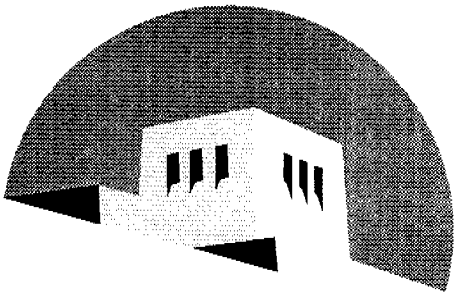

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Factors to Consider When Selecting Radiopharmaceutical Dosages for Diagnostic Procedures

by:

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FACTORS TO CONSIDER WHEN SELECTING RADIOPHARMACEUTICAL DOSAGES FOR DIAGNOSTIC PROCEDURES

By

SUSAN J. BALLINGER, M.S., R.Ph., CNMT, BCNP

STATEMENT OF OBJECTIVES

The purpose of this correspondence lesson is to increase the reader's knowledge of general dosing requirements for various nuclear medicine studies for adult and pediatric patients. The reader should be able to discuss, calculate and understand these dosing requirements.

Upon successful completion of this material, the reader should be able to:

1. Describe reasons why there are dose limitations.
2. Calculate adult and pediatric patient dosages for most nuclear medicine studies.
3. State the relative advantages/disadvantages of dose limitations.
4. Compare and contrast dosing requirements for planar and SPECT imaging.
5. Describe dosing limitations for pregnant and breast-feeding patients.
6. Describe factors that affect image acquisition.
7. List current dosing regimens for diagnostic nuclear medicine.
8. Understand pediatric dosage estimates/calculations.

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VI. SUMMARY AND CONCLUSIONS

FACTORS TO CONSIDER WHEN SELECTING RADIOPHARMACEUTICAL DOSAGES FOR DIAGNOSTIC PROCEDURES

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INTRODUCTION

One of the objectives of Nuclear Medicine is to provide accurate and useful diagnostic information regarding a patient's condition, while keeping the radiation absorbed dose as low as reasonably achievable. This is primarily accomplished by limiting the amount of radioactivity administered, but not to such an extent that the resulting image/data becomes difficult to interpret due to inadequate or suboptimal information (photon density). Patient exposure can also be reduced by using short-lived, photon-emitting (non-particulate) radionuclides that are quickly eliminated from the body, i.e., short effective half-life. Usually, larger amounts of these radionuclides can be administered compared to radionuclides with long effective half-lives, thus allowing more photons available for improved information density per unit time. This phenomenon enhances image quality while shortening the acquisition time. Other characteristics of a radiotracer that may affect image outcome and patient exposure include 1) the relative abundance of photons emitted, 2) the type of emission, i.e., particulate or non-particulate, and 3) the photon energy. When limited radiopharmaceuticals are available to image a specific organ, it is sometimes necessary to use a radiotracer with suboptimal physical and biological characteristics because the benefits of a correct diagnosis, in most cases, outweigh any minimal risks to the patient (1). In this lesson, past and current trends in nuclear medicine dosing will be reviewed, factors affecting dose limitations will be presented, and current dosing regimens for diagnostic radiopharmaceuticals will be discussed.

TRENDS IN RADIONUCLIDE IMAGING

The concept of Nuclear Medicine was first applied in the 1940s, when scientists attempted to quantitate the percentage of ^{131}I taken up by the thyroid gland. Utilizing the Geiger Müller (GM) tube, the efficiency of detecting ^{131}I gamma rays was only 1%, with marginal results. In the late 1940s,

photomultiplier tubes were discovered to detect individual scintillations, and with amplification, large electronic pulses could be produced for each scintillation. When coupled to a gamma ray detector, calcium tungstate, the first trials using ^{131}I produced a detector efficiency of 25.8%, a big improvement from the GM tubes. The first clinical application involved an intravenous dose of 200 μCi of ^{131}I, with the complete mapping of the thyroid gland in one and one half hours. This time-consuming, tedious process led scientists to attempt to improve the sensitivity of this detection system and to also make efforts toward automating the method.

These improvements resulted in a detection system sensitivity so high that a 24-hour thyroid uptake could be measured with as little as 1 uCi of ^{131}I. When Dr. Edith Quimby, a member of the Human Usage Committee of the Atomic Energy Commission, was made aware of this development, she stated that she would recommend this procedure be permitted on hospital patients if the administered dose could be less than 40 uCi. This led to the production of the first scintillation area scanner in 1950.

When hermetically-sealed thallium-activated sodium iodide [NaI (Tl)] in the form of clear single crystals became commercially available, they quickly replaced the calcium tungstate used in commercial scanners. This was followed by the development of focused multichannel collimators that resulted in higher sensitivity, allowing a smaller administered dose, a shorter scanning time, and improved image quality. New imaging agents were developed in the 1950-1960s that allowed for scanning of organ systems other than the thyroid. Examples of these early radiopharmaceuticals include ^{131}I labeled human serum albumin for brain tumor scanning, colloidal ^{198}gold for liver imaging, and ^{131}I labeled rose bengal for imaging the hepatobiliary tract.

Further advancements occurred with the development of a rate-controlled background cutoff system and photoscanning, in which images were printed on standard-size X-ray film, which appealed to radiologists. Again, additional radiotracers became available; ^{51}Cr labeled sensitized red cells for spleen imaging, ^{131}I labeled iodohippurate sodium for kidney function tests, and blood pool imaging agents, among others. Each of the radioisotopes described is characterized by relatively high energy photons. Therefore, the rectilinear scanner, with its thick crystal and special collimator provided an excellent imaging device (3).

In 1957, Anger described a single crystal camera (scintillation camera) that viewed all parts of the radiation field continuously, rather than scanning from point to point as was necessary with the rectilinear scanner (3,5). The collection of gamma photons was markedly improved by use of a parallel-hole collimator. This enabled larger fields of view, shorter imaging times, sharper images, and the possibility of time-sequenced dynamic imaging. This imaging system was not readily accepted in the nuclear medicine community because of the poor detection efficiency of the system when imaging with ^{131}I. It was not until the introduction of ^{99m}Technetium by Harper et al. (3,7) and the wide range of ^{99m}Tc-labeled radiopharmaceuticals developed in the late 1960s, which this scintillation camera was routinely used. Examples of ^{99m}Tc-labeled radiopharmaceuticals developed were ^{99m}Tc-pentetate (DTPA) and ^{99m}Tc-glucoheptonate for brain and renal imaging, ^{99m}Tc-MAA for pulmonary perfusion studies, ^{99m}Tc-labeled polyphosphates and diphosphonates for bone imaging, ^{99m}Tc-sulfur colloid for liver/spleen imaging, and various ^{99m}Tc-labeled hepatobiliary tract imaging agents (3).

Today, commercially-available scintillation cameras employ a single sodium iodide crystal measuring between 11 and 20 inches (25-50 cm) in diameter and from 0.25 to 0.5 inch (0.64-1.27 cm) in thickness as the detector unit. The crystal is viewed by many photomultiplier tubes (19 to 91 or more) usually arranged in a hexagongal array (5).

The development of x-ray computed tomography (CT) in the early 1970s was a stepping stone for the application of the principles of image reconstruction in nuclear medicine. One of the problems with conventional radionuclide imaging is that the images are two-dimensional projections of three-dimensional source distributions. Images of structures at one depth in the patient can be obscured by overlying and underlying structures. An alternative approach is tomographic imaging where two-dimensional representations of structures at a certain depth or plane are viewed in a three dimensional object (8). After the development of CT, tremendous strides were made with emission computed tomography (ECT). The availability of small dedicated computers with high capacity for acquisition of data made this advancement possible (6).

Currently there are two types of ECT utilized in nuclear medicine, and they are based on the type of radionuclides used: 1) single photon emission computed tomography (SPECT), which uses gamma-emitting radionuclides such as ^{99m}Tc, ^{123}I, ^{67}Ga, and ^{111}In, and 2) positron emission tomography (PET), which uses positron (B^+)-emitting radionuclides, such as ^{11}C, ^{13}N, ^{15}O, ^{18}F, ^{68}Ga, and ^{82}Rb, among others (10).

These two imaging modalities have an improved sensitivity over conventional radionuclide imaging

TABLE 1. COMMON RADIOPHARMACEUTICALS IN CLINICAL USE

TRACER	APPLICATIONS
^{99m}Tc-exametazine	imaging of CNS
^{99m}Tc-bicisate	imaging of CNS
^{111}In-pentetate	imaging of CSF kinetics
^{99m}Tc-medronate	bone imaging
^{99m}Tc-oxidronate	bone imaging
^{99m}Tc-pertechnetate	imaging of thyroid, salivary glands, ectopic mucosa, parathyroid glands; dacryocystography, cystography
^{123}I-sodium iodide	thyroid imaging, uptake
^{131}I-sodium iodide	thyroid uptake, therapy
^{99m}Tc-red blood cells	imaging of GI bleeds, cardiac chambers
^{99m}Tc-human serum albumin	imaging of cardiac chambers
^{99m}Tc-macroaggregated albumin	lung perfusion imaging
^{133}Xe-gas	lung ventilation imaging
^{81m}Kr-gas	lung ventilation imaging
^{99m}Tc-pentetate	radioaerosol ventilation imaging; renal imaging and function studies
^{99m}Tc-mertiatide	renal imaging and function studies
^{99m}Tc-gluceptate	renal imaging
^{99m}Tc-succimer	renal imaging
^{125}I-iothalamate	measurement of glomerular filtration
^{131}I-iodohippurate	renal imaging and function studies
^{99m}Tc-sulfur colloid	imaging of RES (liver/spleen), gastric emptying, GI bleeds
^{99m}Tc-albumin colloid	imaging of RES (liver/spleen)
^{99m}Tc-disofenin	hepatobiliary imaging
^{99m}Tc-lidofenin	hepatobiliary imaging
^{99m}Tc-sestamibi	myocardial perfusion imaging
^{99m}Tc-teboroxime	myocardial perfusion imaging
^{99m}Tc-tetrofosmin	myocardial perfusion imaging
^{201}Tl-thallous chloride	myocardial perfusion imaging; parathyroid imaging
^{99m}Tc-pyrophosphate	avid infarct imaging
^{111}In-oxyquinoline	for labeling leukocytes and platelets
^{67}Ga-gallium citrate	imaging of inflammatory processes and soft tissue tumors
^{57}Co-cyanocobalamin	Schilling test
^{32}P-sodium phosphate	therapy of polycythemia vera, palliative treatment of bone pain in patients with skeletal metastases
^{32}P-chromic phosphate	therapy of intracavitary malignancies
^{125}I-human serum albumin	plasma volume determinations
^{51}Cr-sodium chromate	for labeling RBC's
^{131}I-iodomethyl-norcholesterol	adrenal imaging
^{131}I-metaiodobenzyl-guanidine	imaging of pheochromocytomas and neuroblastomas
^{89}Sr-strontium chloride	palliative treatment of bone pain in patients with skeletal metastases
^{111}In-satumomab pendetide	colorectal and ovarian tumor imaging
^{111}In-pentetreotide	somatostatin receptor imaging
Positron Emission Tomography Agents	
^{82}Rb	myocardial perfusion
^{11}C-acetate	metabolism
^{11}C-palmitate	fatty acid metabolism
^{13}N-NH_3	perfusion
^{15}O-H_2O	perfusion
^{15}O-CO_2	perfusion
^{11}C-CO	blood volume
^{18}F-deoxyglucose	metabolism

because the entire organ is imaged instead of just the surface of the organ. More counts are needed to enable evaluation of the entire organ; therefore, the administered activity may be slightly higher than for a planar study (10). The end product is improved clinical results, and in most cases, the benefits outweigh the risks associated with the increased activity administered (6).

The continued introduction of new radiopharmaceuticals (Table 1) that have more desirable physical and biological characteristics, as well as improvements in camera systems, have been, and are, essential for the evolution of nuclear medicine (3). The overall goal should be to reduce a patient's radiation exposure to as low as reasonably achievable (ALARA) while simultaneously obtaining accurate diagnostic information about various disease processes (1).

REVIEW OF RADIATION BIOLOGY

Stochastic and Nonstochastic Effects

Living tissue, when exposed to radiation, can undergo detrimental changes. These changes are a result of physical and chemical reactions in the cells due to absorbed radiation energy. There is a dose threshold point above which acute radiation injuries are produced and this threshold varies with the type of tissue involved. Examples of acute radiation injuries include extensive cellular death, total or partial loss of organ function (e.g., bone marrow depression), and subsequent tissue changes such as decreased blood supply and fibrosis. These effects are referred to as non-stochastic and they are not seen in properly conducted diagnostic nuclear medicine procedures. This is because the absorbed doses from diagnostic nuclear medicine procedures are well below the dose threshold points at which the non-stochastic effects occur. Absorbed doses below these threshold points, however, may eventually result in an increased risk of cancer or inherited disorders. These effects are known as stochastic. As absorbed doses exceed the threshold points for non-stochastic effects, there is an increase in severity of radiation injury to tissue. This does not apply toward stochastic effects because there is no recognized absorbed dose threshold; therefore, even small doses could possibly cause cancer induction (11).

Whenever a nuclear medicine or radiology examination is performed, it is assumed that every increment of absorbed dose to an individual may carry some risk, no matter how small it may actually be. It is difficult to establish a numerical relationship between amount of exposure and frequency of effect. One reason is because the late effects associated with low absorbed doses are not caused exclusively by ionizing radiation; another reason is that these effects may not occur for many years after irradiation. However, risk coefficients have been developed by extrapolation from data involving larger absorbed doses than that used in nuclear medicine and they vary according to the dose-response relationship in the extrapolation process. The cancer mortality risk estimates published by the International Commission on Radiologic Protection are given in Table 2 (11).

TABLE 2: CANCER MORTALITY RISK ESTIMATES BY SITE

Site of Cancer	Mortality Risk ($10^{-3}Sv^{-1}$)
Red bone marrow	2.0
Lung	2.0
Breast	2.5
Bone surfaces	0.5
Thyroid	0.5
Total of all other tissues	5.0

Note: Data is averaged for sex and age, therefore, the average risk estimate for the female breast is twice the given value, and zero for the male.

ICRP Report 52, 1987; p.4, with permission (11).

Radiation Effects on the Fetus

Consideration must also be given to the possible effects of radiation on the developing embryo or fetus. The nature and frequency of developmental effects depend on the stage of development at which exposure occurs, on the absorbed dose received, and on the type of radiation involved. Radiation-induced cancers are also a possibility in this faction of the population and could be expressed during childhood or later in adult life.

Radiation exposure during the month following the first day of the last menstrual period can result in an increase in the probability of spontaneous abortion. Since organogenesis is unlikely during this stage of development, the induction of malformation in the embryo will probably not occur. In the following 2-8 weeks after fertilization, when organogenesis proceeds, there is an assumed increase in radiosensitivity. This is based on malformations observed in exposed experimental animals at corresponding stages of development. However, such malformations have not been observed in human population, most likely due to the slower rate of development of organs in humans. Developing human organs are apparently less susceptable to induction by a brief exposure to radiation because of

the smaller proportion of cells dividing at any one time (11). On the basis of experimental studies, UNSCEAR (1986) (12), assessed the risk of an absolute increase of malformed fetuses to be on the order of 5 x 10^{-1} Gy^{-1} (11).

During the period of 8-15 weeks after fertilization, the human forebrain is developing extensively. Studies of Japanese atom bomb survivors revealed an excess of severe mental impairment in children who received a brief radiation exposure in utero during this period. It may be concluded that the risk of severe mental retardation is a function of the absorbed dose with an estimated risk coeffecient of 4 x 10^{-1} Gy^{-1} (11).

Dose Limitations

Knowing the associated risks of radiation to adult and fetal populations, the ICRP introduced a system of dose limitations (ICRP, 1977) (13). The main features are as follows (11):

1. No practice shall be adopted unless its introduction produces a positive net benefit.

2. All exposures shall be kept ALARA, economic and social factors being taken into account.

3. The dose equivalent to individuals shall not exceed the limits recommended for the appropriate circumstances by the Commission.

The first component refers to justification which implies that more accurate diagnosis or health improvement due to a procedure should outweigh the risk of any eventual stochastic or non-stochastic effects induced by radiation. In other words, by not performing the procedures there is a higher risk to the patient's health than the expected radiation-related risk. The decision of the nuclear medicine physician and referring physician that the procedure will be a net benefit for a patient constitutes justification for the patient's exposure.

A request for the *in-vivo* nuclear medicine procedure should first take in to account the availability, relative efficacy and associated risk of alternative methods. These alternative diagnostic modalities include radiography, x-ray computed tomography, ultrasound, and magnetic resonance imaging (MRI).

The second and third components refer to optimization which means that the effective dose equivalent (a measure of individual organ exposure when radiopharmaceuticals are received by the patient) should not exceed that required to provide the necessary clinical information. This can be achieved by limiting the administered activity to the smallest amount possible without interfering with the outcome of the diagnostic procedure. The Commission has recommended limits of dose equivalents for individuals undergoing certain procedures in nuclear medicine (13).

The optimum activity of a radiopharmaceutical for a given diagnostic procedure can be a complex matter and is difficult to determine, especially when applied to individual patients. Activities needed for procedures that produce quantitative numerical results, i.e., renal clearance, can be assessed with relative ease and precision. On the other hand, activities needed for both dynamic and static imaging procedures are more difficult to determine as one strives to optimize sensitivity and specificity of the study. The amount of activity needed for a nuclear medicine study depends upon many factors. These factors include detector capabilities, radiopharm-aceutical characteristics, and individual patient parameters (11).

IMAGE FORMATION AND LESION DETECTABILITY

Lesion detection is the most important attribute of any image in a clinical setting. The three main factors for lesion detection of an imaging system are image resolution, object contrast, and count density (or information density). These three factors, in combination, allow for optimal image acquisition (14).

Image Resolution

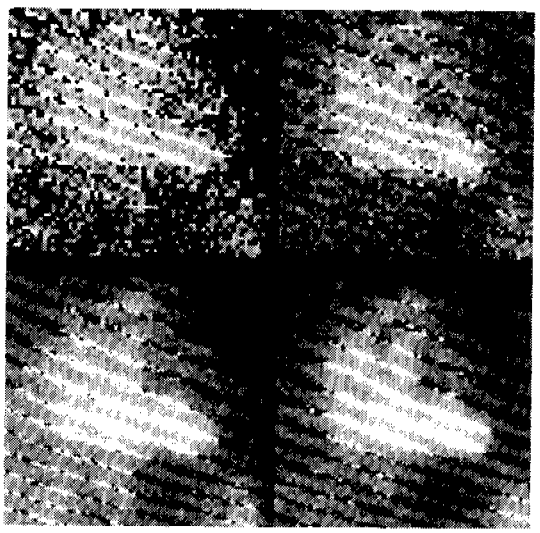
The most important type of resolution is spatial or geometric resolution (14). This varies primarily as a function of the physical characteristics of the imaging device (15). The device is responsible for producing images that clearly separate line sources of activity spaced at various distances or to define different-sized regions of abnormality (4). In other words, the imaging device defines the smallest object that appears as a distinct structure. The limiting factor for a gamma camera imaging system is the collimator resolution. Resolution can be optimized by proper collimator choice and through carefully performed quality control procedures. Even optimal spatial resolution of about 5-10 mm in a nuclear medicine scintiscan compares poorly with the resolution attainable from other imaging modalities. The image sharpness for a radiograph is clearer because the resolution is only a fraction of a millimeter (14). Moreover, patient motion and artifacts can adversely affect image resolution (4).

Object Contrast

Object contrast is the difference between background activity of an image and lesion activity (4,14). In a nuclear medicine scan, this refers to tracer localization in an abnormality compared to tracer localization in normal adjacent tissue. Object contrast is enhanced by selecting the most appropriate radiopharmaceutical and by imaging at the time when the count rate and signal-to-background activity ratio are optimal. Tomographic imaging has improved nuclear image contrast because of the various depths this process can detect, thus allowing isolation of the object of interest from overlying tissue. Nuclear medicine scintiscans have high image contrast compared to other imaging modalities, with target to background ratios as high as 10 times greater (14).

Count Density

Count density is the number of counts recorded per unit area of the radioactive source being imaged (counts/cm^2) (4,15). A minimum number of counts is needed for a difference to be observed between statistical variation and abnormal accumulation of counts in relation to surrounding background (15). All x-ray and radionuclide images result from collecting large numbers of photons. There is an inverse relationship between the square root of the number of photons collected and the degree of statistical uncertainty. Therefore, higher-count density images allow better delineation of edges in the image, less uncertainty, and better detection of lesions (Figure 1).



The images of the heart were recorded to a computer using ^{99m}Tc-labeled red blood cells. The images contain 10,000 counts (upper left), 50,000 counts (upper right), 500,000 counts (lower left), and 1,000,000 counts (lower right). The images have been normalized to a similar image intensity for the purpose of comparison.
Palmer, et al., 1992; p.57, with permission (14).

For most applications, the acceptable range of count density is between 400 and 1200 counts/cm^2, with the upper end of this range being the most optimal for image formation. Count densities higher than 1200 counts/cm^2 add little to image quality. If more photons need to be collected for an optimal count density, the physician can either give a larger tracer dose or image for a longer time. The problem with increasing the patient's dose is the increase in exposure the patient will receive. Administered doses are aimed at delivering a radiation burden of less than 5 rads (50 mGy) to the target organ. With this in mind, an increase in imaging time would be more desirable than an increase in exposure. The downside to increasing imaging time is the possibility of patient motion resulting in a degradation of the image (14).

An adequate combination of all three of the parameters (spatial resolution, object contrast, and count density) are required for lesion detectability (4,15). A high resolution with poor contrast will produce an image that is poor quality and of little value. An example of this is a lesion in the middle of a large organ where the contrast between the two is extremely low. This lesion most probably will not be detected because it can not be distinguished from the surrounding organ. If this same lesion is placed in a small organ with satisfactory object contrast, it will most likely be detected. Another example: If an imaging system has good spatial resolution and favorable object contrast between the lesion and the surrounding tissue, a low count density could be detrimental to the resulting image. Too low a number of counts causes the lesion to be indistinguishable from counts caused by the statistical nature of the random decay process (4).

DETERMINATION OF ACTIVITY TO BE ADMINISTERED

There are many other factors that influence image formation (Table 3) (15). Among them are 1) characteristics of the imaging agent and 2) the administered activity.

Imaging Agent/Radionuclide

Ideal imaging agents will have properties that cause them to localize in various organs of interest. If an agent localizes in a region of abnormality, a "hot lesion" (increased photon density) is created and, if it localizes in an abnormality to a lesser degree than surrounding normal tissue, a "cold lesion" is created. Whether "hot" or "cold" lesions, both are difficult to identify if there is poor object contrast due to low target-to-background ratios. Thus, it is

important to have a favorable object contrast when distinquishing between these two types of lesions compared to surrounding normal tissue (9).

TABLE 3: FACTORS INVOLVED IN IMAGE FORMATION

1. Characteristics of the imaging agent
2. Administered activity
3. Collimator design
4. Detector characteristics
5. Pre-image electronic processing techniques
6. Display and recording medium
7. Image data manipulation techniques
8. Patient motion
9. Artifacts

From Rollo, 1977;p.397, with permission (15).

The type of emission of a radionuclide is also important in nuclear medicine imaging. Particulate emissions, i.e., beta or alpha particles, release a lot of energy per unit length of the path they travel. This energy is imparted to living tissue causing increased radiation exposure to the patient. Non-particulate emissions, i.e., photons such as gamma rays or x-rays, travel at a fast speed and impart less energy along the traveled path, resulting in less tissue interaction. Ideally, it is best to have a radionuclide with a high photon/particle ratio.

Two characteristics that are important involving the radionuclide used to label an agent are photon yield and photon energy (4,15).

Photon Yield. Photon yield is the number of photons produced per disintegration of a radionuclide. High yields of clinically-useful photons are generally desirable because the time to acquire a statistically sufficient count density is decreased (4,15). Many radionuclides release more than one photon per disintegration, including ^{99m}Tc; however, not all of the photons released are useful for imaging. The radiation dose to the patient can be increased if there is a high yield of photons with too low an energy (due to tissue absorption). On the other hand, a high yield of photons with high energies can cause poor system spatial resolution due to an increase in scatter and septal penetration of the collimator (15).

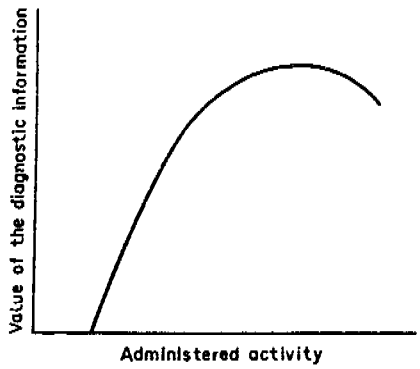
Photon Energy. The photon energy can affect the three parameters previously mentioned, i.e., spatial resolution, object contrast, and count density. Photon energies in the 110 to 160 keV energy range are ideal for scintillation cameras because they are readily absorbed by the sodium iodide crystal and also readily transmitted through body tissues. Their high detection efficiency and high efficiency of being transmitted through the body result in high count densities. Because the photons in this energy range interact with the crystal so well, more electrons can be generated in the photomultiplier tubes, and more information can be gathered, resulting in a good spatial resolution. A good object contrast can be attained when using radionuclides with photon emissions in this energy range. The high count density produces a differential in counts between the organ and the lesion within the organ. Lower photon energies have an increase in attenuation and, therefore, a decrease in this differential. Photon energies greater than 160 KeV have improved object contrast, but less photons are absorbed by the crystal, resulting in poor count densities (4).

Ideally, the radionuclide used to label the imaging agent should have a high photon yield to provide a high count rate. It should also have a sufficiently high photon energy to allow the photons to leave the organ being imaged, but low enough to be sufficiently absorbed by the thickness of the sodium iodide crystal being employed (4,15).

Minimum and Maximum Activity

The administered activity of a radiopharmaceutical, as discussed earlier, is also important. For a given nuclear medicine procedure, the diagnostic information obtained will vary with the amount of administered activity (11).

Threshold. There is an activity threshold point below which no useful diagnostic information can be expected (Figure 2). Above this threshold level, the diagnostic value will go up dramatically with increasing administered activity. When an acceptable quality of the image has been reached, further increases of the administered activity will not significantly improve the results. For each procedure, assessment of optimum activity should be performed. Very little systematic exploration has been done in this area (11).



Schematic representation of the value of diagnostic information as a function of amount of administered activity. From ICRP Publication 52, 1987; p.7, with permission (11).

Additional factors that may limit the amount of activity used are the absorbed dose delivered to the patient and the toxic effects of the radiopharmaceutical.

Absorbed dose. The absorbed dose varies with the physical characteristics of the radionuclide and the biological characteristics of the radiopharmaceutical. For example, radionuclides like ^{131}I deliver a high radiation dose per microcurie of administered dosage, primarily due to the large beta particle component. Conversely, radionuclides such as ^{99m}Tc and ^{123}I have lower associated absorbed doses because they are pure gamma photon emitters (15). In general, radionuclides that have relatively short half-lives and do not have a beta particle component provide the lowest absorbed doses (1,4,15).

The chemical form of the radiopharmaceutical affects the biologic activity. This includes where and how long the agent will remain in the body. Ideally, the agent should only localize within the region of interest, and all other activity should be eliminated rapidly from the body (4).

Toxic Effects. Toxic effects directly related to the administered dosage are rare. The amount of imaging agent administered in a given study is of the order of milligrams or less, which is a very small amount (15). In fact, it is not generally enough to produce a pharmacologic or toxicologic response. For example, a typical 10 uCi diagnostic dosage of sodium iodide ^{131}I will contain only 8×10^{-11} g of iodine. This is only .00005% of the daily dietary intake of iodine. This obviously poses no threat to those who are allergic to iodine (1).

Therefore, the factor that most significantly affects the amount of activity used in a nuclear medicine procedure is the radiation absorbed dose delivered to the patient. In most cases, the toxic effects are rarely, if ever, a concern (15).

The administration of activity levels larger than the optimum amount should be discouraged. There are areas in the world where there are limited resources, and the amount of activity is increased in order to cut down on examination time. This increases the productivity of the medical staff and availability of the services. This practice should only take place if it is justified by the benefits.

The administration of activity levels below the optimum will usually lead to poor quality images and, possibly, errors in the diagnosis. In most cases, there is a small reduction in risk, accompanied by a large reduction in benefit. This practice should also be discouraged (11).

Planar vs. Spect Imaging

The amount of activity administered for a given nuclear medicine scan can have an effect on the method of data acquisition, be it traditional planar views or SPECT. Likewise, the method of data acquisition utilized can affect the amount of activity required for administration.

A planar image requires a minimum number of counts to achieve a reasonable image contrast. The optimum count density is about 1000 counts/cm^2. The count density depends on the amount of activity administered, its uptake in the organ of interest, and the length of time the organ is imaged. In some cases, the examination time may have to be prolonged if a suboptimal amount of imaging agent is administered. Planar imaging usually involves imaging at different projections such as anterior, posterior, lateral and oblique. These views can collectively give some information about the depth of a structure, but a more precise assessment of the depth of a structure in an object can be obtained using tomographic scanners (10).

Improved clinical results are achieved with SPECT because there is an elimination of unnecessary information, both background and foreground, improving the target to non-target ratio, and resulting in a more direct image (6). Most cameras used for tomographic imaging contain one to three detector heads mounted on a gantry to allow rotation around the patient for 180° to 360° angular sampling. The camera systems usually have an on-line computer and display system which allows the user to choose the appropriate display grid and reconstruction filter. The term "noise" means any type of unwanted signal in the data. The reconstruction process used on the raw data propagates some statistical noise, thus requiring that a larger number of counts be acquired for SPECT images. For example, a planar image of high quality requires about 500,000 counts per image, whereas, an image of similar statistical quality with SPECT requires acquisition of a much larger number of counts, on the order of 5-15 million counts (6,8,10).

Image noise, in most cases, is analyzed in terms of signal-to-noise ratio (S/N). The significance of the noise depends on its magnitude compared to that of the signal of interest. When comparing the amount of noise generated in a planar image vs. a tomographic image, one must analyze the square picture elements (or pixels) that form the image. Each pixel can be characterized by a total number of counts, N_p. With standard planar images, the data for individual pixels are independent of other pixels in the image, so the noise in a given pixel is equal to the square root of the pixel counts, $\sqrt{N_p}$. This

relationship does not apply to tomographic images, because the reconstructed value for each pixel is influenced by the values in other pixels crossed by the same sampling lines. Therefore, the signal-to-noise ratio for a reconstructed image over a uniform activity distribution is given by the following equation:

$$S/N = \sqrt{\frac{12N}{\pi^2(D/d)^3}}$$

where D is the diameter of the object or body section, d is the linear sampling distance, and N is the total number of counts in the reconstructed image. Noise is expressed in the above relationship as a standard deviation of recorded signal counts. As total counts increase, the S/N will increase. However, as the number of resolution elements (D/d) increases, the S/N will decrease (8).

The fact that a large number of counts need to be acquired in a reasonable imaging time period demands that the detector system be designed for high photon collection efficiency. One way to design the system is to use multiple detectors around the patient to collect several projections at once. However, even with three detector heads simultaneously acquiring data, many collection intervals are required which increases imaging time. This feature makes gamma camera SPECT less useful for dynamic imaging processes that occur within periods of minutes (8). Otherwise, total counts may be increased either by counting for a longer period of time or by administering more activity (10).

Patient Characteristics and Dosing Regimens

Ideally, all nuclear medicine examinations should be individually planned in relation to the clinical problem. Since each patient has different characteristics, i.e., age, size, and gender, the amount of activity utilized in a particular study may vary (11).

Adult Patients. There is no universally-accepted schedule of activity that should be administered to adult patients (see Table 4). With "state of the art" equipment and use of radiopharmaceuticals which are pure gamma emitters, one should use the amount that will ensure that the examination provides the information which it set out to achieve (16).

The possibility of pregnancy should always be taken into account in ***women of childbearing age***. In light of this information, justification for the use of radiopharmaceuticals must be considered before administration (11).

The absorbed dose received from a diagnostic nuclear medicine study is well below that known to cause adverse effects in humans. However, it is preferable to limit fetal exposure as much as possible (14).

ICRP (11) recommends measures and precautions to ensure the prevention or minimization of exposure to an embryo or fetus, include the following:

- patient must be thoroughly interviewed to assess the likelihood of pregnancy,
- in some cases of question, a pregnancy test may be indicated, and
- advisory notices should be posted at several places within the nuclear medicine department to ensure maximum publicity and less unintentional fetal exposure.

There are no currently-used nuclear medicine diagnostic tests in which tissue radionuclide concentrations have sufficiently long effective half-lives to expose an embryo significantly. Therefore, following the administration of a diagnostic radiopharmaceutical, there is no medical reason to wait in attempting to get pregnant, as the risk to the embryo would be negligible (11).

Most radiopharmaceuticals administered to ***pregnant patients*** deliver some radiation to the fetus either from accumulation in adjacent organs or from excretion in the mother's bladder or colon (14). Some undergo placental transfer and distribute in the fetal tissues themselves, i.e., ^{131}I as iodide or ^{99m}Tc as pertechnetate in the fetal thyroid (11).

The first consideration is to determine if the scan is necessary. Great care must be taken to be certain that the examination is indicated. Therefore, a consultation with the referring physician is warranted. If it is determined that the risk of not making a necessary diagnosis is greater than that of irradiating the fetus, the examination should be performed (11). The danger from maternal illness or death is much greater to the fetus than the theoretical harm of radiation. For example, before performing a ventilation/perfusion lung scan, an estimation of the fetal dose should be considered. The tracer accumulation in the bladder of the mother, with some internal scatter from the lungs would be a large portion of the fetus' exposure. To minimize this exposure, a slightly smaller tracer dose than usual could be used, however the patient must be asked to remain still for longer imaging periods. If the chance of lung disease is small, one might consider omitting the ventilation part of the study. However, this part of the study contributes only a small amount of exposure. Also, the patient should be encouraged to void frequently to minimize accumulation of excreted

TABLE 4: ADULT DOSAGES IN NUCLEAR MEDICIINE

	1		2		3	
Radiopharmaceutical	mCi	MBq	mCi	MBq	mCi	MBq
^{99m}Tc-DTPA(kidney)	5.4	200	8.0	296	20.0	740
^{99m}Tc-DMSA	2.7	100	3.0	111	5.0	185
^{99m}Tc-MAG_3	1.9	70	10.0	370	10.0	370
$^{99m}TcO_4^-$(cystogram)	0.6	20	2.0	74		
^{99m}Tc-MDP	13.5	500	20.0	740	20.0	740
^{99m}Tc-colloid(Liver/Spleen)	2.2	80	3.0	111	5.0	185
^{99m}Tc-colloid(marrow)	8.1	300				
^{99m}Tc-RBC's(denatured)	1.1	40	3.0	111		
^{99m}Tc-RBC's(blood pool)	21.6	800	20.0	740	20.0	740
^{99m}Tc-Albumin(cardiac)	21.6	800				
$^{99m}TcO_4^-$(first pass)	13.5	500	20.0	740		
^{99m}Tc-MAA/microspheres	2.2	80	3.0	111	5.0	185
$^{99m}TcO_4^-$(ectopic gastric)	4.0	150	10.0	370	10.0	370
^{99m}Tc-colloid(GI reflux)	1.1	40	1.0	37	0.3	11.1
^{99m}Tc-IDA(biliary)	4.0	150	2.5	92.5	8.0	296
$^{99m}TcO_4^-$(thyroid)	2.2	80	2.0	74	10.0	370
^{99m}Tc-HMPAO(brain)			20.0	740		
^{99m}Tc-HMPAO(WBC)			20.0	740		
^{123}I-hippuran	2.0	75			1.0	37
^{123}I-(thyroid)	0.6	20	.3	11.1	0.2	7.5
^{123}I-MiBG	5.4	200	10.0	370		
^{131}I-MiBG			1.0	37	0.5	18.5
^{67}Ga-citrate	2.2	80	3.0	111	10.0	370
$^{99m}TcO_4^-$(scrotal)			15.0	555		
^{99m}Tc-MAA(R to L shunt)			1.0	37		
^{133}Xe-in saline(lung perf)			30.0	1110		
^{99m}Tc-sestamibi(cardiac)			30.0	1110	30.0	1110
^{99m}Tc-sestamibi(tumor)			30.0	1110		
^{99m}Tc-gluconate			10.0	370	10.0	370
^{201}Tl(cardiac)			2.0	74	3.5	129.5
^{201}Tl(tumor)			2.0	74		
^{111}In(WBC)			0.3	11.1	0.5	18.5
^{133}Xe(ventilation)			8-30	296-1110	10.0	370
^{111}In-DTPA(cysternogram)			.05-.5	1.875-18.5	20.0	740
^{99m}Tc-sulfur colloid(lymph)			1.0	37		
$^{99m}TcO_4^-$(dacryocystography)			.1-.2	3.7-7.4		

1. Paediatric Task Group of EANM, 1990; p.2 (16).
2. Treves, 1995; p.6 (27).
3. Palmer, et al., 1992 (14)

tracer in the bladder (14).

Another consideration is the scenario of a woman who undergoes a nuclear medicine scan and then learns days or weeks later that she was pregnant at the time of imaging. Nothing can be done to modify fetal exposure at this point in time, but the question of potential damage will arise (14). An estimate of the absorbed dose, and the associated risk to the fetus should be made by a qualified expert, whenever a concern such as this arises. Fetal irradiation from a diagnostic procedure rarely, if ever, justifies terminating a pregnancy when basing it on relative risk increment (11). It is important to be extremely sensitive to the concerns of the parties involved and at the same time provide unequivocal reassurance (14). According to NCRP Report No. 54 (17), doses of less than 10 rem (0.1 Sv) are associated with a smaller risk than normal risks associated with pregnancy itself (14,17). Although there is no available evidence to suggest that the amount of exposure from a diagnostic nuclear medicine study causes any harm, the nuclear medicine physician must strive to avoid irradiation of the fetus whenever possible (14).

Research has determined that the transfer of radionuclides into the milk of ***breast-feeding patients*** varies greatly between individuals. Many radiopharmaceuticals are secreted in breast milk. Of the various ^{99m}Tc compounds, sodium pertechnetate reaches the highest concentrations in milk. Average values for each compound were calculated and very large standard deviations were obtained (18).

An acceptable radiation dose to infants following the intake of radioactive milk is not specified. The most recent publications recommend that the effective dose (ED) to the baby be kept below one mSv. In a study obtained from 60 patients, guidelines were formulated by calculating the total theoretical activity excreted in milk until complete decay of the radionuclide, which is higher than that measured over the actual period of collection. Table 5 summarizes the required interruption periods of breast-feeding (18). The following recommendations were presented by Rubow et al. (18), and Mountford and Coakley (19). There are five categories, one of which is for those radiopharmaceuticals which are not excreted in milk to a large extent, but cause a high contact dose to the infant. This exposure is caused by the radiation emitting from the mother when there is close contact between her and the infant. The recommended time period in which the mother and infant can be near each other is referred to as the close contact time.

I. Interruption not essential
   - ^{99m}Tc-labeled disofenin, sulfur colloid, and gluconate

II. Interruption for a definite period
   - ^{99m}Tc-labeled microspheres, pyrophosphate

III. Interruption with measurement
   - ^{99m}Tc-pertechnetate, pentetate (DTPA), erythrocytes
   - In addition, restriction of the close contact time to five hours over a 24 hour period will reduce the effective dose below one mSv.

IV. Cessation
   - ^{67}Ga and ^{131}I

V. Restriction of close contact only (close contact should be restricted to five hours in a 24 hour period)
   - ^{99m}Tc-sestamibi

In summary, breast-feeding does not need to be interrupted after administration of ^{99m}Tc-disofenin, -sulfur colloid, -gluconate, and -sestamibi. However, close contact with the infant should be restricted after administration of ^{99m}Tc-sestamibi. ^{99m}Tc-pyrophosphate and ^{99m}Tc-microspheres require interruption periods of several hours because of the release of free ^{99m}Tc-pertechnetate *in vivo*. High activities of ^{99m}Tc-pertechnetate may require interruption of breast-feeding longer than two days. For ^{99m}Tc-pertechnetate, ^{99m}Tc-pentetate, and ^{99m}Tc-labeled red blood cells, interruption of breast-feeding and also measurement of activity excreted in expressed milk samples is recommended. The amount of free pertechnetate that gets into breast milk varies according to the method of labeling red blood cells, with the *in vitro* method being the lowest. There is a considerably high contact dose associated with labeled red blood cells. Breast-feeding is contraindicated after the administration of ^{67}Ga and ^{131}I. ^{67}Ga has a long effective half-life in milk (avg. of 51 hours) and this is related to its long physical half-life (78 hours). The interruption period calculated is so long, that breast-feeding should cease completely when ^{67}Ga is given to a breastfeeding woman (18).

Hedrick et al. (20) have recommended that breast-feeding should be discontinued for one and one-half to three days following administration of ^{123}I that contains ^{124}I and ^{125}I contaminants.

It seems that less ^{99m}Tc is excreted in milk after

TABLE 5: RADIOPHARMACEUTICALS IN BREAST MILK: DOSIMETRY AND RECOMMENDATIONS

Drug	Activity (MBq)	Effective Dose (mSv)		*u* (hr)	C_u (kBq/ml)	Recommend[h]
		Milk	**Close Contact**			
^{99m}TcO4-	100	8.28	0.012	30	5.21	III
^{99m}TcO4-	800	66.26	0.94	62	0.36	III
^{99m}Tc-HAM	100	3.86	0.08	18	6.24	II
^{99m}Tc-PYP	600	0.91	0.47	8	4.45	II
^{99m}Tc-Disida	150	0.14	0.11	0	5.19	I
^{99m}Tc-SC	100	0.50	0.12	0	5.59	I
^{99m}Tc-DTPA[a]	600	16.12	0.70	32	2.65	III
^{99m}Tc-DTPA[b]	600	0.48	0.70	6	7.00[e]	III
^{99m}Tc-Mibi	900	0.08	1.40	0[e]	3.33	V
^{99m}Tc-gluconate	600	0.28	0.70	0	5.51[e]	I
^{99m}Tc-RBC's	800	0.08	1.25	0[e]	0.002	III
^{67}Ga-citrate	185	77.75	0.97	738	0.001	IV
^{131}I-iodide[c]	40	3930.40	0.68	153	0.000	IV

u=Interruption period before feeding can be resumed;
C_u=Safe concentration at which feeding can be resumed;
a=patient with very high F;
b=Highest F in remaining DTPA case;
c=Teff from present study;
e=No close contact permitted;
g=Interruption period excessively long;
h=recommendations: I, interruption not essential; II, interruption for period *u*; III, interruption with measurement; IV, breast-feeding contraindicated; V, limit close contact only.
Adapted from Rubow, et al., 1994; p.147, with permission (18)

lung scans with macroaggregated albumin (MAA) than with human albumin microspheres (HAM). Data from two separate sources found 0.9-11.3% (avg=4.3%) and 0.3-5.4% (avg=2.4%) of administered activity in breast milk after injections of ^{99m}Tc-HAM and ^{99m}Tc-MAA, respectively. It appears that dosimetry for the two lung agents should be done independently and that MAA would be the agent of choice for lung perfusion on a breast-feeding patient.

The close contact dose after ^{99m}Tc-pyrophosphate is administered to a breast-feeding patient contributes largely to the infant's dose. Even limiting the close contact to periods of breast-feeding for the 24 hours following administration of the radiotracer will not reduce the total dose to below one mSv. Therefore, interruption of breast-feeding for eight hours post administration is recommended and in this case there is no need to restrict close contact after the administration of ^{99m}Tc-pyrophosphate. This adjustment will reduce the total dose to below one mSv (18). In comparison, ^{99m}Tc-medronate has been found to require no interruption of breast-feeding. This may be due to the fact that the phosphonates are cleared from the blood and excreted by the kidneys somewhat faster than pyrophosphate, thus leaving less activity for excretion into breast milk. Also, pyrophosphate is less stable *in vivo* than phosphonates, probably resulting in more free pertechnetate available for transfer into milk (18,19).

The general principle that nothing which could harm the infant should be administered to a nursing mother, must be followed in nuclear medicine practice. The preparation which would yield the lowest radiation dose to the infant and the lowest amount of activity needed to yield the necessary information on a nuclear medicine image should be used (18).

Pediatrics. Radiopharmaceuticals utilized in nuclear medicine studies are not designed for any one specific age group. The same agents used for adult patients are also used in children by simply modifying the dosage of radioactivity administered according to some index of body size (23). Because the pediatric patient has a smaller total body size and organ mass, a child could receive many times the radiation dose (rad, Sv) of an adult if a properly adjusted amount of radiopharmaceutical is not used (24). The biological distribution, extent of organ uptake, and retention of imaging agents vary considerably throughout childhood and also need to be taken into account (11,25).

The amount of a radiopharmaceutical administered to an adult patient in a variety of procedures is reasonably standardized (Table 4). Calculations for a pediatric dosage can be determined based upon the adult dosages given in Table 4. The pediatric dosage scaling factors are designed to ensure maintenance of an effective concentration of the drug in the blood or other tissues (22). The amount of activity needed for a study is ultimately determined empirically. There is a wide variation in recommended pediatric dosages, indicating either disagreement on what constitutes an adequate examination, or lack of attention in titrating dosages down to the least amount required (26).

The concept of minimal administered activity is another concern. This relates to the minimal amount of radioactivity below which the study will be inadequate due to too low a count rate and an unacceptable imaging time. The suggested minimum radioactivity dosages in Table 6 are based on experiences of institutions in Europe that handle numerous neonates. The schedule of administered dosages in Table 6 are lower than those suggested in certain current pediatric nuclear medicine textbooks (16). In premature and newborn infants, the minimum radioactivity dosage should be applied (16,27). It must be kept in mind that these minimum dosages may be too low for older pediatric patients.

There are several methods available for estimating pediatric radiopharmaceutical dosages. Examples of some of these methods are discussed below and summarized in Table 7.

TABLE 7: CHILD'S DOSE = FRACTION(F) X ADULT DOSE

RULE (F)	FRACTION FORMULA
CLARK'S	$\frac{\text{WEIGHT (LB)}}{150}$
YOUNG'S	$\frac{\text{AGE (YEARS)}}{\text{AGE} + 12}$
FRIED'S	$\frac{\text{AGE (MO'S)}}{150}$
AREA	$\frac{m_1^{(2/3)}}{m_2^{(2/3)}}$
WEBSTER'S	$\frac{\text{AGE} + 1}{\text{AGE} + 7}$
HEIGHT	$\frac{\text{HEIGHT(CHILD)}}{174\ \text{CM}}$
BSA	$\frac{\text{BSA (CHILD)}}{\text{BSA (ADULT)}}$

m_1 = body or organ mass of child
m_2 = body or organ mass of adult
BSA for Adult is 1.73 m^2

TABLE 6: MINIMUM AMOUNTS OF ADMINISTERED ACTIVITY

	1		2	
Radiopharmaceutical	mCi	MBq	mCi	MBq
^{99m}Tc-DTPA(kidney)	0.6	20	0.3	11.1
^{99m}Tc-DMSA	0.4	15	0.2	7.4
^{99m}Tc-MAG_3	0.4	15	1.0	37.0
$^{99m}TcO_4^-$(cystogram)	0.6	20	1.0	37.0
^{99m}Tc-MDP	1.1	40	1.0	37.0
^{9m}Tc-colloid(Liver/Spleen)	0.4	15	0.1	3.7
^{99m}Tc-colloid(marrow)	0.6	20		
^{99m}Tc-RBC's(denatured)	0.6	20	0.5	18,5
^{99m}Tc-RBC's(blood pool)	2.2	80	1.0	37.0
^{99m}Tc-Albumin(cardiac)	2.2	80		
$^{99m}TcO_4^-$(first pass)	2.2	80	2.0	74.0
^{99m}Tc-MAA/microspheres	0.27	10	0.2	7.4
$^{99m}TcO_4^-$(ectopic gastric)	0.6	20	0.2	7.4
^{99m}Tc-colloid(GI reflux)	0.27	10	0.2	7.4
^{99m}Tc-IDA(biliary)	0.6	20	0.5	18.5
$^{99m}TcO_4^-$(thyroid)	0.27	10	0.2	7.4
^{99m}Tc-HMPAO(brain)	2.7	100	1.0	37.0
^{99m}Tc-HMPAO(WBC)	1.1	40	0.5	18.5
^{123}I-hippuran	0.27	10		
^{123}I-(thyroid)	0.08	3	0.025	0.925
^{123}I-MiBG	0.95	35	1.0	37.0
^{131}I-MiBG			0.1	3.7
^{67}Ga-citrate	0.27	10	0.25	9.25
$^{99m}TcO_4^-$(scrotal)			2.0	74.0
^{99m}Tc-MAA(R to L shunt)			0.1	3.7
^{133}Xe-in saline(lung perf)			5.0	185
^{99m}Tc-sestamibi(cardiac)			2.0	74.0
^{99m}Tc-sestamibi(tumor)			2.0	74.0
^{99m}Tc-gluconate			1.0	37.0
^{201}Tl(cardiac)			0.15	5.55
^{201}Tl(tumor)			0.5	18.5
^{111}In(WBC)			0.05	1.85
$^{99m}TcO_4^-$(CSF shunt)			0.5	18.5
^{133}Xe(ventilation)			8.0	296
^{111}In-DTPA(cysternogram)			1.0	37.0
^{99m}Tc-sulfur colloid(lymph)			1.0	37.0
$^{99m}TcO_4^-$(dacryocystography)			0.1	3.7
^{131}I(metastatic survey)			1.0	37.0

1. Paediatric Task Group of EANM, 1990; p.2 (16).
2. Treves, 1995; p.6 (27).

Clark's Rule is based on proportional body weights as related to the standard weight mean of 150 lbs. When radioactivity dosages are calculated by weight, the required dosage is usually underestimated. One reason this occurs is that the ratios of organ to body weights in infants are greater than those observed in adults for the same organs (28).

Young's Rule is based on age and it approximates the body weight rule except during the first years of life and adolescence. This rule cannot be used for newborns and consideration must be made for variability in growth at any given age (28).

Fried's Rule is for pediatric patients that are less than one year of age. If necessary, the minimum dosage requirement may be applied with this rule (24).

The Area Rule is exponentially related to the ratio of pediatric and adult body mass or target-organ mass. An accurate estimation of an imaging dosage can be calculated by this rule because it approximates body or organ surface areas (28).

Webster's Rule (modified Young's Rule) will approximate the Area Rule ($m^{2/3}$) relationship until ages eleven or twelve. For older children, Clark's Rule would be more appropriate because Webster's Rule overestimates the dosage in this age group (21,28).

The Height Rule is based on height of the child compared to the mean adult height. It is not a commonly-used method for pediatric dosage calculations because of the large dosages determined, however, it may be useful for some dynamic imaging procedures (26).

The Body Surface Area Rule has been shown, by experience, to achieve the correct dose-response relationship with therapeutic drugs; therefore, this rule has been adapted for diagnostic dosages. Body surface area (BSA) may be estimated from the body weight since it is proportional to the 0.7 power of body weight (Table 8) (2,23).

Estimation of dosages for pediatric patients based on BSA generally provides a good guide for most children above the age of one year. Organ growth and physiological function conform more nearly to body surface area than to body weight. Typically, hepatic and renal function in young infants exhibit slowed metabolism and excretion compared with that in adults. Also, the total body water and extracellular water, where many drugs distribute, are higher in children than in adults. Dosages calculated by weight usually lead to underdosage in children, whereas dosages calculated by BSA give higher values, and a greater count density. Unfortunately, when dosages are adjusted by BSA, the radiation absorbed doses are slightly higher in pediatric patients than those for adults. If dosages are adjusted by weight, the pediatric patient receives a lower radiation absorbed dose, but much longer imaging times are required (2). Having the child remain still for the length of the procedure can become a problem and sedation may be warranted (25).

TABLE 8: PERCENTAGE OF ADULT DOSE APPLICABLE TO CHILDREN OF VARYING WEIGHT BASED ON SURFACE AREA.

WEIGHT KG	WEIGHT LB	SURFACE AREA (METER)	MULTIPLIER FOR ADUL T DOSE
3	6.6	0.20	0.12
6	13.2	0.32	0.19
10	22.0	0.46	0.27
20	44.0	0.75	0.44
30	66.0	0.99	0.58
40	88.0	1.21	0.71
50	110.0	1.41	0.83
65	143.0	1.70	1.00

TO CALCULATE

$$BSA(m^2) = \frac{[BODY\ WEIGHT(KG)]^{0.7}}{11}$$

From Bell, et al., 1974; p.92, with permission (23).

Most nuclear medicine procedures involve either static imaging studies or dynamic imaging studies, or a combination of both. In the case of static images, it is possible that information density (ID) is the most important consideration. It has been demonstrated that the equivalent ID for adults can be achieved for pediatric patients if dosages are adjusted by organ area (Area Rule). Webster's Rule closely approximates this dosage estimation. There is also a small difference between dosage adjustment by organ area and by BSA, so these three methods can be used interchangeably, as long as the patient is of appropriate size for his/her age.

It has been suggested that static imaging of children with an ID approximately that for an adult can be obtained over the same imaging time if dosages are adjusted by BSA for "thin" organs, i.e., thyroid gland, and by weight for "thick" organs, i.e., liver and brain (26). However, this same publication recommends that all static imaging procedure dosages be adjusted by weight because of the radiation dose received from a BSA-derived dosage. In this case, the imaging time for "thin" organs may be longer in order to obtain an adult ID. Bone imaging is

somewhat different because the tracer is distributed throughout the extracellular fluid and if dosages are adjusted by weight, similar peak blood concentrations are achieved in patients of all ages. Because the entire thickness of the bone is imaged, it is also suggested that bone imaging is similar to imaging a "thin" organ. Therefore, dosages adjusted by either weight or BSA are appropriate for bone imaging. Similar considerations apply to ^{67}Gallium citrate imaging.

Dynamic imaging studies require a different approach, because a lot of information is needed in a short period of time. For dynamic renal imaging, adjustments of dosages by height can provide renograms of quality similar to adult studies. Longer imaging times are not useful in this case because renal function is analyzed during the accumulation phase of the renogram. If a "flow" study is not included, less activity is needed for the analysis of renal function, and this applies to adults also. The pediatric dosage estimated by height can be calculated from an adult dosage of as low as 2 mCi if a flow study is not required.

Gated cardiac ventriculography studies can be performed on a pediatric patient utilizing a dosage adjustment by BSA, and there should be sufficient counts for a decent study. It is possible to compensate for a lower count rate by prolonging image acquisition time or by using fewer frames per cardiac cycle to obtain the desired number of counts per frame.

In the case of first pass ventriculography, additional imaging time is not useful in enhancing studies performed in children. Obtaining sufficient counts for a valid time-activity curve is very important in first pass studies. Since the time-activity curve depends on total counts rather than counts per unit area, it might appear that dosages even larger than those calculated by height would be needed. It has been reported that dosages of 200 μCi/kg of ^{99m}Tc-pertechnetate can produce excellent results with first pass determinations of left ventricular ejection fraction in children. This is similar to an adult dosage of 14 mCi adjusted by weight. They improved results by using fewer frames per cycle which lowered temporal resolution. The need for unnecessarily high dosages can be prevented if the temporal resolution is limited to no greater than that required by the physiologic characteristic being measured (26).

In the case of nonimaging studies, such as thyroid uptake, adjusting dosages by weight or BSA seems reasonable, even though counting times will be increased substantially by this approach (26). Mitchell has suggested that the dosage needed for thyroid uptake (or any other organ counting study) can be reduced in children by decreasing the detector distance (22,26). In general, organ counting studies in children can be hindered by relying on the total radioactivity rather than information density. There is also an increased difficulty in limiting the field-of-view of the detector to the organ of interest in small patients (26).

Another consideration in pediatric dosage determinations is the number of particles that should be administered when performing a lung perfusion study. Because pulmonary development is incomplete at birth, the number of particles injected should be limited in young patients. It is estimated that 10% or fewer of the eventual total number of pulmonary capillaries are present at birth. The capillary number increases to 50% of the adult number by age three years and reaches adult numbers (nearly 300 x 10^9 capillaries) by age eight to 12 years (29). The recommended radioactive dosage of ^{99m}Tc-MAA is 25-50 μCi/kg and the recommended particle values are as follows (30):

Neonates:	10,000
Newborns:	50,000
One year old:	165,000
Three year old:	250,000

It should be noted that the particle number should be reduced for patients with suspected or known right-to-left shunt to decrease the chance of systemic embolization from occurring. The number of particles should also be reduced for patients with pulmonary vascular disease, i.e., pulmonary hypertension to eliminate any further perfusion problems (30).

SUMMARY AND CONCLUSION

There are many things to consider when a radiopharmaceutical dosage is administered to a patient. If more than one radiopharmaceutical can be used for a procedure, one should consider the physical, chemical, and biological properties of each. The type of imaging system that is available in the nuclear medicine department may have a bearing on the type or amount of radiotracer to use. SPECT imaging devices require much more data manipulation and this can cause increased amounts of unwanted noise. Thus a larger amount of radioactivity may be needed with SPECT in comparison with planar imaging. Attention must be given to the particular organ system that is being assessed, and further consideration given to the requirements for dynamic flow studies or static images. Dynamic flow studies may require a larger dosage to increase the count density over the short counting periods. Patient characteristics are very

important in dosage determinations. For example, a pediatric patient will require a much lower administered activity compared to an adult patient. Finally, another related factor in dosage determinations is the experience of the nuclear medicine staff, including the nuclear medicine physician, the nuclear medicine technologist, and the radiopharmacist. If certain information is lacking, it is the responsibility of each party to obtain this missing information prior to performing the procedure. The ultimate goal is to provide an accurate diagnosis without comprimising the care and safety of the patient.

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QUESTIONS

1. Which of the following radiopharmaceutical characteristics is not a significant consideration in determining dosages for diagnostic procedures?

   A. radiation absorbed dose
   B. toxic effects (chemical toxicity)
   C. effective half-life
   D. photon abundance

2. The first images of the thyroid gland in nuclear medicine were obtained using a(n):

   A. GM tube
   B. Anger camera
   C. Rectilinear scanner
   D. SPECT system

3. An increased risk of cancer or inherited disorders are possible results from radiation exposure at low doses and are referred to as:

   A. toxic effects
   B. non-stochastic effects
   C. threshold effects
   D. stochastic effects

4. In a female patient, the cancer mortality risk due to radiation exposure is highest at which site in the body?

   A. lung
   B. breast
   C. red bone marrow
   D. thyroid

5. Which of the following is not a factor that can affect the development of a fetus when it is exposed to radiation?

   A. type of radiation
   B. absorbed dose
   C. development stage
   D. length of nuclear medicine procedure

6. According to the ICRP, when the risk of the patient's health from a disease is greater than the radiation-related risk from undergoing a nuclear medicine procedure, there is adequate _____ for the procedure to be performed.

A. optimization
B. dose limitation
C. remuneration
D. justification

7. An imaging device which produces images that show a clear separation between distinct sources of activity is known to have a good _____.

A. object contrast
B. count density
C. spatial resolution
D. image sharpness

8. The ability to detect tracer localization in a lesion compared to normal adjacent tissue is termed:

A. object contrast
B. count density
C. spatial resolution
D. image sharpness

9. An ideal count density for a planar image would be:

A. 100,000 counts/cm^2
B. 10,000 counts/cm^2
C. 1000 counts/cm^2
D 100 counts/cm^2

10. The best combination for an adequate image would be:

A. low count density/good spatial resolution
B. high count density/poor spatial resolution
C. low count density/poor spatial resolution
D. high count density/good spatial resolution

11. An ideal photon energy range for imaging with an Anger camera is:

A. 50 - 100 KeV
B. 110 - 160 KeV
C. 200 - 500 KeV
D. 140 - 250 KeV

12. The activity level below which no useful diagnostic information is obtained is known as the:

A. threshold
B. saturation point
C. optimum activity
D. plateau

13. Which of the following radionuclides delivers the highest radiation dose per microcurie administered?

A. ^{99m}Tc
B. ^{131}I
C. ^{123}I
D. ^{81m}Kr

14. A response to the non-radioactive chemical portion of a radiopharmaceutical (carrier) would be a _____ effect.

A. radiation-induced
B. diagnostic
C. therapeutic
D. toxicologic

15. SPECT imaging requires more activity than planar imaging because:

A. the acquisition time is longer
B. statistical noise is higher
C. more detector heads are used
D. it requires 500,000 counts/image

16. The signal-to-noise (S/N) relationship for SPECT imaging is described by which of the following statements?

A. as resolution elements increase, the S/N increases
B. as number of counts increases, the S/N decreases
C. as the diameter of section increases, the S/N increases
D. as resolution elements increase, the S/N decreases

17. A woman was injected with ^{99m}Tc-sestamibi for a myocardial perfusion study and then two days later she learned that she was three weeks pregnant. What should be done?

A. The pregnancy should be terminated.
B. The study should be repeated.
C. An estimate of the absorbed fetal dose should be made.
D. All of the above.

18. The amount of radiation exposure to a pregnant mother that is considered safer than normal pregnancy risks is:

A. < 10 rem
B. 20 rem
C. 30 rem
D. 40 rem

19. An acceptable effective dose to an infant that is breast-feeding would be below:

A. 1 mSv
B. 2 mSv
C. 5 mSv
D. 10 mSv

20. The recommendation for a breast-feeding patient that has been injected with ^{99m}Tc-medronate is:

A. no interruption
B. cessation
C. interruption with measurement
D. restrict close contact time

21. The recommended interruption time for breast-feeding if the mother was injected with ^{99m}Tc-pyrophosphate is:

A. 8 hours
B. 16 hours
C. 24 hours
D. 32 hours

22. A pediatric dosage rule that is not based on age is:

A. Webster's
B. Clark's
C. Young's
D. Fried's

23. A normal adult dosage for a bone scan using ^{99m}Tc-medronate is 20 mCi. The pediatric dosage for a child that weighs 40 lbs estimated by utilizing the Body Surface Area Rule is approximately (assuming BSA for an adult is 1.73m^2):

A. 6 mCi
B. 8 mCi
C. 10 mCi
D. 12 mCi

24. Using the same information given in question #23, the pediatric dosage calculated by utilizing Clark's Rule is approximately:

A. 5 mCi
B. 7 mCi
C. 9 mCi
D. 11 mCi

25. Which of the following is not a reason to limit the number of particles of ^{99m}Tc-macroaggregated albumin?

A. pulmonary hypertension
B. pulmonary embolism
C. right-to-left shunt
D. newborn patient