RADIOLOGICAL ENDPOINTS RELEVANT TO ECOLOGICAL RISK ASSESSMENT

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CRITÈRES D'EFFETS RADIOLOGIQUES APPROPRIÉS POUR L'ÉVALUATION DU RISQUE ÉCOLOGIQUE

RÉSUMÉ

En raison du risque potentiel de radiation causé par les rejets de radionucléides provenant d'activités anthropogéniques, un grand nombre d'études ont été faites afin de mesurer la radioexposition des humains, de déterminer les effets de ces radioexpositions et d'élucider les mécanismes d'interaction des rayonnements avec toutes matières vivantes. En ce moment, on note un intérêt accru pour les effets de la radioactivité sur les espèces non humaines. Les méthodes d'évaluation du risque posé aux humains et aux écosystèmes diffèrent. Pour les humains, l'accent est mis sur l'individu et la principale inquiétude est l'induction du cancer. Lorsqu'il s'agit d'écosystèmes, la stabilité de la population est visée et la principale inquiétude est le succès de la reproduction des organismes les plus importants du point de vue de l'écologie et de l'économie. Pour ces organismes, il est nécessaire de se procurer de l'information quant aux effets des irradiations et de l'impact potentiel des doses absorbées sur le taux de succès de reproduction. Nombre de renseignements sont disponibles sur les effets du rayonnement sur les organismes provenant de différents phylla et types d'écosystèmes. Les effets du rayonnement sur la mortalité, la fertilité et la stérilité constituent des bases de données utiles à l'évaluation du risque des radioexpositions des populations. La fertilité et la stérilité sont des facteurs très importants pour le succès de la reproduction. Il existe des données sur les effets de l'irradiation aiguë et chronique sur la mortalité. Par rapport aux effets des rayonnements, le succès de la reproduction d'une population est directement liée à des caractéristiques propres à l'espèce, tels que la radiosensibilité innée des tissus reproducteurs et des premiers stades de vie, la gamètogenèse, la stratégie de reproduction, et le passé radioexpositif. Les données disponibles des radioexpositions aiguës et chroniques pour les invertébrés, les poissons et les mammifères sont passées en revue. Cet examen indique qu'il existe une vaste gamme de réactions parmi les espèces. Nous discuterons des paramètres qui contribuent le plus probablement à la radiosensibilité innée.

ABSTRACT

Because of the potential risk from radiation due to the releases of radionuclides from anthropogenic activities, considerable research was performed to determine for humans the levels of dose received, their responses to the doses and mechanisms of action of radioactivity on living matter. More recently, there is an increased interest in the effects of radioactivity on non-human species. There are differences in approach between risk assessment for humans and ecosystems. For protection of humans, the focus is the individual and the endpoint of primary concern is cancer induction. For protection of ecosystems, the focus is on population stability and the endpoint of concern is reproductive success for organisms important ecologically and economically. For these organisms, information is needed on their responses to irradiation and the potential impact of the doses absorbed on their reproductive success. Considerable information is available on the effects of radiation on organisms from different phyla and types of ecosystems. Databases useful for assessing risk from exposures of populations to radioactivity are the effects of irradiation on mortality, fertility and sterility, the latter two of which are important

components of reproductive success. Data on radiation effects on mortality are available both from acute and chronic irradiation. In relation to radiation effects, reproductive success for a given population is related to a number of characteristics of the species, including inherent radiosensitivity of reproductive tissues and early life stages, processes occurring during gametogenesis, reproductive strategy and exposure history. The available data on acute and chronic radiation doses is reviewed for invertebrates, fishes and mammals. The information reviewed indicates that wide ranges in responses with species can be expected. Parameters that most likely contribute to inherent radiosensitivity are discussed.

1.0 INTRODUCTION

The release of radionuclides from nuclear-weapon testing resulted in concern about their impact on humans and their environment. Since 1945 when the first nuclear detonation occurred, additional anthropogenic radioactivity was released into ecosystems from nuclear waste disposal and nuclear accidents. Because of the potential risk from radiation, considerable research was performed to determine for humans the levels of doses received, their responses to the doses, and mechanisms of action of radioactivity on living matter. More recently, there is an increased interest in the effects of radioactivity on non-human species. Concerns include the possibility of increases in the number of endangered species, in decreases in species diversity, and decreases in ecosystem stability.

Risk assessment, whether for humans or ecosystems, is a process by which critical databases are reviewed and analyzed to determine the potential for an adverse effect to a target group. Assessments of risks to man from radiation were performed for most known releases, and the principal elements of the risk-assessment process identified include hazard identification, exposure assessment, dose-response assessment, and risk characterization. However, there are differences in approach between risk assessment for humans and ecosystems. For protection of humans, the focus is the individual and the endpoint of primary concern is cancer induction from external exposure or from the consumption of radionuclide-contaminated food and water. For protection of ecosystems, the focus is on population stability and the endpoint of concern is reproductive success for organisms important ecologically and economically. For these organisms, information is needed on their responses to irradiation and the potential impact of the doses absorbed on their reproductive success.

2.0 RESPONSES OF NON-HUMAN SPECIES TO IRRADIATION

It is well documented that radiation induces biological effects through the deposition of energy in the cells of the irradiated individuals (UNSCEAR, 1993; 1994). The effects quantified include mortality, life span shortening, changes in morphology and histopathalology, alteration in growth and development, and damage to the cytogenetic constituents of cells. Considerable information is available on the effects of radiation on adult and young organisms from different phyla and from different types of ecosystems (Woodhead, 1984; Anderson and Harrison, 1986; ICRP, 1991; UNSCEAR, 1996). Although data are available for many species, there are entire phyla and groups within phyla for which there is no information.

The biological effects of irradiation of primary concern are damages to the DNA in the nuclei of cells. If the damage from radiation is repaired, then no adverse effects are apparent. In the case when DNA repair is defective or the DNA-repair capacity of the cell is exceeded, then the damage may be transmitted to the progeny of the cells. If the effects are produced in the somatic cells, they must become apparent, by definition, within the life of the irradiated organism, and a consequence of concern is the induction of cancer. If the effects are produced in the germ cells, whose function is to transmit genetic information to new individuals, the effects may be detected in the descendants of the irradiated individual in the first or subsequent generations. Because preservation of the health of ecosystems requires insuring the maintenance of very diverse indigenous populations, there is a need to understand the impacts of radiation on reproductive success.

3.0 RELEVANT RADIOBIOLOGICAL ENDPOINTS

Many different endpoints have been used to provide useful information about radiation. Some of these provide data on effects, radiosensitivity, and mechanisms of damage from radiation while others, such as radionuclide concentrations, show how radioactivity is distributed in ecosystems. The largest database on effects is on whole-animal responses, including increased mortality, reduction in life span, etc. Other endpoints were used to demonstrate effects at the cellular level and molecular levels, i.e., increased chromosomal aberrations, sister chromatid exchanges, micronuclei, anaphase aberrations, and DNA-strand breakage. In general, whole-animal responses require much larger doses to result in an observable effect than those at the cellular levels. The endpoints most relevant to ecological risk assessment are those that provide a measure of changes in the ability of organisms to reproduce. These include factors affecting fertility and sterility, i.e., reduction in the number of gametes produced, gamete death, and increased abnormalities and mortality of early life stages. Thus, databases useful for assessing risk from current and potential exposures of populations to radioactivity are the effects of irradiation on mortality, fertility, and sterility, the latter two of which are important components of reproductive success.

4.0 MORTALITY

The mortality of different species from acute radiation was used traditionally to identify groups of organisms that appeared to be more radiosensitive than others. The response to the irradiation was expressed frequently as the median lethal dose or $LD_{50/30}$, which is the dose killing 50% of the population within 30 days. Data are available both from acute and chronic irradiation.

Some representative data on acute radiation effects on mortality of different taxonomic groups are provided (Table 1). The results show that the range in acute doses that produce mortality in different organisms is very large (< 3 to > 30,000 Gy), that the ranges in responses overlap, and that among animals, mammals are the most sensitive group. However, there is no indication that acute doses less than 1 Gy will result in mortality in animal groups, including mammals.

Table 1. Representative data on the range of acute LD_{50s} for different taxonomic groups.

Group	Radiation Dose (Gy)
Protista	30 - 30,000
Invertebrates	2.1 - 1,100
Vertebrates	
Fishes	10 - > 600
Amphibians	7 - > 22
Reptiles	3 - 40
Birds	5 - 20
Mammals	2.5 ~ 10

The chronic effects of radiation on mortality were assessed in some non-human and human species, but the database is limited (Woodhead, 1984; Anderson and Harrison, 1986; ICRP, 1991; Rose, 1992; UNSCEAR, 1993). For a diverse group of invertebrates and fishes, dose rates resulting in mortality ranged from about 0.1 to >0.48 Gy/h. For mammals, the highest radiosensitivity was found in the rats *Perognathus formosus* and *Dipodomys microps*; they had a dose-rate limit of about 0.4 mGy/h (Rose, 1992).

Mortality data appear to indicate that there is a relationship between radioresistance to high doses of acute radiation and taxonomy of the organism, primitive forms being less radiosensitive than complex vertebrates. However, it must be noted that poikilotherms (animals such as fishes and invertebrates) do not maintain a constant internal body temperature and cell-cycle times are generally more variable and much longer than those in mammals. Furthermore, similar radiosensitivities of related species cannot be assumed, and rules on increasing radiosensitivity with taxonomic position are not absolute. Because such factors as exposure conditions and physiological state can modify responses, the lower limit of radiation inducing mortality in most non-human species is most likely still undefined.

5.0 REPRODUCTIVE SUCCESS

Reproductive success for a given population is related to a number of characteristics of the species. These include the (1) inherent radiosensitivity of reproductive tissues and early life stages, (2) specific processes occurring during gametogenesis, (3) reproductive strategy, and (4) exposure history (Woodhead, 1984; Anderson and Harrison, 1986; ICRP, 1991; UNSCEAR, 1996). Problems met with when assessing data on the effects of radioactivity on reproductive success are the heterogeneity in the kinds of tests performed. It must be re-emphasized that factors other than total dose or dose rate affect the results.

Radiosensitivity. Inherent radiosensitivity factors are those that are controlled by the genetic make-up of the organisms and that determine basic biological repair processes and developmental processes and pathways. Some indication of inherent radiosensitivity is obtained from a comparison of data on effects of acute and chronic irradiation on sterility and fertility.

Numerous experiments were performed to characterize the responses of gametes and early life stages of fishes, invertebrates, and mammals to low levels of acute and chronic radiation. The effects of life stage on radiation responses indicate that sensitivity of early life stages decreases during development (Welander et al., 1948; Welander, 1954; Ravera, 1967). Effects on gametes of fishes were reviewed in Egami and Ijiri (1979). In fishes, irradiation not only may retard development but also alter morphological and physiological characteristics of both early life stages and adults.

Acute irradiation doses affecting reproduction can be assessed from laboratory data on doses that have resulted in decreased fertility or sterility (Table 2). The results demonstrate that effects of acute irradiation on fertility in mammals, fishes, and invertebrates occur over doses ranging over at least two orders of magnitude (0.06 to 20 Gy) and that between 0.05 and 0.5 Gy appear to define a critical range in which detrimental effects on fertility are first observed in a variety of radiosensitive organisms. Also, induction of sterility occurs over a range from 1 to 1,000 Gy and doses less than 1 Gy are not expected to have an observable effect.

Data on chronic radiation show that the dose rates resulting in significant changes to fertility in invertebrates had a larger range of values than those in fishes and mammals. The range for the invertebrates was from 0.07 to 550, for fishes < 0.6 to 4.2, and for mammals 0.023 to 0.07 mGy/h (Table 3). Comparison of the dose rates affecting fertility shows that there is a range of lower values, 0.02 to 0.2 mGy/h, that result in detectable changes in fertility in both mammals and nonmammalian species. The dose rates known to cause sterility in different species also have a large range, from 0.17 to 1,400 mGy/h, but sterility has not been reported for dose rates less than 0.1 mGy/h.

Table 2. Comparison of sensitivity of reproductive tissues of invertebrates, fishes, and mammals exposed to acute radiation (dose in Gy). The doses for fertility are those at which significant changes were noted and for sterility were for when the effect was noted.

	Dose[a] (Gy)		
Invertebrates	**Fertility**	**Sterility**	**References**
Diaptomus clavipes (copepod, embryos)	10	—	Gehrs et al., 1975
Neanthes arenaceodentata (polychaete worm)	0.5	50	Harrison & Anderson, 1994a
Gammarus duebeni (amphipod, adult)	2.2	—	Hoppenheit, 1973
Artemia salina (brine shrimp, juveniles)	9	21	Holton et al., 1973
Crepidula fornicata (slipper limpet, larvae)	20	—	Greenberger et al., 1986
Physa acuta (freshwater snail, adults)	20	1,000	Ravera, 1966, 1967
Fishes			
Oryzias lalipes (medaka, adult males)	5	—	Hyodo-Taguchi, 1980
Oncorhynchus tschawytscha (chinook salmon, embryos)	2.5	—	Welander et al., 1948
Salmo gairdnerii (rainbow trout, 29-d embryos)	6	—	Konno, 1980
Mammals			
Mice (LD_{50}, primordial follicles)	0.1	1	UNSCEAR, 1982
Rat (LD_{50}, primordial follicles)	0.7	8	" "
Monkey 10	20		" "
Human male	0.15	3.5 – 6	" "
Human female	0.06	2.5 - 6	" "

[a] The radiation units provided in references were converted to Grays for comparative purposes. Some values are approximations.

Table 3. Comparison of sensitivity of reproductive tissues of invertebrates and fishes exposed chronically to radiation (dose rate in mGy/h). The doses for fertility are those at which significant changes were noted and for sterility were for when the effect was noted.

	Dose[a] (mGy/h)		
Invertebrates	**Fertility**	**Sterility**	**References**
Pollicipes polymerus (goose barnacle, larvae)	0.07	—	Abbott & Mix, 1979
Neanthes arenaceodentata (worm, single generation)	0.19	20	Harrison & Anderson, 1994b
Ophyrotrocha diadema (worm, seven generations)	3.2	—	Knowles & Greenwood, 1994
Daphnia pulex (water flea, multiple generations)	550	1,400	Marshall, 1962
Fishes			
Ameca splendens (–, single generation)	< 0.6	0.6	Woodhead et al., 1983
Poecilia reticulata (guppy, single generation)	1.7	13	Woodhead, 1977
Oryzias lalipes (medaka, adult males)	2.8	840	Hyodo-Taguchi, 1980
Oncorhynchus tschawytscha (chinook salmon, embryos)	4.2	—	Bonham & Donaldson, 1972
Gambusia affinis	13	—	Trabalka & Allen, 1977
Mammals			
Male Human	0.05	0.23	UNSCEAR, 1982, 1992
Female Human	0.023	—	" " "
Male Dog	0.07	0.17	" " "

[a] The radiation units provided in references were converted to Grays for comparative purposes. Some values are approximations.

The database on chronic effects of radiation on fishes and invertebrates is small, and any conclusions about the significance of the differences may not be valid. In a summary of data for mammals (UNSCEAR, 1993), the reader is cautioned that responses are dependent on the developmental stage of the gonadal tissue at the time and on duration of the irradiation, and that for any species the range in sensitivity may be large. Although such changes in sensitivity are not as well documented in other taxonomic groups, it is likely to be an important factor. It is of interest to note that for invertebrates the low values are in about the same range as those for some fishes and mammals. This indicates that at the cellular and molecular levels, radiosensitivity for these different organisms may not differ much if similar gametogenic stages are exposed.

Gametogenesis Strategy. Reproductive success is affected significantly also by the processes occurring during gametogenesis and their duration. Processes of gametogenesis differ greatly from species to species. Important gametogenesis parameters include the ability to repopulate and repair damage to primary germ cells, the duration and synchrony of stages in gametogenesis, the overall time between production and release of gametes, and the overall time to sexual maturity. Also, within the same species, the responses of male and female gonads is commonly not the same. In general, the testis is more radioresistant than the ovary. In some species, sterility requires dose rates and doses to the testis larger than those causing adult mortality. Recovery of gonads from radiation damage may reflect differences between sexes and among species in radioresistance of the stem-cell population and in the ability of cells to repopulate.

Reproductive Strategy. Reproductive success for a given species may be related also its reproductive strategy (Woodhead, 1984; Anderson and Harrison, 1986). For example, in a species producing large numbers of offspring, the survival of early life stages may be very low. Furthermore, the loss of abnormal embryos induced from radiation exposure may be masked completely by those lost from other ecological factors, such as food limitation and predation. In species that do not produce large number of offspring, strategies for protecting early life stages may be present, such as brooding of the early stages, guarding of nests, or viviparous development.

Important other factors of reproductive strategy, in addition to the total number produced, rate of division, and sensitivity of the gametes, include the time between the formation of the primary germ cells and the release of mature gametes. This becomes important in long-lived species exposed to chronic irradiation because integration of dose may occur. If repair of radiation damage does not occur, the dose to reproductive tissues may be integrated over periods of ten of years. Unfortunately, in many mammals, fishes, and invertebrates the processes involved in radiosensitivity and in gametogenic and reproductive strategies are not known.

Exposure History. Reproductive success of a species in natural ecosystems is affected also by the changes in the population gene pool from multigeneration exposures to radiation and other contaminants. At most radioactivity-contaminated ecosystems, the exposure to the biota is chronic, at low levels, and multigenerational. However, the data available on the effects of this type of irradiation on reproductive success are limited. The database from laboratory studies contains information from only one study that was multigeneration (see Table 3). The duration of most studies was for less than a complete life cycle, and the stages in the life cycle irradiated were not always comparable. The database from field studies includes results from multigeneration investigations, but the results from many of these studies were confounded by the presence in the ecosystem of contaminants other than radioactivity (NCRP, 1991). It is apparent that the database on multigeneration exposure to chronic radiation is very limited.

6.0 IRRADIATION RESULTING IN DETRIMENTAL EFFECTS

The detrimental effects considered in risk assessment are the doses and dose rates that potentially may affect population stability, i.e., causing mortality, sterility, and decreased fertility. From the data reviewed on irradiation doses and dose rates resulting in such responses (see Tables 1-3), it is apparent that the most sensitive endpoint is fertility. In Table 4, the ranges of doses and dose rates eliciting mortality, sterility, and decreased fertility are presented as well as those below which these effects are most likely not produced (NOELs, no observable effects levels). For screening purposes to determine whether a potential ecological risk may be present, the following assumptions about the effects on radiation on biota are proposed: (1) the doses and dose rates causing no detectable effects on fertility in the most radiosensitive species will not result in decreased reproductive success in other species of invertebrates, fishes, and mammals, and (2) doses and dose rates lower than those causing mortality and sterility in the most radiosensitive species will not result in loss of endangered species, loss of populations, or reduced biodiversity in radionuclide-contaminated ecosystems. However, in those ecosystems where the doses and dose rates exceed the proposed NOELs, then these assumptions are not useful, and additional site-specific investigations may be necessary to provide the information required.

Table 4. The doses and dose rates resulting in mortality, sterility, and decreased fertility in groups of mammals, fishes, and invertebrates and the recommended no observable effects levels (NOELs).

	Dose (Gy)		Dose Rate (mGy/h)	
	Range	NOEL	Range	NOEL
Mortality	< 3 - > 30,000	< 1	0.1 - 0.48	< 0.1
Sterility	1 - 1,000	< 1	0.17 - 1,400	< 0.1
Fertility	0.06 - 20	0.05	0.023	0.02

7.0 UNCERTAINTIES AND GAPS

Currently, radioecological risk assessment for almost all ecosystems involves making assumptions about potential effects because the responses to radiation of most non-human species are not characterized. The information reviewed in the preceding section indicates wide ranges in responses with species can be expected. This can be seen by comparing the responses in two widely diverse species, humans and a polychaete worm (Table 5). For the human female, the difference between doses causing mortality and affecting fertility is about a factor of 40 (2.5 vs. 0.06 Gy) but for the worm it is 1,000 (500 vs. 0.5 Gy). Another parameter that may differ greatly from species to species are the differences in doses that cause decreased fertility and cause sterility. In the human female little if any difference exists whereas for polychaete worm the difference is a factor of 100. We need to recognize capabilities that may affect inherent radiosensitivity in widely diverse groups of organisms. Parameters that most likely contribute to inherent radiosensitivity include the capabilities for (1) biological repair, which may affect the dose or dose rate at which effects are first observed and the magnitude of the effect, and (2) cell repopulation and specialization, which may result in replacement of damaged cells and tissues and mask the total impact of the radiation.

Biological Repair. Biological repair consists of repair of nuclear as well as cytoplasmic materials. The main focus of repair in the nucleus is on the processes involved in the repair of DNA; that of cellular repair is on the group of enzymes that are involved in the prevention of and in the repair of damaged constituents within the cytoplasm.

The ability of cells to repair radiation damage was noted early on when organisms were observed to often show reduced sensitivity when exposed to fractionated doses (Woodhead, 1984; Anderson and Harrison, 1984; NCRP, 1991; UNSCEAR, 1996). The conclusion was that splitting the dose allows repair processes to reduce the damage. Currently, there is sufficient information to conclude that repair mechanisms are widely distributed and are important to radiosensitivity responses. The mechanism receiving the most attention is DNA repair, and an extensive database is available on the genes involved and the processes occurring in a wide variety of organisms (UNSCEAR, 1993; UNSCEAR, 1994).

One of the most remarkable capabilities to repair DNA damage was reported for the bacterium *Deinococcus radiodurans*, which is capable of surviving up to 30,000 Gy of ionizing radiation (Daley and Minton, 1995).

Such a dose shatters the organism's chromosomes into hundred of fragments, yet because of an extraordinary ability to recover, due in part to its efficient DNA repair machinery, the organism survives. Because such high radiation doses are not found normally in the environment, it was proposed that the radiation resistance may be the result of its ability to repair its DNA after severe dehydration.

Table 5. Comparison of acute doses resulting in different responses in the human female and male and the polychaete worm, Neanthes arenaceodentata.[a]

Radiation Dose (Gy)	Process	Human		Worm
		Female	Male	
0.001	REPAIR	No Observable Effect	No Observable Effect	No Observable Effect
0.01	REPAIR	Fertility (0.06)		
0.10			Fertility (0.15)	Fertility (0.5) DNA strand breaks (0.5) Sister chrom exchange (0.5)[b]
1.0	CELL REPOPULATION	Mortality (2.5) Sterility (2.5)	Mortality (2.5) Sterility (3.5)	
10	CELL REPOPULATION			Reduced brood size (10)[c] Sterility (50)
100	CELL REPOPULATION			Reduced life span (100)[c]
1,000	CELL REPOPULATION			Mortality (500)

[a] The acute dose resulting in the response is shown in parenthesis, and the references are found in Table 2 except where indicated.

[b] Harrison et al., 1987.

[c] Anderson et al., 1990.

It is well documented that treatment of dividing cells with radiation causes a cell-cycle arrest, and when the pause is absent, the cells are more sensitive to radiation. Specific surveillance mechanisms have been found that detect mistakes, such as DNA damage or in completion of cell-cycle events, and induce inhibitors of key cell-cycle transitions. The surveillance mechanisms are often referred to as "checkpoints." Many proteins in the checkpoint pathway were identified in yeast (Carr et al., 1995; Carr, 1996). Mitotic checkpoints are considered to require three distinct functions: (1) a detection system to determine the change in DNA structure, (2) a signal pathway to transmit this information, and (3) an effector mechanism to interact with the cell-cycle machinery. Checkpoint pathways have components shared among all eukaryotes, indicating that the cell-cycle regulatory mechanisms are conserved (Elledge, 1996).

Information does exist on DNA repair in some aquatic organisms. DNA-strand breakage was investigated in freshwater fishes (Shugart, 1988; Shugart et al., 1989) and in a marine bivalve and polychaete worm (Martinelli et al., 1992). Results from experiments using DNA-strand breakage as the endpoint indicate that after these organisms are irradiated, DNA-strand breakage is repaired. However, the time course of repair is much slower in nonmammals than mammals; the time of repair taking days rather than hours. Also, little is known about the fidelity of the repair, the capacity of the repair processes, and whether the processes differ among different tissues, e.g., liver as compared to gonads of the organisms. Until more information is known about how effective the DNA repair of radiation damage is in non-human animals, the importance of the process in ameliorating the adverse effects of radiation remains undefined.

Indirect damage in genetic material from free radicals produced in the cell's internal milieu from radiation is a likely occurrence (Woodhead, 1984; Anderson and Harrison, 1986). Defense mechanisms against the production of free radicals formation were reviewed by Giulio et al. (1989) who were concerned primarily about xenobiotic molecules, such as quinone, aromatic nitro compounds, aromatic hydroxylamines, biphridyls, and certain metal chelates. They proposed that "antioxidant defenses are of three general classes and include water soluble reductants (glutathione, ascorbate, urate), fat soluble vitamins (alpha-tocopherol, beta-carotene) and enzymes (glutathione peroxidase, catalase, superoxide dismutase)." The enzymes are of special interest because they are inducible under conditions of oxidative stress. Because the kinds and quantities of antioxidant-defense enzymes induced may differ with species, radioresistance in the presence of oxygen may be affected. Therefore, to have a complete understanding of species tolerance to low levels of radiation, it is necessary to consider the capability of the species to reduce concentrations of free radicals by antioxidants. Although little information is known about the role of antioxidants in preventing radiation damage in fishes and invertebrates, some information is available on methods to quantify oxidative stress-related responses induced in these organisms from xenobiotic chemicals (Giulio et al., 1989).

Cell Repopulation and Specialization. The ability of cells to initiate, at any time, repopulation of themselves to replace cells damaged by injury or by radiation and to cause cell specialization or differentiation to form tissues and organs is undoubtedly characterized genetically and varies greatly among species. Even within a species, the ability to continue to divide differs from tissues to tissue. It is well known in humans that cells lining the digestive tract, in haemopoeitic tissues, and primordial cells of the testis continue to divide, but those of nervous tissues and primordial cells of the ovary do not.

In tissue repair, a number of growth-factor genes are induced that help direct repair. However, the molecular signals that initiate the processes are not established completely but are currently under investigation (Khachigian et al., 1995). The cells involved in repopulation and specialization may be cells that never differentiated, such as primordial germ cells, stems cells, and other types of cells that were "set aside" during early development (Davidson et al., 1995), or cells that had dedifferentiated or transdifferentiated (Patapoutian et al., 1995).

Cell division is known to be followed by cell specialization or specification, a process by which the fate of cells is established and the consequences are the installation of differential patterns of gene expression. Some non-human organisms, especially the more primitive ones, have the ability to cause cells to divide and specialize to regenerate tissues and organs even as adults; many of these also appear to be radioresistant as adults. The ability to repopulate cells and initiate specialization is an important component of this regeneration capability and is related to basic developmental processes and pathways. If a species has the abilities to replace cells and to initiate specialization as an adult, the radiation damage observed at the whole organism level, such as increased mortality, may be masked and the species considered to be radioresistant. However, if in this same species, the primary cells in the reproductive organs do not have the ability to repopulate, then as far as reproductive success is concerned, the species may be radiosensitive. Because of the limited database on radiosensitivity of reproductive organs and on processes of gametogenesis in non-human species, the assumptions used in ecological risk assessments should be conservative.

Adaptive Response. Considerable data have accumulated indicating that low doses of radiation may result in changes in the cells that reflect an ability to adapt to the effects of radiation (UNSCEAR, 1993, 1994; Cohen, 1996). This phenomenon is called an "adaptive response," and it may affect our use of the linear, no-threshold theory for predicting radiation damage. The response may remain for several hours in mammals and is sometimes referred to as stress response or response to genotoxic stress. In the UNSCEAR report (1994), it is noted that the "conventional estimates of the risks of stochastic effects of low doses on ionizing radiation may have been overstated because no allowance was made for the adaptive response."

Reported manifestations of adaptive responses in mammals are accelerated growth, increased reproductive ability, extended life span, stimulation of the immune system, and reduced incidence of radiation-induced chromosomal aberrations and mutations. Another important consideration about the adaptive response is that in mammals there is evidence that the lesions that are induced by radiation may also be induced by some other toxic agents. These not only include physical agents but also chemical compounds. The adaptive response and its effect on interaction among contaminants in the environment may become as important issue in the future.

Interaction of Radionuclides with Other Contaminants. In most environments, both organic and inorganic contaminants are present. Yet, little information is available on how these may interact to potentially cause increased damage. The vast majority of laboratory experiments deal with the effects of contaminants singly. Because our concern is on effects of contaminants on fertility, of special interest are the group of organic contaminants reported to be endocrine disrupters. These are organic contaminants that mimic, block, or disrupt the action or production of natural hormones and are reported to have caused significant reproductive effects in wildlife populations (Hileman, 1996).

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9.0 DISCUSSION

Question No.1: Where is the transition between exposure indicators and environmental effects?

Dr. Harrison's comment was that the critical end-point is reproductive success and not mortality. The criteria used would be the most sensitive endpoint, or fertility along with an application factor (e.g., applying 1/10 to be conservative). If this is done, we do not need to worry about effects on a population.

Dr. Thompson added that biomarkers (for example, metallothionein) are used as indicators of exposure or effects on the population level. Biomarkers are useful for monitoring purposes. But it is difficult to gauge reproductive effects using biomarkers, i.e. DNA repair and the length of repair. It is very difficult to go to that level.

Question No. 2: ***What are the measurements of fertility, and what are your criteria for significance?***

Dr. Harrison responded that they measured the control versus the exposed, and look at oocyte survival. A statistical significance of 2 sigmas is generally used as a criterion.

10.0 REFERENCES

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