Abstracts

Reports of Research

On the Production of Sarcoma with Wheat Germ Oil. HARRIS, P. N. [Eli Lilly and Co., Indianapolis, Ind.] *Cancer Research,* 7:26-34. 1947.

Although treatment was prolonged and large amounts of oil were given, no tumors were obtained as a result of oral administration of ether-extracted wheat germ oil to rats. Following repeated subcutaneous or intraperitoneal injections of various types of wheat germ oil, sarcomas were obtained in 2 mice and 16 rats. The tumor percentage for mice was 5% of the effective total, and for rats was 8% of the effective total injected.—Author's abstract.

Production of Sarcoma in Rats with Light Green SF. HARRIS, P. N. [Eli Lilly & Co., Indianapolis, Ind.] *Cancer Research,* 7:35-36. 1947.

Subcutaneous injection into the same region of an aqueous solution of the dye light green SF twice weekly for a period of 33 weeks resulted in development of sarcomas at the site of injection in 15 of an effective total of 24 rats. During the first month a 2% solution was used, but thereafter, the concentration was increased to 3%. The latent period varied from 35 to 85 weeks.—Author's abstract.

Reciprocal Effects of Natural Immune Bodies from Chickens and Ducks on Variants of a Sarcoma Virus. DURAN-REYNALS, F., and KING, J. W. [Yale Univ. Sch. of Med., New Haven, Conn.] *Cancer Research,* 7:21-25. 1947.

This investigation was carried out to determine, first, the nature of the resistance of chickens and ducks to the Rous chicken sarcoma virus, and its variants in ducks, and second, the nature of the changes that took place in the virus in the process of mutation or variation. The immune bodies that develop naturally in the blood of aging chickens neutralize both the viruses of the chicken tumor and its duck variants as tested on both chickens and ducks. Therefore, the resistance of chickens against these viruses is linked with the presence of humoral factors and might be explained on this basis. On the contrary, comparable immune bodies from aging ducks neutralize only duck tumor viruses as tested on ducks, but not as tested on chickens; nor do they neutralize chicken tumor viruses as tested on either chickens or ducks. Therefore, the refractory state of ducks against heterologous chicken viruses, solidly established very shortly after hatching, cannot be linked with humoral factors but rather belongs to the so-called species resistance. However, the resistance of these hosts against the virus after it has varied and has become a duck virus is linked with humoral factors and might be explained on this basis. One may add that, with the tumor viruses here studied, the species resistance is far more effective than is the humoral resistance, and that the presence of natural specific immune bodies against the viruses is an indication of actual or potential susceptibility to these viruses. Analysis of the 8 possible sequences that can be obtained by testing the effect of chicken and duck sera against homologous and heterologous tumor viruses on homologous and heterologous hosts indicates that a pronounced antigenic change has taken place in the virus in the process of variation.—Authors' abstract.

Growth of Avian Tumors Other Than the Rous Sarcoma in the Anterior Chamber of the Guinea Pig Eye. SHRIGLEY, E. W., GREENE, H.S.N., and DURAN-REYNALS, F., [Yale Univ. Sch. of Med., New Haven, Conn.] *Cancer Research,* 7:15-20. 1947.

It has been found that the Rous sarcoma is not the only avian tumor that will grow in the anterior chamber of the guinea pig eye. Two spontaneous growths originating in chickens and 3 methylcholanthrene-induced sarcomas, from chicken, guinea fowl and pigeon respectively, have been found to be transplantable to the eye of the guinea pig. Like the Rous sarcoma, these tumors do not grow to such a size as to completely fill the chamber. In general, tissue fragments in the alien host grow for 10 to 20 days and then regress in size over varying periods of time. However, in the case of one slow-growing spontaneous chicken tumor healthy tissue was recovered from the rodent's eye 83 days after inoculation.—Authors' abstract.

The Role of Heredity in the Etiology of Cancer. MARTYNOVA, R. P. *Bull. Exper. Biol. & Med.,* 19:12-15. 1945.

The author mentions the role of heredity in certain tumors of fish, insects and mammals, but suggests that definite relationship between heredity and cancer has not been established conclusively. She assumes that if cancer is a hereditary disease, susceptibility to cancer in identical (monozygotic) twins is equal and this susceptibility should differ in fraternal (dizygotic) twins. If there is no difference in morbidity between the two groups, she feels that it proves that the hereditary factory is insignificant in cancer etiology. The author bases her report on 478 pairs of twins with cancer included among 45,000 tumor patients collected from 20 cancer institutes in the USSR. Reliable data was obtained only on 126 sets of twins, of whom 31 were identical and 95 fraternal. Among the former, cancer was found in 4 pairs of twins, or 12.9%, and among the latter in 13 pairs or 13.7%. The difference is not significant and a hereditary disposition, based on these figures is not established. She concludes that cancer cannot develop without mutation of a germ or somatic cell, and is not hereditary since somatic mutation is the precursor in the great majority of cases. A detailed theoretical discussion on mutation is included. —J. H.

Cholesterol Content of the Urine in Patients with Cancer. BRUGER, M. [New York Post Graduate Med. Sch. and Hosp., Columbia Univ., New York, N. Y.] *Arch. Int. Med.,* 72:108-114. 1943.

The excretion of cholesterol in the urine in 26 normal subjects ranged from 0.27 to 3.88 mgm. in 24 hours with a mean of 1.69 ± 0.85 mgm. In 28 patients with a variety

of clinical disorders other than cancer, the mean excretion of cholesterol was slightly higher than in the normal subjects (2.01 mgm. in 24 hours), but for the most part the individual variations fell well within the normal range. In 8 of 32 patients with cancer, the excretion of cholesterol in the urine was significantly elevated above normal; the highest value noted was 47.8 mgm. in 24 hours in a patient with adenocarcinoma of the rectum. The mean amount of urinary cholesterol for this group was 6.09 mgm. in 24 hours. No correlation was observed between the sedimentation rate, the plasma cholesterol content and the degree of cholesteroluria. Hypercholesteroluria occurs independently of loss of protein in the urine; some theoretic considerations are offered to account for this phenomenon.—Author's summary. (J. G. K.).

A Study of the Effect of Certain Dietary Factors on the Production of Tar-Carcinoma in Mice. CAMERON, A. T., MELTZER, S., and LEDERMAN, J. M. [Univ. of Manitoba, Canada] *Canad. J. Research,* **23, Sec. E**:50-69. 1945.

The development of carcinoma in mice painted with gasworks tar or with 3,4-benzpyrene was not affected by varying the protein content of the Waddell-Steenbock diet from approximately 14% to 26%. When 1,2,5,6-dibenzanthracene was used as the tarring agent, the results were inconclusive because of the delay in onset of carcinoma. Inconclusive results were also obtained in an experiment designed to study the effect of the dietary content of essential unsaturated fatty acids on 1,2,5,6-dibenzanthracene carcinoma.—M. H. P.

The Solubilization of Polycyclic Aromatic Hydrocarbons by Purines. WEIL-MALHERBE, H. [North of England Council of the British Empire Cancer Campaign, Royal Victoria Infirmary, Newcastle upon Tyne, England] *Biochem. J.,* **40**:351-363. 1946.

Aqueous solutions of caffeine were shaken with solid 3,4-benzpyrene, filtered, passed through alumina and the benzpyrene estimated by fluorimetry. Experiments were also carried out on other polycyclic aromatic hydrocarbons, as well as about 40 purines and purine derivatives. The effects of varying the concentration of purine over a very wide range were also studied.

The discussion is on the mathematical relation of solubility change to concentration, the theory of the mechanism of solubility, constitution and solvent activity, and a comparison of choleic-acid with other hydrocarbon solvents.—I. H.

Effects of Purines on Fluorescent Solutions. WEIL-MALHERBE, H. [North of England Council of the British Empire Cancer Campaign, Royal Victoria Infirmary, Newcastle upon Tyne, England] *Biochem. J.,* **40**: 363-368. 1946.

The fluorescence of 3,4-benzpyrene (1μgm./ml.) in 1% aqueous caffeine solution is reduced to 87% by addition of 0.001 normal H_2SO_4, to 13.5% by 0.02 normal H_2SO_4 and not influenced by 0.2 normal H_2SO_4. This effect is reversible on neutralization of the acid. The compounds resulting in this reduction have to be present in great excess (many thousands of molecules per molecule of fluorescent compound). These observations have been extended by studying the inhibitory effect of different (1) purines and purine derivatives, (2) acids, (3) solvents, and (4) polycyclic aromatic hydrocarbons. The effects of these agents on fluorescent compounds other than hydrocarbons has also been studied. The physicochemical theory and relation of constitution to inhibitory activity are discussed.—I. H.

Succinic Dehydrogenase and Cytochrome Oxidase in Epidermal Carcinogenesis Induced by Methylcholanthrene in Mice. CARRUTHERS, C., and SUNTZEFF, V. [Barnard Free Skin and Cancer Hosp., and Washington Univ. Sch. of Med., St. Louis, Mo.] *Cancer Research,* **7**:9-14. 1947.

The activity of succinic dehydrogenase and cytochrome oxidase in the epidermis of mice undergoing carcinogenesis by methylcholanthrene has been investigated. The activity of succinic dehydrogenase in normal and in hyperplastic (methylcholanthrene-treated) epidermis is the same, but almost a four-fold increase occurs in the activity of this enzyme when the cells become carcinomatous. On the other hand the cytochrome oxidase activity of hyperplastic epidermis (after 6 and 12 paintings on alternate days with methylcholanthrene) was slightly greater than normal, but the activity of late hyperplastic epidermis (18 and 24 applications of the carcinogen) was nearly twice that of normal. In the carcinoma the activity of this enzyme was less than that of late hyperplastic epidermis, but greater than that of normal. Benzene, the solvent for the carcinogen, had a slight inhibitory effect upon the activity of both enzymes. The relationship of the enzymes with the metals, calcium, iron, copper, and zinc, is briefly discussed. Two tables and one figure are appended.—Authors' abstract.

The Inhibition of Urease and Succinoxidase by Metabolic Products of *p*-Dimethylaminoazobenzene and by Some Related Amines. ELSON, L. A., and HOCH-LIGETI, C. [Royal Cancer Hosp., London, England] *Biochem. J.,* **40**:380. 1946.

The compounds tested were aniline, *p*-aminophenol, *o*-, *m*-, and *p*-phenylenediamine, *as*-dimethyl-*p*-phenylenediamine, *as*-diethyl-*p*-phenylenediamine, *N*:*N*:*N'*:*N'*-tetramethyl-*p*-phenylenediamine, benzidine, 2:4'-diamino-5-dimethylaminodiphenyl, and Bindschedler's green. Rat organs were used and included the liver, kidney, spleen, testis, also tumors of the liver. The inhibition of urease by those compounds which are oxidized on exposure to air increased to a maximum during such exposure, indicating that the actual inhibitor is an intermediate product. Aniline and benzidine, which are not readily oxidized thus, are not inhibitory. All the *p*-diamines tested, and *o*-phenylenediamine, are strongly inhibitory; *m*-phenylenediamine is only slightly active. In general, those amines which inhibit urease also inhibit succinoxidase, but with the latter agent the oxidation of the amines by the cytochrome system is so rapid that maximum inhibition is obtained at once and a decrease in activity takes place on exposure to air. In the succinoxidase system with addition of cytochrome *c* the higher concentrations of the inhibitory amines (10^{-3}-10^{-4}M) generally give initially an increase in O_2 uptake followed by complete inhibition of the enzyme activity. With lower concentrations (10^{-5}-10^{-6}M) only a gradually increasing inhibitory effect is observed. Without addition of cytochrome *c* the results are less uniform in that the higher concentrations cause inhibition only in some of the livers; the lower concentrations are often inactive. The succinoxidase of the liver of animals which had been fed *p*-dimethylaminoazobenzene, even in tumor-free parts of the liver of tumor-bearing animals, showed the same general behavior towards the amines as that of control animals. On tissues of low oxidative capaci'y (spleen,

testis, Walker sarcoma, liver tumors induced by *p*-dimethylaminoazobenzene and 2-acetamidofluorene) no inhibitory effect on the O_2 uptake in presence of succinate is produced by amines that inhibit tissues of high succinoxidase content.—E. L. K.

A Note on the Action of Tannin upon Tumour Glycolysis. LASNITZKI, A. [Cancer Research Lab., Med. Sch., Univ. of Birmingham, Birmingham, England] *Biochem. J.*, **40**:263-264. 1946.

Tannic acid (0.1%) added to slices of the Jensen rat sarcoma, inhibited anerobic glycolysis (CO_2 production in an atmosphere of N_2 plus 5% CO_2) by 40%. It is suggested that (1) the tannic acid acts by dehydrating the enzyme proteins, (2) the activity of the enzymes is dependent upon the degree of hydration, and (3) the high water content of rapidly proliferating tissues facilitates the activity of the glycolytic enzymes.—I. H.

Discussion on Leukaemia and Leukosis in Man and Animals. ENGELBRETH-HOLM, J. [London, England] *Proc. Roy. Soc. Med.*, **39**:735-740. 1946.

The discussion opened with a paper on the comparative pathology of animal leukosis by Engelbreth-Holm, who regards the term "leukosis" as properly confined to true autonomous and malignant growths arising from the hemopoietic tissues. Speaking on avian leukemia, Blakemore discussed the connection between this condition and both visceral and neural lymphomatosis, in relation to the unitary theory of Biester and DeVries (*Diseases of Poultry*, Iowa, 1944) which attributes these diseases to a single virus and classifies them as the "leukosis complex." In Blakemore's experience, the neurolymphomatosis virus is much more infective for chicks than for older stock. It can be increased in virulence by rapid animal passage and then the agent produces a markedly different disease characterized by necrosis of the capillary walls.

Other contributors included E. G. White, who discussed leukemia in dogs; J. M. Alston, R. J. Ludford, G. R. Cameron and L. Foulds also contributed to the discussion. —R. H.

Desoxyribose Nucleic Acid from Isolated Chromosome Threads in Experimental Epidermal Methylcholanthrene Carcinogenesis in Mice. GOPAL-AYENGAR, A. R., and COWDRY, E. V. [Barnard Free Skin & Cancer Hosp., and Washington Univ. Sch. of Med., St. Louis, Mo.] *Cancer Research*, **7**:1-8. 1947.

Disruption of nuclear membranes releases into the surrounding medium the chromosomal elements which can then be isolated, concentrated and purified by differential centrifugation. Chromosomes of Swiss mice were thus isolated from normal epidermis, epidermis rendered hyperplastic by methylcholanthrene, and chromosomes from a transplantable squamous cell carcinoma. The concentrations of desoxyribose nucleic acid in the masses of isolated chromosomes were determined. In hyperplastic epidermis the concentration was less than in normal epidermis, whereas in squamous cell carcinoma it was greater.—Authors' abstract.

Relative Sensitivity of Chromosomes to Neutrons and X-Rays. III. Comparison of Carcinoma and Lymphosarcoma in the Rat. MARSHAK, A., and BRADLEY, M., *Proc. Nat. Acad. Sc.*, **31**:84-90. 1945.

Survival curves (log % normal vs. dose) for chromosomes of *Vicia faba* root tips, lymphoma (mouse), lymphosarcoma and carcinoma (rat) obtained at the intervals 3, 8, 12, 18, and 24 hours after treatment with either x-rays or neutrons all fit the equation $Y = e^{-kx}$. When the slopes (k) are plotted as a function of time there is a progressive decrease in k with time in all tissues studied except at the 12-hour interval where there is either a plateau as in the cases *V. faba*, lymphosarcoma, carcinoma, or a peak as found with the lymphoma. It is inferred from this observation that the stage in the nuclear cycle occurring at the time of the 12-hour interval represents a critical period in the physiology of all chromosomes studied.

Relative efficiency of neutrons and x-rays in producing chromosome damage is evaluated from the ratio of k obtained with x-rays (n/x) at each time interval. In all animal tissues and all plant species studied $n/x = 6$ for the phase of the nuclear cycle, which reaches anaphase 3 hours after irradiation. In contrast to this marked uniformity there is striking variation n/x in other phases of the nuclear resting stage not only between species but in a single type of tissue in any one species. Changes in n/x with time in any one type of cell may be used to identify phases in physiological activity of chromosomes in different parts of the resting stage. In terms of the ratio n/x, chromosomes of lymphosarcoma of the rat behave more like those of lymphoma in mouse than chromosomes of carcinoma of the rat. These results are taken to indicate that in the process of differentiation during ontogeny and also during "dedifferentiation" in carcinogenesis the chromosomes become altered in their physiology. One cannot therefore infer that the genetic theory which requires that the genome remain constant during embryogeny also implies that the chromosomes remain unchanged.—Authors' abstract.

Plant Tumours Induced by the Combined Action of Wounds and Virus. BLACK, L. M. [Rockefeller Inst. for Med. Research, Princeton, N. J.] *Nature, London*, **158**:56-57. 1946.

Plant tumors can be induced in numerous host species by a virus previously described (L. M. Black, *Am. J. Bot.*, **32**:408. 1945), and experiments have now confirmed the earlier suggestion that such tumors arise in association with the wounding of plant tissues. That the tumor tissue is capable of indefinite growth without the differentiation of normal plant organs was shown by grafting fragments of the growth to healthy plants, and by growth *in vitro* on White's medium without production of roots, stems or leaves. Two figures illustrate the gross and microscopic appearances of such tumors on the roots of infected sweet clover.—A. H.