9. Pittard, WB III, Geddes, KM, Sutherland, SE, et al.: Longitudinal changes in the bone mineral content of term and premature infants. *American Journal of Diseases of Children* 1990; 144:36-40.
10. Namgung, R, Mimouni, F, Campaigne, BN, et al.: Low bone mineral content in summer-born compared with winter-born infants. *Journal of Pediatric Gastroenterology & Nutrition* 1992; 15:285-88.
11. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research: *Research Involving Children: Report and Recommendations.* Washington D.C., 1976, DHEW Publication No. (OS) 77-0004.
12. Department of Health and Human Services: Final regulations amending basic HHS policy for the protection of human research subjects. *Federal Register* 26 January 1981; 46:8366-86 (p. 8373).
13. Levine, RJ: *Ethics and Regulation of Clinical Research.* New Haven: Yale University Press, 2d ed., 1986, p. 248.
14. 45 CFR 46.102(i).
15. Richardson, RB: Past and revised risk estimates for cancer induced by irradiation and their influence on dose limits. *British Journal of Radiology* 1990; 63:235-45.
16. Mole, RH: Antenatal irradiation and childhood cancer: Causation or coincidence? *British Journal of Cancer* 1974; 30:199-208.
17. Harvey, EB, Boice, JD, Honeyman, M, and Flannery, JT: Prenatal X-ray exposure and childhood cancer in twins. *NEJM* 1985; 312:541-45.
18. Mole, RH: Childhood cancer after prenatal exposure to diagnostic X-ray examinations in Britain. *British Journal of Cancer* 1990; 62:152-68.
19. Yoshimoto, Y: Cancer risk among children of atomic bomb survivors: A review of RERF epidemiologic studies. *JAMA* 1990; 264:596-600.
20. Jonsen, AR: Research involving children: Recommendations of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *Pediatrics* 1978; 62:131-36.
21. Shannon, TA, and Ockene, IS: Approving high risk, rejecting low risk: The case of two cases. *IRB* 1985; 7(1):6-8.
22. Department of Health, Education, and Welfare: Proposed regulations on research involving children. *Federal Register* 21 July 1978; 43:31786-94 (p. 31788).
23. Prentice, ED, Antonson, DL, Jameton, A, et al.: Can children be enrolled in a placebo-controlled randomized clinical trial of synthetic growth hormone? *IRB* 1989; 11(1):6-10.
24. 45 CFR 46.111(a)(1)(ii).
25. Gibbens, DT, Gilsanz V, Boechat, MI, et al.: Osteoporosis in cystic fibrosis. *Journal of Pediatrics* 1988; 113:295-300.
26. Preston-Martin, S, Paganini-Hill, A, Henderson, BE, et al.: Case control study of intracranial meningiomas in women in Los Angeles County, California. *Journal of the National Cancer Institute* 1980; 65:67-73.
27. Preston-Martin, S, and White SC: Brain and salivary gland tumors related to prior dental radiography: Implications for current practice. *Journal of the American Dental Association* 1990; 120:151-58.
28. White, SC: 1992 assessment of radiation risk from dental radiography. *Dentomaxillofacial Radiology* 1992; 21:118-26.

Does Radiation Research in Healthy Children Pose Greater Than Minimal Risk?

William J. Freeman reviewed three studies where X rays were taken of healthy children as part of IRB approved research studies ("Research with Radiation and Healthy Children: Greater than Minimal Risk," this issue). He concluded that using X rays should not be approved for research in healthy children because it represents greater than minimal risk. In one of the studies cited by Dr. Freeman, which was approved by our IRB, Gilsanz performed quantitative computerized tomography (QCT) on 150 children, aged 2 to 20 years (estimated radiation dose approximately one chest X ray).[1]

Dr. Freeman stated that the studies did not fit the criteria of 45 CFR 46.404, 46.405, or 46.406, but "could be approved only under 46.407, by a special panel of experts chosen by the secretary of the HHS." However, under 46.407, the regulations indicate that research may be approvable if

> (a) the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention or alleviation of a serious problem affecting the health or welfare of children; *and*
>
> (b) the Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, education, ethics, law) and following opportunity for public review and comment has determined either that the research satisfies the conditions of 46.404, 46.405 or 46.406; *or* that the research presents a reasonable opportunity to further the understanding of a serious problem affecting the health or welfare of children.

Gilsanz's study was designed to further the understanding of the "differences in the prevalence of osteoporosis and the incidence of vertebral fractures" among white and black *women*. His research did not intend to further the "understanding of a serious problem affecting the health or welfare of *children*." Based on these arguments, the study could not be approved under 46.404, 46.405, 46.406, *or* 46.407.

Our IRB determined that Gilsanz's study proposed research that was designed to develop or contribute to generalizable knowledge regarding osteoporosis and so could be approved under 46.102(d). His study resulted in information that may help to explain why certain groups of women are at higher risk for osteoporosis than others, and may add to the understanding of the mechanisms of osteoporosis in women.

Our IRB also determined that the research involved no greater than minimal risk, which is defined in 46.102(i) as "the probability and magnitude of harm or discomfort anticipated in the research are not greater, in and of themselves, than those ordinarily encountered in daily life, or during the performance of routine physical or psychological examinations or tests." Many children can reasonably expect to receive an X ray in the course of their normal medical examinations during childhood. Although the risk of radiation exposure from one QCT scan is unknown,[2,3] it is believed to be small.[2,4,5] Our IRB thus concluded that the protocol was in keeping with 46.404.

Freeman argues that "minimal risk" can be understood by its meaning in lay person's English. However, Janosky and Starfield found wide disagreement among chairs of pediatric departments on what constitutes "minimal risk" in research on children.[6] IRBs across the country cannot be expected to, and do not, assess risks to common protocols in a uniform manner with uniform results. If one IRB approves a study that another might reject, it does not necessarily imply that the first IRB was wrong and the second right. For ex-

ample, when reviewing research involving child subjects, some adult-oriented IRBs are known to be overly restrictive when compared to pediatric-oriented IRBs.

Freeman's IRB may have found that the study by Gilsanz presented normal children with greater than minimal risk, and not approved it. Our IRB found the risks to be commensurate with those experienced by normal children in routine medical examinations, and the study designed to contribute to generalizable knowledge. Our IRB, therefore, approved the study. Such differences in judgments accentuate the difficulties that confront the IRB in striving to assure that the rights of human subjects are protected and that research is ethically conducted.

Thomas G. Keens, MD
Chair
Gwenn S. F. Oki, MPH
Administrator
Committee on Clinical Investigations
Childrens Hospital Los Angeles
Los Angeles, California

◆

Dr. William Freeman examines three separate studies that used current radiographic techniques to assess bone density in healthy children, one of which represents work done at our institution.[1] He concludes that any exposure to ionizing radiation for research purposes entails risks for the pediatric subjects involved; this conclusion requires careful evaluation and rebuttal.

"We live in a world in which perception of risk is too often confused with real risk. In no field is unjustified risk-related fear more pervasive than in the area of unreasonable concern with hazards of low-level radiation."[2] This statement by Nobel Laureate Dr. Rosalyn Yalow brings sharply into focus the disparity of opinion between the lay community and the scientific community about the risks associated with exposure to low levels of ionizing radiation. The view is commonly expressed in the lay literature that low-level radiation causes malignancy and other adverse biological effects in human populations. This perception is in marked contrast to that held by members of the scientific community who are aware of the data that demonstrates no association between low-level radiation exposure and the frequency of malignant events.

Dr. Freeman's opinion regarding the risk of low-dose radiation is based on extrapolations from observed harmful effects following exposures to high-radiation doses either acutely or chronically. Extrapolations of radiation exposure at such high levels to anticipated effects from low-level radiation doses have generated considerable controversy. The National Academy of Sciences Committee on Biological Effects of Ionizing Radiation concluded that a linear extrapolation is unjustifiably conservative and overestimates the potential harmful effects of low-level ionizing radiation.[2]

All persons are exposed to measurable amounts of radiation in their environment. Sources include cosmic radiation, natural terrestrial radiation, and radiation emanating from chemical elements within the body. There is considerable variation within North America and among various geographic locations around the world with respect to the measurable amounts of natural background radiation (table 1); background radiation levels vary severalfold within the continental United States, and higher levels are found in other countries (table 1). Exposure to these amounts of low-level environmental background radiation is unavoidable.

Many in the lay community are of the opinion that any amount of radiation exposure has adverse biologic effects, and therefore that reductions in exposure to even the lowest level of background radiation reduces the risk of adverse effects. There are no objective data, however, to support this view. Information pertaining to cancer rates in subjects living in geographic regions with differing levels of background radiation does not support the contention that variations in the level of background radiation are related to differences in cancer rates among human populations.[2,3] Thus, subjects living in areas where levels of background radiation are relatively low do not have reduced rates of malignancy. Conversely, there is no increase in the frequency of cancer in populations residing in areas with relatively higher levels of background radiation (table 2).[2,4]

That radiation exposure can result in a number of adverse biologic effects is irrefutable. The level of exposure at which such associations can be demonstrated, however, far exceeds that attributable to background radiation from the environment, which ranges from approximately 65 to 300 millirems per year in the United States (table 1).[6] Prudence dictates that exposure to ionizing radiation be limited to levels known not to cause adverse biologic effects. It appears that the range of exposure defined by the level of natural background radiation conforms to this requirement. Accordingly, variations in annual exposure within the limits of what constitutes naturally occurring yearly background radiation do not deviate from the normal experience.

The amount of additional radiation exposure provided by radiographic diagnostic procedures must be evaluated within the context of radiation exposure from all sources, including background radiation. Statements

Table 1.
Natural Background Levels: Cosmic, Terrestrial, Plus Internal.

Area	Background Level (mrem /year)
U.S. (Atlantic and Gulf Coast)	65-70
U.S. (Noncoastal plains)	80-95
U.S. (Colorado plateau)	125-160
U.S. (Leadville, Colorado)	235
U.S. (Central Florida and New England areas)	200
Brazil (Coastal strips)	500
France (Granite rock areas)	180-350
India (Kerala and Madras states)	1,300
Niue Island (Pacific)	1,000
Egypt (northern Nile Delta)	300-400

Adapted from Brill et al., *Low-Level Radiation Effects.*

about doses of radiation associated with various X-ray procedures lose meaning without a quantitative frame of reference. Careful assessments of the total body equivalent dose of radiation delivered during bone density measurements using quantitative computed tomography (QCT) have been presented.[5,6] For determinations in the lumbar spine, radiation doses are approximately 4 to 7 millirems, and this figure includes the radiation associated with screening digital radiographs used to localize the site of measurement. This amount of radiation is far lower than that associated with other QCT imaging procedures, accounting for the wide range of published figures for the radiation dose associated with QCT measurements of bone density; it is also less than many other commonly used radiographic diagnostic tests (table 3). By comparison, a round-trip transcontinental flight in North America provides an additional exposure to a child of approximately 6 to 8 millirems of ionizing radiation.[5,6]

Members of both the lay and scientific communities should, however, establish levels of concern regarding radiation exposure, whether due to radiographic techniques or other activities such as airplane travel, using currently available knowledge. Dr. Freeman should note that the lack of evidence relating low levels of ionizing radiation from radiographic diagnostic equipment to delayed somatic effects serves as the basis for the recommendation by the American Association of Women Radiologists, American College of Radiology, and the British Institute of Radiology pertaining to acceptable levels of radiation exposure for medical personnel. Accordingly, women radiologists do not interrupt their professional activities during pregnancy although the levels or radiation exposure to both the mother and the fetus are considerably higher than those from natural background radiation.[7-9]

The use of radiation in medical research should always be undertaken with caution and with concern for all parties involved. When children and adolescents are affected, careful assessments of risk, including minimal risk, must be done. Objective information should serve, however, as the final arbiter of these decisions. From the foregoing discussion, it is evident that bone density determinations using CT do not expose children to amounts of ionizing radiation that deviate from the amount that constitutes part of their normal life experience. Based on current knowledge, we have to agree with Dr. Freeman that drawing blood for research purposes in healthy children is not equivalent to exposure to low-dose ionizing radiation for research purposes. Venipuncture is painful, while to date no proven body of evidence has established an increase in any harmful effects of radiation dose-rated and cumulative exposures comparable to those of natural background or even at doses tenfold higher.[2]

Vicente Gilsanz, M.D.
Professor of Radiology
University of Southern California

Thomas F. Roe, MD
Professor of Pediatrics
University of Southern California

William Goodman, MD
Associate Professor of Radiology and Medicine
University of California, Los Angeles

Table 2.
Cancer Rates vs. Background in U.S. White Population, 1950-1967.

State Groupings	7 Highest	14 Next Highest	14 Lowest
Background (mrem/year)	210	178	118
All malignancies	126.3	178	118
Lung	14.5	15.5	21.5
Breast	21.5	22.6	24.4
Leukemia	7.03	7.23	6.91
Thyroid	0.055	0.054	0.054
Malignancies, ages 0-9	8.11	8.31	8.31
Infant/total deaths	0.152	0.159	0.180
Fetal/first year deaths	0.56	0.58	0.61

Adapted from Frigerio and Stowe, "Carcinogenic and Genetic Hazards."

Table 3.
Whole Body Equivalent Doses in Millirems (mrem) for Children at Different Ages.

Exam		Age (years)		
		5	10	20
Chest X ray		4.4	3.9	3.2
Lumbar spine	Anteroposterior	2.1	2.0	1.8
	Lateral	13.1	12.1	11.2
SPA radius		0.2	0.1	<0.02
DPA spine		0.4	0.3	0.3
DPA hip		0.7	0.7	0.6
QCT spine	Scout view	4.8	4.5	4.1
	Axial scan	0.9	0.9	0.8
Natural Background (per month)		22.4	18.1	10.7
Transcontinental flight		3.7	3.0	1.8

SPA — Single Photon Absorptiometry
DPA — Dual Photon Absorptiometry
QCT — Quantitative Computed Absorptiometry

Adapted from Cann, "Why, When and How to Measure Bone Mass."

References

1. Gilsanz, V, Roe, TF, Mora, S, et al. Vertebral bone density in black and in white girls during childhood and puberty. *NEJM* 1991; 325:1597-1601.
2. Brill, B. et al., eds.: *Low-Level Radiation Effects: A Fact Book.* Prepared by Subcommittee on Risks of Low-Level Ionizing Radiation. New York: Society of Nuclear Medicine, 1982.
3. Frigerio, NA, and Stowe, RS: Carcinogenic and genetic hazard from background radiation. In *Biological and Environmental Effects of Low-Level Radiation*, vol. 2. Vienna: International Atomic Energy Agency, 1976, pp. 385-93.
4. National Academy of Sciences, National Research Council, Committee on the Biological Effects of Ionizing Radiations: *Health Effects of Exposure to Low Levels of Ionizing Radiation: Betr V.* Washington, D.C.: National Academy Press, 1990.
5. Cann, CE: Why, when and how to measure bone mass: A guide for the beginning user. In *Expanding the Role of Medical Physics in Nuclear Medicine*, GD Frey and MV Yester, eds. Washington, D.C.: American Physics Institute, 1991, pp. 250-79.
6. Kalendar, WA: Effective dose values in bone mineral measurements by photon absorptiometry and computed tomography. *Osteoporosis Int.* 1992; 2:82-87.
7. Committee on Radiological Units, Standards, and Protection. *Medical Radiation: A Guide to Good Practice.* Reston, Va.: American College of Radiology, 1985.
8. Adler, YT, Fembach, SK, Hayman, LA, et al.: The impact of maternity on radiologists: The AAWR position and its acceptance by women. *American Journal of Radiology* 1986; 146:415-17.
9. Joint Working Party of the Royal College of Radiologists and The British Institute of Radiology: *Pregnancy and Work in Diagnostic Imaging.* London: The British Institute of Radiology, 1992.

◆

The article by Dr. Freeman is interesting. However, to provide some perspective the following points also should be understood.

The study of normal humans is critical to the understanding of the abnormal. Studies in normal babies by definition are not only unavoidable, but essential, so as not to repeat the mistakes of the past, when many studies were done without normal populations and led to erroneous conclusions, diagnoses, and treatment. Numerous misadventures have occurred because of the lack of adequate understanding of normal physiology.

"A baby is not a minor adult" and therefore we cannot extrapolate from adults to babies. Previous studies done on men now have to be reexamined in women. In the past, women were not studied as often, supposedly in part because it was thought they were to be "protected" from the "risks" of research (they might be pregnant, etc.). In reality this approach deprived us of adequate understanding of the health of women. The pediatric and newborn population is suffering similar neglect because of the fear of studying them.

The issue of doing research in healthy versus nonhealthy subjects is important. Obtaining consent in the sick child has more potential for (subconscious) coercion by the physician researcher, since parents may implicitly feel obligated to join a study. This issue is much *less* a problem in the normal newborn infant, since the parent usually is not subjected to any implied pressure. For example, it is well known that normal population studies are most readily performed in well-educated populations, who presumably are able to better sort out ethics and consent issues.

Furthermore, if the argument is made that even a minor increase in risk is an unacceptable risk in normal infants and children, this argument could certainly be made for sick infants and children, because the same incremental increase in risk, even though minor, could be thought of as unconscionable. This nihilistic approach to research, when pushed to the ultimate, would imply that all research is basically unconscionable because it *adds* a small incremental risk. For example, what is a minimal risk if one were to draw blood and the extra blood drawn is only a minimal risk? If the infant or child the next day cuts him or herself and bleeds, and there is a need for transfusion, presumably the incremental blood loss during the study would be enough to tip the child over so that a transfusion may be more likely. The transfusion in turn may result in a minimal risk of exposing the child to hepatitis (especially non-A, non-B), or even HIV. Thus no research, no matter how benign, can be done.

If we are serious about solving problems in infancy and childhood, it is imperative that we examine normal children. For bone, it is extremely important to understand what is normal in order to understand how to treat bone disorders and prevent erroneous treatments (such as huge amounts of vitamin D, or wrong doses of Ca and P). Development of peak bone mass in adulthood may be disrupted by problems of infant bone mineralization especially, which may set the stage for osteoporosis in the future. Osteoporosis is a leading cause of mortality and morbidity, especially in women, and we need to understand how to prevent the disorder. There are minimal risks involved, but it would be a disservice to exaggerate the issues.

Reginald C. Tsang, MD
Executive Director
The Perinatal Research Institute
University of Cincinnati
Medical Center

◆

We would like to respond to the issue of risk from radiation exposure that Dr. Freeman has raised. We strongly believe that normative or control studies are the key to any study of disease states, and prevent the misuse and frequently inappropriate therapeutic adventures that have been part of the history of clinical care. Nevertheless, we will focus on Freeman's estimates of risk from radiation.

Dr. Freeman states, "It was known that intrauterine whole-fetus radiation due to diagnostic, pregnancy-related X rays caused a measurably increased rate of cancer in childhood, with a relative risk of about 2 and an absolute increase of about 1.2 cancer cases per 10,000." Two references are cited.[1,2] What Freeman fails to point out is the dose for which this risk has been estimated. The risks cited are for 1 rad, or 1,000 mrem of exposure. The study by Mole cited by Freeman shows data from Nagasaki and Hiroshima that found an upper risk limit of 124 deaths per million maternal rad. This is equivalent to 1.2 deaths per 10,000 children whose mothers were exposed to 1 rad (1,000 mrem) of radiation, a dose far exceeding those used in the studies analyzed by Freeman. More importantly, it should be noted that this estimate is based on *one death* from malignant disease in 1,292 children less than 10 years of age who were exposed to radiation in utero.[2] This death occurred in a child whose mother was exposed to 40,000 to 179,000 mrem of radiation during pregnancy. It was noted that since only 0.4 deaths were expected, this resulted in an observed increase of 0.6 deaths. The additional reference Freeman cites found a relative risk of 2.4 among twins exposed to an average dose of 1 rad (1,000 mrem) in utero. However, he fails to note that this finding was based on a sample size of 31 and was not statistically significant, with the confidence intervals around this relative risk including 1.0. In addition, it is clearly

stated in one of the papers Freeman cites that "the risk coefficient for irradiation in the third trimester for childhood cancer deaths at ages 0-15 years = 405 x 10^{-4} per cGy fetal whole body dose."[3] This risk is equivalent to 4-5 x 10^{-7} deaths per mrem (1 rem = 1 cGy), or 4 to 5 deaths per *million* individuals: a risk that is not considered a "measurable increase."

There is a point at which risk becomes so low that it can be dismissed. The National Council on Research Protection (NCRP) has defined an annual negligible individual risk level (NIRL) as the boundary below which risk is dismissed from consideration: i.e., at risk of 10^{-7}. The effective dose at which any risk is dismissed due to such a low probability of death is 1 mrem.[4,5]

Because of the sensitivity of an unborn child, the NCRP has recommended that the dose equivalent to the unborn child from occupational exposure of the expectant mother be limited to 50 mrem in a month.[4] As stated by the U.S. Nuclear Regulatory Commission,

> occupational exposure limits are set so low, however, that medical evidence gathered over the past 50 years indicates no clinically observable injuries to individuals due to radiation exposures when the established radiation limits are not exceeded. This was true even for exposures received under the early occupational exposure limits which were many times higher than the present limits. Thus the risk to individuals at the occupational exposure levels is considered to be very low.[6]

However, in any study it is not possible to state categorically that the risk is zero.

Dr. Freeman questions what was known about the risk of radiation at the time the research was conducted. At that time, in 1987, the NCRP determined annual *public* radiation exposure limits to be 100 mrem for continuous or frequent exposure and 500 mrem for infrequent exposure.[5] There was no recommendation given specific to children in this public exposure category, although the setting of public exposure limits is based on the most susceptible group. However, it should be noted that the NCRP Reports nos. 91 and 116 specifically exclude medical procedures from the radiation dose exposure limits and refer to the Food and Drug Administrations's regulations concerning radiation exposure. As Freeman correctly mentions, the FDA regulations state that for research subjects under 18 years of age, the radiation dose shall not exceed 10 percent of the adult dose. However, Freeman does not mention the acceptable exposures. The FDA regulations regarding radiation exposure for research purposes limit total body exposure and exposure to active blood-forming organs, lens of the eye, or gonads to 3,000 mrems per single dose, or 5,000 mrems per annual dose, for adults.[7] These levels result in limits for children participating in medical research of 300 mrems per single dose and 500 mrems per annual dose for total body exposure and exposure to active blood-forming organs, lens of the eye, or gonads. Acceptable doses in children for organs not as sensitive as these are higher, 500 mrem/single dose or 1,500 mrem/annual dose. These exposures include radiation doses from X-ray procedures that are part of a research study.[7] In the studies reviewed by Freeman, the radiation exposures were *well below* these acceptable levels.

Dr. Freeman states that if the added dose from research were 30 mrem, the risk from 125 mrem total (sum of 95 mrem from background and 30 mrem from research) would be 30 percent greater than the minimal risk from whole body background radiation that year, or 10 percent greater than the total background radiation that year including average radon dose to the lung. There are two issues here. The first is the issue of effective dose and second, that the difference in risk between 95 and 125 mrem could even be detected.

All estimates of risk from radiation exposure are based on an effective dose equivalent. This concept, introduced by the International Commission on Radiological Protection, equates the risk from a partial body exposure with that from a whole body exposure.[8] Freeman states that the background radiation exposure, including average radon dose to the lung, is 295 mrem/year to each person. He is implying that the dose from radon is specific to the lung and therefore, would not be included in the background levels. However, in the BEIR V report the dose listed for radon is the average annual *effective dose*, and as such has already been converted to a total body equivalent dose, thus the dose is not specific for the lung. The issue of effective dose also is important in interpreting the

CALENDAR

In honor of its 20th Anniversary, Public Responsibility in Medicine and Research (PRIM&R) is hosting a series of meetings from 30 October to 3 November to coincide with the annual meeting of the Association of American Medical Colleges (AAMC). For information: Joan Rachlin or Danielle Demko, PRIM&R, 132 Boylston Street, Boston, MA 02116; (617) 423-4112; (617) 423-1185 fax.

The following conferences are scheduled:

30 OCTOBER Human Subjects Workshop, sponsored by The Applied Research Ethics National Association (ARENA);

31 OCTOBER-1 NOVEMBER Changes and Choices for Institutional Review Boards: The Inclusion of Women and Minorities in Research, and other Emerging Issues, sponsored by PRIM&R and the Tufts University School of Medicine; and

2-3 NOVEMBER Educating for the Responsible Conduct of Research: The Mandate, the Intent, the Means, sponsored by PRIM&R, the AAMC, the Office of Extramural Research at the National Institutes of Health, Harvard Medical School Division of Medical Ethics, and the Tufts University School of Medicine.

21-22 February 1995 The British Postgraduate Medical Federation will host a two-day course, **Randomised Controlled Trials: Ethical and Legal Issues**, to be held in London. For information: Education Department, BPMF, 33 Millman Sstreet, London WC1N 3EJ; 071-831-6222, ext. 155 or 071-405-5660 (24 hour answerphone); 071-831-1387 fax.

studies cited by Freeman. The radiation doses cited were for a specific site. To equate appropriately these doses with risks from radiation, or those obtained from background radiation, it would be necessary to obtain the *effective dose* from these procedures. This is done by applying a weighting factor and is essentially equivalent to averaging the dose of radiation received at a specific site to what it would be if it were spread over the entire body.[9] Thus, 30 mrem exposure to a 3-mm-wide section of the forearm would result in a minuscule effective dose.

Also, it is important to note that in the BEIR V report it is stated that the largest series of humans exposed to radiation for whom estimates of individual doses are available consists of the populations from Hiroshima and Nagasaki. It also is stated that approximately half of the population of survivors "had radiation doses that were negligible—less than 0.5 rad—and thus serve as a comparison, or 'control' group."[10,p. 162] 0.5 rad is equivalent to 500 mrem exposure. It appears ironic that the risk equations developed from these populations are used to estimate risks at levels significantly lower than what was considered a negligible dose, with those individuals in the population being omitted from the analysis.

The use of comparisons, such as exposure to background radiation, is a way of relating exposures and risks to those presented on an everyday basis. However, since background radiation is not necessarily an exposure that parents choose for their child, perhaps it is better to compare the risk from radiation by choosing to participate in a study to other choices parents make concerning their child. The risk of mortality from 1 mrem of radiation can be equated to the risk of dying from liver cancer by aflatoxin exposure from consuming 20 peanut butter sandwiches (each with 2 tablespoons of peanut butter); the risk of dying from cancer by living in Denver for 2 months or flying 6,000 miles by jet; or the risk of dying from an accident by flying 1,000 miles in a jet, or riding 10 miles by bicycle, or 300 miles by car.[11]

We hope that the readers of Dr. Freeman's article will take the time to check and understand the risk estimates he has provided. These risks should be weighed against the benefits from research on healthy children. How can disease be understood if health is not?

Bonnie L. Specker, Ph.D.
Associate Professor of Pediatrics and Radiology
Children's Hospital Medical Center

Eugene L. Saenger, MD
Professor Emeritus of Radiology
University of Cincinnati Medical Center

References

1. Harvey, EB, Boice, Jr., JD, Honeyman, M, Flannery, JT: Prenatal X-ray exposure and childhood cancer in twins. *NEJM* 1985; 312:541-45.
2. Mole, RH: Antenatal irradiation and childhood cancer: Causation or coincidence? *British Journal of Cancer* 1974; 30:199-208.
3. Mole, RH: Childhood cancer after prenatal exposure to diagnostic X-ray examinations in Britain. *British Journal of Cancer* 1990; 62:152-68.
4. National Council on Radiation Protection and Measurements: *Limitation of Exposure to Ionizing Radiation*. NCRP Report No. 116.
5. National Council on Radiation Protection and Measurements: *Recommendations on Limits for Exposure to Ionizing Radiation*. NCRP Report no. 91.
6. U.S. Nuclear Regulatory Commission, Office of Nuclear Regulatory Research: Instruction concerning prenatal radiation exposure. Regulatory Guide 8.13, Appendix. 1987.
7. 21 CFR 361.
8. International Commission on Radiological Protection: *1990 Recommendations of the ICRP*. ICRP Publication 60. New York: Pergamon Press, 1991.
9. International Commission on Radiological Protection: *Radiological Protection in Biomedical Research*. ICRP Publication 62. New York: Pergamon Press, 1992.
10. National Academy of Sciences, National Research Council, Committee on the Biological Effects of Ionizing Radiation: *Health Effects of Exposure to Low Levels of Ionizing Radiation: BEIR V*. Washington, D.C.: National Academy Press, 1990.
11. Wynne, B: Public perception and communication of risks: What do we know? *Journal of NIH Research* 1991; 3:65-71.

UPDATE

New Presidential National Bioethics Advisory Commission Proposed

The Office of Science and Technology Policy has invited comments on a proposal to establish a new National Bioethics Advisory Commission to examine ethical issues posed by biological and behavioral research with human subjects. The draft charter for the commission (*Federal Register*, 12 August 1994) broadly outlines the NBAC's functions to include consideration of:

> the appropriateness of departmental, agency, or other governmental programs, policies, assignments, missions, guidelines, and regulations as they relate to bioethical issues arising from research on human biology and behavior, and applications of that research. The Commission shall identify broad, overarching principles to govern the ethical conduct of research, citing individual projects only as illustrations for such principles. The Commission shall not be responsible for the review and approval of individual projects.

The NBAC, which will "advise, consult with, and make recommendations to" the National Science and Technology Council, will initially be empowered to examine issues related to "the management and use of genetic information" and "the protection of the rights and welfare of research subjects." Among the more particular issues to be considered under these headings are such questions as genetic privacy, screening for genetic disorders, access to research data or materials developed with public funding, informed consent, and the concept of "minimal risk" prominent in federal regulations governing research with human subjects. Also within the purview of the commission are the adequacy and implementation of federal guidelines for human subjects research. Other potential issues for consideration include rec-