Abstracts

Reports of Research

Induction of Sarcoma of the Liver in the Rat with Methylcholanthrene and Benzpyrene. EISEN, M. J. [Coll. of Physicians & Surgeons, Columbia Univ., New York, N. Y.] *Cancer Research,* **6**:421-425. 1946.

Sarcoma of the liver in the rat was produced in 7 of 27 animals that survived 248 days, the time required for the induction of the earliest tumor, after intrahepatic implantation of paraffin pellets containing 1 mgm. of methylcholanthrene or benzpyrene, or of cotton threads impregnated with 0.8 mgm. methylcholanthrene. Subcutaneous tumors were produced with pellets containing the carcinogens in 10 of 14 animals with a minimal latent period of only 119 days. This would suggest that the liver is less sensitive to the chemicals, but not completely refractory as has been reported by several investigators.—Author's abstract.

The Production of a Carcinogenic Agent in the Degradation of Cholesterol to Progesterone. BISCHOFF, F., and RUPP, J. J. [Santa Barbara Cottage Hosp. Research Institute, Santa Barbara, Calif.] *Cancer Research,* **6**:403-409. 1946.

Progesterone, in the amount and under the conditions that inhibited mammary cancer formation in strain RIII mice, failed to do so in Marsh-Buffalo mice. Ovariectomized Marsh-Buffalo mice that received 10 mgm. of progesterone per mouse subcutaneously over a 6 months period failed to develop mammary tumors; 3 mgm. of progesterone administered subcutaneously, alone or in combination with 500 units of estrone, failed to effect the development of the mammary glands of Marsh-Buffalo female mice. Mice receiving sesame oil containing crude progesterone contaminated with cholestenone, or containing the equivalent of cystalline cholestenone, developed oleomas at the site of injection. Crystalline cholesterol or progesterone under the same conditions was without influence. A crude synthetic progesterone, made by the method of Spielman and Meyer, resulted in a 32% incidence of malignant tumors at the site of injection compared with a 0% incidence in controls and a 1 to 2% incidence in the colony.—Author's abstract.

A Measure of the Stimulating Effect of Simple Injury Combined with Carcinogenic Chemicals on Tumour Formation in Mice. PULLINGER, B. D. [Labs. of Imp. Cancer Research Fund, London, England] *J. Path. & Bact.,* **57**:477-481. 1945.

Multiple simple excisions from mouse skin treated with large or small doses of benzpyrene stimulated the formation of tumors to approximately 2 to 3 times the number obtained in susceptible mice from which only one excision was made.—A. H.

Studies on the Effects of Radioactive Sodium and of Roentgen Rays on Normal and Leukemic Mice. EVANS, T. C., and QUIMBY, E. H. [Columbia Univ., New York, N. Y.] *Am. J. Roentgenol.,* **55**:55-66. 1946.

The effects of radioactive sodium and of whole body roentgen irradiation on white mice have been compared. Results of reduction in the number of white and red blood cells and in shortening the life span are similar for the two types of radiation. Mice with enlarged nodes and extremely high leukocyte counts were found especially sensitive to the radio-sodium. They were not tested with roentgen rays. The marked response was apparently due to radiosensitivity of the abnormal leukocytes rather than to any selective concentration of the material in lymph nodes.—E. H. Q.

The Histologic Effects of Radiophosphorus on Normal and Lymphomatous Mice. GRAFF, W. S., SCOTT, K. G., and LAWRENCE, J. H. [Univ. of Calif., Berkeley, Calif.] *Am. J. Roentgenol.,* **55**:44-54. 1946.

Hematological and histological studies on normal and lymphomatous mice which have been given radiophosphorus revealed characteristic effects on the hematopoietic tissues. Although a few animals recovered from generalized lymphomatosis after treatment with P^{32}, no evidence of any increased radiosensitivity of the neoplastic cells was observed. The limiting factors in the use of roentgen irradiation and P^{32} in the therapy of leukemia and allied diseases are discussed. —E. H. Q.

Restropin Factor in Cancer in Relation to the Reticulo-Endothelial System. CONNELL, H. C., MUNRO, L. A., and MEDLEY, A. [Hendry-Connell Research Foundation, Kingston, Ont.] *Canadian M. A. J.,* **54**:161-164. 1946.

It has been concluded by many that the body function responsible for resistance is resident in the reticulo-endothelial system (R. E. S.). The activity of the R. E. S. is indicated by the elimination of a dye-like congo red when injected into the blood stream (congo red index, C. R. I.). A number of workers have found an impairment of the R. E. S. in cancer as shown by histological examinations paralleled by C. R. I. determinations. There has been reported the recovery of two separate factors in alkaline extracts of the anterior lobe of the pituitary called positive and negative restropin. A positive restropin factor was found in the blood of normal, cancer-free animals whereas a negative factor was obtained from the blood of animals with Walker sarcoma. These findings were also obtained in human beings.

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In the present report blood from 103 cancer patients were studied; 48% gave a negative factor, 34% a positive factor while 18% were neutral. The authors conclude that the whole idea of positive and negative restropin may be in error and now are studying the restropin problem from the standpoint of the effect of x-ray and non-specific substances on stimulation and depression of the R. E. S.—M. E. H.

A Microscopical Study of the Evolution of Mouse Mammary Cancer: The Effect of the Milk Factor and a Comparison with the Human Disease. BONSER, G. M. [Univ. of Leeds, Leeds, England] *J. Path. & Bact.*, **57**: 413-422. 1945.

In a study of the evolution of mammary cancer in the mouse, intra-acinous carcinoma is the first and most frequent form of cancer to be observed and is accompanied in a small number of cases by intraduct carcinoma. Studies of the effect of the milk agent have shown that it acts mainly upon the acini, leading to a high degree of acinous proliferation which progresses ultimately to intra-acinous and extra-acinous carcinoma. There is much variation in the degree of acinous hyperplasia preceding the initiation of the malignant process, but in general the greater this proliferation the more frequently cancer occurs. Extra-acinous or infiltrating carcinoma can be shown in nearly all cases to be preceded by intra-acinous carcinoma. In mice that have received estrogen but not the milk agent, a limit is set upon the growth process at the stage of hyperplasia. Thus the estrogen would appear to act as a developing factor upon breast tissue already sensitized by the milk agent.

There is a difference in the site of origin of mammary cancer in the mouse and in man. Intraduct cancer is far more common than primary intra-acinous cancer in the latter species. This observation raises the question as to whether a milk influence exists in the human subject and, if so, whether it has different tissue specificities. Nevertheless there are many points of similarity in the evolution of breast cancer in the two groups, as for example in both the orgin is frequently multicentric and the development gradual.—A. H.

An Experimental Approach to the Problem of Trauma and Tumours. PULLINGER, B. D. [Labs. of Imp. Cancer Research Fund, London, England] *J. Path. & Bact.*, **57**: 467-476. 1945.

Simple trauma in the form of a single excision of skin, combined with the previous application of a carcinogen, increased the chances of an animal developing a tumor by less than 1% when the carcinogenic stimulus was slight. However when a highly active carcinogen was used by itself the chances of tumor formation was increased 13%. —A. H.

Thymonucleic Acids in Human Tumors. STOWELL, R. E. [Washington Univ. Sch. of Med., and Barnard Free Skin and Cancer Hosp., St. Louis, Mo.] *Cancer Research*, **6**:426-435. 1946.

Twenty human tumors, including a leiomyosarcoma, a primary carcinoma of the liver, 5 epidermoid carcinomas, 2 transitional cell carcinomas, a basal cell carcinoma and 8 adenocarcinomas, were analyzed for their content of desoxyribose and ribose nucleic acids. The nucleic acids were measured in sections of tissue with a special photometric instrument consisting of a stable light source, filters, microscope, photocell, and amplification and recording apparatus. The relative amounts of desoxyribose nucleic acid in adjacent normal and neoplastic tissues were measuered by determining the absorption of monochromatic complementary light by Feulgen-stained material. Similarly, but less satisfactorily, the ribose nucleic acid was estimated by measuring the decreased staining with pyronine after treatment with ribonuclease enzyme. This photometric, histochemical method has the advantage that the exact cells being measured are visualized and identified as one type. The results were expressed as mean amounts per unit volume of tissue and per cell and can be compared with mean volumetric measurements of the cell, cytoplasm, nucleus, chromatin, nucleolus, and nuclear sap.

In 18 of the 20 tumors the amount of thymonucleic acid per unit volume and per cell was greater than in the adjacent homologous normal tissue. Statistical analysis showed that this increase per volume was significant in 11 instances and per cell in 9 tissues. Two-thirds of the tumors had more ribose nucleic acid per unit volume and per cell than the corresponding normal tissue. In half of the tumors this increase was more than 50%. A majority of the tumors had cells of smaller mean size with less cytoplasm. In most instances, the tumor cells had larger mean percentages of nuclear and chromatin material. Correlation coefficients show that the amounts of thymonucleic acid are larger in tissues having small cells and small masses of cytoplasm as well as cells with large percentages of nuclear and chromatin substance. In a total of 34 tissues analyzed to date by this method, no tumor has contained a statistically significant decrease in thymonucleic acid per unit volume. These results add further support to the theory that tumors have disturbances in their nucleoprotein and enzyme systems.—Author's abstract.

Mechanism of the Proteolytic Activity of Malignant Tissue Cells. FISCHER, A. [Biological Inst. Carlsberg Foundation, Copenhagen] *Nature, London*, **157**:442. 1946.

Rous sarcoma cells were grown in rabbit plasma and chick embryo extract throughout many passages without liquefaction of the medium occurring, but on transfer to homologous plasma, liquefaction occurred. The addition of fresh fowl serum to the rabbit-plasma medium induced liquefaction to the same extent as growth in chicken-plasma medium. When the fowl serum was first heated to 56° for 3 to 4 hours, however, liquefaction no longer took place, which suggests that proteolytic enzymes in the culture medium must play a fundamental part in digestion of the plasma clots by sarcoma cells. Confirmatory evidence was afforded by preparing cultures in rabbit plasma with the addition of rabbit serum which had previously been shaken with sand for half an hour. Following this, liquefaction of the plasma then took place as readily as if homologous plasma were used. Presumably, inactive proteolytic proenzymes present in the rabbit serum were activated by the shaking. It is suggested that both normal and malignant tissue cells are able on contact to activate proteolytic proenzymes in homologous blood plasma.—R. J. L.

Induced Antibodies That React *in vitro* with Sedimentable Constituents of Normal and Neoplastic Tissue Cells. Presence of the Antibodies in the Blood of Rabbits Carrying Various Transplanted Cancers. FRIEDEWALD, W. F., and KIDD, J. G. [The Rockefeller Inst. for Med. Research, New York, N. Y.] *J. Exper. Med.*, **82**:21-39. 1945.

Rabbit sera, of animals carrying either the Brown-Pearce carcinoma, the V2 carcinoma, the rabbit sarcoma I, or the Kato sarcoma, have been found to contain an antibody which will *in vitro* fix complement with extracts of various normal and neoplastic rabbit tissues. The portion of the extracts which react with the antibody are readily sedimentable in the high-speed centrifuge. The antibodies found in these rabbits differ from natural antibodies in that they are not found in normal rabbits and are stable for 30 minutes at 65° C.—D. S.

Incidence and Specificity of the Antibody for a Distinctive Constituent of the Brown-Pearce Tumor. MACKENZIE, I., and KIDD, J. G. [Rockefeller Inst. for Med. Research, New York, N. Y.] *J. Exper. Med.*, **82**:41-63. 1945.

Rabbits implanted with a Brown-Pearce carcinoma or injected with extracts of the carcinoma, developed an antibody which reacted specifically *in vitro* with a particular sedimentable fraction of an extract of the tumor. This constituent of the Brown-Pearce carcinoma differed immunologically from other sedimentable fractions which can be extracted from rabbit tissues. The results and implications of the study are discussed.—D. S.

The Heterologous Transplantation of Mouse Tumors Induced *in Vitro*. GREENE, H. S. N. [Yale Univ. Sch. of Med., New Haven, Conn.] *Cancer Research*, **6**:396-402. 1946.

The tumors induced *in vitro* by Dr. Wilton R. Earle of the National Cancer Institute have been successfully transplanted to guinea pigs and to mice of foreign strains. The ability to survive and to grow in animals of alien species identifies the tumors with the chemically induced and naturally occurring sarcomas, and adds further significance to their mode of origin.

The success of the transfer of the tumors to unrelated mice varied with the strain or species of the donor, and an examination of this relationship suggested that the stromal component of the tumor was concerned in the variation.—Author's abstract.

Multiple Malignant Growths. LOMBARD, H. L., LEVIN, M. L., and WARREN, S. *Cancer Research*, **6**:436-441. 1946.

Peller has suggested that a cured cancer protects against the development of other malignant neoplasms and has advocated the experimental induction of a skin cancer to prevent subsequent occurrence of the more fatal cancers of other organs, while Warren and his associates have presented data which indicate that the incidence of multiple primary cancers is sufficiently high to presuppose increased individual susceptibility. This paper, based on 5,078 records from the Massachusetts cancer clinics, suggests that individuals with skin cancers are predisposed to other skin cancers. There is also an indication that males with lip cancers have some predisposition to multiple skin cancers. There is no evidence that immunity to the formation of a second primary cancer is produced by the presence of cancer in any location.—Authors' abstract.

Physiological Studies on Tumor-Inhibiting Agents. II. Effect on Rectal Temperatures in Normal Rabbits of the *Serratia marcescens* Tumor-Necrotizing Polysaccharide of Shear. BECK, L. V., and FISHER, M. [Hahnemann Med. Coll., Philadelphia, Pa.] *Cancer Research*, **6**:410-420. 1946.

The *Serratia marcescens* tumor-necrotizing polysaccharide which Shear and his co-workers have brought to a high state of purity is extremely potent as a pyrogen when injected intravenously into rabbits. Measurable increases in rectal temperature occurred after injection of only 0.005 micrograms per kgm., and elevations of 2 to 3° C. were produced by 0.5 μgm. per kgm. and larger amounts. The fever reaction was intensified and prolonged on very warm days.

Death occurred within 24 hours in some of the rabbits given 20 to 100 μgm. per kgm. Rabbits that died usually exhibited a rather weak fever reaction, and greatly diminished muscular strength.

Elevation of the rectal temperature did not occur as long as the rabbit was tied down on a copper table, or cooled with ice water and cold air. It was possible to minimize the polysaccharide induced fever reaction using the following drugs in amounts that were not acutely toxic to the rabbit: antipyrene, isopropyl antipyrene, acetylsalicylic acid and di-allyl barbituric acid.—Author's abstract.

Clinical and Pathological Reports

Clinical investigations are sometimes included under Reports of Research

MULTIPLE TUMORS

Multiple Primary Tumors. HAYWARD, W. G. [Jamestown, N. Y.] *J. Urol.*, **54**:307-311. 1945.

This is principally a case report of an 82 year old male who in two years had these histologically proved neoplasms: (1) basal cell carcinoma of the perineum; (2) epidermoid carcinoma of the groin; (3) adenocarcinoma of the prostate; and (4) embryonal carcinoma of the testis.—V. F. M.

DIAGNOSIS

Delimitation of Subcortical Tumours by Direct Electrography. WALTER, W. G., and DOVEY, V. J. [Burden Neurol. Inst., Bristol, England] *Lancet*, **250**:5-9. 1946.

It has been shown by means of indirect electroencephalography that a space-occupying lesion has two effects on the electrical activity of the brain. (1) An indirect action due to edema, and vascular change, resulting in the production of delta waves. (2) Disappearance of all electrical activity when there is replacement of nervous