12th meeting on mammary cancer in experimental animals & man

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abstract

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title: MAMMARY CARCINOGENESIS IN THE RAT AFTER SINGLE AND FRACTIONATED X- AND NEUTRON-IRRADIATION AND HORMONE ADMINISTRATION.

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Studies on radiation carcinogenesis are important for the assessment of risks of ionizing radiation during occupational and accidental exposure. Furthermore this type of research is of interest to allow a risk-benefit analysis of diagnostic procedures involving small doses of ionizing radiation. The human data available for X- and gamma-irradiation all pertain to large doses. In order to extrapolate these data to the range of much smaller doses, as required for risk-estimates of X-ray diagnosis and industrial radiation exposure, the shapes of the dose-effect curves for tumour induction and the influence of external factors must be evaluated.

Since 1973 a program on radiation carcinogenesis of the rat mammary gland is performed with three different rat strains, namely Sprague Dawley Wistar WAG/Rij and Brown Norway. The objectives of the program are to investigate the cumulative tumour prevalence over a wide dose range for single and fractionated irradiations, to assess the relative risk of neutron irradiation, to determine the relative biological effectiveness (RBE) of neutrons with energies of 0.5, 4 and 15 MeV and to study the possible synergistic interaction of oestrogen administration and neutron irradiation, so as to gain insight into possible increased risk of women on estrogen containing contraceptive medication.

The animals were irradiated at an age of approximately 8 weeks. Subgroups were introduced of sterilized animals and animals in which estradiol-17β, pellets were implanted into the dorsal region of the neck. A total number of 7,000 animals is included in the experiment. The animals were allowed to live out their natural life span and were killed when moribund. Special attention was paid to the numbers and histological types of mammary tumours as well as to the presence of non-neoplastic mammary gland lesions.

A number of preliminary conclusions can be formulated: 1) the number of induced tumours increases and the latency period for tumour induction decreases with increasing dose. 2) The latency period for non-irradiated controls without hormones (E_2) can be in excess of 22 months. In the hormone treated animals tumours appear earlier than in parallel groups without E_2. 3) There are considerable differences in susceptibility for tumour induction in the three rat strains. 4) The pathology data show that malignant tumours are relatively rare in the BN and SD strain, but quite common in WAG/Rij were they constitute nearly 50% of all tumours. 5) E_2 treatment increases not only the proportion of rats with malignant tumours but also their absolute incidence in both WAG/Rij and SD rats. 6) At a level of 30% cumulative prevalence the RBE for 0.5 MeV neutrons varies between 8 and 25 and for 15 MeV neutrons between 2 and 4 for the three rat strains.