I. DNA LESIONS

Initial damage: in a mere fraction of a second

When radiation enters matter, whether the matter is inert or living, it can interact with the atoms it meets, losing some of its energy at each encounter. This interaction takes only a tiny fraction of a second. The energy of the radiation is transferred to the medium it penetrates, causing ionization (loss of electrons), and transient excitation of the atoms it meets. This ionization subsequently induces structural modifications within the irradiated matter.

Deoxyribonucleic acid (DNA) is an important constituent of the cells of living organisms, making up more than one tenth of their dry weight. Some fifty billion kilometers of DNA are incorporated in the nuclei of the fifty thousand billion or so cells that compose the human body. The state of this DNA, well known for its structure comprising two complementary strands wound in a double helix, is vitally important because DNA supports all the organism's genetic information. It can be compared to a book in which sentences, or genes, are made up of words of three letters chosen from a chemical alphabet of four letters (the four bases).

Other equally vital molecules are also vulnerable to the effects of ionizing radiation, for example water molecules. Water bathes all the cells in the organism, representing more than two thirds of the mass of the human body, and so holds a special place. Ionizing radiation can act on DNA directly, by ionization of the atoms it contains, thereby inducing local modifications of the double helix. The same damage can be caused indirectly by ionization of a water molecule. The decomposition of the water by the action of the ionizing radiation generates chemical species that are unstable because they bear an unpaired electron. These highly reactive entities will oxidize any DNA in their immediate vicinity. The action of ultraviolet radiation and of certain chemical toxicants also leads to the formation of these active oxygen species, which are also involved in the process of cell aging. The same modifications are induced, irrespective of whether the action of the ionizing radiation is direct or indirect. These lesions, which may take the form of damaged or missing bases, breaks in either or both of the DNA strands, or bridges between DNA and certain proteins, will impair the organism's genetic heritage. Various analytical methods are used to study the changes brought about in the structures of damaged molecules.

All these molecular effects take place very rapidly, the whole chain of events taking between one thousandth and one millionth of a second. To study them practically, beyond the global concept of absorbed dose, which quantifies the energy transferred, the technique of microdosimetry is used, which enables us to investigate the microscopic geometry of the energy transfer by dividing up the space around the path of the ionizing particle into very small volumes. This approach makes it easier to estimate the damage sustained by DNA, and together with research on the fundamental mechanisms involved helps us gain a better understanding of how the radiation acts.

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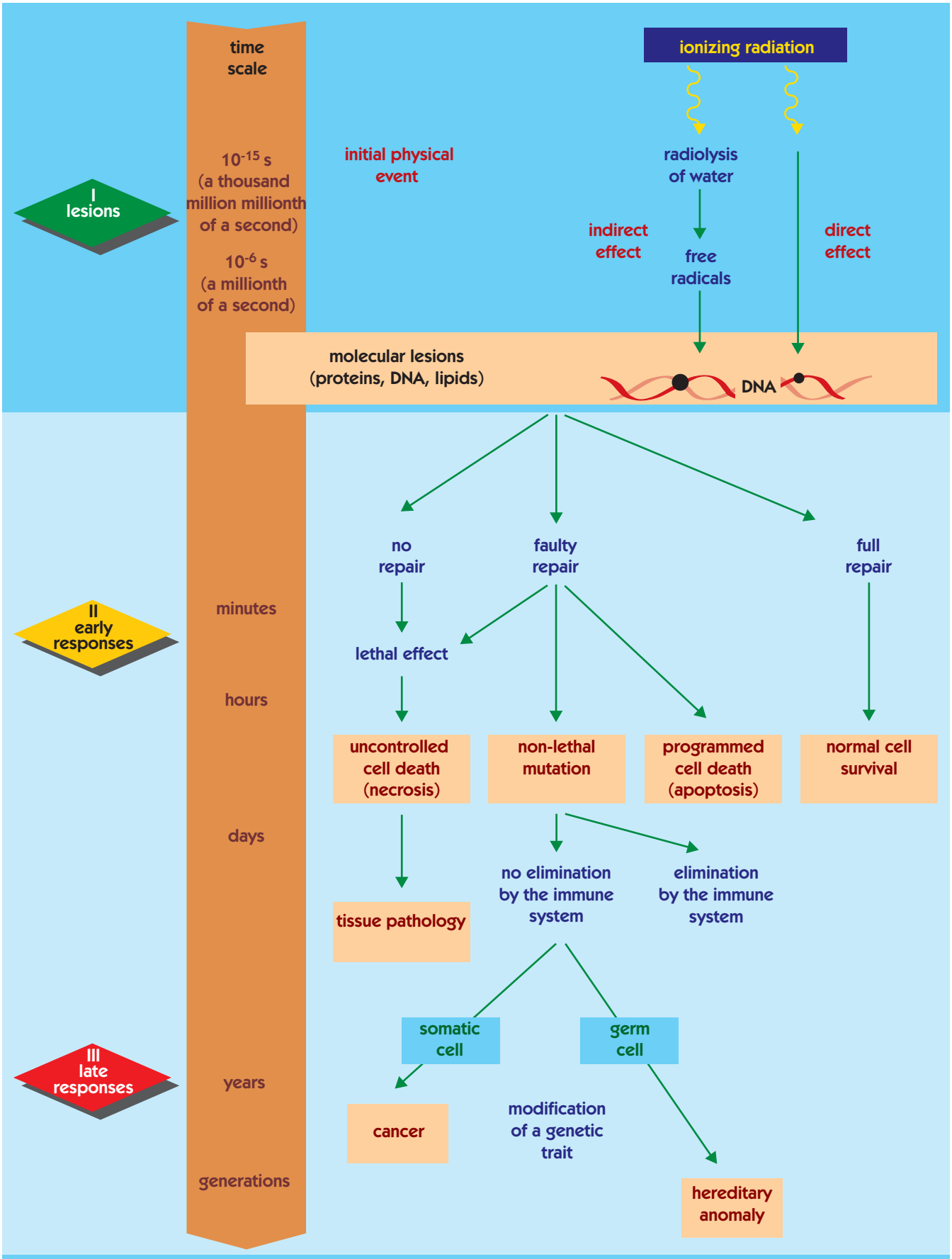

Biological effects of ionizing radiation. Time course of possible outcomes at the cell level.

N.B. *Not all the events indicated have the same probability of occurring. Normal cell survival, for example, is the most frequent outcome after DNA repair.*