Effects of ionizing radiation in children

Wataru W. Sutow, M.D.,* and Robert A. Conard, M.D.**

HOUSTON, TEXAS, AND UPTON, N. Y.

THIS REVIEW of recent literature was undertaken to obtain a perspective of radiation effects on human beings, particularly the effects on children. Although numerous reports indicate the occurrence of specific deleterious effects after high doses of radiation, documentation of damage in man following chronic exposure to low doses and low dose rates is meager.

The question of differential sensitivity in relation to age is particularly relevant to pediatric considerations. The publications suggesting that fetal irradiation at diagnostic roentgenographic dose levels may be associated subsequently with increased leukemogenesis and carcinogenesis[1, 2, 3] have emphasized the need to obtain more data on human beings. The occurrence of thyroid cancer after irradiation of the thymus during infancy[4, 5, 6, 7] and the age pattern of leukemia in the Japanese A-bomb data[8, 9] have suggested that young children might be more susceptible than adults to the carcinogenic action of radiation. Other data, however, show that leukemogenesis also may be associated with diagnostic radiation in the adult[10] and that the incidences of radiation-induced lung tumors among asbestos and coal gas workers, of bladder tumors in chemical workers, and of leukemia among radiation-treated males with spondylitis in England increased with increasing age.[11] Lack of knowledge regarding the basic mechanisms in radiation carcinogenesis (and spontaneous cancer), in addition to the difficulties inherent in the interpretation of epidemiologic data, warns against uncritical acceptance of conclusions seemingly shown.[11-14]

Considerable data have accumulated describing the effects of radiation on adult human beings. However, less is known about the age dependence of such effects, particularly in regard to children. It is believed that the young are somewhat more sensitive to radiation than are adults and this is generally found to be true in studies on animals and from limited experience with irradiated human beings. In this paper, the somatic and genetic effects of radiation in the human being will be reviewed with special attention to what is known about the relative sensitivity of children. Also, the current attitudes toward the hazards of low-level radiation in children will be examined.

From The University of Texas M. D. Anderson Hospital and Tumor Institute, Pediatric Section, Department of Medicine, Houston, Texas, and the Medical Division, Brookhaven National Laboratory, Upton, Long Island, N. Y.

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*Address, The University of Texas M. D. Anderson Hospital and Tumor Institute, 6723 Bertner Drive, Houston, Texas.

**Address, Medical Division, Brookhaven National Laboratory, Upton, Long Island, N. Y.*

SOMATIC EFFECTS OF HIGH DOSES

Somatic effects that result from substantial doses of radiation have been well documented and the causal relationship of early effects to the fact of exposure has been fairly clearly established. The present knowledge regarding the late effects on humans which occur months and years after the exposure is based on meager data from acute exposures, from epidemiologic investigations, and from occupational and medical exposures.[15, 16] These late effects are nonspecific and cannot be differentiated from naturally occurring disease; only the incidence of the disease is increased.[17] The general pattern of somatic effects following irradiation varies with several factors which include the quality of radiation, absorbed dose, and rate and homogeneity of exposure (spatial distribution).

Acute effects. The median acute lethal dose (LD_{50}) in man for short-term total body radiation is not precisely known but is estimated to be somewhere between 300 and 500 rads.[17, 18] Doses over 2,000 rads are fatal within a few hours, producing rapid clinical deterioration in which neurological symptoms are striking. Between 500 and 2,000 rads, effects are characterized by severe gastrointestinal disturbances; death occurs within a week. After an exposure to 100 to 500 rads, less serious gastrointestinal symptoms predominate in the early clinical pattern. Following subsidence of the gastrointestinal symptoms, the effects of injury to the hematopoietic tissue (infections, anemia, bleeding) may become evident in about 3 weeks.[17] Clinical syndromes of acute radiation injury have been described in detail in a number of publications.[19-24]

The relative sensitivity of children compared with adults to high doses of radiation is not precisely known. "In assessing susceptibilities various end points can be used; the apparent radio-sensitivity of a tissue or organ depends on the method of observation. Sensitivity depends on age at the time of exposure, children being more susceptible than adults."[16] Marshallese children irradiated with 175 rads of whole body gamma rays showed a slightly greater degree of nausea and vomiting and greater depression of leukocytes than did the adults.[22, 23] However, the dose may have been greater in these children due to their shorter stature (nearer the ground source) and smaller bodies. The skin of children is known to be more sensitive to radiation than that of adults.[25] The Marshallese children exposed to fallout also developed more widespread "beta burns" of the skin and epilation than did the adults. This greater sensitivity may be related to the thinner skin of the children.[26]

Late effects. In considering the possible late effects of radiation, it should be borne in mind that children have a greater chance of developing some of the late effects since their longer life span would permit effects with prolonged latent periods to become manifest.

Leukemia. The occurrence of leukemia as the result of exposure to ionizing radiation has been established in studies of atomic bomb survivors in Japan[8, 9, 27, 28, 29] and of therapeutically irradiated ankylosing spondylitis patients in England.[30, 31] In the Atomic Bomb Casualty Commission (ABCC) study, calculations based on 82 cases of confirmed leukemia of all types occurring from 1947 through 1958 among the proximally exposed (within 1,500 meters of the hypocenter) survivors demonstrated that the highest calculated annual rate of 673 per million was in the age group 0 through 9 years; the calculated over-all incidence was 455 per million for all age groups combined. During the same period of time, the leukemia rates among the distally exposed (1,500 to 10,000 meters from the hypocenter) survivors, calculated on the basis of 67 confirmed cases, were 26 per million in the 0 through 9 year age group and 35 per million for all ages combined.[8, 9] The expected incidence of leukemia of all types for all ages in Japan was 20 to 30 per million per year.[8] When acute lymphocytic leukemia was considered separately, the calculated annual rates in the 0 through 9 age group were 269 per million

in the proximally exposed and 6 per million in the distally exposed children.[8, 9] Straight-line relationships between irradiation doses and leukemia incidence in the Japanese data were noted over the dose range from 100 to 900 rads.

The British data were obtained from follow-up studies on about 15,000 patients, predominantly males of 14 years and older, who were given radiotherapy for ankylosing spondylitis[11, 30, 31]; 73 cases of leukemia have occurred among these patients. The number of cases of leukemia expected in this study population in the absence of irradiation has been estimated to be four or five.[11] These patients received therapeutic doses of radiation; therefore, "this study does not provide evidence on leukaemia incidence after doses below 500 rad."[17] Other epidemiologic investigations have indicated that children with leukemia have had greater exposure to radiotherapy than have comparison groups[32-35] and that children subjected to therapeutic irradiation, particularly to the thymic area, have a higher incidence of leukemia than expected.[4, 5, 7, 32] In some reported series, however, children who received therapeutic irradiation, including irradiation of the thymus, did not show a significant incidence of leukemia.[36-39] Again, the history of therapeutic radiation is not always a significant finding in leukemic children.[1, 37] The total volume of tissue irradiated (bone marrow) has been suggested as a factor of importance.[40] Although increased frequency of deaths from leukemia among American radiologists has been reported,[41, 42] the data do not contribute toward quantitative aspects of the problem.[28, 40]

Several attempts have been made to determine the probability of leukemogenesis on the basis of radiation dose.[28, 40, 43-48] The conclusions do not definitively answer the question of the existence or nonexistence of a threshold radiation dose for the development of leukemia in man.[28] A cause and effect relationship, however, between high-dose radiation exposure in man and increased incidence of leukemia must be accepted.[40]

Cancer. The correlation between ionizing radiation and the occurrence of malignant neoplasia other than leukemia has been the object of intensive scientific inquiry since the publication of reports of increased carcinogenesis in children who were irradiated in infancy for thymic enlargement.[4, 5] Cancer of the thyroid gland appears to be the most frequent malignant tumor noted in these studies.[4-7, 49] Eleven cases of thyroid cancer developed in a group of 1,644 children given x-ray therapy to the head, neck, or chest. In the same population, 0.12 case would have been expected. Irradiation dosage in the 11 children ranged from 100 to 1,770 r in air.[6] In another prospective study of 2,809 infants who had been therapeutically irradiated for thymic enlargement, 9 cases of thyroid cancer were found (0.10 case expected), in addition to 21 cases of thyroid adenoma (0.9 case expected). The 9 with thyroid cancer had cumulative exposures ranging from 155 to 1,092 r in air with a mean of 598 r.[7] Although the development of "thyroid nodules" has been ascribed to prior therapy with iodine-131,[49, 50] only one case of thyroid carcinoma has been reported among patients so treated.[49, 50] Various data suggest that the formation of the nodules was more frequent in children than in adults (33.3 per cent compared to 0.84 per cent).[50] Clinical observations have indicated that the history of antecedent therapeutic irradiation to the neck area was significantly very common (up to 80 per cent) in children and adolescents with thyroid cancer.[49, 51] In the ABCC survey in Japan, 21 instances of thyroid cancer were found over a three-year period (1958-1961) among more than 19,000 persons in the study sample.[52] Nineteen of the 21 occurred in the exposed group. Two were under 15 years of age at time of exposure; 8, however, were under 21 years of age at exposure. Tentative exposure doses (T_{57}), computed on the basis of exposure distance and shielding history of these cancer cases, ranged from 125 to 3,400 rads with the exception of a single patient whose T_{57} dose was calculated to have been 33 rads.[52] It was concluded from these findings that thyroid carcinoma was significantly more prevalent among survivors

heavily exposed to radiation from the atom bombs.[52, 53, 54]

In another study of Japanese atomic bomb survivors, a higher incidence of cancer of all types (excluding leukemia and lymphoma) among those exposed within 1,500 M. was reported[55]; the increased frequency was not related to age or sex. This finding, however, has not been substantiated.[54, 56]

The development of bone tumors following irradiation with doses in excess of 3,000 r is well documented.[57] An increase in frequency of osteochondromas over the expected number of cases has also been observed[7] in children treated with several hundred r for thymic enlargement. Bone tumors have also been observed in watch dial painters from internal deposition of radium. Radiogenic bone neoplasms from Sr^{90} deposition have been experimentally produced in animals and presumably could occur in man.[57] Malignant tumors of the lung and the skin are also known to be related to radiation exposure. Cancer of the lung has been associated with high atmospheric content of radium and particularly of radon. The risk of radium-induced cancer of the skin is generally considered to be less than that of many other types of tumors.[57]

Growth and development. Several analyses of the growth data on Hiroshima and Nagasaki children subjected to atomic bomb irradiation have suggested a retardation of growth among the exposed group.[58, 59, 60] This deleterious effect seemed more prominent among boys than girls and among those exposed at younger ages.[59, 60] Interpretation of the results is complicated since the children suffered psychic and physical trauma as well as nutritional disturbances and diseases. A similar trend in retardation of growth and development has been noted in a study of 38 Marshall Island native children who were exposed to whole body irradiation of 69 to 175 r from radioactive fallout.[61] Highly suggestive differences were noted, particularly between male children exposed at 12 to 18 months of age and the unexposed comparison group.

Clinical experience has long emphasized the occurrence of developmental abnormalities among children receiving irradiation in utero.[17] Of the offspring of 11 pregnant women who were exposed during the first trimester of pregnancy to the atomic bomb in Hiroshima at distances less than 1,200 M. from the hypocenter, seven had microcephaly and mental retardation.[62] In Nagasaki, the over-all morbidity and mortality were high among babies born to 30 mothers who were exposed during pregnancy and who manifested major radiation symptoms as compared to those among babies born to 68 mothers exposed within 2,000 M. but without histories of major symptoms and to infants born to 113 "control" mothers. Four of the 16 surviving children of mothers with major symptoms were mentally defective.[63] Experimentally, many types of malformations have been produced in the animal fetus by irradiation.[16, 64, 65]

Life shortening. Shortening of the life span and premature senescence have been established in mammals receiving acute or chronic irradiation.[17, 66, 67, 68] It has not been conclusively demonstrated that a similar life shortening effect occurs in human beings exposed to radiation,[17] although mortality statistics from retrospective surveys have been interpreted to show decreased longevity of American radiologists in comparison with other physicians and with the general male population.[17, 69, 70] The Atomic Bomb Casualty Commission—National Institute of Health (Japan) Study of Life Span of A-Bomb Survivors has under surveillance a sample of approximately 100,000 persons.[54] Analyses of these data may provide some firm answers in reference to the relative life span of those exposed to radiation during childhood and infancy, although results thus far have not revealed any positive correlation.

Chromosome changes. Persistent chromosomal aberrations have been noted in the leukocytes of human beings who received whole or partial body irradiation.[71-76] Diagnostic radiation ranges in levels of 12 to 35 r, and even in levels as low as 1 to 12 r, have been associated with postradiation aberrations.[75] The clinical significance, however, of

these chromosomal aberrations has not been established; in the absence of sufficient information, the relationship of these morphologic changes to potential leukemogenesis or other abnormalities which might occur later remains highly speculative.[77, 78]

Other somatic effects. Opacities of the optic lens occur after acute exposure of the lens to doses greater than 200 rads of mixed gamma and neutron radiation,[16, 79] although the minimum effective x-ray dose for the production of clinically significant cataract has been estimated to be 600 to 1,000 rads.[17] In chronic exposures, neutrons are considered to be more cataractogenic than x- or gamma rays.[16] The sensitivity of lenses to radiation seems to be greatest in infants under 1 year of age.[16] Prolonged temporary or permanent sterility has been reported following single local gonadal doses of 500 rads or higher.[16]

HEREDITARY EFFECTS—HIGH DOSE

In the studies of atomic bomb survivors at Hiroshima and Nagasaki by the ABCC,[77, 80, 81] it was concluded that the data could demonstrate "no significant and consistent effect of parental radiation exposure on the number of infants with major defects, among the 76,626 children examined" and failed "to reveal an increase in stillbirths or infant deaths clearly attributable to parental irradiation." The Japanese study, however, has indicated a change in sex ratio among offspring of irradiated parents. Such a shift would be consistent with the occurrence of sex-linked mutations affecting prenatal survival.[82] Schull[83] has examined the genetic interpretation of the data, emphasizing the reality of the effect but indicating that a number of genetic alternatives may account for the change. A slight increase, however, in the number of miscarriages, stillbirths, and neonatal deaths has been reported in the Marshallese women exposed to fallout radiation.[84]

Based on the assumption that children of consanguineous marriages, owing to their increased homozygosity, are "a more sensitive index of radiation induced genetic damage," the ABCC investigated 4,731 births to related parents with varying degrees of radiation exposure[81] and reported: "No demonstrable, consistent effect of parental exposure on the frequency of malformed infants or perinatal deaths was found."

The massive data from the ABCC survey of pregnancy termination in nonrelated parents[30] have been reanalyzed independently, and, on the basis of this separate analysis, a significant total genetic effect has been reported.[85, 86] However, the methodology and interpretations of the reanalysis have been seriously questioned by Neel and Schull.[87]

Experimental studies in organisms other than man have shown that the frequency of mutations was dose dependent, even at the lowest doses investigated, and that the majority of induced hereditary changes had detrimental consequences.[16] Although direct information is lacking, it appears reasonably certain that similar effects occur in the human being.[16] Thus, known exposure to high doses of ionizing radiation requires the disquieting acceptance of genetic hazards, the true magnitude of which may be assessed only with the perspective of time stretching over generations.

SOMATIC AND GENETIC EFFECTS OF LOW-LEVEL RADIATION

The term "low-level" radiation, regardless of source, requires definition. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) has agreed that doses of less than 50 rad short-term exposure and 100 to 1,000 mrad cumulative weekly doses should be considered as "low."[17] Two other frames of reference will be useful in this discussion, one being the amount of radiation from natural sources to which man is constantly exposed and the other being the levels accepted by several advisory and regulatory bodies as protection standards for the general population.

According to UNSCEAR calculations of dose rates from natural radiation sources,[88, 89] cosmic rays and terrestrial sources each deliver about 50 mrem per year to the gonads, bones, and blood-forming cells. The inges-

tion of elements of the radium and thorium series, of potassium-40 and of carbon-14, provides radiation exposure from internal sources in dose rates estimated to be 126 mrem per year to the gonads, 130 mrem per year to the cells lining bone surfaces, and 122 mrem per year to the hematopoietic tissues.

Medical diagnostic radiology constitutes another source of inevitable low-level irradiation, the magnitude of which has been the subject of recent inquiry.[90, 91, 92] The annual genetically significant dose received by an individual in the United States from diagnostic roentgenologic procedures has been estimated to be 50 ± 25 mrem minimum and 140 ± 100 mrem probable.[16] Although estimates of bone marrow dose are based on sparse data and assumptions, the UNSCEAR in two reports has suggested that the estimate of the population per capita dose "might be of the order of 50 to 100 mrem/y."[16] The radiation exposure from radioisotopes in pediatric patients for a number of diagnostic tests has also been calculated.[93]

Adequate information on effects of low doses in both man and experimental animals is lacking. In 1959, Brues[94] commented that the subject of effects of low-level irradiation concerned "hazards which, if they exist, cannot possibly be demonstrated to exist because they are relatively so small." Upton,[95] in reviewing radiation carcinogenesis, stated that "existing data . . . are not adequate to permit confident estimation of the risks of small increases in background radiation."

Somatic effects. The report by Stewart and associates[96] that diagnostic pelvic irradiation of the pregnant mother was associated with subsequent development of leukemia and other malignant neoplasms in the child who was exposed in utero triggered a number of similar epidemiologic studies. In subsequent communications, the original conclusions were confirmed and amplified.[1, 2] The study attempted to trace all children in England and Wales who had died of leukemia (792 cases) or other cancer (902 cases) before the tenth birthday during 1953-1955. It was concluded that the risk of subsequent malignant changes in the child was significantly increased by pelvic irradiation of the mother during the child's intrauterine phase.[1] These findings were supported by data from several other studies.[5, 33, 97]

MacMahon[3] has reported the results of a study of 734,243 children born in and discharged alive from 37 large maternity hospitals in the northeastern part of the United States from 1947 through 1954. For each of three categories, leukemia, neoplasms of the central nervous system, and other neoplasms, the cancer rate was found to be "about 40 percent higher in the X-rayed than in the unX-rayed members of the study population. The excess cancer mortality in the X-rayed group was most marked at ages 3 through 7 years, at which time the relative risk was 2.0. The excess risk apparently was exhausted by age 8." MacMahon has estimated that the probability of death from leukemia for white children in the United States up to the age of 10 years will be increased from 46 per 100,000 children to 62 per 100,000 children by prenatal irradiation.[37]

In a prospective approach,[98] 43,742 women who between 1945 and 1956 received pelvic irradiation during pregnancy were identified from the records of selected hospitals (Edinburgh and London) and the subsequent deaths from leukemia of the children of these pregnancies were then investigated. Court-Brown, Doll, and Hill,[98] in this study, found 9 instances of leukemia among 39,166 liveborn children when 10.5 was the estimated expected number. The study also indicated that "there was no evidence of any disproportionate occurrence of leukaemia among the children who had been most heavily irradiated nor among the children who had been irradiated early in intrauterine life." Data not in accord with those of Stewart and of MacMahon have also been reported from several other studies.[35, 99]

Although the exposure dose cannot be precisely determined in these studies,[47] the reported association between prenatal pelvic irradiation at diagnostic dose levels and increased leukemogenesis (and carcinogenesis)

clearly indicates the need for further data on human beings.[100] "If leukemia does result from pelvimetry, it may indicate that the fetus is extremely sensitive or that in reality there is no threshold."[28] However, no differences in the incidence of leukemia have been found among a number of metropolitan areas of the United States with different cosmic radiation backgrounds.[101] The question regarding the possibility that the irradiated sample may not be representative of the whole childhood population needs to be more precisely answered.[57]

Chromosomal aberrations in peripheral leukocytes have been reported following diagnostic x-irradiation doses of 4 to 12 r.[75] That similar changes may occur at lower doses is suggested by a report of the development of chromosome abnormalities after 825 mr (0.8 rad) total body exposure.[76] None were noted after 20 to 80 mr radiation.[75]

Current available data on human subjects do not permit any definitive assessment of the development of other somatic effects from exposure to low-level irradiation. In reference to life shortening, extrapolation from animal to human has been attempted but the clinical observations are inconclusive.[17, 67, 102] Clinically significant cataract formation probably has not occurred below 600 rads, although it is generally believed that the minimal effective dose is lower in children.[17] Studies of growth and development in children have not been reported other than those carried out on populations exposed to whole-body doses of 69 r or more.[58-61]

Hereditary effect. There exists no body of direct observation of human population which permits the precise quantitative determination of the genetic effect of low-level radiation.[82, 103] The potential genetic consequences of exposure to radiation have been estimated indirectly in such terms as "lethal-equivalents,"[104] total estimated numbers of gross physical or mental defects in future generations,[105, 106] and "gonadal doses" or "doubling doses" of radiation.[77, 105, 107]

Based on radiation-induced mutation rates in man and on the spontaneous incidence of defects in man, the total of gross physical and mental defects from all atomic weapons tests through 1961 and all future generations has been estimated[105, 106] as 1,000 (range 200 to 5,000) from fallout and 2,000 (range 400 to 10,000) from carbon-14. The total number of such defects due to all causes (hereditary and nonhereditary) in children of persons now living has been estimated to be between 4,000,000 and 6,000,000. The number of additional cases occurring in the next generation has been estimated to be 100 (range 20 to 500) due to fallout and 10 (2 to 50) to carbon-14. The risk to the individual of the next generation (of genetic effects manifested by gross mental or physical defect) has been calculated as 1/1,000,000.[106]

The UNSCEAR report concludes that for acute radiation the representative doubling dose for gene mutation for man "is somewhat lower than 30 rad but not less than 15 rad. For chronic irradiation, the most probable value is 100 rad or possibly higher."[103]

FALLOUT RADIATION

The voluminous data on the levels and hazards of environmental contamination with radioactive materials (primarily from nuclear weapons tests) have been effectively summarized, on an international basis, by UNSCEAR.[16, 57] The published records of hearings before the Subcommittee on Research, Development, and Radiation and before the Special Subcommittee on Radiation, both of the Joint Committee on Atomic Energy, Congress of the United States, constitute an authoritative source for basic information on almost all aspects of fallout radiation.[108, 109] The rate and distribution of deposition of radioactive fallout from the testing of weapons depend on the amount of debris, altitude and geographic location of the explosion, meteorological conditions, and other factors.[16, 57, 108, 109, 110] Radiologically important nuclides which account for most of the external irradiation from fallout include the gamma-emitters zirconium-95 (half-life, 9 weeks), niobium-95 (half-life, 5 weeks), and cesium-137 (half-life, 30 years). The chief internal exposure hazards

are strontium-90 (half-life, 28 years), cesium-137 (half-life, 30 years), iodine-131 (half-life, 8 days), and carbon-14 (half-life, 5,760 years).[57, 111] Of particular pediatric medical significance are the hazards of internally deposited radionuclides from tropospheric and stratospheric fallout rather than those from local or near-in fallout.

Strontium-90. The principal source of strontium-90 is dietary, through ingestion of directly contaminated vegetation and through incorporation of strontium-90 into the food chain, both plant and animal.[57, 108, 109] In children, milk is considered an important source of strontium-90, although contaminated potable water may contribute additional amounts of the radionuclide.[57] The distribution of the radionuclide in the body follows the metabolic paths of calcium.[111, 112] The high turnover rate of minerals in the bones of infants and children under 2 years of age is presumed to lead to rapid equilibration of the bone minerals and consequently to uniform deposition of strontium-90 throughout the skeleton.[57, 113] A yearly replacement of 30 to 70 per cent or more of bone mineral has been estimated during the first and second years of life.[57, 115] In the adult, 2.0 to 3.5 per cent of bone calcium is replaced annually.[57, 114] The bones of stillborn fetuses and of newborn infants have a lower strontium/calcium ratio attributed to discrimination by the placenta which favors by a factor of 2 the passage of calcium over strontium from mother to fetus.[57, 113] Metabolic discrimination between strontium and calcium does not become established until the second year of life,[115, 115] the "observed ratios" of strontium and calcium in bone to those in the diet being about 0.8 at 2 to 3 months of age, less than 0.4 at 9 to 10 months, and 0.25 (adult ratio) after 2 years.[57] In 1960, the mean concentration of strontium-90 (as pCi per Gm. calcium) in bones of subjects of different ages in New York City were: 6.81 in infants, 9.84 at 1 year of age, 5.03 at 2 years, 3.41 at 3 years, 2.41 in children from 5 to 19 years, and 1.55 in adults over 19 years of age.[57, 116] The higher concentration in the bones of children is related not only to higher milk consumption but also to greater deposition of Sr^{90} in their growing bones.

Being a beta emitter, the isotope does not contribute significantly to the genetic dose; the effect is localized anatomically where it is responsible for an estimated 50 per cent of the marrow dose and 80 per cent of the bone dose.[106] The potential danger from strontium-90 is assumed to be the development of osteogenic sarcoma and possibly leukemia. Although the behavior of strontium-90 has been examined on ecological and radiophysics bases,[57, 114, 117, 118] the magnitude of the biological risk remains to be determined[14]; a rather high threshold dose of well above 20 rads and probably nearer 1,000 rads has been suggested for bone sarcomagenesis from radium deposition.[119, 120]

Cesium-137. Cesium-137 is not fixed in the body and its distribution is considered to be uniform. The metabolic behavior of cesium-137 resembles that of potassium. It is rapidly absorbed from the intestinal tract and is distributed uniformly in the soft tissues. The biological half-life of cesium in children has been reported in two studies to be about 44 and 38 days and about 100 days in adults.[57, 121] The more rapid turnover partially accounts for the ratio of cesium-137/potassium being lower in children than in adults. Observed levels of cesium-137 in man were two to four times higher in late 1963 than the average levels in 1961.[57] The absorption of this chemical by plant roots is poor, so that the entry of the nuclide into the food chain largely depends on ingestion by animals of food contaminated by direct deposition. Milk and meat are the greatest contributors to human dietary intake.[57] Large age variations in body burdens of this nuclide have not been noted, particularly when related to lean body mass or to potassium.[116, 122, 123, 124, 125] Along with the relatively short-lived zirconium-95, niobium-95, and $Ba\text{-}La^{140}$ (half-life,13 days), cesium-137, which gives off gamma rays, contributes an estimated 90 per cent of the whole body and genetic dose from fallout.[106]

Iodine-131. Iodine-131, with a half-life 7 to 8 days, is a special hazard only during the first few weeks following environmental con-

tamination.[126-129] Food, chiefly milk and its fresh products in children, provides entry into the body where the nuclide concentrates in the thyroid gland.[57, 127, 130] About 5 to 10 per cent of the I^{131} ingested by cows goes into their milk. It is noted that, for the same milk consumption, the thyroid gland of children concentrates much more iodine than that of adults.

Fetal thyroids contain more iodine-131 than maternal thyroid glands on a per gram weight basis.[57, 131] The most critical age in postnatal life in regard to dosage has been estimated to be between 6 months and 2 years of age.[57, 131] Thyroid doses from fallout iodine-131 in infants calculated on the basis of 0.7 liter of fresh animal milk consumed daily were (for the United States) 250, 440, and 21 millirads for 1961, 1962, and 1963, respectively.[57] Evaluations of the relationship of radiation dose to thyroid carcinogenesis have been made on clinical and epidemiological data from populations with known external irradiation by doses in the therapeutic range (50 r to 5,000 r).[132-135] Crude risk estimates for thyroid carcinogenesis, based on average follow-up time of 16 years and thought to be valid for acute irradiation of children only in the exposure range of 100 to 300 roentgens,[57] have been calculated to be 0.3 to 1.6 cases per 10^6 exposed population per year per roentgen.[57] A risk estimate of high magnitude (35 per 10^6 per rad) also has been derived.[134] Reports concerning association of iodine-131 and malignant tumors of the thyroid are scarce.[136, 137] The risk of thyroid cancer from internal exposure to radioiodine has been estimated to be one-tenth that from external x-irradiation.[137] The substitution of radioiodine-free milk (canned or shipped milk) and the feeding of stored feed to cattle have been recommended when critically high levels of iodine-131 are detected.[138, 139] The use of organic and inorganic thyroid-blocking agents (such as iodides, perchlorides, and thiouracil) has been studied as a countermeasure for sudden high radioiodine contamination events.[140]

Carbon-14. The long-term risk is primarily that from carbon-14, the doses from which are delivered at extremely low rates over a very long period of time.[140] Carbon-14 is present almost exclusively as CO_2.[57] Testing in 1961 and 1962 has caused a threefold increase in carbon-14 in the different carbon reservoirs (stratosphere, troposphere, surface oceans, deep oceans).[57] A peak excess of carbon-14 activity at about 70 per cent has been predicted in 1964 or 1965. "The level will then fall to some 60 per cent in seven or eight years' time. Between 1970 and 2040, the level will gradually fall to some 3 per cent and will remain below this level while the excess C^{14} will decay radioactively."[57] Carbon-14 contributes very little to the total body dose to any single individual during his lifetime. The cumulative genetic effect over a number of generations, however, may be significant.[109]

Relative risks. The long-range risk from fallout has been expressed in terms of dose commitment, which is defined as "the total dose that will be delivered as an average for the world population, to the relevant tissues during the complete decay of radio-active material introduced into the environment."[57] The estimates of the dose commitments from all tests before January, 1963, are shown in Table I.

The relative risks from fallout radiation from tests carried out before 1963 have been expressed in terms of the period of time during which natural radiation would have to be doubled to give a dose equal to the dose commitment.[57] Calculated in this way, the periods equal approximately 9 months for the gonads, 32 months for cells lining the bone surfaces, and 20 months for the bone marrow.[57]

The likelihood of developing cancer as the result of chronic fallout radiation from the tests of weapons through 1961 has been estimated by the Federal Radiation Council.[105, 109] During the next 70 years it is expected that 840,000 persons will develop leukemia and 140,000 bone cancer. Of these, the estimated number of cases caused by natural radiation are 0 to 84,000 for leukemia and 0 to 14,000 for bone cancer. The estimated

additional numbers of cases that will be attributable to fallout radiation are 0 to 2,000 for leukemia and 0 to 700 for bone cancer. On the basis of these calculations, the risk of any individual developing cancer as the result of fallout radiation is 0 to 1/100,000 for leukemia and 0 to 1/300,000 for bone cancer.

The existence of potential hazards demands consideration of countermeasures. In relation to this question, the National Advisory Committee on Radiation (NACOR) has advised the avoidance of independent countermeasure action.[141] "Not infrequently, such action involves the use of countermeasures which are associated with risks approaching or exceeding those of the contaminant. Often such action is ineffective in reaching the objective sought. To avoid these and similar problems, recommendations on countermeasures must be promulgated from a single authority, acting after full evaluation of the effectiveness, safety, and feasibility of the measures to be taken."[141]

RADIATION PROTECTION STANDARDS

Among the recommendations formulated for protection from exposure, particularly occupational, to ionizing radiation are those from three qualified bodies: International Commission on Radiological Protection (ICRP), National Committee on Radiation Protection (NCRP), and the Federal Radiation Council (FRC). Each group includes recognized authorities in radiation and in health physics.[103, 109, 142-145] Although varied interpretation of the intent and limitations of the recommendations can occur,[108, 109, 145, 146] these practical and reasonable limits to minimize the hazards of exposure to radiation serve as useful guides.

The International Commission on Radiation Protection (ICRP) was established in 1928 by the Second International Congress of Radiology.[144] Its latest recommendations, revised in 1962, were published in 1964.[147]

The ICRP has introduced the term "permissible dose" which for an individual has been defined as "that dose, accumulated over a long period of time or resulting from a single exposure, which, in the light of present knowledge, carries a negligible probability of severe somatic or genetic injuries."[147]

Table I. Dose commitment from nuclear explosions, 1954-1962[97]

Source of radiation	Dose commitment (mrad)
Gonads	
Short-lived nuclides	21
Cesium-137	42
Carbon-14	13
Total	76
Cells lining bone	
Short-lived nuclides	21
Cesium-137	42
Strontium-90	174
Carbon-14	20
Total	257
Bone marrow	
Short-lived nuclides	21
Cesium-137	42
Strontium-90	87
Carbon-14	13
Total	163

The maximum permissible dose (MPD) for any individual not occupationally exposed has been set at 0.5 rem per year to the gonads and the blood-forming organs,[147] in addition to natural background plus the lowest practicable contribution from medical exposure. It was suggested that the maximum permissible genetic dose to the whole population should not exceed 5 rems to age 30 years. ICRP has also recommended values for maximum permissible body burden of more than 250 radionuclides, and maximal permissible concentrations (MPC) of these nuclides in air, food, and water.[148]

The National Committee on Radiation Protection (NCRP) was set up in 1929 through the collaborative efforts of the American Roentgen Ray Society and the Radiological Society of North America.[108, 142, 149] The NCRP has adopted the "maximal permissible dose (MPD) rate" of 0.1 r per day for the general population.

The Federal Radiation Council (FRC) was set up by Executive order in 1959 to

advise the President with respect to radiation matters and to establish a national policy relative to radiation exposure and health.[108, 109, 142, 148, 149, 150] The membership of FRC includes the Secretary of Health, Education, and Welfare, Chairman; the Secretaries of Defense, Labor, and Commerce; and the Chairman of the Atomic Energy Commission.[148, 150]

The FRC introduced for use by Federal agencies the concept of a Radiation Protection Guide (RPG) defined as "the radiation dose which should not be exceeded without careful consideration of the reasons for doing so; every effort should be made to encourage the maintenance of radiation doses as far below this guide as practicable."[108, 151] Later, a "graded scale of action" was set up for three ranges of exposure for several radionuclides.[145, 152]

PERSPECTIVES

Young and old animals have been shown to have an increased sensitivity to radiation compared with animals in the prime of adulthood. From limited data available, it appears that this situation is also generally true in the human being. Although a number of radiation effects have been shown to be greater in the young human being, there has been no good evidence for any decreased sensitivity to any radiation effects in children as compared to adults. The above statements are based on data involving relatively high doses of radiation. The extremely limited data available do not allow one to make such positive statements in regard to low dose effects.

The sources of low-level radiation are from (a) natural background, (b) fallout from nuclear test explosions, (c) industrial uses of radiation, and (d) medical uses of radiation. Little can be done to alter the dose commitments associated with natural background and the existent fallout. Although monitoring systems exist,[153] the actual application of countermeasures against effects of fallout radiation present public health problems.[96, 142, 145, 154-159] "It is clear that drastic measures to control air, water and food supplies of large population groups might hold threats to health more immediate and serious than the increasing risk from radiation exposures such measures were intended to reduce."[154]

Efforts toward containment of occupational radiation sources and formulation of health safety standards have been effective, reducing radiation exposure in radiation workers. No instance has been recorded in which a radiation worker has stayed within the permissible limits and developed a demonstrable radiation injury.[142]

Estimates of radiation effects at low dose levels are based on assumptions and extrapolations, the accuracy of which must be established. "We still know very little about the frequency with which such (harmful) effects are likely to occur, particularly following small doses of radiation at low dose rates."[160]

Epidemiologic studies have reported increases in the rate of development of leukemia and malignant neoplasia among children exposed in utero to diagnostic doses of radiation.[1, 3] Not all data support this finding.[95] The degree of risk of induction of malignant tumors by low dose radiation is not settled.[15] However, the reports of correlation of radiation exposure and later development of malignancies have made the physician much more cautious in recent years in the use of radiation in both diagnostic and therapeutic procedures. For example, the increasing evidence for development of leukemia in children who were irradiated in infancy for thymic enlargement and the development of thyroid nodules following treatment of children with I^{131} therapy for thyrotoxicosis has resulted in greater conservatism in the use of such treatment in infants and children. For the same reason, the physician has become more circumspect in the use of x-ray pelvimetry on pregnant women. Consequently, the incidence of such late effects of radiation should be greatly reduced in future years.

The degree of conservatism in the medical uses of radiation may be somewhat altered when more is known about linearity of dose response and when the question regarding the existence or nonexistence of a threshold

dose for certain somatic effects is resolved.[162] However, it would seem that the present attitude will likely be maintained in view of the positive correlation of linearity of genetic effects to low doses of radiation. The UNSCEAR report states that "because of the available evidence that genetic damage occurs at the lowest levels as yet experimentally tested, it is prudent to assume that some genetic damage may follow any dose of radiation, however small."[160] On the other hand, the report also points out that "it must be recognized that the human species has in fact always been exposed to small amounts of radiation from a variety of natural sources and that the present additional average exposure of mankind from all artificial sources is still smaller than that from natural sources."[160] Recognition of the risk involved balanced against the objective assessment of the expected benefit should provide the general guidelines for exposure to controlled radiation sources.

Even with the most conservative (and pessimistic) point of view, the consequences of low-level radiation should be examined in context with other pediatric problems.[162] Man is exposed to a number of other mutagenic agents, some of which may be of greater potential importance.[85] Preventable deaths from infections still number in the millions each year. During the same seventy-year period in which fallout from weapons tests to date is estimated to cause (combining all age groups) 0 to 2,000 additional cases of leukemia and 0 to 700 additional cases of bone cancer, automobiles will account for 2,800,000 deaths.[106] Nevertheless, the practice of good preventive pediatrics requires the considered awareness of any avoidable risk of injury, however small, and permits no complacent attitudes or liberalization of the use of irradiation beyond justifiable medical requirements.

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