infants'

urine obtained immediately after birth indicates that the fetal kidneys are well able to concentrate technetium, most of which is in the free form in the fetal plasma. Fetal urination is thus likely to contribute significantly to the relatively high isotope content of the liquor amnii, and intermittent voiding of urine *in utero* may account in part for the wide scatter of results obtained in the liquor measurements.

The explanation for the rapid liberation of the technetium from the albumin after injection remains obscure. There is no reason to suspect that undue denaturation of the albumin occurred during preparation, because the chemical processes involved are not likely to be more destructive than those used to prepare the IHSA. It is notable that in the manufacture of ^{99m}Tc-albumin the pH is a critical factor, and in animal experiments McAfee *et al* (*6*) found that lowering the pH of the solution resulted in more rapid plasma clearance in the early phase after injection. It is therefore possible that displacement of the technetium results from the presence of free halogen or other ions associated with an unfavorable pH in the plasma. Both this and the exact role of the kidneys are worthy of further study.

Initially the relative *in vivo* instability of the preparation was a source of concern in relation to radiation dosimetry. However, it became evident that even with the increased placental transfer compared with IHSA the major contribution to fetal irradiation came from gamma rays in the maternal system. Also the relatively low uptake by the fetal thyroid means that passage of free technetium across the placenta is not a factor of major importance. Indeed, the total thyroid dose was little more than twice the whole-body dose (Table 9), and the administration of agents to block thyroid uptake recommended by Smith (*10*) seems unnecessary.

In general our estimates of radiation dose are in agreement with those of McAfee *et al* (*6*) and Smith (*10*). Smith estimated fetal thyroid irradiation as 5 mrems/100 μCi administered as compared with our figure of 2.8 mrems.

Favorable practical experience in using ^{99m}Tc-albumin for placental localization will be reported elsewhere. From the physical and biological points of view, ^{99m}Tc-albumin is to be preferred to IHSA, and the comparative radiation doses to maternal and fetal gonads and fetal thyroid using amounts commonly recommended for placental localization studies are shown in Table 10. It is possible to use relatively large doses of ^{99m}Tc-albumin, and even when 250 μCi are administered the fetal tissues are subjected to a radiation exposure equivalent to only 2–3 weeks of natural background radiation (Table 10).

TABLE 9. COMPARISON OF CALCULATED RADIATION DOSES (mrems) FROM 100 μCi ^{99m}Tc-ALBUMIN

	Present investigation	Smith (10)	McAfee *et al* (6)	Larson and Nelp (7)
Maternal whole body	1.4	0.5	1.3	—
Maternal blood	4.5	4.7	4.3	—
Maternal gonads	3.8	—	—	—
Fetal whole body	1.2	—	1.4	<5
Fetal blood	1.2	1.4	1.4	—
Fetal gonads	1.2	—	—	—
Fetal thyroid	2.8	5	2–7	—

TABLE 10. COMPARISON OF RADIATION DOSES (mrems) FROM IODINATED AND TECHNETATED ALBUMIN ADMINISTERED IN AMOUNTS COMMONLY USED FOR PLACENTAL LOCALIZATION

	Maternal gonads	Fetal gonads	Fetal thyroid*
^{131}I-IHSA 5 μCi	15	7	4,900
^{131}I-IHSA 50 μCi	10	5	130
^{99m}Tc-albumin 250 μCi	10	3	7

* No pretreatment with thyroid-blocking agents.

SUMMARY

A cross-sectional study of the metabolic behavior of ^{99m}Tc-albumin after intravenous injection to pregnant women was carried out. Serial measurements of the radioactivity of maternal plasma, maternal and infant urine excretion, umbilical cord blood, liquor amnii, neonatal thyroid and whole body were made.

A relationship between percentage uptake and time has been established for these organs and tissues and the radiation exposures in μCi-hr/100 μCi obtained. From these results the radiation doses for mother and fetus have been calculated; maternal gonads, 3.8 mrems/100 μCi; fetal gonads, 1.2 mrems/100 μCi and fetal thyroid, 2.8 mrems/100 μCi.

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