
A chromatographic fractionation of Scottish blue shale oil yielded a carcinogenic fraction (a) showing the fluorescence spectrum of 3,4-benzpyrene; oxidation and reductive methylation of this fraction produced the fluorescence bands of a mixture of 5,8- and 5,10-dimethoxy-3,4-benzpyrene, thus providing additional evidence of the presence of the parent compound, which was not isolated; and a more strongly carcinogenic fraction (b) in which the spectrum of 3,4-benzpyrene was absent. By comparison of the fluorescence spectra with those of standard solutions, the authors estimate the amount of 3,4-benzpyrene in crude shale oil at 0.01%, and in coal tar at 1.5%. In the light of experiments with solutions of the pure compound the authors consider that there is not enough benzpyrene in any fraction of shale oil to account for any large part of its carcinogenic power. Probably the unknown carcinogenic compound or compounds would be isolated more easily from coal tar, in which they are present. From coal tar, benzpyrene-free fractions can be obtained that are more strongly carcinogenic than is a saturated solution of benzpyrene in benzene. Chloroform extracts of unheated shale yield no spectroscopic evidence of the presence of benzpyrene; whether they contain other carcinogenic compounds is as yet uncertain.—E. L. K.


Naphthalene was fed to rats, either dissolved in warm liquid paraffin and given by stomach tube, or mixed with the stock diet to the extent of 1%. As a result, a compound was excreted in the urine, which upon decomposition by acid at pH 1.5 to 2.5 at room temperature yielded naphthalene. Thirteen to 17% of the naphthalene administered was thus recovered. In experiments in which phenanthrene or anthracene was fed, 4% to 7% and 1% to 2.5% of the phenanthrene or anthracene, respectively, were recovered in the urine.

When rats were fed diets containing 1% acenaphthene, chrysene, 3,4-benzpyrene, 1,2,5,6-dibenzanthracene, or methylcholanthrene, no liberation of hydrocarbon was detected in the acidified urine.—M. B.


A lecture that includes a discussion of the carcinogenic action of "styryl 430." When injected subcutaneously (6 to 10 mgm. in mice, or twice such amounts in rats) in water the compound is precipitated by the serum as deep red granules that are gradually taken up by phagocytes; some diffusion over the rest of the body must take place as the substance is trypanocidal. A minute mass of tissue is formed composed of phagocytes packed with red granules; if a tumor develops, non-pigmented areas of sarcoma cells appear among the phagocytes, and the nuclei of some of the phagocytes enlarge. Amounts of 0.1 mgm. can be detected in the subcutaneous tissues for over a year but do not produce tumors. Peritoneal injection, even of large doses, has given negative results. Persistence of a local deposit is necessary; thus intramuscular injection in fowls, when no deposit is formed, does not produce tumors. In rats, numerous metastases occur. The compound is not estrogenic, and no growth-inhibiting action has been detected. A number of other dyes that form similar persistent deposits, and more soluble styryl compounds, have given negative results; the only other carcinogenic compound discovered has been a close analogue of "styryl 430" which is likewise very little soluble in serum. The tumors are not filtrable and are not propagated better by finely ground material than by ordinary grafts (Peacock).—E. L. K.


Three procedures are described for the preparation, from the nonsaponifiable fraction of human livers, of neutral oils exhibiting intense blue or bluish-green fluorescence. Concentrates of a grossly similar character have been obtained from healthy livers, livers of cancer patients showing no liver metastases, and the liver of a patient with lymphosarcoma and hepatic necrosis. The concentrates obtained by the 3 different methods all have ultraviolet absorption spectra with a maximum or plateau at 2550-2600 A., but neither the ultraviolet nor the fluorescence spectra show the fine-banded structure of the type associated with polynuclear aromatic hydrocarbons. The quenching effect of oxygen on the intensity of fluorescence is less than that usually observed for solutions of such hydrocarbons.

The fluorescing component of the concentrate exhibits considerable chemical stability. It is not affected by N aqeous hydrochloric acid or by alkali, nor does it react with reagents that attack the hydroxyl group (succinic

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anhydride, pyridine-sulfur trioxide) or with digitonin, Girard’s reagent, maleic anhydride, or an aqueous solution of sodium hydrosulfite. It appears to be adsorbed specifically on picric acid from an ethanolic solution. Although the spectrographic data do not encourage the view that the fluorescing substance is a polynuclear aromatic hydrocarbon, it has been demonstrated that methylcholanthrene, when added to liver tissue, accumulates in the same fraction.—Authors’ abstract.


Berman and others have drawn attention to the high incidence of cirrhosis, and primary cancer, of the liver in the Bantu of South Africa (abstracted in Cancer Research, 1:176-177, 915. 1941; 2:591. 1942.) The question arises, whether these conditions are due to racial or environmental factors. “Malnutrition among the Africans is widespread in South Africa. The overwhelming majority feed on a diet consisting largely of maize meal (mealie meal) and sour milk. This forms the staple from the time of weaning throughout life.” One hundred and twenty-five rats (40 to 50 gm. weight) were fed solely on mealie-meal porridge and sour milk. No obvious signs of avitaminosis were seen. After 14 months 12 rats were killed, these showed: (a) in the liver either enlargement and fatty change or various degrees of nodular cirrhosis; in one case the left lobe was reduced to 2 small cirrhotic nodules while the right lobe was greatly enlarged; (b) enlargement of heart; (c) thickening of skull; (d) fracture and loosening of upper incisors; (e) enlargement of pituitary.

No such changes in the liver had been seen in several thousand other rats. No tumors are mentioned.—E. L. K.


Mammary tissue of rats (Long-Evans strain) was analyzed, at the end of pregnancy and at the height of lactation, for dry matter and nitrogen content, and its metabolic rate was measured in vitro. It was found that lactation increased the water content of the mammary tissue and the protein content of the mammary dry matter. Lactation did not affect the metabolic rate per unit of fresh tissue in vitro; it increased the metabolic rate per unit of dry matter and decreased the metabolic rate per unit of nitrogen in the tissue.—M. B.


Seven strains of transplanted sarcomas, derived from mouse subcutaneous fibroblasts that had been subjected to various dosages of 20-methylcholanthrene in tissue culture, were found to possess a metabolism highly characteristic of malignant tumors generally, with respect to all criteria tested, including anaerobic glycolysis, aerobic glycolysis, respiratory quotient, oxygen consumption, oxidation re-serve (increase in oxygen consumption on addition of succinate or phenylalanine), Pasteur effect, Meyerhof quotient, extent quotient, and fermentation excess. The biotin and niacin contents of these tumors of in vitro origin were likewise typical of values found in malignant tumors of in vivo origin, whether spontaneous or induced.

The metabolism of the 7 strains of tumors was qualitatively and quantitatively very similar. Analysis of the data indicated, however, a rough, second-order correlation between minor differences in the anaerobic glycolysis values of the tumors and previously reported differences in growth rates and inoculation responses of the original tissue cultural strains. Lowering the pH of the medium containing the tumor tissue slices caused a considerably greater decrease in anaerobic glycolysis in the case of the 3 least altered strains, HW, D, and H, as compared with the 4 most altered tumor strains, J, L, N, and O. This suggests that a more specific correlation between degree of malignancy and ability to glycolyze might be obtained at pH values considerably below that of blood, but closer to those that probably prevail within the tumor intercellularly.—Authors’ summary.


Strain dba mice painted with methylcholanthrene developed essentially the same incidence of leukemia on diets with or without adequate lysine. The data suggest that cystine played a role in the development of induced leukemia, perhaps not associated with its properties as an essential amino acid for growth, but with some other undetermined property. The addition of gelatin to a low cystine diet altered the occurrence of leukemia following methylcholanthrene painting from 10 to 32%. This increase was attributed to the small amount of cystine present in gelatin. The incidence of leukemia in methylcholanthrene-painted mice was increased to the same extent when the low cystine diet was supplemented with methionine as with cystine.—Authors’ summary.


A comparison was made of the incidence of leukemia in physicians and in the general population. Data were obtained from the death lists of the Journal of the American Medical Association, from the mortality reports of the United States Bureau of the Census, and from unpublished compilation of the United States Public Health Service. Comparisons were made on the basis of (1) the ratio of deaths from leukemia to deaths from cancer, (2) the ratio of deaths from leukemia to total death rates, and (3) death rates from leukemia.

Leukemia was recognized approximately 1.7 times more frequently among physicians than among white males in the general population. Possible discrepancies in the data are discussed. While these observations furnish no direct proof that radiation acts to incite leukemia in human beings, they are, nevertheless, in accord with the findings on experimental animals in which exposure to
x-rays has been found to increase the incidence of leukemia.—Authors’ summary.


Spontaneous mammary cancer in virgin C3H female mice showed the same increased incidence in cool environments that was previously found in virgin dba females under these conditions. The tumors appeared 1 month earlier and grew faster at 68°F. F, although they killed the hot-room mice more quickly. In this C3H strain series multiple tumors were 4 times more frequent among mice in the cold-room than among those kept in the heat.—Authors’ summary.


The production of fibromas in female guinea pigs by estrogens (Lipschütz, A., and Iglesias, R. Compt. rend. Soc. de Biol., 129:519-524. 1938) is prevented by simultaneous administration of certain steroids (the naturally occurring progesterone, desoxycorticosterone, dehydrocorticosterone, and testosterone; and dihydrotestosterone, which has not been found in the body). All these 5 compounds are 3-keto-steroids; the last-named lacks the double bond Δ4 which is therefore not essential. Two other compounds lacking this double bond (pregnanedione and allopregnanedione), but having the same side-chain at C17 as progesterone, were inactive, as was also Δ6 dehydroprogesterone, which differs from progesterone by a double bond in ring IV. The activity of testosterone was abolished by oxidation at C17 (Δ4-androstene-3,17-dione) or by elongation of the side-chain (cholesterone). Compounds having hydroxyl at C3 (acetoxypregnenolone, androsterone, androstanediol, and androstenediol) were inactive. All antifibromatogenic 3-keto-steroids are to a varying extent progestational, and no inactive 3-keto-steroid, with the possible exception of androstenediol, is known to be progestational. There is no uniform relation between antifibromatogenic, and either masculinizing or antiestrogenic, activity.—E. L. K.


A technique is described for mice and guinea pigs that permits the intraocular transplantation of brain tumors, both those induced with a chemical carcinogen in mice and those occurring spontaneously in man. This method of study affords the opportunity of keeping the growing neoplasms under constant observation. It has demonstrated certain characteristics of neoplastic growth behavior and appearance that permit differentiation of gliomas from nongliogenous tumors. It has demonstrated, by the standard of autonomous growth in homologous and heterologous strains of mice, that experimentally induced brain tumors represent true neoplasms.—Authors’ summary.


The following conclusions are drawn concerning the Harding-Passey mouse melanoma: (1) Variations in the age of the host did not influence the outcome of transplanation. (2) Suckling mice offered a favorable soil for the continued growth of the melanoma. (3) The survival time after grafting was the same for sucking mice and for adults. (4) Castration in males and females did not significantly affect the growth of the neoplasm. (5) The growth capacity of the melanoma was completely destroyed by immersion in a buffer solution at pH 4 or 10, and at pH 5 or 9 partial inhibition and delayed growth were found. No effect was observable at pH 6, 7, or 8. (6) The viability of the melanoma was completely destroyed by dehydration from the frozen state. (7) The tumor was not filtrable. (8) Grafts grew equally well in C57 black, dba, C3H, agouti, Rockland, Bagg, Swiss, and Paris albino mice. (9) During the past 15 years the tumor has been propagated through many generations by successive graftings. So far no nonpigmented melanoma has appeared.—Author's abstract.


The following observations have been made: Tumor cells introduced into chick embryos by the yolk injection technic become implanted on the mesoderm outside of the endoderm. This is possible because at the time of injection the yolk is not yet enclosed by endoderm. The endoderm grows under some of the injected cells, leaving them in contact with the developing mesoderm, which furnishes the blood supply necessary for further growth. Implantation can occur only before the endoderm encloses the yolk. Experience has shown that the 4 day egg is the most favorable for injection. The most successful implantation is obtained by forcible injection of tumor tissue and by frequent rotation of the egg.—Authors' abstract.


Repeated injection of a solution of mercury-indigo-disulphonate directly into mammary tumors of 40 mice was followed by disappearance of the growths in 30 animals and by regressing of the tumors in the remaining 10. No case of retrogression or disappearance of cancer was noted in the control mice. (The number of mice and the treatment in the controls was not stated.)—A.C.


Recent experiments demonstrate clearly that mammary cancer in mice is communicable from one generation to another. Animals transmitting the disease are, as a rule, carriers of a latent tumor factor and do not themselves display symptoms until they reach the "tumor age." The development of mammary cancer can be entirely avoided in susceptible mice by preventing newly born animals from nursing their potentially cancerous mothers.
The available data on accidental or intentional inoculation of human cancer are reviewed, and the appearance of tumors in several members of the same or successive generations in man is discussed. The conclusion is suggested that human cancer may be similar to that observed in mice and may also, perhaps, be communicable from one generation to another.

Since milk seems mainly responsible for the transmission of certain tumors such as mammary carcinoma, it is suggested that the women of families with any malignant tumors in their ancestry refrain entirely from nursing their progeny. Artificial feeding should be substituted from birth, at least for one generation. This simple preventive measure may bring substantial rewards in the fight against cancer, although results will not become evident until the next generation reaches the tumor age.—Author's summary.

**Chemistry and Cancer.** Cook, J. W. [Univ. of Glasgow, Glasgow, Scotland] Royal Inst. of Chemistry of Great Britain and Ireland. 1943.

A lecture.—E. L. K.

### Clinical and Pathological Reports

#### Etiology


The prevalence of syphilis in a sample of 7,761 cancer patients reported in upstate New York in 1940-1941 was determined by comparing cancer case reports with the registers of reported syphillis cases. Of 3,151 white male cancer patients 3.2% were found also to have been reported as syphilitic. Of 4,610 white female cancer patients 1.7% were found to have syphilis. Syphilis prevalence among males with tongue cancer and females with cervix cancer was significantly greater than in patients with cancer of other sites.

On the basis of the present findings, special efforts are indicated toward early discovery of cervix cancer in women who have had syphilis.—J. L. M.

#### Radiation—Diagnosis and Therapy


Ewing's sarcoma and sympathetic neuroblastoma present definite similarity in histopathology and radiographic appearance. Case histories are given of 4 children with widespread bone tumors, 2 of whom died of the former, and 2 of the latter disease. The differential diagnosis in each case could be made only at postmortem examination.

The author feels that cases of solitary bone tumor diagnosed as Ewing's sarcoma should be treated as if the bone tumor were secondary to an abdominal tumor whether the presence of the latter can be established or not. Amputation for cure should probably not be attempted, and x-ray treatment to retroperitoneal structures should be routine.—E. H. Q.


The biologic, photochemical, and clinical aspects of tissue recovery from radiation are discussed, and a distinction is made between "true recovery" and "pseudo-recovery." Most tissues exhibit pseudo-recovery, which is restoration due to growth of cells uninjured by radiation rather than true recovery of single cells.—R. E. S.


The problem of tumor radiosensitivity is outlined, principally according to the theories of Stewart and Warren. Of 160 cases of carcinoma of the bladder treated by x-radiation 14, or 8.8%, had complete disappearance of the lesion (4 of these, however, had a reappearance of the neoplasm). Marked regression was obtained in 51.9%, and no apparent regression in 30.3%. The solid infiltrating carcinomas responded very poorly, but over 50% of the papillary type showed satisfactory results.—V. F. M.


Following radiation therapy of carcinoma of the cervix, radiation necrosis may occur not only in the bladder and rectum but at or near the site of the cervix itself. These lesions may arise many months after the original carcinoma has disappeared and the radiation reaction has subsided. Such lesions may suggest recurrence of the tumor, and they necessitate biopsy to establish the correct diagnosis and to avoid improper treatment. Four illustrative cases are described.—J. L. M.


Seven cases of hemangioma were treated with implantation of radon. Each seed (0.25 to 1.0 mc.) was used to irradiate approximately 1 cc. of tissue. Photographs after this procedure are given as evidence favoring its use where cosmetic results are important and surgery and scarring are undesirable.—W. J. B.


The subdivision of laryngeal cancer into intrinsic and extrinsic forms is much less satisfactory to the radio-
# Experimental Research, Animal Tumors


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