noninvasively. The scientific, economic, and regulatory problems that have been discussed eventually will be solved.

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Henry D. Royal
Washington University School of Medicine
St. Louis, Missouri
Mallinckrodt Institute of Radiology
St. Louis, Missouri

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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 numbered options related to that heading. Select those options you think are true and those that you think are false. Answers may be found on page 344.

The anticipated effects on an individual of a whole-body radiation dose of 100 rads include:

1. a significant reduction in immune responsiveness
2. permanent sterility
3. a lifetime risk of about 1% for radiation-induced fatal cancers
4. a high likelihood of genetic effects in his or her children
5. epilation and bleeding of gums

True statements concerning nonstochastic effects of ionizing radiation include:

6. The severity of the effect varies with dose.
7. The probability of the effect varies with dose.
8. There often is a threshold dose.
9. The aim of radiation protection should be to prevent these effects.
10. They are limited by cell killing.

The genetically significant dose (GSD)

11. is the dose of radiation each person receives from birth to death.
12. is the dose of radiation that can be shown to have led to a genetic death.
13. from medical exposure in the U.S. is approximately equal to that from background sources.
14. is an index of the presumed genetic impact of radiation exposure to the population.

True statements concerning the genetic "doubling dose" for radiation-induced genetic abnormalities include:

15. It is the amount of radiation that would be expected to add as many new mutations as occur spontaneously.
16. The higher the doubling dose, the greater the risk of *mutations* for a given amount of exposure.
17. A doubling dose administered to a population would produce twice the spontaneous number of mutations in the next generation.
18. It is the reciprocal of the relative mutation risk.
19. The BEIR 1980 estimate of a doubling dose of 50–250 rads was obtained from human epidemiologic studies.

True statements concerning the genetic effects of radiation include:

20. Mutations are usually harmful.
21. Genetic effects observed in the progeny of the A-bomb survivors provide the best estimate of human risk.
22. They appear to depend very little on the stage of germ cell development at irradiation.
23. They are independent of the rate of delivery of the radiation.
24. Their likelihood decreases as the time interval between irradiation and conception increases.

Statements that support the concept of multistage development of cancer following irradiation include:

25. In irradiated populations no excess risk of breast cancer has been seen until exposed individuals reached ages at which spontaneous cancers are observed.
26. The excess incidence of radiation-induced bone cancer and leukemia appear within a few years.
27. There is a long latent period for radiation induction of most tumors.
28. Latent periods for radiation-induced cancers are reduced by "promoters."
29. Transformation to malignancy by viral oncogenes appears to require activation of more than one cellular oncogene.

Cancers induced in humans by acute whole-body radiation exposure

30. generally can be distinguished from those occurring naturally.
31. typically develop after latent periods of 10 years or more after irradiation.
32. are the most important late somatic effect.
33. are more often leukemias than solid tumors.

The risk of radiation-induced cancer is *strongly* dependent on gender for which of the following tumors?

34. breast carcinoma
35. bronchogenic carcinoma
36. leukemia
37. thyroid carcinoma
38. bone sarcomas

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ITEMS 1-5: Effects of Acute Whole-Body Radiation Exposure

ANSWERS: 1, T; 2, F; 3, T; 4, F; 5, F

In general, whole-body doses over 100 rads have significant effects on immune system responsiveness. A whole-body exposure of 100 rads will reduce the peripheral blood lymphocyte count by about 50%. In fact, the immunosuppressive properties of whole-body radiation have been used to prevent rejection of transplanted organs.

The dose in humans that produces permanent sterilization is about 500–600 rads. Such an effect is highly unlikely from a whole-body radiation exposure because a dose of this magnitude is likely to be lethal before sterility is manifest. In males, doses as low as 15–30 rads markedly reduce the sperm count at about 8 wk after exposure. The sperm count slowly recovers over the next several months. At doses above 100–150 rads, the sperm count begins to fall earlier, and after falling practically to zero may recover, but very slowly.

Even with high doses of radiation the likelihood of radiation-induced cancer in an irradiated individual is small. For a whole-body dose of 100 rads the lifetime risk of radiation-induced fatal cancer is about 1%. The risk of radiation-induced genetic effects in the offspring of such irradiated individuals would be quite small. In fact, the study of 18,946 children born to parents who were A-bomb survivors (with a mean dose of 117 rads received jointly by the two parents) showed no statistically significant increase in stillbirths, congenital defects, premature death, and abnormal blood proteins.

Epilation and bleeding of gums would be quite unlikely after a dose of 100 rads; these effects generally occur after doses of about 400 rads.

ITEMS 6-10: Nonstochastic Effects

ANSWERS: 6, T; 7, F; 8, T; 9, T; 10, F

Nonstochastic effects of radiation are those for which the severity, rather than the probability, of an effect varies with the dose, and for which a threshold may occur. Nonstochastic effects of radiation include nonmalignant damage to the skin, cell depletion of the bone marrow, induction of cataracts, and gonadal cell damage leading to impaired fertility. Because the thresholds for these effects are well above the dose equivalent limits for occupational exposure, these nonstochastic effects can be prevented.

Stochastic effects (carcinogenesis) appear to saturate at high doses—the likely explanation for this phenomenon is cell killing. Many nonstochastic effects, on the other hand, specifically occur as a result of cell killing.

ITEMS 11-14: Genetically Significant Dose

ANSWERS: 11, F; 12, F; 13, F; 14, T

The genetically significant dose (GSD) is *not* the dose of radiation each person receives from birth to death and is *not* the dose of radiation that can be shown to lead to a genetic death. Rather, the GSD is an index of the presumed genetic impact of radiation exposure on the population. The GSD is defined as the dose that, if received by every member of the population, would be expected to produce the same total genetic injury to the population as is produced by the actual doses received by various individuals. The GSD for medical radiations is calculated from the frequency of the particular examination in a certain age group of the population, the corresponding gonadal doses and the appropriate weighting factors that take into account the expectancy of offspring in the population. Because the presumed genetic injury is *only* associated with the offspring of irradiated individuals, estimation of GSD from the gonadal doses received by these individuals requires that these doses be weighted for the probability of offspring, i.e., not only must there be gonadal radiation, there must be a probability of offspring for it to have a genetic effect. A nuclear medicine procedure resulting in gonadal radiation exposure to a 70-yr-old woman would not contribute to the GSD because the probability of offspring is nil. The annual contributions to the GSD from background, diagnostic radiology, and nuclear medicine procedures in the U.S. are: 82, 20, and 2–4 mrems/year, respectively.

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ITEMS 15–19: Genetic "Doubling Dose"

ANSWERS: 15, T; 16, F; 17, F; 18, T; 19, F

By definition, the doubling dose is the amount of radiation that would be expected to add as many new mutations as occur spontaneously. Thus, the higher the doubling dose, the lower would be the risk of mutation from any particular radiation dose. The doubling dose is the reciprocal of the relative mutation risk, the fraction by which each added rad of radiation dose would increase the mutation rate above the spontaneous level. Thus, a relative mutation rate of 0.01/rad, a risk of 1/100 per rad, would give a doubling dose of 100 rads. A doubling dose would not double the incidence of mutations in the next generation but would require several generations to be fully expressed, i.e., to reach a new equilibrium. This is because elevations in radiation dose must persist over many generations to result in a new and higher mutation burden in the gene pool of the population. Mutant genes are eliminated from the population faster as the number of mutant genes in the population increases. Eventually (after perhaps ten or more generations) a balance will occur between the rate of increase and elimination of mutations and a new "equilibrium" will be established.

The BEIR-1980 estimate of a doubling dose of 50–250 rads was obtained from data on mice because no genetic effects have been observed in humans.

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ITEMS 20-24: Genetic Effects of Radiation

ANSWERS: 20, T; 21, F; 22, F; 23, F; 24, T

Mutations are almost always detrimental to the organism. Any gene, presumably, is the bearer of some bit of valuable genetic information, a particular command that must be executed if the cell is to function properly. In its mutated form the gene's "action" will be missing.

Because there is no direct evidence in humans of radiation-induced genetic damage (even in the progeny of the A-bomb survivors) it has been necessary to rely on animal studies to estimate the risk to humans. Animal studies have revealed that the type and magnitude of the genetic effect depends on: (1) the stage of germ cell development at irradiation (immature germ cells appear to be capable of repair, whereas, in mature germ cells there is little or no repair); (2) dose rate (lower dose rates and fractionation produce fewer mutations); and (3) the interval between

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exposure and conception (it has been observed that avoiding conception for a time interval after irradiation greatly reduces the production of mutations).

ITEMS 25-29: Multistage Development of Radiation-Induced Cancer

ANSWERS: 25, T; 26, F; 27, T; 28, T; 29, T

For many types of radiation-induced cancer, the epidemiologic evidence suggests that events subsequent to irradiation are required to produce a cell that is capable of uncontrolled proliferation. For example, in irradiated populations no excess risk of breast or lung cancer has been seen until the exposed individuals have reached ages at which these cancers usually are observed in nonirradiated populations. This suggests that induction of these cancers requires one or more time-dependent factors in addition to whatever role ionizing radiation plays in their causation.

Bone cancer and leukemia, on the other hand, have appeared in excess within a few years after exposure, suggesting that the multiple stages must occur rapidly or that they may not be required to complete the carcinogenic process. These observations do not support the concept of multistage tumor induction by radiation.

Another marked contrast that distinguishes radiation-induced leukemia and bone cancer is the return of risk to near normal levels within a period of 30 yr or less after irradiation, whereas, with other cancers the risk period may extend to the end of life. These long latent periods again imply a multistage process. The literature of experimental carcinogenesis abounds with examples in which cocarcinogens or promoting agents modify the dose–response curve and the latent period for radiation carcinogenesis. This reduction in latent period by "promoters" indicates that the process (promotion) is at least a second step after initiation.

Recent studies of malignant transformation by viral oncogenes and activated cellular oncogenes suggest that cellular malignant transformation may require activation by more than one cellular oncogene. It is possible, thus, that the long latent periods that characteristically elapse between irradiation and clinical appearance of the cancer may result from the need for activation of recessive oncogenes or other sequential steps.

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ITEMS 30-33: Radiation-Induced Cancer in Humans

ANSWERS: 30, F; 31, T; 32, T; 33, F

The presence of radiation-induced cancers in a human population is difficult to detect and to quantitate because the cancers induced by radiation are indistinguishable from those occurring naturally. Their existence can be detected only on the basis of a statistically significant excess in irradiated individuals above the natural incidence. Detection of radiation-induced cancers is also difficult because of the long latent periods (typically 10 yr or more for solid tumors) between irradiation and detection, as shown in the following table.

Approximate Latent Periods (yr) for Radiation-Induced Cancers in Humans

Type	Minimum	Mean	Total Period of Expression
Leukemia	2–4	10	25–30
Bone	2–4	15	25–30
Thyroid	5–10	20	>40
Breast	5–15*	23	>40
Other solid tumors	10	20–30	>40

*Varies with age at exposure
Adapted from Ref. 2, below.

Radiation-induced cancers are considered to be the most important late somatic effect of radiation. Leukemia induced by radiation stands out because of the natural rarity of the disease, the relative ease of its induction by radiation, and its short latent period (2–4 yr). When the *total* risk of radiation-induced cancer is considered, however, it is clear that the risk of induced solid tumors exceeds that of leukemia. For the A-bomb survivors, the ratio of radiation-induced solid tumors to leukemias is now approximately 4:1. The major sites of solid cancers induced by whole-body radiations are breast (in women), thyroid, lung, and some digestive organs.

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ITEMS 34-38: Sex Dependence of Radiation Carcinogenesis

ANSWERS: 34, T; 35, F; 36, F; 37, T; 38, F

The incidence of radiation-induced human breast and thyroid cancer is such that the total cancer risk is greater for women than for men. Breast cancer occurs almost exclusively in women, and absolute-risk estimates for thyroid cancer induction by radiation are higher for women than for men (as is the case for the natural incidence). With respect to other cancers, the radiation risks in the two sexes are approximately equal.

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