Abstracts
Experimental Research, Animal Tumors


Intracerebral implantation of pellets of 1,2,5,6-dibenzenanthracene in 21 female C3H mice yielded 13 tumors. Of these, only 2 were gliomas—a glioblastoma multiforme and an ependymoblastoma. There were only 2 other intracranial neoplasms; one was a meningeal sarcoma and the other a fibrosarcoma. Eight tumors were extracranial fibrosarcomas. The remaining new growth was a squamous cell carcinoma of the scalp. Eight animals failed to develop any type of tumor. With the single exception of the possible glioma produced by Weil with a lard solution of dibenzenanthracene in a white rat, the 2 gliomas reported here are the first gliogenous neoplasms produced with this chemical carcinogen.—Author's abstract.


In reply to inquiries, the author states that in 17 dusting experiments (Brit. M. J., 1:179-183. 1943; see abstract, Cancer Research, 3:486. 1943) “the average number of lung tumours per mouse with a tumour was 2.4 for the dusted mice, compared with 1.9 for the controls.” The largest number of tumors in any one mouse was 17 for the dusted group and 9 for the controls.—E. L. K.


Further evidence is adduced to show that a continuous exposure of the mouse skin to methylcholanthrene, which involves the application of relatively large total doses in order to induce skin cancer, is not essential. Skin cancer can be induced by much smaller doses if the applications are made at long intervals such as 1 month. This implies a discontinuous exposure of the skin to the carcinogen.

These facts necessitate revising current conceptions of the mode of action of chemical carcinogens. In discussing these implications the following conclusions have been drawn. Increasing the dosage applied to a large area of skin increases the number of multiple skin cancers. Minimal dosages induce single skin cancers even in the more susceptible individuals of a strain. A multiplicity of skin cancers is therefore not in itself an indication of an increased susceptibility of the skin to a carcinogen.

Increasing the dosage shortens the time at which cancer develops in resistant animals; it does not materially shorten the time of induction in the most susceptible animals. The quantitative evaluation of the carcinogenic potency of chemical substances should be based on the use of minimal doses of the carcinogen. It can be determined by the percentage of cancerous tumors and the dose, rather than by the percentage of cancerous animals and the time of induction.

The etiology of multiple skin cancer in man is discussed in the light of our findings.—Author's abstract.


The liver from a person who had died of primary liver carcinoma was minced and extracted with benzene. At the boundary between the benzene and water phases, a fat-like material separated from which a waxy material was obtained by distillation. From the benzene fraction a solid material was prepared. The tissue residue was dried, powdered, and extracted in succession with benzene, cold ether, and warm ether. From the warm ether extract a more solid material and an oil were obtained. The solid material was extracted with cyclohexane. The different extracts were injected subcutaneously into mice twice weekly. With the cold ether extract, it was possible to produce tumors in mice near the site of injection. The tumors formed pulmonary metastases, but were not transplantable.—Of the hydrocarbons prepared by Diels, only the 3'-methylcyclopentenophanthrene was found to be carcinogenic. (Translation of abstract in Chem. Zentralbl.)—C. J. L.


A fluorescent phenolic derivative has been isolated from the feces of mice and rats injected with 1,2-benzanthracene by the intraperitoneal route. On methylation of the metabolite a product was obtained that possessed identical chromatographic behavior, fluorescence spectrum, and absorption spectrum (in the range longer than 300 mμ) with those of synthetic 4'-methoxy-1,2-benzanthracene. It seems suggested, therefore, that the metabolite is 4'-hydroxy-1,2-benzanthracene. The mechanism of metabolic oxidation of carcinogenic hydrocarbons is discussed briefly.—Authors' summary.

The author studied the fluorescence spectra obtained from 1,2-benzopirene, from natural purified cholesterol, and from Cd-irradiated cholesterol [irradiated with a cadmium vapor lamp] in a benzol solution of 1:20,000.

The fluorescence spectrum of benzopirene extends from 3,950 to 4,900 Å. It shows bands with maxima at 4,140, 4,260, and 4,460 Å, and minima at 4,180 and 4,425 Å. The spectrum of Cd-irradiated cholesterol lies between 3,800 and 5,000 Å. It also shows 3 bands, the maxima being at 4,050, 4,280, and 4,460 Å, and minima at 4,160 and 4,425 Å. The total fluorescence of the Cd-irradiated cholesterol is 0.8 that of the 1,2-benzopirene. The natural purified cholesterol does not show any fluorescence in the concentration used.—M. D. R.


The author gives a general discussion concerning the type of investigation in which radioactive tracers are useful and presents data on the distribution of radioactive phosphorus in normal and tumor-bearing human beings and laboratory animals. Some of the studies of iodine metabolism in the normal, diseased, and tumor-bearing thyroid gland are reviewed as well as the work done on the metabolism of radioactive calcium, strontium, carbon, nitrogen, and iron, in plants and animals. The use of radioactive elements in the investigation and treatment of tumors is only one aspect of this general review.—C. E. D.


The incidence of hepatomas was observed in 133 untreated breeding and nonbreeding strain C3H mice over 12 months of age. Although the number of animals in some groups was rather small, the results of these studies suggested that there was a relatively equal incidence of liver tumors in the nonbreeding animals of both sexes, 6% in the males and 10% in the females. In breeding animals the incidence of hepatomas was 27% in the males and 0% in the females. There was no great difference in the average age at which the neoplasms appeared in the various groups.—Authors’ abstract.


Because the incidence of spontaneous liver tumors is higher in male than in female mice of strain C3H, the influence of the male sex hormone and of estrogens on the tumor rate was studied. Nonbreeding mice were used in the experiment. Forty-eight were treated with testosterone propionate, 69 with a-estradiol benzoate, and 39 with ketohydroxyestrin. None of the 24 males and 4% of the 24 females injected with testosterone propionate developed hepatoma; 25% of the 59 males and none of the 10 females injected with a-estradiol benzoate developed hepatomas; 17% of the 25 males and none of the 9 females injected with ketohydroxyestrin exhibited hepatomas.—Authors’ abstract.


Intracytoplasmic inclusion bodies and mitochondria were studied in the liver and hepatoma cells of 88 strain C3H mice. Two types of intracytoplasmic inclusion bodies were found. One was a large hyaline body found almost exclusively in the cytoplasm of tumor cells; the other was a smaller lipoprotein body found exclusively in the cytoplasm of the tumor cells. The staining reactions of these bodies are described and their possible modes of origin discussed. Mitochondrial studies made under conditions that did not permit accurate assay of their number or forms suggested that there were few mitochondria in hepatoma cells as compared to nonneoplastic cells. It is also suggested that the administration of testosterone propionate did not alter the number, and that the administration of a-estradiol benzoate reduced the number, of mitochondria in nonneoplastic liver cells.—Authors’ abstract.


Twenty-three plant hormones were tested for their effect upon the takes and subsequent growth of the Flexner-Jobling rat carcinoma, the Walker rat carcinosarcoma 256, and on a transplantable fibrosarcoma of the mouse. The following results were obtained: (1) When tumor mince was allowed to stand before inoculation in direct contact with the plant hormones a pronounced decrease in the number of takes and subsequent growth rate was generally observed. (2) Subcutaneous injection of the same substances, however, exerted no significant effect upon neoplasms already established.—Authors’ abstract.


The problem of the relationship between filterable and nonfilterable chicken tumors was reinvestigated. A nonfilterable chicken tumor (sarcoma 16) originally induced by methylicholanthrene was transmitted for 27 generations in chickens. In young chicks the tumor was invasive and often metastasized, but in older birds it frequently regressed. The frequency of regression was in direct relation to the age of the chickens at time of injection.

No erythroleukosis or myeloleukosis was found in any of the chickens injected with sarcoma cells, 190 of which
were observed for more than 2 months. All attempts to isolate a filterable agent from the tumor failed. Sarcoma 16 grew readily in newborn ducklings, but no filterable agent was found in the duck-grown tumor.

The regression of sarcoma 16 rendered chickens resistant to a subsequent injection of a filterable agent of leukemia and sarcoma (agent 13).

The resistance of chickens to the growth of sarcoma 16 was proportional to the amount of antibodies to agent 13 in their sera. Chickens with sarcoma 16 that had regressed had neutralizing antibodies to agent 13 in much larger amounts than normal birds of the same age. The sera of chickens in which sarcoma 16 was growing but did not metastasize also strongly neutralized agent 13. The sera of chickens having tumors and metastases contained no neutralizing antibodies. Sarcoma 16 appeared or recurred in a few chickens several months after the graft of particles; these birds had a smaller amount of neutralizing antibodies to agent 13 than chickens in which sarcoma 16 did not recur.

Neutralizing antibodies to agent 13 were also produced by the injection into rabbits of high speed sediments from sarcoma 16. These antibodies could not be absorbed by cells from normal chicken spleen, which removed the complement-fixing antibodies. The injection into rabbits of heavy material from normal chicken spleen did not produce neutralizing antibodies to agent 13.

It is concluded that a nonfilterable chemically induced chicken tumor (sarcoma 16) contains an antigen not found in normal fowl cells. This antigen is related to an antigen contained in a filterable agent of leukemia and sarcoma (agent 13).

It is possible that the specific antigen is contained in a tumor agent that loses its infectivity when freed from cells, or that the nature of the association of the specific antigen with tumor cells precludes the isolation from the cells of an active tumor agent.—Author's abstract.


It was found that small benign papillomas occur quite frequently on the oral mucous membranes of domestic rabbits. These papillomas contain a filterable virus that is very stable. The virus was not inactivated at -22°C and retained its activity when kept at 65°C for 30 minutes. The virus was also found in the mouths of rabbits having no growths. It is believed that the virus may be spread by transfer from the mother to the young during the period of suckling and that it may be latent in the mouth, doing no harm unless the mucous membrane is injured. The virus has a special affinity for the mucous membranes and differs from the Shope virus.—D. S.


Rous sarcoma cells have been cultivated in vitro, without the addition of normal tissue, for a period of 6 months. The character of the cultures depended upon the amount of embryonic extract in the culture medium. With little or no embryonic extract liquefaction of the culture medium did not occur, and the spindle cells that migrated from explants formed continuous sheet growths.

It was not possible to maintain growth for more than 6 months (40 to 50 passages). After the first 30 passages growth declined. The cells underwent pronounced alterations, degenerated, and died. During the entire period of cultivation the cells retained their malignant properties (tested by inoculating cultures into chicks).—R. J. L.


The alterations undergone by cells of the Rous sarcoma growing in vitro are described and illustrated. There is a pronounced hypertrophy of the individual cells that may proceed to the formation of cells of monstrous dimensions. These retain, however, the form and architecture of their prototypes, the basophilic round cell and the spindle cell. The cultures also contain elements of unusually small sizes. Next to cell hypertrophy, changes in the nucleoplasm are conspicuous. In many cells, granular eosinophilic material accumulates in the center, leaving a clear zone between it and the nuclear membrane. Easily defined, small, rounded, homogeneous intranuclear inclusions that stain bluish gray with Giemsa's method are often found. Similar larger bodies occur singly or may fill the nucleus. The nucleoli are frequently hypertrophic and may become broken into fragments. The entire nucleus becomes vesicular and almost free from basophilic chromatin. It is often extremely lobulated. The most striking of the cytoplasmic alterations is a marking off of the central zone with the formation of a roundish, more deeply staining area at the center of the cell. The peripheral cytoplasmic layer often contains basophilic thread-like and granular structures that sometimes form extensive nets, and in addition, eosinophilic material in the form of fine granules and clumps. In a few of the cells crystalline structures also are encountered. Vacuoles are present in abundance. The large round cells may project pseudopodia in the form of rigid rods that move freely as if on a jointed base. The distal ends may swell to spherical masses that may become detached. Atypical mitosis is frequent. Multinucleated cells are often found.

The nature and significance of these changes are discussed.—C. J. L.


This tumor is rarely reported in this country but has been noted in India. The growth described herein followed injury and removal of the horn. The tumor was removed but recurred 5 months later.—E. E. S.


A large mass in the lung of a dog was visible on roentgenographic examination and was associated with cough and bony symmetrical enlargements of the 4 legs. —E. E. S.