Abstracts

Abstracts are grouped under the following main headings: Reports of Experimental Research, Clinical and Pathological Reports, Statistics, and Cancer Control and Public Health. Subheadings are used in accordance with the subjects of papers abstracted.


REPORTS OF EXPERIMENTAL RESEARCH

Carcinogenic Compounds


Thirteen carcinogenic compounds were injected intravenously into strain A mice. The incidence and latent periods of the induced pulmonary tumors were regular enough to make this method valuable as a quantitative biologic test for carcinogenic substances. A comparison of the carcinogenicity, however, of the same compounds for the lungs, skin, and subcutaneous tissues of mice showed that there was no quantitative or qualitative correlation in this respect. The carcinogens tested were 2-methylcholanthrene, 1,2,5,6-dibenzanthracene, 9 other related hydrocarbons, 2-amino-5-azotoluene, and colloidal thorium dioxide.—L. L. W.


Rats of the Wistar, Osborne-Mendel, and Buffalo strains were fed purified 2-amino-5-azotoluene for periods up to 614 days. The diet included, besides the dye, 15.0% whole milk powder, 75.47% ground wheat, 4.0% dried yeast, 4.0% cod-liver oil and salt mixture. The increase in weight of the rats on the experimental diet was much less than those of the controls. For the first 7 months of dye feeding, changes in the liver consisted of injury, regeneration, and hyperplasia. The first gross tumor was observed at 211 days. Between 401 and 614 days, 81 of 91 animals showed gross tumors and all of 33 rats examined between 451 and 614 days had gross liver involvement.

Microscopically, the tumors were mostly hepatomas up to 500 days, but thereafter 4 of 7 rats had anaplastic liver cell tumors classified as carcinoma. Tissue injected from 9 hepatomas and 2 carcinomas into other rats failed to grow.

In vitro, liver tissue from normal embryonic, young and adult rats were studied as a base line for comparisons with hepatomatous tissues. Early embryo liver was kept alive 133 days, but the survival time decreased with the age of the rat. With normal adult rat liver, there was very little epithelial proliferation. Tissue cultures of hepatomas showed a great increase in growth over the normal liver controls. This growth increase is described.——L. L. W.


In a series of mice of strains C57 brown, C57 black, C3H, A and A backcross ingesting methylcholanthrene or dibenzanthracene emulsions over a period of 9 months, 10 developed squamous carcinoma of the fore-stomach and 30 developed hyperplastic changes in the gastric mucosa. All the gastric carcinomas arose in strain A and strain A backcross mice receiving methylcholanthrene emulsions. A mineral oil emulsion seemed more effective than one prepared with olive oil. Thirteen of the animals with gastric lesions showed adenocarcinoma of the small intestine as well. Metastases from the gastric tumors were found in 3 cases in the mesentery, pancreas, mesenteric lymph nodes, spleen, diaphragm, lungs, and chest and abdominal walls.—L. L. W.


A list of the factors to be considered in such biologic testing of carcinogens and related substances includes the following: I. Experimental animal: A. Species, B. Strain, C. Age, D. Diet, E. Condition of animals, 1. Intercurrent infection, 2. Ulceration at injection site, F. Environmental conditions. II. Carcinogen: A. Chemical structure, B. Purity, C. Physical state, D. Vehicle (solvent), E. Dose and concentration. III. Mode of administration: A. Route, B. Number of injections, C. Site. IV. Interpretation of results: A. Diagnosis, 1. Gross diagnosis, 2. Histologic examination, 3. Transplantation, B. Presentation, 1. Number of animals, 2. Average, 50%-latent time or carcinogenic index. The author's summary follows: "The carcinogenicity of any given compound is modified by so many factors that it is necessarily a relative term, applicable only to the specific conditions of the reported experiment."

"As one standard test, the subcutaneous-injection technique into mice is recommended. Several widely divergent doses of the chemical, from 0.01 to 10 mgm., are dissolved in a solvent of known chemical composition, such as tricaprylin. A single subcutaneous injection into the right axilla is made into C3H male mice, at least 20 per group. The animals are 2 to 3 months of age and are maintained under constant conditions of diet and environment. The presence of tumor is determined by weekly palpatory examination. As soon as a growing hard mass is detected and has reached appreciable size, it is removed for histologic examination. Detailed data for the incidence and the latent periods of the neoplasms are presented."—L. L. W.


In an effort to determine if possible the role played by chronic irritation in the production of lung tumors, strain A mice were
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given a single intravenous injection (5 mgm.) of finely ground arsenopyrite, chromite, thorite, or quartz (1 mgm.). These ores produced chronic inflammatory lesions in the lungs but no tumors within 6 months. Furthermore, they seemed to have no effect upon the number of tumors occurring after the intravenous injection of 0.1 mgm. of 20-methylcholanthrene. The tumors produced by this carcinogen did not arise more frequently in the foci of chronic inflammation than elsewhere in the lung.

A benzene extract of soot from a chimney burning soft coal produced spindle cell sarcomas and pulmonary tumors in C3H male mice. The intravenous injection of 2.5 mgm. of the unextracted soot increased the incidence of primary pulmonary tumors in strain A mice. The authors point out the possible industrial hazards indicated by such studies—L. L. W.


Pure cultures of E. typhi were carried through 240 daily transfers into 10 cc. of broth containing 12 mgm. of methylcholanthrene. Other cultures of E. typhi were transferred 192 consecutive days to tubes of broth into which a 10 mgm. radium-emanation needle had been inserted. Much care was given to control material. After these long periods of exposure to methylcholanthrene and radium emanations, "no structural, functional, or immunological changes were observed other than an immediate stimulation of the rate of cell division which had been previously reported by other investigators." These negative results contrast strongly with the effect of methylcholanthrene and radium on a strain of Paramecium. A report of this latter experiment will be published later.—L. L. W.


An extract of the saponifiable residue prepared from the liver of patients with carcinoma was dissolved with sesame oil and injected in mice. Thirteen tumors, all spindle or polymorphous cell sarcomas, were observed in a total of 56 mice. Similar tumors had never been observed in 2,000 controls. The non-saponifiable residue of the liver from 7 persons who had died from nonneoplastic diseases and the non-saponifiable residue from carcino tissue failed to produce tumors.—J. J. B.

Hormones


An experiment was made to determine whether or not the correction of a deficiency of vitamin B₃ in hypothyroidism would alter the effect of the hormone on tumor growth. No consistent difference was observed in the growth of Walker sarcoma 319 in the 5 experimental groups; namely, (a) thyroid-fed, (b) thyroid-fed plus vitamin B₃, (c) controls, (d) thyroid-ectomized, (e) weight control. No consistent differences in the pH drop or lactic acid production of the tumors was noted among the groups. The state of hypothyroidism in which the deficiency of vitamin B₃ was corrected had no significant effect on the growth and metabolism of Walker sarcoma 319.—Authors' summary.


Seven female rats receiving 2 R.U. of antuitrin-S daily from the 6th to the 24th day of life and 17 receiving 0.25 mgm. testosterone propionate from the 6th to the 28th day were characterized by a continuous estrous smear and only follicular development of the ovary. When the same androgen treatment was started on the 4th day the results were the same except that development of the lower vagina was inhibited in 13 of 16 rats treated. Most of the experimental pathology produced by prolonged injection of estrogens was obtained on these constant estrous rats. Marked vaginal and cervical hypertrophy were observed in 2 animals and in 2 cases gross pyometra occurred. Tubo-ovarian abscesses were numerous. The infectious abscesses were associated with the prolonged estrous condition and were the result of continuous endogenous estrogen production. The after effects of APL or androgen treatment were probably mediated by altering the hypotheses to the male type.—C. A. P.


The uteri, cervices, and vaginae of rats of the Albany (A-S) and Vanderbilt (V-S) strains, killed at ages ranging from 30 to over 800 days, were examined histologically to determine the effects of age and endocrine factors upon connective tissue. As age advanced the collagenous tissue increased in amount and density in the uterus, cervix, and vagina of the normal rat. In the endometrium this increase was greatest from the immature to the 2-month stage. Thereafter the deposition of collagen varied, influenced not only by age but also by the sexual activity of the animal. The observations tended to associate the deposition of collagenous tissue in the accessory reproductive organs of the rat with the long-continued unmodified influence of estrogen in the nonpregnant state. Beginning with 1 year of age, connective tissue increased in the muscle layers of the uterus. Large amounts of collagenous tissue developed around the uterine arteries, especially between the muscle coats. The paper is illustrated with 8 photomicrographs and 1 diagram.—S. B-J.


The femurs and other bones, especially of the appendicular skeleton, of mice which received estrogens had greatly thickened walls. Following prolonged treatment the marrow was largely or completely replaced by new osseous tissue (Proc. Soc. Exper. Biol. & Med., 37:678. 1938; 38:599. 1938; Anat. Rec., 76: suppl. 22. 1940). The breaking strength of femurs of 30 estrogen-treated mice averaged 2,499 gm. This was 844 gm. greater than that of untreated controls. Details of diet, estrogen treatment, and ages of mice are given.—S. B-J.


Slight growth of mammary glands of some hypophysectomized male mice was induced within 15 days by the injection of desoxycorticosterone acetate, progesterone, and estradiol propionate. A more extensive and more rapid proliferation of the mammary ducts of hypophysectomized mice occurred when desoxycorticosterone acetate or progesterone was injected with the estradiol dipropionate.—Author's summary.


The inhibitory effects of large doses of estrogen on mammary gland development were tested on 67 male C3H mice, 1 young male and 6 immature or young mature female monkeys (Macaca rhesus), and 4 female dogs (fox terriers). In the mice some
inhibition followed prolonged administration of weekly doses of 50 mg of estradiol benzoate while almost complete inhibition resulted from the same treatment with 50 mg of estradiol dipropionate. Of the 17 mice receiving 50 mg of estradiol dipropionate weekly, only 1 developed a mammary carcinoma while, associated with better mammary growth, tumors developed in more than 80% of the cases (normal incidence for multiparous female C3H mice) when 250 mg of estradiol benzoate was weekly administered. Inhibition of the mammary glands followed prolonged treatment with weekly doses of over 400 mg of estradiol benzoate to monkeys and of 1337 mg to the 4 dogs. Much higher doses administered for brief periods to 3 of the dogs failed to produce any mammary growth.—C. A. P.


An experiment of Cramer and Horning (Lancet, 2:72. 1938) was repeated on a larger scale, using the same strain of mice, RIII, and the same pituitary extract, ambonin, purchased from N. V. Organon Co., Oss, Holland. This impure preparation contained 50 units of gonadotropic hormone in addition to 150 units of thyrotropic hormone per cc. Thirty-three mice were injected and 100 mice were used as controls. The treatment was begun when the mice were just under 2 months of age and 0.1 cc. of the hormone solution was injected twice weekly for 15 months. Twenty-nine mice survived at least 6 months and 13 were alive 15 months after the start of the experiment. The results with the 29 mice are presented in a table. This long-continued subcutaneous injection of an anterior pituitary preparation containing thyrotropic hormone and some gonadotropic hormone did not definitely affect the incidence of mammary carcinoma in female mice of the RIII strain. S. B. J.


Stilbestrol in oil solution in amounts of 0.5 to 3.0 mgm. was injected subcutaneously into 40 castrate female rats. About 55 of the rats died within 18 days. Eight rats lived over 1358 weeks. All showed marked estrous reactions. Some uterine metaplasia and pyometra appeared. Body weight and blood cell counts decreased. Liver damage was not observed. The adrenal glands showed marked hyperemia. The rats were compared with estradiol-treated animals.—W. U. G.


The following differences were noted between 2 high and 1 low breast tumor strains of mice when ovariecctomized at birth and examined in later life (beyond 1 year of age). The high tumor JAX dba and JAX C3H strains showed stimulated uterus, vagina, and mammary glands. Mammary adenocarcinomas appeared. The adrenal glands exhibited extensive nodular, hyperplastic areas. All of the above organs of the low tumor JAX C57 black strain remained essentially unstimulated. No mammary gland tumors appeared.—G. W.

GENETICS


Fi hybrid mice derived from C3H mothers and 1 and Y strain fathers together with backcross generations procured by mating the hybrids to their parental strains were tested for their susceptibility to induced dibenzanthracene tumors, to induced pulmonary tumors, and to the occurrence of spontaneous mammary cancer. It was found that susceptibility to all 3 types of tumor is inherited in a dominant manner and that multiple, modifying genetic factors are involved. Although the susceptibility of the 3 inbred strains to induced and spontaneous tumors was known, it was impossible to predict the degree of susceptibility of their hybrid offspring because of these modifying factors.—L. L. W.

Viruses


The paper presents an attempt to purify the filtrable agent transmitting chicken tumor I by the medium of a precipitate which formed when a basic protein was added to the tumor extract. A first step in the procedure was to reduce the viscosity of crude extracts by treatment at 37° C. with a pneumococcus enzyme (hyaluronidase), which hydrolyzes a tumor polysaccharide of high viscosity. Subsequently, the extract was passed through a Berkefeld V filter. A proper amount of neutral papain solution was added to the filtrate, the precipitate washed with cold water and finally redissolved in 3% NaCl solution. The crude papain complex was then fractionated twice by tenfold dilution with distilled water and redissolved in 3% NaCl. Fifty to 70% of this purified papain complex was papain, along with a certain amount of lipids and possibly nucleic acid. The smallest amount of material which was required to produce a tumor, when injected into 3 week old chicks was 10^-7 gm. of the purified papain complex, in terms of nitrogen, as compared with 10^-5 gm. of the original tumor filtrate. The purified papain complex was examined in the Tiselius apparatus and fractions obtained after 7 to 11 hours electrophoresis were tested for tumor producing activity. The material from the cathode compartment was inactive and consisted mainly of papain. The papain producing power of the material from the anode compartment was not higher than that of the material from the "middle" compartment, and was equal to that of the untreated preparation, the minimal active dose in each case corresponding to about 10^-7 gm. nitrogen. Study of the electrophoretic pattern indicated that the purified fraction contained other material beside the basic protein and the tumor agent.—A. C.
The experiments were controlled by using non-fostered litter-mates.—L. L. W.


The author reviews his own extensive work and that of others on inherited tendencies toward breast cancer in mice. By correlating the results of successive experiments (which are given in some detail), he is able to ascribe the occurrence of breast cancer in mice to the combined activity of at least 3 etiological influences: (1) The milk influence. This extrachromosomal, maternal factor is transferred in the milk to the progeny in the first 24 hours of life. It is the active influence that has been found in normal tissues and organs transplanted from 1 strain to another. (2) Inherited susceptibility. Studies of breast tumor ratios in hybrid animals are in accord with the genetic theory that this susceptibility is inherited as a single dominant factor. (3) Ovarian hormonal stimulation of the mammary gland.—L. L. W.


The paper presents a condensed report of experimental investigation of the effect of foster nursing upon the incidence of spontaneous mammary cancer in several strains of mice and tests for the presence of the milk influence in various organs. A bibliography of publications of the author and others working on this problem since 1936 is included with a review.

The "breast cancer producing influence" is an actual active "influence" present in the milk of high cancer stock females. It is probably present and active during the entire lactation period. The active influence may be transferred by the inoculation of spleen, thymus, and lactating mammary gland tissue from cancerous stock animals. The active influence is probably not present (or has been destroyed) in the liver of high tumor stock mice. The active influence may be given to 4-week-old females by feeding by mouth milk obtained from lactating females of a cancerous stock. Fasted females of low breast tumor strains need not develop breast tumors to transmit the active milk influence by nursing. An active milk influence may be necessary for the development of induced estrogenic breast tumors.—S. B. J. and Author's summary.


Chemical mechanisms, chemical participants, and chemical determinants are used by heredity in the production of normal and cancerous structures. For the better understanding of the abnormal growth, cancer, it is necessary to learn more about normal growth and its chemistry.—J. J. B.


The authors determined the incidence of mammary tumors in virgin females of the Murray-Little strain of dilute brown mice (to be called "D") and the C57 stock of Little (to be called "B"). Eighty-five per cent of the control mice of the D stock had cancer and 9% of the D females fostered by B mothers. The incidence in mice of the B stock (194 mice) was 9%, and when fostered by D females was 13%. Mice of the oaw Luekenvloekhuis strain had an incidence of 1%. The incidences in F1 females were: D × B, 69% in controls, 4% in fostered (by D); B × D, 2% in controls, 46% in fostered (by D). Backcrosses were made by mating hybrids having D stock maternal parents to males of the B stock and hybrids having maternal parents from the B stock to males of the D strain. These matings were continued for 11 generations to the paternal stocks and in each group the incidence of mammary tumors was 1%.

From these results the workers concluded that the extrachromosomal factor was independent of and not a product of the genetic composition. The genetic susceptibility for mammary cancer is of little importance if the extrachromosomal factors are inactive. Because the incidence was lower in backcross mice of the 11th generation than in mice of the B stock fostered by D females, they believed that the extrachromosomal factors might become inactive after a number of generations.

Mice in the same stage of diestrus were selected for study of the architecture of the mammary glands. The structure of the glands of the mice of the B stock was described as resembling a tree in winter and the glands of the females of the D stock resembled a budding tree in spring—buds along the primary ducts and at the beginning of the secondary ducts. Females of the D strain fostered by B females had primary ducts of the normal D type but the gland tree possessed characteristics of the B type. The B females fostered by females of the D stock had primary ducts of the normal B type. The gland tree, on the whole, had the architecture of the B type but some areas were identical with the D type. The architecture of the primary ducts was believed to be determined by the plasma and/or uterus factor, and the structure of the gland tree determined by the genetic and the extrachromosomal factors—milk, plasma, and uterus factors.

In different types of mice there is a correlation between the architecture of the mammary gland and the degree of the disposition for mammary cancer.—J. J. B.


Foster nursing, by which the incidence of mammary tumors in mice may be reduced, exerted no influence upon the course of, or mortality rate of, encephalitis.—J. J. B.


Mice of the CFX strain inoculated with Crocker mouse sarcoma 180 were refrigerated at 5 to 7° C. intermittently or continuously from 8 to 48 hours. Tumors disappeared completely in 5 mice; in others a small decrease or temporary arrest of tumor growth occurred. Tumors which had attained relatively large size 16 to 18 days after inoculation were not affected by the reduction of temperature of the tumor-bearing animals. Metabolic studies using tissue slices failed to show significant changes in the oxygen consumption, respiratory quotients, and aerobic glycolysis of sarcoma 180 excised from refrigerated mice as compared with the tumor excised from control mice. The author concluded that "the high mortality rate, the comparatively few successful results, and the unaffected viability of tumor cells, indicate the inadequacy of refrigeration in the treatment of malignant growths."—S. B. J.

Radiation

Pecher, C. (Crocker Radiation Lab., Univ. of California, Berkeley, Calif.) Biological investigations with radioactive...
in mice is enhanced by 1-proline probably through its favoring death, 78 mice were given daily by intrascapular subcutaneous injection 0.2 cc. of M/125 solution of 1-proline in distilled water. The influence of terminal B avitaminosis with attending low body temperature upon the growth characteristics of sarcoma 180. Cancer Research, 1:217-219. 1941.


From the time of the first appearance of mammary tumor until death, 78 mice were given daily by intraperitoneal subcutaneous injection 0.2 cc. of M/125 solution of l-proline in distilled water. The controls were 76 untreated mice kept under similar conditions. The mice injected with l-proline had more multiple primary tumors than the controls. A second tumor appeared in 56.4% of the proline-treated group, and in 44.7% of the controls; and a fourth tumor developed in 9.0% in the proline-treated mice and in 2.6% of the controls. 56.4% of the proline-treated group, and in 44.7% of the controls; and a fourth tumor developed in 9.0% in the proline-treated mice and in 2.6% of the controls. A third tumor appeared in 20.5% of the prolines and in 13.2% of the controls; and a fourth tumor developed in 9.0% in the proline-treated mice and in 2.6% of the controls. A third tumor appeared in 20.5% of the prolines and in 13.2% of the controls; and a fourth tumor developed in 9.0% in the proline-treated mice and in 2.6% of the controls. The author emphasizes that these experiments deal with the selective fixation of radioactive strontium in the skeleton, the suitable energy of its beta-rays (1.5 million electron-volt), its half life of 55 days, and the innocuousness of small doses provide a specific method of irradiation of the skeleton. The experiments furnished 2 practical findings: (1) a method of selective irradiation of the skeleton for therapeutic purposes, and (2) the secondary production of appreciable amounts of a long-lived radioactive yttrium, the most likely among the artificially made radioactive elements now known, which may be substituted for radium as a penetrating gamma-ray source. The paper is illustrated with autographic pictures of bones containing radioactive phosphorus and strontium.—S. B-J.

Biochemistry and Nutrition—Chemotherapy


Radioactive strontium and calcium have been used to study the mineral metabolism in mice during pregnancy. It appears that part of the calcium and strontium previously fixed in the skeleton of mice migrates to the fetus during the last days of pregnancy and to the offspring through the milk. When radio-active strontium lactate is injected intravenously into lactating mice and cows, appreciable amounts are excreted in the milk.—Authors' summary.


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Chemical methods were used to determine the amounts of phospholipids present in rat carcinosarcoma 256. It was found that the ratio of lecithin to cephalin was 45:55, comparing favorably with a 40:60 ratio previously determined in the same laboratory. Also, after giving rats a tracer dose of radioactive phosphorus, the activity of the phospholipid fractions of the tumors was observed at intervals up to 20 days. The activity of the lecithins reached a peak after 30 hours and the cephalins after 40 hours. Thereafter, the tagged phosphorus began to disappear from both fractions at about the same rate. It was felt that the rapid rate of turnover of lecithin indicated that its function in the tumor was predominantly metabolized, while the cephalin was more concerned with structure.—L. L. W.


When limited amounts of 20-methylcholanthrene were applied to the skin of mice receiving a control diet, tumors developed in only 12% of the animals. The addition of fat to the diet increased tumor formation to 83%. The tumor-promoting activity of the fat was found to reside in the fatty acid fraction. Ethyl laurate was as effective as natural glycerides; glycerol and the unsaponifiable fraction had only slight activity. The action of fat was increased by heating at 300°C. for 1 hour. Rancidification with ultraviolet light, or oxygenation in the presence of copper oleate failed to alter the effectiveness of the fat for tumor formation. The highest incidence of tumors appeared when fat was given throughout the experiment, but measurable increases were also observed when fat was fed either during the first 2 months while the carcinogen was applied, or after the 2nd month; e.g., after the application of hydrocarbon had ceased. The most effective period was 1 ½ to 3 months after the beginning of the application of hydrocarbon. Dietary fat was much less effective in promoting induced skin tumors in the rat than in the mouse. Oil applied locally increased the rate of tumor formation in rats. It is suggested that the difference between the 2 species may be due to differences in skin thickness, in the rates of destruction of the hydrocarbon, and in the ability of the 2 species to metabolize fat.—Authors' summary.


A macromolecular fraction isolated from chick embryo extracts by differential high-speed centrifugation essentially according to Claude, exerts a definite growth-stimulating effect on cultures of mouse heart fibroblasts.—Authors' summary.


Rats fed a basal diet lacking choline developed hyperplasia of the epithelium of the forestomach. The addition of 0.15% choline hydrochloride to the basal diet prevented the development of these lesions.—S. B-J.


Dibenzyl disulfide was fed to rats and hippuric acid was isolated from the urine and identified by analysis. The results support the suggestion that benzyl mercaptan or dibenzyl disulfide may be formed in vivo from S-benzyl-d-cysteine via S-benzyl-thio-
IMMUNOLOGY


The mean quantity of purified-papilloma protein necessary to bind 1 unit of complement was 0.95 ± 0.06 γ, or 10^{-9.26} gm, with a coefficient of variation in the individual estimates of ± 29.8%. In previous work, the infectious unit (defined as that amount of protein injected under standard conditions necessary to produce papillomas at 50% of the injection sites), was found to be 10^{-13.6} gm. Thus the ratio of the complement-fixing unit to the infectious unit as far as their protein content was concerned was 2151:1. The authors believe that the complement-fixation test may be useful not only in assaying the proteins of such materials but also in indirectly measuring their infectivity.—L. W.

LEUKEMIA


The progressive development of cultures of leukotic blood cells, leukemic bone marrow, and heart muscles from leukotic chickens is described. The fowls used were inoculated with Englebreth-Holm's strain T of chicken hemocytoblastosis. Leukosia and sarcoma were produced by this agent. The agent remained virulent in tissue cultures as long as 181 days, through several transfers. In the authors' opinion fibroblasts developed from leukotic blood cells and “the agent of fowl leukosis is capable of remaining active and of increasing in the presence of nonspecific mesenchymal cells (fibroblasts).” The paper includes 15 photomicrographs.—S. B-J.


Mice of the inbred F strain which shows a high incidence of spontaneous leukemia were painted with methylcholanthrene twice weekly according to the technic of Morton and Mider. Mice of the C3H strain received similar treatment. Other non-leukemic strains (NH, CHI, CBAN, and C57) were painted once a week. Painting with methylcholanthrene was begun when the mice were about 3 ~ days old. Details are presented in several transfers. The authors' opinion fibroblasts developed from leukotic blood cells and “the agent of fowl leukosis is capable of remaining active and of increasing in the presence of nonspecific mesenchymal cells (fibroblasts).” The paper includes 15 photomicrographs.—S. B-J.

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pyruvic acid. Certain phases of the metabolic transformation of sulphydryl and cystine derivatives of certain carcinogenic compounds are discussed.—Author's summary.

REFERENCES

10. The leucocytic response in the peripheral blood to transplanted normal tissues which had previously been shown to parallel closely the changes occurring locally about transplanted tissues, as described by Loeb, was used to determine the presence of the organisinal differentials in tumors. Pieces from various kinds of rat and mouse tumors were homoio- and hetero-transplanted into rats, mice, and guinea pigs; benign as well as malignant tumors were used. They all exerted the same effects on the leucocytes in the circulating blood as did normal tissues, the degree and kind of changes depending mainly upon the relation of the organisinal differentials of host and transplant. However, benign tumors reacted with a slightly diminished intensity. Successive transplantsations of tumor pieces likewise acted like those of normal tissues, and tumors and normal tissues interacted in the same way as did normal tissues; transplanted tumor pieces successively transplanted; that is, a 1st homotransplantation of either tumor or normal tissue caused an accelerated leukocytic response to a 2nd transplantation of either tumor or normal tissue. However, when tumor homotransplants reached a large size the animals became progressively debilitated, developed an anemia and a leucocytosis, with a secondary hyperplasia of red and white cell elements of the bone marrow. This leucocytosis must be distinguished from the increase in polymorphonuclear leucocytes caused by the transplantation of heterogeneous normal or tumor pieces; it is a condition which was not found after homotransplantation of normal tissues. The anemia and accompanying leucocytosis are the only significant differences in the reactions of the host to normal and to tumor tissues, and this particular reaction to tumors is not connected with the organismal differentials of the tissues.—Author's abstract.

BLUMENTHAL, H. T. The effects of spontaneous and transplanted tumors on the red and white cells in circulating blood and bone marrow. Cancer Research, 1:196-204. 1941.

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The adenocarcinoma of the leopard frog, when implanted into the anterior chamber of the eye, offers excellent material for the study of the influence of temperature on the growth of neoplasms. The transplants can be observed directly. Changes due to differences in temperature can be studied over a wider range in the frog than in warm-blooded animals since the body temperature is practically that of its surroundings. In this work, the temperatures to which the inoculated frogs were exposed ranged from 4 to 28°C, these being the extremes at which frogs could be maintained satisfactorily. Under these conditions, the temperature within the eye corresponded to that of the environment, as ascertained by thermocouple measurements. Regardless of temperature, frog carcinoma in the eye has a definite cycle of growth. After a period of lag comes a relatively rapid increase in size, followed by a slowing down of the rate of growth, then a stationary period and finally regression. The most important difference observed was an increase in the rate of growth at higher temperatures, and retardation at lower. At the higher temperature, there was earlier and more effective vascularization, the tumors forming long, branching, tubular outgrowths and cysts. At lower temperatures, the outgrowths were short and straight and cysts were uncommon. These differences were accentuated by repeated passages in the eye. Growth was checked during hibernation at 4°C for 80 days, but no injury to the tumor resulted from this long exposure at low temperature and growth was resumed when the frogs were brought to higher temperatures. The paper is illustrated by 28 photographs.—A. C.

BLUMENTHAL, H. T. The effects of spontaneous and transplanted tumors on the red and white cells in circulating blood and bone marrow. Cancer Research, 1:196-204. 1941.

The leucocytic response in the peripheral blood to transplanted normal tissues which had previously been shown to parallel closely the changes occurring locally about transplanted tissues, as described by Loeb, was used to determine the presence of the organisinal differentials in tumors. Pieces from various kinds of rat and mouse tumors were homoio- and hetero-transplanted into rats, mice, and guinea pigs; benign as well as malignant tumors were used. They all exerted the same effects on the leucocytes in the circulating blood as did normal tissues, the degree and kind of changes depending mainly upon the relation of the organisinal differentials of host and transplant. However, benign tumors reacted with a slightly diminished intensity. Successive transplantsations of tumor pieces likewise acted like those of normal tissues, and tumors and normal tissues interacted in the same way as did normal tissues; transplanted tumor pieces successively transplanted; that is, a 1st homotransplantation of either tumor or normal tissue caused an accelerated leukocytic response to a 2nd transplantation of either tumor or normal tissue. However, when tumor homotransplants reached a large size the animals became progressively debilitated, developed an anemia and a leucocytosis, with a secondary hyperplasia of red and white cell elements of the bone marrow. This leucocytosis must be distinguished from the increase in polymorphonuclear leucocytes caused by the transplantation of heterogeneous normal or tumor pieces; it is a condition which was not found after homotransplantation of normal tissues. The anemia and accompanying leucocytosis are the only significant differences in the reactions of the host to normal and to tumor tissues, and this particular reaction to tumors is not connected with the organismal differentials of the tissues.—Author's abstract.


The adenocarcinoma of the leopard frog, when implanted into the anterior chamber of the eye, offers excellent material for the study of the influence of temperature on the growth of neoplasms. The transplants can be observed directly. Changes due to differences in temperature can be studied over a wider range in the frog than in warm-blooded animals since the body temperature is practically that of its surroundings. In this work, the temperatures to which the inoculated frogs were exposed ranged from 4 to 28°C, these being the extremes at which frogs could be maintained satisfactorily. Under these conditions, the temperature within the eye corresponded to that of the environment, as ascertained by thermocouple measurements. Regardless of temperature, frog carcinoma in the eye has a definite cycle of growth. After a period of lag comes a relatively rapid increase in size, followed by a slowing down of the rate of growth, then a stationary period and finally regression. The most important difference observed was an increase in the rate of growth at higher temperatures, and retardation at lower. At the higher temperature, there was earlier and more effective vascularization, the tumors forming long, branching, tubular outgrowths and cysts. At lower temperatures, the outgrowths were short and straight and cysts were uncommon. These differences were accentuated by repeated passages in the eye. Growth was checked during hibernation at 4°C for 80 days, but no injury to the tumor resulted from this long exposure at low temperature and growth was resumed when the frogs were brought to higher temperatures. The paper is illustrated by 28 photographs.—A. C.
into the anterior chamber of the eye of animals of the same species. The method permits direct observation of the growth with the naked eye or under the microscope. The present paper deals with an attempt to establish whether or not the frog carcinoma can proliferate in the eyes of alien hosts. Two species belonging to the same family (green frog and bullfrog), a species from a different family (toad), and 2 different classes of cold-blooded vertebrates (gold fish and alligator) were used. The tumor was found to grow as readily in the eyes of frogs of alien species as in the eye of the natural host. In toads, the tumor grew well but the proportion of successful transplantations was distinctly less (37% as compared to 61 to 67% in the frogs). In frogs and toads, the character and rate of growth of the transplants was practically the same. The neoplastic cells retained their acinar arrangement, supported by a stroma which developed as well from the tissues of alien hosts as from those of the natural host. No progressive growth occurred in the fish, although characteristic acini persisted and a few mitoses could be found long after implantation. In the alligator, no growth occurred and the transplant deteriorated rapidly. No reaction developed in the eyes of any of the amphibians whereas a marked inflammatory reaction did occur in the eyes of fish and reptiles. The results indicate that, among cold-blooded vertebrates, the tumors and tissues of the eye have a high degree of tolerance for foreign tumor grafts and that the success of transplantation into alien species decreases as the relationship to the original species becomes more distant. Seventeen photomicrographs illustrate the paper.—A. C.

**REVIEWS**


This comprehensive review, covering the period from 1916 to 1940, presents summaries, discussions, and interpretations of investigations of the role of hormones of the ovary, adrenal, and pituitary glands in the production of cancer. While most of the material presented deals with the relation of hormones to carcinomas of the mammary gland and genital tract of mice and rats, other species and other types of tumors are included, and some features of cancer of the breast in women are discussed. Genetic factors and the possible role of viruses are analyzed. After discussing both rhythmic and noncyclic growth processes the author concludes that "the study of the origin of cancer is, at the same time, a study of the mechanisms which in the normal organism tend to prevent the development of these abnormal growth processes." The bibliography contains 153 references.—S. B-J.

**CLINICAL AND PATHOLOGICAL REPORTS**


Ilford film, artificial light, and radiations of from 7,000 to 9,000 Å were used. Twelve sets of ordinary photographs compared to infra-red photographs are included.—M. D-R.


The author reviews the recent literature on the subject and summarizes his own method used successfully for 16 years. Procedure less than 0.5 cm, thick were fixed 1 minute in boiling 15% formaldehyde solution. This is followed by sectioning in the freezing microtome, staining of the sections on a slide with 0.5% toluidine blue for 20 seconds, rapid washing with water, and mounting and observation in neutral glycerol. Four photomicrographs are appended.—M. D-R.


This is a further report on the use of a new biopsy needle devised and previously described by the junior author.—E. A. L.

**RADIATION—DIAGNOSIS AND THERAPY**


Various methods of irradiation of carcinomas of the skin are presented and illustrated with case reports. Massive doses of medium or low voltage x-rays with little or no filtration are used for practically all small lesions. High voltage, heavily filtered x-rays in fractionated doses are preferred for the large indurated lesions, all lesions involving cartilage, and all carcinomas of the lip. In selected cases x-ray therapy is supplemented with interstitial low intensity radium element needles.—E. A. L.


One case of leiomyosarcoma and 3 of lymphosarcoma of the small intestine are reported, and the literature is reviewed. Thirty-four cases of leiomyosarcoma of the small intestine and over 400 of lymphosarcoma have been recorded in the literature. The author's case of leiomyosarcoma was the only one to have been irradiated. It responded well. Lymphosarcomas are radio-sensitive.—E. A. L.


A new radium applicator, called a hysterostat, for the intracavitary radiation of carcinomas of the corpus uteri is described. It consists of a central crosspiece and 2 to 4 lateral tandem inserters. The central crosspiece is attached to a stem permitting variation of the angle between them. The lateral inserters are not fixed instruments but are separate pieces which can be interchanged to make various shapes to correspond to the shape of the uterine cavity.

Eight of the 13 patients treated with this instrument were subjected to total hysterectomy 4 to 6 weeks after the radium treatment. Seven of the 8 showed no residual cancer. Three of the remaining 5 are alive and well 6 to 24 months after treatment. The dose varied between 4,000 and 7,660 mg.—E. A. L.


A method is described for rotation x-ray therapy in which the beam is directed horizontally towards the tumor area and the patient is rotated on a vertical axis. The advantage of this method is that there is a volume of tissue surrounding the axis of rotation which is continuously in the beam and receives the most intense radiation, whereas the skin receives the least radiation owing to the fact that it is moving most rapidly and is in the narrowest portion of the beam.—E. A. L.


The use of radioactive isotopes as tracers and as substitutes for radium in direct radium therapy is discussed. Four representative cases of chronic myelogenous leukemia and 1 of chronic
Reports of Experimental Research

Cancer Res 1941;1:250-256.

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