Abstracts

Reports of Research


The authors have devised a method whereby the epidermis of mouse embryos, implanted in the voluntary muscles of adults of the same inbred (C) strain, can be selectively exposed to the action of a chemical carcinogen. It was found that the encysted epidermis underwent neoplastic changes with great regularity and rapidity under the influence of methylcholanthrene. The growths that arose from the embryo epidermis, papillomas and carcinomas, were like those appearing on the skin of adult mice after exposure to methylcholanthrene.—D. S.


Attempts to show that an agent out of the blood would localize in inflammatory lesions of the skin failed. Neoplastic changes arose only occasionally in skin of C3H and Webster-Swiss mouse embryos, transplanted with methylcholanthrene into the muscles of adults of these strains. The skin of new-born and suckling mice proved resistant, while that of their mothers and of young adults was susceptible, to the carcinogenic effect of methylcholanthrene. Gastric carcinomas, which can be elicited only after months when ordinary carcinogenic technics are applied to adult mice, arose rapidly and regularly in stomach fragments from C strain embryos, implanted, together with the carcinogen 6SM (olive oil containing 1% of methylcholanthrene and 1% of Scharlach R), into the muscles of adult mice of the same strain. Tumors from fragments of the lung, ovary, and bile passages have been similarly produced. The implications of the findings in papers I and II are discussed. The results do not support the idea that carcinogenesis of the transplanted embryo tissue is due to the lodgment therein of tumor-producing viruses.—M. H. P.


Squamous cell carcinomas of the prostate were induced by 3 mgm. pellets of compressed methylcholanthrene crystals in 1 of 9 Fischer line 344 and in 10 of 17 A x C line 9935 rats that survived an average of 241 and 329 days, respectively, after the pellets were implanted in the organ. One of these induced tumors had generalized peritoneal and skeletal metastases. The litter sisters of these males, 9 Fischer line 344 and 15 A x C line 9935 females, survived an average of 257 and 528 days, respectively, after similar pellets were implanted in the parenchyma of the liver but failed to develop any liver neoplasms. A study of the history after subcutaneous transplantation of one of the induced prostate carcinomas showed that it regularly metastasized to the lungs, superficial lymph nodes, and skeleton. Five successful transplants of a mammary adenocarcinoma to the prostate were followed by weekly x-ray examinations, but no skeletal involvement was observed.—Authors' abstract.


Hyperplastic mouse epidermis contained about 45% less copper and 30% less zinc than did normal epidermis. A transplantable squamous cell carcinoma contained even smaller quantities of copper and zinc than did hyperplastic epidermis. Judged from the mineral composition, the sequence is normal to hyperplastic tissue to carcinoma.—H. J. C.


Data are presented to show that the process of epidermal carcinogenesis in mouse and man is similar with respect to calcium, copper, and zinc. Normal mouse epidermis contained almost three times as much calcium as did normal human epidermis, about twice as much zinc, but about the same amount of copper as did normal human epidermis. Methylcholanthrene-treated mouse epidermis was quite similar chemically to normal human epidermis, which agrees somewhat with their histology. The calcium, zinc, and copper contents of a transplantable squamous cell carcinoma were 80, 67, and 83% less than those of normal mouse epidermis, while these 3 metals in human squamous cell carcinomas were respectively, 47, 30, and 70% less than in normal human epidermis.—Authors' abstract.


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In human material, gastric carcinomas were found to contain relatively less calcium and more potassium than the adjacent uninvolved gastric mucosa. In a benign papilloma of the stomach situated between 2 separate carcinomas the K/Ca ratio was of the same order as in the carcinomas and differed in like manner from the K/Ca of the surrounding uninvolved mucosa.—Authors' abstract.


In human material, carcinomas of the colon were found to contain less calcium and more potassium than adjacent normal mucosa. In papillomas of the colon an increase in potassium of the same order as that found in carcinomas was observed, but the degree of reduction in calcium was not so pronounced as in the latter.—Authors' abstract.


Twenty mice of the Street strain bearing Crocker sarcoma 180 transplants received (l+)-glutamic acid, as a suspension containing 2 gm. in 10 ml. of 0.1540 M NaH-glutamate, in 4 subcutaneous injections of 0.2 ml. at intervals of 2 days beginning 2 days after transplantation. The average tumor weight 2 days after the last injection was 0.35 gm., as compared with 0.50 gm. in controls bearing the sarcoma transplants but receiving no glutamic acid. In another experiment, the results of which were judged to be statistically not significant, both l(+) -glutamic acid and D,l-glutamic acid reduced the average weight of the tumors by about the same amount. The findings are discussed in connection with Kögl's theory of the role of glutamic acids in tumor growth.—M. H. P.


Among 26 women with carcinoma of the breast, instances of high basal metabolism, hypercalcemia, and functional uterine bleeding were present. Water-soluble extracts of 3 tumors produced a rise in basal metabolic rate in rabbits. Water-soluble extracts of 2 tumors gave rise to hypercalcemia when injected into dogs. Fat-soluble extracts of 2 of 4 tumors had an estrogenic effect in ovariectomized rats.—C. A.


A high incidence of breast cancer was induced by administering dried mammary tumor tissue of mice of the A and RII strains to 4 month old hybrid female mice (C57 × A), whose mammary glands were completely developed in the absence of the mammary tumor agent. With the dried RII tumor tissue the cancer incidence was 83% at an average age of 18 months, with the A tissue it was 60% at 20 months. A similar tumor incidence resulted when 4 month old hybrids were given 12 times the amount of dried tumor tissue as was given to 4 week old hybrids.—R. J. L.


Breast cancer was induced by dried mammary tumor tissue of mice of: (1) RII strain in C57 × C3H hybrids and Ax mice; (2) C3H strain in C57 × C3H and C57 × A hybrids and Ax mice; (3) A strain in C57 × C3H hybrids. The tumor-producing potency of the dried RII tumor tissue (as shown by the breast tumor incidence and average tumor age) is greater than that of dried C3H tumor tissue, while dried A tumor tissue is the least potent. Whether the potency of the agent varies in different strains, or whether tumors of different strains contain varying amounts of the same agent requires further investigation.—R. J. L.


During the course of this study mammary tumors were not found in any of the descendants of the fostered females of the cancerous A and Z (C3H) stocks and their reciprocal hybrids, mice that were susceptible to mammary cancer but did not have the milk agent. Observations made upon breeding females of the cancerous A and Z stocks and their reciprocal F₁ and F₂ hybrids were in accord with the theory that the mice of these 2 strains may have the same inherited susceptibility to mammary cancer. The difference in the incidence of mammary cancer in the virgin females of the A and Z strains was due to gene action in controlling some hormonal mechanism. This effect has been called the inherited hormonal influence, and is probably the result of the action of multiple genes. The same genes probably do not produce the inherited susceptibility and the inherited hormonal influence. The characteristics (concentration and/or activity) of the milk agent may differ in the A and Z stocks and possibly influenced the incidence of mammary cancer that was observed in the hybrids when they were maintained as virgins. These differences were not apparent in the breeding hybrids. Each inciting influence in the genesis of mammary cancer in mice may be almost completely determining in its effects, and thus equally important.—Authors' summary.


A comparative study of the right ovaries of virgin dba and C57 black mice revealed the following differences: (a) The average number of ova escaping from one ovary at a given ovulation is 5.2 in dba, and 4.2 in C57 black mice. Since the growing follicles are the source of estrogen, it can be presumed that this hormone is pro-
duced in larger quantity in the dba mice. (b) In C57 black virgin females 3 sets of corpora lutea are the most that can be found in an ovary. In the ovaries of dba mice the corpora lutea persist for a longer period, and 7 or more sets may be present. Consequently it can be presumed that a larger quantity of progesterone is produced in the ovaries of the dba mice. (c) In older animals hyaline changes occur in the lutein cells of persistent corpora in dba mice, and in some ovaries large hyalinized areas are present; this alteration does not occur in the ovaries of C57 black mice. (d) Groups of yellow lipochrome cells originating in corpora lutea atretica undergo atrophy and become dispersed in the ovarian stroma of dba mice, whereas in C57 black mice these cells hypertrophy and form aggregated nodules. (e) Ovarian cysts occur more frequently in dba mice (30.7%) than in C57 black mice (13.4%).—Author's abstract.


By numerous passages, a transplantable carcinoma originating from squamous cell epithelium in mice has been transformed from a keratinizing to a basal cell type and has been rendered more virulent. Photomicrographs illustrating the change are presented.—M. H. P.


A filterable agent of leukosis and sarcoma of chickens (agent 13) was sedimented from tumor extracts at a speed of 15,000 r.p.m. in an angle centrifuge. When resuspended and diluted in buffer, the sediments contained only a small fraction of the infectivity of the original extracts. The total activity was recovered when the sediments were kept in concentrated solution, or resuspended and diluted in buffer containing inactivated rabbit serum. A preparation of agent 13, purified by 3 successive centrifugations at 15,000 r.p.m., was infectious in amounts containing $8.6 \times 10^{-4}$ mgm. of nitrogen. The 50% response dose (calculated from latent period values) contained $3.2 \times 10^{-2}$ mgm. of nitrogen. Inactivated supernatants of extracts from sarcoma 13 did not afford a better protection than solutions of inactivated serum. Inactivated extracts of a nonfilterable chicken tumor (sarcoma 16) had no inhibitory action on agent 13. It was thus shown that protein solutions have a nonspecific protective action on preparations of agent 13.—Author's abstract.


The literature on the behavior of blood elements in tissue culture is reviewed, and a point is made of the fact that all attempts to cultivate lymphocytes unaltered for any considerable length of time have failed. Similarly it has been impossible to find cells in leukemias that would behave as many malignant cells do and grow indefinitely in vitro. The author describes his attempts to culture a transmissible mouse leukosis. It was found that the leukosis cells would show continued growth only when provided with the support of other cells, and for this purpose he cultured fibroblasts of chick embryo satisfactorily. The leukosis cells invaded the peripheral portions of the fibroblast colony and there multiplied. By transferring such mixed cultures, the in vitro cultivation of the leukosis cells was kept up for 4½ months and probably could have been continued indefinitely. They never transformed to other types, and when inoculated into mice, reproduced the original leukosis. The author feels that these results substantiate the correctness of the concept that mouse leukosis is a neoplastic disease.—K. P.


 Cultures from 3 human synovial sarcomas revealed two main elements: flattened, spindle-shaped cells and mem- branous or epithelioid cells, both of which showed fibroin- lytic activity and were associated with the formation of reticulin and refractive vacuoles. The predominant type of cell may not be the same in vivo and in vitro; this is also true of mesotheliomas. Macrophages were seen quite late, and fibroblasts appeared in older cultures. Studies of normal synovial cultures indicated that the synovial cell is a specific cell.—W. J. B.


Four human tumors, 3 carcinomas of the breast and 1 adenoma of the thyroid, were grown in roller tube cultures and subcultured in hanging drop preparations for cytological study. Growth patterns of fibroblasts and epithelial cells were typical of those previously reported except for the early formation of acini in an adenoma of the thyroid and the development of whorls of cells at the peripheries of the zones of outgrowth in 2 carcinomas of the breast. The separation of the whorls from the zones of outgrowth and the subsequent proliferation of new cells from the whorl-like clusters, suggest a similarity to the metastatic behavior of malignant epithelial cells in vivo. Cytological examination showed stroma cells of the tumors to be bipolar or multipolar cells with broad or long oval nuclei. Spherical mitochondria predominated in epithelial cells, rod-like and filamentous mitochondria in fibroblasts. Neutral red granules were found in perinuclear arrangements and scattered in the cytoplasm of both types of cells. The cytoplasm of epithelial cells of carcinoma cultures was generally dense and diffusely granular; however, epithelial cells of the adenoma and fibroblasts of the adenoma and the 3 carcinomas of the breast were homogeneous with localized granular areas. Binucleate and trinucleate cells were seen in carcinoma cultures.—Author's abstract.
Experimenal Imitation of Tumour Conditions.


One section of this article reviews the literature on the relation of plant growth substances to crown gall. The histological similarity of auxin-induced tumors to crown galls and the fact that plant reactions that follow application of auxins also accompany gall formation suggest that crown gall development is associated with increased auxin content. Measurements of the auxin content of galls have not yet established whether they actually contain more auxin than normal tissues. However, experiments with attenuated Phytophthora tumefaciens show that growth substances are somehow involved in gall formation. In these experiments the attenuated bacteria by themselves fail to produce galls, but if extra growth substance is supplied to the infected tissue large galls develop.—R.B.


This review presents a summary of work on the effects of colchicine and x-rays on tumors. Plant tumors produced by Bacterium tumefaciens are not prevented from developing, but when they are well formed they may be destroyed by colchicine. Some animal tumors regress or grow at a retarded rate following colchicine injections, but others appear not to be affected. Experiments having to do with the effect of colchicine on the sensitivity of animal tumors to x-rays have likewise given variable results. The drug in some instances appears to render tumors more sensitive to irradiation and in others to have no effect. This article also reviews the literature on the nature of the changes produced in cells by colchicine and x-rays, and summarizes the applications of colchicine in genetics and endocrinology.—R.B.


A consideration of certain experimental data led to the following conclusions: The change from a normal to a malignant cell is of the nature of a mutation. This might be brought about by an increase in the amount of heterochromatin, or by a mutation in nuclear genes, or in cytoplasmic plasmagens. The malignant cell is characterized by increased nucleic acid metabolism and more rapid mitosis. A comparable condition is said to be brought about in yeast cells by the action of camphor and chemical carcinogens. The increased production of lactic acid by malignant cells brings about changes in the physical state of their cytoplasm, which results in abnormal spindle development and consequent nuclear aberrations. Similar disturbances of the spindle mechanism can be induced with lactic acid in the root-tip tissue of rye.—R. J. L.


A photograph of the tumor in situ is presented. The tumor was said to be a melanin-impregnated sarcoma near the udder, a rarity in young animals of the bovine species. The cow was observed for several years; no metastases or recurrence developed. Photomicrographs of the tumor are not given.—E. E. S.

**Clinical and Pathological Reports**

**Clinical investigations are sometimes included under Reports of Research**

**GENERAL**


A review and discussion, with an extensive bibliography. The author's morphogenetic theory embraces the blastomere, the parthenogenesis, and pole-cell-theory. The organizer-theory is rejected as not clear and not directly applicable to the entire vertebrate organism.—M. H. P.

**ETIOLOGY**


A general discussion for practitioners, touching upon biological factors, hormones, genetics, carcinogens, and viruses.—M. E. H.


Multiple neurofibromatosis (von Recklinghausen's disease) appeared as a dominant hereditary disease in 4 generations of a family observed for 37 years. One boy of the third generation, who had multiple neurofibromas in practically every nerve, died at the age of 9 years of gliomatosis (or neurinomatosis) spreading in the meninges especially along the spinal cord and medulla oblongata, and on the base of the brain. A girl of the third generation died at the age of 23 of an intrathoracic tumor that had developed in a nerve trunk. In many of the neurofibromas in this case there were hemangiomas with...