Abstracts

Experimental Research, Animal Tumors


Olive oil solutions of o-aminoazotoluene or p-dimethylaminoazobenzene were administered subcutaneously to mice of strains C, C57 black, C3H, and A. Hepatic changes, hepatomas, pulmonary tumors, hemangioendotheliomas, and fibrosarcomas at the site of injection were induced by o-aminoazotoluene. The strains differed somewhat in the type of tumors developed, and females appeared more susceptible to liver damage than males of the same strain. Olive oil solutions or glycerol suspensions of p-dimethylaminoazobenzene were much less carcinogenic than similar preparations of o-aminoazotoluene under the same conditions of administration.—H. Q. W.


An experiment was planned to determine the minimum amount of o-aminoazotoluene that, when administered by subcutaneous injection to female strain A mice, would produce liver or other tumors. It was found that a single dose of 10 mgm. would induce cirrhosis within 27 weeks, and hepatomas and pulmonary tumors within 35 weeks. Doses of 20, 30, 40, 50, or 60 mgm. induced the same changes more promptly, and, in addition, caused hemangioendotheliomas.—H. Q. W.


A technic is described for producing fluorescence spectrograms of biological specimens. Benzpyrene (BP) painted on the skin of mice is transformed within 1 or 2 days into a derivative with blue fluorescence (spectrum maxima at 450 and 425 m/μ). This spectrum resembles that of the orthorhombic metastable crystals of BP, but other evidence indicates that the two substances are not identical. The derivative is soluble in alkali (blue fluorescence) and becomes ether-soluble from an acid watery medium. It is precipitated by half-saturation ammonium sulfate from an alkaline extract of BP-painted skin, is probably phenolic, but is not identical with 6- or 4-hydroxybenzpyrene. The fluorescence spectrum is not identical with that of the hydroxybenzpyrene (green fluorescence in alkaline solution) that Chalmers and Crowfoot isolated from the feces of BP-treated animals and that they assumed to be identical with the derivative called "BPX" by Peacock.

After intravenous injection of colloidal BP into mice and rabbits, the derivative can be detected in the cortex of the kidney, in the lungs, liver, intestine, and mammary gland. The evidence concerning the latter organ is provided by the spectrum of extracts of milk taken from the stomachs of sucklings of mothers injected with BP.

Observations by microscopy in ultraviolet light are recorded of the behavior of ciliates such as Paramecium, etc., towards colloidal suspensions of BP.

If mouse skin is painted with BP the hydrocarbon is no longer extractable after 48 hours, but the blue fluorescent derivative appears in a few hours, increases to a maximum at the 4th to 6th day, and persists for 2 to 3 weeks. It appears at the site of painting with BP and not elsewhere on the skin, thus indicating that the transformation occurs locally. It is concentrated in the epithelial cells of the hair bulbs, which form a continuous layer with the Malpighian layer from which tumors arise.

The persistence and distribution of the derivative in the skin, and its appearance in those organs (kidney excepted) liable to the induction of cancer by BP, suggest that this derivative represents an intermediate stage in the production of tumors by BP.—I. H.


Five series of mice were treated by: (1) feeding with benzpyrene (BP); (2) intravenous injection with BP; (3) feeding with "BPX" (see abstract immediately preceding this); (4) feeding with BP after the common bile duct had been ligated and cut; (5) intravenous injection with BP after this operation. Examination of the tissues in ultraviolet light showed that BPX is not absorbed from the intestine and that substances with much the same blue fluorescence (spectrum maxima near 450 and 425 m/μ) are present in (a) tissues: kidney cortex, liver, lung, skin (after painting only), walls of stomach and intestine; and milk, (b) bile, and (c) plasma. The authors suggest that the relation between "tissue-BPX," "bile BPX," and "plasma BPX," is possibly due to the linking of the same blue fluorescent benzpyrene derivative as a prosthetic group to various cell constituents.—I. H.

**Sebaceous Glands and Experimental Skin Carcinogenesis in Mice.** Simpson, W. L., and Cramer, W. [Barnard Microfilm copies of such papers here abstracted as are available may be obtained from Medicofilm Service of the Army Medical Library at 25¢ for each complete article, not exceeding 25 pages in length—and 10¢ for each additional 10 pages or fraction thereof. Repayment is not requested. Remittance may be made with subsequent orders and in such manner as found most convenient. Address—Medicofilm Service, Army Medical Library, Washington D. C.
Fluorescence microscopic studies of mouse skin have shown that the sebaceous glands absorb much of a benzene solution of methylcholanthrene and subsequently pour out sebum containing the carcinogen onto the surface of the skin. The authors have now studied the effects of single and multiple applications to mouse skin of 20-methylcholanthrene dissolved in wool fat (anhydrous lanolin), a vehicle chosen as most likely to resemble mouse sebum.

Two experiments, comprising a total of 110 Swiss mice, were carried out by applying a 0.3% solution of the carcinogen 3 times weekly for 14 weeks. In these experiments the lanolin almost completely prevented the carcinogenic activity of methylcholanthrene. The mice did not become epilated; there was no hyperplasia of the epidermis or hair follicles; the sebaceous glands, which are usually destroyed rapidly by benzene solutions of the carcinogen, were still present after 42 applications, though small and less numerous. Six months after the first painting, no neoplasms had appeared except for one precancerous papilloma in a mouse that died and 2 small papillomas in surviving animals. In this same strain similar treatment with the carcinogen in benzene leads to the development of malignant tumors in all survivors at 6 months. If a protective mechanism against the carcinogenic action of methylcholanthrene is reversed by replacing the gas with NO. Irradiation of the NO-hydrocarbon complex with ultraviolet light leads to the production of a substance having a blue fluorescence in the ultraviolet beam.—Author's summary.


Fifty-one C3H mice were fed in unrestricted amount a diet of glucose, lard, casein, dry yeast, dry alfalfa leaf, and salt mixture. Forty-four animals received a similar diet but with restriction of carbohydrates and fat so that the total caloric intake was decreased by about one-third. After 16 months 32 mice on the unrestricted diet had developed mammary carcinoma and 15 were tumor-free. Of the mice on the restricted diet 25 survived 16 months and none had mammary tumor.—W. A. B.


Vitamin C was injected into mice and rats bearing transplantable tumors (melanosarcoma S39, Crocker sarcoma 180) and was observed to stimulate tumor growth mildly in some instances. In some groups of animals this stimulatory effect on the tumors was not demonstrable.—Author’s abstract.


Inositol was given intravenously in doses from 38 to 1,000 gm to female Rockland mice carrying sarcoma 180. The degree of inhibition depended on the dose. The mean terminal tumor weight of the mice receiving the highest dose was about one-third that of the mice with the lowest dose, or of the controls (saline). Sodium phytate...
and liposol showed an inhibition similar to that of inositol.

Subcutaneous or oral administration of inositol was without effect. Also ineffective were intravenous injections of γ-inositol, inosose, and crystalline factors of the vitamin B complex.—M. B.


In 3 experiments (122 Marsh-Buffalo mice), a synthetic diet containing vitamins of the B group other than B₆ produced a significant decrease in the rate of tumor growth, which was corrected by the addition of vitamin B₆ to the diet; and in a single experiment (30 mice) the addition of vitamin B₆ to a diet otherwise completely deficient in the B complex produced a significant increase in tumor growth. The findings are considered to establish the essentiality of vitamin B₆ for the maximum growth of sarcoma 180.

Pantothenic acid deficiency was without influence on the tumor in 31 mice.—J. G. K.


Extracts of normal rat liver were incubated at different temperatures with extracts of transplanted Jensen sarcoma, and with serum and extracts of other tissues of tumorbearing rats. Similarly, rat liver slices were incubated with tumor slices, and extracts of normal mouse liver with extracts of sarcoma 37. None of these mixtures affected the catalase activity of the livers. Thus tumor tissue apparently has no direct action *in vitro* on liver catalase.

Dialysis at low temperatures of extracts of normal rat liver and of the livers of tumor-bearing rats caused the same proportionate drop in the catalase activity of both extracts. This fact indicates the absence of readily dissociable inhibitor from the liver catalase of the tumor-bearing animals.

Aqueous extracts were prepared at the same concentrations from livers of normal and of tumor-bearing rats. On dilution of the extracts from the livers of normal animals with boiled normal liver extract in the ratio of 1:2.2, values for catalase activity were obtained similar to those of the undiluted extracts of the tumor-bearing animals. The rates of reaction of such extracts with hydrogen peroxide were practically identical, and the drop in activity in each on dialysis was the same.

Extracts of a transplanted hepatoma injected intraperitoneally into normal rats produced no change in the liver catalase activity of these animals.

The view is advanced that the low liver catalase activity of tumor-bearing animals is ascribable to the presence of only about half the normal amount of total catalase in this organ.—F. L. H.


The paper presents a comprehensive summary of enzyme data relevant to the cancer problem. The enzymatic activity of tumors is compared with that of the normal tissues of origin. The tumors studied in this manner include hepatomas, lymphomas, mammary tumors, rhabdomyosarcomas, adenocarcinomas of the stomach and intestines, carcinomas of the prostate, and osteogenic sarcomas.

The enzymatic activity and the concentrations of certain components of the tissues of normal animals are compared with those of tumor-bearing animals. The study includes liver, kidney, spleen, adrenals, and muscle, as well as blood and serum. The observations indicate that the systemic effects elicited by the tumor generally parallel in degree the growth of the tumor and are reversible with removal of the tumor.—F. L. H.


Values for the copper content of tissues of tumor-bearing and normal animals are compared. The copper content of the whole blood of tumor-bearing rats was lower than that of normal rats and unequally distributed between cells and serum. The copper content of normal and regenerating rat livers was the same, but that of the livers of tumor-bearing rats was distinctly higher than normal. Normal mouse livers were considerably higher in copper content than normal rat livers, but the increase in copper in the livers of tumor-bearing mice over that of the normal was less than in rats. The kidneys of normal rats and mice had a higher copper content than the livers of these species. In tumor-bearing animals, however, the copper content of the kidneys decreased as compared with values in normal animals.—F. L. H.


Cathepsins prepared from normal rat liver, livers of rats resistant to hepatoma 31, normal spleen and kidney, and hepatoma 31 hydrolyzed the glycine bond of glutathione at an optimum pH of 4.3.

The order in which the peptide bonds of glutathione were attacked was proved by the absence of free cysteine and the separation of γ-glutamylcysteine and glycine from the digests when the alkalimetric titration indicated that the equivalent of one peptide bond had been hydrolyzed.

The cathepin from normal rat livers hydrolyzed the glycine peptide bond of glutathione at a rate twice that of the hepatoma cathepin. But the hepatoma cathepin was able to hydrolyze slowly the remaining γ-glutamylcysteine while the normal liver cathepin did not attack this dipeptide. The normal spleen cathepin also hydrolyzed both bonds of glutathione and at a much more rapid rate than did the hepatoma cathepin. The rate of hydrolysis of glutathione by the cathepin from livers of resistant rats was very slightly higher than by the cathepin from normal rat livers. The rate of the kidney cathepin was about one-half that of the normal liver cathepin.—F. L. H.


The activity of cytochrome oxidase and d-amino acid oxidase in a number of tumors and normal tissues was...
measured. Particular attention was given to tissues of hepatic origin.

The ratio of cytochrome oxidase activity of normal liver to hepatoma was about 4 or 5, to regenerating liver 1, to fetal liver 2.5, and to liver of tumor-bearing animals about 1.1. A variety of other tumors possessed low cytochrome oxidase activities of the same order of magnitude as hepatoma.

The ratio of d-amino acid oxidase activity of rat liver to hepatoma 31 was about 10, to regenerating liver 1.2, to fetal liver 7, and to liver of rats bearing hepatoma 31 about 1.5. Neither mouse liver nor mouse hepatomas exhibited measurable d-amino acid oxidase activity.

The significance of these results to oxygen utilization by tumor tissue is discussed.—F. L. H.


Injection of culture filtrates, or suspensions, of certain bacteria into tumor-bearing animals may induce severe hemorrhage in the tumor, frequently followed by complete regression of the neoplasm. The effect is especially pronounced with transplanted tumors but has been observed also with tumor-induced and certain spontaneous tumors.

In the present work about 100 strains of bacteria, representing a number of principal genera, were examined in respect to their ability to elaborate tumor hemorrhage-producing materials. Both bacterial filtrates and suspensions were tested in mice bearing the transplantable sarcoma 180. Organisms producing tumor hemorrhagic materials were found to be characterized by the following common features: (1) They are gram-negative; (2) they contain complex endotoxin antigens; and (3), their pathogenesis is marked by vascular damage, disturbances in carbohydrate metabolism, and enteric irritation. Recent studies of certain endotoxin nonprotein O antigens lead to the conclusion that tumor-hemorrhagic agents produced by many gram-negative bacteria are probably identical with a polysaccharide compound of the complex endotoxin antigens.—A. C.


Thrombocytopenia produced by anti-mouse-platelet serum, of the same amount as that produced by a concentrate of Bacillus prodigiosus filtrate and by moccasin venom, did not produce hemorrhage in transplanted sarcoma 37 in strain A backcross mice. The action of the bacterial filtrate and of the snake venom on the transplanted sarcoma 37 is primarily that of an endothelial toxin.—F. L. H.


Mice of similar strains were united by means of parabiosis, and inoculated with alien mouse tumors known to induce an immunity in the hosts. Primary injection of tumor into the left parabiont, 25 days after operation, resulted in rapid proliferation and growth of the implanted fragments. Inoculation of the same tumor 10 days later into the opposite parabiont was not followed by any perceptible growth of the implanted cells. It is suggested that inoculation of an immunizing tumor into one parabiont leads to simultaneous development of resistance in both animals.—Author's abstract.


A method is described whereby tumors from the mouse and rat can be cultivated in the yolk sac of the developing chick embryo. Rapidly growing neoplastic tissue is dispersed and suspended in 0.85% saline solution and then injected by means of a hypodermic syringe into the yolk sac of an embryo at the fifth day of development. The inoculated egg is incubated for another 12 to 13 days, for a total of 17 to 18 days. The yolk sac tumor, which may attain a weight of several grams, resembles the donor material both in the gross and microscopically, and is generally located just beneath the area known as the umbilicus. Dba mouse mammary carcinomas, both spontaneous and transplanted, and the Walker rat carcinosarcoma 256 have been grown successfully in this manner.—Authors' abstract.


A study was made of the effect of yolk sac-grown mammary carcinomas of dba mice on the hemoglobin level of 51 white Leghorn embryos that served as hosts for the tumors. The results obtained demonstrated a notable decline in the hemoglobin level of the experimental embryos. The severity of the effect tended to be in direct relation to tumor size, although a completely consistent, straight line relationship was not observed. Any growth of carcinomatous tissue (even as little as 0.03 gm.) in the yolk sac effected a measurable decrease in blood hemoglobin concentration. Individual tumors induced depression of hemoglobin level by as much as 50%. These results strengthen the conclusion reached previously in a similar investigation reported from this laboratory, in which mice and rats were used as the experimental animals; i.e., tumors exert a direct inhibitory action upon the blood hemoglobin of the host.—Authors' abstract.


Urine from patients with chronic myeloid leukemia was extracted with chloroform, the latter removed by distillation, and the residue suspended in 200 to 300 cc. of 10% NaOH. This suspension was extracted 8 to 10 times with 100 cc. portions of ethyl ether. The ethyl ether-soluble fraction (A) was recovered by removal of the solvent. The residual alkaline solution (B) was reacidified with 30 to 50 cc. of concentrated HCl, extracted with chloroform, and after the removal of the chloroform, extracted with successive portions of petroleum ether (C); these extracts were then combined and distilled in vacuo.
Four guinea pigs receiving fraction B showed proliferation of myeloid cells. Three animals receiving fraction A showed no such proliferation. Five guinea pigs given fraction C showed, on autopsy, proliferation of myeloid cells in the liver, lungs, spleen, and adrenals. Blood smears showed 10 to 20% myelocytes.

Three similar fractions from urine of patients with chronic lymphoid leukemia showed proliferation of lymphoid cells with no apparent variation.

Urine of normal animals yielded fractions which gave no specific cellular response.—M. B.


The method of Gomori and of Takamatsu was used for the demonstration of alkaline phosphatase in histological preparations. Tissues from mouse, cat, chicken, and man were studied. In normal tissues, alkaline phosphatase was found to be present in the endothelium of the blood vessels of the central nervous system and in the arachnoid. In the parenchyma of the nervous system, the amount of phosphatase activity was found to vary in different localities and in the same locality in different species, but, except in the chicken, the parenchymal reaction was much less striking than that of the vascular endothelium and the arachnoid. The suggestion is made that the phosphatase in the vascular endothelium may play a role in the passage of dextrose through the capillary wall, a view similar to that advanced by Lundsgaard to explain the transfer of dextrose through the intestinal wall and the convoluted tubules of the kidney.

Phosphatase activity was demonstrated in a number of common tumors of the nervous system, more frequently in meningiomas and in astrocytomas. Apparently the phosphatase content of tumors of the nervous system can be correlated roughly with that of the homologous normal tissue and with the tendency of the tumor to become calcified. The method has a limited usefulness in diagnosis of tumors when employed in conjunction with other techniques.—A. C.

**Studies of Normal and of Abnormal Mitotic Activity. II. The Rate and the Periodicity of the Mitotic Activity of Experimental Epidermoid Carcinoma in Mice.** Blumenfeld, C. M. [Cleveland City Hosp. and Western Reserve Univ., Cleveland, Ohio] Arch. Path., 35:667-673. 1943.

Squamous cell carcinomas produced experimentally with methylcholanthrene in 60 male CBA mice were procured at stated times during the day and night and fixed immediately in Bouin's fluid, together with normal epidermis from the same animals. Detailed histological studies showed that mitotic activity in the cancer cells remained at a practically constant level throughout the day and night, whereas the normal epidermal cells manifested the characteristic diurnal rhythm. The rate of mitotic activity in the carcinomas proved no greater than the maximum rate in an equal volume of normal epidermis. Certain implications of the findings are discussed.—J. G. K.


A cytologic study of various lesions of the livers of Buffalo rats fed p-dimethylaminobenzene was made. In all neoplasms derived from the hepatic parenchymal cell, the Golgi apparatus had shifted to a completely juxtanuclear position. The type of mitochondria was found to vary from lesion to lesion, one mitochondrial form predominating in any one neoplasm. With some exceptions spherical mitochondria were characteristic of hepatoma type I. Tenuous, fine, filamentous mitochondria were characteristic of hepatoma type II.

Cytologic evidence indicates that the transplantable hepatoma 31 originated as a primary hepatoma of type II, and that the hepatic adenocarcinoma of the rat is derived from hepatic parenchymal cells rather than from cells of proliferating bile duct epithelium.—F. L. H.


Cells derived from pleural and peritoneal effusions were grown in tissue culture by the roller tube method. Macrophages, polymorphonuclear leukocytes, lymphocytes, mesothelial cells, and fibroblasts were cultured from all fluids. In one instance endothelial cells were found, and these produced structures resembling capillaries. Cells from carcinomas and sarcomas were cultured and grew vigorously, thereby indicating that such cells remain viable and capable of proliferation after floating in pleural or peritoneal fluids if given a satisfactory surface to which they may become attached. Thus support is given to the view that carcinomatosis of serous membranes can occur by implantation. Small colonies were observed to develop from single neoplastic cells that had become isolated in the supporting plasma of the tissue culture. The significance of this observation is discussed as opening a field for further exploration. It is suggested that the culture of cells from pleural and ascitic fluids can be of aid in diagnosis under favorable circumstances.—Author's abstract.


Many hundred cultures of normal and malignant fibroblasts from rat and mouse tissues were made in various media and examined for nucleolar vacuoles. Some cultures of normal fibroblasts had no nucleolar vacuoles, some had a few or a moderate number, and some had many cells containing them. Malignant fibroblasts from some tumors had no nucleolar vacuoles, those from other tumors had a few or a moderate number, and those from a few had many cells with them. No consistent correlations were found in either normal or malignant cells between the number of cells with nucleolar vacuoles and the culture medium, the extent of migration, the life of the culture, the number of mitoses, the amount of pinocytosis, or any cytological feature—such as the number and size of the nucleoli, the condition of the nucleo-
plasm, the number of nuclei, the number of fat globules, the mitochondria, the neutral red-staining vacuoles and granules, and the size of the central area. Normal fibroblasts had 1 to 30 and malignant ones 1 to 60 vacuoles per nucleolus. The number of vacuoles per nucleolus usually varied directly with the number of cells containing them and with the size of the nucleolus. The relative number of cells with nucleolar vacuoles may increase or decrease during the life of a culture. Malignant fibroblasts cannot as a rule be distinguished from normal ones by the relative number of cells with nucleolar vacuoles, by the number of vacuoles per nucleolus, or by the size of the vacuoles.—Author's abstract.


A cytological investigation of the nucleus and chromosomes was carried out on 565 human tumors (carcinoma of the skin, esophagus, colon, rectum, larynx, lung, cervix, uterus, and breast). The characteristic abnormalities exhibited by malignant cells such as polyplody, multinucleate, and giant cells, multipolar spindles, stickiness, and displacement of chromosomes at metaphase, as well as increased rate of division, are attributed to a quantitative change in nucleic acid synthesis. Since "it is known that the heterochromatic regions of chromosomes primarily concerned with nucleic acid synthesis can undergo spontaneous mutation and structural change more easily than other parts" it is suggested that a gene mutation in such a chromosomal region may initiate the alteration in nucleic acid metabolism. The ultimate cause of the somatic mutation is unknown. "The cytological analysis reveals only the fact that in the tumour cell there is a disturbed nucleic acid metabolism."—R. J. L.


Marshak counted the relative numbers of normal and abnormal mitotic figures present in transplantable mouse lymphoma at various time intervals after exposure to x-rays and to neutrons. There was a sharp increase in the percentage of abnormal mitoses 3 hours after exposure to x-rays and to neutrons and a greater increase at 12 hours. Cells observed in mitoses at 12 hours must have been in the resting stage at the time of exposure, and hence the cells of this lymphoma differ from those of tumors previously investigated in that their radiosensitivity is maximal during the resting phase of the nuclear cycle and not in early prophase. As the dose of x-rays or neutrons was increased, it was found that the percentage of normal mitoses decreased as a negative exponential function of the dose, indicating that the damage resulted from a single encounter of the effective agent with a sensitive portion of the chromosome and not from the gradual accumulation of diffusible toxic substances.

The relative efficiency of neutrons as compared to x-rays in producing nuclear damage was not constant when calculated at different time intervals but was maximal at 12 hours after exposure, indicating that nuclei irradiated at one stage during the resting phase were relatively more vulnerable to neutrons than to x-rays.

It is suggested on the basis of these findings that neutron radiation may prove effective in treating some tumors that are resistant to x-ray therapy.—C. E. D.


A patient with cutaneous melanoma and 2 patients with mycosis fungoides were given radioactive phosphorus by mouth. Determinations of the radioactivity of the superficial tissues were made with a special Geiger-Müller counter. In all 3 patients the radioactivity was greater in the region of the skin lesions than in other parts of the body surface. The variations of radioactivity in various parts of the body, as a function of time, are shown in 4 charts.—C. E. D.


Anterior hypophyses and ovaries from rats of the Albany strain, in which the incidence of spontaneous mammary fibroadenomas is high, were compared histologically with those of the Vanderbilt strain, in which such tumors rarely occur. Rats ranging in age from 1 to 28 months were used. In all age groups the anterior hypophyses of the Albany rats were characterized by significantly lower percentages of eosinophils and higher percentages of chromophobes than were found in the Vanderbilt rats. The relative numbers of basophils were practically the same in the two strains. In both strains advancing age was associated with structural changes in the anterior lobe, including a progressive decrease in the relative number of eosinophils, an increase in the relative number of chromophobes, a decrease in mitotic activity, the appearance and increase in number of vacuolated basophils, the appearance and increase of colloid degeneration of anterior lobe cells and of intercellular colloid, and adenomatous changes. With the exception of the latter, these changes appeared earlier and were more intense in the Albany rats. In the ovaries advancing age was associated with a progressive decrease in the numbers of normal follicles, total follicles (normal plus atretic), and corpora lutea. A partial failure of ovulation and an increased follicular atresia occurred. Interstitial tissue became more abundant and wheel cells appeared and became more numerous. The alterations occurred earlier and were more pronounced in the Albany rats.—Authors' abstract.


In a group of 10 patients with prostatic carcinoma and roentgenographic evidence of skeletal metastases, the average value of urinary 17-ketosteroids (in 6 day samples) before operation was 7.6 mgm. per 24 hours. The range
was 3.6 to 11.7 mgm. After castration the values were less; the lowest were observed 2 to 14 days after operation, at an average of 6.5 days. The role played by operative procedures in these lowered titers could not be identified. The postoperative fall in values was not sustained. Levels of these steroids returned after castration to a point higher than they had been previous to operation; per 24 hours the range was 7.3 to 24.4 mgm., the average 11.4 mgm. Ten other patients, studied only subsequent to bilateral orchietomy carried out as a therapeutic measure for prostatic cancer, had values with a range of 1.8 to 18.2 mgm. per 24 hours, and an average of 6.6 mgm. Beta forms, which represented about 10% of the total amount of 17-ketosteroids prior to castration, did not account for the rise in values after operation.

Preoperatively, the titers of urinary estrogens were 12 to 13 I.U. per 24 hours. In 4 of 6 patients studied the amounts were reduced after operation.

The quantities of urinary gonadotropins were increased after castration, but the amounts were considered to be less than those observed in younger eunuchs.—J. B. H.


In the effort to find a more convenient method of administering stilbestrol than by daily oral doses, pellets of diethylstilbestrol were implanted subcutaneously in 9 male patients, and were removed and weighed after varying periods. The pellets were cylindrical in shape, weighed 50 mgm., and were prepared either by compression or by fusion. It was found that such pellets were absorbed at a rate of 0.35 to 0.45 mgm. per day for at least 100 days. Clinical evidence of the efficacy of this method of administration was found in the development of gynecometasia and, in one patient with prostatic cancer, in a drop in the serum acid phosphatase.—H. Q. W.


When mice of the extreme dilution strain (ce) were gonadectomized at 2 days of age, carcinoma of the adrenal cortex occurred, its frequency increasing with age up to 1 year when it reached 100%. No such tumors have so far been observed in normal male and female mice of the ce strain. This observation is linked with the theory that hormonal imbalance may be one of the factors leading to this and other types of cancer.—M. B.


This paper gives a short review of tumors and cancers occurring in experimental animals after long-continued treatment with estrogenic hormones. Genital organs are involved primarily, but nongenital tissues also are affected. The uterus may develop cancer of the cervix (in mice) or fibromyomas of the cornua (in guinea pigs). The mammary glands are especially susceptible to cancer. In certain inbred strains of mice, low tumor incidence among females is increased by estrogenic treatment. Males of strains in which the females are susceptible to spontaneous mammary cancer may have the disease after injections of estrogen. The tests of mice respond to this estrogenic treatment by hypertrophy of the interstitial cells. In the A strain, unilateral nodules may become large tumors. These are transplantable into other mice of this strain if estrogen is injected into the host. The tumor tissue may secrete androgenic hormone. Pituitary hypertrophy and chromophobous tumors of considerable size can be induced in high incidences in mice of certain strains and in rats. The suprarenal cortex may develop tumors after long estrogenic treatment in mice. Mice ovariectomized at early ages resumed estrous cycles late in life. Cortical tumors found at autopsy are considered responsible for the secretion of estrogen in these cases. Growth of new bone in the marrow cavities of mice and several species of birds may be induced by estrogenic hormone. Osteogenic tumors have been reported in albino mice. Several hyperplastic or hypertrophic conditions, definitely atypical, have followed excessive estrogenic stimulation. These include cystic hyperplasia of the uterus, metaplastic changes of male accessory organs, leukemia (lymphatic), and hypertrophy of the bile ducts. Cystic ovaries may be induced by unbalanced pituitary stimulation. In these cases hypertrophic uterine conditions are induced by endogenous estrogen. From these experiments endocrine secretions appear as important factors in the genesis of some atypical growths, including certain tumors and cancers.—C. A. P.


The acinar tissue of the pancreas in many species of snakes undergoes unexplained focal necrosis followed by abortive regenerative growth, apparently of the terminal ducts, producing small, edematous, adenoma-like structures. These areas presumably enlarge, and with their enlargement, leukocytes infiltrate the organ, fibrous tissue is increased, and there is further degeneration of acinar and islet epithelium, until occasionally the whole organ is replaced by tissue that has the histologic characters of carcinoma. Among 136 snakes of five families of the order Serpentes, all of which died in captivity, 45 presented some stage in the development of this disease. But of 261 snakes of species that seemed most susceptible to the disease, killed for examination 60 to 90 days after capture, only 10 had developed lesions of this sort, and none presented the more advanced stages of the disease. Metastases were not found, and local extension occurred infrequently. Transplantation was not attempted.—J. G. K.


A general discussion.—A. C.
Experimental Research, Animal Tumors


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