
APPENDIX C: INHERENT RADIOSENSITIVITY FACTORS

Ecological risk assessment of the Alaskan environment requires an understanding of basic processes that affect radiosensitivity because the responses to radiation of most species in the Arctic have not been characterized. The information reviewed in Section 5 indicates that comparison of responses during reproduction and development represent better the radiosensitivity of the species than the mortality responses of adults. The RAIG needs to recognize factors that may contribute to inherent radiosensitivity in widely diverse group of organisms. Parameters that most likely reflect inherent radiosensitivity include the capabilities for (1) cell repopulation and specialization or differentiation, (2) biological repair, and (3) adaptive responses.

C.1 CELL REPOPULATION AND SPECIALIZATION OR DIFFERENTIATION

The ability of cells to initiate at any time repopulation of themselves to replace cells damaged or injured by radiation and to cause cell specialization or differentiation to occur undoubtedly is characterized genetically and varies greatly among species. 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., 1996). The cells involved in repopulation and specialization may be cells that never differentiated, such as primordial germ cells, stem 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). If organisms have the abilities to replace cells and to initiate specialization, the radiation damage observed at the whole organism level may be masked. Both these abilities are most likely related to basic developmental processes and pathways and are important components of tissue and organ recovery from radiation damage.

C.2 BIOLOGICAL REPAIR

Inherent radiosensitivity is also related to the biological repair capability of cells. 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 when organisms were observed to often show reduced sensitivity when exposed to fractionated doses (see reviews Woodhead, 1984; Anderson and Harrison, 1986; NCRP, 1991; and UNSCEAR, 1996). The conclusion is 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).

Indirect damage in genetic material from free radicals produced in the cell's internal milieu from radionuclides accumulated internally is a likely occurrence (Woodhead, 1984; Anderson and Harrison, 1986). Defense mechanisms against the production of free-radical 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).

Some information does exist on DNA repair in aquatic organisms. DNA-strand breakage was investigated in freshwater fishes (Shugart, 1988; Shugart et al., 1989) and in a marine bivalve and a polychaete worm (Martinelli et al., 1990). Results from experiments using DNA-strand breakage as the endpoint indicate that after these organisms are irradiated, DNA-strand breakage is repaired. However, the course of repair is much slower in these animals than in mammals; the time of repair takes 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 aquatic animals, the importance of the process in ameliorating the adverse effects of radiation remains undefined.

C.3 ADAPTIVE RESPONSES

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. The following are some of the mechanisms proposed to be involved in the adaptive response that might be reflected in

radiosensitivity responses quoted from the UNSCEAR report (1994):

- (a) Effects of radiation on the up-regulation of genes and their influence on cell-cycle kinetics;
- (b) Identification of activated genes and their enzyme products specifically involved in radiation-induced DNA repair;
- (c) Relationship between radiation-induced repair genes and those activated by other mutagens;
- (d) Ability of cells to remove toxic radicals;
- (e) Activation of membrane receptors and the release of growth factors; and
- (f) Effects of radiation on the proliferative response to mitogens.

Although these factors may come into play at low doses and low dose rates, which are characteristic of many of the conditions found in the environment, very little is known about the mechanisms in fishes and invertebrates. The presence of adaptive responses in fauna of concern in our assessment should make our findings even more conservative.

Another important consideration about the adaptive response is that in mammals there is evidence that the lesions induced by radiation also can be induced by some other toxic agents, including physical agents as well as chemical compounds. The adaptive response and its effect on interaction among contaminants in the environment may become an important issue in the future.