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Experimental Research. Animal Tumors


Eggs of the sea urchin Strongylocentrotus lividus were suspended for 1 hour in sea water saturated with benzpyrene. They were then fertilized, and their development in normal sea water was observed for the first 7 days after fertilization. At the pluteus stage giant forms appeared. None appeared among several hundred controls, which were either not treated or treated with noncarcinogenic substances.—Z. D.


Methylcholanthrene was applied to the skin of mice for a period just short of that necessary for the formation of visible tumors. The skin was then treated with naphthoquinone, croton oil, croton oil resin, or sodium sulfide, or was subjected to frequent incisions. In every case many tumors developed subsequently, except after sodium sulfide, which was ineffective.

Frequent incisions made through the abdominal wall of rats with primary hepatomas resulted in nests of proliferating hepatoma cells in the regions of the wound. These neoplasms regressed during the later stages of the healing process. It is suggested that such transplanted cancer cells found a favorable environment for growth in the region of the healing wounds, and that the defense mechanism of tissues that inhibit such growth normally is decreased in areas where reparative processes are active.

These results are correlated with the suggestion that tumor formation may be divided into three phases: (a) period of induction, during which the neoplastic cell is formed; (b) critical or reversible period, in which the growth of the neoplastic cell is in delicate balance and depends upon the local tissue environment; and (c) the final period of progression, during which growth is relatively unchecked.—Authors' abstract.


The carcinogenic action of 3,4-benzpyrene on mouse skin is inhibited and sometimes prevented by local applications of bromobenzene to the skin 4 times weekly. In a precancerous area of skin, bromobenzene greatly delays and often prevents the emergence of visible tumors. The influence of bromobenzene is local, and evidence is given that it is due to intermittent interference with sulphur metabolism. Glutathione and ascorbic acid levels in the skin are lowered quickly after bromobenzene treatment, but recover to normal values after a few hours. All the chemical and biological evidence supports the view that bromobenzene is detoxicated by mercapturate formation in the skin before being excreted in the urine.

The possible relation of sulphur metabolism to carcinogenesis is discussed.—Author's abstract.


A pronounced increase in the number of tissue mast cells accompanies the carcinogenic process induced in mouse skin by minimal total doses of methylcholanthrene. The mast cell reaction is evident long before a carcinoma appears. It occurs in association with, and seems to be conditioned by, the development and degree of nonneoplastic epidermal hyperplasia. Mast cells disappear from the cancer itself probably by being destroyed, although contiguous areas of dermis beneath precancerous hyperplastic epithelium often show the most striking accumulations of these cells.

Histochemical studies reveal that the mast cells in areas of considerable hyperplasia are altered from the normal prototype. Two kinds of chromatase substance were found, one soluble, one insoluble in watery fixatives. Progressive changes in the kind and amount of these substances, in the total load of stainable granules, and in the size of the cells suggest that a continuous process of histogenous development and maturation of these cells occurs in such areas. From the superficial dermis to the deeper parts, the mast cells fall into general classes of "agranular," "ametachromatic," and "metachromatic" types. Further evidence of structural change is the fact that "agranular" and "ametachromatic" cells exhibit strong golden-brown fluorescence in ultraviolet light. Normal mast cells fluoresce weakly or not at all. The possible significance of the mast cell reaction in the light of recent work on heparin, hyaluronic acid, and other polysulfuric acid esters of high molecular polysaccharides is discussed.

The regular occurrence of a mast cell reaction beneath hyperplastic epidermis, absence of these cells from carcinomas, and their presence to an abnormal degree in the skin of mice resistant to limited methylcholanthrene treatment suggest that the response is associated with a defensive process against the development of skin cancer.—Authors' abstract.


In mouse epidermis painted with methylcholanthrene in benzene, the ribonuclease-pyronin technic indicated a
notable increase in cytoplasmic ribonucleic acid concentration by one-half day after treatment. Ribonucleic acid was at a maximum from the third to the tenth day and thereafter dropped to an intermediate value by the 57th day. It was high again in the one cancer studied and remained at normal levels in controls treated with benzene alone.

Nuclei bearing multiples of the normal number of heterochromatid segments were in evidence from the second day of methylcholanthrene treatment on through carcinogenesis and were predominant in the cancers, as a study of acetocarmine preparations revealed. Such nuclei, which also contained increased numbers of plasmosomes and were relatively large, were closely paralleled in frequency by metaphases containing enlarged chromosomes. It is doubtful that there is any increase in number or size of heterochromatid segments in either hyperplasia or carcinoma induced by methylcholanthrene that is not explicable on the basis of multiple-stranded chromosomes and polyploidy.—Author's abstract.


Alkaline phosphatase was studied histochemically in mouse skin painted with methylcholanthrene in benzene. By the second and third days after the beginning of treatment, considerable phosphatase activity was evident in the nuclei of the epidermal basal cells and in the reticular layer of the dermis. As epidermal hyperplasia progressed and the hair follicles were destroyed, the enzyme became less concentrated in the epidermis and the reticular layer, but it was still abundant in the skin on the edge of the region of greatest histological reaction to the carcinogen, much like the collar of positive cells about a healing skin wound. The enzyme concentration in the basal cells was in direct proportion to the closeness of positive dermal elements, such as capillaries. In the carcinomas and papillomas studied the alkaline phosphatase reaction was very intense both in the stroma and moved.—Authors' abstract.


—H. J. C.


A comparison was made of the activities of d- and l-peptidases in water extracts from fresh human organs, 3 mammary carcinomas, and a liver metastasis of one of them. No significant difference between normal and tumor cells was found. The fact is reported without any experimental details, that when a mixture of d- and l-peptidases acts on a mixture of d- and l-peptides only the latter is split. The possible importance of this phenomenon from the point of view of Kögl's tumor theory is discussed at length.—Z. D.


The l- and d-amino di- and tripeptidases of the ascitic fluid and of the cells suspended in it (tumor and exudate cells) were compared with normal cells (previously investigated) as to their activity and sensitivity to heavy metals and to substances forming complexes. The cell enzymes were extracted with 10 parts of water from the cell powder obtained by drying with acetone. Tumor cells growing on the peritoneum also were examined. No significant differences between tumor and normal cells were found.—Z. D.


The peptidases of tissue cells were examined as to their activity and sensitivity to heavy metals and complex-forming inhibitors in glycerol extracts from the acetone-dried tissue. One part of the desiccate was extracted with 2 parts of glycerol for 2 days at room temperature. No significant difference with respect to “natural” and “unnatural” peptidases was found between extracts from the various tissues tested, whereas the blood serum of tumor rats contained more d-peptidase than did the serum of normal rats.—Z. D.


This posthumous paper contains a large number of experiments on the behavior towards extraction and drying procedures, of “natural” and “unnatural” dipetidases and “natural” aminopolypeptidas of the liver and kidney tissue of rabbits, guinea pigs, and rats, as well as of mouse carcinoma and sarcoma, and rat sarcoma tissue. The substrates employed were leucyl-glycine, alanyl-glycine, glycyl-alanine, glycyl-leucine, glycyl-glycine, leucyl-glycyl-glycine, alanly-glycyl-glycine, glycyl-glycyl-
glycine (all containing the "natural" forms) and the "un-
natural" d-leucyl-glycine, glycyl-d-leucine, and glycyl-
d-alanine.

The bulk of the liver, kidney, and tumor peptidases appears to be present in the tissues either in dissolved or in readily soluble form, i.e., as lyo-enzymes in Willstätter's terminology, since they are extracted from the dried tissue powder by treatment with water for 10 min. at 0°C. Only a minor fraction of these enzymes is present in the form of insoluble dermo-enzymes or endo-enzymes. There appear to be small but significant differences in the solubility behavior of liver and tumor peptidases on the one hand, and kidney enzymes on the other. The ratio of lyo-enzymes to dermo-enzymes is subject to certain variations from enzyme to enzyme, species to species, and individual to individual. However, the ratio is invariably strongly in favor of the soluble forms.

Drying of the tissues with acetone, which is a rapid process, is always accompanied by more or less far-reaching impairment (denaturation) of the peptidases examined. Upon drying the tissue from the frozen state over P₂O₅ in high-vacuum, which is a relatively slow method, no appreciable damage to these enzymes was observed, the activity being equal to that of glycerol or water extracts of the fresh materials.—K. G. S.

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The concentration of ascorbic acid in the liver has been compared in pregnant and nonpregnant mice, and in the pregnant condition an increase was found that was significant in 3, and probably significant in 3 more, of the 7 strains examined. No other sexual conditions have been found in which such an increase occurs. Glutathione does not behave in this way. Some data are given on the increase in weight of the liver in pregnancy.—Authors' abstract.


The oxygen consumption of liver tissue from mice with lymphoid leukemia was greater than that of normal liver tissue; the rate of aerobic glycolysis, somewhat lower, and of anaerobic glycolysis, much higher.

It is concluded that the increase in the rate of anaerobic glycolysis is attributable to two factors: (1) the presence in the liver of malignant lymphocytes that are carrying on anaerobic glycolysis at a rate similar to that of the same cells in the lymph nodes; and (2) a considerable increase in the glycolytic activity of the parenchymal cells of the liver, which can be independent of the presence of leukemic cells in the organ and which appears to be due to the leukemic state of the animal.—Author's abstract.


The present study deals with the changes occurring in the adrenal glands of rats subjected to lowered oxygen tension in single (4 hours) and repeated exposures of short duration (4 hours, 6 days a week). Immediately after a single exposure, the zona fasciculata usually contained less lipid than did the same zone in normal glands and resulted in the appearance of lipid droplets in the "lipid free zone" of the outer fasciculata. Twenty hours later all adrenals contained less lipid than normally, and the "lipid free zone" became unidentifiable as a result of the accumulation of numerous lipid droplets within it. Repeated exposure to lowered oxygen tension caused adrenal hypertrophy, which reached a maximum at 6 weeks, and with continued exposure a gradual return toward the original size occurred. Also, animals exposed for more than 6 weeks possessed adrenal glands that contained approximately normal amounts of lipid, which was distributed in a normal pattern. The authors suggest that adaptation to conditions of lowered oxygen tension may result from discontinuous exposure after 6 weeks and discuss the significance of the changes in the lipid free zone in relation to the life history and functional activity of the adrenal cortical cells.—D. S.


The presence in the rat of spontaneous mammary tumors, of induced skin tumors, or of inoculated Flexner-Jobling tumors does not cause a prolongation of the normal prothrombin time (12.5% plasma). On the other hand the presence of primary hepatic tumors due to p-dimethyl-aminoazobenzene may cause a mild hypoprothrombinemia. A standard dose (2.5 mgm.) of 3,3'-methylenebis(4-hydroxycoumarin) usually causes a more severe hypoprothrombinemia in rats with primary hepatic tumors than in normal rats or in rats bearing tumors in other parts of the body. The extent and duration of the hypoprothrombinemia is probably influenced by the amount of normal hepatic tissue present. While vitamin K protects normal rats against the hypoprothrombinemic action of a single dose of 3,3'-methylenebis(4-hydroxycoumarin), in rats with hepatic tumors this protective action is either lessened or abolished.—Authors' abstract.


Calorie-restricted diets inhibit the formation of various types of tumors in mice. Previous work suggested that the inhibitory effect occurs during the period in which tumors appear, rather than in the period of carcinogenic stimulation. The present experiment was designed to test this view. Four groups of 50 mice each were given equal applications of 3,4-benzpyrene to the skin; treatment was terminated before any tumors appeared. The groups differed in that the first received a calorie-restricted diet during painting, the second after painting, the third both during and after painting; the fourth received the ad libitum diet throughout. The percentages of skin tumors formed in these groups were 55, 34, 24, and 65 respectively.
The results suggest that carcinogenesis can be divided into 2 distinct phases: (1) a stage of preparation or initiation in which the normal cells become prepared or biased toward forming a tumor, and (2) a stage of development or formation that eventuates in a perceptible tumor. Furthermore, it was shown that (a) the initial fundamental changes due to the application of a carcinogen occur regardless of whether the mice are on a full or calorie-restricted diet, and (b) a full diet promotes the development of tumors from these initial changes, while a calorie-restricted diet inhibits such development.—Author’s abstract.


This communication is not a report of new experimental results. Pertinent reports in the literature are utilized in an attempt to clarify and extend the present concepts of the stages of carcinogenesis—initiation (pre-neoplastic) and development (neoplastic). Particular emphasis is placed on cocarcinogenic and anticarcinogenic effects of various agents and procedures, and an attempt is made to show that cocarcinogenic and anticarcinogenic actions may be, and generally are, effective during only one stage or the other (pre-neoplastic or neoplastic) of carcinogenesis.

As examples of the above, such procedures as wound healing, application of croton resin, and caloric restriction can affect the neoplastic stage, but have little or no effect on the pre-neoplastic stage. On the other hand, treatment with certain solvents and other procedures can have a definite effect during the pre-neoplastic stage, yet may be without significant effect during the neoplastic stage. It is possible that a particular agent or procedure may have one effect, cocarcinogenic, anticarcinogenic, or none, on the development of the pre-neoplastic stage, and another effect, cocarcinogenic, anticarcinogenic, or none, on the outcome of the neoplastic stage. The author stresses the desirability of testing, when feasible, the effect of a particular agent or procedure (solvent, chemical, hormone, inflammation, trauma, dietary change) during each stage of carcinogenesis as well as during the whole experimental period. Also discussed is the likelihood that such practice would increase our knowledge of the mechanism of carcinogenesis and its clinical implications.—Author’s abstract.


A high-fat diet facilitates the formation of skin tumors. In the experiments reported, applications of 3,4-benzpyrene were made to the skin of mice for a limited period, being discontinued before any of the mice developed tumors. A group of mice that were fed a high-fat ration only during the period of carcinogen application developed no more tumors than did a control group on a low-fat ration. On the other hand, a group of mice receiving the high-fat ration in the period subsequent to application of carcinogen developed as many tumors as did a group that received the high-fat diet throughout the experiment. It was assumed that the period of application of carcinogen roughly corresponds to the initiatory stage of carcinogenesis, and that the period in which tumors appeared corresponds to the developmental stage. On the basis of this assumption, it was concluded that dietary fat has little or no effect on the initiatory stage, but that it has a significant facilitating effect on the developmental stage. This effect of ingested fat is differentiated from the effect of fat applied intentionally or by chance to the skin.—Author’s abstract.


Fifteen groups of 15 rats each were fed various lipids in synthetic diets containing 0.06% p-dimethylaminoazobenzene for 4 months followed by dye-free diets for 2 more months. The strong anticarcinogenic effect of 5% of hydrogenated coconut oil was confirmed by the occurrence at 6 months, of 8% or less of hepatic tumors. When the hydrogenated coconut oil was replaced by corn oil, the tumor incidence increased to 73%. The removal of antioxidants from either oil did not affect these tumor incidences, and the addition of α-tocopherol to hydrogenated coconut oil likewise had no effect. When mixtures of the two oils were fed, the response tended to be characteristic of the major component of the mixture, though a greater effect was produced by a small amount of corn oil than of hydrogenated coconut oil.

The formation of hepatic tumors by rats kept on the diets studied did not depend upon the development or prevention of the syndrome characteristic of a deficiency of essential fatty acids. Relatively slight protection against hepatoma formation was obtained with diets containing 2½% trilaurin, the equivalent of the lauric acid contained in 5% hydrogenated coconut oil. Similar results were obtained with raw coconut oil. A tumor incidence of 69% was obtained with a diet free of added fat, thus demonstrating that dietary fat is not indispensable for the action of the dye. High tumor incidences were observed following both corn oil and hydrogenated coconut oil fed in diets containing crude casein and rice bran concentrate. A very low tumor incidence still occurred in rats given a diet containing hydrogenated coconut oil and 0.12% p-dimethylaminoazobenzene. No tumors were found in rats fed a corn oil diet with only 0.03% of the azo dye. It is suggested that the partition of the dye between the portal and lymphatic systems (Frazer) may be affected by the nature of the fat fed, with subsequent differences in metabolic breakdown.—Authors’ abstract.


The object of the experiment was to determine whether
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\[ \Delta^1 \text{-} 3 \text{-} \text{keto} \text{s} \text{teroids that have little or no pr} \text{ogestational}
\text{activity are ant} \text{ifibromatogenic. Tablets of androstenedione}
\text{or of cholestenone were implanted in castrated female}
guinea pigs simultaneously with estrogenic tablets.}
\text{The latter when present alone induce abdominal fibroids in}
\text{most animals in the course of 3 months.}
\text{The androstenedione was mixed with 20\% cholesterol;}
\text{1 to 2 tablets of 25 to 30 mgm. each were implanted}
\text{subcutaneously. Three to four tablets of pure cholestenone}
\text{were implanted similarly. Autopsy was done 90 to 95}
\text{days after tablet implantation.}
\text{Quantities of androstenedione up to 40 times greater than}
\text{the antifibromatogenic threshold of progesterone were}
\text{not sufficient to prevent abdominal fibroids induced by}
\text{\( \Delta^1 \text{-} \text{estradiol. These quantities were also many times}
\text{greater than the antifibromatogenic amounts of testo-
\text{sterone. The masculinizing action on the guinea pig}
\text{clitoris was as great as with testosterone.}}
\text{Amounts of cholestenone 10 times those of progesterone}
\text{showed no antifibromatogenic activity.—M. B.}}


Pellets of stilbestrol or of hexestrol were implanted subcutaneously, intrasplenicly, or intraperitoneally in 152 castrated female guinea pigs. Autopsy was performed 70 to 100 days later, and the fibrous tumoral reaction was classified in units previously employed by the authors.

The synthetic estrogens, stilbestrol and hexestrol, were more resistant to hepatic inactivation than were the natural ones. Abdominal fibroids could not be induced with intrasplenic pellets of natural estrogens, free or esterified; they were induced with the synthetic estrogens, although the incidence of tumors of a certain size was greatly diminished when compared with that resulting from subcutaneously implanted pellets. Toxic actions characteristic of prolonged treatment with estrogens were present also after intrasplenic implantation of pellets of the artificial estrogens.—M. B.


Castrate female guinea pigs were given subcutaneous implants of pellets of the following estrogens: \( \Delta^1 \text{-} \text{estradiol, estrone, estriol, \( \Delta^1 \text{-} \text{dihydroequilenin, \( \Delta^1 \text{-} \text{di}-
\text{hydroequilenin. The pellets weighed from 3.5 mgm. for estradiol}
\text{and estrone to 43 mgm. for the others. The ability of these}
\text{estrogens to produce abdominal fibroids decreased among them in the order in which they are listed above. Ninety-one animals were used.—M. B.}}

The Urinary Excretion of Estrogens, 17-Keto-


Metabolic differences between high and low tumor strains of mice and between litters of high and low tumor strain mice foster-nursed by the reciprocal mother are reviewed.

Comparative observations were made on C57 (low tumor strain) virgin and C3H (high mammary tumor strain) virgin and once-pregnant female mice. The C3H required more food than the C57 mice to maintain body weight. Both strains excreted approximately 0.5 mgm. creatinine per 20 gm. mouse per day.

The males and females of both strains excreted relatively large quantities of creatine in their urine. The creatine-creatinine ratios in the C57 and C3H females were similar until the tenth to 12th months of age, when the creatine output rose in the C57 and fell in the C3H strain mice. The C57 male mice consistently excreted more creatine than the C3H males.

Each mouse excreted in its urine an average of 1.2 to 3.3 international units of estrogens a month. The C57 mice appeared to excrete on the average slightly more estrogenic material (30\%) than the C3H mice, but the difference is not considered significant. Both strains excreted 0.46 to 1.93 mgm. of a 17-ketosteroid-like substance per mouse per month with no appreciable strain differences.

Therefore, judged from urinary excretion rates there is as yet no evidence that high mammary tumor strain mice form or metabolize estrogens or 17-ketosteroid-like material in any significantly different fashion from a low tumor strain. Estrogens are to be regarded as an essential but not a specifically carcinogenic factor in the development of spontaneous mammary tumors in mice.—Authors’ summary.


Various kinds of growth processes are described in the sex organs of older female mice that have passed the breeding period and have been subjected to long-continued treatment with an estrogen in addition to the earlier action of the endogenous ovarian hormones. These proliferative changes are classified into (a) intensified normal growth processes, (b) abnormal growth processes, (c) precancerous and (d) cancerous changes.

Chronic mechanical stimuli, as well as long-continued inflammatory changes due to infection, may help to intensify some of the growth processes caused by hormones. There is no indication that acute regenerative processes have such an effect.

In the course of these carcinogenic stimulations conditions may develop that affect the stimulated tissues in such a way that their growth response is inhibited.

The various tissues of the secondary sex organs differ in their ability to respond to stimuli with proliferative changes that ultimately may lead to cancer. In the same individual, organ and tissue differences may be involved that are determined only indirectly by genetic factors; there exist also differences in the responsiveness of corresponding organs and tissues in different individuals and species, which are determined by genetic factors more directly and in a manner that is specific for these individuals and species.
It has been shown that within the same inbred strain or individual there probably exists, in addition to these differences in the mode of reaction of different tissues and organs to stimuli, a parallelism in intensity of the reactions of the various tissues and organs. This parallelism depends on the intensity of the hormonal stimuli, which differs in different animals, but which affects all the tissues in a given mouse with the same relative strength.

These experiments indicate that the increase in the incidence of cancer with advancing age of animals belonging to inbred strains is largely due to the accumulation of chronic stimulations of growth. At far as growth processes and cancerous processes are concerned, the tissues of older and those of younger organisms seem to differ only quantitatively in their reactions; the modes of their reactions seem to be similar.

It has, furthermore, been shown that the addition of an exogenous estrogen to the previously active endogenous ones may intensify certain growth processes initiated by the latter or may initiate other growth processes.—Authors' summary.


Twenty-three out of 26 control breeding females of strain dba (subline 12) developed spontaneous mammary cancer at an average age of 370 days (range: 300 to 460 days).

Two groups of female progeny, 6 to 8 weeks old, from these breeders, were put on similar diets and given 2 cutaneous applications weekly of a 0.5% solution of methylcholanthrene in benzene. The 27 females in group I were bred, each mouse having one or more litters. Thirty-one females in group II were maintained as virgins. Forty-eight male mice were similarly treated with methylcholanthrene.

All animals in group I developed mammary cancer after an average treatment period of 105 days. In group II only 4 of 31 mice produced mammary cancer; the average induction period was 190 days. Sixty-five percent of the males and virgin females developed leukemia; none of the untreated control breeders developed leukemia spontaneously.—M. B.


Mice of the F strain, which have a spontaneous leukemia incidence of 53%, were crossed with animals of strains A, CBA, and C57, in which the leukemia incidence is less than 1%. In F1 hybrids and backcrosses to the high leukemia stock, the incidence of leukemia was about the same as in the pure F stock; in the backcross to the low leukemia stock the incidence of leukemia was decreased. The retarded appearance of leukemia in the hybrid animals may be significant and might be correlated with the degree of inheritance from strain F or with the increased life expectancy in hybrids.

Gonadectomy did not alter the incidence of spontaneous leukemia in either sex; and there was no evidence for the existence of a leukemia "milk influence."—M. B.


Reciprocal F1 hybrids produced by mating mice of one low cancer (C57 black) and one high cancer (A) strain and nursed by females of the cancerous stock gave, in breeding females, approximately the same incidence of spontaneous mammary cancer. No evidence was secured to suggest any intrauterine influence for the development of mammary cancer in mice. The incidence in the total number of F1 hybrids nursed by females of the A stock did not differ significantly from the incidence found in mice of the cancerous A stock.

Although the pooled data obtained in all the various types of hybrid generations could be accounted for on the genetic theory that the inherited susceptibility for mammary cancer in this cross was transmitted as a single dominant factor, it became evident on analysis of the incidence of cancer in the several subgroups that such a simple interpretation is inadequate and that other factors are probably involved. Detailed analysis showed: (1) That the incidence of mammary carcinoma in the F1 hybrids with brown coat color was significantly higher than in their litter mates with black or albino coats. (2) That not all brown mice became cancerous, nor was the incidence in brown mice as high as in mice of the high cancerous A stock. (3) The progeny of brown mothers had a higher incidence than did the progeny of black or albino mothers, but not all brown mothers transmitted the inherited susceptibility to their progeny. (4) The incidence of cancer was significantly greater, in some groups, in the mice born in the third and later litters than in mice born in the earlier litters from the same mothers. (5) The incidence in the progeny was influenced also by the age at which the mothers developed mammary cancer.

It has previously been shown that a considerable proportion of mice of the so-called nonsusceptible stock developed mammary cancer when given the active milk agent. It is probable that some cancerous hybrid animals are likewise genetically nonsusceptible. Thus the tumor incidence would not represent the true percentage of susceptible animals, and should not serve as the only basis for a genetic interpretation of the data.

It is concluded that the inherited susceptibility for spontaneous mammary cancer in mice, as transmitted by mice of the cancerous A stock, probably depends upon multiple genetic factors, one of which may be linked with the gene for brown coat color.—Author's abstract.


Tumors were produced on healthy plants of Nicotiana glauca, a species that is never subject to spontaneous tumefaction, by implanting under the bark fragments of tissue cultures originally obtained from near the growing points of young plants of the hybrid Nicotiana langsdorffii ×
N. glauca. The tissue cultures used had been maintained in vitro for 5 years and were isolated from plants that were healthy appearing but known to be subject to spontaneous tumefaction. The induced tumors were anatomically similar to those that appear spontaneously on the hybrid.

The writer considers the retention of the tumefacient property after 5 years in vitro and its expression in a non-tumefacient host as evidence of the fundamental character of this property, in this case a property of genetic origin.—Author’s abstract.

**The Serial Passage of an Avian Lymphoid Tumor**


The reaction of a chicken after receiving an implant of the lymphoid tumor will vary depending upon the activity potential of the tumor and the resistance of the host.

In ascending order of severity these reactions are: failure of the graft, growth and regression, progressive local growth only, growth with localized metastasis, and growth with diffuse metastasis.

Serial transfer of the tumor enhanced its ability to produce the more severe reactions.

Transfer of the tumor at 10 day intervals was more effective in raising the growth activity of the tumor than transfer at 15 day intervals.—Author’s summary.

**Beitrag zur Beziehung zwischen der Mitosegiftwirkung und der Konstitution von Colchicin Derivaten [Relation between the Antimitotic Effect of Colchicine Derivatives and their Constitution]**


A series of derivatives of colchicine, mostly those obtained by Windaus and Cook in their investigations of the constitution of this substance, were tested as to their inhibitory effect on the growth of chicken heart fibroblasts in tissue culture and of the mouse ascites tumor. Thus the importance of certain atom groups in the colchicine molecule for the antimitotic effect could be established.

The study was carried further by the determination of the antimitotic activity of synthetic products, similar in their structure to the “backbone” of the colchicine molecule. The phenyl-(p-methoxyphenyl) derivatives of methyl-, ethyl-, and propylmonoamines were investigated. Of these only the ethyl compound showed activity. From this it is concluded that the configuration: benzene ring-C-C-NH₂, is essential for the antimitotic action of colchicine and its derivatives.—Z. D.

**Hemmung der Zellteilung durch östrogene Faktoren. [Inhibition of Cell Division by Estrogens.]**


Diethylstilbestrol inhibits completely the growth of chicken heart fibroblasts in tissue culture at a concentration of 150-200 μg/cc. Even 40 μg/cc. has some effect. The author assumes that this is due to an addition of NH₂ to the double bond of the ethyl bridge, because the addition product shows the atom grouping, phenyl-C-C-NH₂, which was recognized in a previous paper as antimitotic. Na₂ estradiol phosphate (Schering), a water-soluble ester of estradiol, at a concentration of 100 μg/cc. gave a marked inhibition of culture growth. The author reports without giving experimental details that an oxidation product of diestradiol proved to be a “mitosis poison” in so small a concentration that it can be taken into consideration as a physiological antimitotic principle.—Z. D.

**Mitosegifte aus der Steringruppe. (Vorläufige Mitteilung). [Mitosis Poisons in the Steroid Group (Preliminary Communication)]**


The monomethyl ester of the 17,17-diamino-3-hydroxyestratriene-1,3,5 poisons mitosis in cultures of chicken heart fibroblasts at a concentration of 1 μg/cc.—Z. D.

**The Influence of Malignant Cells Upon the Growth of Fibroblasts in Vitro.**


The growth of mouse fibroblasts in tissue cultures is influenced by the proximity of other tissues.

A considerable stimulation of growth has been observed in the presence of the following tumors: (a) Spontaneous and transplanted mammary carcinomas of the high cancer strains Stron A, C3H, and RI1. (b) Mammary carcinomas induced in susceptible hybrids by the injection of dried RI1 tumors.

Fibroblasts cultivated between 2 explants of these tumors grew more rapidly and were mitotically active over a longer period than those of control cultures, so that the maximum growth attained by cultures of the former was 8 to 10 times that of the controls in most experiments.

Fibroblastic growth was also stimulated to a lesser extent by cultures of embryo kidney and of the transplantable carcinoma 63. The latter is the most rapidly growing of the tumors employed in these experiments, hence it can be concluded that fibroblastic growth stimulation is not directly related to the rate of tumor growth.

Growth stimulation of fibroblasts occurs irrespective of: (a) their age, whether embryonic or adult; (b) their organ of origin, whether from heart, kidney, dermis, or mammary gland; (c) their genetic constitution, whether from high cancer or low cancer strains or from hybrids.

Sarcomas of both high mammary and low mammary cancer strains of mice inhibit fibroblastic growth under the experimental conditions described.—Authors’ summary.

**Transformation of Cells and Viruses.**


A review.—E. L. K.

**Heredity, Development and Infection.**


A review.—E. L. K.