



January 28, 2002

U. S. Nuclear Regulatory Commission
Region II
Sam Nunn Atlanta Federal Center, Suite 23T85
61 Forsyth Street, SW
Atlanta, GA 30303-3415

Attn: Cynthia Taylor

Dear Ms. Taylor,

Enclosed is the dosimetry information on the two pregnancy cases you requested during your January 22nd visit of our facility. Specifically, I have included the original dosimetry information from our consultant (letters dated August 23, 2001 and September 11, 2001), a copy of page 533 and 534 from Human Embryology 2nd Edition and two pages from "Radiation Dose Estimates for Radiopharmaceuticals" (NUREG/CR-6345). The reference from Patten is intended to validate our claim that the fetal thyroid has low affinity for iodine before the 3rd to 4th month. Note the reference to formation of colloid at the bottom of page 533. The tables from NUREG/CR-6345 are the ones used by Mr. Lairmore in his dose estimates. I confirmed the fetal (uterine) doses by multiplying the factors in column two (RAD/mCi) by the given radiopharmaceutical dosage. Please call at 540-536-8912 if you further assistance.

Sincerely,

Dana Hare
Radiation Safety Officer

Enc.

NATIONAL PHYSICS CONSULTANTS, Ltd.

72 BUSTEED DRIVE
MIDLAND PARK, NJ 07432
Telephone (201)447-3303

August 23, 2001

Facsimile (201)447-3170
Phonemail (201)646-6219
(800)789-6434

Dana Hare, M.S.
Radiation Safety Officer
Winchester Medical Center
Department of Radiation Oncology
1870 Amherst Street, Suite B
Winchester, VA 22601

RE: Fetal Dose Calculation

Dear Dana:

Pursuant to our conversation, the following information has been prepared estimating the radiation exposure received to a pregnant patient undergoing diagnostic testing on the mobile van.

It is my understanding that this individual received a 3.4 mCi dose of Tc-99m Hepatolite. Following testing, the patient contacted the nuclear medicine technologist and informed him she was pregnant. Through this conversation, it was determined that her conception date was estimated as June 25, 2001. At the time of testing, the patient was approximately four (4) weeks pregnant.

The patient's physician contacted Mr. Hare and requested, the fetal dose be calculated and a summary report be forwarded for examination.

Based on the data provided, the results are as follows:

Internal Dosimetry Calculation

<u>Organ</u>	<u>Absorbed Dose (rems)</u>
Total Body (Effective Dose Equivalent)	.316 rems
Kidney	.075 rems
Ovaries	.241 rems
Uterus	.174 rems
Gall Bladder Wall	1.36 rems
Small Intestine	.544 rems
ULI Wall	1.088 rems
LLI Wall	.748 rems
Red Marrow	.061 rems

Using the information, data, assumptions and the current sources of calculation data^{2,3,4}, I estimate the embryo absorbed a dose of radiation of 0.174 rads +/- 10% as a result of the nuclear medicine exams performed at the mobile van.

At the time of exposure, the embryo was determined to be in the "pre-implantation period". During this stage, it has been shown that large doses of radiation to an embryo can result in prenatal death in the form of resorption of the embryo. At this early stage of development, death of even a few cells of the embryo results in severe, irreparable detriment. However, it should be stressed, that these findings are based on animal studies in which very large doses of radiation were delivered - absorbed dose in the range of 25 rads or more.

Obviously, this embryo received nowhere near the 25 rad level. Please be reminded the embryo's absorbed dose was well below 1 rad.

No ill effects have been demonstrated to occur at doses less than 15 - 20 rads to the embryo. I hope you can see that the risk to the fetus is negligible.

In addition, it was found that embryos which did implant successfully following irradiation went on to experience normal gestation or birth with no defects or abnormalities. In other words, there appears to be an "all-or-none" type of effect at this early stage of fetal development, resulting in either prenatal death or normal birth.

For your additional benefit, the general risk information is provided for your examination:

- ▶ The National Council on Radiation Protection and measurements suggests that radiation doses below five rads are considered to be acceptable risk. However, their report dose not go as far to indicate the dose at which "unacceptable risk" begins.
- ▶ Human data has shown a discouraging array of risk factors, and must be considered somewhat unreliable. Nevertheless, this data indicates few examples of congenital abnormalities from doses below twenty to twenty-five rads.

I hope this report has been helpful in assessing the risk of the embryo of this patient. If you have additional questions, please contact me at (201) 447-3303.

Sincerely,



Michael W. Lairmore, M.S.
Licensed Medical Physicist

Bibliography

¹Regozzino, M., R. Beckie, L. Hill, and J. Gray. Average Dose in Utero: Data for Estimation of Fetal Absorbed Radiation Dose. Medical Physics, 1988, Vol. 15, Number 2; 513 - 515.

²John, H., and J. Cunningham. The Physics of Radiology, 1983. Charles C. Thomas, Pub. Springfield, IL.

³Harriett, R. Central-axis Depth Dose Data for Diagnostic Radiology. Physics in Medicine and Biology, 1981. Vol. 26, Number 4; 657-670.

⁴Wagner, L., R. Lester, and L. Selders. Exposure of the Pregnant Patient to Diagnostic Radiation: A Guide of Medical Management. Lippincott Pub.

⁵Hall, Eric J. Radiobiology for the Radiologist, 1978. Harper and Row, Pub. New York.

⁶Fullerton, G.D., D.T. Kopp, R.G. Waggener, and E.W. Webster. Biological Risks of Medical Irradiations, 1980. American Institute of Physics, Pub. New York.

⁷NCRP report 54. Medical Radiation Exposure of Pregnant and Potentially Pregnant Women, 1985. National Council on Radiation Protection and Measurements, Pub. Bethesda, MD.

To: Dana Hare R.S.O.

From: Sean M Blue

Date: 06 September, 2001

Re: [REDACTED] Fetal Exposure

Dana,

Below is the pertinent information regarding the incident regarding the exposure of [REDACTED] to I131 MIBG during pregnancy.

Patient - [REDACTED] Ht 5' 5", Wt 140lbs

Isotope - I131 MIBG

Dose - 1.1 mCi

Form - liquid

Delivery - injection

Date of injection - 27 August, 2001 @ 09:52

Referring Physician - Dr. Gaviria

Obstetrician - Dr. Wanger

Of note, the patient was given Lugols solution beginning 26 August, 2001 for thyroid blockade. The patient was instructed to take .3 mL/day for a total of 5 days post injection per Dr. Blake Watts.

See the attached from the patients physician regarding fetal age.

If you need anything else, please do not hesitate to let me know.

Thanks,



Sean M. Blue

September 11, 2001

Dana Hare, M.S.
Radiation Safety Officer
Winchester Medical Center
Department of Radiation Oncology
1940 Amherst Street
Winchester, VA

RE: Fetal Dose Calculation - [REDACTED]

Dear Dana:

Pursuant to our conversation on September 7, 2001, a fetal dose calculation has been completed for [REDACTED]. Please refer to the following paragraphs for details.

I. INVESTIGATION:

- On August 27, 2001, [REDACTED] received a 1.10 mCi dose of Iodine 131 MIBG. Prior to administration, the patient informed the nuclear medicine technologist that she was not pregnant. Approximately one week following administration, the patient contacted the nuclear medicine technologist and informed him she was pregnant at the time of testing.

Through this conversation, it was determined that her estimated conception date was calculated as August 6, 2001.

II. CORRECTIVE ACTION:

- All female patients scheduled for any nuclear medicine procedure will be interviewed by the nuclear medicine technologist to assure the patient is not pregnant prior to administration. In addition, all female patients will be required to sign a non-declaration pregnancy form. If pregnancy is questionable, a pregnancy test will be completed before testing is initiated.

ALREADY
U.H.S.
POLICY
G.W.H.

III. FETAL DOSE CALCULATION:

- The patient received approximately 1.10 mCi of I-131 MIBG intravenously for diagnostic testing. The radiation dose received to the fetus was calculated at 3.3E-1 rads/mCi. The total absorbed fetal dose was calculated at 363 mrems.

Due to the patient's apparent body habitus, it was assumed that the mid-line depth of the embryo is five centimeters from the anterior maternal skin surface, fifteen centimeters from the posterior maternal skin surface, and ten centimeters from the side (lateral) maternal skin surface.

At an age of approximately four weeks or less the embryo is said to be in the "pre-implantation period" of development. If a sufficient high dose of radiation is received by the embryo, the results would most likely be resorption of the zygote, or abortive death.

Between the ages of two to four weeks, the embryo is said to have moved into the "organogenesis period" of development. At this stage, if a high dose of radiation is received, the endpoint of damage would be a congenial anomalies of the organ systems developing at the time of irradiation. The total dose to the patient was determined to be less than one rad (.363 rad). In my opinion, the radiation risk for congenial anomalies is quite low.

In addition, the thyroid of the fetus does not begin to develop until the 14th week of pregnancy. Therefore, the absorbed dose and fetal exposure (to the thyroid gland) was of no significance.

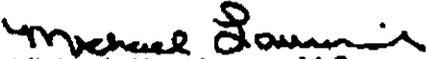
The National Council on Radiation Protection and Measurements suggests the doses below five rads are considered to be an acceptable risk. However, the report does not go as far to indicate the radiation dose where "unacceptable" risk begins.

Human data has shown an encouraging array of risk factors and must be considered to be somewhat unreliable. Nevertheless, this data indicates few examples of congenial abnormalities from dose below twenty to twenty-five rads have been noted.

A major consideration in assessing risk to the embryo/fetus is the stage of development during which irradiation occurred. If the fetus is exposed during the very early stages of pregnancy (two - four weeks post fertilization), the dominant endpoint will be prenatal death, if a sufficient dose was absorbed. After approximately three weeks post-fertilization, teratogenesis becomes a consideration, as the various organ systems undergo proliferation and differentiation.

If you have additional questions regarding this report, please contact me at (201) 447-3303.

Sincerely,


Michael W. Lairmore, M.S.
Medical Physics Consultant

IVATIVES

um of larynx
 Left int. carotid art.
 Parathyroid III
 Pedicle of thymus
 Thyroid gland
 Thyroid isthmus
 Intrabronchial body
 Trunk
 Monocary trunk

Human embryo
1 of primordia
Weller, Carnegie

ular pouch
 Epithelium
 carotid art.

External carotid art.
Parathyroid III

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DUCTLESS GLANDS AND PHARYNGEAL DERIVATIVES

As these cells proliferate they become progressively smaller. (Cf. 326, A, B with C, D.) This is a phenomenon which occurs quite generally in the differentiation of specialized tissues from their embryonic primordia. (See, for example, Fig. 143 on the histogenesis of connective tissue, and Fig. 280 on the histogenesis of the epithelial lining of the esophagus.) As the primary cellular mass expands, it becomes arranged in cords with vascular mesen-

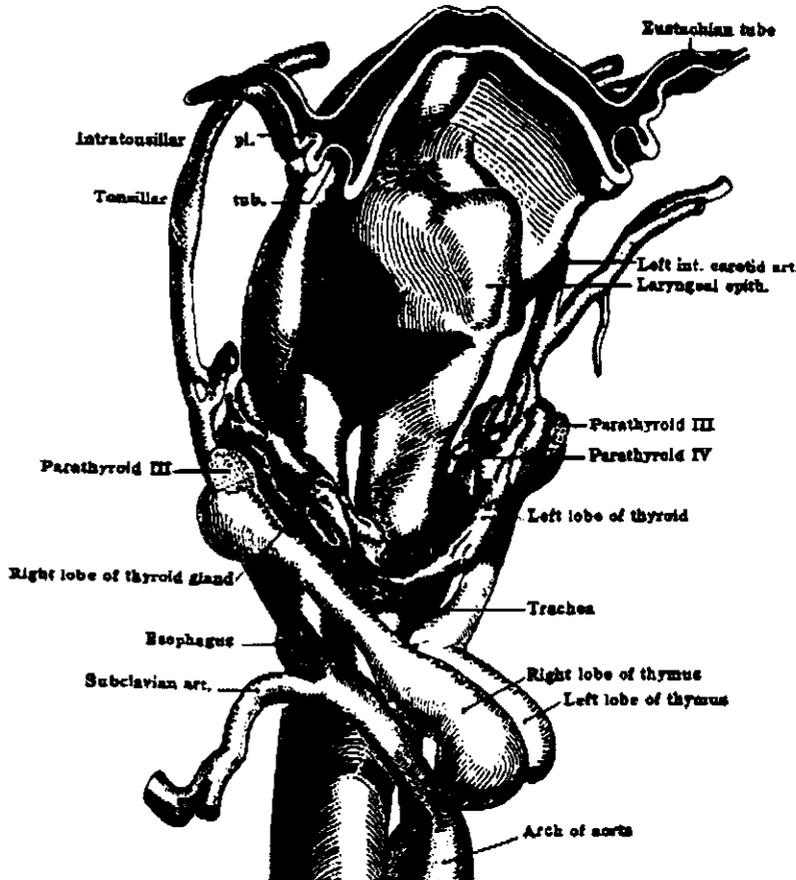


FIG. 325. Reconstruction of pharyngeal region of a human embryo of 23 mm. (middle of eighth week) to show migration of primordia of thymus, thyroid, and parathyroid glands toward their definitive positions. (After Weller, Carnegie Cont. to Emb., Vol. 24, 1933.)

chyme between them (Fig. 326, C). During the third month, these epithelial cords break up to form cell nests surrounded by young, vascular connective tissue (Fig. 326, D). To a slight degree toward the end of the third month (Fig. 326, D), and more markedly during the fourth month (Fig. 326, E), an acidophile material known as colloid begins to accumulate in the center of the cell nests. When this occurs we have the characteristic thyroid follicle established with its central mass of colloid surrounded by a simple cuboidal or low columnar epithelium. The later changes involve the accumulation of

DUCTLESS GLANDS AND PHARYNGEAL DERIVATIVES

PHARYNGEAL DERIVATIVES



Vascular Mesenchyme



Projection drawings (A, Four weeks; B, Middle of eighth month; C, Fourteenth month; D, Twenty-

greater amounts of colloid in increasing numbers of follicles, and the gradual differentiation of the surrounding embryonic connective tissue into the characteristic fibro-elastic tissue of the stroma of the adult gland. As is so characteristic of the ductless glands as a group, the connective tissue interspersed between the epithelial units is highly vascular providing an effective arrangement facilitating the entrance of the hormone into the blood stream.

Parathyroid Glands. There are ordinarily two pairs of parathyroid glands formed. One pair is derived from the third and the other from the fourth pair of pharyngeal pouches. Because of their origin they are commonly designated as parathyroids III and parathyroids IV (Fig. 322, A). Parathyroids III arise in close association with the thymic primordia (Fig. 323). During the seventh week both these primordia are freed from the parent pouches and start to move caudad in association with each other. Although these two primordial cell masses become quite distinctly differentiated during the eighth week, parathyroids III are very likely to remain for a time attached to the young thymus or even become encased in its cephalic tip (Fig. 322, B). With the further caudal migration of the thymus, parathyroids III are usually left embedded in the adjacent capsular tissue of the thyroid. They lie caudal to parathyroids IV, having passed them in their migration. Thus the cephalocaudal relations of the two pairs of parathyroids are reversed in the adult as compared with their position of origin in the embryo.

Parathyroids IV arise in close association with the postbranchial bodies, and when the postbranchial bodies merge with the lateral lobes of the median thyroid primordium, parathyroids IV usually become adherent to the thyroid capsule. Not infrequently they become more or less embedded in the substance of the thyroid gland (Fig. 322, B).

The histogenetic changes are alike in the two pairs of parathyroids. Both start as solid cell masses on the craniodorsal aspect of the respective pharyngeal pouches. These cell masses break up into cords and nests with large, irregular capillary spaces (sinusoids) between them in the manner so highly characteristic of many of the ductless glands. The secretory cells show a rather pale clear cytoplasm. The oxyphile cells which are so striking in the adult gland are not differentiated until long after birth—ordinarily about the tenth year.

Thymus. In mammals as a group, thymic tissue may arise either from the third or the fourth pharyngeal pouches, or from both. This situation has given rise to designating these primordia as thymus III and thymus IV. Thymus III is in most mammals the more important primordium. Thymus IV may be absent altogether and, even when formed, is likely to be quite rudimentary and give rise only to vestigial tissue masses. These masses usually become associated with the thyroid as it migrates caudad and may ultimately become actually embedded in its substance (Fig. 322, B). In man thymus IV is so unimportant and inconstant that we may confine our attention to thymus III. In the following section, unless otherwise stated, all references to thymic primordia refer to thymus III.

September 18, 1992

**Radiation Dose Estimates for Tc-99m for the Adult
for Disofenin, Lidofenin and Mebrofenin**

ORGAN	Estimated Radiation Dose	
	<u>mGy</u> <u>MBq</u>	<u>rad</u> <u>mCi</u>
Adrenals	3.6E-03	1.3E-02
Brain	6.9E-05	2.6E-04
Breasts	4.7E-04	1.7E-03
Gallbladder Wall	1.1E-01	4.0E-01
LLI Wall	6.0E-02	2.2E-01
Small Intestine	4.4E-02	1.6E-01
Stomach	5.6E-03	2.1E-02
ULI Wall	8.6E-02	3.2E-01
Heart Wall	1.4E-03	5.4E-03
Kidneys	6.0E-03	2.2E-02
Liver	1.4E-02	5.2E-02
Lungs	1.1E-03	4.2E-03
Muscle	3.0E-03	1.1E-02
Ovaries	1.9E-02	7.1E-02
Pancreas	5.6E-03	2.1E-02
Red Marrow	3.9E-03	1.5E-02
Bone Surfaces	3.8E-03	1.4E-02
Skin	9.2E-04	3.4E-03
Spleen	2.5E-03	9.3E-03
Testes	1.7E-03	6.3E-03
Thymus	3.7E-04	1.4E-03
Thyroid	1.2E-04	4.5E-04
Urinary Bladder Wall	2.7E-02	9.9E-02
Uterus	1.4E-02	5.1E-02

Effective Dose Equivalent 2.5E-02 mSv/MBq 9.3E-02 rem/mCi

Biological model based on ICRP 53 (data gathered in human subjects).

Kidneys	$\tau = 0.012$ hour	Gallbladder contents	$\tau = 0.77$ hour
Liver	$\tau = 0.80$ hour	Small Intestine	$\tau = 1.79$ hour
Upper Large Intestine	$\tau = 2.34$ hour	Lower Large Intestine	$\tau = 1.14$ hour
Urinary bladder	$\tau = 0.53$ hour	Remainder of body	$\tau = 0.14$ hour

Dynamic bladder model with 4.8-hour voiding interval

Estimate calculated using phantom of Cristy & Eckerman (Report ORNL/TM-8381/V1 & V7).

The effective dose equivalent is a quantity which may be suitable for comparing risks of different procedures in nuclear medicine, radiology, and other applications involving ionizing radiation, but should not be construed to give information about risk to individual patients.

Source: Radiation Internal Dose
Information Center

September 18, 1992

Radiation Dose Estimates for I-131 mIBG (i.v. injection)

ORGAN	Estimated Radiation Dose	
	mGy	rad
	MBq	mCi
Adrenals	2.1E-01	7.6E-01
Brain	4.7E-02	1.7E-01
Breasts	5.4E-02	2.0E-01
Gallbladder Wall	1.4E-01	5.2E-01
LLI Wall	7.2E-02	2.7E-01
Small Intestine	7.5E-02	2.8E-01
Stomach	7.8E-02	2.9E-01
ULI Wall	7.9E-02	2.9E-01
Heart Wall	3.8E-01	1.4E+00
Kidneys	8.8E-02	3.3E-01
Liver	7.8E-01	2.9E+00
Lungs	7.4E-02	2.7E-01
Muscle	6.2E-02	2.3E-01
Ovaries	7.4E-02	2.7E-01
Pancreas	1.1E-01	3.9E-01
Red Marrow	7.4E-02	2.7E-01
Bone Surfaces	6.5E-02	2.4E-01
Salivary glands	2.4E-01	8.8E-01
Skin	4.8E-02	1.8E-01
Spleen	5.8E-01	2.2E+00
Testes	5.8E-02	2.2E-01
Thymus	6.4E-02	2.4E-01
Thyroid	9.0E-02	3.3E-01
Urinary Bladder Wall	7.6E-01	2.8E+00
Uterus	8.9E-02	3.3E-01

Effective Dose Equivalent

2.1E-01 mSv/MBq

7.8E-01 rem/mCi

Dose - 363
to Fetus mRms
CT

Based on data gathered in patients - Jacobsson et al, 4th International Radiopharmaceutical Dosimetry Symposium, CONF-851113, pp. 389-398. Assumed distribution and retention:

Total body	63 %	T _b = 32.8 hours	36 %	T _b = 3.05 hours	1 %	T _b = ∞
Liver	21 %	T _b = 32.8 hours	15 %	T _b = 3.05 hours	0.3 %	T _b = ∞
Spleen	0.6 %	T _b = 178 hours				
Sal. glands	0.04 %	T _b = 32.8 hours				
Thyroid	0.005 %	T _b = 168 hours				
Adrenals	0.02 %	T _b = 48.6 hours				
Heart wall	0.8 %	T _b = 120 hours				

Dynamic Bladder Model used (4.80 hour void)
36 % T_b = 3.00 hours 63 % T_b = 33.6 hours

Dose to salivary glands is self-dose only, based on 77 g mass and photon absorbed fractions from MIRD Pamphlet No. 8. Salivary gland activity did not contribute to other organ doses. Estimate calculated using phantom of Cristy & Eckerman (Report ORNL/TM-8381/V1 & V7).

The effective dose equivalent is a quantity which may be suitable for comparing risks of different procedures in nuclear medicine, radiology, and other applications involving ionizing radiation, but should not be construed to give information about risk to individual patients.

Source: Radiation Internal Dose Information Center