EXTRAPOLATION OF ANIMAL DATA TO MAN

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INTRODUCTION

Experimental radiation research is devoted to the evaluation of the biological effects of radiation on man under various conditions. While the animal experiments can be selected according to the question raised, direct conclusions for man are restricted to the observations available on selected groups of people (cohorts). Thus, it is necessary to evaluate under which conditions an extrapolation of animal data to man is possible. Such an extrapolation could be done for a number of biological radiation effects, but there are also many limitations for it. Therefore we have to discuss the various radiation effects relevant for radioprotection. The following topics will be addressed:

- acute radiation effects after total body irradiation;
- teratogenic effects;
- late effects in normal tissues;
- radiation induced carcinogenesis;
- genetic effects of radiation.

ACUTE RADIATION EFFECTS

Acute radiation sickness in various animal species can be quantified by using the dose effect curve for survival within 30 days and calculating the lethal dose in 50% of the exposed animals (LD50/30). This dose reflects the extent of the damage to the bone marrow and the resistance of the animal against infection. There is a great variation of the LD50/30 values and the slope of the dose effect curve between the various animal species, for instance mice, rats, dogs or monkeys (Hall, 1978). Accordingly it is difficult to obtain a reasonable curve for man. In the German Risk Analysis Study for Nuclear Power Plants (Deutsche Risikostudie, 1980) the LD50/30 value for monkeys of 5 Gy is used for man. In addition, it assumed that about 10 percent of the population would exhibit a higher radiosensitivity than the other healthy persons, due to various pre-existing conditions.

such as anaemia, bronchitis, hyperthyreose and others. The only large population of people, receiving whole body irradiation are among the survivors of atomic bombs exposure, but this survival depended also on many other factors such as mechanical and thermal injury, as well as the state of general exhaustion.

TERATOGENIC EFFECTS

One of the acute radiation effects of special interest is the impairment of development of the embryo and fetus, the so-called teratogenic effect of irradiation. According to early classical studies (Hall, 1978; Brent et al., 1987), the radiation effect depends greatly on the respective stage of development. In the preimplatation period, mostly prenatal death is observed, while during organogenesis, malformations and neonatal death occur. During the fetal period no severe damage has been noted; consequently relatively low radiosensitivity has been reported in developing mices. The stages of development mentioned differ in various animal species. Malformations during organogenesis occur in a precise time schedule, depending on the type of teratogenic agent administered.

Recent studies have shown that in man also the fetal period is rather sensitive for damage of the brain development leading to mental retardation. This could be demonstrated by Otake and Schull (1984) on children exposed in utero in Hiroshima and Nagasaki (cf UNSCEAR 1986). According to the frequency of severe mental retardation, an exposure between the 8th and 15th week of gestation was particularly effective. The dose effect relation for this effect seemed to be linear from about 1 Gy down to a few cGy. This is in contrast to many animal experiments, in which malformation exhibited a distinct threshold dose (for a no-effect-level) of about 0.25 Gy (Konermann, 1982). Yet, this mental retardation in man after irradiation in the fetal period could not be detected in animals despite various attempts to test brain function.

LATE RADIATION EFFECTS ON NORMAL TISSUES

Much more information is available for the comparison of late radiation effects in animals and man. This concerns the carcinogenic effect of radiation, but also the late damage of various normal tissues. Late radiation effects on normal tissues were first observed as side effects of radiotherapy of malignant tumours. Later, experimental studies on animals were made, leading to the conclusion that the mechanisms and time course of late effects are quite comparable in animals and man. Hence animal studies are suitable to achieve progress in understanding the mechanisms leading to late effects in normal tissues.

In man and in animals late effects develop after a short latency period following a fraction of irreparable injury. It was proposed by Rubin (1984) that these effects are due "to parenchymal cellular hypoplasia of stem cells and to alterations in the fine vasculature and fibroconnective tissues". Due to the impairment of the renewal system in the