

Abstracts

Reports of Experimental Research

CARCINOGENIC COMPOUNDS

BRIGGS, J. B., and BRIGGS, R. W. [McGill Univ., Montreal, Canada] **THE EFFECTS OF A WATER-SOLUBLE CARCINOGEN ON EARLY FROG DEVELOPMENT.** *Cancer Research*, 3:1-12. 1942.

Eggs of the frog, *Rana pipiens*, were reared in solutions of a water-soluble carcinogen in order to determine whether there would be any effect on the rate of development, or on the morphological organization of the embryo. The carcinogen used was Na-1,2,5,6-dibenzanthracene-9,10-endo- α,β -succinate (*trans*). Exposure began 1 hour after fertilization, and the concentrations used were 0.02, 0.213, 2.13, 4.26, and 10.0 mgm. per 100 cc.

The results were: (1) No evidence of stimulative effect in any concentration. (2) Retardation of developmental rate (after beginning of gastrulation) in solutions containing 2.13, 4.26, and 10.0 mgm. per 100 cc., the degree of retardation being proportional to the concentration. (3) Degeneration of embryos in these same three concentrations—degeneration following a definite uniform pattern, and beginning always at the same developmental stage for a given concentration. (4) Differential retardation of development of capacity for muscular movement relative to morphological development. (5) Lack of any effect on the morphological organization of the embryo.

Various control experiments, with a surface tension-reducing agent (aerosol O.T.), Na-succinate, a related noncarcinogen (anthracene-succinate), metabolic poisons, and miscellaneous substances, indicated that the effects noted above were specific for dibenzanthracene-succinate, and suggested further that the carcinogenicity of this chemical might be responsible for the effects. Treatment of eggs with another water-soluble carcinogen, Na-3-methylcholanthrene-6,12b-endo- α,β -succinate, gave confirmatory evidence on this latter point.—Authors' abstract.

COLLINS, V. J., GARDNER, W. U., and STRONG, L. C. [Yale Univ. Sch. of Med., New Haven, Conn.] **EXPERIMENTAL GASTRIC TUMORS IN MICE.** *Cancer Research*, 3:29-35. 1943.

Benzpyrene dissolved in sesame oil was administered orally or by intravaginal instillation to 133 mice of 5 inbred strains, namely C₃H, NH, C₅₇, A, and CHI, to determine its effect upon the formation of tumors of the gastrointestinal tract. All the resulting gastric tumors arose in the forestomach and were of the squamous cell type. The highest incidence of gastric papillomas and carcinomas occurred in mice of the C₃H strain. A high incidence of gastric tumors was observed in mice of the C₅₇ and NH strains and a low incidence of carcinomas in mice of the CHI and A strains. No definite sex difference in the

incidence of gastric tumors was noted in the C₃H strain. However, the incidence of carcinomas was higher in ovariectomized mice of the C₃H and NH strains than in intact mice treated similarly with the carcinogen. Most gastric tumors appeared at the greater curvature of the forestomach, the fundus of which was more frequently involved than the area near the limiting ridge. Tumors occasionally developed on the lesser curvature and on the anterior or posterior wall. Carcinomas and papillomas appeared in 22 and 69 of the treated mice respectively. They were of the squamous cell type showing a mixture of keratinized flat cells, prickle cells, and basal cells. The 22 carcinomas infiltrated the gastric wall, extended to the serosa, and invaded the lymphatics. Papillomas and carcinomas of the skin occurred at the sites contaminated by the benzpyrene in nearly all animals. Whenever a carcinoma of the skin was found the gastric tumor was usually small and benign; on the other hand, mice with carcinoma of the stomach usually had benign skin lesions. A gastric carcinoma from a C₅₇ mouse was successfully transplanted to 3 normal mice of the same strain.—Authors' abstract.

CRAMER, W., and STOWELL, R. E. [Barnard Free Skin and Cancer Hosp. and Washington Univ. Sch. of Med., St. Louis, Mo.] **SKIN CARCINOGENESIS BY A SINGLE APPLICATION OF 20-METHYLCHOLANTHRENE.** *Cancer Research*, 3:36-42. 1943.

Cancer can be induced in the skin of mice in response to a single cutaneous application of a potent carcinogen such as 20-methylcholanthrene. In the experiment recorded in this paper 6 of 14 female Swiss mice developed malignant tumors after intervals of 13 to 42 weeks. Five of these malignant neoplasms were squamous carcinomas developing at the site of application. The significance of this phenomenon lies in the fact that methylcholanthrene applied cutaneously disappears from the skin after 1 to 2 weeks. The bearing of these observations on the interpretation of the mode of action of chemical carcinogens is discussed.—Authors' abstract.

LAURIDSEN, J., and EGGERS, H. E. [Univ. of Nebraska Med. Coll., Omaha, Nebr.] **CARCINOGENESIS AFTER MULTIPLE IRRITATION.** *Cancer Research*, 3:43-46. 1943.

An attempt was made to determine whether carcinogenesis is facilitated by the additive effect of diverse irritations. Approximately 100 mice were taken from each of two inbred strains, one with a low tumor incidence and the other with a high incidence of spontaneous mammary tumors. Half the animals in each group were subjected to cutaneous applications of 1,2,5,6-dibenzanthracene and to repeated light cauterization, the other half to dibenzan-

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thracene only. Cutaneous and subcutaneous tumors developed more rapidly in the cauterized animals. This effect was shown more decidedly by the animals from the low tumor strain. In the mice from the high tumor strain, the higher incidence of induced tumors among the cauterized mice was largely due to the greater number of sarcomas that developed rather than to induced skin tumors. It is suggested that in these animals the higher incidence of sarcomas may be an expression of a constitutional predisposition that is masked in the skin by some accessory factor.—Authors' abstract.

HORMONES

HEIMAN, J. [Coll. of Physicians and Surgeons, Columbia Univ., New York, N. Y.] **COMPARATIVE EFFECTS OF ESTROGEN, TESTOSTERONE, AND PROGESTERONE ON BENIGN MAMMARY TUMORS OF THE RAT.** *Cancer Research*, 3:65-69. 1943.

Abstracted in the Report of the Endocrine-Cancer Conference, *Cancer Research*, 2:726. 1942.

GENETICS

BURDETTE, W. J., and STRONG, L. C. [Yale Univ. Sch. of Med., New Haven, Conn.] **THE INHERITANCE OF SUSCEPTIBILITY TO TUMORS INDUCED IN MICE. I. TUMORS INDUCED BY METHYLCHOLANTHRENE IN FIVE INBRED STRAINS OF MICE.** *Cancer Research*, 3:13-20. 1943.

The susceptibility to neoplasms induced with a single subcutaneous injection of methylcholanthrene was determined for 5 inbred strains of mice. Differences in the time of appearance of tumors were found. The predominant type of growth was rhabdomyosarcoma in some strains and spindle cell sarcoma in others. The survival time of mice of the several strains was not always the same and did not necessarily parallel their susceptibility to induced tumors.—Authors' abstract.

STRONG, L. C., COLLINS, V. J., and DURAND, E. A. [Yale Univ. Sch. of Med., New Haven, Conn.] **A GENETIC ANALYSIS OF THE INDUCTION OF TUMORS BY METHYLCHOLANTHRENE. IV. THE PROBABLE REMOTE INDUCTION OF VARIOUS TYPES OF GASTRIC LESIONS.** *Cancer Research*, 3:21-28. 1943.

A variety of gastric lesions, including glandular hyperplasia, adenoma, adenocarcinoma or potential adenocarcinoma, squamous cell papilloma, and squamous cell carcinoma have been obtained in mice of the NHO strain after subcutaneous injection, at 60 days of age, of 1 mgm. of methylcholanthrene dissolved in 0.1 cc. of sesame oil.

It appears, although it is not definitely proved, that the presence of the carcinogen may have had some influence on the appearance of these lesions.

The gastric lesions occurred in mice that had also developed adenocarcinoma of the lung or spindle cell sarcoma, or quite independently of any other form of lesion.—Authors' summary.

BIOCHEMISTRY AND NUTRITION

CHALKLEY, H. W. [Nat. Cancer Inst., Bethesda, Md.] **EFFECT OF CERTAIN SULFUR-CONTAINING COMPOUNDS ON THE INITIATION OF MITOSIS IN AMOEBA PROTEUS.** *J. Nat. Cancer Inst.*, 2:425-447. 1942.

A method was devised to permit detection and measurement of rapid changes in the rate of entry into mitosis in

Amoeba proteus. Sulfur-containing organic compounds were added in high dilution (2×10^{-4} to 5×10^{-3} mols per liter) to cultures of selected amoebae, and their effect on the number of cells entering prophase as a function of time was studied. Methionine and cysteine gave negative results. Cystine, cysteine, glutathione, cystinyldiglycine, and β, β' -dithiodipropionic acid, cystinyldiglycine, and a mixture of glutamic acid and glycine all affected the entrance of the amoeba into mitosis.

The effects obtained were: (1) a sudden increase or decrease in rate, and (2) a change from one level of constant acceleration to another. The effect of each compound studied was generally a mixture of these two results. The most effective reagents used were those containing sulfur in labile form as $-SH-$ and $-SS-$. These reagents in general exerted a stimulative action but cysteine, β, β' -dithiodipropionic acid, and cystinyldiglycine exerted partial or total depressive actions. It is concluded that the presence of labile sulfur alone does not insure a stimulative action. Seventeen figures showing forms of amoeba and control and experimental curves are included.—F. L. H.

GREENSTEIN, J. P. [Nat. Cancer Inst., Bethesda, Md.] **TITRATION OF THE LIVER CATALASE ACTIVITY OF NORMAL AND OF TUMOR-BEARING RATS AND MICE.** *J. Nat. Cancer Inst.*, 2:525-530. 1942.

Heretofore data on the liver catalase activity of normal and of tumor-bearing rats and mice have been obtained by the volumetric method. This method cannot conveniently be used to measure activities over a wide range of varying enzyme and substrate concentrations. The titration method, which is free from this disadvantage, follows the rate of disappearance of the hydrogen peroxide by the use of either permanganate or hydriodic acid. Descriptions of the two methods are given.

Three tables give results obtained by the titration method, of determinations of the liver catalase activity of normal rats and of rats bearing the transplanted hepatic tumor 31 and the transplanted Jensen sarcoma, as well as of normal mice and of mice bearing the transplanted sarcoma 37. These activities are expressed as ratios (under identical conditions) of k , the monomolecular reaction constant for each tissue. The ratios are equivalent to ratios of *Kat. f*. The liver catalase activity ratio of tumor-bearing to normal rats was 1:3-4 and of tumor-bearing to normal mice was 1:5. These values, while lower than those obtained by the volumetric method, are consistent with them in the finding of a much lower liver catalase activity in tumor-bearing as compared with normal animals.—F. L. H.

WHITE, F. P., and WHITE, J. [Nat. Cancer Inst., Bethesda, Md.] **EFFECT OF A LOW CYSTINE DIET ON THE GROWTH OF VARIOUS STRAINS OF MICE.** *J. Nat. Cancer Inst.*, 2:449-450. 1942.

A diet was devised in which the cystine level could be readily controlled. This diet could be used over prolonged periods of time with various types of mice. The percentage composition of the low cystine diet and of a cystine-supplemented diet is given, the difference between the two being the replacement of 0.5% starch by 0.5% *l*-cystine in the high cystine diet. The two diets were tested on mice of both sexes of the C₃H, ABC, Bagg albino,

C, A, dba (subline 212), I, and AK strains; all showed essentially the same type of response.

Mice fed on the low cystine diet for 12 months or longer showed no structural changes in organs or tissues but had a tendency toward rough coats and slow breeding. No permanent stunting occurred, as normal growth was resumed immediately and rapidly on addition of cystine to the diet. Mice were usually placed on the diets at 4 weeks of age. If started at 8 weeks they showed a tendency toward a slight loss of weight during the first week, but after that maintained their weight or gained slightly.—F. L. H.

WOODARD, H. Q., and KENNEY, J. M. [Memorial Hosp., New York, N. Y.] **THE RELATION OF PHOSPHATASE ACTIVITY IN BONE TUMORS TO THE DEPOSITION OF RADIOACTIVE PHOSPHORUS.** *Am. J. Roentgenol.*, **47**: 227-239. 1942.

Nine patients with osteogenic sarcoma, 4 with non-osteogenic malignant tumors, and 2 without tumors were studied in an attempt to correlate the phosphatase activity of tissue with actual phosphorus metabolism. Through the use of radioactive phosphorus as a tracer, it was found that phosphorus deposition in normal and hyperplastic bone was a function of the alkaline phosphatase activity of the tissue but this rule did not hold in all cases of osteogenic sarcoma. The osteogenic sarcomas which failed to store phosphorus in proportion to their high phosphatase content were generally the highly malignant tumors. Failure of the tumors to store phosphorus would constitute a limitation of the effectiveness of radioactive phosphorus in the treatment of osteogenic sarcoma.—C. E. D.

TRANSPLANTATION

CLOUDMAN, A. M. [Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine] **REACTIONS OF HYBRID AND PARABIONTIC PSEUDO-HYBRID MICE TO INOCULATIONS OF TUMOR C198.** *Cancer Research*, **3**:47-52. 1943.

More than 1,000 pure stock leaden mice were used as hosts in 55 successive transplant generations and all were positive to inoculation with the hepatic neoplasm C198 which arose spontaneously in this strain. Other stocks were negative after the usual methods of transplantation. No growths were obtained in 118 mice of the inbred strain C57 black. F₁ hybrids between the leaden and black C57 strains were completely susceptible to inoculation with grafts from the later transplant generations of C198.

A study was made of tumor inoculations following parabiosis. In 23 pairs of parabionts within the leaden strain, one mouse only was inoculated. In every case both members of the pair developed tumors in the liver. Black mice from the nonsusceptible C57 stock were united to susceptible leaden mice and, after healing was complete, inoculated with tumor C198. In 30 of 34 pairs the black mouse developed either subcutaneous or internal tumors. The tumor also passed from the black mouse into the leaden member of the pair.

The term "pseudo-hybrids" was employed to describe pure stock mice that showed a change from nonsusceptibility to susceptibility to C198 following parabiosis with susceptible mice. The altered pure stock mice react somewhat like hybrids between the stocks.—Authors' abstract.

RUSS, S., and SCOTT, G. M. [Barnato Joel Labs., Middlesex Hosp., London, England] **EXPERIMENTS SHOWING THE INFLUENCE OF ONE GROWING TUMOUR UPON ANOTHER.** *Brit. J. Exper. Path.*, **23**:127-133. 1942.

The growth of the Jensen rat sarcoma in one flank of an animal was accelerated by inoculation of another graft in the opposite flank, when the second graft was derived from a tumor growing much more rapidly than the original graft. The reverse effect was obtained by inoculating a graft growing much more slowly than the tumor already growing from the first implantation. In consistent experiments with adequate numbers, the tumors in the rats given the stimulating graft in the opposite flank eventually became twice the average volume of the controls; the tumors of the rats treated with the slowly growing grafts on the opposite flank were only one-third of the volume of the controls. Similar stimulation of Jensen sarcoma tissue, which had been given a sublethal dose of x-rays, was shown after the inoculation of a graft of rapidly growing normal tumor. Conversely, the inoculation of a graft of Jensen sarcoma, which had been given a sublethal dose of x-rays *in vitro* and was growing slowly, had an inhibiting effect on a normal tumor already growing in the rat, the average volume being only one-half that of the controls.—A. H.

MISCELLANEOUS

SELBIE, F. R. [Bland-Sutton Inst. of Path., Middlesex Hosp., London, England] **CARCINOMATOUS TRANSFORMATION IN A TRANSPLANTABLE RAT FIBROADENOMA.** *Brit. J. Exper. Path.*, **23**:61-68. 1942.

In a transplantable rat fibroadenoma (obtained from a spontaneous tumor in 1934) a substrain has arisen in which 5 tumors in 3 successive passages have become manifestly carcinomatous at long intervals after inoculation. It is suggested that these changes can be ascribed to an increased proliferative capacity of the glandular tissue acquired by the parent tumor of the substrain. By its increased powers of proliferation the epithelium can overcome the restraint of the fibrous component of the tumor and can thus make manifest its intrinsic malignancy. Changes had previously been described in the fibrous component of this tumor (*Brit. J. Exper. Path.*, **22**:156. 1941; abstract in *Cancer Research*, **1**:909. 1941) leading to the appearance of new sarcomatous tumors.—A. H.

COMPARATIVE ONCOLOGY

GREENE, H. S. N., and BROWN, W. H. [Rockefeller Inst. for Med. Research, Princeton, N. J., and Yale Univ. Sch. of Med., New Haven, Conn.] **A TRANSPLANTABLE SQUAMOUS CELL CARCINOMA IN THE RABBIT.** *Cancer Research*, **3**:53-64. 1943.

The course of a squamous cell carcinoma in the skin of a rabbit was followed from inception of the growth to the death of the animal, and clinical observations were supplemented by frequent biopsies and attempts to transfer the tumor. Histologically the primary tumor conformed in part to a type known in man as spindle cell epidermoid carcinoma, but the metastases were all squamous cell in character. The tumor was successfully transplanted and the histological character of the subsequent growths varied according to locality.—Authors' abstract.