25. Makrigiorgos GM, Adelstein SJ, Kassis AI. Limitations of conventional internal dosimetry at the cellular level. *J Nucl Med* 1989;30:1856–1864.
26. Fenech M, Morley A. Measurement of micronuclei in lymphocytes. *Mutat Res* 1985;147:29–36.
27. Almassy Z, Krepinsky AB, Bianco A, Koteles GJ. The present state and perspectives of micronucleus assay in radiation protection. A review. *Appl Radiat Isot* 1987;38:241–249.
28. Cole A. Absorption of 20-eV to 50,000-eV electron beams in air and plastic. *Radiat Res* 1969;38:7–33.
29. Kassis AI, Adelstein SJ, Haydock C, Sastry KSR. Thallium-201: an experimental and a theoretical radiobiological approach to dosimetry. *J Nucl Med* 1983;24:1164–1175.
30. Feinendegen LE. High LET-emitters and their relative biological effectiveness. In: Schubiger PA, Hasler PH, eds. *Radionuclides for therapy.* Proceedings of the 4th Böttstein colloquium; Villigen, Switzerland; June 13–14, 1986:39–57.
31. Cole J, Arlett CF, Green MHL et al. Comparative human cellular radiosensitivity. II. The survival following gamma-irradiation of unstimulated (G_0) T-lymphocytes, T-lymphocyte lines, lymphoiblastoid cell lines and fibroblasts from normal donors, from ataxia-telangiectasia patients and from ataxia-telangiectasia heterozygotes. *Int J Radiat Biol* 1988;54:929–943.

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 question or incomplete statement followed by five lettered answers or completions. Select the *one* lettered answer or completion that is *best* in each case. Answers may be found on page 1182.

True statements concerning radiation-induced thyroid cancer include:

1. All types of thyroid cancer are increased in incidence by radiation exposure.
2. It is unlikely to develop as a consequence of administration of ^{131}I in doses used in the diagnosis or therapy of thyrotoxicosis.
3. It can be distinguished from that occurring spontaneously.
4. It is more likely to result from exposure to the thyroid during adolescence than in early childhood.
5. It is more common following external than internal radiation exposure.

True statements concerning probability of causation (PC) calculations for radiation-induced cancers include:

6. They pertain to a particular cancer diagnosed at a particular time following a particular radiation exposure.
7. The PC is equal to the relative risk for radiation-induced cancer divided by the sum of that risk and the spontaneous risk.
8. They may be applied to patients exposed to diagnostic and therapeutic radiation.
9. They consider age, sex, and cigarette smoking habits as well as radiation exposure.
10. They are based on the linear–quadratic model for all cancers.

Iodine-131 therapy for carcinoma of the thyroid has been shown to cause

11. excess deaths from cancer of the bladder.
12. excess deaths from leukemia.
13. increased incidence of malignant salivary gland tumors.
14. reduced fertility.
15. overt evidence of genetic damage.

True statements concerning ^{131}I therapy for thyroid cancer include:

16. Radiation effects on the parathyroid glands occur in about 10% of patients.
17. The limiting tissue response occurs in the bone marrow.
18. Radiation nephritis occurs in about 5% of patients.
19. Cytogenetic changes in circulating lymphocytes are directly related to the blood dose.
20. Radiation-induced vomiting occurs in more than 20% of patients.

Radiation-related effects from high-dose ^{32}P therapy of polycythemia vera include:

21. thyroid cancer
22. leukemia
23. leukopenia

True statements regarding radiation therapy with radiolabeled monoclonal antibodies include:

24. It is effective primary therapy for several types of cancer.
25. The radiation dose distribution within a typical tumor is sufficiently uniform to ensure a tumoricidal dose throughout the tumor volume.
26. The dose to normal tissues does not limit the effectiveness of radiolabeled monoclonal antibodies as a sole method of treatment.
27. Alpha-emitting radionuclides are preferred.

For radiation protection purposes it is generally assumed that a dose to a portion of the bone marrow can be averaged over the entire marrow. Concerning this concept,

28. a dose of 800 rads to 40% of the marrow is equivalent to 320 rads to the whole marrow.
29. the dose calculated in this fashion is the same as the mean marrow dose.
30. the assumption is consistent with a dose–response model incorporating quadratic terms.
31. the assumption applies if partial body doses are high enough to kill cells.
32. the assumption is the basis of the dose equivalent concept.

(continued on page 1182)

REFERENCES

1. Hui KY, Haber E, Matsuda GR. Monoclonal antibodies to a synthetic fibrin-like peptide bind to human fibrin, but no fibrinogen. *Science* 1983;222:1129–1132.
2. Rosebrough SF, Grossman ZD, McAfee JG, et al. Aged venous thrombi; radioimmunoimaging with fibrin-specific monoclonal antibody. *Radiology* 1987;162:575–577.
3. Knight LC, Maurer AH, Ammar IA, et al. Evaluation of indium-111-labeled anti-fibrin antibody for imaging vascular thrombi. *J Nucl Med* 1988;29:494–502.
4. Rosebrough SF, Grossman ZD, McAfee JG, et al. Thrombus imaging with indium-111 and iodine-131-labeled fibrin-specific monoclonal antibody and its $F(ab')_2$ and F(ab) fragments. *J Nucl Med* 1988;29:1212–1222.
5. Jung M, Kletter K, Dudczak R, et al. Deep vein thrombosis: scintigraphic diagnosis with In-111-labeled monoclonal anti-fibrin antibodies. *Radiology* 1989;173:469–475.
6. Hashimoto Y, Stassen JM, Leclef B, et al. Thrombosis imaging with an I-123-labeled $F(ab')_2$ fragment of an antihuman fibrin monoclonal antibody in a rabbit model. *Radiology* 1989;171:223–226.
7. Rosebrough SF, McAfee JG, Grossman ZD, et al. Thrombosis imaging: a comparison of radiolabeled GC4 and T2G1S fibrin-specific monoclonal antibodies. *J Nucl Med* 1990;31:1048–1054.
8. Rubin RH, Fischman AJ, Needleman M, et al. Radiolabeled, nonspecific, polyclonal human immunoglobulin in the detection of focal inflammation by scintigraphy with gallium-87 citrate and technetium-99m-labeled albumin. *J Nucl Med* 1989;30:385–389.
9. Kairemo KJA, Wiklund TA, Liewendahl K, Miettinen M, Heikkonen JJ, et al. Imaging of soft-tissue sarcoma with indium-111-labeled monoclonal antimyosin Fab fragments. *J Nucl Med* 1990;31:23–31.
10. Fischman AJ. When magic bullets ricochet [Editorial]. *J Nucl Med* 1990;31:32–33.

(continued from page 1174)

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

Your nuclear medicine clinic operates from 8AM to 5PM Monday through Friday and is closed on Saturdays and Sundays. On Friday afternoon at 1PM a technologist who was preparing ^{99m}Tc macroaggregated albumin dropped the [^{99m}Tc] pertechnetate stock vial. The vial, which contained 20 GBq (about 500 mCi) of [^{99m}Tc] pertechnetate, broke and its contents splashed on the floor, the wall, and the adjacent cabinets. The contaminated area was in front of the radioactive material storage and waste disposal area, which is about 4 m from the dose preparation area and the dose calibrator. Which of the following statements concerning this accident are true?

33. The amount of ^{99m}Tc spilled is too large to be ignored and to be allowed to decay to background levels.

34. The amount of ^{99m}Tc spilled is sufficiently great that the person who cleans up the debris and decontaminates the area should wear lead gloves, a lead apron, and special disposable clothing.

35. The exposure rate (mR/hour) in the dose calibrator/dose preparation area will be sufficiently great to require that work in this area be discontinued for the remainder of the day.

36. The contaminated area should be completely decontaminated to background levels before leaving for the weekend so that housekeeping personnel will not be exposed to excessive radiation levels.

SELF-STUDY TEST

Skeletal Nuclear Medicine

ANSWERS

ITEMS 1–5: Radiation-Induced Thyroid Cancer

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

Thyroid cancer, in its papillary form, is the predominant radiation-induced entity, with a lesser increase in follicular cancer. The incidences of medullary and anaplastic cancers are not increased by radiation exposure. The etiology of individual cases of thyroid cancer cannot be attributed to radiation by any pathological criteria currently known. Exposure to ^{131}I has not been shown to cause an increased incidence of thyroid cancer in medically treated human subjects, whereas x-ray therapy has been shown to be a potent cause, especially in the youngest exposed individuals, females being more sensitive than males. Adolescents are less sensitive than younger children. The relative risk following external irradiation is at least three times greater than that following irradiation by internal emitters.

References

1. Schneider AB, Recant W, Pinsky SM, Ryo UY, Bekerman C, Shore-Freedman E. Radiation-induced thyroid carcinoma. Clinical course and results of therapy in 296 patients. *Ann Intern Med* 1986;105:405–412.
2. Shore RE, Woodard ED, Pasternack BS, Hempleman LH. Radiation and host factors in human thyroid tumors following thymus irradiation. *Health Phys* 1980;38:451–465.

ITEMS 6–10: Calculating Probability of Causation

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

The radioepidemiologic tables that provide probability of causation (PC) values were designed to estimate the likelihood that a person who has or has had a "radiation-related" cancer and who received a specific dose of radiation prior to its onset developed the disease as a result of the irradiation. Probability of causation tables pertain to a particular cancer in a particular individual.

The relative risk per unit of radiation dose can be used to determine the PC that a given cancer is the result of a previous exposure; this is calculated by use of the following relationship:

$$PC = R/(1 + R),$$

where R is the relative risk due to radiation exposure and the spontaneous risk is 1.

Patients exposed to diagnostic and therapeutic radiation are different from the general population to some degree. Because of selection factors other than radiation, PC values based on radiation risk factors and

(continued on page 1215)

rests. These relatively simple measures usually, but not always, maintain the patient probably within a centimeter and/or a few degrees between the transmission and emission measurements. This has been verified at our institution in a number of cases by carrying our two blood-pool imaging procedures before and after measurements to verify the correct position of the patient. This approach offers the added advantage of keeping the patient relatively stationary during transmission and emission measurements, in addition to maintaining alignment between emission and transmission images.

It is very useful to know the magnitude of the effect produced by misalignment as a function of patient translations and/or rotations. With proper care, these motions can be kept to a minimum, under which circumstances the described effect introduces a, so far, unavoidable but often tolerable source of error.

M.M. Ter-Pogossian
Washington University
St. Louis, Missouri

REFERENCE

1. Thompson CJ, Ranger N, Evans AC, Gjedde A. Validation of simultaneous PET emission and transmission scans. *J Nucl Med* 1991;32:154–160.

(continued from page 1182)

SELF-STUDY TEST ANSWERS

baseline rates in the general population would not apply. For instance, an organ transplant patient may be at a much greater risk, as much as 30 times higher in some cases, for cancer during his or her lifetime compared with a typical member of the population.

Because of the established variation in incidence for spontaneous and radiation-induced cancer, PC tables must take into account both age and sex. Because tobacco smoking (particularly cigarette smoking) is the single most important external risk factor for human cancer, estimated to cause 25%–40% of all cancer deaths in the U.S., it is also taken into account.

The weight of radiobiological evidence favors a linear-quadratic dose response to low-LET radiation for most cancers. Thyroid cancer and female breast cancer are exceptions in that the epidemiologic data for these cancers strongly favor a linear dose response.

Reference

1. Gur D, Wald N. Probability of causation tables and their possible implications for the practice of radiology. *Radiology* 1986;158:853–854.

ITEMS 11–15: Risks of ^{131}I Therapy for Thyroid Carcinoma

ANSWERS: 11, T; 12, T; 13, F; 14, F; 15, F

Edmonds and Smith have reported the follow-up of 258 patients treated with high doses of ^{131}I for thyroid cancer. They observed a small but significant excess of deaths from cancer of the bladder and from leukemia. Despite the high levels of irradiation of the salivary glands, no malignancies and only one adenoma were found. No evidence of reduced fertility or of overt genetic damage has been reported in individuals (and their offspring) treated with ^{131}I for thyroid cancer

References

1. Edmonds CJ, Smith T. The long-term hazards of the treatment of thyroid cancer with radioiodine. *Br J Radiol* 1986;59:45–51.
2. Sakar SD, Beierwaltes WH, Gill SP, Cowley BJ. Subsequent fertility and birth histories of children and adolescents treated with ^{131}I for thyroid cancer. *J Nucl Med* 1976;17:460–464.

ITEMS 16–20: Adverse Effects of ^{131}I Therapy for Thyroid Carcinoma

ANSWERS: 16, F; 17, T; 18, F; 19, T; 20, F

Undesirable side-effects of radiation therapy with internal emitters are much less prominent than those encountered with external beam radiation therapy or chemotherapy. The parathyroid gland is rarely clinically impaired by even the highest dose procedures to the thyroid with ^{131}I; only isolated cases of hypoparathyroidism have been reported. The limiting tissue dose is that to the bone marrow, which receives approximately 0.5 rad/mCi of ^{131}I administered to the patient with thyroid cancer. Radiation nephritis is not a reported complication of ^{131}I therapy (or of other nuclear medicine therapy). Mild nausea may occur, but vomiting is a rare complication (<1%). Cytogenetic changes in circulating lymphocytes occur after internal irradiation as they do after external radiation exposure. Their frequency is correlated with the exposure to blood.

Reference

1. Edmonds CJ, Smith T. The long-term hazards of the treatment of thyroid cancer with radioiodine. *Br J Radiol* 1986;59:45–51.

ITEMS 21–23: Adverse Effects of ^{32}P Therapy of Polycythemia Vera

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

Phosphorus-32 administered as the phosphate in high doses to treat polycythemia vera has the desired effect of decreasing the number of circulating platelets and erythrocytes. Leukopenia, predominantly lymphopenia, is noted as with any other high whole-body radiation exposure. Leukemia does occur in increased frequency in these patients, although it is not certain whether this is due to the radiation exposure per se or to the longer lifespan of ^{32}P-treated patients, giving more time for the natural evolution to leukemia that occurs in this diease. No elevated incidence of thyroid cancer has been reported in patients with polycythemia vera treated with ^{32}P.

ITEMS 24–27: Therapy with Radiolabeled Monoclonal Antibodies

ANSWERS: 24, F; 25, F; 26, F; 27, F

Radiolabeled monoclonal antibodies show great promise for use in diagnosis. However, the tumor-to-background ratios achieved with radiolabeled monoclonal antibodies generally have been too low to permit use of these agents as the sole means of treatment of tumor metastases. The radiosensitivity of the bone marrow usually limits the ability to obtain a full therapeutic effect. Nonuniform dose distribution is due in part to regional blood flow variations, which along with antigenic heterogeneity, nonspecificity of tumor-associated antigens, and changing antigenic composition of tumors, limit the current utility of monoclonal antibody therapy. Because it is difficult to ensure that antibodies will bind to each cell of the tumor, the use of radionuclides emitting short-range, high-LET radiations (e.g., alpha particles) is not optimal. Beta emission is more likely to result in a more uniform dose distribution within the tumor.

References

1. Carrasquillo JA, Krohn KA, Beaumier P, et al. Diagnosis and therapy for solid tumors with radiolabeled antibodies and immune fragments. *Cancer Treat Rep* 1984;68:317–328.
2. Grossman ZD, Rosebrough SF. *Clinical Radioimmunoimaging*. Orlando, FL: Grune & Stratton, 1988.
3. Maners AW, Sanders MM, Pappas AA. Current status of radioligand antibodies in the treatment of malignancy. *Ann Clin Lab Sci* 1988;18:53–57.
4. Order SE. Radioimmunoglobulin therapy of cancer. *Compr Ther* 1984;10:9–18.
5. Vaughan AT, Anderson P, Dykes PW, Chapman CE, Bradwell AR. Limitations of the killing of tumours using radiolabelled antibodies. *Br J Radiol* 1987;60:567–578.

ITEMS 28–32: Dose-Equivalent Concept with Bone Marrow Exposure

ANSWERS: 28, T; 29, T; 30, F; 31, F; 32, F

There is controversy regarding the comparability of risk coefficients based on partial-body radiation exposure with those based on whole-body exposure. For the purposes of radiation protection, it has been assumed that a dose to a portion of the bone marrow could be "averaged" over the entire marrow (i.e., as in the example in the question, a dose of 800 rads to 40% of the marrow would be equivalent to a dose of 320 rads to the whole marrow).

(continued on page 1242)

Med 1986;27:1830–1836.
2. Garcia E, Van Train K. Maddahi J, et al. Quantification of rotational thallium-201 myocardial tomography. *J Nucl Med* 1985;26:17–26.
3. O'Brien A, Gemmell H. Effectiveness of oblique section display in thallium-201 myocardial tomography. *Nucl Med Comm* 1986;7:609–616.
4. DePasquale E, Nody A, DePuey E, et al. Quantitative rotational Tl-201 tomography for identifying and localizing coronary artery disease. *Circulation* 1988;77:316–327.
5. Tamaki N, Yonekura Y, Mukai T, et al. Segmental analysis of stress thallium myocardial emission tomography for localization of coronary artery disease. *Eur J Nucl Med* 1984;9:99–105.
6. Senda M, Yonekura Y, Tamaki N, et al. Axial resolution and the value of the interpolating scan in multislice positron computed tomography. *IEEE Trans Med Imaging* 19854:44–51.
7. Hicks K, Ganti G, Mullani N, Gould KL. Automated quantitation of three-dimensional cardiac positron emission tomography for routine clinical use. *J Nucl Med* 1989;30:1787–1797.
8. Raylman R, Hutchins G, Schwaiger M, Paradise A. Axial sampling requirements for 3-dimensional quantification of myocardial function with positron emission tomography. *IEEE Trans Nucl Sci* 1989;36:1030–1033.
9. Schafer RW, Rabiner LW. A digital signal processing approach to interpolation. *Proc IEEE* 1973;61:692–702.
10. Carter WH. Image sampling and interpolation. *SPIE* 1983;397:477–486.
11. Keys RG. Cubic convolution interpolation for digital image processing. *IEEE Trans Acoust, Speech, Signal Processing* 1981;ASSP-29:1153–1160.
12. Maeland E. On the comparison of interpolation methods. *IEEE Trans Med Imaging* 1988;7:213–217.
13. Gambhir S. Quantitation of the physical factors affecting the tracer kinetic modeling of cardiac positron emission tomography data. PhD dissertation. University of California, Los Angeles 1990.
14. Bard Y. *Nonlinear parameter estimation*, 1st edition. New York: Academic Press; 1974:341.
15. Karp J, Muehllehner G, Mankoff D, et al. Tomograph with volume imaging capability. *J Nucl Med* 1990;31:617–627.
16. Mullani N, Gould K, Hartz R, et al. Design and performance of posicam 6.5 BGO positron camera. *J Nucl Med* 1990;31:610–616.

(continued on page 1215)

SELF-STUDY TEST ANSWERS

This concept is consistent with the "mean marrow dose," which incorporates a linear dose-response model (500 rads to 50% the marrow would have the same effect as 250 rads to 100% of the marrow). Such an approach is clearly inconsistent with a dose model that incorporates terms that are quadratic or otherwise nonlinear (the model assumes that 50 rads to 10% of an organ is equivalent to 5 rads to the whole organ—a *linear* extrapolation). Furthermore, if partial-body doses are high enough to kill a significant number of cells, the hypothesis is surely invalid.

The dose-equivalent concept is not related to partial organ irradiation, but provides a method of expressing all kinds of radiation exposures on a common scale for calculating the effective absorbed dose.

References

1. International Commission on Radiological Protection. *Radiosensitivity and Spatial Distribution of Dose, Publication* 14. New York: Pergamon, 1969.
2. Rosenstein M. *Organ Doses in Diagnostic Radiology.* U.S. Department of Health, Education, and Welfare, HEW Publication (FDA) 76-803. Washington, D.C.: U.S. Government Printing Office, 1976.
3. Shleien B, Tucker TT, Johnson DW. The mean active marrow dose to the adult population of the United States from diagnostic radiology. *Health Phys* 1978;34:587–601.

ITEMS 33–36: Management of ^{99m}Tc Spill

ANSWERS: 33, T; 34, F; 35, F; 36, F

The amount of ^{99m}Tc spilled, 20 GBq, is slightly more than 500 mCi. This clearly is a major spill, and it cannot be ignored under any circumstances. The exposure rate constant for ^{99m}Tc is approximately 70 mR/hr/Ci at 1 m, from which it can be calculated that the exposure rate at the dose preparation area (4 m from a spill of 0.5 Ci) will be on the order of about 2 mR/hr. This is not an alarmingly high exposure rate, and work in this area can continue as necessary. However, it would most assuredly be inconsistent with ALARA philosophy to ignore the spill and to allow personnel to continue to work in the area without efforts to reduce exposure levels.

Because of the large activity of ^{99}Tc involved and the relatively high probability of contaminating large areas of the nuclear medicine clinic and hospital if the contamination were not contained, most radiation safety officers would agree that some decontamination is necessary. The activity is not so large, however, that extraordinary precautions must be taken during the clean-up. The first step is to contain the contamination, i.e., prevent it from spreading beyond the immediate area of the spill. The person who dropped the vial should have immediately placed enough absorbent material on the spill to soak up all of the liquid on the floor. He or she should then have called for assistance and remained in the area until a survey meter was brought to check for contamination of clothing and shoes. The second step should be stopping work long enough to plan how best to proceed. Because the radiopharmaceutical is not significantly volatile, so long as people are excluded from the contaminated area, there is no immediate hazard to anyone. The third step is to put on disposable foot covers, two pairs of disposable plastic gloves, and either a laboratory coat or a surgical scrub suit. The fourth step is to quickly remove all of the broken glass and wet absorbent material and place these into a heavy plastic bag or two nested thin plastic bags; the plastic gloves should be placed in the bag after all of the other debris has been picked up. The fifth step is to attempt to remove the remaining superficial contamination on the walls, cabinets, and floor. All of these contaminated materials should be removed from the clinic area and placed in an approved radioactive waste storage area over the weekend for decay. The dose rate in the area of the spill, which now will be substantially lower than initially, should be reassessed with a survey meter. At this point most radiation safety officers probably would recommend labeling the area with the proper radioactive materials caution signs, cautioning nuclear medicine personnel to avoid the area of the spill for the remainder of the day and over the weekend, and allowing the ^{99m}Tc to decay over the weekend. The contaminated regions of the floor might also be covered with polyethylene sheeting to further reduce the likelihood of dissemination.

If the accident had occurred on Monday morning instead of Friday afternoon, the first five steps for handling the spill should be the same. In fact, this would be true regardless of the time of the week or the activity of ^{99m}Tc involved. However, because the area will be occupied more intensively during the 24–48 hr necessary for ^{99}Tc to decay, greater attention must be paid to the dose rate from the residual contamination and to determine whether any of the residual contamination is removable and might be disseminated on individuals' shoes or clothing. The radiation safety officer should survey the laboratory and make recommendations about avoidance of the contaminated areas or other adjustments in work practices that will be required until the contamination has decayed completely.

For further in-depth information, refer to the syllabus pages in Nuclear Medicine Self-Study I.