Abstracts

Reports of Research

Azotoluene Bladder Tumours in Rats. STROMBECK, J. P. [Surg. Clin., Lund, Sweden] *J. Path. & Bact.*, **58**:275-278. 1946.

Azotoluene given by the mouth to rats does not produce neoplastic changes in portions of the bladder transplanted to the liver.—E. L. K.

The Induction of Mammary Carcinoma in "IF" Mice by Cutaneous and Intraperitoneal Administration of Methylcholanthrene. ORR, J. W. [Dept. Exper. Path. and Cancer Research, Univ. of Leeds, Leeds, England] *J. Path. & Bact.*, **58**:589-592. 1946.

The IF strain of mice appears to be resistant to the development of mammary cancer, only one possible mammary carcinoma having been found in an untreated female. On the other hand, fortnightly cutaneous applications of methylcholanthrene dissolved in almond oil induced mammary carcinoma, frequently multiple, in 30 of 37 females of the strain. Tumors developed in all female mice surviving this treatment for 126 days or more, the mean induction time being approximately 140 days. Intraperitoneal injections of methylcholanthrene in sesame oil induced mammary carcinoma in 1 of 12 IF mice after 105 days, the maximum survival period of the group being 113 days.—A. H.

Measurement of the Photodynamic Effect of Cancerogenic Substances with Biological Indicators. MATOLTSY, G., and FÁBIÁN, Gy. [Biol. Research Inst., Tihany, Hungary] *Nature*, **158**:877. 1946.

When *Drosophila* flies were fed in the dark on a standard diet containing carcinogens (1 mgm. per 13 gm.), the hydrocarbon could be detected in the organs and cells of of the larvae by fluorescence microscopy. The survival time after raying with ultraviolet light was found to be as follows: benzpyrene treated for 6 minutes 30 seconds; methylcholanthrene 13 minutes 35 seconds; dibenzanthracene 19 minutes 34 seconds; controls *i.e.* larvae bred on standard diet, survived 39 minutes 51 seconds. (No mention is made of controls which should have been made where fluorescent noncarcinogenic hydrocarbons were added to the diet.)—I. H.

Test of a Cancerogenic Substance in Respect to the "Non-disjunction" Frequency of the X-Chromosomes in Drosophila. FÁBIÁN, Gy., and MATOLTSY, G. [Biol. Research Inst., Tihany, Hungary] *Nature*, **158**:911-912. 1946.

Drosophila larvae and adult flies were fed on a diet containing benzpyrene, and the hydrocarbon could be detected by fluorescence microscopy in the larvae, eggs and ovaries. Some tests have been made on the effect of carcinogenic substances on *Drosophila* in respect to mutation frequency (Auerbach, C., *Proc. Roy. Soc. Edinburgh*, **60**:164; Friedrich-Freksa, H., *Biol. Zentralbl.*, **60**: 498). The results showed that the mutation rate does not increase following applications of carcinogenic chemicals. The cultures were kept in darkness, while the primary nondisjunction was investigated. Bar males and white females were used from 2 inbred stocks which had been kept pure for 5 years, and so may be considered well-balanced stocks from the point of view of modifying factors. In this standard arrangement the frequency of exceptions was 1:500, or 0.2 ± 0.05% without benzpyrene. There was not a significant difference between the control and the treated cultures in respect to the number of exceptional offspring. In a succeeding test, the adult females were fed entirely on food containing benzpyrene, and in this case, using the fluorescence microscope, it was evident that the benzpyrene was also present in the eggs when they were laid. In this test the ratio of exceptions was 1:2,300, or 0.04 ± 0.03%. The standard errors showed a statistically significant difference (0.16 ± 0.059) in the negative direction between controls and the second test. None of the treatments used gave any detectable increase in the nondisjunction frequency; but treatment with benzpyrene decreased the number of exceptional flies, that is, the mutation rate. The reason for this is not known.—I.H.

Uncoordinated Growth in Paramecium Induced by "Gammexane." LLOYD, L. [Univ. of Leeds, Leeds, England] *Nature*, **159**:135. 1947.

The γ-isomer of hexachlorocyclohexane produces in *Paramecium* large multinucleated forms, as the late J. C. Mottram observed, after treating these organisms with carcinogenic hydrocarbons.—E. L. K.

Induction of Glandular Carcinomas of the Prostate in the Mouse. HORNING, E. S. [Imperial Cancer Research Fund, London, England] *Lancet*, **2**:829-830. 1946.

The epithelium from either the anterior or dorsal lobes of the prostate of 6 months old Strong A mice was cut into strips, wrapped around some crystals of 20-methylcholanthrene, and implanted subcutaneously in male mice of the same strain. Three such grafts can be made in one host. In 10½ weeks small tumors appear; of 11 tumors 10 were glandular and 1 squamous cell in nature. Some are growing in the eighth grafted generation, and show considerable secretory activity.—E. L. K.

Significance of Carcinogenic Agents. ŠULA, J. *Časop. lék. česk.*, **80**:698-700. 1941.

The author discussed the similarity of the chemical structure of methylcholanthrene and bile acids and the

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possibility of the production of methylcholanthrene from some products of the sterol metabolism in the organism. The relationship to the sex hormones is also considered. —B. S.

Relations of Steroid Hormones and Anhydro-Hydroxy-Progesterone to Fibromatosis. IGLESIAS, R., and LIPSCHÜTZ, A. [Nat. Health Service and Univ. of Chile, Santiago, Chile] *Lancet*, **2**:488-490. 1946.

Anhydro-hydroxy-progesterone has an inhibitory action upon uterine fibroids, and to a lesser extent upon other abdominal fibroids, induced in castrated female guinea-pigs by 2-estradiol. No masculinizing action was observed. The authors suggest clinical trials of this compound, together with small quantities of testosterone propionate, in cases of uterine fibroids.—E. L. K.

Genes and Nucleoproteins in the Synthesis of Enzymes. SPIEGELMAN, S., and KAMEN, M. D. [Mallinckrodt Inst. of Radiol., and Washington Univ. Sch. of Med., St. Louis, Mo.] *Science*, **104**:581-584. 1946.

Yeast cells were grown in a medium containing radioactive phosphorus (P^{32}) for 48 hours, at which time all fractions contained P^{32} in equilibrium with the P^{32} in the medium. The cells were then washed, and were allowed to ferment glucose anaerobically in absence of nitrogen. Under these conditions no protein synthesis or cell division occurred, and there was no loss of P^{32} from the nucleoprotein fraction of the cells even though the non-nucleoprotein, acid soluble phosphorus was rapidly equilibrated with that of the medium. The same result was obtained in the presence of nitrogen when cell division was inhibited by sodium azide or dinitrophenol. When, however, the cells were allowed to synthezise protein and to divide, it was found that large amounts of P^{32} were lost from the nucleoprotein, indicating a flow of phosphate from this fraction in the course of synthesis. The same flow of P^{32} from nucleoprotein was observed when the cells were induced to form a new enzyme in the course of adaptation to a new substrate.

These results plus other evidence reviewed in this paper have led the authors to suggest that nucleoproteins are the controlling elements in protein formation. They hypothesize that genes continually give off at different rates partial replicas of themselves to the cytoplasm. These replicas are nucleoprotein in nature, possess in varying degrees the capacity for self reproduction, and together determine the types and amounts of proteins and enzymes synthesized. Furthermore, it is supposed that a competitive balance exists among the various cytoplasmic nucleoproteins, that this balance may be changed by changing certain conditions under which the cells live, and that such altered relationships among the cytoplasmic nucleoproteins may be passed on to subsequent cell generations. This theory thus attempts to bring together under a unified interpretation (1) Mendelian, or "gene" controlled inheritance, (2) cytoplasmic inheritance, (3) cellular differentiation, and (4) enzymatic adaptation. The origin of cancer as a sudden heritable change in somatic cells, analogous in many ways to enzyme adaptation or cellular differentiation, also comes within the scope of this theory.—R. B.

Ultra-Violet Absorption in Living and Dead Cells. BRUMBERG, E. M., and LARIONOW, L. TH. [Optical Inst., and Central Roentgenological, Radiological and Cancer Inst., Leningrad, U. S. S. R.] *Nature*, **158**:633-664. 1946.

An ultraviolet microscope equipped with a special achromatic objective (aperture 0.5) was employed for photographing living tissue cultures. The source of light was a high-pressure quartz mercury lamp. All radiations except of wave length 254-275 $\mu\mu$ were eliminated by filters. Focussing was performed by ordinary lighting, so that no ultraviolet rays reached the cells prior to their being photographed. When living mouse mammary carcinoma cells and mouse and chick fibroblasts were examined, only nucleoli and the cytoplasm of cancer cells revealed moderate absorption in the region 254-275 $\mu\mu$. The cytoplasm of cancer cells vitally stained with neutral red lost its capacity for absorption. Preliminary exposure of cultures to direct ultraviolet irradiation (without filters) for 2 minutes resulted in definite cytological changes. Nuclei then acquired the property of absorption and photographs presented the same appearance as those published by Caspersson.

It is suggested that desoxyribonucleic acid is contained in the nuclei of living cells in a form which does not absorb ultraviolet rays of wave length about 260 $\mu\mu$, and that absorption only occurs in injured and dead cells.—R. J. L.

Studies in Vitro on Cellular Physiology. The Effect of X-rays on the Survival of Cells. SCHREK, R. [Veterans Administration, Hines, Ill.] *Radiology*, **46**:395-410. 1946.

Cellular suspensions of thymus, spleen, bone marrow, and testes of rabbits and from leukocytes of normal and leukemic blood of men were irradiated with 20 to 5,000 r and incubated at 37° C. for 1 to 7 days. Periodic examination of cell counts and stained smears were made and graphed as to the 50 and 10 % survival time. A dose of 1,000 r to thymic and splenic suspensions produced no perceptible change in 3 hours but produced a relatively rapid decrease in the unstained cell counts after this period. Irradiated leukocytes from normal and lymphocytic blood had a shorter survival time than non-irradiated blood. Suspensions from myelogenous leukemia, bone marrow and testes showed no effect of irradiation. Tests made under anaerobic conditions showed no perceptible decrease in the number of eosin-resistant lymphocytes which had been irradiated.—R. E. S.

Mechanism of Radiation Effects Against Malignant Tumors. WARREN, S. [Boston, Mass.] *J. A. M. A.*, **133**: 462-463. 1947.

It is the radiant energy absorbed by the tissue or cell that is effective, not that which is delivered to it. The first noticeable effect on cells is interference with mitosis —both diminution in mitotic activity and the appearance of chromosomal abnormalities followed by vacuolization and swelling of the cytoplasm. There are concomitant effects produced on the connective tissue stroma and blood vessels within the irradiated area. The vascular endothelium is damaged inducing thrombosis. Hence local impairment of circulation in the tumor and tumor bed results. Hyaline changes leading to the formation of dense

collagen thus act as an added barrier to the metabolic activities of tumor cells and hinders their spread to adjacent structures. The same general order of sensitivity prevails among the tissues exposed to radiation by an atomic blast as by therapeutic means.—M. E. H.

Biochemical Aspects of Over-Activity of the Adrenal Cortex. SCOWEN, E. F., and WARREN, F. L., *Proc. Roy. Soc. Med.*, **40**:39-43. 1946

Adrenal cortical carcinoma in females of all ages is associated, except in rare cases, with increased excretion of 17-ketosteroids; an excessive excretion of dehydroisoandrosterone is characteristic of these tumors. Owing to the rarity of adrenal carcinoma in males it is not yet possible to say whether the sterol metabolism is the same in them as in female patients.—E. L. K.

The Disposition of C^{14} in Bone. BLOOM, W., CURTIS, H. J., and MCLEAN, F. C. [Univ. of Chicago, Chicago, Ill., and Monsanto Chemical Co., Dayton, Ohio] *Science*, **105**: 45. 1947.

C^{14} injected as carbonate into rats was deposited in bone primarily in non-growing areas, and persisted there apparently undiminished for the 4 months' duration of the experiment. In contrast, the C^{14} deposited in the liver and kidney remained there for only 2 weeks. The authors suggest that the health hazards involved in working with this radio-isotope of carbon should be studied with special reference to the possible development of bone tumors. —R. B.

A Plan for Analysis of the Biologic Factors Involved in Experimental Carcinogenesis of the Thyroid by Means of Radioactive Isotopes. HERTZ, S. [Boston, Mass.] *West. J. Surg.* **54**:487-489. 1946.

A plan is presented for the analysis of experimental carcinogenesis in animals, drawn up from experience to date, from the study of normal and pathologic thyroid physiology, chemistry and therapeutics by means of radioactive isotopes of iodine. It is hoped that a logical theory of carcinogenesis and an understanding of important preventive and therapeutic factors may be evolved.—M. E. H.

The Effect of Certain Azo Dyes upon the Storage of Riboflavin in the Liver. GRIFFIN, A. C., and BAUMANN, C. A. [Univ. of Wisconsin Coll. of Agric., Madison, Wis.] *Arch. Biochem.*, **11**:467-476. 1946.

Since riboflavin is known to counteract the carcinogenicity of several of the azo dyes, investigations were carried out to determine whether the effect of a given dye on hepatic riboflavin might parallel its potency in inducing liver tumors. Such a parallelism was observed. The addition of many carcinogenic azo dyes to the diet of rats caused some decrease in the riboflavin content of the liver. The decrease appeared to be roughly equivalent to the carcinogenicity of the dye: *m'*-methyl-*p*-dimethylaminoazobenzene was most effective, *p*-dimethylaminoazobenzene and *p*-monomethylaminoazobenzene were fairly effective, whereas *o'*-methyl-*p*-dimethylaminoazobenzene, *p'*-methyl-*p*-dimethylaminoazobenzene, aminoazotoluene, aminoazobenzene, or azobenzene had little or no effect.

More riboflavin was stored in the liver when the basal diet contained 24% of casein than when 12% was fed. The relative effects of the carcinogens were essentially the same on both diets.

The presence of carcinogenic azo dyes in the diet resulted in a decreased food intake, but this was not responsible for the impaired vitamin storage. Rats fed restricted amounts of the control diet free from the dye showed only a slight decrease in the total amount of riboflavin per liver while the concentration of vitamin per gm. of liver tissue was usually higher than in rats fed *ad libitum*.—Authors' abstract.

The Influence of Liver L. casei Factor on Spontaneous Breast Cancer in Mice. LEWISOHN, R., LEUCHTENBERGER, C., LEUCHTENBERGER, R., and KERESZTESY, J. C. [Mount Sinai Hosp., New York, N. Y.] *Science*, **104**:436. 1946.

Among 28 Rockland mice injected intravenously daily with 5 μgm. of fermentation *L. casei* factor over a period of 4 to 6 weeks there were 11 in which the mammary cancer regressed completely; after 100 days 23 mice were still alive. Among 39 mice injected in the same way with a daily dose of 5 μgm. of liver *L. casei* factor there was only 1 complete regression, and the mean life span was 75 days. Lung metastases in this group were more numerous than among the controls. Thirty-one additional mice were treated with daily doses of 100 μgm. of liver *L. casei* factor. In this group there were no regressions; in fact the mammary tumors grew faster than did those of the controls. The mean life span was 55 days. Among the 71 control mice there were no regressions and the mean life span was 74 days.—R. B.

Les facteurs antiblastiques d'origine alimentaire. [**The Anti-Blastic Factors of Dietary Origin.**] MAISIN, J., and POURBAIX, Y., *Bull. Assoc. franç. p. l'étude du cancer*, **29**:223-251. 1940.

A review with 31 references is presented. Protocols are presented of 13 experiments, previously reported by Maisin and his colleagues, showing the cancer-inhibiting action of various foods, including fresh beef heart, whole rye flour, and fresh baker's yeast.—G. H. H.

Tumors in Intrasplenic Ovarian Transplants in Castrated Mice. LI, M. H., and GARDNER, W. U. [Yale Univ. Sch. of Med., New Haven, Conn] *Science*, **105**:13-15. 1947.

Ovaries grafted into the spleens of castrated mice (A strain, C_3H strain, $C_3H \times A$ F_1 hybrids) developed tumors 130 to 346 days after grafting. Among 21 castrated males there developed 5 (possibly 7) granulosa cell tumors plus 1 mixed tumor. Among 33 castrated females, in which the intrasplenic ovarian grafts showed no adhesions to adjacent structures, there developed 4 luteomas plus 7 mixed tumors. Among 19 additional castrated females, in all of which the intrasplenic ovarian grafts showed vascularized adhesions, there developed only 1 luteoma in a mouse that had irregular estrus cycles during the latter part of the experimental period. No tumors developed from control grafts of ovaries into

the subcutaneous tissue of castrated females, normal and castrated males, and into the testes of normal males; except for one questionable granulosa cell tumor developing from a subcutaneously transplanted ovary in a castrated female mouse.

The development of tumors from intrasplenic ovarian grafts appears to be due to an increased production of gonadotropins in the host following castration. Grafts placed in the spleen are exposed to these hormones before they reach the liver where they appear to be inactivated. —R. B.

Hypervolemia in Mice Bearing Transplantable Granulosa Cell Tumors. FURTH, J., and SOBEL, H. [Cornell Univ. Med. Coll., and New York Hosp., New York, N. Y.] *Science*, **105**:41. 1947.

Mice bearing transplanted granulosa cell tumors were previously found to have livers and other abdominal organs congested with blood. In the present study these animals were shown to have striking increases in blood volume. By the exsanguination-perfusion technic, the blood volume, in per cent of body weight, was found to be 13.6 for the experimental mice compared with 5.2 for the controls. By the Evans blue (T-1824) dye technic, the values were 34.3 and 10.9 respectively. The hematocrit values of the blood of the experimental mice were normal, indicating a large increase in both plasma and red cells. Control mice bearing any of four other types of tumors showed no increase in blood volume.

It is suggested that the granulosa cell tumors may secrete a substance causing the hypervolemia, and that this may be accompanied by the appearance of excessive amounts of a vaso-depressor material which would account for the observed vasodilation associated with the blood volume increase.—R. B.

The "Cytogenetics" of Black and White Guinea Pig Skin. BOILLINGHAM, R. E., and MEDAWAR, P. B. [Univ. of Oxford, Oxford, England] *Nature*, **159**:115-117. 1947.

Black guinea pig epidermis "infects" and thus blackens white epidermis upon which it is grafted. This is due, not to invasion and displacement of white cells by black, but to some agent which enters the white cells and brings about a permanent heritable change that causes them and their descendents to become and remain black.—F. L. K.

Interpretive Morphology. MOORE, R. A. [Washington Univ. Sch. of Med., St. Louis, Mo.] *Proc. Inst. Med. Chicago*, **16**:306-312. 1947.

The theme of the lecture was that pathologic anatomy can take a place beside experimental pathology as a dynamic science. In the mind of the observer of morphologic changes, there may be the consideration of the contraction of muscles, the secretion by cells, the action of enzymes, and the elaboration effects of hormones, as well as parthogenetic development of the sex cell. Examples of the histogenesis and development of various tumors of the genitourinary tract served as examples.—M. E. H.

General Pathology of Tumors of Endocrine Glands. KARSNER, H. T. [Western Reserve Univ. Sch. of Med., Cleveland, Ohio] *Bull. New York Acad. Med.*, **22**:503-510. 1946.

A general review of tumors of endocrine glands including brief discussions of the genesis, morphology, chemical components and physiological manifestations of these tumors.—M. T.

Protective Action of Desoxycorticosterone Acetate Against X-Ray Induced Liver Changes. ELLINGER, F. [Long Island Coll. of Med., Brooklyn, N. Y.] *Science*, **104**: 502-503. 1946.

This paper reports a study of desoxycorticosterone acetate as a remedy for radiation sickness, this sterone being selected because it counteracts effects of histamine or histamine-like substances which may be the cause of radiation sickness.

One hundred and sixty-eight male white mice were given 500 and 1,000 r/air in one exposure or in fractions of 100 r daily. Seventy-nine of these animals were given in addition daily subcutaneous injections of 0.25 or 0.50 mgm. desoxycorticosterone acetate (in oil), the total dose varying between 2.5 and 8.0 mgm. The most striking effect of the sterone was a reduction in the amount of sudanophile fat appearing in the liver as a result of the irradiation. There was also a slight decrease in mortality among the injected animals, but no definite alteration in the radiation effects on spleen and bone marrow.—R. B.

A New Method of Making Radon Ointment. CARDENAS, L., and WEATHERWAX, J. L. [Philadelphia Gen. Hosp., Philadelphia, Pa.] *Radiology*, **46**:381-384. 1946.

A method of making radon ointment by impregnating charcoal or other adsorbent with radon is described.—R. E. S.

Les tumeurs mammaires bénignes chez l'animal. Leur intérêt biologique. [Benign Mammary Tumors of Animals. Their Biological Aspect.] ROUSSY, G., and GUÉRIN, M. [Cancer Inst., Paris, France] *Presse méd.*, **52**:313-314. 1944.

A review.—C. A.

Some Notes on the Cancer Problem. KOSOLAPOFF, G. M. [Monsanto Chemical Co., Dayton, Ohio] *Science* **104**:491-492. 1946.

In a preceding letter to *Science* (**104**:167. 1946.) K. S. Pilcher proposed that the cancer problem should be attacked through a large-scale, well planned, completely co-ordinated program directed by a group of experts following, as examples, the successful wartime programs in atomic physics, penicillin production, and so on. In the present letter Kosolapoff points out that the successful wartime programs were based on discoveries already in existence, which indicated a clearly defined line of approach. No such clear-cut line of approach to a solution of the cancer problem can be said to exist at present. Therefore, while promising fields of investigation now known should be supported in co-ordinated research, there should be at least equal support given to independent groups of investigators not tied to any definite approach.—R. B.

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