Abstracts

Reports of Experimental Research

Carcinogenic Compounds

LASNITZKI, A., and WOODHOUSE, D. L. [Univ. of Birmingham, England] FORMATION OF HAEMOLYMPH NODES IN RATS TREATED WITH 1:2:5:6-DIBENZANTHRACENE. Nature, 150:660. 1942.

Normal rats show some hemolymph nodes, of which the most conspicuous lie near the kidneys. After injections *sub cutem* of colloidal 1,2,5,6-dibenzanthracene in a glucose-gelatin aqueous solution, many lymph nodes in various parts of the body show a red or brownish red color and, microscopically: (1) widening of lymph spaces and diminution of lymphatic tissue, (2) red corpuscles in the lymph spaces, and (3) increase of macrophages containing red corpuscles and "hemosiderin." The nodes in this condition resemble the normal hemolymph nodes. Injection of the solvent alone does not produce these changes. Experiments still in progress indicate that two other carcinogenic hydrocarbons (3,4-benzpyrene, methylcholanthrene) have the same effects, while two noncarcinogenic hydrocarbons (anthracene, phenanthrene) do not alter the appearance of the lymph nodes.—E. L. K.

LORENZ, E., and SHIMKIN, M. B. [Nat. Cancer Inst., Bethesda, Md.] DISAPPEARANCE OF INTRAVENOUSLY INJECTED METHYLCHOLANTHRENE IN MICE OF DIFFERENT SUSCEPTIBILITY TO PULMONARY TUMORS. J. Nat. Cancer Inst., 2:491-498. 1942.

Mice of strain A (highly susceptible to pulmonary tumors) and of strain C57 black (insusceptible) were injected intravenously with 0.5 mgm. of 20-methylcholanthrene dispersed in 0.5 cc. horse serum saturated with cholesterol. They were killed at various periods after injection and the lungs or whole bodies extracted for determination of the hydrocarbon content. The presence of the hydrocarbon was detected in amounts as small as 5×10^{-4} mgm. per cc. for a 1 cm. cell by a photographic method of absorption spectrum analysis in the ultraviolet.

The rate of disappearance of ether-extractable methylcholanthrene from the body was found to parallel that from the lung. In 4 days the concentration in the lung decreased to one-tenth its original value. No spectroscopic evidence of chemical change of the hydrocarbon was found, and no significant divergence was observed in the curves for the A strain or C57 black. Therefore the difference in susceptibility to pulmonary tumor shown by these strains cannot be explained by a difference in rate of elimination of methylcholanthrene.

The results indicate that intravenously injected methylcholanthrene disappears rapidly from the lungs and whole body of the mouse. Since pulmonary tumors arise within 6 weeks in strain A and within 6 to 8 months in C57 black after injection of methylcholanthrene, it seems probable that the tumors arise long after the introduction of the stimulus and long after its removal from the body.—F. L. H.

MILLER, J. A., and BAUMANN, C. A. [Univ. of Wisconsin, Madison, Wis.] THE EFFECT OF NAPHTHACENE ON THE FLUORESCENCE OF HYDROCARBONS. Cancer Research, 3: 217-222. 1943.

Details are given for the purification of carcinogenic and related hydrocarbons, for the quantitative determination of fluorescence in liquid solution, and for the photography of the fluorescence spectra of these hydrocarbons in solution and in the solid state.

One-tenth per cent of naphthacene (2,3-benzanthracene) in solid solution in 3,4-benzpyrene, 20-methylcholanthrene, 9,10-dimethyl-1,2-benzanthracene, or anthracene caused the appearance of bands in the fluorescence spectrum. These bands differed from those of either component and appeared to be characteristic of the fluorescence of naphthacene in solid hydrocarbon solution. The solid hydrocarbons and their solid solutions with naphthacene lost their ability to fluoresce upon fusion in air or *in vacuo* and immediately regained it on resolidification. 3,4-Benzpyrene when heated in liquid solution to its melting point did not lose its fluorescence.

When added to liquid solutions of the hydrocarbons, naphthacene was without effect as a fluorescence inhibitor. The so called "naphthacene effect" therefore offers no obstacle to the fluorometric determination of hydrocarbons in liquid solution.—Authors' abstract.

MILLER, J. A., and BAUMANN, C. A. [Univ. of Wisconsin, Madison, Wis.] FACTORS THAT ALTER THE FLUORESCENCE OF CERTAIN CARCINOGENS. Cancer Research, 3: 223-229. 1943.

The intensity of fluorescence in solution was measured for seven hydrocarbons in 37 solvents. In most solvents the intensity increased in the following order: napthacene < 1,2,5,6-dibenzanthracene < 1,2-benzanthracene < anthracene < 9,10-dimethyl-1,2-benzanthracene < 20-methylcholanthrene < 3,4-benzpyrene.

The fluorescence of each hydrocarbon varied with the solvent in which it was dissolved. Fluorescence was most intense in tetrahydrofurfuryl alcohol, pyridine, methyl collosolve, and dioxane; it was low in the lower alkanes, and it was zero in CS_2 or aniline.

With the exception of 1,2,5,6-dibenzanthracene, the fluorescence of these hydrocarbons was partially destroyed in solution by prolonged exposure to strong ultraviolet light. Each hydrocarbon was stable to refluxing in 10% alcoholic KOH for 1 hour.

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The most potent inhibitor of fluorescence encountered was tetranitromethane; other inhibitors studied included nitromethane, nitrobenzene, benzaldehyde, aniline, and carbon disulfide. The inhibition by tetranitromethane was irreversible; the inhibition due to CS_2 was readily reversible. $C(NO_2)_4$ inhibited the fluorescence of all compounds studied; namely, hydrocarbons, riboflavin, thiochrome, vitamin A, tissue substances, and impurities in paraffin or in ordinary solvents. It can be used in determining the "fluorometric purity" of a solvent.

The fluorescence of the unsaponifiable matter of mouse tissue was measured in 18 solvents; on a weight basis the fluorescence of these extracts was very weak as compared with that of the carcinogenic hydrocarbons. The fluorescence of the unsaponifiable matter did not vary greatly with solvent and in mixtures it was strictly additive to the fluorescence of the hydrocarbons.—Authors' abstract.

MOTTRAM, J. C., and WEIGERT, F. [Mt. Vernon Hosp., Northwood, Middlesex, England] TRANSFORMATION OF BENZPYRENE IN THE LIVING SKIN OF MICE INTO A COMPOUND SOLUBLE IN DILUTE ALKALI. Nature, 150: 635. 1942.

Benzpyrene painted on mouse skin is transformed locally into a derivative with blue fluorescence that can be found also in certain organs and in the milk of mice injected with the hydrocarbon. The fluorescence spectrum resembles that of BPX (a benzpyrene derivative found in the bile of animals injected with the hydrocarbon) but is not identical with it nor with the spectrum of the monohydroxybenzpyrene isolated from the excreta of rats injected with benzpyrene.

The derivative in the skin, which is not removed by benzene, is soluble in alkali and can be extracted with ether after acidification. It can be detected 6 hours after one painting with benzpyrene and persists for several weeks.

Microscopic study in ultraviolet light shows that this blue-fluorescing derivative is confined to the quickly proliferating cells of the malpighian layer and therefore its formation may be an important step in the production of tumors.—I. H.

NELSON, A. A., FITZHUGH, O. G., and CALVERY, H. O. [Food and Drug Administration, Washington, D. C.] LIVER TUMORS FOLLOWING CIRRHOSIS CAUSED BY SELENIUM IN RATS. Cancer Research, 3:230-236. 1943.

Eleven of 53 rats developed adenoma or low grade carcinoma in cirrhotic livers and 4 others showed decided adenomatoid hyperplasia after surviving for 18 to 24 months on diets containing 5, 7, or 10 parts per million of selenium in corn, or in wheat, or as inorganic selenide. No tumors occurred in 73 rats surviving less than 18 months, although after 3 months cirrhosis was frequent. In control rats 18 to 24 months of age, the incidence of spontaneous hepatic tumors was less than 1%. This appears to be the first report of tumors arising in experimentally cirrhotic livers after the cirrhosis had been present without tumor for a relatively long period of time.—Authors' abstract.

STEINER, P. E. [Univ. of Chicago, Chicago, Ill.] COMPARATIVE PATHOLOGY OF INDUCED TUMORS OF THE SALIVARY GLANDS. Arch. Path., 34:613-624. 1942.

By means of methylcholanthrene, 1,2,5,6-dibenzanthracene, or 3,4-benzpyrene a wide variety of cell changes, ranging from metaplasia to neoplasia, were induced in the salivary glands of mice, rats, guinea pigs, and rabbits. Metaplasia of the acinous and terminal duct cells to a squamous type of epithelium was seen as early as the 3rd day. Later epidermoid cysts, squamous cell carcinoma, and adenocarcinoma developed from the epithelium; from the connective tissue, spindle and mixed cell sarcoma developed. The mixed tumor types seen were adenocarcinosarcoma, acanthocarcinosarcoma, and acanthoadenocarcinoma, but none were composed of epithelium and cartilage as in the common human tumors. Epithelial tumors were produced in rats and guinea pigs, in which the induction of epithelial tumors is generally considered to be difficult, but no neoplasia was produced in rabbits. The ease of induction of tumors in the salivary glands is interesting in view of the rarity of such spontaneous tumors in the lower animals.—H. G. W.

STOWELL, R. E., and CRAMER, W. [Barnard Free Skin and Cancer Hosp., St. Louis, Mo.] OSTEOSIS CUTIS IN METHYLCHOLANTHRENE EPIDERMAL CARCINOGENESIS IN MICE. Arch. Dermat. & Syph., 46:276-282. 1942.

A report of 4 examples of osteosis of the skin adjacent to rather anaplastic carcinomas in Swiss mice that had been painted on a large area of the back with a 0.6% solution of 20-methylcholanthrene in benzene. Necrosis and calcification of the tissues was absent, and it is suggested that the heterotopic bone was produced by the differentiation of fibroblasts to osteogenic cells.—H. G. W.

WHITE, J., DALTON, A. J., and EDWARDS, J. E. [Nat. Cancer Inst., Bethesda, Md.] PATHOLOGY OF RAT HEPATOMA 31. J. Nat. Cancer Inst., 2:539-554. 1942.

The history and pathology of rat hepatoma 31 are presented. The tumor, a malignant hepatoma, arose in the liver of an Osborne-Mendel rat fed *p*-dimethylaminoazobenzene. It is readily transplantable in the homologous strain of rats and is now in the 16th generation. It is suitable for studies in which liver and a tumor of hepatic parenchymal cell origin are to be compared.—F. L. H.

WHITE, J., and EDWARDS, J. E. [Nat. Cancer Inst., Bethesda, Md.] EFFECT OF ORAL ADMINISTRATION OF ANILINE AND p-AMINODIMETHYLANILINE ON THE GROWTH OF THE RAT. J. Nat. Cancer Inst., 2:531-533. 1942.

This paper records the effect on the growth of the rat of the oral administration of 2 possible split products of *p*-dimethylaminoazobenzene (butter yellow); namely, aniline and *p*-aminodimethylaniline. Male Osborne-Mendel rats were raised from weaning to a weight of 75 to 80 gm. on an adequate basal diet of relatively low protein content. The transfer of these rats to a diet containing either 80 mgm. of aniline hydrochloride or 120 mgm. of *p*-aminodimethylaniline monohydrochloride per 100 gm. of the basal diet resulted in retardation of growth (failure to gain weight normally). The addition of *l*-cystine (500 mgm.) or *dl*-methionine (500 mgm.) to each 100 gm. of basal diet containing the amine stimulated growth and gave weight increases comparable to those of rats on the basal diet alone. The addition of glycine, taurine, or cysteic acid to the amine-containing diet failed to stimulate growth.—F. L. H.

Radiation

BLUM, H. F., and LIPPINCOTT, S. W. [Nat. Cancer Inst., Bethesda, Md.] ABSENCE OF HYPERVITAMINOSIS D IN MICE SUBJECTED TO ULTRAVIOLET RADIATION. J. Nat. Cancer Inst., 2:623-624. 1942.

Microscopic examination of all tissues, except those of the nervous system, from 15 mice that had received sufficient ultraviolet radiation to produce tumors of the ear revealed no lesions characteristic of hypervitaminosis D. A table giving radiant energy values and estimated amounts of the vitamin D formed, is included.—F. L. H.

Biochemistry and Nutrition

GREENSTEIN, J. P. [Nat. Cancer Inst., Bethesda, Md.] DISTRIBUTION OF ACID AND ALKALINE PHOSPHATASE IN TUMORS, NORMAL TISSUES, AND THE TISSUES OF TUMOR-BEARING RATS AND MICE. J. Nat. Cancer Inst., 2:511-524. 1942.

For various ratios of enzyme to substrate (phenylphosphate) for all the tissues studied, a linear relation, either for acid phosphatase hydrolysis (Q acid) or for alkaline phosphatase hydrolysis (Q alk.), was found to exist between the amount of hydrolysis and the nitrogen content of the tissue extract. The tissues fell into 3 groups: (1) Q (acid) > Q (alk.): Liver of the rat and mouse and the adult and fetal rabbit; muscle, skin, and spleen of the rat and mouse; and of mice, the lymph nodes, hyperplastic mammary tissue, gastric mucosa, transplanted intestinal, stomach, lung, and hepatic tumors, transplanted malignant endothelioma and melanoma, sarcoma 37, sarcoma 180, and primary induced tumor (benzpyrene). (2) Q (acid) = Q (alk.): Normal lung and bone marrow, and spontaneous mammary tumors and transplanted lymphoma 72942, all of mice. (3) Q (acid) < Q (alk.): Intestinal mucosa of the mouse; kidney of the mouse and rat; and of the rat, blood serum, Jensen sarcoma, transplanted hepatoma 31.

Mouse tumors.—Only the spontaneous mammary tumors and the lymphoma possessed alkaline phosphatase activities. The acid phosphatase activities of all were high.

Rat tumors.—The alkaline phosphatase activities were very high. Acid phosphatase activities were higher than those of mouse tumors and normal tissues.

Tumors and comparable normal tissues.—(1) Hepatic tissues: In mice the acid phosphatase was practically the same in normal and neoplastic hepatic tissues; the alkaline phosphatase was much less in the tumors than in liver. In rats both acid and alkaline phosphatase were much greater in the transplanted tumor than in normal liver. (2) Mouse mammary tissue: The acid phosphatase was nearly the same for hyperplastic mammary tissue and spontaneous tumors; the alkaline phosphatase was much higher in the latter than in the former tissue. (3) Mouse gastric and intestinal tissue: Both acid and alkaline phosphatase were much lower in the transplanted adenocarcinomas than in the respective normal mucosas. (4) Mouse lymphatic tissue: The lymphoma was lower in acid phosphatase than were the lymph nodes or bone marrow; the alkaline phosphatase of the tumor was similar to that of the nodes and less than that of the marrow.

The phosphatase activities of tissues (liver, kidney, spleen, skin, muscle) and sera of normal mice and rats and of those bearing transplanted tumors were similar.—F. L. H.

GREENSTEIN, J. P., ANDERVONT, H. B., and THOMPSON, J. W. [Nat. Cancer Inst., Bethesda, Md.] KIDNEY AND BLOOD CATALASE ACTIVITY OF TUMOR-BEARING ANIMALS. J. Nat. Cancer Inst., 2:589-594. 1942.

The liver and kidney catalase activities of the same animal were compared in normal and tumor-bearing rats and mice. The tumor-bearing animals included dilute brown mice bearing the transplanted tumors: sarcoma 37, 180, and malignant melanoma; dilute brown × I mice bearing the transplanted hepatoma 1; C3H mice bearing the transplanted hepatoma, transplanted gastric adenocarcinoma, and spontaneous mammary tumors; strain A mice bearing a primary subcutaneous tumor (benzpyrene-induced); Osborne-Mendel rats bearing the transplanted hepatoma 31; and Buffalo rats bearing the transplanted Jensen sarcoma.

The kidney catalase activity in normal mice was about half that of the livers; in normal rats it was only slightly less than that of the liver of this species. As in previous findings, the liver catalase activity of animals bearing rapidly growing tumors was much less than that of normal animals. On the other hand, with the exception of C3H mice bearing spontaneous mammary tumors, the kidney catalase activity of tumor-bearing animals was lowered relatively little so that values for catalase activity were higher for the kidney than for the liver. The decrease in catalase activity in the kidney of mice bearing spontaneous mammary tumors was greater than in the liver.

The blood catalase activity of rats bearing the Jensen sarcoma was like that of normal rats despite a lower red cell count and lower hemoglobin concentration in the blood of the former group of animals.—F. L. H.

GREENSTEIN, J. P., and STEWART, H. L. [Nat. Cancer Inst., Bethesda, Md.] NOTE ON THE ENZYMATIC ACTIVITY OF THE TRANSPLANTED ADENOCARCINOMA OF THE GLANDULAR STOMACH OF A MOUSE. J. Nat. Cancer Inst., 2:631-633. 1942.

The pepsin and thymonucleodepolymerase activity of normal gastric mucosa is compared with the enzyme activity in the transplanted adenocarcinoma of the pyloric stomach in C3H mice. The normal gastric mucosa exhibited strong pepsin activity at pH 1.39 and none at pH 5.03 as determined by hydrolysis of egg albumin and horse serum substrates. The gastric adenocarcinoma had no protease activity at either pH. Similar results were obtained in determinations of the milk-clotting activity of the two tissues.

The thymonucleodepolymerase activity of the gastric adenocarcinoma was like that of the normal gastric mucosa but considerably less than the activity of normal intestinal mucosa and intestinal adenocarcinoma.— F. L. H.

LIPPINCOTT, S. W., and MORRIS, H. P. [Nat. Cancer Inst., Bethesda, Md.] PATHOLOGIC CHANGES ASSOCIATED WITH RIBOFLAVIN DEFICIENCY IN THE MOUSE. J. Nat. Cancer Inst., 2:601-610. 1942.

C3H mice of both sexes were placed on a basal diet at weaning or at 3 months of age. A control group of 20 mice received this diet plus 10 mgm. of crystalline riboflavin. Another group was maintained on the basal diet

until the state of acute deficiency was produced and then given sufficient riboflavin to produce a state of chronic partial ariboflavinosis.

The animals of the control group grew about as well as did those on a stock diet of natural foodstuffs and showed no lesions. The young mice on the deficient diet had a maximum life span of 8 weeks. They showed retarded growth, thinned hair about the snout, ears, scapulae, and forelegs, and cracks and fissures on the snout and legs. The adult mice during a life span of 14 weeks lost weight and were similar in appearance to the young mice.

The young mice suffering a chronic partial deficiency for at least 3 months appeared smaller than the controls and exhibited more frequent and intensified cutaneous lesions. The animals assumed a hunched position on standing and on walking showed a dragging, jerky gait with mild ataxia.

The internal viscera showed no obvious lesions in mice of any group but were generally smaller than normal. Lesions were observed only in the skin, nervous system, and eyes. The skin showed atrophia and hyperkeratotic dermatosis followed occasionally by dermatitis. Myelin degeneration appeared in the spinal cord chiefly in mice in the chronic deficiency state. In the eye keratitis and occasionally the capsulolenticular type of cataract were present.—F. L. H.

MORRIS, H. P., and LIPPINCOTT, S. W. [Nat. Cancer Inst., Bethesda, Md.] PRODUCTION OF GASTRIC LESIONS IN RATS BY FASTING, PARTIAL INANITION, AND DEFICIENCY OF CERTAIN DIETARY CONSTITUENTS. J. Nat. Cancer Inst., 2:459-477. 1942.

Fourteen groups of 20 to 25 three month old Wistar strain rats were used in studying the relation of fasting, partial inanition, and specific deficiencies of protein, fat, or carbohydrate, to the production of papillomas of the forestomach or ulcers of the glandular portion of the stomach of the rat.

It was found that both types of lesions occurred after fasting and partial inanition. Choline in the drinking water increased the survival of fasting rats, but did not prevent lesions in the forestomach, and choline in 25% aqueous glucose solution prevented the formation of glandular ulcers in an otherwise fasting rat. Small amounts of any energy-producing food helped to prevent the formation of papillomas. Papillomas that formed during a 7 day period of fasting disappeared most rapidly after rats were placed on a fat-deficient diet, less rapidly on a diet deficient in carbohydrate, and least rapidly on a protein-deficient diet. Rats fed any of these diets without a preliminary fasting period did not tend to have increased numbers of papillomas, and under these conditions no papillomas became malignant. Such diets were not factors in the genesis of glandular ulcers.

Microscopic examination of material from 225 rats showed that a circulatory disturbance in the peripheral capillaries of the glandular mucosa followed by a local interference in nutrition resulted in necrosis of the acini and the overlying mucus-secreting cells, with the formation within 5 to 14 days of superficial mucosal ulcers. It was not primarily a break in continuity of the layer of mucus-secreting cells *per se* that initiated the formation of this type of ulcer.—F. L. H.

ROBERTSON, W. v.B., and KAHLER, H. [Nat. Cancer Inst., Bethesda, Md.] RIBOFLAVIN CONTENT OF TUMOR TISSUES. J. Nat. Cancer Inst., 2:595-600. 1942.

A fluorometric method, described in detail, was used in determining comparative amounts of riboflavin in primary and transplanted mouse hepatomas, and in fetal, normal, and regenerating livers of rats and mice.

Free riboflavin made up about 25% of the total amount in both hepatoma and liver. The riboflavin concentration in normal liver was 3 to 6 times that in primary or transplanted liver tumors on both a wet weight and a dry weight basis. Values for fetal liver and for tumors of 15 types ranged from 20 to 30 μgm. of riboflavin per gm. of dry tumor with the exception of mouse hepatomas, spontaneous and induced, in which the values were higher.

The total solids of 12 tumors ranged from 17 to 20% while mouse hepatomas contained 24%. The macroscopically normal livers of all tumor-bearing rats and mice had less total solids than the livers of normal controls but riboflavin was lowered only in the rats bearing hepatoma 31.—F. L. H.

WHITE, J., and EDWARDS, J. E. [Nat. Cancer Inst., Bethesda, Md.] EFFECT OF DIETARY CYSTINE ON THE DEVELOPMENT OF HEPATIC TUMORS IN RATS FED p-DIMETHYLAMINOAZOBENZENE (BUTTER YELLOW). J. Nat. Cancer Inst., 2:535-538. 1942.

Male and female Osborne-Mendel rats were raised from weaning to a weight of 75 to 86 gm. on an adequate basal diet of relatively low protein content. *p*-Dimethylaminoazobenzene was then added to the diet (60 mgm. per 100 gm. of diet). At this time, one group of rats was given a 0.5% *l*-cystine supplement (high cystine-*p*-dimethylaminoazobenzene diet) while a second group received no supplement (low cystine-*p*-dimethylaminoazobenzene diet). Two groups of rats ingesting the high and low cystine diet, respectively, with no *p*-dimethylaminoazobenzene supplements were used as controls. Results are presented only for animals that had been on the *p*-dimethylaminoazobenzene diets and were studied pathologically. The tumors of the liver were first detected by palpation through the abdominal wall. From 120 to 500 days after the beginning of the experiment the animals were killed and autopsied. The liver and other tissues were examined microscopically.

At the end of 200 days, 96.3% of the autopsied rats that had ingested the high cystine-*p*-dimethylaminoazobenzene diet proved to have developed primary hepatic carcinoma, while only 15.4% of the autopsied animals that had been on the low cystine-*p*-dimethylaminoazobenzene diet had developed such tumors. At 390 days, 61.4% of the autopsied rats of the low cystine group had developed hepatomas; and at 500 days only 60.0% of the total number in this group had developed cancer of the liver. The conclusion is reached that the major effect of the low cystine diet was to increase the latent period rather than to prevent tumor formation.—F. L. H.

Milk Influence

BITTNER, J. J. [Roscoe B. Jackson Memorial Lab., Bar Harbor, Maine] THE MILK-INFLUENCE OF BREAST TUMORS IN MICE. Science, 95:462-463. 1942.

This report presents further data on the characteristics of the active milk influence that plays an important role

in the development of spontaneous carcinoma of the mammary glands of mice.

Females were selected from the fostered C3H strain (with normal breast tumor incidence of 2%) and from the BAF_1 hybrids (C57 black ♀ × A ♂, with normal breast tumor incidence of 1%). They were given, by mouth or by subcutaneous or intraperitoneal injection, filtrates or extracts of glycerin-treated mammary tissue from lactating mice. Sixty-three experimental mice gave a mammary tumor incidence of 41%. Thirty-six mice receiving unfiltered or untreated material showed an incidence of 67%.

Previous studies have indicated that the milk influence is not inactivated by desiccation. After ultracentrifugation the active influence appeared in traces in the fat fraction and in the final supernatant fluid. It is possible that the active agent is a colloid of high molecular weight.—M. B.

BRYAN, W. R., KAHLER, H., SHIMKIN, M. B., and ANDERVONT, H. B. [Nat. Cancer Inst., Bethesda, Md.] EXTRACTION AND ULTRACENTRIFUGATION OF MAMMARY TUMOR INCITER OF MICE. J. Nat. Cancer Inst., 2:451-455. 1942.

Fresh tissue of spontaneous mouse tumors from C3H females was ground with sand, diluted with 0.9% NaCl to a 20% by volume solution, and fed in 0.2 or 0.4 cc. amounts to 46 female mice 7 to 14 days of age. The high and significant tumor incidence (45.6%) shows the presence of mammary tumor inciter in such extracts.

Milk from C3H female mice, after separation of the cream and some of the heavy curd, was centrifuged for 1 hour at 60,000 times gravity in the ultracentrifuge. The resultant fractions consisted of (1) a clear, slightly yellow, supernatant fluid, and (2) an opaque, chalky white pellet surmounted by a thin layer of clear, amber-colored, gelatinous material at its centripetal surface. After the pellet material was suspended in phosphate buffer (pH 7.0, $M/15$) and diluted to the original ultracentrifuged volume of 4.5 cc., each fraction was fed in 0.2 cc. quantities to 17 mice. Twenty-three mice served as controls. The test animals were C3H females that had been removed from their mothers (high tumor strain) and foster nursed by C57 black (low tumor strain) mothers. The incidence of tumors was: pellet suspension 82.3%, supernatant 41.2%, and controls 4.3%. The differences between groups were significant. From 79% to 96% of the tumor-inciting agent was estimated present in the pellet suspension with 4% to 21% remaining in the supernate.—F. L. H.

Immunology

GROSS, L. [Inst. Pasteur, Paris, France] A PROPOS DE LA NATURE DE L'IMMUNITÉ ANTI-NÉOPLASIQUE CHEZ LE LAPIN. [CONCERNING THE NATURE OF ANTI-TUMOR IMMUNITY IN THE RABBIT] Bull. internat. Acad. polon. d. sc. et d. lett., Cl. méd., 581-584. 1938.

The mechanism of immunity acquired against the Brown-Pearce epithelioma was investigated in male rabbits recovered from intradermal implants of this tumor. Active tumor cell suspension was injected in both testicles of the immunized animals; after an interval of 1 to 16 days, one of the testicles was removed from each animal, ground, and the resulting suspension injected into testicles of normal rabbits. It was observed that the tumor cells remaining as long as 7 days in the testicles of the immunized animals proved viable and capable of producing fatal metastases when removed and implanted in new animals. The same tumor cells lost their potency after 24 hours when placed *in vitro* in the incubator at 37° C., or after 48 hours when placed in a collodion sac in the peritoneum of a normal rabbit, or in from 1 to 3 days when injected into testicles of normal guinea pigs.—Author's abstract.

Transplantation

HOFFMAN, J. G., GOLTZ, H. L., REINHARD, M. C., and WARNER, C. G., [State Inst. for Study of Malignant Diseases, Buffalo, N. Y.] QUANTITATIVE DETERMINATION OF THE GROWTH OF A TRANSPLANTABLE MOUSE ADENOCARCINOMA. Cancer Research, 3:237-242. 1943.

The rate of growth of the tumor known as the Marsh-Simpson mouse adenocarcinoma was determined in the following manner: Suspensions of known numbers and sizes of live tumor cells were inoculated into 317 mice of the Marsh-Simpson strain, and the relation was established between the number of cells inoculated and the latent period (time in days from inoculation of the cells to palpation of the tumor). When the tumor reached approximately 0.1 cc. in size, it was removed and measured by means of a special volumetric pipette. The three values, final volume (V), volume of the cells inoculated (V_0), and time (t), were plotted and showed that the rate of growth was exponential; the exponent μ in the equation $V = V_0 e^{\mu t}$ was 0.37 per day.—Authors' abstract.

Cytology

DALTON, A. J., and EDWARDS, J. E. [Nat. Cancer Inst., Bethesda, Md.] MITOCHONDRIA AND GOLGI APPARATUS OF INDUCED AND SPONTANEOUS HEPATOMAS IN THE MOUSE. J. Nat. Cancer Inst., 2:565-575. 1942.

The mitochondria and Golgi apparatus of induced and spontaneous hepatoma cells are compared with those of normal hepatic cells and with those of livers after partial hepatectomy, bile duct ligation, and CCl_4 treatment. Mitochondria of cells of induced hepatoma are regularly fine filaments while those of the spontaneous hepatoma are spherical. The mitochondrial type characteristic of a primary hepatoma is also characteristic of the tumor in transplant. The Golgi apparatus of hepatoma cells is in the form of a variably condensed juxtanuclear network.

It is suggested that some relationship exists between the presence of this type of Golgi apparatus and the absence of exocrine secretory activity in the hepatoma cell.

The diagnostic value of the mitochondria and the Golgi apparatus with respect to neoplasms of the mouse liver is discussed.—F. L. H.

MOTTRAM, J. C. [Mt. Vernon Hosp., Northwood, Middlesex, England] OBSERVATIONS ON THE MORPHOLOGY OF TUMOUR CELLS. J. Path. & Bact., 54:511-514. 1942.

In 2 cancer cases large numbers of free malignant cells were present in aspirated pleural exudates. The cells were in good condition and many were seen dividing. Films were made of these cells for morphological study. Cell diameters ranged from 10 μ to nearly 70 μ, and the shapes of the nuclei varied considerably. Binucleate cells were seen as well as mononuclear and multinucleate giant cells.

Occasionally clusters of cells were observed that had originated presumably as the result of cells dividing but not separating. The cells of each cluster tended to be of the same morphological type. These observations are adduced as confirmatory evidence of the view previously advanced by the author as the result of the study of tar tumors of mice, that primary tumors are composed of groups of similar cells, which vary in morphology and in growth rate from group to group.—R. J. L.

Review

MURPHY, JAS. B. [Rockefeller Inst. for Med. Research, New York, N. Y.] AN ANALYSIS OF THE TRENDS IN CANCER RESEARCH. J.A.M.A., 120:107-111. 1942.

A lecture reviewing the evidence on the etiology of cancer, with the conclusion that at the present time there is no theory concerning the nature of the disease sufficiently comprehensive to be taken seriously. The experimental results offer definite support for certain conclusions. Malignancy is a universal cell potentiality in that any cell has inherent in its makeup the latent capacity for unlimited or uncontrolled growth. The degree of this potentiality for malignancy is a variable quantity for each tissue or cell type, and this degree is determined largely, if not entirely, by hereditary or predisposing factors. The malignant potentiality of a cell may be developed in the more sensitive subjects by the strain of normal physiological processes but may be set off even in resistant groups by a variety of inciting agents. The change from a normal to a malignant cell represents an alteration in the cell itself by virtue of which proliferation becomes an automatic process independent of a continuously acting provocative agent. The new property of the cell appears to develop suddenly, and this becomes a fixed character, which is transmitted to all its descendents. It may possibly be the result of a somatic mutation. There is insufficient indication at present that viruses play any important role in the general picture.—H. G. W.

Miscellaneous

REICH, C., and DUNNING, W. F. [Coll. of Physicians and Surgeons and Lenox Hill Hosp., New York, N. Y., Wayne Univ. Coll. of Med. and Detroit Inst. of Cancer Research, Detroit, Mich.] STUDIES ON THE MORPHOLOGY OF THE PERIPHERAL BLOOD OF RATS. I. NORMAL RATS. Cancer Research, 3:248-257. 1943.

The peripheral blood picture was studied in a series of 2,656 rats that included both sexes from 7 inbred strains and a group of hybrids at age levels varying from nearly full term embryos to over 400 days. Significant differences were observed in the mean hemoglobin values and the red and white cell counts in several inbred strains. Rats under 100 days of age had lower hemoglobin values and red and white cell counts with a lower percentage of polymorphonuclear leucocytes and higher percentages of lymphocytes and monocytes than older rats. Cyclic changes in hemoglobin values and red cell counts were observed in pregnant and lactating females, but the white cell counts and differential values were little affected by either pregnancy or lactation. The maximum decrease in hemoglobin value and red cell count was observed during the first 7 days after birth. The strains with the longest average life span had the highest mean white cell count and the greatest proportion of polymorphonuclear neutrophil leucocytes. The lowest mean hemoglobin value was observed in the strain of rats with a history of the highest spontaneous tumor incidence.—Authors' abstract.

DUNNING, W. F., and REICH, C. [Wayne Univ. Coll. of Med. and Detroit Inst. of Cancer Research, Detroit, Mich., and Coll. of Physicians and Surgeons and Lenox Hill Hosp., New York, N. Y.] STUDIES ON THE MORPHOLOGY OF THE PERIPHERAL BLOOD OF RATS. II. RATS INJECTED SUBCUTANEOUSLY WITH CARCINOGENIC HYDROCARBONS. Cancer Research, 3:258-265. 1943.

The peripheral blood pictures of rats were studied before and after the injection of varying localized doses of methylcholanthrene or benzpyrene. No significant changes were observed in 339 rats examined from 10 to 30 days after the subcutaneous injection of 1 to 12 mgm. of methylcholanthrene. After 40 days, however, 132 rats showed a significant decrease in the mean hemoglobin value and in the mean number of red cells and a notable increase in the percentage of monocytes. Fifty days after the injection of 1 to 6 mgm. of methylcholanthrene, 153 rats showed an average decrease of approximately 3 gm. of hemoglobin per 100 cc., with little change in the mean number of red and white cells and an increase of more than 100% in the proportion of monocytes. The latter picture persisted in rats with early tumors observed 60 to 140 days and 140 to 300 days after the injection of methylcholanthrene.

A significant increase in the mean number of red cells and in the proportion of monocytes was observed in 668 rats examined from 30 to 40 days after the subcutaneous injection of 0.2 to 3.0 mgm. of 3,4-benzpyrene. When the early benzpyrene tumors were discovered 60 to 300 days after the injection, the mean hemoglobin value had decreased significantly.—Authors' abstract.

DUNNING, W. F., and REICH, C. [Wayne Univ. Coll. of Med. and Detroit Inst. of Cancer Research, Detroit, Mich., and Coll. of Physicians and Surgeons and Lenox Hill Hosp., New York, N. Y.] STUDIES ON THE MORPHOLOGY OF THE PERIPHERAL BLOOD OF RATS. III. RATS WITH INDUCED AND TRANSPLANTED TUMORS. Cancer Research, 3:266-274. 1943.

Observations were made on the peripheral blood of rats with methylcholanthrene or benzpyrene tumors and of rats with progressively growing transplanted sarcomas of diverse origin. The peripheral blood pictures of 101 rats with advanced tumors induced by 1 to 3 mgm. of methylcholanthrene and of 122 with tumors induced by 4 to 10 mgm. of methylcholanthrene were compared with their blood pictures before injection, after injection, and when the growths were first discovered. Similar observations were made on 101 rats with advanced neoplasms induced by 0.2 to 2.0 mgm. of benzpyrene and of 89 with tumors induced by 2.0 to 3.0 mgm. of benzpyrene. In each group the continued growth of the tumor reduced the hemoglobin value and the red cell count and significantly increased the total white cell count and the percentage of polymorphonuclear neutrophil leucocytes. Observations on 431 rats bearing progressively growing transplanted sarcomas of 7 different strains showed that the progressive growth of each of these significantly reduced the hemoglobin value and increased the white cell count and the

percentage of polymorphonuclear leucocytes. The degree of anemia observed in the hosts of induced and transplanted sarcomas seemed to be related to the malignancy of the neoplasm, but the leucocytosis was apparently independent.—Authors' abstract.

TUBOI, S. [Path. Inst. d. med. Akad., Kioto.] INFLUENCE OF POTASSIUM α-NAPHTHALENE ACETATE UPON THE GROWTH OF MOUSE AND RAT CARCINOMAS. Mitt. a. d. med. Akad. zu Kioto, 32:176-188. 1941.

Mice with growing transplants of the Bashford carcinoma, and rats with growing transplants of the Sasaki-Yoshida hepatoma were treated daily with subcutaneous injections of respectively 0.5 and 1.5 cc. of a 1% solution of potassium α-naphthalene acetate. This substance (hormodin B, Boyce Thompson Institute) is effective in promoting the growth of various plant tissues. After 3 weeks of such treatment, the tumors in the treated groups were somewhat smaller than the tumors in the control animals, which had received similar daily injections of saline solution. The author concludes that α-naphthalene acetate inhibits the growth of carcinoma.—A. C.

COMPARATIVE ONCOLOGY

EDWARDS, J. E., ANDERVONT, H. B., and DALTON, A. J. [Nat. Cancer Inst., Bethesda, Md.] A TRANSPLANTABLE MALIGNANT HEMANGIOENDOTHELIOMA OF THE LIVER IN THE MOUSE. J. Nat. Cancer Inst., 2:479-490. 1942.

The original tumor, a solitary, spontaneous hemangioendothelioma found in the liver of a 15 month old male C3H mouse of the Andervont line, was successfully transplanted subcutaneously into 4 mice of the same line, 2 of these showing hepatic metastases. Transplantation has been continued from one subcutaneous transplant and from the liver metastasis in the same mouse for 5 and 4 generations respectively. The rate of growth has increased in successive transplants.

Histologically, the primary tumor had the appearance of a typical cavernous hemangioendothelioma. The transplanted tumors differed from the primary tumor only in details, such as evidence of less differentiation and of greater rate of growth of tumor cells, and the presence of numerous solid sheets of cells. The metastases were similar in general structure to the primary neoplasm; there were a few small, solid areas of cells.

Although the picture of the primary tumor suggested a benign character, the occurrence of liver metastases in 2 mice bearing transplanted tumors attested to its actual malignancy. The difficulty of correlating the expected behavior of a hemangioendothelioma with its histologic picture is stressed.—F. L. H.

EDWARDS, J. E., DALTON, A. J., and ANDERVONT, H. B. [Nat. Cancer Inst., Bethesda, Md.] PATHOLOGY OF A TRANSPLANTABLE SPONTANEOUS HEPATOMA IN A C3H MOUSE. J. Nat. Cancer Inst., 2:555-563. 1942.

Studies on a transplantable hepatoma arising spontaneously in a male mouse of the C3H strain are presented. The primary tumor and all transplants exhibited the structure of a well differentiated hepatoma. The tumor cells of the transplants contained fat and glycogen but little or no stainable alkaline phosphatase. The Golgi apparatus of the cells was similar to that in induced hepatomas of the mouse and rat and differed from that in the parenchymal cells of normal and regenerating liver. The mitochondrial pattern differed both from that in the cells of normal liver and from that in induced hepatomas.

The weight of evidence indicates that the spontaneous hepatoma of the mouse is a neoplasm, but whether it is benign or malignant is as yet an unsettled matter.—F. L. H.

LUCKÉ, B. [Univ. of Pennsylvania Sch. of Med., Philadelphia, Pa.] TUMORS OF THE NERVE SHEATHS IN FISH OF THE SNAPPER FAMILY (LUTIANIDAE). Arch. Path., 34:133-150. 1942.

Nerve sheath tumors have been found in 76 fish representative of 3 species of the snapper family. These tumors have been observed in no other species, though many fish have been examined. The growths were all subcutaneous, occurring particularly in the dorsal regions and the head, and although some were invasive none produced metastasis. They occurred in mature fish; the distribution was about equal in the sexes; and it is estimated that 0.5 to 1.0% of the fish in the Tortugas area were affected.—H. G. W.

NEUBUERGER, K. T., and DAVIS, C. L. [Univ. of Colorado Sch. of Med. and Hosps., and U. S. Dept. of Agriculture, Denver, Colo.] CEREBRAL TUMOR IN A DOG RESEMBLING HUMAN MEDULLOBLASTOMA. Cancer Research, 3:243-247. 1943.

A spontaneous cerebral tumor in a 3 year old male English bulldog is reported with clinical and anatomical findings. The neoplasm destroyed large areas of the brain substance, particularly the left basal ganglia, and obliterated most of the lateral ventricles. Histologically, it resembled human medulloblastoma. The probable origin of the growth was in the periventricular layers of immature cells. The differential diagnosis from oligodendroglioma and medulloblastoma is discussed.—Authors' abstract.

PAPANICOLAOU, G. N., and OLCOTT, C. T. [Cornell Univ. Med. Coll., New York, N. Y.] STUDIES OF SPONTANEOUS TUMORS IN GUINEA PIGS. II. TUMORS OF THE STOMACH AND INTESTINE. Arch. Path., 34:218-228. 1942.

About 100 spontaneous tumors have been observed in autopsies on approximately 7,000 guinea pigs. Tumors were rarely seen in animals less than 4 years old. Eight of the growths were found attached to the stomach or intestines. Four of the tumors of the stomach were classified as leiomyoma, 1 as a lipoma; of the tumors attached to the intestine, 1 was a liposarcoma and 2 were neurilemmoma. In addition to the tumors named, 1 animal had a tumor of the cervix, 1 a fibrosarcoma of the thoracic wall, and a third, an adenoma of the thyroid.—H. G. W.