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Radiation Safety Issues Related to Nuclear Medicine and Pregnant Patients

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RADIATION SAFETY ISSUES RELATED TO

NUCLEAR MEDICINE AND PREGNANT PATIENTS

STATEMENT OF OBJECTIVES

The primary purpose of this lesson is to increase the reader's knowledge and understanding of radiation safety issues related to the embryo/fetus from the performance of nuclear medicine procedures in women who are pregnant.

On completion of this continuing education lesson, the reader should be able to:

1. Describe the stages of embryo/fetal development and common congenital anomalies.

2. Discuss radiation effects on embryo/fetus including types of effects, relationship to gestational age, and dose-response relationships.

3. Discuss the risks to the embryo/fetus from low doses of radiation in comparison with risks from other factors.

4. Discuss the influence of radiopharmaceutical biodistribution on fetal dosimetry.

5. Using appropriate reference tables, estimate the radiation absorbed dose to a fetus of a specified gestational age from a specified dose of a specified radiopharmaceutical.

6. Describe the rationale, utility, and limitations of pregnancy testing in women of child-bearing potential scheduled for a nuclear medicine procedure.

7. State recommendations/guidelines for the evaluation of female patients regarding pregnancy and the performance of nuclear medicine procedures in these patients.

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RADIATION SAFETY ISSUES RELATED TO NUCLEAR MEDICINE AND PREGNANT PATIENTS

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INTRODUCTION

Perceptions of radiation effects and malformed babies carry an abundance of emotion. Spurred by sensationalistic media reports, the public seems quick to blame radiation for any deleterious health effect, including congenital anomalies. Moreover, in many nuclear medicine departments, 45-65% of patient procedures are performed in females of child-bearing age.[1] Hence, it is important that health care workers, especially those involved in the use of radioactive materials and/or ionizing radiation, have a working knowledge of radiation safety issues related to the embryo/fetus from the performance of nuclear medicine procedures in women who are pregnant. In addition, an understanding of these issues affords the foundational knowledge and perspective necessary for the provision of superior pharmaceutical care of these patients. [A discussion of pharmaceutical care is beyond the scope of this lesson].

Health Professional Ethics

Dating from the time of Hippocrates, the "prime directive" for medical practice has been to work for "the benefit of patients, and abstain from whatever is deleterious." The concept of providing benefits while avoiding harm is also embodied in the second line of the Code of Ethics for Pharmacists[2]: "A pharmacist promotes the good of every patient..." Although an embryo/fetus does not generally have the status of "patient," the concept of avoiding harm to the fetus while caring for the mother is generally accepted as appropriate professional practice in all but life-threatening circumstances or purposeful abortions.

Medicolegal

The presumption of cause and effect has medicolegal ramifications for abnormalities in fetuses exposed to radiation in utero. A number of malpractice lawsuits has been filed over the last two decades alleging that an abortion or fetal anomaly was caused by medical radiation procedures.[3] In the area of nuclear medicine, such lawsuits are more likely associated with I-131 administration.[3]

Regulatory

No government regulation explicitly requires that pregnancy status be determined prior to a woman receiving a medically indicated radiation procedure. In fact, the Nuclear Regulatory Commission (NRC) has stated that, "NRC does not believe that it is appropriate to propose a rule that would require a licensee to assess the pregnancy or nursing status of patients."[4] However, pursuant to Section 208 of the Energy Reorganization Act of 1974, NRC has established a policy that it submit to Congress an Abnormal Occurrence Report for any unintended radiation exposure to any embryo/fetus that results in a dose equivalent of 50 mSv (5 rem) or more[4]. Therefore, in order to obtain the necessary information to generate such reports, NRC has proposed to include the following reporting requirements [excerpted] in its medical use regulations[4]:

[Proposed] 35.3047 Report of a dose to an embryo/fetus or a nursing child.

(a) A licensee shall report any dose to an embryo/fetus that is greater than 5 mSv (500 mrem) absorbed dose that is a result of an administration of byproduct material or radiation from byproduct material to a pregnant individual unless the dose to the embryo/fetus was specifically approved, in advance, by the authorized user.

(c) The licensee shall notify by telephone the NRC Operations Center within 5 days after the discovery of a dose to the embryo/fetus that requires a report in paragraph (a) of this section.

(d) The licensee shall submit a written report to the appropriate NRC Regional Office listed in § 30.6 no later than 15 days after discovery of a dose to the embryo/fetus that requires a report in paragraph (a) of this section.

(1) The written report must include –

(i) The licensee's name;

(ii) The name of the prescribing physician;

(iii) A brief description of the event;

(iv) Why the event occurred;

(v) The effect on the embryo/fetus;

(vi) What improvements are needed to prevent recurrence; and

(vii) Actions taken to prevent recurrence.

(2) The report must not contain the individual's name or any other information that could lead to identification of the individual.

(e) The licensee shall notify the referring physician and also notify the pregnant individual, hereafter referred to as the mother, within 5 days of discovery of an event that would require reporting under paragraph (a) of this section, unless the referring physician personally informs the licensee that either he or she will inform the mother or that, based on medical judgement, telling the mother would be harmful;

(f) To meet the requirements of this section, the notification of the mother may be made instead to the mother's responsible relative or guardian, when appropriate.

(g) The licensee is not required to notify the mother without first consulting the referring physician. If the referring physician or mother cannot be reached within 5 days, the licensee shall make the appropriate notifications as soon as possible thereafter. The licensee may not delay any appropriate medical care for the embryo/fetus, including any remedial care as a result of the event, because of any delay in notification.

(h) If notification was made pursuant to paragraphs (e) and (f) of this section, the licensee shall also furnish, within 15 days after the discovery of the event, a written report to the mother or responsible relative or guardian, by sending either –

(1) A copy of the report that was submitted to the NRC; or

(2) A brief description of both the event and the consequences as they may affect the embryo/fetus.

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EMBRYONIC/FETAL DEVELOPMENT[5-8]

Before discussing the effects of radiation on the embryo/fetus, a brief review of normal embryonic/fetal development, as well as congenital abnormalities, is in order.

Review of Normal Development

Embryo/fetal development is generally divided into three stages: pre-implantation, major organogenesis, and the fetal (growth) stage. The pre-implantation stage occurs from conception until the time of implantation, generally at about one week. During this time, the fertilized ovum repeatedly divides forming a ball of cells (termed an embryo) that are highly undifferentiated. Implantation of the embryo in the uterine wall signals the onset of the second stage, major organogenesis. During this stage, lasting for approximately 6 weeks, the cells of the embryo begin differentiating into the stem cells that will eventually form all organs of the body. For many organs, the initial differentiation of cells occurs on a specific gestational day. At the end of the second stage, the embryo is termed a fetus and enters the third and final stage, called simply the fetal (or growth) stage. The fetus contains most organ systems and many types of cells ranging from undifferentiated stem cells to more differentiated parenchymal cells. Continuing until birth, this is primarily a period of growth. One specific system requiring further mention, however, is the central nervous system (CNS). Although neuroblasts appear very early in the organogenesis stage and undergo some differentiation during fetal development, the majority of these cells continues to exist throughout the fetal growth stage and beyond birth into infancy.

Congenital Abnormalities

Although often used synonymously, congenital abnormalities may be defined as congenital malformations (limited to structural defects present at birth) or as congenital anomalies (a broader term including abnormal behavior, function, or chemistry in addition to structural defects).[9] Congenital abnormalities can be categorized either as hereditary (i.e., genetic) or as teratogenic (i.e., resulting from external influences such as viral infection, drugs, tobacco, alcohol, radiation, etc.). If a teratogenic insult occurs during organogenesis, the result may be major structural abnormalities of various organs, especially the skeleton (e.g., limb deformities), CNS (e.g., microcephaly), and eyes (e.g., microphthalmia). If a teratogenic insult occurs during the second or third trimesters, the result may be limited to general growth retardation, mental retardation, or minor malformations.

The "normal" incidence of congenital anomalies is difficult to determine precisely.[9] Diverse values for the incidence of congenital abnormalities have been reported, ranging from 0.03% to 14.7%. The diversity of values is related, at least in part, to (1) under-reporting of congenital malformations on birth certificates (up to 40-50% not reported); (2) reporting only "major" malformations (up to 7X higher incidence when "minor" malformations are also considered); and (3) reporting only those external malformations observed at birth (up to 3X higher incidence when internal abnormalities discovered later are considered).

The number and rate of selected congenital anomalies reported on birth certificates in 49 states and the District of Columbia in 1996 are detailed in Table 1. Although the data in this report[10] indicate an incidence of congenital abnormalities of 2.6%, the actual value is undoubtedly higher, for reasons discussed above. Hence, the often cited value of approximately 4-6%[5,11-12] appears to be a

Table 1. Live Births with Selected Congenital Anomalies[*10]

	Number Reported	Rate/100,000 Life Births
All Life Births	3,864,266	- - -
Congenital Anomaly (Total)	101,007	2614
microcephalus/anencephalus	796	21
spina bifida/menigocele	984	26
hydrocephalus	1,047	27
other CNS anomalies	854	22
heart malformations	4,398	115
other circulatory/respiratory anomalies	5,234	137
esophageal/rectal atresia/stenosis	905	24
omphalocele/gastroschisis	1,029	27
other GI anomalies	1,259	33
malformed genitalia	2,875	75
renal/urogenital anomalies	5,016	131
cleft lip/palate	3,307	86
polydactyly, syndactyly, adactyly	3,242	85
clubfoot	2,224	58
Musculoskeletal/integumental anomalies	8,274	217
Down's syndrome	1,676	44
other chromosomal anomalies	1,463	38
not specified	56,424	1460

* Total of 49 reporting states and the District of Columbia, 1996. Adapted from data reported by the National Center for Health Statistics.

reasonable estimate of the true incidence of congenital abnormalities.

RADIATION EFFECTS ON EMBRYO/FETUS[5-6,8,11,13-15]

The embryo/fetus tends to be more sensitive to many insults, including radiation, as compared to adults and even children. Although much is known about radiation effects, there still exists much controversy, especially with radiation at low doses.

Types of Effects

Radiation exposure of an embryo/fetus may result in three different types of effects: prenatal death, congenital malformations, or late effects. Radiation exposure, especially early in pregnancy, may result in death of the embryo/fetus. This effect, especially during pre-implantation or shortly thereafter, is generally an "all or none" response; i.e., either embryo death or no detectable effects at all. Prenatal death during early pregnancy is very difficult to evaluate given that the "normal" incidence of spontaneous abortion may be as high as 30-50%.[6,8]

Radiation is considered a teratogen; radiation exposure, especially during organogenesis, may result in congenital malformations such as those described above. Radiation-induced congenital malformations are not unique, however, and cannot be distinguished individually from malformations that occur spontaneously or are caused from by other factors.

Radiation also is considered a carcinogen; radiation exposure may result in the development of cancer as a late effect. For example, radiation exposure to a fetus could result in the development of leukemia several years later during childhood. Radiation-induced cancer is not unique, however, and cannot be individually distinguished from cancer that occurs spontaneously, or is caused from other factors.

Relationship to Gestational Age

One factor that influences the type of radiation effect that may be produced is the gestational age of the embryo/fetus. During the pre-implantation stage, radiation effects tend to be limited to either prenatal death or no effects at all. During the organogenesis stage, prenatal death becomes less frequent while the likelihood of congenital malformations and neuropathologies tend to be relatively greater. Figure 1 shows the critical period during gestation for radiation effects on selected organs. After major organogenesis is complete, the predominant radiation effects on the fetus are general growth and mental retardation. The relative incidence of adverse radiation effects at different stages of gestation is summarized on Figure 2.

Dose-Response Relationship

The earliest identification of adverse radiation effects on the embryo/fetus followed the use of therapeutic pelvic irradiation during pregnancy during the 1920's and 1930's. In many instances, radiation therapy, for indications such as uterine myoma, malignant tumors, and metrorrhagia, was initiated before pregnancy was recognized. Absorbed doses were usually 1-2.5 Gy (100-250 rad) or greater, and were typically delivered during the first trimester (organogenesis and early fetal stages). Doses of this magnitude resulted in reported cases of microcephaly, mental retardation, eye defects, skeletal and genital deformities, cleft palate, and generalized growth retardation.[6,15] None of these effects was identified at absorbed doses of less than 1 Gy (100 rad).[6]
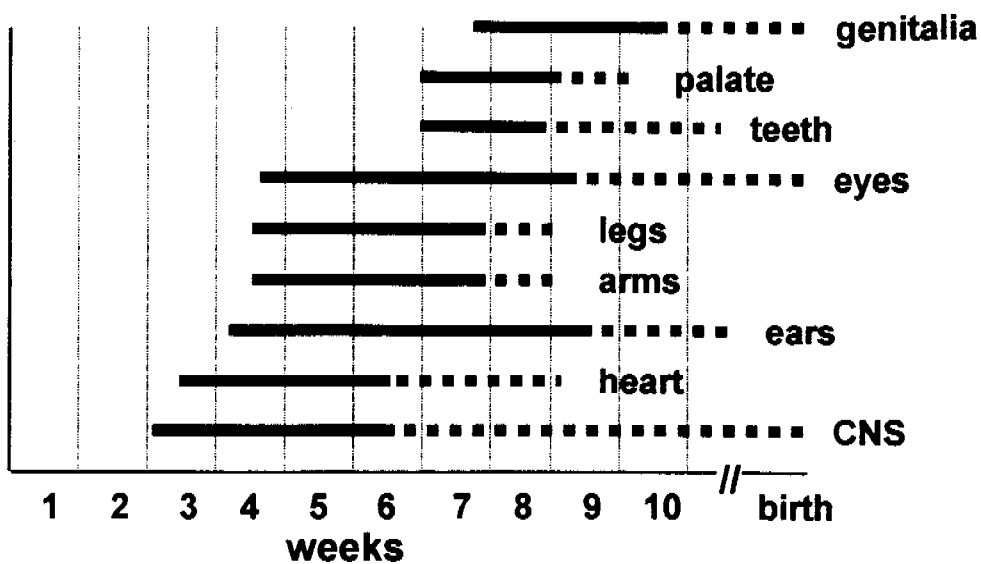
6

Figure 1. Embryo/fetus sensitivity to radiation effects at critical periods during organ development. Adapted from Stabin.[18]
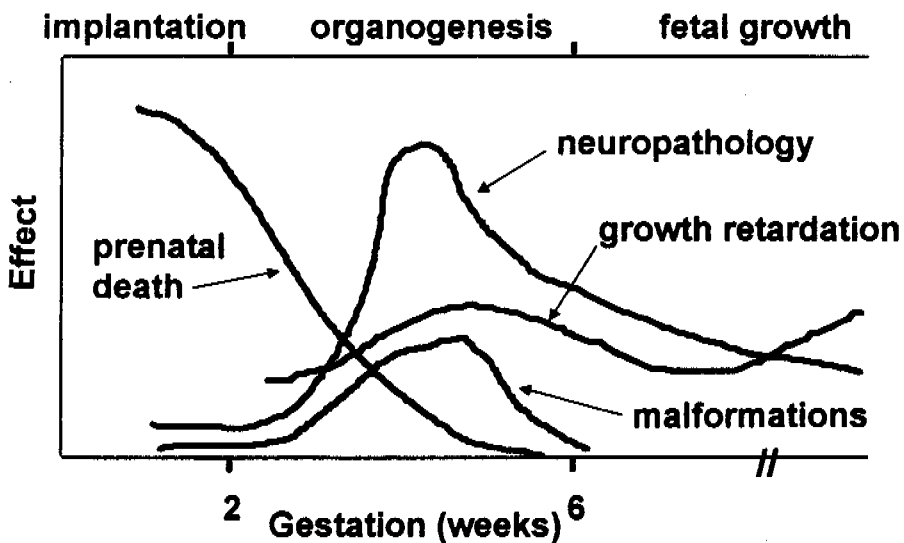

Figure 2. Relative incidence of adverse radiation effects at different stages of gestation. Adapted from Mettler and Upton.[6]

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Absorbed doses greater than 3 Gy (300 rad) usually resulted in abortion.[6,15]

Additional knowledge of radiation effects on the embryo/fetus has been obtained from studies of A-bomb victims in Japan. At Hiroshima, of the 93 victims who received > 0.25 Gy (25 rad) in utero, 21 had microcephaly with 10 of these also being mentally retarded.[13] At Nagasaki, of the 30 victims (who probably received > 0.5 Gy (50 rad)) in utero, there were 7 fetal deaths, 6 neonatal deaths, and 4 with mental retardation.[5] Gross congenital malformations associated with external radiation exposure were not observed unless the individual also exhibited either growth retardation or a CNS abnormality. For example, 80% of malformed children who were exposed to > 1 Gy (100 rad) in utero were also microcephalic.[6] Although linear and linear-quadratic dose-response relationships are consistent with data on microcephaly and mental retardation at high doses, the data suggest that the threshold for these effects is about 0.1-0.2 Gy (10 to 20 rad).[15]

Another source of information comes from studies of diagnostic maternal X-rays of the pelvis or abdomen.[6] Although many of the procedures were performed for pelvimetry during the third trimester, some procedures (either pelvic or abdominal) were performed early in pregnancy. Estimated fetal exposures ranged from 0.003 to 0.1 Gy (0.3 to 10 rad), although most were less than 0.05 Gy (5 rad). These studies showed that radiation effects on the fetus were either non-existent or were not increased above control groups.

A final source of information comes from the 1986 Chernobyl nuclear power plant accident. Average radiation doses this event were calculated to be 0.43 Gy (43 rad) to the 24,000 residents living near the plant, 0.03 Gy (3 rad) to the 110,000 residents of Pripyat and other evacuated communities, and 0.005 Gy (0.5 rad) to 600,000 residents just outside the evacuation zone.[16] Follow-up studies of populations living in the affected Soviet republics, as well as others from Hungary and Scandinavia, have each reported that no increase in congenital malformations was detected.[6]

Childhood Leukemia Controversy

The risk of radiation carcinogenesis and childhood leukemia following fetal radiation exposure has been a major concern and the subject of much controversy. Nearly all epidemiological studies in this area are comprised of children who received in utero exposure from pelvimetries or placentograms performed during the third trimester.[6,11] Radiation exposures generally fell in the range of 0.01 to 0.02 Gy (1 to 2 rad). The original conclusions from these studies purported that this level of fetal exposure resulted in a 1.5 - 2 times higher probability of developing childhood leukemia. Upon careful review and criticism from others, this relationship has now been rebutted.[6,11,14] For example, the non-exposed control group (born to normal healthy mothers) is felt to be inappropriate for comparison with the exposed group (born to mothers who required X-ray procedures for medical care). Also, additional information concerning the increased incidence of childhood leukemia in non-exposed siblings demonstrates that the original findings of in utero exposure and childhood leukemia were merely an association rather than a causal relationship. Some of these data are summarized in Table 2.

Table 2. Reported Incidence of Leukemia in Various Groups.[11]

Population	Incidence of Childhood Leukemia
control population (no radiation exposure)	1:3000
1-2 rad in utero radiation exposure	1:2000
non-exposed siblings of exposed children	1:2000
non-exposed siblings of leukemic children	1:720

Adapted from Marcus.[1]

A second source of information regarding in utero exposure and childhood leukemia comes from studies of atomic bomb survivors in Japan. More than 2000 children were born to mothers who were pregnant at the time of the bombing; they received an average dose in utero of 0.14 Sv (14 rem). Of these children, only one developed leukemia. This incidence is far less than that predicted (on a per radiation dose basis) from the studies described in the preceding paragraph, and is almost exactly equal to that seen throughout the rest of Japan.[14]

Summary and Comparison of Risks

To summarize the effects of radiation on the embryo/fetus, the following statements are applicable[6,11]:

• High doses of radiation, i.e., > 1 Gy (>100 rad), result in a high incidence of microcephaly and mental retardation. Approximately 30 other abnormalities or malformations have been identified and correlated with high doses of radiation, but these rarely occur in the absence of neurologic abnormalities.

• Available evidence strongly supports the statement that major malformations are highly unlikely to be produced by doses under 0.25 Gy (25 rad).

• Doses of < 0.05 Gy (5 rad) have not been observed to cause any congenital malformations or growth retardation.

• The extrapolated incidence of effects at low radiation doses is negligible compared to the baseline incidence of "spontaneous" effects.

• A working limit of 0.1 Gy (10 rad) appears to be reasonable.

Any discussion of risks should not be carried out in isolation. Rather, risks should be put in perspective by comparing them with other voluntary and involuntary risks. Risks from various factors during pregnancy are summarized in Table 3.

FETAL DOSIMETRY[1,8,17-19]

Human studies of the biodistribution of radiopharmaceuticals during pregnancy are rarely found in the literature. The limited human data available come largely from determinations of radionuclide content in fetuses; radioanalyses of embryonic tissues, abortuses, and placentas; and in vitro studies using perfused human placentas. Hence, extrapolations from animal studies comprise the majority of available information on the subject.[1,8]

In addition to biokinetic information, anatomical and physical

Table 3. Risks to the Fetus from Various Factors During Pregnancy.[6]

Risk Factor	Pregnancy Outcome	Risk of Occurrence
German measles	defects of heart, lens of eye, muscles, inner ear, teeth	2 in 3
cigarette smoking	low birth weight	1 in 5
> 1 pack/day	infant death	1 in 3
alcohol consumption	low birth weight	1 in 10
> 4 drinks/day	fetal alcohol syndrome	1 in 3
0.5-1.0 Gy (50-100 rad) radiation exposure	small head size, mental retardation	1 in 4
unknown (natural incidence)	congenital abnormalities	1 in 16
maternal age = 20	Down's syndrome	1 in 2300
maternal age >40	Down's syndrome	1 in 64
0.01 Gy (1 rad) radiation exposure	childhood cancer (?)	1 in 2000
0.0 Gy (1 rad) radiation exposure	congenital malformations	not detectable

Adapted from Mettler and Upton.[6]

properties are necessary for estimation of absorbed doses. Anthropomorphic models representing the pregnant woman at 3, 6, and 9 months of gestation have been recently developed, and "S" factors for common radionuclides have been published as well as incorporated into the MIRDOSE 3 software.[1,18] This schema provides more reliable absorbed dose estimates than do previous approaches that equated fetal doses with absorbed doses for the uterus or the ovaries.[18]

Placental Transfer of Radiopharmaceuticals

Several radiopharmaceuticals are known to undergo placental transfer and accumulate in fetal tissues. Perhaps the best example is radioiodide. Iodide readily crosses the placenta and is concentrated in the fetal thyroid after about the 10-13th week of gestation.[6,18] High radiation doses are possible with I-131, which can result in hypothyroidism or athyria. Fetal thyroid doses from I-123 and I-131 sodium iodide at various gestational ages are summarized on Table 4. Tc-99m pertechnetate also crosses the placenta and is concentrated in the fetal thyroid as well as in the fetal GI tract.[6,20]

Tc-99m medronate accumulates on the fetal skeleton by 30-32 weeks,[21] but not at 8-18 weeks.[22] This may be due to increased ossification of the fetal skeleton and/or increased permeability of the placenta by 30 weeks. Tc-99m exametazime accumulates in the fetal liver and brain, especially later in pregnancy.[23,24] Tl-201 thallous chloride accumulates in the fetal liver and heart;[25] in contrast, Tc-99m sestamibi and tetrofosmin do not cross the placenta and are not transferred into the fetal circulation.[25] Other radiopharmaceuticals that may cross the placenta and accumulate to some degree in fetal tissues include Tc-99m oxidronate, Tc-99m pyrophosphate, Tc-99m albumin aggregated, Tc-99m pentetate, Tc-99m gluceptate, Tc-99m succimer, Tc-99m red blood cells, and Ga-67 citrate.[1,6,18,26-27]

Gamma Radiation from Other Maternal Sources

In most cases, the majority of the fetal radiation dose comes from gamma radiation emitted by radioactive material localized in nearby maternal organs. Because of proximity, a major source organ for fetal irradiation is the placenta (both placental tissue and placental blood pool), especially during the second and third trimesters.[1,18] Radiopharmaceuticals that concentrate in the placenta include Tc-99m pertechnetate, Tc-99m medronate, Tc-99m oxidronate, Tc-99m pyrophosphate, Tc-99m sulfur colloid, Tc-99m albumin aggregated, Tc-99m pentetate, Tc-99m gluceptate, Tc-99m succimer, Tc-99m red blood cells, Tc-99m exametazime, and Ga-67 citrate.[1,18,24,26-27]

Another major source organ for fetal irradiation, especially during the first trimester, is the urinary bladder. Radiopharmaceuticals that concentrate in the urinary bladder include Tc-99m pertechnetate, Tc-99m medronate, Tc-99m oxidronate, Tc-99m pyrophosphate, Tc-99m albumin aggregated, Tc-99m pentetate, Tc-99m gluceptate, Tc-99m mertiatide, Tc-99m exametazime, Tc-99m red blood cells, Tc-99m sestamibi, Ga-67 citrate, In-111 pentetreotide, F-18 fludeoxyglucose, I-123 iodide, and I-131 iodide.[1,18]

Other major source organs for fetal irradiation may include the intestines (e.g., Tc-99m pertechnetate, Tc-99m disofenin, Tc-99m exametazime, Tc-99m sestamibi, Tl-201 chloride, Ga-67 citrate, I-123 iodide, and I-131 iodide); liver/spleen (e.g., Tc-99m sulfur colloid, Tc-99m leukocytes, Ga-67 citrate, and In-111 leukocytes); lungs (e.g., Tc-99m aggregated albumin, Xe-133); bones (e.g., Tc-99m medronate, Tc-99m oxidronate, Tc-99m pyrophosphate, and Ga-67 citrate); and

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Table 4. Fetal Thyroid Dose Following Maternal Administration of Radioiodide. [18]

Gestational Age	I-123 mGy/MBq	(rad/mCi)	I-131 mGy/MBq	(rad/mCi)
3 months	2.7	(10)	230	(850)
4 months	2.6	(10)	260	(960)
5 months	6.4	(24)	580	(2100)
6 months	6.4	(24)	550	(2000)
7 months	4.1	(15)	390	(1400)
8 months	4.0	(15)	350	(1300)
9 months	2.9	(11)	270	(1000)

Adapted from Stabin. [18]

kidneys (e.g., Tc-99m gluceptate and Tc-99m succimer). [1,18]

Fetal Dosimetry for Common Radiopharmaceuticals

Absorbed doses from common radiopharmaceuticals at selected gestational ages are presented in Table 5. In summary, fetal doses are < 10 mGy (<1 rad) from routine administered dosages of Tc-99m radiopharmaceuticals (except sestamibi), F-18 fludeoxyglucose, In-111 leukocytes, I-123 iodide, and Xe-133. Fetal doses are 10-50 mGy (1-5 rad) from routine administered dosages of Tc-99m sestamibi, In-111 pentetreotide, Tl-201 chloride, Ga-67 citrate, and diagnostic dosages of I-131 iodide. Fetal doses range up to 500 mGy (50 rad) from therapeutic doses of I-131 iodide. [1,18]

PREGNANCY TESTING [28-30]

Because a substantial fraction of nuclear medicine procedures is performed in females of childbearing age, [1] evaluation of pregnancy status is a frequent concern. Fortunately, modern pregnancy tests are fast, sensitive, and relatively inexpensive.

Rationale

Human Chorionic Gonadotropin (hCG) is a 39,000-dalton glycoprotein hormone that is biosynthesized and secreted during pregnancy by the trophoblastic cells of the placenta. It is composed of two dissimilar noncovalently linked subunits, termed simply α and β. The alpha subunit contains 92 amino acids and has a molecular weight of 16,000. This subunit is identical to the alpha subunits of the pituitary hormones luteinizing hormone (LH), follicle-stimulating hormone (FSH), and thyroid-stimulating hormone (TSH). The beta subunits, on the other hand, are different and distinct for each of these hormones. The beta subunit of hCG consists of a 145 amino acid sequence and has a molecular weight of 23,000.

Table 5. Fetal Dosimetry for Common Radiopharmaceuticals at Selected Gestational Ages, mGy/MBq (rads/mCi) administered to mother.

Radiopharmaceutical	Early	3-month	6-month	9-month
Tc-99m pertechnetate	0.011 (0.041)	0.022 (0.081)	0.014 (0.052)	0.0093 (0.034)
Tc-99m sulfur colloid	0.0018 (0.007)	0.0021 (0.008)	0.0032 (0.012)	0.0037 (0.014)
Tc-99m albumin aggregated	0.0028 (0.010)	0.004 (0.015)	0.005 (0.019)	0.004 (0.015)
Tc-99m pentetate aerosol	0.0058 (0.021)	0.0043 (0.016)	0.0023 (0.0085)	0.0030 (0.011)
Tc-99m medronate	0.0061 (0.023)	0.0054 (0.020)	0.0027 (0.010)	0.0024 (0.009)
Tc-99m oxidronate	0.0052 (0.019)	0.0054 (0.020)	0.0030 (0.011)	0.0025 (0.009)
Tc-99m pentetate	0.012 (0.044)	0.0087 (0.032)	0.0041 (0.015)	0.0047 (0.017)
Tc-99m mertiatide	0.018 (0.067)	0.014 (0.052)	0.0055 (0.020)	0.0052 (0.019)
Tc-99m gluceptate	0.012 (0.044)	0.011 (0.041)	0.0053 (0.020)	0.0046 (0.017)
Tc-99m succimer	0.0051 (0.019)	0.0047 (0.017)	0.0040 (0.015)	0.0034 (0.013)
Tc-99m disofenin	0.017 (0.063)	0.015 (0.056)	0.012 (0.044)	0.0067 (0.025)
Tc-99m exametazimeO	0.0087 (0.032)	0.0067 (0.025)	0.0048 (0.018)	0.0036 (0.013)
Tc-99m albumin	0.0051 (0.019)	0.0030 (0.011)	0.0026 (0.010)	0.0022 (0.0081)
Tc-99m red blood cells (in vivo)	0.0064 (0.024)	0.0043 (0.016)	0.0033 (0.012)	0.0027 (0.010)
Tc-99m red blood cells (in vitro)	0.0068 (0.025)	0.0047 (0.017)	0.0034 (0.013)	0.0028 (0.010)

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Table 5. Fetal Dosimetry for Common Radiopharmaceuticals at Selected Gestational Ages, mGy/MBq (rads/mCi) administered to mother. (Continued)

Radiopharmaceutical	Early	3-month	6-month	9-month
Tc-99m sestamibi	0.015 (0.056)	0.012 (0.044)	0.0084 (0.031)	0.0054 (0.020)
Tc-99m leukocytes	0.0038 (0.014)	0.0028 (0.010)	0.0029 (0.011)	0.0028 (0.010)
In-111 leukocytes	0.13 (0.48)	0.096 (0.36)	0.096 (0.36)	0.094 (0.35)
In-111 pentetreotide	0.082 (0.30)	0.060 (0.22)	0.035 (0.13)	0.031 (0.12)
Tl-201 chloride	0.097 (0.36)	0.058 (0.22)	0.047 (0.17)	0.027 (0.10)
Ga-67 citrate	0.093 (0.34)	0.20 (0.74)	0.18 (0.67)	0.13 (0.48)
F-18 fludeoxyglucose	0.027 (0.10)	0.017 (0.063)	0.0094 (0.035)	0.0081 (0.030)
Xe-133 gas	0.0002 (0.001)	0.0003 (0.0001)	0.00002 (0.0001)	0.00002 (0.0001)
I-123 iodide	0.020 (0.074)	0.014 (0.052)	0.011 (0.041)	0.0098 (0.036)
I-131 iodide	0.072 (0.27)	0.068 (0.25)	0.23 (0.85)	0.27 (1.00)
I-131 iodohippurate	0.064 (0.24)	0.050 (0.19)	0.019 (0.070)	0.018 (0.067)
I-131 iobenguane	0.11 (0.41)	0.054 (0.20)	0.038 (0.14)	0.035 (0.13)

Adapted from Russell et al.[1] and Stabin.[18-19]

In contrast to the similar pituitary hormones mentioned above, it possesses a distinctive 28-30 amino acid tail.

Immunoassays for hCG are often referred to as β-hCG assays because the antibodies used are directed against the specific beta subunit of hCG. These antibodies, however, do detect the intact molecule, so the assay does properly measure hCG rather than just measuring free β-subunits. Because of some variation in immunoreactivity, the World Health Organization has established that all bioassays of hCG be calibrated to standardized International Units. Hence, hCG concentrations are typically reported as values of mIU (milli- International Units) per ml.

After implantation, hCG concentrations in maternal blood rise rapidly, with a doubling time of 1.7 - 2 days. By the time of the missed menstrual period, the circulating hCG concentration reaches approximately 100 mIU/ml. The expected ranges of hCG concentrations in maternal blood at various times during the first trimester of pregnancy are outlined below in Table 6.

Table 6. Expected Range of hCG Concentrations in Blood at Various Times During the First Trimester of Pregnancy.

Time after Conception	hCG Concentration (mIU/ml)
Non-pregnant females	< 5
0 – 1 week	0 – 50
1 – 2 weeks	40 – 300
2 – 3 weeks	100 – 1000
3 – 4 weeks	500 – 6000
1 – 2 months	5000 – 200,000

Adapted from Pathology Laboratories Services Handbook.[30]

Urine Vs. Serum Testing

Because urine concentrations of hCG approach those in serum, urine pregnancy testing has gained widespread acceptance as a convenient, reliable, and inexpensive diagnostic method. If possible, the testing should be performed on a sample of the first urine voided in the morning. This is because the first void generally contains the highest concentration of hCG; urine collected at other times may be diluted by intake of liquids and thus have a lower hCG concentration. Urine testing is typically qualitative, i.e., the results are either negative or positive for pregnancy.

Serum testing may be more sensitive than urine testing, especially if the urine sample is not from the first void in the morning. A 5 ml blood sample collected by standard venipuncture into a conventional "red top" tube is required. Serum testing is typically qualitative (i.e., negative or positive for pregnancy) but, if desired, it can be performed to yield

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quantitative results (i.e., numerical value for hCG concentration).

Accuracy/Sensitivity

Quantitative serum testing is capable of detecting hCG concentrations at about 1 mIU/ml. Using a cut-off value of 5 mIU/ml, this test has the ability to detect pregnancy at 7-10 days after conception. Qualitative "pregnancy" testing, either serum or urine, generally uses a cut-off value of 25 mIU/ml; hence, this test has the ability to detect pregnancy at about 2 weeks after conception.

False positive pregnancy test results are uncommon, but can occur in the following situations:

• Certain germ cell neoplasms such as choriocarcinomas and trophoblastic tumors (these neoplasms secrete hCG);

• Recent abortion, including spontaneous abortion from an unknown pregnancy (hCG is slowly cleared from the blood and may be detectable for up to 2-4 weeks after abortion);

• Recent transfusion of blood obtained from a pregnant donor (hCG from donated blood may be detectable even after dilution in recipient's bloodstream).

False negative test results are somewhat more common, and can occur in the following situations:

• Early pregnancy (hCG concentrations may still be below the cut-off value for positivity);

• Ectopic pregnancy (hCG concentrations with extra-uterine preg-nancies are generally lower and rise more slowly);

• Low specific gravity of urine (hCG may be diluted to a concentration below the cut-off value for positivity);

• Procedural error(s) in test performance.

RECOMMENDATIONS

Based on concerns about possible deleterious effects of radiation exposure to the embryo/fetus, the International Commission on Radiological Protection (ICRP) in 1966 and the National Council on Radiation Protection and Measurements (NCRP) in 1968 issued recommendations advising the avoidance or postponement of certain diagnostic radiation exposures of pregnant or potentially pregnant patients.[12] The emphasis of these recommendations focused on procedures that were elective or not of immediate benefit to the patient. These recommendations stated that elective procedures should be performed only during the first 10 days of the menstrual cycle. NCRP subsequently revised its recommendation to restrict elective procedures to the first 14 days of the menstrual cycle,[12] but the initial "10-day rule" continued to enjoy widespread acceptance for many years.

Several problems are associated with routinely using the 10-day rule. These include: poor patient compliance; scheduling difficulties, especially for women who have irregular periods; and the potential that a delay for an unknowingly pregnant women may require that a procedure be performed at a later date when the fetus is more susceptible to malformation and CNS effects than it would have been during pre-implantation. Additionally, the vast majority of diagnostic procedures exposes the embryo/fetus to less than 50 mGy (5 rad), a level below which the radiogenic risk of congenital abnormalities appears to be essentially nonexistent, and certainly far less than other risks normally associated with pregnancy. Therefore, the classic 10-day rule has been largely abandoned.[6]

The current philosophy is to ascertain the possibility of pregnancy and then use best medical judgment. Considerations include changing the radiation procedure to a non-radiation procedure such as ultrasound, or tailoring the radiation procedure to minimize the dose to the fetus while still obtaining the

necessary diagnostic information. If, in the best judgement of the attending physician, the radiation procedure is deemed advisable to the medical well being of the patient (i.e., the benefits outweigh the risks), it should be carried out immediately.

Diagnostic Radiopharmaceuticals

In recent years, professional/ scientific organizations have begun formally defining "standards of practice" or "practice guidelines" for certain activities commonly performed by their members. Regarding pregnancy testing prior to the administration of diagnostic radiopharmaceuticals, the Society of Nuclear Medicine procedure guidelines contain the following statements:

> "Female patients who are post-menarche and pre-menopause should be asked about pregnancy, lactation, and breast-feeding prior to administration."[31] "A pregnancy test is not required prior to performing most diagnostic imaging procedures."[32]

The American College of Radiology standards contain the following statements:

> "All imaging facilities should have policies and procedures to reasonably attempt to identify pregnant patients prior to the performance of any diagnostic examination involving ionizing radiation. If the patient is known to be pregnant, the potential radiation risks to the fetus and clinical benefits of the procedure should be considered before proceeding with the study."[33]

Therapeutic Radiopharmaceuticals

Regarding pregnancy testing prior to administration of therapeutic radiopharmaceuticals, the Society of Nuclear Medicine procedure guidelines contain the following statements:

> "A pregnancy test should be performed in all women physically capable of becoming pregnant when the effective dose to a fetus potentially exceeds 5 rems. An example of such a test is whole body imaging following a diagnostic dose of I-131 (typically 2 - 5 mCi)."[32]
> "Negative pregnancy test in women of childbearing age. No breastfeeding. These [pregnancy and breastfeeding] are absolute contraindications to therapy."[34]

The American College of Radiology standards contain the following statements:

> "Female patients must not be pregnant or breast-feeding at the time of orally, intravenously or intraperitoneally administered therapy. Pregnancy may be ruled out by a negative beta human chorionic gonadotropin (hCG) test obtained within 48 hours prior to administration of the radiopharmaceutical, by a postmenopausal state with absence of menstrual bleeding for two years, or by premenarche in a child."[35]

Author's note: Even when a pregnancy test is performed, it must be remembered that any pregnancy test is unreliable for some period of time after conception (approximately ten days for a quantitative test and two weeks for a qualitative test); hence, the patient also must be carefully and tactfully questioned regarding the possibility of recent conception. Additionally, because of the unreliability of pregnancy test results early in pregnancy, some physicians recommend that women of childbearing potential use sufficient contraception for at least one month before receiving radioiodine treatment.[36]

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REFERENCES

1. Russell JR, Stabin MG, Sparks RB, Watson E. Radiation absorbed dose to the embryo/fetus from radiopharmaceuticals. *Health Phys* 1997; 73(5):756-769.

2. *Code of Ethics for Pharmacists*. Washington, DC: American Pharmaceutical Association. October 27, 1994

3. Berlin L. Malpractice issues in radiology: radiation exposure and the pregnant patient. *AJR* 1996; 167:1377-1379.

4. Nuclear Regulatory Commission. Medical use of byproduct material: proposed revision. *Federal Register*, Vol. 63, No. 156, Thursday, Aug. 13, 1998: 43516-43580.

5. Travis EL. *Primer of Medical Radiobiology*. Chicago; Year Book Medical Publishers. 1975.

6. Mettler FA, Upton AC. *Medical Effects of Ionizing Radiation, 2nd Edition*. Philadelphia; WB Saunders. 1995.

7. Guyton AC, Hall JE. *Textbook of Medical Physiology, Ninth Edition*. Philadelphia: WB Saunders. 1996.

8. Sikov MR, Robertson JS, Wegst AV, et al. *NCRP Report No. 128: Radionuclide Exposure of the Embryo/Fetus*. Washington, DC: National Council on Radiation Protection and Measurements. 1998

9. Warkany J. *Congenital Malformations: Notes and Comments*. Chicago, IL: Year Book Medical Publishers. 1971.

10. Ventura SJ, Martin JA, Curtin SC, Mathews TJ. Report of final natality statistics, 1996. *Monthly Vital Statistics Report* 1998; 46(11)Suppl:1-99.

11. Marcus CS. Radiation biology. In: Tubis M, Wolf W (eds): *Radiopharmacy*. New York; John Wiley & Sons. 1976; 123-150.

12. Gorson RO, Brent RL, Moseley RD, et al. *NCRP Report No. 54: Medical Radiation Exposure of Pregnant and Potentially Pregnant Women*. Washington, DC: National Council on Radiation Protection and Measurements. 1977.

13. Advisory Committee of the Biological Effects of Radiation. *The Effects on Populations of Exposure to Low Levels of Ionizing Radiation*. Washington, DC; National Academy of Sciences. 1972.

14. Hall EJ. *Radiation and Life, 2nd Edition*. New York: Pergamon Press. 1984.

15. Mayr NA, Wen BC, Saw CB. Radiation therapy during pregnancy. *Obst Gyn Clin North America* 1998; 25:301-321.

16. Wilson R. A visit to Chernobyl. *Science* 1987; 236:1636-1640.

17. Cloutier GJ, Smith SA, Watson EE, et al. Dose to the fetus from radionuclides in the bladder. *Health Phys* 1973; 25:147-161.

18. Stabin MG. *Fetal Dose Calculation Workbook (ORISE 97-0961)*. Oakridge, TN; Radiation Internal Dose Information Center. 1997.

19. Stabin MG. Health concerns related to radiation exposure of the female nuclear medicine patient. *Environ Health Perspect* 1997; 105(Suppl 6):1403-1409.

20. Saunders M, Palmer AM, Preece AW. Fetal accumulation of technetium-99m administered during pregnancy. *Eur J Nucl Med* 1997;24:965.

21. McKenzie AF, Budd RS, Yang C, et al. Technetium-99m-methylene diphosphonate uptake in the fetal skeleton at 30 weeks gestation. *J Nucl Med* 1994; 35:1338-1341.

22. Hedrick WR, DiSimone RN, Wolf BH, Langer A. Absorbed dose to the fetus during bone scintigraphy. *Radiology* 1988; 168:245-248.

23. Kume N, Hayashida K, Shimotsu Y, Matsunaga N. Hyperventilation technetium-99m-HMPAO brain SPECT in Moyamoya disease to assess risk of natural childbirth. *J Nucl Med* 1997; 38:1894-1897.

24. Owunwanne A, Omu A, Patel M, et al. Placental binding and transfer of radiopharmaceuticals: technetium-99m *d*,l-HMPAO. *J Nucl Med* 1998; 39:1810-1813.

25. Owunwanne A, SadekS, Omu A, Patel M. Placental binding and transfer of myocardial perfusion imaging radiopharmaceutical. *J Nucl Med* 1995; 36:154P.

26. Palmer AM, Preece AW. Placental transfer of technetium labelled radiopharmaceuticals in the guinea pig. *J Nucl Med* 1993;34:159P.

27. Palmer AM. Placental transfer of gallium (67) citrate in guinea pigs. *Eur J Nucl Med* 1997;24:965.

28. Jacobs DS, Demott WR, Finley PR, et al. *Laboratory Test Handbook, 3rd Edition.* Hudson, OH; Lexi-Comp Inc. 1994.

29. Product literature. *Uni-Gold hCG™.* Jamestown, NY; Trinity Biotech USA. Oct., 1997.

30. *Pathology Laboratory Services Handbook.* Iowa City, IA; University of Iowa

Hospitals and Clinics. 1999. *http://www.medicine.uiowa.edu/pathology/*

31. Callahan RJ, Chilton HM, Goodwin DA, et al. Society of Nuclear Medicine procedure guideline for imaging with radiopharmaceuticals: 2.0. Reston, VA: Society of Nuclear Medicine. February, 1999. *http://www.snm.org/*

32. Parker JA, Yester MV, Graham LS, et al. Society of Nuclear Medicine procedure guideline for general imaging: 2.0. Reston, VA:

Society of Nuclear Medicine. February, 1999. *http://www.snm.org/*

33. Brill DR, Abreu SH, Alderson PO, et al. ACR standard for diagnostic procedures using radiopharmaceuticals [res. 19-1998]. Reston, VA: American College of Radiology. 1998. *http://www.acr.org/*

34. Silberstein E, Taylor A. Society of Nuclear Medicine procedure guideline for bone pain treatment: 2.0. Reston, VA: Society of Nuclear Medicine. February, 1999. *http://www.snm.org/*

35. Brill DR, Abreu SH, Benedetto AR, et al. ACR standard for the performance of therapy with unsealed radionuclide sources [res. 11-1996]. Reston, VA: American College of Radiology. 1998. *http://www.acr.org/*

36. Bohuslavizki KH, Kröger S, Klutmann S, et al. Pregnancy testing before high-dose radioiodine treatment: a case report. *J Nucl Med Technol* 1999;27:220-221.

QUESTIONS

1. Which of the following concerns is LEAST relevant regarding nuclear medicine procedures in pregnant patients?
   a. Ethical
   b. Medicolegal
   c. Regulatory
   d Third- party reimbursement

2. According to the **proposed** rule 10 CFR 35.3047, which of the following situations would require reporting to the NRC of embryo/fetus doses from administration of byproduct material to a pregnant individual?
   a. All cases involving radiation exposure of the embryo/fetus.
   b. All cases in which the embryo/fetus dose is >500 mrem.
   c. All cases in which the embryo/fetus dose is >5 rem.
   d. Cases in which the embryo/fetus dose is > 500 mrem without specific

approval, in advance, by the authorized user.

3. The gestational stage that occurs from about one week to about seven weeks after conception is referred to as the _____ stage.
   a. Fetal
   b. Growth
   c. Major organogenesis
   d. Pre-implantation

4. Compared to the actual incidence of congenital abnormalities, the reported incidence is falsely low for all of the following reasons, EXCEPT:
   a. Reporting only external malformations observed at birth.
   b. Reporting only hereditary abnormalities.
   c. Reporting only "major" malformations.
   d. Underreporting of congenital malformations on birth certificates.

5. An all-or-none effect (i.e., prenatal death or no effects at all) is typical of which gestational stage?
   a. Fetal
   b. Major organogenesis
   c. Pre-implantation
   d. All of stages throughout gestation

6. Studies of radiation effects on the embryo/fetus from therapeutic pelvic radiation during pregnancy showed that congenital anomalies involving the CNS, skeletal system, genitalia, and other tissues were associated with absorbed doses of:
   a. 1-2 rad.
   b. 25-50 rad.
   c. 100-250 rad.
   d. >300 rad.

7. Linear and linear-quadratic dose-response relationships between in utero irradiation and microcephaly/mental retardation have been observed in which of the following situations?
   a. Atomic bomb victims in Japan
   b. Chernobyl nuclear power plant accident
   c. Diagnostic maternal X-rays of pelvis or abdomen
   d. Nuclear medicine imaging procedures

8. Which of the following individuals has the highest risk of developing childhood leukemia?
   a. Child exposed in utero to 1-2 rad
   b. Member of the general population
   c. Non-irradiated sibling of a child who received 1-2 rad in utero
   d. Non-irradiated sibling of a child who developed leukemia

9. Which of the following is most likely to be caused by high radiation doses to a fetus?
   a. Cataracts
   b. Cleft palate
   c. Hypoplastic genitalia
   d. Microcephaly

10. Which of following best describes the relationship between CNS abnormalities and other congenital malformations?
    a. CNS abnormalities rarely occur in the absence of other congenital malformations
    b. Other congenital malformations rarely occur in the absence of CNS abnormalities
    c. Both exhibit the highest incidence when irradiation occurs during the fetal stage
    d. No relationship between these two effects has been described

11. Which of the following factors carries the LOWEST risk of an adverse pregnancy outcome?
    a. Consuming four alcoholic drinks/day
    b. Maternal age of 40 years
    c. Radiation exposure of 1 rad
    d. Smoking 1 pack of cigarettes/day

12. The majority of information on the biodistribution of radiopharmaceuticals during pregnancy has come from which of the following sources?
    a. Clinical trials involving pregnant women
    b. Extrapolations from animal studies
    c. In vitro studies using perfused human placentas
    d. radioanalyses of embryonic tissues, abortuses, and placentas

13. For estimation of fetal absorbed doses from radiopharmaceuticals administered to the mother, which of the following provides the most reliable values?

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a. Equating them to absorbed doses for the ovaries

b. Equating them to absorbed doses for the remainder of the body

c. Equating them to absorbed doses for the uterus

d. Using anthromorphic models representing the pregnant woman

14. Which of following radiopharmaceuticals does NOT cross the placenta and localize in fetal tissues?
a. Tc-99m exametazime
b. Tc-99m medronate
c. Tc-99m sestamibi
d. Tl-201 thallous chloride

15. A whole body scan for thyroid cancer metastases using 2 mCi I-131 sodium iodide in woman who is six months pregnancy would result in a fetal thyroid dose of about _____ rad.
a. 1.7
b. 48
c. 1100
d. 4000

16. Which of the following is an especially important source organ for fetal irradiation during the first trimester?
a. Intestines
b. Liver
c. Placenta
d. Urinary bladder

17. Which of the following procedures would generally result in the lowest fetal dose?
a. Abscess imaging using Ga-67 citrate
b. Infection imaging using In-111 leukocytes
c. Myocardial perfusion imaging using Tc-99m sestamibi
d. Tumor imaging using In-111 pentetreotide

18. With regard to fetal dosimetry, which of the following would be the best radiopharmaceutical to use for evaluation of renal transplant function in a woman who is 6 months pregnant?
a. I-131 iodohippurate, 0.1 mCi
b. Tc-99m pentetate, 15 mCi

c. Tc-99m gluceptate, 15 mCi
d. Tc-99m mertiatide, 10 mCi

19. A perfusion lung scan is requested for a 29-year-old woman who is 8 months pregnant. What would be the radiation dose to the fetus from administration of 2 mCi Tc-99m albumin aggregated to the mother?
a. 16 mrem
b. 32 mrem
c. 320 mrem
d. Negligible, because albumin aggregated particles do not cross the placenta

20. Which of the following is identical in the structures of hCG, LH, TSH, and TSH?
a. Alpha subunit
b. Beta subunit
c. Neither the alpha nor beta subunits
d. The distinctive 28-30 amino acid tail

21. A quantitative serum level of 2 mIU/ml hCG at one week after a missed menstrual period would most likely indicate that the woman:
a. Has a normal intra-uterine pregnancy.
b. Has an ectopic (extra-uterine) pregnancy.
c. Has spontaneously aborted.
d. Is not pregnant.

22. Which of the following could produce a falsely negative urine pregnancy test result?
a. choriocarcinoma
b. Low specific gravity of urine
c. Recent abortion
d. Urine collected from first void in the morning

23. Which of the following represents the current philosophy regarding performance of a diagnostic radiation procedure in a potentially pregnant patient?
a. Contraindicated; do not perform any radiation procedure; switch to ultrasound
b. Perform the radiation procedure only during the first 10 days after onset of menses

c. Perform the radiation procedure only during the first 14 days after onset of menses

d. Tailor the procedure to minimize the radiation while still obtaining the necessary information

24. A 23-year old women with hyper-thyroidism is scheduled to be treated with 8 mCi I-131 sodium iodide. When asked about pregnancy, she states that she is not pregnant. Should a pregnancy test be performed in this patient anyway prior to administration of the I-131 treatment?

a. No, according to both SNM guidelines and ACR standards

b. No, according to SNM guidelines; but Yes, according to ACR standards

c. Yes, according to both SNM guidelines and ACR standards

d. Yes, according to SNM guidelines; but No, according to ACR standards.

25. Even when a pregnancy test is performed and yields a negative result, the patient should be questioned about the possibility of recent conception because:

a. Pregnancy tests are unreliable for the first two weeks after conception.

b. Such questioning is required by NRC regulations.

c. Such questioning is recommended in professional practice guidelines/standards.

d. Such questioning is specifically advocated by NCRP recommendations.

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