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

Lars Ahlgren, Sten Ivarsson, Lennart Johansson, Sören Mattsson, and Bertil Nosslin

Departments of Radiation Physics, Paediatrics, and Nuclear Medicine, Malmö General Hospital, Malmö; Research Institute for National Defence, Umeå; and Department of Radiation Physics, University of Gothenburg, Sahlgren Hospital, Göteborg, Sweden

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 ($^{51}$CrEDTA) and $^{99m}$TcRBC, 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 $^{51}$CrEDTA, 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.


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
and the radiopharmaceuticals that have been used. 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 Keriaikes 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 1.2 g 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.

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

### 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>
<thead>
<tr>
<th>Radio-pharmaceutical</th>
<th>Number of patients</th>
<th>Number of hours</th>
<th>Mean value</th>
<th>Range</th>
<th>Mean value for breast milk activity</th>
<th>Operation</th>
<th>Effective dose</th>
<th>Stomach wall</th>
<th>Thyroid mGy</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc</td>
<td>MAA</td>
<td>6</td>
<td>3.7</td>
<td>3.3–4.5</td>
<td>3.2–10$^{-2}$</td>
<td>0.4–5.2–10$^{-2}$</td>
<td>0.9–10$^{-2}$</td>
<td>11.0–10$^{-2}$</td>
<td>3.2–10$^{-2}$</td>
</tr>
<tr>
<td>$^{99m}$TeO$^{4-}$</td>
<td>1</td>
<td>3.2</td>
<td>—</td>
<td>10.8–10$^{-2}$</td>
<td>—</td>
<td>3–10$^{-2}$</td>
<td>36–10$^{-2}$</td>
<td>10.8–10$^{-2}$</td>
<td></td>
</tr>
<tr>
<td>$^{99m}$Te</td>
<td>plasmin</td>
<td>2</td>
<td>3.2</td>
<td>2.2–4.1</td>
<td>2.0–10$^{-2}$</td>
<td>0.9–3.2–10$^{-2}$</td>
<td>0.6–10$^{-2}$</td>
<td>7–10$^{-2}$</td>
<td>2.0–10$^{-2}$</td>
</tr>
<tr>
<td>$^{99m}$Te</td>
<td>DTPA</td>
<td>1</td>
<td>3.7</td>
<td>—</td>
<td>1.5–10$^{-2}$</td>
<td>—</td>
<td>0.4–10$^{-2}$</td>
<td>5–10$^{-2}$</td>
<td>1.5–10$^{-2}$</td>
</tr>
<tr>
<td>$^{99m}$Te</td>
<td>RBC</td>
<td>1</td>
<td>7.7</td>
<td>—</td>
<td>6.1–10$^{-5}$</td>
<td>—</td>
<td>1.7–10$^{-5}$</td>
<td>2–10$^{-5}$</td>
<td>6.1–10$^{-5}$</td>
</tr>
<tr>
<td>$^{99m}$Te</td>
<td>MDP</td>
<td>2</td>
<td>4.3</td>
<td>3.5–5.1</td>
<td>1.9–10$^{-2}$</td>
<td>1.1–2.7–10$^{-2}$</td>
<td>0.5–10$^{-2}$</td>
<td>6–10$^{-2}$</td>
<td>1.9–10$^{-2}$</td>
</tr>
<tr>
<td>$^{125}$I</td>
<td>Hippuran</td>
<td>1</td>
<td>4.8</td>
<td>—</td>
<td>2.4–10$^{-2}$</td>
<td>—</td>
<td>1.7</td>
<td>0.03</td>
<td>55</td>
</tr>
<tr>
<td>$^{125}$I</td>
<td>Hippuran</td>
<td>6</td>
<td>4.5</td>
<td>2.5–5.8</td>
<td>2.8–10$^{-2}$</td>
<td>1.8–4.9–10$^{-2}$</td>
<td>7.0</td>
<td>0.23</td>
<td>227</td>
</tr>
<tr>
<td>$^{51}$Cr</td>
<td>EDTA</td>
<td>2</td>
<td>6.0</td>
<td>5–7</td>
<td>4.0–10$^{-4}$</td>
<td>1.5–6.5–10$^{-4}$</td>
<td>1.6–10$^{-4}$</td>
<td>1.2–10$^{-4}$</td>
<td>—</td>
</tr>
</tbody>
</table>
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 amounts 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$]^{\text{MAA}}$ and $[^{99m}$Tc$]^{\text{pertechnetate}}$.

**Technetium-99m-RBC**

For this single patient, only $6\times10^{-5}$ 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

### TABLE 2

<table>
<thead>
<tr>
<th>Radiopharmaceutical</th>
<th>Stomach wall mGy/MBq</th>
<th>Lower large intestine wall mGy/MBq</th>
<th>Thyroid mGy/MBq</th>
<th>Total body mGy/MBq</th>
<th>Effective dose equivalent mSv/MBq</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$TcO$_4^-$</td>
<td>3.3</td>
<td>0.21</td>
<td>1.0</td>
<td>0.04</td>
<td>0.3</td>
</tr>
<tr>
<td>$[^{131}$I$]^{\text{ion}}$</td>
<td>9.5</td>
<td>1.0</td>
<td>8,100</td>
<td>—</td>
<td>250</td>
</tr>
<tr>
<td>$[^{125}$I$]^{\text{ion}}$</td>
<td>1.2</td>
<td>0.4</td>
<td>2,300</td>
<td>—</td>
<td>70</td>
</tr>
<tr>
<td>$[^{51}$Cr$]^{\text{EDTA}}$</td>
<td>0.29</td>
<td>3.4</td>
<td>—</td>
<td>0.027</td>
<td>0.4</td>
</tr>
</tbody>
</table>

![Fraction of injected activity per ml](image-url)

![Fraction of injected activity which was present per ml breast milk at various times after the injection of $[^{99m}$Tc$]^{\text{MAA}}$](image-url)
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) [131I]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 ~4–10⁻⁴ of the administered activity was excreted in the breast milk. The effective half-life for the [⁵¹Cr] 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 [⁵¹Cr]EDTA in man (24).

If 110 µCi (4 MBq) [⁵¹Cr]EDTA is given to the mother, the highest absorbed dose in the child will be found in the lower large intestine which will receive ~0.005 mGy if all the [⁵¹Cr]EDTA passes the gastrointestinal tract. An uptake of 10% will decrease the effective dose equivalent ~10%, since the [⁵¹Cr]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 [⁹⁹mTc] pertechnetate, [⁹⁹mTc]MAA, [⁹⁹mTc]plasmin, [¹²⁵I]hippuran, or [¹³¹I]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 [⁹⁹mTc]RBC, [⁹⁹mTc]DTPA, [⁹⁹mTc]MDP, and [⁵¹Cr]EDTA, only the first milk fraction need to be discarded. As outlined in our earlier investigations (17,18), when [¹²⁵I]fibrinogen is used breast feeding must be stopped for at least 3 wk.

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