Cell Proliferation and Chromosomal Damage after Irradiation.

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For cell death after irradiation two fundamental different mechanisms are described. While in interphase death the cells die before the first mitosis occurs, for reproductive death the irradiated cells and their daughters go through several mitoses and the cells die in the following generations. At least for this second mechanism energy deposition in the cell nucleus is more effective than in the cytoplasm. The experimental evidence will be described. Apparently chromosomal damage, which is induced directly after irradiation, is modified and amplified in such a way that the progeny cells can no longer contribute to cell proliferation. Cell death is the consequence;the number of cell generation cycles is besides other factors dependent on the radiation dose and radiation quality, before cell death occurs. After exposure with high LET radiation the number of cell generation cycles is smaller than after exposure with low LET radiation.

Beside the quality of the primary radiation events cell proliferation is very important for the development of the radiation damage. With synchronized cell populations it has been demonstrated that the radiosensitivity of cells differs in

the various phases of the cell generation cycle. Usually the sensitivity is comparatively low in late S-phase and high in G_2-phase. It is assumed that the differing intensity of repair processes is responsible in part for the difference.

Quite often it is observed that irradiated cells arrest in the G_2-phase of the cell cycle before the first post-radiation mitosis, G_2-block. With preimplanted mouse embryos it has been found that apparently no further repair processes take place when the cells have gone through one mitosis. - This biological system is advantageous for such studies, as the cells are naturally synchronized for some cell generation cycles and it can easily be determined through how many mitoses the cells have migrated after irradiation. Those cells which arrest longer in the first G_2-phase show less chromosomal damage and cell death.

The chromosomal damage is partly expressed by loss of chromatin from the cell nucleus into the cytoplasm. The formation of these micronuclei can be correlated to certain types of chromosome aberrations. The development of chromosome breaks, chromatid breaks and micronuclei is studied after the first, second and third mitosis post-radiation exposure with X-rays and neutrons. The consequences for cell death will be discussed.