Abstracts
Reports of Experimental Research

CARCINOGENIC COMPOUNDS


Data from other workers indicate that (a) sarcoma can be induced in a small proportion of rats injected with hard alone, (b) mice on the other hand are not susceptible, and (c) heated domestic fats (when fed to rats) can induce stomach tumors.

Cottonseed oil heated to 350° C. for 1 hour was injected (0.5 cc.) subcutaneously into 12 mice; 6 survived more than 414 days when sarcoma appeared in one animal and in another on the 53th day. No tumors were found in 3 survivors living more than 414 days after the injection in 12 mice of oil heated for 12 hours at 210° C. Controls, 10 mice living more than 414 days after injection of unheated oil, were also negative.

Spectroscopic examination of the heated oils gave no indication of the presence of carcinogenic hydrocarbons.

The long latent period in these tests suggests that either (a) absorption of the active factor is very slow or (b) that it is present in very low concentration.


After subcutaneous injection into rats, 3,4-benzpyrene is in part excreted as a fluorescent derivative, BPX, in bile, feces, and urine. Purification by extraction, alumina adsorption, and vacuum sublimation gave a crystalline product.

Solubility in alkalies suggests a hydroxy derivative, but melting point, fluorescence spectra, alkali solubility differences, morphological and optical examination of the crystals, and seeded recrystallization (hot wire stage), indicate that BPX is not identical with 6-hydroxy-benzpyrene. Spectroscopic examination of the heated oils gave no indication of the presence of carcinogenic hydrocarbons.

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Twelve sarcomas were induced in 37 mice at the site of subcutaneous injection of the nonsaponifiable lipid fraction extracted from pooled noncancerous livers of persons who died with cancer. The induction time was 182 days and the percentage yield was 32.4.

An extract similarly prepared from the livers of noncancer-bearing persons had less carcinogenic activity, having an induction time of 12 months and a percentage yield of 14.3 (5 sarcomas in 35 mice). Neither of these extracts induced tumors in rats.

A benzene extract of liver from a person who died with cancer, and various fractions of such an extract failed to induce tumors at the site of injection.

Extracts of cancer tissues also did not induce tumors.

A theory for the chemical causation of cancer is outlined, and its possible relationship to the theory of chronic irritation is pointed out. — Author's abstract.


Methylcholanthrene was used to produce malignant tumors in the cottontail rabbit, a new host for this type of work. The carcinogenic agent was injected into each of 11 cottontails at 4 sites, 2 subcutaneous and 2 intramuscular, in amounts of 250 mgm. in 1 ml. of tricaprylin.

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These animals were permitted to survive without operative interference for the duration of their natural lives. Five died before the 175th day from intercurrent infection or injury; at the time of death no histological evidence of neoplasia was found. The remaining 6 died between the 176th and the 295th day after injection. Of this group, 2 had carcinomas, and 5 had soft-tissue sarcomas with metastases to a regional lymph node in 2 and in a single animal to the lungs, liver, and kidneys in addition. Attempts to transmit the methylcholanthrene-induced tumors by serial passage in cottontail rabbits was unsuccessful. No evidence was encountered to suggest that a virus was playing any rôle in the reactions observed—Authors’ abstract.


The autoxidation of benzaldehyde and of heptaldehyde in the presence of anthracene, 3,4-benzpyrene, 1,2,5,6-dibenzanthracene, 20-methylcholanthrene, phenanthrene, dimethylaminobenzene, and hydroquinone in concentrations of M/1000 to M/10,000 was studied in an ordinary Warburg manometric apparatus at 25° C. All these compounds except phenanthrene noticeably inhibited the autoxidation of the aldehydes. Evidence from absorption spectra indicated that the inhibition of the autoxidation of benzaldehyde by 3,4-benzpyrene involves the induced oxidation of the latter to one or more quinones.---Authors’ abstract.


Certain sulfhydryl and cysteine derivatives of 1,2-benzanthracene, 10-methyl-1,2-benzanthracene and 3,4-benzpyrene (J. Am. Chem. Soc., 62:2574. 1940) have been found not to exhibit any carcinogenic activity. It is concluded that these sulfur-substituted derivatives cannot function as intermediates in the process of hydrocarbon carcinogenesis but that these or isomeric substances may possibly afford one route for the metabolic detoxification of the hydrocarbons. The observations on the thiocyanation of carcinogenic hydrocarbons support the view that the initiation of carcinogenesis by a hydrocarbon is associated with a substitution into either a meso position or an alkyl group located at such a position and involves interaction with a cell constituent containing a disulfide group. The opening of a disulfide linkage of a protein might occur by the utilization of either an active nuclear hydrogen atom or the hydrogen of a meso methyl or methylene group.---H. J. C.

Biochemistry and Nutrition


The transaminase activity of livers from rats fed a brown rice diet, with and without butter yellow, was determined at various intervals up to 200 days. The changes in these livers were followed by histological examination. With continued butter yellow feeding it was observed that the transaminase activity fell to one-third the initial value in the resulting tumor tissue. There was a high correlation between the transaminase activity and the days of butter yellow feeding. Dilution experiments resulted in curves which showed progressively decreasing values for transaminase activity. The dilution curves for the butter yellow tumor tissue were practically identical with those previously reported for transplanted mouse tumors. Livers from rats fed 15% yeast in addition to the rice-butter yellow diet showed normal values. The inhibitory effect on transaminase of the following metabolic intermediates of butter yellow, arranged in order of their potency, was investigated: quinone, N,methyl-p-phenylenediamine, N,N-dimethyl-p-phenylenediamine, and p-phenylenediamine.---Authors’ abstract.

Leukemia


The oxygen consumption of the lymph nodes of mice with spontaneous and transmitted lymphoid leukemia is not significantly different from that of normal lymph nodes. The rate of aerobic glycolysis is often, but not invariably, increased; that of anaerobic glycolysis is invariably increased. The Pasteur effect is greatly increased in the leukemic as compared with the normal lymphoid tissues studied. The metabolic activity of the leukemic tissue is similar to that of malignant tumors of mice but differs from that of human and rat tumors by a lower rate of aerobic glycolysis and a slightly negative value for the fermentation excess.

In leukemic hybrids between high and low leukemia stock mice, the rate of oxygen consumption is higher and that of aerobic and anaerobic glycolysis is lower than in high leukemia stock mice. The relative significance of the percentage inheritance from leukemia-resistant and leukemia-susceptible stock remains to be determined.

In those leukemic lymph nodes which contain considerable normal tissue, the aerobic glycolysis rate of the malignant lymphocytes is higher and the anaerobic glycolysis rate is lower than in the nodes consisting almost entirely of malignant cells. With increasing age the character of the metabolism of the leukemic lymph nodes changes, the aerobic glycolysis rate increasing, the anaerobic glycolysis rate decreasing. These changes appear to be due rather to differences in the glycolytic activities of the lymph nodes themselves than to factors in the body of the host.---Authors’ summary.

Transplantation


One hundred and eight rabbits apparently free from intercurrent disease and having each of 9 blood factor
Clinical and Pathological Reports


Previous work (Roffo) has shown that muscle extracts inhibit tumor growth. Muscle was acid-extracted, dialyzed, precipitated with trichloracetic acid, and the filtrate precipitated with phosphotungstic acid for the preparation of the bases. At each stage tests (daily oral administration; about 1/5th the lethal dose) were made on spontaneous mouse carcinoma and on grafted mouse sarcoma M.C.D.B.I., using the muscle fractions, the bases likely to occur, and related compounds (β-alanine, aminurine, arcanate sulfate, betaine, carnosine nitrate, choline chloride, creatine, creatinine, ethanolamine, methylguanidine, trimethylamine oxide hydrochloride, ethylenediamine hydrochloride, putrescine, cadaverine hydrochloride, spermine hydrochloride, tetradecamethylenediamine dihydrochloride). Ethanolamine and cadaverine hydrochloride were the most effective inhibitors but were not much superior to the "muscle extract trichloracetic acid-soluble fraction." These results (a) indicate that the activity of the muscle fraction is due to a combination of factors and (b) suggest some speculations on the correlation of chemical structure and tumor growth-inhibiting capacity.—I. H.

Breast


An analysis of 29 cases of recurrence after apparently successful operation has been made, but no evidence of qualitative difference between cases with long and short latency was found, except that latency was shorter in cases with rapid preoperative growth or with local metastases at the time of operation. On comparison of cases of breast cancer with delayed metastases compiled from the literature no trait common to all these cases was found.—Author's abstract.


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