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TABLE IV-2 Genetic Effects of an Average Population Exposure of 1 Rem per 30-Yr Generation

Type of Genetic Disorder[a]	Current Incidence, per Million Liveborn Offspring	Effect per Million Liveborn Offspring, Rem per Generation	
		First Generation[b]	Equilibrium[c]
Autosomal dominant and X-linked	10,000	5-65[d]	40-200
Irregularly inherited	90,000		20-900[e]
Recessive	1,100	Very few; effects in heterozygotes accounted for in top row	Very slow increase
Chromosomal aberrations[f]	6,000	Fewer than 10[g]	Increases only slightly

[a] Includes disorders and traits that cause serious handicap at some time during lifetime.
[b] Estimated directly from measured phenotypic damage or from observed cytogenetic effects.
[c] Estimated by the relative-mutation-risk method.
[d] No first-generation estimate available for X-linked disorders; the expectation is that it would be relatively small.
[e] Some estimates have been rounded off to eliminate impression of considerable precision.
[f] Includes only aberrations expressed as congenital malformations, resulting from unbalanced segregation products of translocations and from numerical aberration.
[g] Majority of Subcommittee feels that it is considerably closer to zero, but one member feels that it could be as much as 20.

with that of the other classes of genetic disorders, especially in the early generations. When the disorder is not completely recessive, the equilibrium frequency is approximately proportional to the mutation rate. Whatever mechanisms of elimination operate, equilibrium is reached very slowly, and any effect of an increased mutation rate on the incidence of recessive traits would be spread over a very large number of generations.

The population survey in British Columbia reported that at least 9% of all liveborn humans will be seriously handicapped at some time during their lifetimes by genetic disorders of complex etiology, manifested as congenital malformations, anomalies expressed later, or constitutional and degenerative diseases. This, the larges- category of genetic disorder listed in Table IV-2, we refer to as "irregularly inherited" disorders. The mutations responsible for the many hundreds of disorders in this category are

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NUCLEAR REGULATORY COMMISSION

Docket No. 50-352/353 Official Exh. No. Ap. 147

In the matter of Philadelphia Electric

Staff ✓

Applicant

Intervenor

Comm'g Cit'y

Contractor

Other

Reporter Ann Riley

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Witness

TABLE V-15 Derivation of Ratios for Transforming Mortality-Risk Estimates to Incidence-Risk Estimates, by Sex

Site (i)	Males				Females			
	Weight (ω_i)[a]	Percentage Expectation at Birth of Eventually Developing or Dying from Cancer		Ratio ($R_i = M_i / I_i$)	Weight (ω_i)[a]	Percentage Expectation at Birth of Eventually Developing or Dying from Cancer		Ratio ($R_i = M_i / I_i$)
		Mortality (M_i)[b]	Incidence (I_i)[b]			Mortality (M_i)[b]	Incidence (I_i)[b]	
Esophagus	0.26	0.4	0.4	1.00	0.28	0.2	0.2	1.00
Stomach	1.53	0.9	1.2	0.75	1.68	0.7	0.9	0.78
Intestine	1.02	2.3	4.4	0.52	1.12	2.8	5.1	0.55
Pancreas	0.90	1.0	1.1	0.91	0.99	0.9	1.0	0.90
Lung	3.64	4.9	5.9	0.83	3.94	1.2	1.6	0.75
Urinary	0.81	1.0	2.7	0.37	0.88	0.6	1.3	0.46
Lymphoma	0.27	1.1	1.5	0.73	0.23	0.9	1.2	0.75
Breast	0	0	0	—	5.82	3.0	7.7	0.39
Thyroid	2.20	0.03	0.17	0.18	5.80	0.09	0.46	0.20
Liver	0.70	0.20	0.20	1.00	0.70	0.18	0.18	1.00
Sum[c]	11.33	—	—	—	21.48	—	—	—
Weighted sum[c]	—	—	—	7.37	—	—	—	10.76
Expansion factor[d]	—	1.84		—	—	2.00		—

[a] Age-adjusted risk estimate, Table V-14.

[b] Data from Seidman et al.[88] or calculated directly (thyroid, liver).

[c] The ratios of mortality to incidence for specific types of cancer derived from vital statistics are not generally in close agreement with survival probabilities based on long-term clinical followup studies of cancer patients, nor is there any reason that they should be.

[d] Sum $= \sum \omega_i$, weighted sum $= \sum \omega_i R_i$, expansion factor $= \sum \omega_i / \sum \omega_i R_i$.

Somatic Effects: Cancer

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spermatocyte is relatively radioresistant, in comparison with its progenitor cells. Single acute doses of 500 rads or less cause significant cellular damage in the testis; these changes are dose-dependent, with complete recovery after doses of 600 rads or less, and with the time until recovery also dose-dependent, extending up to 5 yr.

Atomic-Bomb Survivors

Information on impairment of fertility in man is available from the study of atomic-bomb survivors and from Marshallese and Japanese who were inadvertently exposed to fallout during atomic-bomb testing in the Pacific.[15,90,106,148,165] The data lack precision, but demonstrate the following: Relatively low doses can decrease production of sperm cells, but effects on spermatogenesis are transient; the sterilizing dose in the male is probably much greater than about 400–500 rads, i.e., it probably exceeds the mean lethal dose to the whole body. Fertility is impaired in the oocyte population only after moderately high doses—200–400 rads. Little is known regarding the delayed effects of radiation on fertility in these exposed populations, nor is there information on the extent of impairment, if any, in the male and female populations exposed *in utero* and in the F_1 populations of exposed parents.[15,78,148] Followup studies of the Japanese atomic-bomb survivors and the Marshallese women exposed to fallout have failed to demonstrate any long-term effect on fecundity.[6,15,148,165]

Radiotherapy Patients and Victims of Nuclear-Reactor Accidents

Clinical data are available on male radiotherapy patients and men exposed during criticality accidents at nuclear-reactor installations.[90,165] Careful sperm-count studies after limited partial-body radiation exposure have indicated that, if sterility occurs, normal sperm counts can return in about 1 yr after doses of 100 rads and even in 3 yr after exposures in the near-lethal range.[90,165] Acute whole-body exposure has not been shown to cause permanent sterility in males.[165] The sterilizing dose therefore exceeds the lethal whole-body dose for acute radiation. Similarly, sterilization of the human testis has never been shown to result from continuous or fractionated (protracted) low-dose exposure.[30,90,144,148]

In women, radiotherapy experience has suggested that acute doses of 300–400 rads or slightly higher doses given in two or three fractions result in permanent sterility.[2,15,45,53,165] If fractionation is protracted over a 2-wk period, much larger doses (possibly 1,000–2,000 rads) are required for sterilization, depending on the age of the woman.[2,15,45,165] The ovaries of younger women are much less radiosensitive; permanent sterility is more likely as the menopause is approached.

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Conclusions

Populations of mature spermatozoa in the human testis are maintained by proliferating spermatogonial stem cells. Provided that the dose remains below 400 rads (low-LET radiation, acute exposure), radiation depletion of the spermatogonial-cell population is only temporary, and the seminiferous epithelium is repopulated and regenerates from surviving and proliferating spermatogonial cells in the damaged tissue. Exposure much greater than this (perhaps by an order of magnitude) directed only at the testis could probably result in permanent sterility.

Impairment of fertility can result from absorbed doses to the human ovary in the range of 300–400 rads (low-LET radiation, acute exposure), but this depends, in part, on age. Radiotherapeutic experience has shown that women approaching the menopause may have long-term impairment of fertility or permanent sterility, whereas in younger women only transient infertility associated with amenorrhea may result. This may be associated, in part, with oocyte populations, which decrease primarily by physiologic atresia (and to a much lesser extent by ovulation) with age.

CATARACTS

A causal involvement of radiation-induced damage of epithelial cells in the germinative zone of the lens in radiation cataractogenesis has not yet been proved. However, the available evidence from animal studies strongly suggests this mechanism, on the basis of the differentiation of the affected cells into abnormal lens fibers and the time coincidence between the appearance of lens opacification and the rate of migration of lens epithelial cells into the posterior lens cortex. Accumulation of aberrant cells in the posterior cortex causes alteration in the lens cytoarchitecture, resulting in a loss of transparency.[177] There is no direct evidence that lens opacification depends on the killing of epithelial cells in the germinative zone. The sigmoid cataract dose-response curves and the protective effect of partial lens shielding provide evidence that other factors are involved in radiation cataractogenesis in addition to cell-killing.

The available data suggest a sigmoid dose-response relationship with an apparent threshold for lens opacification. Threshold doses in man for x rays and gamma rays delivered in a single exposure vary from 200 to 500 rads, whereas the threshold for doses fractionated over periods of months is around 1,000 rads.[78] Continuing observations of lens changes in survivors of Hiroshima and Nagasaki have been reported.[47,48,58,72,84,160,161] The subjective nature of the lens assay techniques used by the several investigators involved in these studies, as well as the limited dose informa-