Abstracts

Experimental Research, Animal Tumors

**Under den Versuch, mit β-Anthrachinolin Nieren- tumoren zu erzeugen. [Attempt to Induce Renal Tumors by β-Anthrachinoline.]**


No carcinogenic action on the rat kidney was exerted by β-anthrachinoline injected subcutaneously in poppy-seed oil, when the author attempted to repeat and extend the experiments of Sempronj and Morelli (Am. J. Cancer, 35:534. 1939). The positive results of the latter investigations may have been due to the hereditary disposition of the animals employed.—M. H. P.

**Über die Beeinflussbarkeit der Krebshilbung nach Benzpyrenepinselung. [Effect of Various Factors on Tumor Formation after Benzpyrene Painting.]**


When mice (not genetically uniform) were painted twice a week in the interscapular region with 2 drops of 0.4 or 0.8% benzpyrene in benzene, tumor formation was greatly accelerated and the number of tumors increased by incorporation of o-aminoazotoluene or chlorophyll in the benzpyrene solution. The chlorophyll effect was characterized by significant morphological deviations of the neoplasms from those produced by benzpyrene alone. When vitamin A was applied locally at the same time as benzpyrene, tumor formation was appreciably inhibited. Painting with benzpyrene in lanolin was not carcinogenic within the usual experimental period, even with intensive dosage; lanolin apparently exerts active or passive protective power, the nature of which should be investigated. Ultraviolet irradiation, ionone, and interazine did not affect carcinogenesis.—M. H. P.

**A Sensitising Factor in Experimental Blasto- genesis.**


The author describes the action of noncarcinogenic agents (croton oil, croton resin, cantharidin) applied to the skin of the mouse either before (sensitizing action, A) or after (developing action, B) one or more applications of 3,4-benzpyrene. Experiments of the following type are described. Croton oil (1% in acetone) is applied to the right flank 5 times in 10 days. Then 3,4-benzpyrene (0.02 cc. of 0.3% in acetone, *i.e.*, 0.06 mgm. hydrocarbon) is applied once to both flanks, followed by the croton oil solution, also to both flanks, thrice weekly for 20 weeks. This procedure applied to 12 mice gave, in 20 weeks, 22 benign and 3 malignant tumors on the right, and 6 benign tumors on the left, flank. When the same benzpyrene solution was applied twice weekly to another series of mice for 20 weeks (*i.e.*, 2.4 mgm. hydrocarbon), without croton oil, the same number of tumors was obtained, but the tumors appeared 5 or 6 weeks later than those produced by a single application.

Other experiments in which a single application of 3,4-benzpyrene was combined with the action of croton oil or croton resin showed that A alone gave no tumors, but A+B gave more tumors than did B alone. Application of cantharidin (0.3% in acetone) on 2 days followed by benzpyrene on 3 days and croton oil during 20 weeks gave no tumors within the area of application of cantharidin although tumors appeared outside this area. But if the preliminary treatment with cantharidin were prolonged (7 applications in 14 days), a cocarcinogenic action appeared, the tumors on the flank receiving cantharidin being more numerous than those on the opposite flank.

Counts of mitoses in the epidermis showed (a) that croton oil or resin produced a fourfold to ninefold increase; (b) that cantharidin caused a complete cessation of mitosis during the first week, followed by a stimulating action as great as that of croton oil or resin. These effects upon mitosis are held to bring about the observed effects upon carcinogenesis.—E. L. K.

**Loss of Carcinogenic Activity when Methylcholanthrene is Dissolved in Anhydrous Lanolin.**


Experiments on 312 mice have shown that methylcholanthrene when dissolved in anhydrous lanolin, a vehicle closely resembling sebum, and applied to the skin of mice loses its carcinogenic effect. After 42 applications, given 3 times weekly for 14 weeks, it fails to induce skin cancer. It does not even induce those early changes that represent the initiation of the carcinogenic process, such as epilation, destruction of the sebaceous glands, epidermal hyperplasia, and a diminution in the calcium and iron content of the epidermis, which follow the single application of a benzene or acetone solution of the carcinogen. Fluorescence-microscopic and spectrographic studies show that this loss of carcinogenic activity cannot be attributed to a lack of absorption or to a rapid destruction of the methylcholanthrene by the skin. After 42 applications of the lanolin solution of the carcinogen to the skin, the morphological and chemical criteria that were studied revealed no differences from normal skin. There is, however, a striking biological change produced in the skin, in that it has become sensitized to the action of a benzene solution of methylcholanthrene. This effect will be described in a following paper.—Authors’ abstract.

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The authors have previously shown that a solution of methylcholanthrene in anhydrous lanolin is carcinogenically inactive to mouse skin and fails even after prolonged and repeated applications to produce the specific early structural and chemical changes that initiate the carcinogenic process. All these changes are regularly produced by the same carcinogen when it is applied in a lipid solvent such as benzene. The carcinogen can therefore exist in an active or inactive state depending on the medium in which it is dissolved.

Two experimental series of mice that had received 42 applications thrice weekly of the inactive solution of methylcholanthrene in lanolin and untreated controls of the same age were painted with a benzene solution of methylcholanthrene in an effort to determine whether the prolonged exposure to the inactive carcinogen had conferred any resistance to the carcinogen in lipid solvents. Quite the opposite had occurred, for the mice that had been pre-treated proved much more sensitive to the benzene solution of methylcholanthrene than the controls. This enhanced sensitivity manifested itself in a great increase in the incidence of skin cancer and a great shortening of its period of induction.

The significance of these findings in relation to a concept of a mode of carcinogenic action of methylcholanthrene is discussed.---Authors' abstract.


It appears from the experiments that pigeons, guinea fowls, and possibly ducks may be added to the list of animals responding to the injection of methylcholanthrene with malignant tumors. The incidence in 21 pigeons was 47% and in 12 guinea fowls 66%, whereas only one tumor developed in 52 ducks and none in 10 turkeys injected.

The results show that there is no species relationship between the susceptibility of birds to the virus of the Rous sarcoma and to methylcholanthrene.

Transplantation of 1 guinea fowl and 2 pigeon tumors through from 2 to 9 generations of birds of their respective species was accomplished, but attempts to transplant the pigeon tumors by means of Berkefeld N filtrates ended in failure.

All the tumors induced were ordinary spindle cell sarcomas that frequently gave rise to metastases in the liver and, in the case of 2 pigeon tumors, in the bones of the lower extremities.

Benzol solutions of methylcholanthrene proved to be far more effective than lard solutions.---Authors' summary.


Rats received subcutaneous injections of colloidal 1,2,5,6-dibenzanthracene (d.b.a.) (27.8 mgm. in 100 cc., i.e., 0.001 mole per liter in isotonic glucose and gelatine solution) 5 times weekly for 20 to 22 injections, while controls received the suspending solution only. In the normal rat, hemolymph nodes occur only in the renal region. In rats given d.b.a., lymph nodes all over the body (those of 10 regions were examined) tended to take on the hemolymph structure. These nodes showed (1) widening of the lymph channels and diminution of lymphoid tissue, (2) red corpuscles in the lymph spaces, sometimes in large numbers; and (3) increase in macrophages containing red corpuscles and pigment. Many of the macrophages, and the reticulum cells, gave a reaction for iron. The nodes of the controls did not differ from the normal condition. Anthracene produced in a few nodes in some animals some degree of these changes, but the experiments are being repeated with anthracene specially purified. The growth rate of rats receiving d.b.a. was slowed; anthracene had not this effect. The possibility is considered that the red blood corpuscles in the nodes of the d.b.a. treated rats have passed through the walls of blood capillaries and passed with the lymph stream to the nodes. An abstract of a preliminary statement of these results was given in Cancer Research, 3:337. 1943.---E. L. K.


In a rat that had been inoculated with aqueous, absolutely cell-free extracts of rat benzpyrene-tumors, a fibrosarcoma developed at the injection site after a few months. It is possible that the extracts might have contained traces of the hydrocarbon.---M. H. P.


Benzpyrene irradiated with x-rays or y-rays produces tumors in rats more rapidly, but not in greater number, than does nonirradiated benzpyrene.---M. H. P.


The author describes the nature of cosmic rays and reports briefly on the results of experiments of Eugster and Hess on tumor mice that had been exposed to intensified radiation. These animals developed carcinoma much more frequently than did controls in radiation-free atmosphere.---M. H. P.


Strain dba (subline 12) and strain F mice were used in 3 experimental groups. Mice of Group I received irradiation alone; those of Group II had 0.5% methylcholanthrene applied percutaneously twice a week; those of Group III received both kinds of treatment. The irradiated
animals received a daily dose of 80 r, 140 kv., 30 cm. skin target distance, 2 mm. Al filter, including the entire body in the field. Nine successive daily treatments were given to the strain F mice for a total of 720 r, while the dba animals received a total dose of 880 r.

There was no evidence that irradiation, under these experimental conditions, when used in conjunction with methylcholanthrene, increased the incidence or accelerated the onset of carcinogen-induced leukemia in strain dba and strain F mice.—M. B.


Spayed C3H mice of the Andervont subline strain were divided into three groups at 2 months of age and kept at 68, 79, and 91° F., evenly divided litters being used. Mammary tumors developed earliest and in largest numbers in the 68° F. group, next best in the 79° F. group, and least at 91° F. Tumor incidence in all groups was considerably less than in unspayed mice of the same strain but showed the same stimulating effect of cold (or depressive effect of heat).—Authors' abstract.


As a preliminary to an investigation of the metabolism of the carcinogenic azo compounds, a study of the changes undergone by azobenzene, which is the simplest azo compound and is not known to be carcinogenic, was undertaken. The compound was injected intraperitoneally in arachis oil in rats. The amino compounds in the urine were estimated colorimetrically by diazotization and coupling with N-sulfatoethyl-m-mluidine. Aniline and benzo- 
diazine were isolated; the latter appears to be formed on metabolism with N-sulfatoethyl-m-mluidine. Aniline and benzo- 
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The two methods used were: (1) determination of oxygen consumption in the Warburg respirometer upon oxidation of p-phenylenediamine by an oxidase prepara-
tion from beef heart (method of Keilin and Hartree), and activation of this process by cytochrome c or hemolyzed blood corpuscles, and (2) determination of indophenol-blue formation by Sehrt's method (Sehrt's carci-

noma reaction). Erythrocytes of healthy and sick persons showed differences in ability to activate oxidase. Those of cancer patients showed pronounced impairment of the cytochrome oxidase system, apparently because of decrease in the amount of cytochrome c present in such erythrocytes. Diagnostic evaluation is difficult, since the oxidase prepara-
tions show different values with regard to activity and to activation by cytochrome c or erythrocytes. The indophenol blue determination method is also not applicable to practical diagnosis.

The autoxidation of p-phenylenediamine remains almost the same in a given time, the solutions of dimethyl-p-phenylenediamine and 2-naphthol show great differences in their autoxidation and oxidizability in individual series of experiments, and a norm has not been found. Within the same experimental series, indophenol blue formation is generally decreased by hydrolyzed erythrocytes of sick persons. Erythrocytes of cancer patients form less indophenol blue than those of healthy persons. Results of both methods show that action of oxidation enzyme systems may be injured in persons with or without cancer, and that the effects of oxidase and cytochrome c or other factors in these systems are not separable.—M. H. P.


A triphosphatase ("preparation M") obtained from benzpyrene rat sarcoma 616 by the preparation method for myosin (PLIMMER—Organic and Bio-Chemistry, 6th ed., p. 415) catalyzed the hydrolysis of neutralized sodium triphosphate but not that of nonneutralized (alkaline) sodium triphosphate. Activity was optimal at pH 5.5 to 6 in the absence of magnesium or manganese, 4.8 in the presence of Mg (and probably also Mn). Both Mg and Mn accelerated the enzymatic hydrolysis more markedly at pH 4.8 than at pH 8.4, and hardly affected it at pH 6. At pH 5.5 to 6, potassium fluoride slightly inhibited the hydrolysis.—M. H. P.


Seven types of experimental tumors were assayed for their adenosinetriphosphatase (ATP-ase) content. They were found to contain about the same amount as adult specialized tissues, in contrast to the findings for various respiratory enzymes. It is pointed out that the assay measures potential ATP-ase rather than the effective ATP-ase concentration of the tissues. The factors that determine the effective ATP-ase concentration in normal and tumor tissue are discussed, and it is suggested that the activity coefficient in neoplasms is likely to be at least as great as in normal tissue. The data are discussed in relation to the theory of cancer that relates growth to the balance between ATP and its breakdown products.—Authors' abstract.

Brain and liver from late embryonic and newborn rats up to the 30th day of postnatal life were compared with adult tissues with respect to their content of succinic dehydrogenase, cytochrome oxidase, and adenosinetriphosphatase (ATP-ase). In brain the enzymes studied remained constant from about 3 days before birth until about 6 days after birth, and then increased rapidly so that the adult level was reached by the 30th day of life. The wet weight of the brains increased steadily throughout this period. In liver the enzymes studied increased rapidly during late embryonic and early postnatal life, and the adult level was approximated within 10 to 15 days. Up to this time there was very little increase in the wet weight of the liver, but at this point its weight began to increase rapidly. The results show that profound changes occur in both types of enzyme increased, that is to say, the potential rate of energy mobilization was increased. The results of enzymes mentioned above.--Authors' abstract.


A valuable review of the literature (about 250 references) with a section on tumors. --E. L. K.


The protective colloids of 78 cancer sera were compared with those of normal sera from 70 persons. After 0.075 ml. of serum, and then the coagulating electrolyte, are added to 5 ml. of Congo red, and the mixture is incuabted at 30° C. for 30 minutes, the residual color is determined in a photoelectric colorimeter. Average values of 9.26 and 40.52γ per ml. respectively were obtained; 89.6% of the cancer patients and 4.3% of normal subjects gave values below 15γ per ml. The albumin/globulin ratio showed only rough agreement with the protective colloid index. It is suggested that other factors, such as molecular dispersion and even molecular species, are more important in determining this index. The protective colloid test may be useful in diagnosis of cancer or in following clinical progress in patients with this disease, in absence of other diseases that affect the protective colloid index, i.e., cardiac edema, pernicious anemia, chronic nephritis, gastroenteritis, pertussis, malaria, active tuberculosis, and active asthma.—R. N. J.


The cystine and cysteine distribution as well as the complete sulfur distribution of the extractable proteins of the neoplastic tissues of rats and rabbits were studied and compared with the corresponding relationships in the normal tissues of these species. Earlier work by Greenstein and his associates (J. Nat. Cancer Inst., 1:91-104, 1940; 2:305-306, 1941) had indicated that extractable tissue proteins possess a species-specific cystine/cysteine ratio. The experimental methods employed are described in a forthcoming paper in the Journal of Biological Chemistry.

It was found that the cystine and cysteine content of adult liver is higher, and the methionine content is lower, than that of fetal liver. At about equivalent periods of gestation, the total sulfur, cystine-cysteine sulfur, and methionine sulfur of fetal rabbit liver amount to only about 50% of that of fetal rat liver. The sulfur distributions of normal adult and of regenerating rat liver are nearly the same, as are those of fetal rat liver and of transplanted rat hepatoma.—K. G. S.


Mice on low carbohydrate diet from the time of inoculation of Ehrlich mouse carcinoma showed a lower number of takes of the carcinoma than did controls (on normal diets). Growth of the successful implants showed a small but statistically significant inhibition in the mice on the low carbohydrate diets, and the life of these animals was prolonged. Administration of insulin with the low carbohydrate diet did not alter the effects on the tumors. When mice with tumors were given the low carbohydrate diet, some of the tumors regressed, but the possibility that such regression was spontaneous was not completely excluded.—M. H. P.


Shortly after weaning, mice from strain F, which has a high incidence of spontaneous leukemia, were placed on diets relatively high (32%) and low (3%) in fat. Litters were divided, and half received one diet and half the other. At the end of 300 days the data indicated a slightly earlier appearance of leukemia in the group fed the high fat diet, although the total incidence of leukemia was about the same in the 2 groups. It is unlikely that the earlier appearance of the disease can be attributed to the dietary fat content, since differences in caloric intake and rate of growth in the 2 groups could account for the results.

Methylcholanthrene (0.5% in benzene) was applied percutaneously twice weekly to 2 groups of strain dba mice (subline 12) fed the high fat and low fat diets, respectively.
This strain is susceptible to the induction of leukemia with methylcholanthrene. The results indicated that there was a significant delay in onset of carcinogen-induced leukemia in the mice on the high fat diet, although the incidence of leukemia was the same for both dietary groups. It is possible that the oil on the fur of the animals given the high fat diet retarded absorption of the carcinogen and thus prolonged the induction period.—M. B.


The final incidence of mammary carcinoma in virgin C3H mice maintained on a diet supplying the same amounts of protein, vitamins, and salts as an ad libitum fed control group received, but restricting the caloric intake by one-third, was 0% as compared to 72% for the control animals. The histological picture of the ovaries, uteri, and mammas of the restricted animals that were living at 17 to 18 months of age was that of pseudo-hypophysectomy due to inanition. It was suggested that the mechanism by which caloric restriction per se reduces the incidence of mammary carcinoma is pituitary insufficiency producing: (a) a lowered level of ovarian secretion; (b) a relative refractoriness of the mammary gland to estrogenic substances.—Authors' abstract.


The average tumor weight was less in 20 white rats that had been injected with 2 cc thymus-Henning (equivalent to 10 gm. fresh thymus gland) daily for 18 days, starting when transplanted Flexner carcinomas were first palpable, than in 31 control rats not so treated. On the 18th day after the first injection, the difference in average tumor weight between the two groups was 40%. However, some of the treated animals showed larger tumors than did several controls.—M. H. P.


Antigonadotropic factor occurs more frequently in the serum of cancer patients than in that of noncancerous persons, but cannot be considered as specific diagnostic evidence of cancer. The incidence of antigonadotropic factor (manifested in the corpus luteum test and in the ovarian weight increase test) was 79% in 61 sera from cancer patients, 65% in 64 sera from noncancerous patients. Some of the sera of the latter group increased, rather than antagonized, the gonadotropic reaction.—M. H. P.


Melanophore hormone inactivating substance occurred in 22% of sera from carcinomatous subjects, in 12% of other sera. The 22% incidence in carcinoma serum is too small to permit application of the inactivation reaction to the diagnosis of carcinoma. The results differ from those of Rodewald, who found the melanophore hormone inactivator in almost all carcinoma sera tested, and in only occasional samples of other sera. The technic employed by von Dehn was the same as that described by Rodewald.—M. H. P.


Five groups of rats (154 animals) were treated with estrogen for various periods between birth and the 28th day of life. Rats of Group I were suckled by mothers injected with 0.1 mgm. stilbestrol daily, and those of Group II by mothers receiving 0.5 mgm. estrone daily. Rats of Group III received direct injections of 0.01 mgm. stilbestrol. Group IV animals were affected by stilbestrol injections into litter mates given 0.01 mgm. daily. Group V animals were exposed to small amounts of stilbestrol placed on nesting material. Abnormalities appeared in the smear histories in all groups. In mice more than 120 days of age, gross changes appeared in ovaries, uteri, and fallopian tubes. The most marked change was the formation of roughly spherical or multilobular cysts in one or both ovaries. Pyo-ovarium, pyometra, pyosalpinx, and uterine metaplasia were also found.—M. B.


White rats, 3 months old, from the University of Denver strain were used. In this strain the spontaneous tumor incidence is practically zero.

Small methylcholanthrene pellets, 20% suspension in paraffin, were introduced into various reproductive organs, i.e., uterus, ovaries, testes, seminal vesicles, and prostate. The total dose per animal was 10 mgm. Each animal also received injections of progesterone, stilbestrol, gonadotropin from pregnancy urine or serum, or testosterone, 3 times weekly.

The gonads themselves were highly resistant to the carcinogenic action of methylcholanthrene. Administration of stilbestrol increased the incidence of uterine tumors. Progesterone inhibited the stilbestrol effect. The action of testosterone upon tumors of the male adnexa was contradictory: although, after methylcholanthrene application, castrated rats (having neither endogenous nor exogenous testosterone) showed 100% tumor incidence, and noncastrated rats (having an endogenous testosterone supply only) showed 30% tumor incidence, the provision of additional testosterone to noncastrated rats by exogenous administration, instead of lowering the tumor incidence, raised it to 50%.—M. B.

The excretion of 17-ketosteroids was determined in the urines of 19 male and 73 female patients. In 4 cases of adrenal cortical tumor in adult females extremely high excretions were found; in 2 of these cases dehydroandrostenedione was isolated. Two cases of prepubertal virilism in girls also showed very high excretions, but isolation procedures showed the excess of androgen to be due to androstenedione. A pregnant woman with virilism excreted large quantities of 17-ketosteroid; the child resulting from this pregnancy also showed an excessive excretion, but no explanation of these observations can yet be offered. About 10 times the normal excretion of 17-ketosteroids was observed in a patient suffering from carcinoma of the splenic flexure of the colon.—Author's summary.


Some physicochemical and biological properties of the well known mammary tumor agent (Bittner's milk influence) were studied with a view to securing further information about its nature. Strain CSH mice were used as the source material, and 7 to 14 day old strain C or 1×CSH hybrid female mice were employed as test animals.

When mouse milk containing the tumor-producing agent was held at 61 or 66°C for 30 minutes the agent was inactivated. The same holds for mammary tumor extracts kept at 56 or 66°C for the same period of time.

On the other hand, the agent contained in mouse milk was stable over a period of 2 weeks when the milk was stored at 8°C. Whole tumors, after storage for 80 days in a 50% saline-glycerine solution at 8°C, failed to exhibit tumor-producing activity. The active principle was filterable through Berkefeld N candles. When a tumor extract was administered to litter mates, many tumors were induced in the animals receiving the extract intraperitoneally, although only few tumors resulted from oral administration. Mice of unknown ancestry developed mammary tumors after being nursed by CSH foster mothers. This was also true for mice not derived from inbred strains. Crude or partially purified and concentrated mouse tumor extracts produced neutralizing antibodies when injected intraperitoneally into rabbits. The antibodies thus produced neutralized the agent both in vitro and in vivo. Resemblances to certain properties of viruses are pointed out.—K. G. S.


From the present and a previous investigation on the same subject it appears that following the injection of adult domestic rabbits with the virus of the rabbit fibroma no virus is ever found in the blood, generalized spread of the virus in the viscera occurs only during the first 8 days after infection, immunity to reinfection is already noticeable after 24 hours, and the antibody response is prompt and vigorous.

Following similar injections into newborn rabbits, virus is detected in the blood for at least 13 days and in the viscera for at least 21 days after injection, immunity to reinfection is not yet well established 12 days after infection, and the antibody response is slow and poor.

When large amounts of virus are injected into newborn rabbits an acute, lethal disease with traits largely destructive and inflammatory, but also with typical proliferative features, results. This disease shows many analogies with the disease induced in the adult domestic rabbit by another but highly pathogenic virus, that of rabbit myxomatosis, the agent of which is a variant of the fibroma virus.

If small amounts of virus are injected into newborn rabbits a progressively growing tumor results, which induces satellite nodules, sometimes generalized fibromas, and often kills the host. In other cases the tumors regress after having attained a large size. The generalized fibromas are very similar to the generalized lesions obtained by other investigators in rabbits prepared by carcinogens and injected intravenously with fibroma virus.—Author's summary.


When a solution containing 100 mgm. diphenyl sulfoxide, 4 cc. 10% gum acacia in distilled water, and 1 cc. 95% ethyl alcohol was given in dosage of 0.1 cc. subcutaneously on 6 of every 7 days of the experimental period to inbred descendents of Bar Harbor “D” strain mice bearing spontaneous tumors, the duration of tumor growth, the maximum tumor volume attained, and the gain in tumor volume were generally less than in controls not given the diphenyl sulfoxide solution. However, while the tumors were growing their daily increase was the same in both treated and control animals, and the treated mice died earlier than the controls, apparently because of the toxic action of the diphenyl sulfoxide. When 0.25 cc. of the solution was given at one time, the mice became paralyzed one-half hour afterward. The 0.1 cc. injections were followed in 2 instances by fatal respiratory paralysis. The acacia-ethyl alcohol solvent without diphenyl sulfoxide, given to the controls, caused no paralysis in 0.25 or 0.1 cc. dosage.—M. H. P.


The incidence and development of benzpyrene sarcoma in 62 mice given intravenous injections of Vipera ammodytes and Naja tripudians venoms were the same as those in 78 control mice not given the venoms. In previous experiments the author was unable to influence spontaneous mammary carcinoma of mice by intravenous injections of Naja venom antiserum.—M. H. P.

Neither protoporphyrin nor hematoporphyrin exerted a therapeutic effect on ascites carcinoma of the mouse, when these compounds were given intraperitoneally or subcutaneously in single doses of 0.25 to 0.5 mgm., starting at implantation of the tumors and repeated every 2 days. The results were not improved by simultaneous ultraviolet irradiation.—M. H. P.


A review, with 74 references, of the relations of proteins, amino acids, and enzymes to cancer, with special reference to the author's studies on amino acids and to Potter's enzyme-virus theory of carcinogenesis (Cancer Research, 3:358-361. 1943). Hitherto unpublished data are also presented that show the disappearance of 56% of transplanted Emge sarcomas in rats that received l-arginine-HCl, d-histidine-HCl, l-lysine-HCl, dl-leucine-HCl, dl-isoleucine, dl-phenylalanine, dl-methionine, dl-threonine, dl-tryptophan, and dl-valine, parenterally, daily for 7 weeks starting on the day of transplantation. Results were as good with 18 mgm. of each of the amino acids alone as with 50 mgm. of a mixture containing equal parts of all of them, daily.—M. H. P.


Subcutaneous injection of 3 cc. of a solution containing 50 mgm. arginine-HCl, lysine-HCl (both neutralized), or creatine into the abdomen of rats every other day for 10 weeks after transplantation of Emge sarcoma into both sides of the abdomen caused the disappearance of 50, 44, and 30% of the tumors, respectively; only 3.7% of the tumors disappeared in the controls. The average increase in tumor weight from the 3rd to the 10th week after transplantation was 8.3, 9, 11.7, and 22 gm. respectively for the rats receiving arginine, lysine, and creatine, and for the controls. When the injections were stopped, the tumors grew rapidly.—M. H. P.


Thirty-two Bagg albino mice bearing implants of a sarcoma native in this strain were injected repeatedly over periods ranging from 3 to 5½ days with total doses of Merck's purified salt of penicillin ranging from 1,000 to 33,333 Oxford units per mouse. At the end of 7 days the injected mice and 2 uninjected control mice all had tumors of approximately the same size.

Roller tube tissue cultures of sarcoma, heart, spleen, muscle, and kidney were similarly unaffected by the highly purified, colorless penicillin in amounts ranging from 20 to 160 units per tube. However, when an impure, yellow sodium salt of penicillin (Squibb) was tested in the same way, it was found that 60 to 80 units per tube damaged sarcoma cells and left normal cells unaffected, while 100 to 120 units killed sarcoma cells and damaged normal ones. These results indicate that a differential damaging agent is present in the yellow penicillin preparation, and that it is lost in the course of producing the highly purified, colorless penicillin salt.—R. B.


By the method of unstained cell counts, the survival of cells at 45°C was determined under aerobic and under anaerobic conditions, in the presence and in the absence of dextrose. The major factor determining the length of survival was the type of cell. In most cases the survival of cells was not affected appreciably by dextrose or oxygen. Most types of cells studied were able to survive for prolonged periods in the absence of both dextrose and oxygen. In contrast, the thymic cells of the rabbit required the presence of either oxygen or a fermentable sugar for survival.

It appeared from these experiments that the survival of cells in vitro depended not on respiration nor on glycolysis but on some other cellular reaction, possibly the metabolism of nucleoproteins.

Aerobic and anaerobic glycolysis of cells was studied by determining the number of viable cells and the pH of the suspensions before and after incubation. Decrease in the pH of the suspension depended on such factors as the number and the type of cells and the duration of incubation. In peritoneal fluid and suspensions derived from the testicle as much acid developed aerobically as anaerobically. Thymic cells produced less acid under aerobic conditions. The thymic cells of the rabbit were able to ferment dextrose and mannose and possibly galactose but not fructose, xylose, sucrose, and maltose. Polymorphonuclear leukocytes of peritoneal exudate and of human blood produced acid in a dextrose-free medium, apparently by utilization of glycogen in the cells.

Leukemic cells derived from patients were able to survive as long in vitro as the normal leukocytes of blood. Myelogenous and lymphatic leukemic cells differed markedly in their capacity for aerobic and anaerobic glycolysis.—Author's summary. (J. G. K.)


The incidence of amyloid infiltration and renal disease was studied microscopically in strain A, strain C3H, and hybrid ABC mice. It was concluded that spontaneous amyloidosis is of frequent occurrence in strain A and hybrid ABC, while it is infrequent in strain C3H animals. An association was found between the development of amyloidosis and renal disease, and it is suggested that an amyloid deposit in the papilla with blockage of the collecting tubules is responsible for a kidney change that resembles microscopically a chronic or healed pyelonephritis in man.
Papers dealing with amyloid infiltration and renal disease in the mouse are reviewed, and the comparative pathology of these changes in the mouse and similar processes in man is briefly considered. Eleven photographs are included, which illustrate the characteristic appearance of these two conditions in the mouse.—T. I. D.


The object of this report is to provide more definite information than has been available in the past on the morphological characteristics of the various types of neoplasia found in chickens, and on the relative incidence of the specific types.

The classification employed follows in general the simple scheme by which tumors are arranged according to their tissue of origin. In 2,304 chickens examined the incidence for all tumors, benign and malignant, was 12.9%. Three hundred and eighty-four neoplasms in 365 chickens were studied. Lymphohyctoma, the most common, accounted for 55.5% of the 384; 6 other types (leiomyma, embryonal nephroma, myelocytoma, leukemia, epithelioblastoma, and fibrosarcoma) for 33%.

The different varieties are described, and their incidence is discussed in relation to season and to age, sex, and breed of the host, each of which appeared to be of significance in one or more types of tumor.—W. H. W.


On the basis of recent biological and biophysical data, the author seeks a hypothesis for the mode of origin of tumor cells. He systematically reviews previous theories.—M. H. P.


A review with 25 references. Among the reports discussed are those dealing with injurious action of biliary backflow into the stomach upon the gastric mucosa, production of stomach cancer by carcinogens, relation of diet to experimental stomach cancer, growth patterns and diagnosis of early cancer of the human stomach, precancerous changes in the gastric mucosa, metabolic abnormalities in patients with gastrointestinal cancer, possible role of viruses in gastric disease, and progress in organization of cancer research and prevention.—M. H. P.

Clinical and Pathological Reports

Etiology


Description of 2 cases.—M. H. P.


Seven patients with chronic arsentic poisoning showed carcinoma of the skin, and 2 of these also had mucosal carcinoma of the esophagus and bronchi, respectively. Clinical observations and experimental investigations indicate that chronic arsenic poisoning increases the general susceptibility of the organism to cancer and can promote cancer development locally, especially in the skin.—M. H. P.

Diagnosis—General


The tests considered in this review fall into 3 categories: (1) Those that measure comparative concentrations of blood constituents, or chemical and physical properties dependent upon these constituents, in cancer and non-cancer patients. Several of these tests are listed, but no appraisal of them is given. (2) Immunologic tests: Immune reactions specific for cancer and useful in diagnosis have not yet been discovered. (3) Enzymic tests: These depend upon the presence, or absence, of some specific crotolytic, proteolytic, or lipolytic activity in the blood of cancer patients. Several of these tests, including those devised by Freund and Kaminer, Bernhard, Adlerhalden, and Fuchs, have been found by some workers to give high percentages of correct diagnoses. However, their value has not been confirmed by all investigators, and none of the tests is known to provide diagnoses of early stages of cancer.

Recently several tests have been developed that indicate the presence of malignant disease in organs with well defined secretory function, or highly specialized activity. Although successful in many cases these tests are limited to certain types of cancer, and therefore a general test for cancer is still needed.—R. B.


Confirmation is offered of Koster's observation (Acta med. Scandinav., 93:420. 1937) that blood from patients with malignant neoplastic disease is slower than blood from other persons to show a decline in erythrocyte sedimentation rate during 24 hour storage. The average sedimentation rate after such storage was 64% of the presedimentation rate in 40 patients with cancer, leukemia, or Hodgkin's disease, 78% in 6 patients suspected of having
Argentaffin Tumors of the Gastrointestinal Tract.

A case is reported of argentaffin carcinoma of the ileum with metastases in the liver and spleen.—J. G. K.

Carcinoma of Appendix.

Report of 3 cases in which morphological changes served to differentiate the growths from so-called carcinoid tumors.—J. G. K.

Lesions of the Sigmoid and Rectum, and Pelvic Colon.

General discussion of preoperative and postoperative care as well as the surgical problems involved in treating polyposis, carcinoma, and diverticulitis.—M. E. H.

Clinical Features, Diagnosis, and Treatment of Carcinoma of the Colon and Rectum.

The clinical features, diagnosis, and surgical treatment of carcinoma in the various regions of the colon and rectum in 117 cases are presented.—R. E. S.

Results of Treatment of 173 Cases of Carcinoma of the Rectum.

The end results of treatment in 173 cases of carcinoma of the rectum showed a 5 year survival following surgery in 34% of 69 cases that were considered operable. The remaining 104 patients were treated by irradiation and 5% of them survived 5 years. However in this series adequate irradiation was felt to be of appreciable palliative value, and in some cases previously inoperable tumors were made amenable to surgery.—R. E. S.

Adenoma of Apocrine Sweat Glands (Hidradenoma) of the Anal Canal.

Case report, with discussion and photomicrographs.—J. G. K.

Liver and Biliary Tract

Hepatoma of the Liver with Metastasis to Bone Occurring in a Patient Known to Have Had Advanced Cirrhosis Eight Years Previously.

A case history, with photomicrographs.—E. E. S.

Malignant Hepatoma in an Infant.

A case of malignant hepatoma in a 2 month old white male infant is reported with a brief review of the subject.—J. L. M.

Primary Carcinoma of the Biliary Tract: Case Report.

Primary biliary tract carcinoma, involving the pancreas and ductus choledochus by direct extension, and hepatic cirrhosis were found at autopsy.—M. E. H.

Pituitary

Acromegaly.

Attention is called to the facial changes of early acromegaly that occur before recognizable prognathism. The importance of roentgenograms of the skull in the early diagnosis of acromegaly in patients with headache or unexplained amenorrhea is emphasized.—M. E. H.

Cancer Control and Public Health

Cancer Reporting in New York State.

Cancer reporting in upstate New York began on Jan. 1, 1940, following legislation enacted in accordance with recommendations made by the State Legislative Cancer Survey Commission. As would be expected in the reporting of any chronic disease, the largest number of reports was received during the first year. The number of reports of new cases has decreased each year by approximately 20%; this decrease is expected to continue until the number of new cases is stabilized at a level approximating the number of deaths plus the number of cured cases. In 1942, the number of new cases reported exceeded the number of deaths by 36%.
The total number of known persons with cancer alive at some time in 1942, as indicated by reporting for 1940 to 1942, was 35,378, giving an annual prevalence rate of 579 cases per 100,000 population. This is 3.6 times the mortality rate. It is the general practice for estimations of cancer prevalence to be based upon a ratio of 3 cases per death. Allowing for incompleteness of morbidity reporting, these figures for New York state indicate that this ratio is probably too low, and that prevalence may be 4 or 5 times as great as mortality. The factors of duplication of reports and the maintenance of a statewide cancer roster are discussed.
Cancer reporting has proved useful: first, in providing material for epidemiologic investigation and for evaluation of progress in cancer control; second, in public education; third, in professional education; fourth, in aiding the follow-up of cancer patients; and fifth, in the administration of public health nursing service to cancer patients.—J. L. M.

Corrections

Cancer Research, 5:249. April, 1945. Line 29 from top of column 2: For "Xiphurus" read "Xiphophorus."
Experimental Research, Animal Tumors

Cancer Res 1945;5:120-127.

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