1.

ARE VIRUSES IMPLIED IN HUMAN BREAST CANCER ? A SHORT REVIEW.
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Ever since it was established that mammary carcinoma in mice can be induced by a retrovirus, researchers have looked for retroviruses that could cause breast cancer in humans. So far it was not possible to isolate such a virus. Indications for the presence of virus proteins were reported and they will be discussed.

Recent work with retroviruses in animals has shown that normal cells contain so-called onco-genes which are inactive. Activation of these genes leads to cell transformation and tumor formation. Using hybridization techniques it was possible to find genes in human cells which are homologous to animal oncogenes. Some of these genes are active in cells derived from human tumors. Whether viruses are implied in the activation of these genes is not known.

2.

CROSS REACTION OF ANTIGENS IN SECTIONS OF HUMAN BREAST CANCERS WITH THE ENVELOPE GLYCOPROTEIN gp52 OF THE MOUSE MAMMARY TUMOR VIRUS MMTV: A MARKER FOR HUMAN MAMMARY CARCINOMA ? *

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Recently, antigens crossreacting with MMTV-gp52 have been demonstrated in breast cancers of US-patients by immunoperoxidase staining (Spiegelman et al., 1980). We detected similar antigens in specimens from breast cancer patients, mainly from southern Germany.

A total of 103 breast cancers, 60 normal breast tissues, 42 benign breast lesions and 10 other carcinomas were tested for antigens crossreacting with MMTV-gp52. Positive reactions were observed in 89 breast cancers (86%) and in 10 benign lesions (24%), whereas normal breast tissues and other carcinomas remained negative. The results, however, depended on the antisera used. With another antiserum 14 out of 69 breast cancers and 5 out of 34 benign breast lesions yielded positive staining results, whereas normal breast tissues and other carcinomas again were negative.

These crossreacting antigens might be useful for the confirmation of diagnosis in doubtful cases, for the early detection of micrometastases, for the assignment of metastases from unknown primary tumors and - possibly - as additional criteria for the classification of mastopathies.

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3.

MOUSE MAMMARY TUMOR VIRUS : A MODEL SYSTEM FOR MAMMARY GLAND TRANSFORMATION.
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Infection of mice with milk borne mouse mammary tumor virus (MMTV) leads to a high mammary tumor incidence early in life. Most mice also carry endogenous MMTV proviruses as mendelian genetic elements, but these genes are generally inactive and cause no tumors or tumors only late in life. Glucocorticoids enhance the expression of the exogenous MMTV, but have no effect on the silent endogenous viral genes.

In order to elucidate the different biological behaviour of exogenous and endogenous MMTV we cloned both forms of the viral DNA using recombinant DNA techniques. The biological activity of the cloned viral DNA's was analyzed after their introduction into mouse L cells or mink lung cells. Our experiments demonstrate that cloned exogenous and endogenous MMTV DNA can be expressed in transfected mouse and mink cells and that viral gene expression is stimulated by glucocorticoid hormones. Using subgenomic pieces of viral DNA for transfection we were also able to localize DNA sequences responsible for the hormone response within a 1.45 kb fragment of MMTV DNA containing the long terminal repeat sequence. This DNA fragment also contains a large coding region which could give rise to a protein of 36 k with so far unknown function. Experiments are in progress to search for this protein in mammary gland cells and mammary tumor cells.

4.

RADIATION INDUCTION OF HUMAN BREAST CANCER.
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In the last years the interest for genetical damage by low radiation doses have been extended also for somatic risks. In agreement with experimental studies (mainly on rats) the human mammary tissues seems to be the most sensitive for cancer induction. So the risk factor (regardless of age and sex) for development of breast cancer has been estimated 1977 (ICRP, 26) as $2.5 \cdot 10^{-5}$ pro rad and for leukaemia induction with $2.0 \cdot 10^{-5}$ pro rad. In these studies the linear model of dose effect have been choosen. From epidemiologic studies on atomic-bomb survivors, New York mastitis patients and Massachusetts tuberculosis fluoroscopy patients risk estimates can be presented depending strictly on the age at first exposure (e.g. 9 excess cases per 10^6 women per rad per year of life after 10 years after exposure at age 10 - 19, against 3.3 cases after irradiation at age 50). New risk estimates (BEIR III) are discussed in connection with the problem of risk/benefit for mammography. Some aspects of the mechanism of radiation induction and the possible high efficiency of high LET (dense ionizing radiation) will be presented.

Ref.: BEIR III: The effects on populations of exposure to low levels of ionizing radiation. Washington, D.C. 20418: National Academy Press, National Academy of Sciences, N.Y., 1980.

ICRP Publication 26: Radiation Protection. Recommendations of the International Commission on Radiological Protection. Pergamon Press: Oxford, New York, Frankfurt, 1977.

NCRP Report No. 66: Mammography. Recommendations of the National Council on Radiation Protection and Measurements, Washington, July 15, 1980.

5.

EPIDEMIOLOGICAL ASPECTS OF BREAST CANCER.
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In this review some of the important results from studies in descriptive and in analytical epidemiology of breast cancer will be discussed. Descriptive data show a substantial geographical variation in incidence and mortality. High rates are found in most countries of Western and Northern Europe as well as in the United States and Canada. Cancer registries in Switzerland report age-adjusted incidence rates (European population) from 75-100 per 100'000 and mortality rates from 30-38 per 100'000 women. Low rates are found in most Asian and African countries. Most of these differences seem to be due to environmental rather than to genetic factors, possibly operating at a young age. To a certain degree it is possible to define risk factors for developing the disease (family history (especially of premenopausal breast cancer), social class, reproductive variables (especially early age at first birth), radiation, certain types of benign breast disease, history of primary cancer in ovary or endometrium and possibly body build). The majority of these risk factors are fairly modest and some of them may be related to some common underlying mechanism. At present it is rather difficult to implement preventive measures on the basis of current epidemiological knowledge.