



Calculation of radiation dose to infants from radioactive breast milk and precautions necessary to constrain dose to prescribed limits



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agazine

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WOMEN





Many Substances Consumed by the Mother Transfer to Breast-Milk







The infants sucked more frequently during the first minute of feedings after their mothers had consumed alcohol, but they consumed significantly less milk during the testing sessions in which their mothers drank the alcoholic beverage.

Mennella JA, Beauchamp GK. The transfer of alcohol to human milk. Effects on flavor and the infant's behavior. *New England Journal of Medicine* 1991; 325 :981-5



Typical Doses to Infant

No Interruption to Feeding

R a d i o p h a r m a c e u t i c a l		A c t i v i t y (M B q) A d m i n i s t e r e d t o M o t h e r	E f f e c t i v e D o s e t o I n f a n t (mS v)
Tc -99 m M D P		1000	0.04
Tc -99 m S C		400	1.5
Tl -201 C h l o r i d e		200	2.7
In -111 p e n t e t r e o t i d e		220	86
Ga -67 C i t r a t e		400	123
I -131 I o d i d e		200	13660

Absorbed Dose from Ingested Milk

The absorbed dose to the infant, D , is given by

$$D = A_0 Fe$$

where

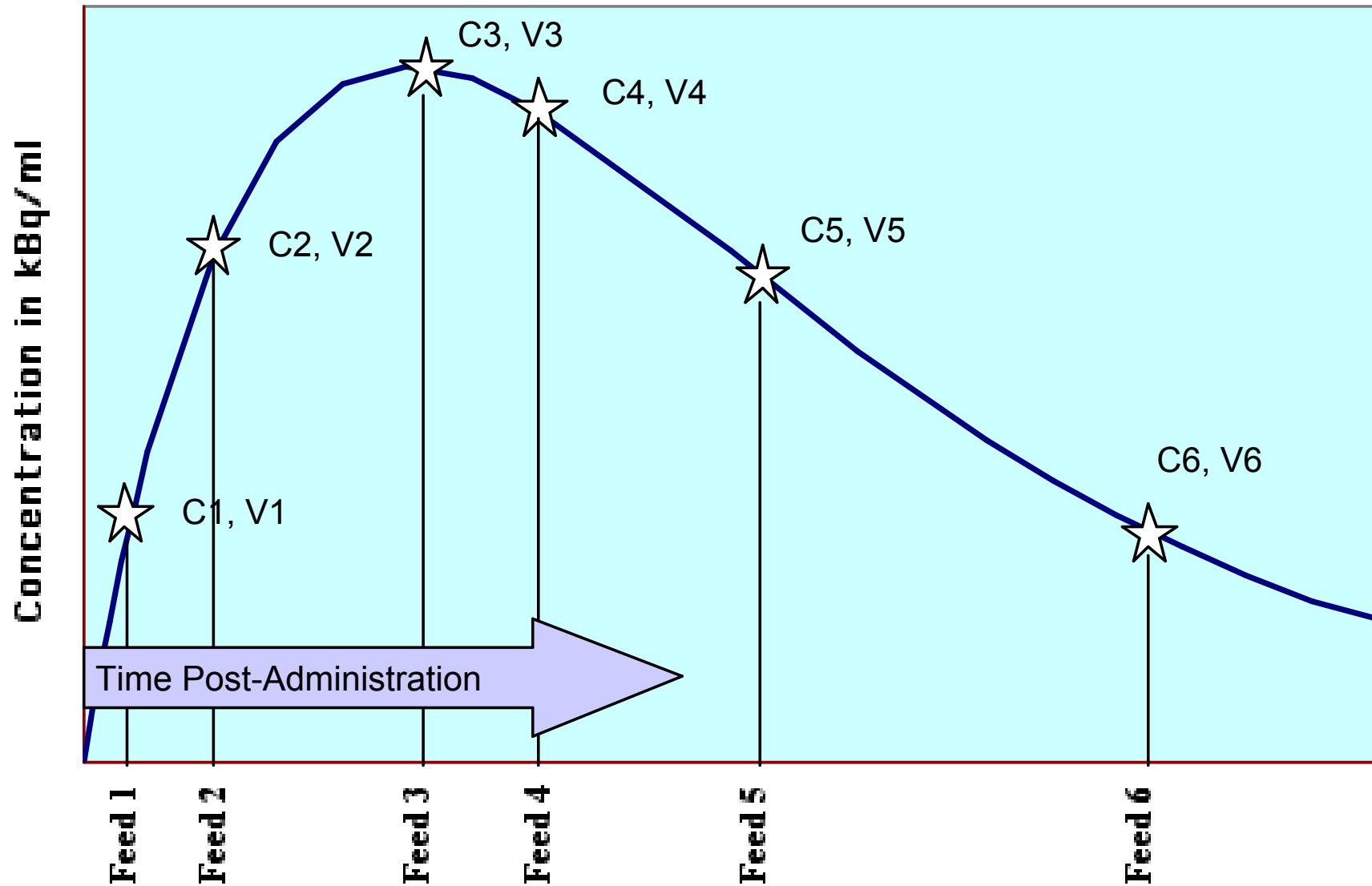
A_0 is the activity administered to the mother

e is the dose to the infant per unit activity ingested

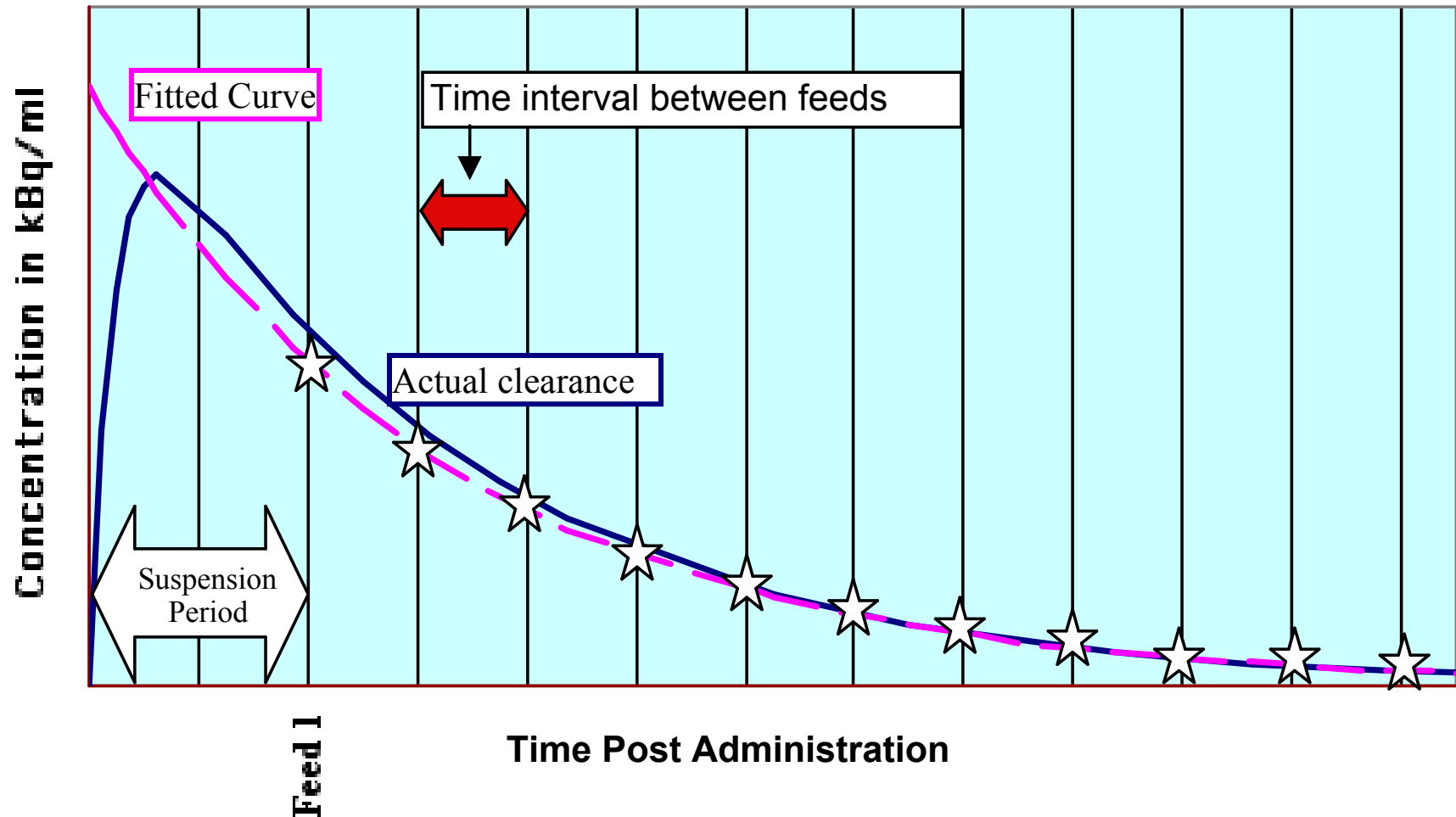
F is the ingested fraction,

$$F = \frac{\text{Total activity ingested by infant}}{\text{Activity administered to mother}}$$

Calculation of Absorbed Fraction from Measured Data



Deriving an Analytic Model





Analytic Expression for F

$$F = V f_p \xi \sum_{i=1}^n a_i \left[\frac{e^{-\lambda_i (\tau - t_p)}}{1 - e^{-\lambda_i \delta}} \right]$$

F = ingested fraction

V = volume of milk ingested at each feed

f_p = peak ingested fraction per unit volume of milk

τ = time for which breast feeding is suspended



Spreadsheet Implementation



- **Allows better sources of raw data to be utilised as they become available.**
- **Allows rapid calculation of patient-specific doses and interruption periods from measured data.**
- **Allows adjustments to be made for different feeding schedules, maturity of child and activity administered.**



Input Section of Spreadsheet

Breast Milk Dosimetry

Print

Nuclear Medicine Section
 Medical Imaging Division
 Flinders Medical Centre
 Telephone (08) 8204 4642



Patient Name/Infant Name

****WARNING** Ensure Measured Data has been entered and fitted correctly!**

Input Data for Radiopharmaceutical

Component	Effective Half-life(hrs)	Percent	Correction factor	
1	9.11E+00	99.63818852		1.114757276
2	5.61E+01	0.361811477		
3	0.00E+00	0		

Peak Fraction(per ml of breast milk) 5.57E-04

Time to peak (hours) 3

Dose to child per MBq ingested (mSv/MBq) 160

****WARNING** Ensure Measured Data has been entered and fitted correctly!**

Input Data for Patient

Volume of milk per feed (ml) 142

Activity administered to mother (MBq) 1740

Time between feeds (hours) 4

Time(post-administration) to first feed (hours) 670

Ancillary Dose Limit (mSv) 5



Output Section of Spreadsheet

Output Data	RESET	
Ingested Fraction	1.74E-06	
Dose to Child (mSv) *	4.85E-01	
Dose to Child (mSv per Mbq to mother) *	2.79E-04	
Interruption Period in hours(1 mSv Limit) **	611.4	Comments Calculated equivalent dose to lactating breast was 460 millisieverts, using actual clearance data from patient.
Interruption Period in hours (5 mSv Limit) **	481.2	
Milk Conc. (kBq per ml) at resumption of feeding (using time post-administration to first feed)	1.03E-03	
Peak Milk Conc. (kBq per ml)	9.70E+02	Milk Uptake/Clearance Data (Radiopharmaceutical administered to mother) Peak Fraction
Max. Milk Conc. allowed (kBq per ml, 1 mSv Limit) #	2.12E-03	**MEASURED data for this patient**
Max. Milk Conc. allowed (kBq per ml, 5 mSv Limit) #	1.06E-02	Uptake/Clearance Curve
Advice Level (MBq)	3.59E+03	**MEASURED data for this patient**
Recording Level (MBq)	1.79E+04	Dosimetry Data (Milk Ingestion) Radiopharmaceutical appearing in milk
<p>* Dose assumes feeding resumes at the time post-administration specified in the patient input data. For uninterrupted feeding, this time will be equal to the time between feeds minus the time pre-administration at which the last feed took place.</p> <p>** Time (post-administration) for which breast -feeding should be interrupted in order to limit dose to the value specified.</p> <p># Maximum milk concentration (post-peak) allowable if dose to child is to be limited to the specified limit.</p>		I-131 Iodide
		Maturity of infant
		Newborn

NOTE

The chemical form of the radionuclide appearing in the breast milk may not be the same as the chemical form administered to the mother.

Assumed milk intake by young infants (ICRP) is usually 850 ml per day (6 feeds of 142 ml), but will obviously vary. As a rule of thumb, a value of 175 ml per kg body weight per day (up to a maximum of about 1300 ml per day) may be used.

For more mature infants use the "1 year old" dosimetry.

Print



Derivation of Clearance/Uptake Parameters from Patient-Specific Data

Single Exponential Fit			Measured Milk Uptake/Clearance Data					Print
Dual Exponential Fit			Patient Name: Jane Doe/baby Charlotte		Time to Peak Fraction (h)		3.00E+00	Enter New Data
			Initial Value	Half-life (h)	Amount (%)	Correlation	mse %	
			0.001	9.11	99.638	0.992047285	21.98	
Max Half-Life			192	56.09	0.362	Correct. Fact.	1.114757276	
PostPeak(h)	Fraction (M)	Fraction(F)						
0	5.00E-04	5.57E-04						
2	4.84E-04	4.79E-04						
4.9	4.09E-04	3.84E-04						
8.3	3.11E-04	2.97E-04						
10.7	2.76E-04	2.48E-04						
13.7	2.30E-04	1.98E-04						
17.8	1.27E-04	1.45E-04						
26.3	5.91E-05	7.66E-05						
35.3	4.40E-05	3.92E-05						
133.3	4.85E-07	4.10E-07						
480.3	3.17E-09	5.33E-09						
632.3	1.17E-09	8.15E-10						
Enter fraction per ml of milk at various times post-peak, starting with peak fraction per ml								
NOTE If you alter any of the above data, please remember to RE-FIT. (Click on the single or dual exponential FIT button)								



Guidance Parameters

Derived from Spreadsheet -1

- **The effective dose in mSv to the infant per MBq administered to the mother (assuming no interruption of the feeding schedule).**
- **The administered activity level at which advice needs to be given to the mother (dose exceeds 1 mSv for uninterrupted feeding).**
- **The administered activity level at which a record needs to be maintained of the advice given (dose exceeds 5 mSv for uninterrupted feeding).**



Guidance Parameters

Derived from Spreadsheet-2

- **The interruption period (if any) required to limit the dose to 1mSv and 5 mSv for the typical activity administered.**
- **The safe milk concentration of activity at which feeding can resume if dose is to be limited to 1 mSv and 5 mSv.**
- **A category rating of 1 to 4 (Mountford-Coakley categorization scheme) relating to the action to be taken.**



Problems



- **Paucity of information on uptake and clearance of radioactive materials in breast milk.**
- **Lack of information as to the exact chemical nature of the breast milk activity.**
- **Insufficient information on the dosimetry of **INGESTED** radiopharmaceuticals.**
- **Radiochemical purity of administered substance.**



Additional Items to Consider



- In the early post-partum period (especially in the first 5 days or so) there may be a larger transfer of activity to the infant .
- For some radiopharmaceuticals, close contact dose from external exposure may also have to be considered.
- Dose varies considerably with age of infant, volume ingested per feed and frequency of feeding
- Inter-patient variation in uptake/clearance rates



Practical Details-1



- Should be a sign (preferably multilingual) prominently displayed.
- All female patients of child-bearing age should be asked if they are breast-feeding.
- Appropriate instructions and advice should be given to the patient.



Practical Details-2



- Arrangements need to be made for feeding child before and after the study; expressed milk or formula for missed feeds
- Arrangements may need to be made for weaning child.
- Appropriate records and documentation should be maintained.



Ell and Gambhir Volume 2

Third Edition, Page 1890-1892

- **List compiled by Cormack and Towson, based on the UK model and using best breast milk uptake /clearance data currently available.**
- **Gives dose to infant per MBq administered to mother along with 1 mSv and 5 mSv suspension periods for typical activities administered.**



ICRP 52

- **Group 1:** *Stop nursing for at least 3 weeks*
All I-131 and I-125 radiopharmaceuticals except labelled hippuran, Na-22, Ga-67, Tl-201, Se-75 methionine
- **Group II:** *Stop nursing for at least 12 hours*
I-131, I-125 and I-123 hippuran. All Tc-99m compounds except labelled red blood cells, phosphonates and DTPA.
- **Group III:** *Stop nursing for at least 4 hours*
Tc-99m red blood cells, phosphonates and DTPA
- **Group IV:** *No necessity to stop nursing*
Cr-51 EDTA



NRC 10 CFR 35.75

If the effective dose to the infant from continued breast feeding is calculated to be:

- **less than 1 mSv:** Patient must be informed that continuation of breast feeding poses little risk to the child, and that discontinuation or interruption is unnecessary.
- **1 mSv or more:** Patient must be provided with instructions relating to the discontinuation or interruption of breast feeding, and the consequences of failing to follow these instructions.
- **5 mSv or more:** Record of instructions given must be maintained for a period of three years.



NRC Regulatory Guide 8.39

- Gives prescriptive information relating to compliance with NRC 10 CFR 35.75
- Gives, for various radiopharmaceuticals, administered activities at which the 1 mSv and 5 mSv limits will be exceeded, along with recommended interruption periods.
- Available in full from the NRC Web Site at <http://www.nrc.gov/nrc.html>



Mountford-Coakley Scheme

- **Category 1** Suspension not essential except possibly for short period for reassurance of mother
 - **Category 2** Suspension for period indicated
 - **Category 3** Suspension for period indicated, with measurement of samples to ensure radioactive concentration in milk is sufficiently low to resume feeding
 - **Category 4** Cessation of feeding as the period of suspension would be very long. If mother insists on maintaining her milk supply, treat as Category 3.
- *NOTE*** During the early stages of lactation when colostrum is being secreted, all patients in Categories 1 and 2 should be upgraded to Category 3.



Further Information

Further information, full paper and spreadsheet available from authors

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Breast feeding restrictions

category	compound	NRC	Stabin	E&G	notes
1	Tc-aerosols	0 (40)	0 (40)	0 (40)	and Tcgas
	Tc-DISIDA	0 (300)	0 (300)	0 (300)	
	Tc-MAG3	0 (370)	0 (370)	0 (400)	NRC: like DTPA
	Tc-DMSA	-	-	0 (400)	
	Tc-DTPA	0 (740)	0 (740)	0 (800)	
	Tc-PYP	0 (740)	0 (740)	0 (800)	
	Tc-MDP	0 (740)	0 (740)	0 (800)	
	Tc-mIBI	0 (1110)	0 (1119)	0 (800)	
2	Tc-S colloid	12 (444)	0 (444)	5 (400)	
	Tc-O4-	4 (185)	4 (185)	23 (200)	thyroid scan
	FDG	-	-	7 (400)	close contact only
	Tc-MAA	12 (148)	12 (148)	8 (200)	
	Tc-RBCs	12 (740)	12 (740)	12 (800)	in vivo
	Tc-O4-	24 (1110)	-	40 (800)	venogram etc.
3	Tc-WBCs	24 (185)	48 (185)	24 (400)	NRC: like Tc-O4
	Tc-HMPAO	-	-	25 (800)	
	I123 iodide	0 (15)	cessation	9 (50)	Stabin: I125 impurity
	I123-mIBG	24 (370)	48 (370)	11 (400)	Stabin: I125 impurity
	Tl-chloride	168 (111)	96 (111)	32 (200)	
4	Ga-citrate	cessation	cessation	cessation	
	I131-mIBG	cessation	cessation	cessation	
	I131-iodide	cessation	cessation	cessation	