

# Abstracts

## Reports of Research

**Induction of Mammary Cancer with Methylcholanthrene. I. Histogenesis of the Induced Neoplasm.** KIRSCHBAUM, A., WILLIAMS, W. L., and BITTNER, J. J. [Univ. of Minnesota Med. Sch., Minneapolis, Minn.] *Cancer Research*, 6:354-362. 1946.

When the skins of forced-bred female mice of certain genetic types were painted with methylcholanthrene dissolved in benzene, they developed grossly visible, multiple nodules in the mammary gland. Forced breeding alone did not induce this type of nodule formation. These nodules are considered to be carcinogen-induced, and they developed in either the presence or the absence of the milk agent. Although in whole mount preparations, as viewed under low magnification, the nodules resembled the "hyperplastic nodules" which precede "milk agent tumors," sections of the carcinogen-induced nodules revealed a decidedly different histology. The nodules developed as a result of injury to the epithelium of the ducts and proximal alveoli by the carcinogen, followed by a proliferative epithelial response. These alterations were succeeded by neoplasia. The frank cancers, which developed from carcinogen-induced nodules, were of mixed squamous and alveolar structure. Susceptibility to the carcinogenic induction of mammary cancer is not common to all strains, and this susceptibility cannot be correlated with susceptibility to spontaneous mammary cancer. The histological evidence does not favor the concept that the carcinogen accelerates the sequence of alterations seen in the histogenesis of spontaneous "milk agent tumors" of mice.—Authors' abstract.

**Carcinogens and the Regeneration Patterns after Injury.** HOWES, E. L. [Coll. of Physicians & Surgeons, Columbia Univ., New York, N. Y.] *Cancer Research*, 6:298-310. 1946.

Carcinogens destroy reticulin and collagen. This destruction could be seen both when the carcinogen was painted on the skin of rats and mice and also when a thread containing the carcinogen was buried in the muscle. Leukocytes and giant cells were also destroyed but epithelial cells and fibroblasts survived the injury and proliferated in response to it, especially after the damaged reticulin and collagen were absorbed. Following this the epithelial cells and fibroblasts grew distortedly in sheets and developed into malignant tumors. The absorption of collagen and reticulin and their failure to regenerate could explain the long latent period between the initial application of the carcinogen and the development of the tumor. No evidence could be found to justify the theory that the

carcinogen stimulated cells directly into the formation of a tumor or that the rate of proliferation exceeded any other form of injury. The leukocytes of the guinea pigs studied, phagocytized the carcinogen, a fact which offers a possible explanation of the resistance of the species. A plea is made for more careful observation of changes in reticulin and collagen in the study of neoplasms.—Author's abstract.

**The Carcinogenicity of Wood Soot from the Chimney of a Smoked Sausage Factory.** SULMAN, E., and SULMAN, F. [Hebrew Univ., Jerusalem, Palestine] *Cancer Research*, 6:366-367. 1946.

Thirty-six female rats implanted subcutaneously with fragments of soot from the chimney of a sausage factory developed sarcoma in 16.6% of the cases. No tumor developed in 36 male rats implanted intrascrotally with bits of the same soot. Ten female mice treated for 2 years with an ether and alcohol extract of wood soot showed tumor formation in 3 cases (2 sarcomas and 1 carcinoma). Twenty rats fed for 2 years on a diet containing an unlimited amount of smoked sausage failed to develop tumors.

The conflicting finding, carcinogenic effect in parenteral treatment versus absence of carcinogenic effect after oral administration, indicates the need for further study of the carcinogenic activity of smoked food, in view of the practical importance of the problem for human nutrition.—Authors' summary.

**Tissue Changes in Experimental Mice Treated with Pentose Nucleotides.** BARKER, G. R., GULLAND, J. M., and PARSONS, L. D. [Bernhard Baron Inst. of Path., The London Hosp., and Univ. Coll. Nottingham, London.] *Nature*, London, 157:482-483. 1946.

Adenylic (I), guanylic (II), cytidylic (III), and uridylic (IV) acids were injected into mice (C57, CBA) grafted with homologous methylcholanthrene sarcomas. I and II had an inhibitory action on the growth of these tumors while III had little or no effect. On the other hand IV had a stimulating action. Details are given concerning the effects of these compounds upon the size of the spleen and on the number of giant cells in it. Stock or pure line mice treated with I or III showed a leukocytosis; the absolute numbers of lymphocytes, polymorphs, and immature myeloid cells were increased and the lymphocytes were often more numerous than the polymorphs. A rise in the eosinophils was infrequent and did not exceed 6%. Amyloid infiltration of the spleen and liver followed treatment with I and II but not with III. Mice treated with II

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showed no, or only moderate, leukocytosis while the eosinophils rose from 12 to 16% (normal 1 to 3%). I and II produced reticulosis and plasmacytosis of lymph nodes.

The systemic effects of the growth of primary and grafted sarcomas in mice include leukocytosis, with increase of myeloid cells and crossing of the lymphocyte line by the polymorphs, reticulosis and plasmacytosis of the lymph nodes and amyloid infiltration of spleen and liver. These results suggest that nucleotides may be liberated during the development of primary and grafted sarcomas.—E. L. K.

**The Effects of Suramin (Germanin), Azo Dyes, and Vasodilators on Mice with Transplanted Lymphosarcomas.** WILLIAMS, W. L. [Yale Univ. Sch. of Med., New Haven, Conn., and Louisiana State Univ. Sch. of Med., New Orleans, La.] *Cancer Research*, 6:344-353. 1946.

Sixty-one C3H mice received subcutaneous transplants of an estrogen-induced lymphosarcoma and were killed 21 days later. During the terminal 7 to 16 days of this period, 34 mice were injected (subcutaneously) daily with 1 mgm. (0.1 cc. of an aqueous solution) of one of the following: suramin, 20 animals; trypan red, 4; trypan blue, 3; chlorazol fast pink, 7; histamine dihydrochloride, 6. Four animals received 0.1 cc. of depropanex in the same manner.

The azo-dyes had no effect upon the growth or morphology of the transplanted lymphosarcoma but prolonged the bleeding and clotting times. The vasodilators (histamine and depropanex) did not alter the amount or pattern of tumor growth. In these animals and in the untreated controls the weights of the tumors ranged from 7 to 16 gm. (average 10.9 gm.).

In the suramin-treated animals the tumors weighed 1 to 7 gm. (average 3.5) and the inhibition of tumor growth apparently resulted from necrosis of neoplastic lymphocytes. Many of these necrotic cells as well as remnants of them were observed in the tumors. Cytologically normal tumor cells were also present. In the lymph nodes and spleens of suramin-treated animals there was an obvious diminution in the number of lymphocytes. The usual lymphoid areas of these organs consisted almost entirely of reticular cells, macrophages, fibroblasts, large lymphocytes and plasma cells. The lymph nodes showed less actual necrosis of lymphoid elements *in situ* than did the tumors. Bleeding and clotting times were prolonged in the suramin-treated animals and in most cases there was renal damage. Tissue from 2 tumors which grew in suramin-treated animals was successfully transplanted to other C3H mice.

Smaller doses of suramin given to an additional group of ten C3H mice during the immediate interval subsequent to transplantation did not significantly inhibit the eventual growth of the tumor.—Author's abstract.

**Quantitative Studies on the Latent Period of Tumors Induced with Subcutaneous Injections of the Agent of Chicken Tumor I. I. Curve Relating Dosage of Agent and Chicken Response.** BRYAN, W. R. [Nat. Cancer Inst., Bethesda, Md.] *J. Nat. Cancer Inst.*, 6:225-237. 1946.

In a series of experiments with partially purified chicken tumor I agent, injected subcutaneously into several breeds

of chickens, it was found that a linear relationship existed between the reciprocal of the latent period of tumor development and the logarithm of the dosage of agent injected. This relationship held, except in an occasional discordant chicken group, throughout a ten million fold dilution of the chicken tumor agent. Under controlled conditions, therefore, it is felt that the latent period is a satisfactory criterion of biological activity of the chicken tumor agent. Employing statistical methods based on this dose-latent period relationship, evidence of heterogeneity among chicken groups was obtained.—R. A. H.

**On the Anatomical Character of the Infectious Myxoma of Rabbits.** AHLSTRÖM, C. G. [Path. Inst., Lund, Sweden] *Acta path. et microbiol. Scandinav.*, 17:377-393. 1940. Description.—M. H. P.

**Genetic Analysis of the Induction of Tumors by Methylcholanthrene: XII. The Effects of Selection Toward Resistance.** STRONG, L. C. [Yale Univ. Sch. of Med., New Haven, Conn.] *Yale J. Biol. & Med.*, 18:145-155. 1946.

Further evidence is presented to show that the two phenomena, (1) segregation and recombination of genes and (2) mutations or other suddenly acquired biological alterations, are both effective in changing susceptibility to local tumors induced by methylcholanthrene. This is true when the carcinogen has been administered to both parents over a period of several generations of hybrid mice (from the F<sub>4</sub> to F<sub>12</sub>) and a regime of continued selection toward resistance to such local tumors is consistently employed.

Hybrid mice of 6 separate lines of descent were injected subcutaneously at 60 days of age with 1 mgm. of methylcholanthrene. These lines were continued through 4 to 6 generations by a rigid regime of selection toward resistance to the appearance of the expected local tumors at the site of the injection. No discrimination was practiced in the different lines. Diversified effects of selection were obtained as follows: (1) no effect in changing tumor susceptibility in one subline; (2) an intermediate or rapid decline in the incidence of local tumors in the succeeding generations in 4 sublines, and (3) a gradual shift toward increased local tumor susceptibility counter to the trend of genetic selection. Earlier data of the author have previously disclosed the appearance of a sudden increase of local tumor susceptibility in another subline of methylcholanthrene-injected hybrid mice. The conclusion is drawn that the two phenomena referred to above are involved in shifting susceptibility to local tumors induced by methylcholanthrene.—J. L. M.

**Degradation of Cystine Peptides by Tissues. IV. Dehydropeptidase Activity in Normal and Neoplastic Tissues.** GREENSTEIN, J. P., and LEUTHARDT, F. M. [Nat. Cancer Inst., Bethesda, Md.] *J. Nat. Cancer Inst.*, 6:197-201. 1946.

The authors have reported previously that aqueous extracts of liver, kidney and pancreas contain dehydropeptidase activity when chloroacetyldehydroalanine is used as a substrate whereas extracts of spleen, brain, muscle and a variety of neoplastic tissues are nearly inactive as far as the hydrolysis of this substrate is concerned. The present investigations reveal, however, that when glycyldehydroalanine is employed as a substrate all tissues tested, both

normal and neoplastic, show dehydropeptidase activity and to about the same degree. This would indicate the existence of two separate dehydropeptidase systems, the one acting upon glycyldehydroalanine being tentatively designated as dehydropeptidase I and the other, active in the hydrolysis of chloracetyldehydroalanine, as dehydropeptidase II. The similarity of distribution of exocystine desulfhydrase and dehydropeptidase II is pointed out.—R. A. H.

**Enzymatic Hydrolysis of Benzoylarginineamide in Normal and Neoplastic Tissues.** GREENSTEIN, J. P., and LEUTHARDT, F. M. [Nat. Cancer Inst., Bethesda, Md.] *J. Nat. Cancer Inst.*, 6:203-206. 1946.

The activity of the amidase system capable of hydrolysing benzoylarginineamide at the amide linkage with the evolution of ammonia was investigated in whole extracts of several normal and neoplastic tissues. The order of descending activity of the various normal tissues was found to be spleen, liver, kidney, pancreas, brain and muscle. The rate of hydrolysis appeared to be the same for normal liver and for primary rat and transplanted mouse hepatomas. The activity in fetal rat liver was less, and that of transplanted rat hepatoma was greater, than the activity of normal adult rat liver. Similarities of distribution of this amidase and of catheptic protease and nucleodesaminase are discussed.—R. A. H.

**Note on Some Aspects of the Effect of Nucleates in Primary and Transplanted Rat Hepatomas.** GREENSTEIN, J. P., and CHALKLEY, H. W. [Nat. Cancer Inst., Bethesda, Md.] *J. Nat. Cancer Inst.*, 6:207-209. 1946.

The activity of the desaminases for ribosenucleate and desoxyribosenucleate and the effect of added nucleate on the dehydrogenase activity in extracts of primary rat hepatomas were investigated. In both respects, primary hepatomas were found to correspond very closely to normal adult liver but to differ considerably from a transplanted hepatoma.—R. A. H.

**Enzymatic Activity in Primary and Transplanted Rat Hepatomas.** GREENSTEIN, J. P., and LEUTHARDT, F. M. [Nat. Cancer Inst., Bethesda, Md.] *J. Nat. Cancer Inst.*, 6:211-217. 1946.

Combining data from the literature with new experimental results, a comparative tabulation is given of a large number of components, enzyme systems, coenzymes and vitamins, of extracts of non-neoplastic rat liver (fetal, normal adult and regenerating adult), primary induced rat hepatomas and a transplanted rat hepatoma. These components are classified into six categories according to different patterns of alterations noted in the different types of hepatic tissue, and some of the implications of these alterations are discussed.—R. A. H.

**Protective Effect of Thymus Nucleate on the Heat Coagulation of Proteins.** CARTER, C. E., and GREENSTEIN, J. P. [Nat. Cancer Inst., Bethesda, Md.] *J. Nat. Cancer Inst.*, 6:219-223. 1946.

It has been reported previously that the addition of thymus nucleate to tissue extracts protect the proteins of such extracts from coagulation at 100° C. The present experimentation shows the same protective influence of thymus nucleate for purified egg albumin, 1 mgm. of nucleate being sufficient to prevent the coagulation of

600 mgm. of the protein when kept at 98° C for longer than 120 minutes. This protective action of the nucleate is obviated by the addition of 3 to 4 × 10<sup>-5</sup> mols of NaCl, the concentration of NaCl necessary being independent of the concentration of the nucleate. Fresh aqueous extracts of liver were found to possess a natural protection against heat coagulation. Both the natural protection and that imparted by the addition of nucleate were found to decrease as the extracts were allowed to stand at room temperature or upon incubation. Experiments with the effects of desoxyribonuclease upon the protective ability of thymus nucleate suggest that the loss of protection upon standing or incubation is due to the enzymatic degradation of the nucleate. Although protein coagulation did not occur in the "protected" liver extracts, the enzymatic activity of the extracts, at least in the case of several enzyme systems, was destroyed by the heating.—R. A. H.

**The Microscope or the Guinea Pig?** GREENE, H. S. N. [Yale Univ. Sch. of Med., New Haven] *Yale J. Biol. & Med.*, 18:239-242. 1946.

The author emphasizes the value of heterologous transplants as an aid to the diagnosis and classification of human tumors. The ability to survive in an alien host is not shared by normal adult tissue, benign tumors, or chronic granulomas, and the mere fact that growth takes place immediately identifies the tissue in question as cancer. The value of heterologous transplantation is further emphasized from a diagnostic point of view by the fact that increased differentiation and organization exhibited by the tissue takes place in the foreign host. Completely disorganized tumors often undergo alterations in stromal-parenchymal relationships and reveal an organized structure indicating the tissue or organ of origin. In other instances, as in the present, an increased differentiation of the transplanted cells betrays their proper classification.

In the reported case, the primary diagnosis of hemangioblastoma was made on a purely morphological basis. In contrast to the disorderly anaplastic appearance of the human biopsy specimen (recurrent tumor), microscopic examination of the transplants in the eye of the guinea pig showed a fairly well organized growth of cells whose structure and arrangement were typically those of a chondrosarcoma. At autopsy several months later widespread metastases were found and the classification of the tumor based on histological examination was chondrosarcoma. The author states that the method of transplanting human cancer into the anterior chamber of the guinea pig's eye is extremely simple, requiring no special technical ability, and can be applied in any hospital laboratory.—J. L. M.

**Toxin Therapy of Experimental Cancer. The Influence of Protozoan Infections upon Transplanted Cancer.** ROSKIN, G. [Univ. of Moscow, Moscow, U.S.S.R.] *Cancer Research*, 6:363-365. 1946.

Cancer cells may be particularly sensitive to certain protozoan endotoxins and bacterial toxins, while normal cells of a given animal species are immune. Some bacterial toxins and protozoan endotoxins in adequate dosages inhibit the development of certain experimental tumors

and cause complete regression of others. Toxin therapy may become one of the methods for treating malignant tumors.—Author's summary.

**The Utilization of Intravenously Injected Salt in Normals and in Patients with Cushing's Syndrome before and after Administration of Desoxycorticosterone Acetate.** SOFFER, L. J., LESNICK, G., SORKIN, S. Z., SOBOTKA, H. H., and JACOBS, M. [Mt. Sinai Hosp., New York, N. Y.] *J. Clin. Investigation*, 23:51-54. 1944.

This report deals with the findings in 12 normal individuals and 4 patients with Cushing's syndrome. In normal individuals the intravenous injection of salt following the intramuscular injection of a single dose of desoxycorticosterone acetate resulted in a considerable retention of injected salt, above that seen prior to the injection of the hormone. In contrast to these results, patients with Cushing's syndrome showed a pronounced sodium chloride diuresis. Five case reports are presented.—J. L. M.

## Clinical and Pathological Reports

*Clinical investigations are sometimes included under Reports of Research*

### DIAGNOSIS—GENERAL

**Diagnostic Aspects of Bronchiogenic Carcinoma.** MOERSCH, H. J., *Proc. Staff Meet., Mayo Clin.*, 19:357-361. 1944.

This discussion includes the following topics: roentgenographic examination, bronchoscopy, bronchography and tomography. A filling defect or obstruction of the bronchial tree as demonstrated on bronchography or tomography does not necessarily indicate that the obstruction is due to carcinoma. If possible, tissue should be obtained from the lesion itself to establish the diagnosis. Needle biopsies and thoracoscopic examinations are other diagnostic procedures that may be of help. However needle biopsies possess some element of risk and thoracoscopic examinations frequently yield negative results.—J. L. M.

**The Significance of Fluid in the Pleural Space: A Study of 274 Cases.** TINNEY, W. S., and OLSEN, A. M. *Proc. Staff Meet., Mayo Clin.*, 20:81-85. 1945.

A review of 444 cases is given in which fluid was present in the pleural space and in which a diagnostic thoracentesis was performed. All cases of pleural effusion which developed as a postoperative complication or as the result of trauma were excluded. In 170 of the 444 cases (38%) diagnosis of the underlying disease was not established, although a tentative diagnosis of tuberculosis was made in 58 cases and metastatic carcinoma of the pleura was suspected in 46 cases. The present study on the significance of fluid in the pleural space was limited to the 274 cases in which the cause of this condition was determined.

The etiologic factors responsible for production of pleural fluid are tabulated. There was a low incidence of inflammatory lesions, such as pneumonia and tuberculosis, in contrast to the high incidence of carcinoma. These figures may be explained by (1) the types of cases encountered at the Clinic, which include a relatively large number of cases of carcinoma and lymphoblastoma and (2) the fact that all patients who had received collapse therapy were excluded. The highest incidence of pleural effusion occurred in cases of intrathoracic tumor and of carcinoma of the breast. In 42 of the 141 cases of carcinoma (30%) malignant cells were found in the aspirated fluid. The technic described by McDonald and Broders was used

in studying pleural effusion for malignant cells. In 193 of the 274 cases (70%) the pleural fluid was serous in type, and in 81 cases (30%) it was hemorrhagic. The total number of cases of carcinoma and lymphoblastoma reveal that a malignant process was the underlying disease in 85% of cases of hemorrhagic effusion. In an additional 10%, the cause was congestive heart failure. This observation is of clinical significance because if congestive failure can be eliminated as a cause of bloody effusion in a specific case there is a 95% chance that a malignant process, either carcinoma or lymphoblastoma, is present. Pulmonary embolus was a complicating condition in 5 of the 8 cases of congestive failure in which the fluid was hemorrhagic.—J. L. M.

### FEMALE GENITAL TRACT

**Indications for Oophorectomy.** HODGE, R. H. [Med. Coll. of Virginia, Richmond, Va.] *Virginia M. Monthly*, 72:286-288. 1945.

Radical surgery (bilateral salpingo-oophorectomy and hysterectomy) is indicated in carcinoma of the ovary of moderate or high malignancy and in adenocarcinoma, sarcoma, and solid teratoma of that organ. Simple oophorectomy is recommended for Brenner tumor, fibroma, and other relatively benign growths.—M. E. H.

**Fatal Bronchial Asthma Showing the Asthmatic Reaction in an Ovarian Teratoma.** THOMSON, J. G. [Med. Sch., King's Coll., and Roy. Victoria Infirmary, Newcastle-on-Tyne, England] *J. Path. & Bact.*, 57:213-219. 1945.

At the postmortem examination the characteristic picture of asthma was found, comprising blockage of bronchi by mucus, eosinophilous infiltration of bronchial mucosa and submucosa, hyaline thickening of the basement membranes, hypertrophy of the bronchial muscles and mucous glands, the presence of mucus in some of the air vesicles, and, in addition, Charcot-Leyden crystals and Curschmann's spirals. The case was one of status asthmaticus in which adrenaline was ineffective in relieving the condition during life. A unique feature was the presence of a typical asthmatic reaction in some epithelium of respiratory type, which was found in an ovarian teratoma. Histological appearances similar to those in the lungs were found.—L. W. P.