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Reports of Research


This article is confined to a discussion of the recent work in carcinogenic substances, as the aromatic hydrocarbons, with special reference to the conversion of physiological bile acids, and the relationship of sex hormones to carcinogenesis. The influence of female sex hormones on cancer formation is illustrated by its carcinogenic capacities when the hormone is injected in great quantity into experimental animals. This is regarded as of particular significance in the light of present treatment of the menopausal syndrome. Testosterone is discussed briefly as inhibitory to tumor formation. A report from the Cancer Research Laboratory of the Mt. Sinai Hospital is given.

—A. C.


Livers without metastases (group 1) from 5 patients and livers with metastases (group 2) from 5 patients, who had died from epidermoid or glandular carcinoma, were treated in the following manner. After desiccation, the liver pulp was treated by hot benzene and the lipid fraction obtained saponified by potassium hydroxide in alcohol. The non-saponifiable fraction was extracted by petroleum ether and dissolved in olive oil (0.20 gr. per cc.). The livers of 12 patients (group 3) who had died from non-neoplastic diseases, were used as controls.

One cc. of the extract solution from each group was injected subcutaneously in the dorsal region of mice, 20 mice being used for each group. No tumors were obtained with the non-saponifiable fraction from control livers. Four tumors (3 sarcomas and 1 mammary adenocarcinoma) developed in the mice injected with the fraction from group 1, and 2 tumors (1 sarcoma and 1 epidermoid carcinoma) in the mice injected with the fraction from group 2. These tumors appeared 16 months or more after the moment of inoculation.—C. A.


Intravenous injections of 20 to 50 micrograms of mesothorium into 12 rabbits were followed by the death of 5 animals before the tenth month. Among the 7 surviving rabbits, 5 developed osteosarcomas. Fracture sites were not always the place of localization of the cancerous growths. Very small amounts of radioactive substances were successful in producing tumors, but larger amounts apparently destroyed the susceptible cells since no growths appeared.—R. J.


Benzopyrene produced tumors in 80% of the white rats treated. Guinea pigs were, on the other hand, almost completely refractory to the action of this chemical, even when large doses were used. The authors tried to establish whether the differences were due to a different metabolism of the product in the two animals. Photometric technics were used to detect the presence of the carcinogen and to localize and measure the amounts of the chemical in the host after certain lengths of time. The conclusions were that benzopyrene remains at the site of injection, and is eliminated very slowly in the case of the rat, an observation which was not seen in the guinea pigs. Here, the oil solution diffused widely and was relatively rapidly eliminated.—R. J.


Experimental study in mice (strain XVII) with an anthracenic oil showed that the acid fraction of the oil had the property of diminishing the carcinogenic action of the non-saponifiable fraction. The acid fraction, in some cases, was not responsible for the production of stomach cancer in mice.—R. J.


A solution of 2-anthramine in acetone was applied to the skin of 19 male rats (10 Wistar, 9 piebald). Between the 180th and 260th day spindle-cell tumors of the dermis
Spontaneous Mammary Adeno-Carcinomas

mental Production of Tumors by Repeated Stitching.--R. A. H.

To investigate the relationship between liver necrosis and repair and the induction of hepatomas in strain mice, a quantitative study of necrosis and repair following a single dose of carbon tetrachloride was made and the minimal necrotizing dose established. By using a graded series of necrotizing and non-necrotizing doses, a non-necrotizing dose was found which, when administered daily, would produce hepatomas, thus indicating that repeated liver necrosis and repair are, in all probability, not necessary for the induction of hepatomas. Also, although there was a correlation between the dose of carbon tetrachloride administered and both the degree of lobular disorganization and the increase of reticular fibers, some increase of reticular fibers was observed after the daily administration of sub-necrotizing doses of the agent. Some of the implications of these findings are discussed.—R. A. H.


To investigate the relationship between liver necrosis and repair and the induction of hepatomas in A strain mice, a quantitative study of necrosis and repair following a single dose of carbon tetrachloride was made and the minimal necrotizing dose established. By using a graded series of necrotizing and non-necrotizing doses, a non-necrotizing dose was found which, when administered daily, would produce hepatomas, thus indicating that repeated liver necrosis and repair are, in all probability, not necessary for the induction of hepatomas. Also, although there was a correlation between the dose of carbon tetrachloride administered and both the degree of lobular disorganization and the increase of reticular fibers, some increase of reticular fibers was observed after the daily administration of sub-necrotizing doses of the agent. Some of the implications of these findings are discussed.—R. A. H.


Hypophysectomy does not have any appreciable effect on the growth or the behavior of spontaneous adenocarcinomas in mice. The authors were unable to detect any change in the histological aspect of the cancer. Cancerous cells are not changed, whereas the normal mammary epithelium surrounding the tumor shows its usual process of atrophy following hypophysectomy.—R. J.


A discussion is given of the author's theory concerning the myotropic nature and mode of action of the chicken tumor agent—i.e., certain nodules of the myocardium, called "pseudo-metastases," are believed to be due to the proliferation of local muscle elements, caused by the polyvalent virus circulating in the blood.—G. H. H.


A method for a more accurate estimation of the latent period of Chicken Tumor I is given.—R. A. H.


It is possible to imitate the appearance of small tumors by repeated pricking of a cabbage leaf in the same place. If the needle is soaked in bee venom, the effect on the leaf is the same, with increased intensity.—R. J.


The following technic was used: the opened end of a small ampoule of bee venom was gently introduced into the leaf tissue. After 5-6 days a tumor appeared at the site where the venom had been constantly applied.—R. J.


The introduction of bee venom into flower staff of Pelargonium zonale produces the same effect as that obtained on the cabbage leaf. A localized tumor begins to appear 3-4 days after the beginning of the application of venom.—R. J.


Strain A mice were exposed daily, over an 8 hour period, to 8.8 r of gamma radiation for 267 consecutive days and were autopsied when 10.5 to 11.5 months of age. Whereas 47.3% of the control animals had lung tumors at autopsy, 76.7% of the irradiated mice were so afflicted. The relationship of gamma radiation to lung tumors is discussed.—R. A. H.


Prolonged daily feeding of large amounts of splendothélan, "a splenic and reticuloendothelial product of Braunstein," (BRAUNSTEIN, A., ZÉLINSKI, J. Krebsforsch, 39:321. 1933.) to rats, mice, and guinea pigs did not produce any immunity to experimental tumors.—G. H. H.


Cells in process of active proliferation are 2 or 3 times richer in ribonucleic acid than resting cells of the same kind of tissue. Cancerous and healthy tissues of the uterus, stomach, breast, rectum, and also rat epithelioma and chick embryo were tested.—R. J.


A study of the action of vitamin B on the growth of spontaneous breast cancers in mice showed that daily...
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subcutaneous injections of 0.04 to 0.06 mgm. and even 1 mgm. were well tolerated, and the rate of growth of the tumor was consistently slowed, the treated animals surviving longer than the controls. It is possible that the vitamin B., plays an active role in the metabolism of tumors gluclides.—R. J.


Daily feedings of an oil solution of α-tocopherol, 50 parts per 100 and one drop per animal, delays the growth of spontaneous tumors in the breast of mice. However, similar amounts given once or twice a week seem to have a stimulating effect on the growths.—R. J.


The subcutaneous injection of large amounts of nicotinamide (25 mgm. for each injection) lowered the rate of growth of breast tumors in mice and prolonged the life of the animals.—R. J.


Forty mice were fed different amounts of whole wheat. Among 57 adenocarcinomas observed, 28 showed a low rate of growth, as compared with the controls, but the other 29 tumors showed a faster growth rate during the first months; later the growth became slower. Actually, no very significant changes were observed. The animals fed with whole wheat survived longer than the controls.—R. J.


Injections of ascorbic acid were started the day after the transplantation of the tumor and were continued until the death of the animal, a total of 0.250 to 0.600 gm. being injected. The treated mice survived longer than the controls, and microscopic metastases in the lungs, adrenals, kidneys and liver were more frequent in the experimental animals than in the controls.—R. J.


The activity of 12 enzyme systems were tested in several normal and neoplastic tissues of the rat. The data show that the range of enzymic activity among normal tissues is considerably greater than among the three transplanted tumors studied.—R. A. H.


The effects of the so-called sulhydryl reagents upon the activity of purified cathepsin of the Murphy rat lymphosarcoma indicate that this enzyme system contains -SH groups which are essential for its activity. These groups are oxidized and the enzyme thus inactivated by iodine and sodium iodosobenzoate. P-Chloromercuribenzoic acid also reversibly inactivates the enzyme, and the quantity needed for complete inactivation correlates closely with the total quantity of -SH groups as determined by chemical titration. The -SH groups necessary for enzymic activity do not combine extensively with 3-amino-4-hydroxyphenyl dichlorarsine hydrochloride or with iodacetamide. The cathepsin activity is activated by sodium cyanide.—R. A. H.


Intraperitoneal or subcutaneous injections of lyophilized A strain mammary carcinoma 15991a were given mice of the C57 brown, C57 black and B alb C stocks over a period of 7 weeks, and, 8 to 12 days after the final injection, fresh tumor tissue was inoculated subcutaneously. In the majority of the treated animals the inoculated tumor grew progressively and killed the host, whereas in the majority of the untreated control animals the tumor either did not grow or regressed after a period of growth. The growth of C57 black sarcoma L946-AII transplanted to F hybrid mice (Swiss X B alb C) was also stimulated, but to a lesser degree, by the prior injection of the recipient mice with lyophilized sarcoma tissue. On the other hand, lyophilized C57 black myeloid leukemia C1945 tissue administered to C57 leaden mice produced a distinct inhibition of growth of subsequent leukemic transplants. The relation of the genetic theory of tumor transplantation to tumor-immunity experiments is discussed.—R. A. H.


Twenty lymphosarcomas were found in 4,000 autopsies of rats. Almost all the tumors appeared in albino rats, males and females. These tumors must be considered as spontaneous in origin, although most of the rats had been inoculated with various types of tumors or treated with various carcinogenic substances. All the tumors developed in the ileocecal region with the exception of 2 cases. Histologically they represented, in 18 cases, reticulo-lymphoblastic sarcoma; in 2 cases, lymphoid sarcomas. Metastases were very frequent. The tumor was successfully transplanted in 3 cases among 7 trials. One tumor was carried for 20 passages.—R. J.


Lesions of the reticular system of the liver, varying from reticulo-endotheliosis to reticulum-cell sarcoma, were found in 22 mice in a total of 2,000 animals examined. Most of these animals had been used for experimental purposes and had received tar, benzpyrene or methylcholanthrene or had been grafted with transplantable tumors.—C. A.


A spontaneous chloroleukemia in a rat was transplanted
It is the opinion of the authors that the discordance in the results of inoculation of the same tumors in rats primarily resistant to a first inoculation, is due to the fact that different kinds of tumors were tested. They found that Jensen's sarcoma resulted in the immunity of the host following one injection. On the other hand, other varieties of sarcomas had to be injected several times before a strong immunity was developed in the host.—R. J.


Immunity is difficult to obtain by serial injections of transplantable rat epitheliomas. There are differences in acquired immunity with different varieties of tumors; for example, uterine epitheliomas do not cause immunization even after a relatively large number of inoculations. One animal, however, did give a positive result after the fifth injection.—R. J.


This technic of transplantation was used in the study of the mechanism of action of chemical carcinogenesis, and also to study the behavior of tissue grafts in the process of becoming cancerous. Preliminary results seem to indicate that: 1) auto-grafts of such tissues have more chances to develop cancer than homo-grafts; 2) the development of a tumor does not depend on the general dissemination in the organism of the carcinogenic substance, but is due to its local action.—R. J.


Both intraperitoneal and peritumoral injections of novocaine were capable of increasing considerably the number of microscopic metastases in various organs. Instead of 70% of the mice surviving as was observed on the average in the controls, 50 to 60% of them in the treated group showed microscopic metastatic lesions.—R. J.


A round cell sarcoma which appeared in a rat treated over a period of time with estrogen has been studied in successive transfer generations.—A. K.


It was found that cancer induced in rats and mice, by agents such as benzpyrene, methylcholanthrene, or 7-dimethylaminozobenzene, could be influenced by diet in two ways: (1) The induction of some cancers could be retarded by certain pure substances that are not growth-inhibiting, such as glycuronic acid, nicotinamide, and vitamin B, mixed with pyrophosphate. (2) In other
experiments, with animals on a deficient diet and given p-dimethylaminozoabenzene, and similar compounds, the induction of liver tumors was prevented by making up the dietary deficiency. In the conclusion, the author states that a specific growth-inhibiting substance found in animal tissues, particularly in brain and liver, and effective in the prophylaxis of skin cancer induced in mice and benzpyrene and methylcholanthrene, is ether-soluble and thermostable. —G. H. H.

The technic is more of a short-distance radiotherapy (3 to 5 cm.) than a real contact radiotherapy. Twenty tumors were treated, and 17 animals survived much longer than the controls. In many cases there was no complete destruction of the tumors, and recurrences were observed. —R. J.

Former investigations have shown that female white mice of the strain RIII (DOBROVOLSKAIA-ZAVADSKAIA) give a percentage of 53.5% of spontaneous mammary adenocarcinomas. Almost 100% of the males of the same strain treated with estrogen developed mammary carcinomas (Lacassagne). These observations, in both females and males, were not substantiated by this study in which 6 generations of females, all suckled by mothers bearing carcinomas, and 10 males were treated with estrone benzoate. All animals were kept on a low fat, low protein diet. —R. J.

Clinical and Pathological Reports

**Multiple Tumors**


Double cancers with different histological structure are relatively rare (1.5%). They can grow simultaneously in the same patient or be successively. The possible clinical latency of one of the tumors may be misleading in the appreciation of their real chronological appearance. The evolution of such tumors seems more rapid than other cancers. Their study does not throw any light on the etiological problem of cancer in general. —R. J.

**Diagnosis—General**

The theoretical foundation of two kinds of polarographic serum reactions concerning typical changes in human serum from individuals suffering from cancer, sarcoma, inflammations, infections, or certain bile or liver disorders is discussed in detail.

Some experimental facts elucidating the nature of the pathological changes in sera are reviewed. The erroneous objections to the author's original interconnection, brought forward by certain authors, especially V. Moravský and his collaborators, are dealt with. It is shown that the experimental results of the latter authors concerning the polarographic examination of two horse sera, one normal and the other sarcomatous, are not, as these authors believe, contradictory to the present author's theory, but on the contrary, when investigated more exhaustively than these authors were able to do, even yield valuable evidence in support of it. Closely analogous results to those of the authors mentioned have been obtained by the present author with human sera and are fully explained.

Finally the cause of the pathological change in the blood stream is discussed. —Author's summary.

The aim of this communication is a critical examination of the polarographic test for cancer given by serum filtrates after deproteination with sulfosalicylic acid. On the basis of experiments with different deproteinating agents, evidence of the albumin-like character of the substance, the increase of which indicates the pathological state, is brought forward.

A detailed study of the deproteination of sera with sulfosalicylic acid is described which reveals some important facts in diagnostic tests: (1) proper caution must be paid to the rigorous maintenance of a fixed time interval between the precipitation of proteins and the filtration of the precipitate, (2) the test is improved by introducing an excess of ammonia in buffered ethylalcoholamine solution. The improved test was checked by tests on 183 cancer patients and was found positive in 177 cases.