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SELF-STUDY TEST

Radiobiology and Radiation Protection

Questions are taken from the *Nuclear Medicine Self-Study Program I*, published by The Society of Nuclear Medicine

DIRECTIONS

The following items consist of a heading followed by lettered options related to that heading. Select the options that you think are true and those that you think are false. Answers may be found on page 101.

1. Suppose that a nuclear medicine clinic's patients were almost exclusively geriatric, i.e., older than about 60 yr of age. Suppose further that the clinic's work load for skeletal imaging has been increasing steadily and throughput is now limited by available camera time during the work day. It occurs to the hospital administrator that the hospital could save the expense of buying a new camera ($200,000) and of hiring a new technologist ($25,000/yr) by simply increasing the usual 20-mCi dosage of ^{99m}Tc-MDP to 50 mCi and reducing the time of imaging for any patient older than 60 yr of age. Although this action might cause a theoretically increased risk of cancer in these patients, this might not be a real concern because the latent period probably would be longer than their remaining life spans. The attitude of an NRC inspector to this policy is likely to be which one of the following?

A. It is acceptable because the NRC does not regulate dosage range.
B. It is acceptable because this is an FDA responsibility and the FDA does not regulate dosage range.
C. It is acceptable because the patients probably will excrete most of the excess radiopharmaceutical into the urine anyway.
D. It is unacceptable because this policy is not conistent with the ALARA philosophy.
E. It is unacceptable because this policy is not consistent with the de minimis philosophy.

2. How does a nuclear medicine physician determine the maximum dosage of a radiopharmaceutical that can be administered to a patient for a routine clinical study?

A. FDA regulations contained in Title 21 of the Code of Federal Regulations
B. NRC regulations contained in Part 35 of Title 10 of the Code of Federal Regulations (Medical Use of Byproduct Material)
C. NRC regulations contained in Part 20 of Title 10 of the Code of Federal Regulations (Standards for Protection Against Radiation)
D. NCRP Report No. 70 (Nuclear Medicine—Factors Influencing the Choice and Use of Radionuclides in Diagnosis and Therapy)
E. Radiopharmaceutical package insert and clinical judgment

3. Current radiation protection philosophy holds that efforts should be expended continually to reduce the radiation exposure of patients, radiation workers, the general public, and the environment, so long as the expenditure of resources to accomplish this reduction does not outweigh the incremental gain in radiation protection. This philosophy is known as

A. de minimis
B. benefit-risk ratio
C. ALAP
D. ALARA
E. relative biological effectiveness

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SELF-STUDY TEST
Radiobiology and Radiation Protection
ANSWERS

ITEM 1: ALARA Philosophy in Nuclear Medicine Practice
ANSWER: **D**
The Food and Drug Administration (FDA) is responsible for establishing the safety and efficacy of drugs, including radiopharmaceuticals, prior to allowing their commercial distribution. As part of the safety evaluation, the toxicity of the pharmaceutical portion of the radiopharmaceutical is tested at the usual doses administered to a patient and at doses many times greater than would ever be administered to a patient. The package insert (label) furnished by the manufacturer (and approved by the FDA) provides a range of suggested dosages; this range is a guideline, not a legal stipulation. Physicians may choose to vary from the conditions of the package label, using either lower or higher dosages than suggested, based on their clinical assessment of the needs of individual patients. A physician's decision to vary substantially from the recommendations in the package insert should be made only after careful consideration, since justification of these doses becomes the physician's responsibility.

The Nuclear Regulatory Commission (NRC) is responsible for ensuring the safe use of by-product material. Its rules stipulate that only those individuals with appropriate education and experience are licensed to use radioactive materials in humans for diagnosis, therapy, and research. The NRC relies on the FDA to establish the safety and efficacy of radiopharmaceuticals and does not attempt to include or exclude radiopharmaceuticals based on its own independent judgment. The NRC has established groups of radiopharmaceuticals that require similar levels of experience, types of instrumentation, and radiation protection precautions. A physician may use any or all of the radiopharmaceuticals in a group for which he or she has gained approval, and may use any new radiopharmaceutical that is subsequently added to that group (as a result of approval by the FDA). The NRC does not stipulate or suggest any dosage ranges for any radiopharmaceuticals, whether diagnostic or therapeutic. The physician is expected to be familiar with the package insert and with the standard of care nationwide with respect to each radiopharmaceutical. The physician's clinical judgment is the deciding factor in determining the actual dosage given a patient.

Radiation protection regulations in the United States are based on the conservative assumption that radiation effects at low doses can be predicted from high-dose effects by extrapolating the dose–response curve from the high-dose region to zero-dose. A consequence of this assumption is that some small effect must be presumed for all doses, even very small doses where the occurrence of the effect may not be established. Many radiation protection specialists have argued for years that surely there must be some radiation dose that is so small (de minimis) that any expected effect would constitute a negligible additional risk to the exposed population. The implication of the de minimis dose is that efforts by radiation users and regulators alike would not need to be expended in order to reduce the radiation dose below this level. The de minimis concept, however, does not apply to the situation posed in this question, because the dilemma is whether or not the dosage administered to patients can be increased above that normally used.

In the usual procedure for skeletal imaging with ^{99m}Tc-MDP, imaging is delayed until several hours have elapsed after administration of the radiopharmaceutical. This delay period allows that portion of the ^{99m}Tc-MDP not taken up in bone to be cleared via urinary excretion from the soft tissues, yielding an enhanced target-to-background ratio and improved image appearance. As with all diagnostic radiopharmaceuticals, the actual amount of ^{99m}Tc-MDP injected is small (in the range of 1 mg); an increase from 20 mCi to 50 mCi would have essentially no pharmacologic effect and probably would cause no difference in the distribution of ^{99m}Tc-MDP between bone and extraskeletal structures. There is no evidence that the excess radiopharmaceutical would be preferentially excreted into urine rather than going to bone.

Although it is true that the FDA and the NRC do not regulate the dosage range of a radiopharmaceutical that a physician may use, it is not true that these agencies would sanction the routine use of a radiopharmaceutical at dosage levels substantially different from those suggested in the package insert or reported in the literature. The ALARA (*as low as reasonably achievable*) philosophy applies equally to clinical practice as it does to radiation protection of workers and the environment. If radiation or radioactive materials must be used in order to obtain clinically important information or to effect therapy, there must be a clear benefit to the patient. Furthermore, the patient should not be subjected to unnecessary amounts of radiation, because the benefits derived from the radiation might be eroded by the additional risk of the unwarranted radiation. In an individual patient, the decision may be made to use more than 20 mCi, perhaps even as much as 50 mCi, but that decision should be made for that particular patient and not for a general class of patients. For example, if an elderly patient has difficulty remaining motionless long enough for satisfactory imaging with the lower dosage, a higher dosage may be warranted in order to obtain diagnostic-quality images. This decision to use a higher dosage would be in keeping with the ALARA philosophy because the benefit–risk ratio for this patient would be unacceptable at the lower dosage but acceptable at the higher dosage.

ITEM 2: Maximum Dosage of Radiopharmaceuticals
ANSWER: **E**
FDA regulations do not stipulate dosage levels of any pharmaceutical, whether it is radioactive or not. Radiopharmaceuticals are subjected to the same review procedure as nonradioactive pharmaceuticals, i.e., the filing of a "Notice of Claimed Investigational Exemption for a New Drug" (IND) to authorize the premarketing clinical research on the drug and the subsequent approval of a "New Drug Application" (NDA), which authorizes commercial distribution of the drug. The FDA regulations do not directly impose any limits on the dosage of a pharmaceutical any time during this process. Rather, dosage range during clinical investigation is predicated on available preclinical evidence, and the dosage range suggested in the package insert reflects the scientific evidence submitted to FDA in support of the claims of safety and effectiveness for particular

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SELF-STUDY TEST
Radiobiology and Radiation Protection
ANSWERS

indications. Whereas the IND-NDA process is intended for the development of new commercial pharmaceuticals, there is occasionally a desire to study a radioactive drug in a very limited number of patients strictly for the purpose of obtaining fundamental metabolic or biochemical information. The FDA has provided for this type of investigation in Part 361 of Title 21 of the Code of Federal Regulations. Because the information obtained from these studies will not directly benefit the patients being studied, the FDA has imposed maximum limits on the pharmacologic dose and absorbed radiation doses, which cannot be exceeded in such studies.

Title 10 of the Code of Federal Regulations contains all of the regulations published by the U.S. Nuclear Regulatory Commission. Part 20 deals strictly with radiation protection standards that apply to radiation workers, members of the general public, and the environment. Discussions of exposure to patients in Part 20 are limited to: (1) a section that excludes a radiation worker's dose due to a medical procedure from being added to his occupational exposure and (2) a section that excludes patient excreta from the waste disposal standards. Part 35, which was extensively revised in 1986, sets forth the regulations that control the safe use of by-product radioactive materials or the associated radiations in the clinical practice of medicine. The regulations in Part 35 stipulate the training and experience of physicians who may be authorized to use by-product material, the radiopharmaceuticals that may be used by NRC-licensed physicians, and other requirements related to quality assurance, record-keeping, etc. Part 35 makes no mention of the maximum allowable dosage for any radiopharmaceutical.

NCRP Report No. 70 provides a detailed review of the nuclear medicine imaging process and the factors that must be considered in the design of a radiopharmaceutical or a new imaging procedure. The report discusses typical values of absorbed doses from currently used radiopharmaceuticals and cautions that the ALARA concept should be applied to administered dosage levels; however, it does not offer any suggestions about maximum administered dosages.

There are no regulations that stipulate the maximum dosage of a radiopharmaceutical that a physician may administer to a patient. The FDA has a long-standing policy that the way a drug is administered to a patient is a medical decision best left to the judgment of a qualified physician. In the FDA's view, this policy has always applied to radiopharmaceuticals as well as to nonradioactive pharmaceuticals. In contrast, the NRC formerly restricted the use of a radiopharmaceutical to the chemical form, route of administration, and dosage range stipulated in the package insert; this restriction no longer appears in the complete revision of Part 35 that was published in October 1986 and took effect in April 1987. The FDA's position that dosage levels are to be determined by the physician now applies fully to radiopharmaceuticals. A nuclear medicine physician should prescribe the smallest dosage that will yield a study result of acceptable quality, based on considerations of the sensitivity of the counting or imaging equipment being used and the weight (and sometimes age) of the patient. Patient throughput should be only a minor consideration. However, certain clinical circumstances might justify a higher dose, e.g., a critically ill or unstable patient in whom completing the examination faster would be of definite benefit to the patient. Thus, the maximum dosage of a radiopharmaceutical is to be determined by the nuclear medicine physician using information on absorbed dose from the package insert and exercising his or her best clinical judgment. Dosages significantly above those suggested in the package insert may be used, but the physician should be ready to defend the dosage as being medically justified in each specific instance.

ITEM 3: ALARA Philosophy

ANSWER: **D**

A fundamental tenet of radiation protection philosophy is that no person should be exposed to radiation and radioactive materials unless there is a demonstrable benefit to that person in particular, to society in general, or to both. This posture is based on the conservative but prudent hypothesis that even small amounts of radiation have the potential to cause irreparable damage. The balancing of benefit and risk results in the semiquantitative relationship "benefit-risk ratio," but the benefit-risk ratio does not take into account the costs involved in achieving reduced risk. In high-quality medical practice, the benefit-risk ratio (with regard to radiation exposure) is always clearly greater than one. Benefits and risks are much more difficult to define in other instances, such as the selection of the site for a low-level radioactive waste disposal facility. In these types of cases, the people or institutions accruing the benefit usually are not the same people or communities who are exposed to the risk.

The mandate to reduce risk regardless of the magnitude of the costs (time, personnel, money) is embodied in the philosophy of ALAP, or *as low as possible*. ALAP was the operating philosophy of radiation safety regulatory agencies until recently. Although there is nothing inherently wrong with attempting to control radiation exposures to ALAP, there is a practical problem—how do we define ALAP so that we know when we have accomplished it? A regulatory agency inspector may tell you that 15 mrems/month is ALAP for a nuclear medicine technologist, but your experience may have shown that 20 mrems/month is ALAP for your clinic. Whose definition should be accepted, and who will arbitrate these disputes? ALAP can be extended to the point of requiring that exposures be essentially zero, because additional shielding or other alterations

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no higher than a few names. But looking forward, the visitor sees the names of the dead rising higher and higher, a statistical blur of marks in the distance with micro-detail at hand . . . ."

While illustrating the uses of space-time grids, he draws on our specialty of nuclear medicine. The esophageal transit study, as presented by Herbert Klein, employs dimensional compression of the horizontal component of a series of images, yielding one final image which depicts the important vertical dimension.

Tufte has done it again. If you enjoyed his well-received book *The Visual Display of Quantitative Information*, this sequel will delight by further distilling and extending Tufte's penetrating observations—126 pages of unstirred graphical amalgam, refining a coherent viewpoint on effective communicating.

The more we all must know, the less we can afford inefficient or misleading graphic communication. From the astronomical to the atomic, scientists can accomplish much by embracing Tufte's principles. In the bargain, our work will become more understandable, even to ourselves.

Richard Moore
Massachusetts General Hospital
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Books Received

Therapeutic Endoscopy and Radiology of the Gut (Second Edition). John R. Bennett and Richard H. Hunt, eds, Williams & Wilkins, York, PA, 386 pp, Price: $120.00.

The Language of Fractures (Second Edition). Robert J. Schultz, Williams & Wilkins, York, PA, 333 pp, $49.95.

Radiology in the Management of Cancer. Richard J. Johnson, Brian Eddleston, and Robin D. Hunter, Churchill Livingston, Inc, Chicago, IL, 472 pp, $125.00.

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SELF-STUDY TEST
Radiobiology and Radiation Protection

ANSWERS

in technique could theoretically reduce exposures to negligible levels.

The de minimis concept, as applied to radiation safety, states that there is some level of radiation exposure low enough that any risk posed by that exposure is negligible, and that regulatory resources should not be expended to reduce exposures further if they are below the de minimis level. Health physicists have been urging the adoption of the de minimis concept for many years, but regulatory agencies have been cautious in doing so, because of the political sensitivity of the topic. At the present time, there seems to be a general consensus that the de minimis concept is valid; the difficulty lies in defining a politically acceptable exposure or dose level. The debate now centers on how to define a negligible risk. Here again, what is an acceptable, negligible risk to one person may be unacceptable to another person, e.g., skydiving or off-road motorcycle racing.

Relative biological effectiveness (RBE) is the quantitative expression of the efficiency with which a specified type of radiation causes a particular type of radiation effect, compared with some reference radiation. The reference radiation in early radiobiological work was usually 250 kVp X-radiation. An RBE of greater than one indicated that the radiation being tested was more effective in inducing the effect under study than 250 kVp X-rays, whereas an RBE of less than one indicated that it was less effective. From a radiobiological standpoint, RBE is a useful quantity, and in fact it is the basis of the quality factor used to weight absorbed doses (in rads or grays) to obtain dose equivalents (in rems or sieverts). The RBE is not especially useful for radiation protection purposes, however, because there will be a unique value of RBE for each type of radiation (beta particle vs. gamma ray vs. neutron), for different energies of a given type of radiation (140 keV vs. 511 keV), and for every imaginable radiation effect (induction of cancer, cataracts, tissue necrosis). The quality factor attempts to relate linear energy transfer and RBE for the purpose of controlling personnel exposure to radiation.

The correct answer is ALARA, the acronym for *as low as reasonably achievable*. Unless one's radiation exposure is zero (neglecting background radiation for the time being), there is always room for improvement in lowering the exposure. The proper goal of each radiation worker and each radiation safety officer should be to adopt every reasonable technique that will allow the worker's dose to be decreased. Ultimately, however, a dose level will be reached below which doses can be reduced only by installation of expensive modifications to the building or by implementation of special work rules that impose a heavy burden on the worker or supervisory personnel. The ALAP philosophy told us to take whatever steps were possible, regardless of the burden it placed on the worker or the employer. The ALARA philosophy, on the other hand, allows us to make the judgment that every reasonable effort is being made and that further efforts would merely waste time, money, or both, and not accomplish very much of a dose savings. A formal, written ALARA program must be included in every license application submitted to the U.S. Nuclear Regulatory Commission. Licensees tend to have only two main complaints with this requirement: the paperwork burden of the radiation safety officer is increased, and the definition of what constitutes a quantitative ALARA level is still left to the judgment of the user and/or the regulator.

Note: For further in-depth information, please refer to the syllabus pages included at the beginning of *Nuclear Medicine Self-Study Program I: Part I.*