HORMONAL FACTORS IN HUMAN CARCINOGENESIS

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The epidemiologic study of hormonal factors in human carcinogenesis initially was confined to the study of variables like pregnancy or use of oral contraceptives which obviously exert their effect through hormonal mechanisms. At a later stage actual measurement of hormones on a mass scale became possible. Biological sample banks are now being developed for this purpose.

Hormones may play a role in the development of a variety of cancers. Cancers of the reproductive system probably form the majority of these. The hormonal mechanisms are virtually unknown for cancers of the ovary, the testis and prostate, partly understood in cancer of the breast and more or less settled in cancer of the endometrium.

Insight is growing as to how parity and age at first birth affect breast cancer risk. Results so far seem to indicate that the protective effect of these factors is to limit the occurrence of precancerous lesions.

EFFECTS OF THE ASSOCIATION OF PHENOBARBITAL-LIKE COMPOUNDS ON LIVER HYPERPLASIA AND ENZYME INDUCTION.

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In studies on the relationship between enzyme induction, liver hyperplasia and promotion of hepatic carcinogenesis, we have evaluated the effects of phenobarbital (PB), amobarbital (AB), diphenytoin (DP) and 1,4-bis[2-(3,5-dichloropyridyloxy)]-benzene (TCPOBOP) on liver hyperplasia (measured as liver DNA/body wt ratio) and on the p-nitroanisole-O-demethylase and aminopyrine-N-demethylase activities. Groups of B6C3F1 mice were treated with PB, and with AB, DP or TCPOBOP alone or in association with PB. PB and TCPOBOP increased the liver DNA/body wt ratio, the latter being more effective, whereas DP and AB were ineffective. The 4 chemicals increased the demethylase activities to various extents: TCPOBOP was the most effective, PB and DP were equally effective, whereas AB was the least effective. The association of TCPOBOP with PB gave the same results as TCPOBOP alone, both in liver hyperplasia and enzyme induction. The association of DP with PB increased only slightly the liver DNA/body wt ratio, but increased the demethylase activities by about 50%. No changes of the PB effects were produced by AB association. The influence of the observed differences on promoting activity of hepatic carcinogenesis are being tested in the mouse, using the 4 chemicals alone or in association as promoters after initiation with NDEA.

A MURINE RENAL CELL CARCINOMA AS A POTENTIAL SCREENING MODEL IN CANCER CHEMOTHERAPY

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The principal requirement of a primary screening in cancer chemotherapy is to ensure the selection of the highest number of active drugs. L1210 and P388 leukaemias failed to detect a few clinically-active drugs. A new renal cell carcinoma (RC) was used to evaluate a number of such active drugs in the hope of obtaining a more predictive pre-screening system.

Eleven drugs with clinical activity were tested against intraperitoneally- or subcutaneously-implanted RC following two schedules, i.e. from day 1 to 9 or on days 1, 5, 9, 13 and 17. The most effective drugs were cyclophosphamide, BCNU, cis-platin and Me-CCNU which induced an increase in lifespan of over 100% and from 50 to 100% of long-term survivors (LTS). Other drugs such as methotrexate, bleomycin, 5-fluorouracil, vindesine, vinblastine and adriamycin were moderately active. Four drugs, i.e. hexamethylmelamine, busulfan, 2-deoxycoformycin and op'-DDD, which were not selected by P388 or L1210 leukaemias, were tested on RC. All except op'-DDD were active. Hexamethylmelamine induced up to 70% LTS against early, as well as advanced RC. We conclude that RC is an appropriate pre-screen model because it is able to detect clinically active drugs that were previously rejected by the P388 and L1210 systems.