Excretion of Radionuclides in Human Breast Milk After the Administration of Radiopharmaceuticals

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The fraction of injected activity that was excreted through the breast milk of nursing mothers at different times after the injection of various radiopharmaceuticals has been measured in 21 patients. For ^{99m}Tc-labeled radiopharmaceuticals the total excreted fraction was 10% for pertechnetate and 1.5–3% for MAA, plasmin, diethylenetriaminepentaacetic acid (DTPA), and methylene diphosphonate (MDP). For [^{125}I]hippuran and [^{131}I]hippuran the corresponding value was 3%. For the above mentioned radiopharmaceuticals the activity concentration in the milk decreased exponentially with an effective half-life of approximately 4 hr. For chromium-51 ethylenediaminetetraacetic acid ([^{51}Cr]EDTA) and [^{99m}Tc]RBC, much smaller amounts were excreted in the breast milk. The absorbed dose to various organs of the baby has been calculated. We conclude that when [^{99m}Tc]pertechnetate, [^{99m}Tc]MAA, [^{99m}Tc]plasmin, [^{125}I]hippuran, or [^{131}I]hippuran are used the child should be fed just before the administration of the radionuclide to the mother and the next three milk fractions should not be used. For [^{99m}Tc]DTPA and [^{99m}Tc]MDP as well as [^{51}Cr]EDTA, only the first fraction should not be used. According to our earlier investigations breast feeding has to be stopped for at least 3 wk after investigations with [^{125}I]fibrinogen.

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The usual practice in nuclear medicine is to avoid administration of radiopharmaceuticals to nursing mothers. It is, however, sometimes necessary to carry out emergency nuclear medicine investigations, mostly for pulmonary embolism or kidney failure. For some of these investigations, it will be necessary to interrupt the breast feeding because of high absorbed doses to the child. This interruption may cause feeding problems.

There are only limited biokinetic and dosimetric data available that are needed to estimate the absorbed dose to a breast-fed child. In the literature, these data are normally published as case reports (*1–16*). There is a need for systemic studies on more patients. We have earlier measured the activity concentration in breast milk from a small number of nursing mothers after the injection of various radiopharmaceuticals (*17,18*). In the present work, we have measured the activity concentration in the breast milk from 21 additional mothers and improved our estimates of the absorbed dose to the child. On these grounds, we propose simple recommendations for interrupted or continued breast feeding in clinical practice.

MATERIALS AND METHODS

Because of suspected pulmonary embolism, six mothers underwent lung scintigraphy with macroaggregated human serum albumin (MAA) labeled with ~2.2 mCi (80 MBq) technetium-99m (^{99m}Tc). The activity concentration in milk samples taken up to 47 hr after the injection was studied.

Because of renal dysfunction, six mothers underwent renography with hippuran labeled with approximately 8 μCi (0.3 MBq) iodine-131 (^{131}I). For one of these patients, 10 μCi (0.4 MBq) iodine-125 (^{125}I) hippuran was used to localize the kidneys prior to the [^{131}I]hippuran injection. The activity concentration in the breast milk was studied up to 68 hr after injection.

For two of the mothers, the glomerular filtration rate ("clearance") was determined using 100 μCi (3.7 MBq) chromium-51 ethylenediaminetetraacetic acid

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TABLE 1.
Total Fraction of Injected Activity Excreted in Breast Milk Assuming Milk Production of 850 ml/day and Absorbed Dose to Child per MBq Given to Mother

Radio-pharmaceutical	Number of patients	Effective half-life hours Mean value	Effective half-life hours Range	Total fraction of injected activity excreted in breast milk Mean value	Total fraction of injected activity excreted in breast milk Range	Effective dose eqiv mSv Mean	Stomach wall mGy Mean	Thyroid mGy Mean
[^{99m}Tc]MAA	6	3.7	3.3–4.5	$3.2 \cdot 10^{-2}$	$0.4–5.2 \cdot 10^{-2}$	$0.9 \cdot 10^{-2}$	$11.0 \cdot 10^{-2}$	$3.2 \cdot 10^{-2}$
$^{99m}TcO_4^-$	1	3.2	—	$10.8 \cdot 10^{-2}$	—	$3 \cdot 10^{-2}$	$36 \cdot 10^{-2}$	$10.8 \cdot 10^{-2}$
[^{99m}Tc]plasmin	2	3.2	2.2–4.1	$2.0 \cdot 10^{-2}$	$0.9–3.2 \cdot 10^{-2}$	$0.6 \cdot 10^{-2}$	$7 \cdot 10^{-2}$	$2.0 \cdot 10^{-2}$
[^{99m}Tc]DTPA	1	3.7	—	$1.5 \cdot 10^{-2}$	—	$0.4 \cdot 10^{-2}$	$5 \cdot 10^{-2}$	$1.5 \cdot 10^{-2}$
[^{99m}Tc]RBC	1	7.7	—	$6.1 \cdot 10^{-5}$	—	$1.7 \cdot 10^{-5}$	$2 \cdot 10^{-5}$	$6.1 \cdot 10^{-5}$
[^{99m}Tc]MDP	2	4.3	3.5–5.1	$1.9 \cdot 10^{-2}$	$1.1–2.7 \cdot 10^{-2}$	$0.5 \cdot 10^{-2}$	$6 \cdot 10^{-2}$	$1.9 \cdot 10^{-2}$
[^{125}I]Hippuran	1	4.8	—	$2.4 \cdot 10^{-2}$	—	1.7	0.03	55
[^{131}I]Hippuran	6	4.5	2.2–5.8	$2.8 \cdot 10^{-2}$	$1.8–4.9 \cdot 10^{-2}$	7.0	0.23	227
[^{51}Cr]EDTA	2	6.0	5–7	$4.0 \cdot 10^{-4}$	$1.5–6.5 \cdot 10^{-4}$	$1.6 \cdot 10^{-4}$	$1.2 \cdot 10^{-4}$	—

([^{51}Cr]EDTA). The excretion of the radionuclide in breast milk was studied up to 68 hr after injection.

Seven mothers were injected with various ^{99m}Tc-labeled radiopharmaceuticals, one with 3.1 mCi (115 MBq) $^{99m}TcO_4^-$ for thyroid scintigraphy, two with ~0.5 mCi (20 MBq) [^{99m}Tc]plasmin for diagnosis of suspected deep vein thrombosis, two with approximately 11 mCi (400 MBq) ^{99m}Tc methylene diphosphonate (MDP) for bone scintigraphy, and one with 3.8 mCi (140 MBq) [^{99m}Tc]diethylenethiaminepentaacetic acid (DTPA) for kidney scintigraphy. On one patient, a multigated heart study was carried out with red blood cells labelled in vivo using an i.v. injection of 2 mg Sn(II) DTPA kit 20 min prior to the injection of 15 mCi (545 MBq) $^{99m}TcO_4^-$. Table 1 summarizes the number of patients and the radiopharmaceuticals that have been used.

Immediately after the injection of the radiopharmaceutical, breast feeding was stopped and the mother was asked to use a mechanical breast pump during the child's regular feeding times. All milk was taken to the laboratory for analysis. The milk volume was noted and the activity concentration in it was measured in 10-ml samples using a background-shielded 46 cm^3 Ge(Li)-detector. The ^{125}I activity was measured with a 124 (diam) × 1.5 mm NaI(Tl)-detector in a low-background iron room.

The absorbed dose to the child has been calculated assuming an intake of 850 ml breast milk per day (*19*), which is equivalent to 142 ml breast milk at each feeding six times per day. Iodine-125 and ^{131}I in the breast milk like that of $^{99m}TcO_4^-$ has been assumed to be in ionic form (*4,7,16*). Chromium-51 EDTA is known to be a very stable complex. We have therefore assumed that ^{51}Cr is present as [^{51}Cr]EDTA in the milk and not taken up from the intestinal tract of the child.

For ^{99m}Tc, the absorbed dose to the child was estimated using S-values that give the absorbed dose in different organs in the new-born child per unit cumulated activity (*20*). For the calculation of the cumulated activity, the biokinetic data given for the resting adult in the MIRD Dose Estimate Report 8 (*21*) were used with the exception that the data have been modified for oral administration according to the biokinetic model of the gastrointestinal tract for the newborn given by Crawford-Brown (*22*).

In order to calculate the cumulated activity in the thyroid from ^{125}I and ^{131}I, a 50% immediate uptake and a biological half-life of 14 days in the newborn have been assumed (*23*). The absorbed dose per unit activity of ^{131}I given to the baby was estimated to 8,100 mGy/MBq using absorbed fractions that have been transformed from the values for adults to newborn with a thyroid mass of 1.2 g (*19*) using a method described by Yamaguchi (*25*). S-values from Keriakes and Rosenstein (*20*) result in an absorbed dose per activity unit to the thyroid of 10,200 mGy/MBq. However, the absorbed dose to the thyroid of the newborn child, as given by Heinrichs, et al. (*22*), only amounts to 3,500 mGy/MBq. As a simple control, we have calculated the absorbed dose to a sphere of tissue or water having a mass of 1.2g and the same cumulated activity as that of the baby's thyroid by using MIRD tabulated absorbed fractions (*21*) for a source uniformly distributed in small spheres. The result 8,200 mGy/MBq is in good agreement with that of the first described method. The result of this first method has been used in our further calculations. The absorbed doses per activity unit given to the baby from ^{125}I and ^{51}Cr have also been estimated with the first described method.

The effective dose equivalent was primarily designed by the International Committee on Radiological Protection (ICRP) for the protection of occupationally exposed workers (*26*). The concept may also serve, however, as a crude indicator for detriment in other cases of irradiation. It also offers a tool for the comparison of risks from different radiation sources. The effective dose equivalent has therefore been included in our tables where we use the weighting factors given by the ICRP, which for the want of better data have been approved for all ages (*26*).

Table 2 shows the calculated absorbed dose per activity unit in the breast milk for various organs. For MAA, the external irradiation of the child caused by activity in the lungs of the mother has been estimated on the basis of results from phantom measurements and calculations of the absorbed dose to the breast with a source in the lungs (*27*).

RESULTS AND DISCUSSION

Figures 1, 2, and 3 show the fraction of activity that was present per ml of breast milk at various times after the injection. The amount of milk produced by the nursing moth-

TABLE 2
Effective Dose Equivalent and the Absorbed Dose to Child per MBq Given to Baby

Radiopharmaceutical	Stomach wall mGy/MBq	Lower large intestine wall mGy/MBq	Thyroid mGy/MBbq	Total body mGy/MBq	Effective dose equivalent mSv/MBq
$^{99m}TcO_4^-$	3.3	0.21	1.0	0.04	0.3
[^{131}I]ion	9.5	1.0	8,100	—	250
[^{125}I]ion	1.2	0.4	2,300	—	70
[^{51}Cr]EDTA	0.29	3.4	—	0.027	0.4

er varied greatly (50–1100 ml/24 hr, mv 687) during the time when breast feeding was stopped. However, the activity per ml milk followed a monoexponential curve for most of the mothers studied even if the daily production of milk varied considerably for the same mother.

Technetium-99m-MAA

There are large differences in the initial ^{99m}Tc concentration in the breast milk presumably caused by various amount of free pertechnetate in the MAA preparation and on various rates of breakdown of macroaggregate in the lungs. The activity is excreted with an effective half-life of approximately 3.7 hr. A small increase in the activity concentration in the milk can be noticed during the first few hours (Fig. 1). If the infant has been fed just before the injection of the radiopharmaceutical, the next fraction, 4 hr later, will contain about 60% of the total activity which is excreted in the milk.

Assuming a milk production of 850 ml/day, according to ICRP 23 (*19*), the total fraction which is excreted in the milk has been calculated to be 0.4–5.2% with a mean value of 3.2% (Table 1). Corresponding values given by other authors (*7,10,12,14*), are somewhat lower, 0.2–0.8%. If 2.2 mCi (80 MBq) is injected, the effective dose equivalent to the child will be 0.7 mSv. The highest absorbed dose will be found in the stomach wall, 8 mGy (Table 2).

Assuming that the child remains in close contact to the mother for 2 hr, during the first 24 hr after the injection, the mean value of the absorbed dose from external radiation from the mother will be approximately 0.1 mGy in the worst case.

Technetium-99m-pertechnetate

For this single patient, 11% of the injected activity was excreted in the breast milk. This value is considerably higher than those reported by Wyburn (*8*) 1%, by Rumble, et al. (*11*) 0.6%, and by Pittard, et al. (*13*) 0.3%.

Technetium-99m-plasmin, DTPA, and MDP

For these radiopharmaceuticals, 1.5–2.0% of the injected activity is excreted in the milk with the same effective half-life as [^{99m}Tc]MAA and [^{99m}Tc]pertechnetate.

Technetium-99m-RBC

For this single patient, only $6 \cdot 10^{-5}$ of the injected activity was excreted in the milk, indicating that the binding of the pertechnetate of the red blood cells is very stable. This fact is also shown by the effective half-life of the activity concentration which is approximately the same as the physical half-life.

Tables 1 and 2 summarize the absorbed dose to the child. The absorbed dose in the case of ^{99m}Tc-labeled substances can

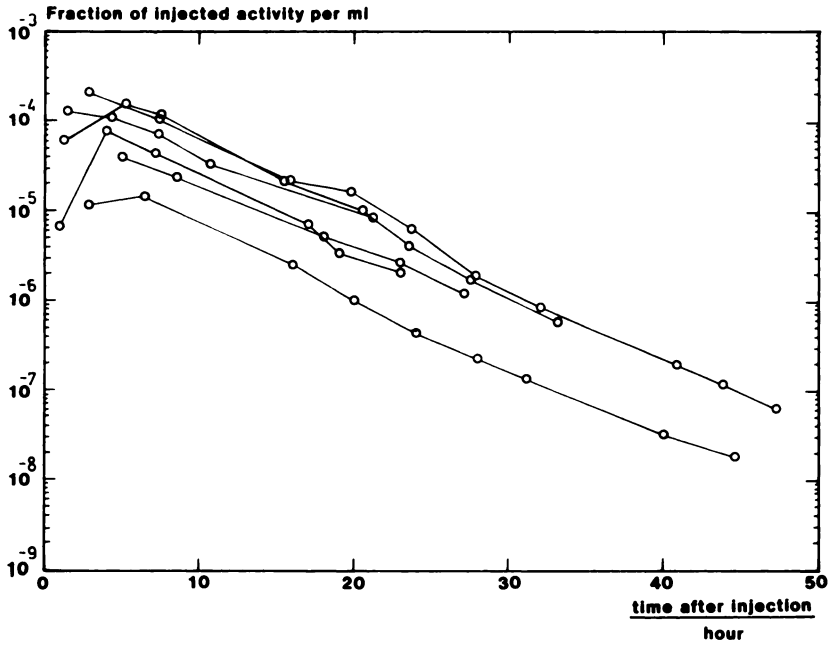

FIGURE 1
Fraction of injected activity which was present per ml breast milk at various times after the injection of [^{99m}Tc]MAA

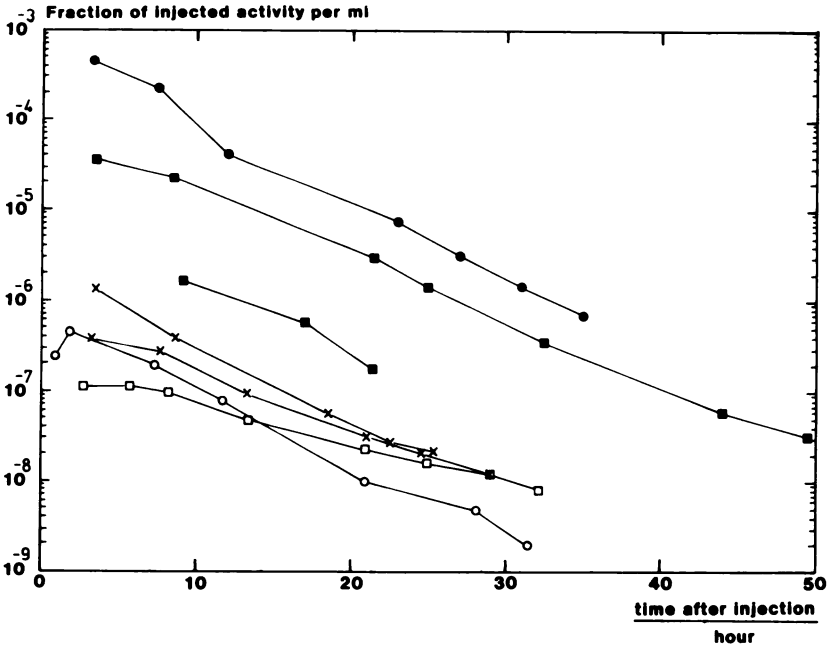

FIGURE 2
Fraction of injected activity which was present per ml breast milk at various times after injection of various ^{99m}Tc-labeled radiopharmaceuticals. (●) [^{99m}Tc]pertechnetate; (■) [^{99m}Tc]plasmin; (X) [^{99m}Tc]MDP; (O) [^{99m}Tc]DTPA; (□) [^{99m}Tc]RBC

be reduced by at least 60% by feeding the child just before the administration of the activity and then not using the next milk fraction taken 4 hr later. If the investigation is not acute, the mother can be instructed to save some milk from a few days feeding before the injection. This milk can be stored in a refrigerator and given to the child as the first meal after the investigation.

Iodine-131-Hippuran

Approximately 3% of the injected activity was excreted in the breast milk. The effective half-life of the activity in the milk was between 2.2 and 5.8 hr (Fig. 3). The half-life was longer for patients with a lower kidney clearance. The absorbed dose to the child's thyroid will be approximately 70 mGy if 8 μCi (0.3 MBq) [^{131}I]hippuran is given to the mother. Approximately 50% of this activity will appear in the first fraction within 4 hr after the administration of the activity, and the absorbed dose could therefore easily be reduced by omitting this milk. The thyroid uptake and the absorbed dose to the child could also be reduced by almost two orders of magnitude by giving the mother 60–100 mg potassium iodine just before the investigation, which also gives subsequent blocking of the child's thyroid.

Chromium-51-EDTA

For the two patients studied $\sim 4 \cdot 10^{-4}$ of the administered activity was excreted in the breast milk. The effective half-life for the ^{51}Cr concentration in the milk was 5–7 hr for 97–99% of it, and, in certain percentages, it showed a significantly longer half-life (Fig. 3). A similar slow retention component has been seen in studies of the longterm retention of [^{51}Cr]EDTA in man (*24*).

If 110 μCi (4 MBq) [^{51}Cr]EDTA is given to the mother, the highest absorbed dose in the child will be found in the lower large intestine which will receive $\sim$0.005 mGy if all the [^{51}Cr]EDTA passes the gastrointestinal tract. An uptake of 10% will decrease the effective dose equivalent $\sim$10%, since the [^{51}Cr]EDTA is washed out very quickly through the kidneys.

CONCLUSIONS

Even if the effective dose equivalent and the absorbed dose to the stomach wall of the child is rather low, caution is advised when recommendations are made as to when breast feeding should be resumed. We recommend that when [^{99m}Tc] pertechnetate, [^{99m}Tc]MAA, [^{99m}Tc]plasmin, [^{125}I]hippuran, or [^{131}I]hippuran are used the child should be fed just before the administration of the radionuclide and that the next three milk fractions should not be used. Following this period, breast feeding may resume without restrictions. If possible, the mother should be asked to save some milk before the nuclear medicine investigation, which can then be used instead of the discarded fractions.

For [^{99m}Tc]RBC, [^{99m}Tc]DTPA, [^{99m}Tc]MDP, and [^{51}Cr]EDTA, only the first milk fraction need to be discarded. As outlined in our earlier investigations (*17,18*), when [^{125}I]fibrinogen is used breast feeding must be stopped for at least 3 wk.

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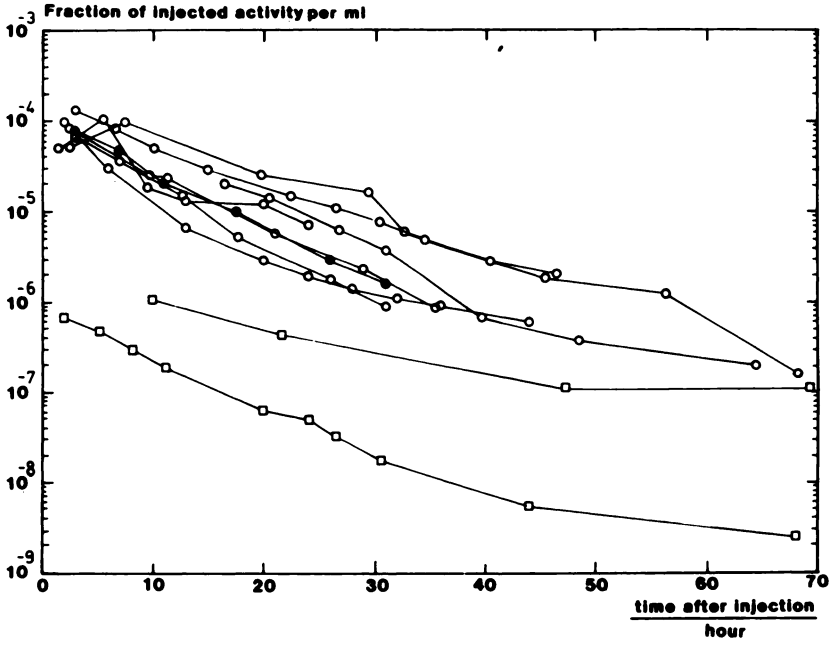

FIGURE 3
Fraction of injected activity which was present per ml breast milk at various times after injection of [^{125}I],[^{131}I]hippuran and [^{51}Cr]EDTA. (○) [^{131}I]hippuran; (●) [^{125}I]hippuran; (□) [^{51}Cr]EDTA

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