Abstracts
Experimental Research, Animal Tumors


From 1934 to 1936, inclusive, amounts of 0.1 to 0.15 gm. of chromium, arsenic, or cobalt were deposited in the marrow cavity of the femur in rabbits. Among 21 survivors of an epidemic no tumors were found 3 years later. For one reason or another connected with the war 9 of these animals disappeared, but of the remaining 12, 7 developed carcinomas or sarcomas after 3½ years or more, some at the site of the metal depot, others at a remote site (lungs). Some of the growths metastasized.

The author suggests that the metals must have been slowly distributed throughout the body, where they became active in traces.

A full report is promised, as well as a resumption of the investigation when favorable conditions are restored.—W. H. W.


Experiments are described of the following type: 3,4-benzyrene in acetone was applied three times on alternate days to both flanks of a mouse; subsequently acetone was applied to the left side and croton oil in acetone to the right side. After 20 weeks, there were 5 tumors, one malignant, on the right, and none on the left side. Application of croton oil before benzpyrene also promotes the development of tumors. The author discusses (1) the results of earlier workers, (2) the part played by hyperplasia and chronic irritation in the genesis of cancer, and (3) the statistical value of comparative experiments on both sides of the same mouse “... blastogenic agents are likely to be missed unless a developing agent is applied at the same time. ... The combination of croton oil with benzpyrene provides a much more delicate test than the sledge-hammer treatment of continuous painting.”—E. L. K.


Diets containing o-aminoxotoluene and p-dimethylaminoazobenzene were fed to strain C mice of both sexes. The former induced many hepatic changes, hepatomas, pulmonary tumors, and hemangiopericytomas, whereas the latter induced only a few hepatic reactions and few hepatomas. Female mice were more susceptible than males to hepatic reactions, hepatomas, and hemangiopericytomas induced with o-aminoxotoluene. When orally administered, this compound elicited many pulmonary hemangiopericytomas. Authors' summary.


Three groups of rats were fed diets containing 3,5-cholestadiene at graded levels. No characteristic pathology of gastric or hepatic tissues, which would distinguish one experimental group from another or from the controls, was noted. Hyperkeratosis of the forestomach was rather evenly distributed among all the groups. No papillomas were found in the stomachs of the control rats, whereas 1, 1, and 3 were found in the forestomachs of rats fed the low, intermediate, and high concentrations of the hydrocarbon, respectively.

The highest level of ingested hydrocarbon appeared to exert a low-grade systemic toxicity characterized by loss in weight of the rats; all animals in this group were dead after 8 months. The animals maintained on the diet containing the intermediate level of 3,5-cholestadiene exhibited a similar reaction, but to a much lesser degree. Pellets of 3,5-cholestadiene, when implanted subcutaneously in Wistar rats and in strain C3H mice, were inert. Autopsies up to 16 months after implantation revealed intact pellets and no evidence of hyperplasia in adjacent tissues.

Dicholesteryl ether, implanted subcutaneously in strain C3H mice in the form of pellets, remained intact and caused no tissue reaction.

3,5-Cholestadiene, administered orally or subcutaneously, presented no evidence of carcinogenicity in these experiments. —Authors' summary.


Three groups of rats were fed diets containing desoxycholic acid at graded levels for as long as 20 months without evidence of toxic effects. No characteristic pathological picture, which would distinguish one experimental group from another or from the controls, was noted in the gastric tissues.

Pellets of desoxycholic acid, implanted subcutaneously in rats, incited a temporary local tissue reaction, which subsided within 2 weeks. Autopsy of 41 animals after 13 to 16 months revealed neither gross nor microscopic evidence of neoplasia or hyperplasia. Subcutaneous implantation of pellets consisting of equal parts of the acid and cholesterol likewise led to negative results as far as tumor genesis was concerned.

Subcutaneous implantation of desoxycholic acid pellets in 46 strain C3H mice led to necrosis, sequestration, and sloughing of the pellet in most cases. Twenty-six mice that survived for 6 months showed no evidence of hyper-
plasia at the pellet site. Similar implantation of acid-cholesterol pellets was followed by sloughing in about half the mice. Pellets that were retained in the remainder of the mice appeared to be completely absorbed within 35 days. These mice, autopsied 8 months later, showed no reaction at the pellet site.

Desoxycholic acid, as administered in these experiments, showed no evidence of carcinogenicity.—Authors' summary.


When azobenzene is given to rats benzidine can be isolated from the urine (Elson and Warren), and evidence has been obtained that p-dimethylaminobenzene undergoes a similar rearrangement to 2,4-diamino-5-dimethylamino diphenyl. Both these products have a strong inhibitory action on urease and succinoxidase systems. p-Phenylene diamine and dimethyl-p-phenylenediamine on oxidation give products that inhibit the succinoxidase system; the rate of oxidation of the diamines seems to be related to the amount of cytchrome c present. When the diamines are added to the complete system the rate of oxygen uptake is first increased, presumably due to the oxidation of the diamine by the cytchrome, and then inhibited, often completely.—E. L. K.


The data indicate that the cells of the V2 rabbit carcinoma possess a glycolyzing capacity which, calculated on a dry weight basis, is about as great as that of the cells of 2 other transplanted rabbit cancers (the Brown-Pearce carcinoma and sarcoma I of Andrews and Ahlström), and is considerably greater than that of the benign papilloma cells of the sort from which they originally derived. The derived metabolic quotients, which relate glycolysis to oxygen consumption independently of dry weight, lend further support to the view that the metabolism of the V2 carcinoma is characteristic of malignant cells generally, whereas that of the Shope virus papilloma is characteristic of benign tumor cells and distinguishable in certain respects from that of normal rabbit skin cells. The differences in metabolism between the benign papilloma cells and the homologous V2 carcinoma cells are more noteworthy since the former proliferate quite as rapidly as the latter. It remains to be ascertained whether the metabolic differences have something to do with the differences in the form and behavior of the papilloma and carcinoma cells, with the failure of repeated attempts to procure a causative virus from the V2 carcinoma, or with antigenic differences in the sedimentable constituents of the two sorts of cells.—Authors' abstract.


In 23 (36%) of 65 patients with cancer of the colon and rectum hypoproteinemia, as determined by the falling-drop method, was present. The number of patients with serum proteins below 6.5 gm. per cent increased to 86% during the first postoperative week. Whole blood, where there was associated anemia, and plasma were used to combat this condition in the early stages, and later dietary nitrogen was effective. In all but 1 of 14 of the cases the serum protein levels were higher from 20 to 150 days after the parenteral injection of protein than during the first postoperative week. It was more difficult to combat hypoproteinemia in cases where there were infections.—W. J. B.


In patients with gastrointestinal cancer, the development of significant postoperative hypoproteinemia is an almost uniform finding. The condition is the result of numerous factors including the disease itself, poor liver function, and reduced protein intake following resection of some portion of the alimentary tract. The preoperative ingestion of considerable amounts of protein for from 10 to 22 days prevents the development of serious degrees of hypoproteinemia in patients with gastric cancer during their postoperative periods of negative nitrogen balance. These conclusions are the result of nitrogen balance studies on 6 patients with carcinoma of the stomach, receiving diets containing 101 to 196 gm. of protein daily.—M. E. H.


From previous studies it appears that the liver of patients with gastrointestinal cancer is infiltrated with fat, but in 11 patients who received 8 gm. of lipocai before laparotomy the fat content was found to be normal. Since lipocai contains relatively large amounts of choline and inositol, each of which is lipotropic, the effect of these substances was tested separately.

Supplement of either 8 gm. lipocai, 3 gm. choline chloride, or 1.2 gm. inositol was found to correspond to a reduction of hepatic lipid of 51, 39, and 58% respectively. A reduction of 50% lipid was observed when 0.28 gm. inositol was administered 10 hours before intervention. Since this amount is equal to the quantity of inositol present in an effective dose of lipocai, it is suggested that inositol alone may account for the lipotropic properties of the crude preparation.—M. B.

Five patients showing postoperative hypochloremia resistant to the administration of large amounts of saline solution were found to have an associated hypoproteinemina. In those instances in which the level of serum protein was increased therapeutically, the disturbed electrolyte equilibrium was corrected. The existence of hypoproteinemia may seriously prevent the correction of the chloride imbalance by the administration of saline solution alone.—M. E. H.


Patients with gastrointestinal cancer have low levels of plasma vitamin A not explainable by inadequate ingestion, or poor absorption of the vitamin, or by inability of the liver to store vitamin A. The administration of yeast, lipocaic, or choline raised the plasma vitamin A levels in these patients although the mechanism involved is not clear.

Fifty-nine per cent of patients with gastric cancer suffer from hypoproteinemia. This is not because of dietary deficiency or excess bleeding but more likely is the result of metabolic abnormality that interferes with the maintenance and replacement of serum albumin, possibly hepatic dysfunction.

Patients with cancer of the gastrointestinal tract have a high incidence of hepatic dysfunction as indicated by diminished ability of the liver to synthesize, store, conjugate, and excrete metabolites.

Postoperative metabolic abnormalities include the following: (1) Absorption of fat after total gastrectomy is low, and the steatorrhea is apparently related to the dietary content of fat and possibly to the fat-splitting pancreatic enzymes. (2) Hypoprothrombinemia is frequent in patients with gastrointestinal cancer and may persist for months in those from whom the cancer is removed. (3) Postoperative anemia of mild degree may persist in patients whose gastrointestinal neoplasms have been removed, although the degree of anemia is less than in those still bearing tumors.—W. A. B.


Fractionation of α-ketosteroid extracts of urines from patients with neoplastic diseases yielded several homogeneous substances some of which were not obtained from normal persons or from those with certain nonneoplastic disorders.

An analysis of the relative amounts of these substances gave distribution patterns that were definitely abnormal for patients with lymphatic leukemia and cancer, while the pattern obtained from a patient with myeloid leukemia was very similar to the pattern for normal persons.—R. B.


Only one among several investigators has found that photosensitizing agents such as hematoaphorin or cosin increase the activity of carcinogens.

In an attempt to settle this question the author exposed mice sensitized with anthracene, which is not carcinogenic, to light from which the ultraviolet and heat rays had been filtered out.

No tumors appeared, and the conclusion is drawn that even a strong and long-continued photodynamic reaction in the skin can be of little significance in carcinogenesis.

In the one positive result mentioned in the opening paragraph photosensitization facilitated carcinogenesis in some non-specific manner. In any case, there is no warrant at present for regarding photosensitization as a new and specific carcinogen.—W. H. W.


Transplanted tumors grew and benzpyrene carcinomas developed in rats and mice kept in an atmosphere ionized with various preparations of radium as they did in the controls.

Though the experiments are not yet finished they give no support so far to the suggestion of several authors that the ions of the atmosphere are concerned in carcinogenesis.—W. H. W.


Measurements of growth rates of tumors induced with ultraviolet radiation are described. The growth rates of the gross tumors are not correlated with the time required for their appearance but are the same for early and late appearing tumors. The growth rates are not correlated with the age of the animals, nor with the recency of exposure to ultraviolet radiation. Estimates based on individual tumors show that the growth rate does not remain constant throughout development and does not follow the same pattern in all tumors of the same type. Experiments to determine the effect of interruption of the schedule of exposures on development time suggest that opposing growth and regressive processes determine the time at which a tumor becomes established so that it may continue to grow. The general evidence indicates that the tumor cells do not escape and assume their own essential proliferation rates, but that rates of tumor growth are to a great extent dominated by the controlling influence of the tissues.—Author's summary.

Both virgin and breeding female C3H mice developed mammary tumors earlier when kept segregated, 1 mouse to a cage, than they did when living together, 8 to a cage.

Vaginal smears taken from virgin mice indicated that estrous cycles in the segregated animals occurred earlier, were more frequent, and lasted longer than they did in nonsegregated animals. Thus, hormonal stimulation was presumably greater in the segregated mice and could account for the earlier development of tumors amongst them.—R. B.


Spontaneous mammary carcinoma from mice of the A and C3H stocks were tested in chick embryos. The A tumor gave large growths following the primary inoculation, but the second or third yolk-sac transfer resulted in the death of the embryos after 3 to 6 days. One mammary carcinoma from a C3H female was implanted in eggs after 13 passages in mice. During the early serial yolk-sac passage the tumor was transferred at 12-day intervals, but after the eighth serial passage the tumor had to be transferred at shorter and shorter periods because of the death of the embryos. The tumor was lost in the 20th passage owing to the death of the embryos on the night of the seventh day. The increasing mortality rate of the embryos was not related to the size of the tumor.

Following the fifth serial passage in eggs the C3H mouse tumor was inoculated into mice. It grew progressively in mice of the A stock and C3H stock and their hybrids but did not give temporary growth in mice of the A stock. Following the 11th serial passage in eggs, the C3H stock tumor gave temporary growth in 44 of 50 mice of the C57 black, C, A, and dilute brown (sublines 212 and 12) stock; 3 mice of the 212 line of the dilute brown stock showed progressive growth. After the regression of their tumors, the mice were resistant to reinoculation. These data suggested that the genetic constitution of the mouse tumor had changed during serial passage in chick embryos.

A limited number of attempts to find a cell-free agent in the yolk from tumor-bearing eggs that would produce tumors in mice within a few days resulted in failure. Material for injection was obtained by means of the following technics: filtration through Berkefeld N candles; rapid freezing and thawing; use of supernatant from an ether suspension; and centrifugation of the blood and allantoic fluid from embryos with tumors.

When untreated and unfiltered yolk surrounding large tumors was injected into mice, tumor resulted within 10 to 30 days in 6 of the 8 mice tested, which suggested the transfer of living tumor cells.—Authors’ abstract.


Among 143 mice with benzpyrene carcinomas of the skin, or spontaneous mammary carcinomas, treated with modifications of the mixture of powdered organs suggested by Vlés and de Coulon (Proc. II. Internat. Cancer Congr., 1936) the tumor was inhibited, or made to disappear, in 12 and 13% respectively.

Among 114 mice that received injections or inunctions of colchicine in addition, the inhibition was evident in 23 and 28%.

Except in those few cases where the tumors disappeared life was not prolonged, and there is no reason, therefore, to hope that the treatment might be of practical value.—W. H. W.


Certain steroids caused mitotic anomalies in tissue cultures, and growth disturbances that seemed to be related to the mitotic anomalies in malignant new growths—W. H. W.


Chromosome sizes in normal rat organs vary to some extent with nuclear volume, but they do not form a polymeric series by progressively doubling in volume from one tissue to another. The changes in chromosome volume are small, although often significant, and are not accompanied by changes in the number of plasmosomes carried by the diploid set of chromosomes. Since the average chromosome volume of normal rat organs does not vary in accordance with the cytoplasmic concentration of ribonucleic acid nor with the development of heterochromatin and plasmosomes, differences in chromosome size are probably not determined by differences in the quantity of polynucleotides on the chromosomes. However, the average chromosome volume is directly proportional to the total concentration of B vitamins, with the exception of inositol, reported in the literature. It is proposed that the difference in chromosome size from one normal cell type to another in rats depends on the development and activity of the euchromatin, i.e., the larger the chromosomes, the greater is the bound vitamin capacity of the organ.—Author’s abstract.


Chromosomes in hepatoma 31 and Walker carcinosarcoma 256 are of 3 sizes: small ones of about the size found in newborn rats or in adult organs poor in B vitamins; chromosomes about twice as large, that are in the majority; and chromosomes about 4 times as large. The chromosomes of double and quadruple size in the 2 cancers are probably composed of more discrete strands
than are chromosomes of normal tissues, since in the tumors the proportion of division figures that are polyploid is greatly exceeded by the proportion of resting nuclei with more plasmosomes than are carried by the diploid set of normal chromosomes. Most of the hepatoma chromosomes are double the size of newborn or perhaps fetal rat liver chromosomes rather than double the volume of actively functioning adult liver chromosomes.

Because of the double nature of most of the cancer chromosomes, one-half their average volume is to be used in assessing their synthetic activity. On this basis the two tumors should have a low over-all rate of synthesis of chromosomal products, and this is made probable by evidence from the literature of low B vitamin content, low activity of a number of enzymes, and a decrease in certain metals in these and other cancers.—Author's abstract.


Mitochondria and Golgi material were demonstrated in both carcinogen-treated and control cultures of mouse fibroblasts, with no differences between them that could be related to the process of malignant transformation in vitro. However, the orientation of the Golgi material was found to be correlated with the growth pattern of cultures treated with the carcinogen for different lengths of time, being located distally (toward the periphery of the cultures) more frequently in cells of the faster growing cultures.

Studies of mitochondria in (1) tumors arising in mice from implants of carcinogen-treated cultures, (2) transplants of spontaneous fibrosarcomas, and (3) normal fibroblasts, revealed no differences associated with malignancy; but the Golgi material was hypertrophied in both types of tumors and in the endothelial cells of host blood vessels supplying them, compared with its condition in normal fibroblasts.—R. B.


Ciliated cells were found in histologic sections of the thyroids of C3H and A strain mice. Ten of 22 C3H mice 10 months of age, and 5 of 25 A mice of the same age had some of the ciliated thyroid cells. None of these cells were found amongst 3 strain A mice, 11 weeks old, but a number of them were present in the thyroids of 10 newborn C3H mice.—R. B.


A method for use in the study of vascular structure.

Clinical and Pathological Reports

Etiology


It is highly improbable that there is anything in military predisposing to cancer. The author finds no evidence that bodily exertion has any influence on the growth of a malignant tumor. The question whether a malignant growth was present at the time of enlistment, or developed later, cannot be answered, because the latent period is unknown.—W. H. W.

Radiation—Diagnosis and Therapy


The article is a fairly comprehensive survey of all leading American papers on the subject. The bibliography includes 126 titles. Since the paper is a digest of other articles, the original should be consulted.—A. C.


The results of treatment with million volt x-rays of 315 cancer patients are tabulated. Of the total number 213 are dead. Of these, 145 were in a very advanced stage of the disease and were treated palliatively; many of the others presented more complicated problems than usually seen in the radiation therapy patient. However, in those who died, considerable palliation was obtained. Survival rates even on the living group are not a fair indication of the value of million-volt therapy, because, as is usually the case when a new method of treatment is employed, the majority of the first patients were in advanced stages of the disease. An analysis is made of factors which should determine what types of cancer might be expected to present better results with million volt than with 200 kilovolt therapy.—E. H. Q.


A review is presented of 466 cases of malignant disease and 294 of non-malignant, treated by 40-60 kv. x-rays, at target skin distances of 2 to 10 cm. Depth dose and isodose charts are given for various voltage-filter-distance combinations. Practical methods for shielding eyes and other normal parts are discussed.—E. H. Q.
Experimental Research, Animal Tumors


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