Excretion of Iodine-123-Hippuran, Technetium-99m-Red Blood Cells, and Technetium-99m-Macroaggregated Albumin into Breast Milk

Marjorie R. Rose, Mary C. Prescott, and Kenneth J. Herman

*Departments of Nuclear Medicine and Medical Physics, Manchester Royal Infirmary, Manchester, United Kingdom*

The amount of radioactivity excreted in breast milk following three different nuclear medicine procedures on twelve nursing mothers has been measured. Some of this information has already been incorporated into the latest guidelines on suspension of feeding after maternal radiopharmaceutical administration. The overall radiation dose that the patients' babies would have sustained had breast feeding not been interrupted has been estimated as an effective dose equivalent. A model has been developed to describe the relationship between clearance of activity from the milk, time between expressions, and the fraction of milk expressed. Some simple guidance is given on calculation of suitable interruption times for any individual mother from counts on her milk samples.

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Data on the excretion of radiopharmaceuticals into breast milk following nuclear medicine procedures is available for some of the tests commonly performed. However, there is only one set of published data for iodine-123-hippuran (\(^{123}I\)-hippuran) (1); in addition, results obtained following in-vivo labeling of red cells with technetium-99m (\(^{99m}Tc\)) are scarce (2) and might be expected to vary between patients since the labeling efficiency is known to vary.

Results obtained on six nursing mothers are therefore presented and six others who received \(^{99m}Tc\)-macroaggregated albumin (MAA) have been included for comparison with other published data. The twelve women were advised to stop feeding for a short period and they kindly consented to send us a sample of milk expressed at each nominal feed time over this period. Initially, the interruption period was always 24 hr but this varied latterly as new guidelines appeared (3) and our experience grew.

**MATERIALS AND METHODS**

**Patients**

Details of the radiopharmaceuticals administered to the mothers and the ages of their babies are given in Table 1. Three patients underwent renography. The \(^{123}I\)-hippuran administered to Patient H1 was estimated to contain 5% free iodide, 5% iodobenzoic acid, and 0.2% \(^{125}I\) (Harwell, England). Frusemide (Furosemide) was administered to this patient 19.5 min after the start of the test. The \(^{123}I\)-hippuran administered to Patients H2 and H3 contained <2% free iodide and no \(^{125}I\) (Mallinckrodt Diagnostica).

Venography was performed on three of the patients. For Patients R1 and R2, the red cell labeling agent, stannous medronate (Amersham International) was administered intravenously followed by \(^{99m}Tc\) pertechnetate 20 min later. For Patient R3, Pyrolite (NEN Du Pont, N. Billerica, MA) was used as the red cell labeling agent and the pertechnetate was administered after 5 min. The activity administered is higher where first-pass images were requested.

The remaining patients had lung scans using \(^{99m}Tc\)-MAA. Pulmolite (NEN Du Pont) was used for Patient M6 but all the others received MAA from the Mallinckrodt kit. All the patients except M3 also inhaled krypton-81m \((^{81m}\text{Kr})\) gas but this was not considered in the calculations.

**RESULTS**

The results are summarized in Figure 1 and Table 2. This table also includes previously published data from other centers for comparison (1,2,4–7). The percentage of the dose excreted into breast milk was calculated in two parts. This section outlines the estimation of the most significant part which is the fraction excreted over the interruption period. The next section outlines the reasoning behind the estimation of the actual percentage of the dose ingested by the child after breast feeding was resumed.
TABLE 1
Results of Radiopharmaceuticals Administered to Nursing Mothers

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Activity admin. (MBq)</th>
<th>Age of baby</th>
<th>Volume expressed (ml)</th>
<th>Interruption period (hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>123I-hippuran</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H1</td>
<td>10</td>
<td>18 d</td>
<td>nm</td>
<td>24</td>
</tr>
<tr>
<td>H2</td>
<td>9</td>
<td>7 mo</td>
<td>410</td>
<td>24</td>
</tr>
<tr>
<td>H3</td>
<td>10</td>
<td>7 mo</td>
<td>nm</td>
<td>8</td>
</tr>
<tr>
<td>99mTc in-vivo RBC</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R1</td>
<td>303</td>
<td>4 d</td>
<td>nm</td>
<td>24</td>
</tr>
<tr>
<td>R2</td>
<td>500</td>
<td>3 d</td>
<td>500</td>
<td>24</td>
</tr>
<tr>
<td>R3</td>
<td>425</td>
<td>4 d</td>
<td>nm</td>
<td>24</td>
</tr>
<tr>
<td>99mTc-MAA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M1</td>
<td>83</td>
<td>6 d</td>
<td>nm</td>
<td>24</td>
</tr>
<tr>
<td>M2</td>
<td>38</td>
<td>15 d</td>
<td>640</td>
<td>24</td>
</tr>
<tr>
<td>M3</td>
<td>44</td>
<td>6 d</td>
<td>75</td>
<td>16</td>
</tr>
<tr>
<td>M4</td>
<td>44</td>
<td>9 d</td>
<td>120</td>
<td>20</td>
</tr>
<tr>
<td>M5</td>
<td>68</td>
<td>11 wk</td>
<td>nm</td>
<td>24</td>
</tr>
<tr>
<td>M6</td>
<td>37</td>
<td>6 d</td>
<td>nm</td>
<td>16</td>
</tr>
</tbody>
</table>

nm = not measured.

Dose Excreted Fraction

The fraction of the dose excreted into breast milk over the interruption period was estimated from the injected activity and the measured concentration of activity in each expression, assuming a total volume excreted over 24 hr of 850 ml (8). Almost all of the babies involved in this study were either so young that breast feeding had not been properly established or much older so that weaning had begun. It is not surprising, therefore, that, where complete milk collections were obtained, the volume was always less than this figure. Table 1 gives the individual values. However, since there are good reasons to doubt that the volume of milk expressed would be as much as would have been ingested naturally (8), it was felt that no reasonable approximation could be made and the larger volume should be used in the calculations. This volume was assumed to be spread equally over the expressions since milk was expressed as typical feed times. Hence:

\[ F_i = \left( \frac{\sum_{n=1}^{\infty} (C_i \times 850/n \times t/24)}{D} \right) \]

where \( F_i \) is the fraction of the dose excreted in breast milk over the interruption period of t hr, \( C_i \) is the concentration of activity in MBq/ml from the ith expression, and D is the injected activity in MBq. This fraction is expressed as a percentage in Table 2. The number of expressions, n, varied between 3 and 6 for those patients studied over 24 hr.

The percentage of the dose excreted in breast milk is most often reported as an estimate to infinity from an exponential fit of the data. We have used a different method but our estimate for Patient H1 is within the published range for 123I-hippuran and 131I-hippuran (2). After changing the supplier, the percentage excreted was reduced and is consistent with the only other set of published data for 123I-hippuran, which was obtained from the same source (4). This confirms the warnings often given in the literature that the fraction of activity excreted in breast milk after administration of hippuran is critically dependent on chemical purity which varies from supplier to supplier and at different times from the same supplier as the radiopharmaceutical is improved.

The percentage excreted after 99mTc-red blood cells is around two orders of magnitude higher than that found by Ahlgren (2). This suggests that we obtained a poorer labeling efficiency than Ahlgren did in his patient.

For 99mTc-MAA, our results are within the published range which is wide.

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TABLE 2
Dose Excretion Results

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Patient no. or ref.</th>
<th>T\textsubscript{eff}</th>
<th>% dose excreted</th>
<th>H\textsubscript{s} (baby) mSv/MBq to mother</th>
<th>f</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hippuran</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{123}I</td>
<td>H1</td>
<td>5.1</td>
<td>3.5</td>
<td>0.12</td>
<td>0.31</td>
</tr>
<tr>
<td>\textsuperscript{123}I</td>
<td>H2</td>
<td>5.0</td>
<td>2.0</td>
<td>0.06</td>
<td>0.23</td>
</tr>
<tr>
<td>\textsuperscript{123}I</td>
<td>H3</td>
<td>5.7</td>
<td>1.2</td>
<td>0.04</td>
<td>0.20</td>
</tr>
<tr>
<td>\textsuperscript{123}I</td>
<td>ref. 1</td>
<td>3.5</td>
<td>1.2</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{123}I</td>
<td>ref. 2</td>
<td>4.8</td>
<td>2.4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>\textsuperscript{123}I</td>
<td>ref. 2</td>
<td>2.2—5.8</td>
<td>1.8—4.9</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-red blood cells</td>
<td>R1</td>
<td>6.8</td>
<td>0.6</td>
<td>0.0019</td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-red blood cells</td>
<td>R2</td>
<td>7.2</td>
<td>1.0</td>
<td>0.0034</td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-red blood cells</td>
<td>R3</td>
<td>9.5</td>
<td>0.2</td>
<td>0.00056</td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-red blood cells</td>
<td>ref. 2</td>
<td>7.7</td>
<td>0.006</td>
<td>0.00002</td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>M1</td>
<td>—4.7</td>
<td>5.4</td>
<td>0.019</td>
<td>0.31</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>M2</td>
<td>4.1</td>
<td>5.4</td>
<td>0.019</td>
<td>0.25</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>M3</td>
<td>3.6</td>
<td>3.7</td>
<td>0.012</td>
<td>0.28</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>M4</td>
<td>2.6</td>
<td>0.5</td>
<td>0.0018</td>
<td>0.55</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>M5</td>
<td>5.4</td>
<td>0.4</td>
<td>0.0005</td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>M6</td>
<td>4.4</td>
<td>2.0</td>
<td>0.0006</td>
<td>0.19</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>ref. 2</td>
<td>—3.3—4.5</td>
<td>0.4—5.2</td>
<td>0.001—0.018</td>
<td></td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>ref. 4</td>
<td>2.8</td>
<td>0.5</td>
<td>0.002</td>
<td>0.68</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>ref. 5\textsuperscript{+}</td>
<td>4.6</td>
<td>3.3</td>
<td>0.012</td>
<td>0.31</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>ref. 6</td>
<td>3.4—4.8</td>
<td>0.2—2.8</td>
<td>0.001—0.010</td>
<td>0.37</td>
</tr>
<tr>
<td>\textsuperscript{99m}Tc-MAA</td>
<td>ref. 7</td>
<td>—</td>
<td>0.4</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{+} As originally reported.
\textsuperscript{+} Calculated by our method.
\textsuperscript{+} Includes a contribution from \textsuperscript{99m}Tc-DTPA aerosol.

For all radiopharmaceuticals, the effective half-life calculated from our results was in reasonable agreement with any previously published data. This aspect of the work is also considered in more detail in the next section.

DISCUSSION

The Expressed Milk Model

We have noted the wide range of effective secretion half-lives obtained by ourselves and others. In particular, we were intrigued by the results we obtained after administration of \textsuperscript{123}I-hippuran. In all three cases, these were similar to those reported for \textsuperscript{125}I-hippuran and \textsuperscript{131}I-hippuran (2). If we use the well-known relationship:

\[
T_{\text{eff}} = \frac{T_b}{T_p/(T_p + T_b)},
\]

where \(T_{\text{eff}}\) is the effective half-life, \(T_p\) is the physical half-life of the radionuclide, and \(T_b\) is the biologic half-life, then this implies a biologic half-life of 8.1, 8.4, and 10.2 hr for Patients H1, H2, and H3, respectively. One might expect that the figures should be similar to those published for hippuran labeled with other radionuclides. However, the corresponding biologic half-lives are 2.2—6.0 hr for \textsuperscript{131}I-hippuran and 4.8 hr for \textsuperscript{125}I-hippuran. Certainly the results of Mountford et al. are more consistent than our own since these workers obtained a biologic half-life of 4.8 hr with \textsuperscript{123}I-hippuran (\textsuperscript{1}).

This discrepancy could be due to variations in the biologic distribution of tracer between patients. However, we have developed a model which offers a more plausible explanation and it is based on consideration of the nature of the 'biologic' decay for this type of data. It seems to us that the decrease in the activity of the milk over and above the physical decay will be almost entirely due to the previous expressions of milk. Resorption of label from the milk back into the mother's body is likely to be insignificant by comparison.

We consider the breast to be a reservoir of milk which is completely mixed. If it can be assumed that uptake of tracer by the breast is complete by the time of the first expression and that a constant fraction \(f\) of the available milk is expressed each time, then the fractional decrease in milk activity between any two samples corrected for physical decay will equal \((1 - f)\) as long

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as the time between expressions is sufficient for the breasts to fill to the same capacity as before. That is:

\[
\frac{\text{activity conc. in (n + 1)th sample}}{\text{activity conc. in nth sample}} = (1 - f). \tag{3}
\]

This can be proved by extension from the following argument. Say the total milk supply has a volume of V ml and, at the time of the first expression, the activity within this volume is B MBq. At the first expression, a fraction \( f_1 \) of the volume will be removed and this will contain \( f_1 B \) MBq leaving an activity of \((1 - f_1)B\) MBq in the breast. At the time of the second expression, the volume of milk in the breast will again have reached V ml but the activity within it will remain at \((1 - f_1)B\) MBq so that, when a fraction \( f_2 \) is removed it will contain \( f_2(1 - f_1)B\) MBq. Assuming that an equal aliquot of milk is counted each time, the concentration of activity in the second expression as a fraction of the first is \( f_2(1 - f_1)/B \). If \( f = f_1 = f_2 \), then this expression reduces to \((1 - f)\).

This model does not predict an exponential decrease in the activity for the general case although, in the particular case where the time between expressions is a constant \( h \) hours, a graph of activity in the expressed milk \( A \) (corrected for physical decay) against time \( t \) would take the form:

\[
A = \exp\left( t \ln (1 - f)/h \right) \tag{4}
\]

and hence the corresponding biologic half-time would be given by:

\[
T_\text{b} = h \ln 0.5/\ln (1 - f). \tag{5}
\]

Most researchers express their results as the fraction of the dose excreted in milk corrected to the time of expression which is more relevant to the dosimetry. They therefore measure effective half-life directly. The observation that most have obtained a reasonably good fit to an exponential can be explained as a result of the fact that most women will express a constant fraction of milk at reasonably regular intervals, so \( f \) and \( h \) will not vary appreciably and, for the shorter-liver isotopes, the contribution of physical decay will add a strong exponential component.

Equation 4 was applied to every consecutive pair of samples provided by 9 of the 12 patients in this study, and the mean value of \( f \) obtained for each of these patients is shown in Table 2. The three patients who received \( 99m\text{Tc-RBCs} \) were excluded from this calculation as the prominent peak in two of the sets of data several hours after the administration of the isotope is good evidence that there is further uptake of the tracer into milk after the first expression. The model is therefore invalid for this radiopharmaceutical until this late uptake has finished. Although the results for \( 99m\text{Tc-MAA} \) show some evidence of late uptake of tracer, it was possible to estimate \( f \) with some degree of certainty for some of the later samples.

Twenty-six separate calculations were made but six were excluded because the delay between samples was either too short or too long for the assumption of an equal volume of milk present in the breast at the beginning of each expression to be valid. As long as the delay between samples was between 2 and 6 hr, the value of \( f \) computed averaged out at 0.28 with a s.d. of 0.09. In four of the five cases where the delay was over 6 hr, the values obtained for \( f \) were higher at between 0.43 and 0.56. This may reflect a larger initial milk volume at the later expression leading to a lower concentration of activity and hence a depressed value for \((1 - f)\).

The model predicts that mothers would reduce the radioactivity in their milk more quickly if they expressed as much as possible of the available milk each time and also expressed more often. There is supporting evidence from the results of Ahlgren et al. on two mothers who received \( 51\text{Cr-EDTA} \) (2). One expressed milk every 3–4 hr and the activity in her milk decreased much more rapidly than in the case of the other mother who only expressed four times in three days.

We have calculated values of \( f \) from data in the literature on the three radiopharmaceuticals we studied. This was only possible if full details of counts were given. The results are shown in Table 2. They are more variable than those we obtained from our own studies. Where a patient is shown as having a larger value of \( f \) than average, this always reflects consistently high values for that particular patient. It may be that some women can empty their breasts of milk more completely than others.

The expressed milk model can be used to predict the percentage of the dose that will be excreted after the resumption of feeding. If Equation 1 is taken as a starting point and \( N \), the number of feeds per day, replaces \( 24n/t \), then the fraction of the dose excreted after resumption of feeding is given by:

\[
F_\text{resum} = \left\{\sum_{n=n+1}^{\infty} C_i \times 850/N\right\}/D. \tag{6}
\]

However, from the expressed milk model, we can write:

\[
C_i = (1 - f) C_{i-1} \times \exp(-\lambda h), \tag{7}
\]

allowing for the physical decay of \( h \) hours between feeds and where \( \lambda \) is the radioactive decay constant for the radionuclide. If we define \( g = \exp(-\lambda h) \), then it can be shown that:

\[
F_\text{resum} = \frac{g(1 - f)}{1 - g(1 - f)} \times C_n \times 850/(N \times D). \tag{8}
\]

The fraction excreted after resumption of feeding can therefore be estimated from the known physical half-
life of the radionuclide, the number of feeds per day, the administered dose, the concentration of activity in the last expressed milk sample, and the fraction of her milk supply that the patient is able to express which can be estimated from any two consecutive milk samples from the patient for most radiopharmaceuticals.

This equation was used to complete the calculation of total percentage of dose excreted in breast milk for each patient and referenced article as given in Table 2. Where the estimate of \( f \) was uncertain as in the case of the patients who received \(^{99m}\text{Tc-RBCs} \), a value of 0.3 was assumed. As long as the peak in the data had been reached before feeding was resumed, this is a reasonable assumption. In all cases, it was assumed that there was 4 hr between feeds, corresponding to six feeds per day.

Estimation of Radiation dose to the Baby

Whole-body radiation doses pertaining to the baby have been estimated as an effective dose equivalent (EDE). The EDE can be considered to be the uniform whole-body dose which would carry the same risk as the actual nonuniform dose. The International Commission on Radiological Protection (ICRP) consider this to be a useful means of comparing the radiation exposure from different procedures in nuclear medicine (9). The ICRP collates information from the literature and then calculates doses to individual organs using the MIRD methodology. They then sum those doses with different organs being weighted according to the relative radiation sensitivity of the organ. Our figures were derived using the lists of EDE for various radiopharmaceuticals published by ICRP.

In order to estimate the EDE to the child from the ingestion of milk, we made certain simplifying and 'worst case' assumptions. The assumption that the total volume of milk produced was 850 ml over 24 hr has already been discussed. We assumed the body weight of the baby to be 3 kg and employed the rule of thumb that the EDE for a child will remain the same as for an adult, provided the administered activity is scaled down in proportion to body weight (10).

The biodistribution of milk after ingestion by the child was derived from the assumed chemical nature of the activity in the milk. Only in the case of Patient R2 was an attempt made to determine the chemical nature directly. The results are difficult to interpret but suggest that at least some of the activity was bound to protein. The prediction of the chemical form is not straightforward since the composition of milk is complicated and responds to many factors. One can either assume that it is the same as that of the original preparation given to the mother or some well-known contaminating chemical to which the original is likely to revert (e.g., free pertechnetate has been found in breast milk after \(^{99m}\text{Tc-MAA administration} \), or that all the activity has been incorporated into protein. In view of the lack of information, it was thought safest to assume that the chemical nature of the activity was the one out of the three above possibilities which gives the highest EDE per MBq as calculated by the ICRP (9). For the oral route, this is pertechnetate for the two radiopharmaceuticals incorporating \(^{99m}\text{Tc} \) and iodide for \(^{123}\text{I-hippuran} \).

The ICRP gives values of absorbed dose for \(^{123}\text{I-iodide} \) for different values of thyroid uptake. A value of 30% was taken in this study.

The EDE in mSv/MBq which the baby would have sustained due to the ingestion of milk, \( H_b(baby) \) for each MBq of activity administered to the mother was therefore estimated as follows:

\[
H_b(baby) = (F_i + F_{\text{sum}}) \times (70/3) \times H_b(\text{adult}), \quad (9)
\]

where \( H_b(\text{adult}) \) is the EDE in mSv/MBq for the particular chemical form ingested by a 70-kg adult (9), \( F_i \) is as defined in Equation 1, and \( F_{\text{sum}} \) is as defined in Equation 8.

The results are summarized in Table 2. They are shown together with results from the literature which have been reworked according to our assumptions if the data was given in enough detail to enable us to do this. The results of Mountford (1) have been given both as originally reported and as estimated using our method.

As has already been discussed in the Results section, our figures are in reasonable agreement with previously published data except for the large discrepancy with Ahlgren for \(^{99m}\text{Tc-RBCs} \) which is thought to be due to poorer labeling efficiency.

As well as the dose to the infant from the ingestion of milk, there is also the close contact dose to consider in estimating the total absorbed dose to the child. This has been shown to be \( <1 \mu\text{Sv}/\text{MBq} \) for the radiopharmaceuticals under consideration here (11). In the worst case therefore, this leads to an additional dose of \( <0.5 \) mSv to the child of Patient R2.

We have had the opportunity of investigating the assumption of Mountford that a child is held in close contact for a total of 5 hr per day (11). Between 3 and 9 wk after the birth of her baby, our volunteer logged the total number of hours per day that she held her daughter on a certain number of days each week. The number of days varied between 2 and 4 over the 7 wk. The number of hours of close contact per day averaged 7.3 with a s.d. of 0.9. The maximum number of hours recorded was 9 corresponding to times when the child was fretful and the minimum number was 6. Individuals will differ of course but it seems that 5 hr may be an underestimate.

In the particular cases of the patients involved in this study, the possible revision of close contact dose would not have caused any change in our advice to the patients which was not to be concerned about any limitation of close contact. However, our results may affect advice to patients receiving other radiopharmaceuticals.
**Interruption of Feeding**

The latest guidelines on interruption of feeding after maternal radiopharmaceutical administration have been provided by Mountford et al. (3). These workers advise that the EDE to the baby from the ingestion of milk should be kept below 1 mSv. Radiopharmaceuticals for which data are available have been divided into four categories based on the likely radiation dose to the child calculated from measurements of milk activity and the confidence that can be placed in the data. Confidence increases as more data become available which are consistent with previous values. The categories are:

1. Interruption not essential.
2. Interruption for a specified period.
3. Interruption with measurement of activity in the milk until it reaches a particular radioactive concentration.

Some of the data detailed in this paper have already been used in the formulation of these guidelines for the three radiopharmaceuticals involved. Technetium-99m-MAA has been placed in Category 2 and a stoppage of 6 hr is recommended. Because of the sparse amount of data on the other two radiopharmaceuticals, they have both been placed in Category 3, with a provisional estimate of 13 hr stoppage after $^{99m}$Tc-RBC and 8 hr after $^{123}$I-hippuran.

We have used slightly different assumptions in the calculation of EDE than those used in the guidelines. In particular, we assumed a body weight of 3 kg for the child whereas they used 4 kg. We also chose to estimate the radiation dose to the child over the interruption period from the actual milk samples provided and the dose after the interruption period from a consideration of the expressed milk model. The calculations for the guidelines were based on a consideration of the total committed dose derived from a best fit of the data to a monoexponential.

Although the guidelines are useful and do contain an equation to enable estimation of interruption times from a best fit of the data, we would like to suggest an alternative and issue a note of warning. It seems to us that, since tests on breast-feeding women are not common and most departments will have access to sample counting facilities, it is preferable to measure the activity in milk individually for each patient. The point at which breast feeding can be resumed without incurring a dose to the baby above 1 mSv can then be estimated from a modification of Equation 9, that is:

$$H(baby) = F_{\text{mex}} \times (70/W) \times H_{a}(\text{adult}) \times D_{r},$$  

(10)

where $H(baby)$ is the actual dose in mSv incurred by the baby and $W$ is the weight of the baby in kg. This would allow due account to be taken of physiologic differences between mothers and the actual quality of the pharmaceutical used. In addition, other factors can be taken into account, such as the high thyroid uptake exhibited by neonates (12) and, if $F_{\text{mex}}$ is adjusted accordingly, the smaller volume of milk which can be assumed for a very young baby (6). Individual attention is also reassuring for the mother in our experience.

There has been an attempt to provide simpler guidance on when feeding can safely be resumed from measurement of the activity concentration of the radionuclide in milk until it falls below a threshold level (13). When we applied these thresholds to our results, we obtained reasonable estimates for $^{99m}$Tc-RBCs and $^{99m}$Tc-MAA but the activity in milk after $^{123}$I-hippuran did not fall below the recommended threshold over the 24 hr of interruption. However, these researchers assumed five times the radiation dose from $^{123}$I that we did and this presumably reflects the radiochemical purity of the radionuclide they were considering. They also assumed twice the total milk volume per day. When these differences were taken into account, interruption times consistent with the current guidelines were obtained by this method. We do not consider it necessary to empty the breasts as completely as possible just before collection of the sample for counting as these workers suggest.

The guidelines state that milk must be expressed at normal feed times and discarded if the interruption times it recommends are to be valid. In view of the conclusions reached from a consideration of our expressed milk model, it may actually be helpful to encourage mothers to express as much and as often as possible. Of course this will only decrease interruption times if the mothers are treated as individuals as suggested previously. Expressing more often would also encourage milk production which might cause a temporary increase in supply but would be more likely to offset the decrease often experienced by mothers who express milk but do not nurse their babies for an extended period. In practice, we have found it difficult to investigate this aspect of the work because we have only had experience with short-lived nuclides and the supply and demand system works on a delay of ~24 hr so that any short-term increase in frequency is difficult to accommodate. Normally, we would of course avoid using the longer-lived nuclides on breast-feeding patients but, if such a test were to be performed, we would certainly investigate this aspect of the work further.

To the advice on the interruption of breast feeding, a note of caution must be added. Under certain circumstances, the real risks of bottle feeding as an alternative can far outweigh any potential radiation hazard from the continuation of breast feeding. Where the water supply and facilities for sterilization of bottles are inadequate, it may be preferable to accept the small risk to the infant from the continuation of breast feeding.
The maximum dose that any of the babies would have received in our study was only 2.3 mSv without interrupting feeding and including the close contact dose.

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