Abstracts
Reports of Experimental Research

CARCINOGENIC COMPOUNDS

BERENBLUM, I. [Univ. of Oxford, Oxford, England] THE MECHANISM OF CARCINOGENESIS: A STUDY OF THE SIGNIFICANCE OF COCARCINOGENIC ACTION AND RELATED PHENOMENA. Cancer Research, 1:807-814. 1941. The effect of croton resin on carcinogenesis was studied under varying conditions. No cocarcinogenic effect was observed when croton resin was applied to the skin and benzpyrene was injected intraperitoneally. Subcutaneous injection of croton resin and benzpyrene together did not augment the carcinogenic effect of benzpyrene. While augmentation of carcinogenesis was pronounced when croton resin was applied to the skin concurrently with a dilute solution of a potent carcinogen (3,4-benzpyrene), none was observed with concentrated solutions of different carcinogens irrespective of whether their potency was high (3,4-benzpyrene), moderate (1,2,5,6-dibenzanthracene), or low (1,2-benzanthracene). Preliminary treatment with croton resin failed to influence the response of the mouse's skin to subsequent application of benzpyrene, but croton resin applied to the skin subsequent to a limited period of benzpyrene treatment led to an increase in the development of tumors. Croton resin applied to papillomas appeared to facilitate their conversion to malignancy. It is suggested that the 3 phases of carcinogenesis—precarcinogenic, or latent; epicarcinogenic, or wart-stage; and metacarcinogenic, or malignant transformation, are independent processes. Croton resin having only epicarcinogenic and metacarcinogenic properties cannot produce tumors.

Cocarcinogenic action is discussed and attention drawn to the clinical implications of cocarcinogenic, epicarcinogenic, and metacarcinogenic actions on the part of noncarcinogenic agents affecting human beings.—From author's summary.

BRUES, A. M., B. B. MARBLE, and B. RIESEL. [Collis P. Huntington Memorial Hosp., Boston, Mass. and Northwestern Univ., Evanston, Ill.] THE MECHANISM OF CARCINOGENIC HYDROCARBONS AND RELATED COMPOUNDS ON THE AUTOXIDATION OF OILS. Cancer Research, 1:815-817. 1941. An attempt was made to detect effects of different solvents used as vehicles for methylcholanthrene and 9,10-dimethyl-1,2-benzanthracene on the induction time of tumor formation in rats. Rat fat, linseed oil, lard, lanolin, and spermaceti were used and a single injection of 0.4 cc. of a 2% solution of the carcinogen made into the right flank. A series of 44 rats received methylcholanthrene and 32 received dimethylbenzanthracene. One special group of 9 received 3 doses of methylcholanthrene in linseed oil, lanolin, and lard respectively. Control doses of lipids without carcinogen were injected on the opposite side. Of the total number of 85 rats, 76 survived longer than 80 days after injection, at which time the first tumor appeared. Between 80 and 287 days, 61 tumors appeared among the 70 which received one injection of carcinogen, and 10 tumors occurred among 6 survivors which received three injections each. The average time of induction in the methylcholanthrene series for each solvent was as follows: rat fat, 120; linseed oil, 153; lard, 123; lanolin, 160; spermaceti, 144; and the 3-injection group, 147 days respectively. The times in the dimethylbenzanthracene series were: rat fat, 115 days; linseed oil, 120; lard, 153; and lanolin, 140. Spermaceti was not used in this series. There was so much overlap in the various times of induction, and the groups so small that the averages are not significant except to indicate that dimethylbenzanthracene is somewhat more active than methylcholanthrene. Any influence of the solvent was probably overwhelmed by the high concentration and large amount of carcinogen used. No tumors developed at the sites of injection of lipids alone.—Authors' abstract.

DEUTSCH, H. F., D. L. MINER, and H. P. RUSCH. [McArdle Memorial Lab., Univ. of Wisconsin, Madison, Wis.] THE EFFECT OF CARCINOGENIC HYDROCARBONS AND RELATED COMPOUNDS ON THE AUTOXIDATION OF OILS. Cancer Research, 1:818-820. 1941. An effort was made to determine whether the antioxidative action of the carcinogens is specific for catalyzed phospholipid oxidation or whether other types of fat oxidation are also affected by the hydrocarbons. The effect of various carcinogenic chemicals and related compounds on the autoxidation of corn oil, cod liver oil, lard, and ethyl linolate was investigated. The degree of autoxidation in the presence or absence of these compounds was determined by the Kreis test, peroxide numbers, and measurement of the total oxygen consumption. When ethyl linolate was employed, dibenzanthracene acted as a mild inhibitor whereas hydroquinone and ascorbic acid gave marked inhibition. Alloxan, aminozotoluene, and desoxycholic acid stimulated autoxidation. The effect of other hydrocarbons was variable but, in general, the oxidation of freshly prepared ethyl linolate was accelerated by most carcinogens while that of older samples was inhibited. When other oils were employed, the results were even more variable and depended upon several factors.—Authors' abstract.

HORMONES

JONES, E. E. [Wellesley Coll., Wellesley, Mass.] THE EFFECT OF TESTOSTERONE PROPIONATE ON MAMMARY GROWTH IN RATS. Cancer Research, 1:821-824. 1941. An attempt was made to determine whether the anti-estrogenic action of the carcinogens is specific for catalyzed phospholipid oxidation or whether other types of fat oxidation are also affected by the hydrocarbons. The effect of various carcinogenic chemicals and related compounds on the autoxidation of corn oil, cod liver oil, lard, and ethyl linolate was investigated. The degree of autoxidation in the presence or absence of these compounds was determined by the Kreis test, peroxide numbers, and measurement of the total oxygen consumption. When ethyl linolate was employed, dibenzanthracene acted as a mild inhibitor whereas hydroquinone and ascorbic acid gave marked inhibition. Alloxan, aminozotoluene, and desoxycholic acid stimulated autoxidation. The effect of other hydrocarbons was variable but, in general, the oxidation of freshly prepared ethyl linolate was accelerated by most carcinogens while that of older samples was inhibited. When other oils were employed, the results were even more variable and depended upon several factors.—Authors' abstract.

Female mice of the C3H strain were injected with testosterone propionate from the 2nd to the 12th month of life. None developed tumors during the period of treatment. Three (25%) of those living to cancer age developed mammary gland tumors at an average age of 20 months. Eighteen controls (47%) developed tumors at an average age of 12.0 months. Thus, tumor incidence was lowered and age at macroscopic appearance of tumors may have been increased. Mammary glands of treated and virgin control mice of comparable age are described. Glands from treated females had fewer cystic and more narrow branching ducts, more localized areas of alveolar proliferation, and a greater amount of periductal infiltration. Sixteen females of normal breeding history, injected with testosterone, all developed tumors at an average age of 9.6 months. Sib controls all developed tumors at an average age of 9.0 months. Testosterone injections into mice in which a tumor was already established were ineffective in inhibiting tumor growth.—Author's abstract.

VIRUSES


Tissue from spontaneous mammary carcinoma of mice was lyophilized as follows: The tissue was removed aseptically, minced, placed in tubes, immediately frozen at \(-72^\circ\)C, and dried in vacuo. The tubes were then sealed with a blowtorch till used.

Thirty cc. of water were added to 10 cc. of the lyophilized tumor tissue and filtered. Ten cc. of this filtrate was placed in small dishes before each of 2 groups of 5 mice. The mice receiving this filtrate were of the Ax strain and were from 4 to 5 weeks old. The incidence of breast cancer in breeding females of this strain is 34.1%; average tumor age 13.9 months. Females of this strain are so genetically constituted that breast tumors may be expected to develop if they are nursed by females which have the milk influence, and are used as breeders. Of the mice of the Ax strain receiving filtrate of the lyophilized tumor tissue 6 developed breast tumors (13.4 months), 1 was missing at 12 months of age, and 3 are living (17.5 months). These mice were bred. The 10 experimental animals were the progeny of 3 females, 2 of which had 21 additional young. As none of these mice has developed breast tumors it is improbable that the mice receiving the filtrate were subjected to an active influence in the milk of the mother, or that the influence developed de novo. The technic used in the preparation of the lyophilized tumor tissue was similar to that of others for preservation of viruses of other diseases. Hence the results obtained suggest that the milk influence may be a virus.—M. B.


This large article brings together practically all the known data on the biochemical and infectious properties of the Shope rabbit papilloma virus. Much original work is included. The wealth of material reported is so great and its exposition so detailed that any abstract would be inadequate. The reader is referred to the original paper.—L. L. W.


The duck, heretofore considered resistant to Rous virus, can be infected if (a) newborn ducks are injected, preferably intravenously; (b) large amounts of virus are used. Intravenous infection of the duckling with the Rous virus is manifest in two ways: by development of a hemorrhagic disease, fatal in a few weeks with blood blebs and extra-vasations in viscera, and by development of one or a few sarcomas in various locations several weeks or even months after infection. Once tumors have been induced in ducks by the chicken virus, the disease can easily be transmitted by grafts or filtrates to other ducks without much regard for the age of the host.

When the virus has acquired the capacity to infect ducks, it has lost its original capacity to infect chickens. This change seems to take place suddenly as soon as the chicken virus has infected the duck cells, since extracts of hemorrhagic and neoplastic lesions from ducks injected with Rous virus consistently fail to induce tumors in adult chickens. When young chicks (1 to 3 days) are injected intravenously with the duck variant of the Rous virus they develop (in 20 to 40 days) multiple sarcomas of flat and long bones, skeletal muscles, and occasionally in viscera. This disease is quite different from that induced in chicks by the original Rous virus.—M. B.


Virus-induced papillomas of domestic rabbits contain an inhibitor capable of neutralizing the active papilloma virus. Experiments were undertaken to determine whether or not this inhibitor is identical with the specific antiviral antibody which develops in the blood of rabbits carrying papillomas. It was found that the amount of inhibitor present in papilloma extracts varies concurrently with the serum antibody titer of the host. The inhibitor fixed complement in mixture with papilloma virus, in proportion to its neutralizing capacity. It was specifically absorbed from papilloma extracts when mixed with the papilloma virus. The infectivity and complement-fixing property of a virus filtrate could be completely absorbed with the inhibitor, findings similar to those previously reported for blood antibody. The inhibitor and the blood antibody were both completely inactivated by heating 30 minutes at 86° C. and they were precipitated together upon treatment with ammonium sulfate. The inhibitor was not confined to the papillomas but was present in extracts of liver, muscle, and skin from rabbits bearing the papillomas, and in amounts proportional to the titer of antibody in corresponding serums. It is assumed that the greater proportion of inhibitor in papilloma extracts, as compared to organ extracts, is probably blood antibody which has become localized in the papilloma tissues, not merely circulating antibody. This view is supported by
the fact that perfusion with saline failed to effect any large reduction in the inhibitor content of the papillomas. The author concludes that the “inhibitor” demonstrable in extracts of papillomas is identical with the antiviral antibody found in the blood of rabbits bearing the growth.—A.C.


Observations presented in this paper indicate that the rabbit papilloma virus (Shope) elicits an antibody of one type only, this being capable both of neutralizing the virus and of fixing complement in mixture with it. The virus and its antibody have a specific affinity for one another, each being capable of absorbing the other in great excess when they are brought together in the test tube. These conclusions are based on elaborate experiments which are reported in great detail. The results reveal important properties of the virus and its antibody. General findings can be summarized as follows: 1. The virus-neutralizing and complement-fixing capacities of immune sera are, however, of widely different origin and potentials, invariably parallel one another closely. 2. The complement-fixing and virus-neutralizing capacities of any given serum were absorbed simultaneously, the amount of antibody remaining after absorption varying inversely with the concentration of virus used for absorption. 3. Visible flocculation was noted in mixtures of virus filtrate and immune sera when proportions were optimal. In mixtures containing an excess of either, there was less, or no flocculation. 4. The papilloma virus itself appeared to be responsible for the absorption of antibody, no absorption being observed when extracts derived from domestic rabbit papillomas (inactive), Brown-Pearce tumor, or various mammalian organs, were used. 5. When virus filtrates were fractionated by high speed centrifugation, it was found that absorption occurred only with the fraction containing the virus. 6. In experiments in which the virus had been treated at various temperatures, or had been submitted to ultraviolet light, it was found that infectivity of the virus was affected sooner than the capacity to fix complement or to absorb antibody, but the two latter properties were affected in a comparable manner. The union between the papilloma virus and its antibody in vitro appears to be rapid and stable. After 5 minutes contact at room temperature, no evidence of any dissociation could be detected, either by dilution or by centrifugation.—A.C.

GENETICS


A high incidence of spontaneous tumors of the breast was observed in breeding females of the A strain and a low incidence in breeding females of the same strain following fostering by mothers of the CBA or X stock (low incidence). Reciprocal matings were made between individuals of these two sublines of the A stock. All the hybrids were used as breeders.

When the maternal parents had high incidences there was no reduction in the F1—F2 hybrids; the reciprocal cross gave only 1 tumor in mice of the F1—F2 generations. The total number of hybrids observed was 859.

Thus, foster nursing, with a reduction in the incidence of tumors, does not alter the genetic constitution of mice for the development of mammary carcinoma.—Author’s abstract.


An unusually high rate of infanticide was observed in a strain of rats (Albany or A-S strain) characterized by a high incidence of benign mammary tumors. The cannibalistic habit was manifested too early to be interpreted as an eventual deterioration of the maternal behavior pattern and occurred most frequently in those rats which eventually developed tumors. The data, taken with other observations on breeding abnormalities of these rats, were interpreted as tending to indicate that common factors may be operating in producing both the greater degree of abnormality in reproductive physiology characterizing the tumor-bearing animals and the susceptibility to tumor development.—Authors’ abstract.


Leukemic cells arising in hybrids (F1, F2, and backcross) between the “susceptible to leukemia” F strain and “resistant to leukemia” CBA strain were inoculated into the parent stocks; leukemias arising in F1 hybrids were also inoculated into F1 hybrid mice. Leukemia arising in hybrid mice was transplatable in the same manner as mammary cancer and normal splenic tissue of hybrid mice; that is, the leukemic cells of F1 hybrids grew in neither parent stock but in all F1 hybrids. Leukemic cells of F2 hybrids grew in neither parent stock; leukemic cells from a small percent of backcross mice grew in the parent stock to which the F1 hybrid parent had been backcrossed.—Authors’ abstract.


In this paper an attempt is made to separate and evaluate the parts which chromosomal and extrachromosomal influences play in the development of mammary carcinoma in mice.

Data from 9 experiments totaling 2,330 animals are offered as evidence that the ratios in which mammary tumors occur in inbred strains and experimental crosses may be reasonably explained upon the basis of the strength of the milk stimulus which the mice receive and the resistance of the physiological systems produced by these matings to various concentrations of the milk stimulus.—Author’s abstract.
PHYSICAL FACTORS


Significant changes in electrodynamic fields were observed during the growth of transplanted tumors. This supplements previously reported similar observations concerning spontaneous tumors and those induced with methylcholanthrene or benzpyrene.

When the rapidly growing Yale carcinoma No. 1 was implanted into the right axillary region of Strong A mice, the implantation site became significantly positive relative to the other side of the chest at the time of appearance of the tumor. The readings then also exhibited greater variations from the mean than at first. In the sternum-pubis gradient, the former also reversed its polarity and became significantly positive relative to the pubis after the tumor appeared. In the case of the slowly growing tumor No. 139,658 (Strong) the findings were in the same direction. Also in the cross-chest measurements, the values at first clustered about the mean but after the tumor became manifest they tended to scatter. The opposite was observed in the xiphoïd-symphysum readings.

These observations concerning gradients are discussed as a frame for a general theory of cancer.—A. A. L.

RADIATION


This is a study of massive and fractionated doses of x-ray, delivered by a Chaoul contact therapy on transplanted rat sarcoma 39. The control animals usually died in the 7th week. Spontaneous regression never exceeded 5%. Tumors 10 to 15 mm. in diameter were used. A single dose of 10,000 r caused complete destruction of all tumors. When this total dose was divided and given in daily treatments so that 10,000 r would be delivered within 7, 14, 28, 42, or 70 days, the destructive effect on the tumor decreased. If the total dosage was given in 6 or 12 successive treatment days, 60% of the animals survived. There was no destructive effect on the tumor if it required 70 days to reach a total dose of 10,000.—E. A. L.


This is a report of studies on the effect of magnetic fields on cells cultivated in vitro, on the repair of cutaneous wounds, and on the growth of Ehrlich adenocarcinoma. The experiments were performed with electromagnets capable of functioning either with direct or pulsating currents and of generating fields of from 1,500 to 1,700 gauss. White mice were used and were placed in cellophane cells between the poles of the magnet.

It was concluded from reviewing the experiments of others that the direct magnetic field acts on the course of mitosis of cells cultivated in vitro while the alternating field acts on the order and orientation of the entire culture. Wounds treated in the direct magnetic field showed an initial slowing of the rate of healing compared with the controls followed by an increased rate. This phenomenon has not yet been adequately interpreted.

Grafts of the Ehrlich adenocarcinoma previously kept in a magnetic field show a greater percentage of takes than the control tumor. When the animals were placed in a constant magnetic field, immediately after the graft, for 8 hours a day for 12 days, there was a marked delay in the taking and a smaller percentage of taken neoplasms. With the animals placed in a similar manner in an alternating magnetic field the taking was delayed even more, so that at the end of the 12th day there were 25% takes as compared to 92% in the controls. When animals bearing 12-day-old tumors were used, there was no effect on the further development of the tumors with either type of magnetic field.—E. A. L.


The spinal ganglia of rats which had had their extremities irradiated with varying amounts of low voltage x-radiation were studied cytologically. Changes in the cell outlines, the size and shape of the nuclei, and in the Golgi apparatus and mitochondria were noted. Ganglion cells that had received direct radiation showed similar changes. The authors conclude that these changes are morphological evidence of functional disturbances in the cells brought about either directly or by circulating products of irradiation.—L. L. W.


A method for determining the dosimetry of radiation is described which depends on the rate of cleavage of sea-urchin eggs after fertilization by sperm irradiated with varying doses of roentgen rays. These workers found that at a given temperature the time of the first cleavage is determined only by the quantity of radiation administered, and depends neither on the duration of irradiation nor on the time between irradiation and insemination within certain limits. The depth-dose determined by this biological method showed some discrepancy when compared with ionization chamber measurements. The significance of this discrepancy is discussed.—P. P. C.


The reactions of neoplasms to radiation fall into three groups: the radiosensitive, which respond strikingly to a total dosage of 2,500 r or less of protracted radiation; radiosensitive, which require from 2,500 to 5,000 r for similar regression; and radioresistant tumors which require over 5,000 r. Radiosensitivity and radioresistance are not, however, synonymous. Although many tumors of higher grades are radioresistant and some of the lower
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glands, and raw milk. This enzyme oxidizes aldehydes
potentials. A possible relationship to previous work on
LIVERS OF MICE OF CANCER-SUSCEPTIBLE AND
in so doing, maintains very negative oxidation reduction
Baltimore, Md.] XANTHINE OXIDASE ACTIVITY IN
substrates and end products by dialysis. Xanthine oxidase
xanthine oxidase activity units per gin. of liver. The JK
activity was determined quantitatively in livers of 21 mice
of mouse livers, utilizing the Thunberg methylene blue re-
summary.

Biochemistry and Nutrition—Chemotherapy

FIGGE, F. H. J., and L. C. STRONG. [Yale Univ. Sch. of
Med., New Haven, Conn., and Univ. of Maryland Sch. of Med.,
Baltimore, Md.] XANTHINE OXIDASE ACTIVITY IN
LIVERS OF MICE OF CANCER-SUSCEPTIBLE AND
CANCER-RESISTANT STRAINS. Cancer Research, 1:779-784.
1941.
Xanthine oxidase occurs abundantly in liver, mammary
glands, and raw milk. This enzyme oxidizes aldehydes
as well as some of the constituents of nucleoproteins and,
in so doing, maintains very negative oxidation reduction
potentials. A possible relationship to previous work on
salicylaldehyde tolerance and heptaldehyde influence on
tumors was, therefore, postulated.

A method for determining the xanthine oxidase activity
of mouse livers, utilizing the Thunberg methylene blue
reduction technic, was devised. The essential and new
feature of this method was the removal of naturally occurring
substrates and end products by dialysis. Xanthine oxidase
activity was determined quantitatively in livers of 21 mice
of the C3H cancer-susceptible strain and 22 mice of the
JK cancer-resistant strain. The C3H livers averaged 0.81
xanthine oxidase activity units per gm. of liver. The JK
livers averaged 1.64 xanthine oxidase activity units per gm.
of liver. These values correspond to a methylene blue
reduction time of 33 minutes per C3H and 16 minutes
for JK livers.

It is thus apparent that the xanthine oxidase activity in
livers of the mammary cancer-resistant JK strain of mice is
about double that observed in the livers of C3H mam-
mary cancer-susceptible strain of mice. A discussion of
a possible correlation between xanthine oxidase activity
and cancer susceptibility is included.—Authors’ abstract.

LASNITZKI, A., and A. K. BREWER. [Univ. of Manches-
ter, Manchester, England, and U. S. Dept. of Agric., Wash-
ington, D. C.] THE ISOTOPIC CONSTITUTION OF POTAS-
SIUM IN ANIMAL TUMORS AND MUSCLE FROM TUMOR-
BEARING ANIMALS. Cancer Research, 1:776-778. 1941.
The isotopic constitution of potassium in Jensen rat sarcoma and mouse sarcoma S 37 has been studied. Com-
pared to mineral potassium as contained in ordinary pot-
tassium chloride (A. R.), a slight but definite increase of the isotopic ratio K 39/K 41 was found, indicating a cor-
responding decrease in the percentage of the heavy iso-
otope K 41. In rats, since potassium in bone including
narrow and blood plasma has shown similar deviation in the
opposite direction, and as potassium in other normal
tissues usually showed no deviation, it appears that the
isotopic constitution of potassium in normal and tumor
tissue is appropriately different. Comparison was also made
of the potassium in muscle from normal and tumor-bearing
rats and mice. In muscle from normal animals the isotopic
ratio was generally the same as that of mineral potassium;
but in tumor-bearing animals a deviation was observed similar
to that found with tumor tissue.—Authors’ summary.

LEWISohn, R., C. LEUCHTENBERGER, R. LEUCHTEN-
BERGER, D. LAZLO, and K. BLOCH. [The Mount Sinai
Hosp., New York, N. Y.] ACTION OF YEAST EXTRACT
ON TRANSPLANTED AND SPONTANEOUS MALIGNANT
TUMORS IN MICE. Cancer Research, 1:799-806. 1941.
In testing the action of fractions of yeast extract on the
regression of spontaneous adenocarcinoma of the mouse,
the following results were obtained. The active principle
is water-soluble and comparatively thermostable at neutral
pH. It is not protein in nature, not affected by nitrous acid,
nor precipitated by high concentration of ethanol. The
active material is precipitated by lead acetate and silver
nitrate. Active preparations can be obtained by precipita-
tion with barium and ethanol, and also by phosphatungstic
acid. The active material is adsorbed by Fuller’s earth and
by norite but not by permutit. It has not been possible to
remove it by elution. None of the known vitamins of the
B group appears to be responsible for the activity.

Results with yeast extract on four different malignant
tumors in mice are reported. These were spontaneous
mammary adenocarcinomas in mice of the following strains: 1. strain A, Jackson Memorial Laboratory; 2.
Rockland Farms strain; 3. strain R III. One tumor was
the highly malignant transplanted carcinoma 2163 in the
R III strain. With all these tumors 30% complete dis-
appearance was produced.

In the spontaneous carcinoma (R III strain) results ob-
tained in biopsied and nonbiopsied tumors were found to
be identical. As a rule small tumors respond to the yeast
extract more quickly than large tumors. Recurrences are
noted in about 25% of the apparently healed animals,
usually after 6 to 8 months.

Fifty spontaneous mammary carcinomas are presented. Biopsy performed before treatment was started had estab-
lished the diagnosis of carcinoma. Intravenous treatment
either with spleen or yeast extract was given. The tumors
had disappeared completely for i to 12 months when the
animals died. Careful post-mortem and microscopic ex-
amination failed to show any evidence of remaining tumor
cells. Twenty animals are still living and apparently
healed. Among the 70 healed animals, 50 belonged to the
strain A Jackson Memorial Laboratory and 20 to the Rock-
land Farms strain.

The interpretation of the regressive changes in the
tumors of the treated animals is difficult, as similar changes,
though not as extensive, may be observed in untreated tumors. However, in successfully treated animals the whole tumor undergoes marked changes in a relatively short time, whereas in the controls these changes occur more slowly. Remnants of unchanged malignant tumors are always present in the controls. Histological pictures of marked changes in treated tumors (as compared with the original biopsy specimen) after 7 and 43 intravenous injections respectively are presented.—Authors' abstract.


In continuation of previous experiments which showed that liver feeding prevented carcinogenesis by butter yellow, the author investigated the effect of the following tissues: beef kidney, spleen, muscle, brain, lung, fore and glandular stomachs, small intestine, pancreas, and testicle. In addition, the effect of feeding bile was investigated. The different tissues were dried on a steam bath and pulverized. The diets consisted of 880 gm. of polished rice, 190 gm. of dried tissue, and 20 gm. of an olive oil solution of butter yellow. The amount of butter yellow used was 0.2 gm. per kg. of food at the beginning of the experiments, and was gradually increased to 0.6 gm. per kg. A small slice of carrot was fed every other day. The experiments were terminated after 150 days and the livers were examined macroscopically and microscopically. Forty to 50 animals were used for each experiment. Of the above tissues kidney alone showed an inhibitory effect on carcinogenesis, though the effect was not as marked as with liver feeding. In the case of the bile feeding experiments, the mortality was so high that no rats survived beyond 131 days, and as many as 31 of 40 animals died during the early part of the experiment. Thus of the animal tissues, liver and kidney are the only ones which exert an inhibitory influence on butter yellow carcinogenesis.—P. P. C.


One hundred rats were placed on a diet consisting of polished rice (900 gm.), o-aminooazotoluol (0.2 to 1 gm. per kg. of food) in olive oil, dried beef liver powder (100 gm.), and fresh carrots. A second group of 100 rats was placed on the same diet except that no liver powder was present. The experiment was discontinued after 350 days at which time 38 rats on the liver diet and 24 rats on the nonliver control diet survived. In the liver fed group, 23 (60.5%) of the total 38 rats showed apparently normal livers. In 13 other animals (34.2%) the liver changes were not advanced beyond the stage of a granular surface, and only in the remaining 2 animals (5.3%) were the hepatic changes sufficiently advanced to warrant the diagnosis of cancer, but without cirrhosis. In contrast, the group not fed liver included 8 animals (33.3%) with liver cancer plus cirrhosis and 16 animals (66.6%) with typical cirrhosis. None of the control rats showed normal livers macroscopically.—P. P. C.


Forty rats were fed a diet consisting of polished rice, butter yellow (0.2-0.6% of diet in olive oil), cystine (1 gm. per kg. of polished rice), plus a daily slice of carrot. An equal number of animals were fed the above diet without added cystine. The animals were sacrificed after 150 days. In the cystine-fed group 16 rats survived, 6 (37.5%) of which showed cirrhosis, and the remaining 10 (62.5%) liver cancer. In the control group 8 animals survived, 3 (37.5%) of which showed cirrhosis and 5 (62.5%) of which showed liver cancer. The author concludes that on the basis of this study the inhibiting effect of liver on butter yellow carcinogenesis cannot be due to the high sulphydryl content of these tissues.—P. P. C.


Fifty rats were placed on a diet of husked and polished rice, 20 cc. of 3% butter yellow in olive oil, green vegetables, and dried sardines. An equal number of animals were placed on the same diet except that husked Japanese millet was used in place of rice. All the livers of the animals which died were carefully examined histologically. At the end of 165 days all the surviving animals, 5 in the rice group and 10 in the millet group, were sacrificed for histological examination. Liver cancer was found in 100% of the animals surviving in the rice group. No cancer was found in the 10 animals surviving on the millet diet. The livers of the latter animals showed minimal pathological changes.—P. P. C.


An examination of Nakatani's statement that during carcinogenesis by butter yellow (dimethyl yellow, p-di-methylaminooazobenzene) the glycolytic properties of normal liver tissue change progressively to those of liver tumor tissue. The steps in the process were classified histologically, (normal, degenerative changes, periportal changes, nodular hyperplasia). Anaerobic glycolysis, $Q_{240}$, stated by Warburg and Nakatani to be low in normal liver was found to depend in some degree upon the glycogen content. When comparison is made giving due regard to glycogen content, no significant difference was seen between $Q_{240}$ for normal, regenerating or precancerous liver. $Q_{240}$ as a measure of the capacity to deal with added glucose (i.e. glycolysis) was small in amount and there was no great difference in this respect between normal, regenerating, or precancerous liver. Normal liver has also a very small aerobic glucolysis; i.e., conversion of added glucose to lactic acid aerobically. Liver tumors have quite different glycolytic characteristics. Two hepatomas had high anaerobic glucolysis, and 3 cholangiomas, and 2 hepatomas had considerable aerobic glucolysis (about as high as the anaerobic glucolysis). Thus the change in metabolism during carcinogenesis seems to be sudden
and not progressive and the substrate is glycogen in liver tissue and glucose in liver tumors.

The authors point out that comparison of the metabolism of a parent tissue and of the tumors derived from it has been investigated only for liver and for skin (Berenblum et al.), who found no qualitative differences between normal skin and skin tumors.—I. H.


With the fluorescence microscope 219 tumors were examined for vitamin A fluorescence, which was encountered only in certain groups of tumors. The findings suggest that the presence or absence of vitamin A does not influence tumor formation. Vitamin A fluorescence is seen in tumors originating from a parent tissue normally containing vitamin A. The presence and distribution of vitamin A fluorescence helps to determine the origin of some tumors; e.g., ovarian tumors. The fluorescence microscopic picture suggests an adrenal origin of hypernephroma. The visualization of vitamin A in tumors further suggests an important histologic method for the study of the histogenesis of tumors.—Authors’ summary.


Previous experiments concerning the effect of sulfur-containing amino acids, and of glutathione and cystine disulfide in terminating the growth inhibition produced by certain compounds is reviewed. The question had arisen as to whether a chemical detoxicating mechanism or one of general growth stimulation is concerned. In the present experiments the introduction of 5% of sodium benzoate into a low protein diet was found to inhibit the growth of young rats. This inhibition of growth was abolished by adding to the diet glycine, sarcosine, or both sarcosine and, to some extent, glycolic acid can be converted to glycine. Ineffective, however, were the sulfur-containing amino acids, and glycocyamine, creatine, hydroxypropilene, serine, threonine, sodium sulfate, or sodium citrate.

These results were taken as evidence that a detoxicating reaction is concerned in the growth inhibition: the effective dietary supplement supplies for conjugation a substance that otherwise would be withdrawn from the tissues of the animal subsisting on a low protein diet.—A. A. L.

IMMUNOLOGY


The serum of rabbits convalescent from infectious myxoma possessed the power to neutralize the virus of the disease.—M. J. E.

CYTOLOGY


Upon direct contact with the genital tissues of spayed and subsequently estrogenized mice, colchicine (0.1 mgm. in 0.05 cc. of H2O) produced surface and systemic effects. Local action upon the vaginal epithelium was demonstrated within half an hour after contact with the drug, reached a maximum between the 6th and 8th hour, was on the decline at the 10th, and was largely absent at 24 hours. After the 6th hour colchicine effect was visible also in the uterus and rectum; this indicated systemic action. No effect was observed in mice spayed but not treated with estrone. Colchicine introduced in similar amount into a ligated uterine horn produced effects only on the homolateral horn. In the periovarian capsule colchicine action was local; it was manifest only in the 6 to 8 peripheral layers of cells and in the outer portions of the larger follicles.—A. A. L.

MISCELLANEOUS


Active agents of dialyzed extracts of giant ragweed, short ragweed, and timothy pollen can be transported by diffusion and electrophoresis into the skin. Three main channels of transport are considered, (a) the pores or coils of the sweat glands, (b) the hair follicles and sebaceous glands, (c) the keratin matrix of the skin itself. Electrophoretic studies show that copper ions, and basic and acidic dyestuffs localize primarily in the sweat glands, and that pore patterns of the skin, persisting for several weeks may be “developed” by electrophoretic transport of such pigments. Pore patterns in scar tissue and in such skin diseases as scleroderma and poriosis may also be mapped in this manner and certain characteristics of the disease defined. Although not specifically mentioned by the authors, it would seem that such a technic might be useful in studies of cancerous skin lesions.—R. N. J.


An improved form of an operation devised for the study of the metabolism of carcinogenic compounds.—E. L. K.

RONDONI, P. [Inst. für exper. Path. der Univ. und Klinikum, Milan, Italy] DAS NEPHELOMETRISCHE VERHALTEN VON SERUM UND VON ORGAN- UND TUMOREIWEISS BEI DER ERWARMUNG. [NEPHELOMETRIC REACTION OF SERUM, ORGAN, AND TUMOR PROTEIN TO HEAT. Ztschr. f. Immunnsforsch., 99:115-121. 1940.

Variations in the Tyndall phenomenon observed in sera, and extracts of normal and neoplastic tissues at different temperatures were studied with the aid of a nephelometer. On heating rabbit and horse serum there is a relative decrease in the Tyndall effect between 44° and 62° C. prior to the rapid flocculation of the protein
molecules at the latter temperature. A 10% sodium chloride extract of the normal subcutaneous tissue of the rat reacted somewhat similarly although the relative increase in clarity was restricted to a zone between 45° and 55° C. This biphasic reaction was absent in comparable concentrations of protein of induced benzpyrene or methylcholanthrene sarcoma of the rat. Further, in tumor extracts an increase in Tyndall effect was noted at a temperature of 46-51° C, thus indicating the presence of more labile proteins. In more dilute tumor protein suspensions a slight relative increase in clarification occurred at lower temperatures. Rabbit liver and kidney proteins reacted similarly to tumor extracts.—M. J. E.


With the aid of a microcinematographic apparatus active phagocytosis of leucocytes and wandering cells by tumor cells was observed in explants of a mouse carcinoma. At a later stage remnants of the phagocytosed cells are frequently encountered as inclusion bodies in the cytoplasm of the malignant cells.—M. J. E.

Clinical and Pathological Reports

HEREDITY


Of 9 pairs of monozygous twins in whom neoplastic disease occurred in one or both members, both were affected in 6 and one in 3 instances, while of 10 pairs of dizygous twins both were affected in only 2 and one in 8 instances. Tumors occurring in twins were frequently similar in each member of a pair.—M. J. E.


A review of the literature discloses an incidence of primary multiplicity of between 3.5 and 4% of all malignant lesions. Report of a case of simultaneous occurrence of cancer of the face and the breast, and another of carcinoma of the lip and the thyroid. The hypothesis is advanced that the genesis of multiple cancers depends on the interaction of a functionally mature gene bearing the unit character for cancer inheritance with a functionally mature gene bearing the unit character for localization but endowed with the faculty to affect various structures similarly.—H. G. W.

DIAGNOSIS—GENERAL


The average areas of the nuclei and nucleoli, and the average nucleonucleolar ratio, are not the same in all normal tissues; they vary, probably according to the function of the organ, and in the same organ they vary with the metabolic activity. In nonmalignant lesions the average area of the nucleoli is smaller and the average nucleonucleolar ratio is larger than in carcinoma. In the cells of the fetus, normal liver, membrana granulosa of the ovary, and exophthalmic goiter the areas of nucleoli and the nucleonucleolar ratios approximate those found in carcinoma. This is probably attributable to the great metabolic activity of these cells. There is more variation in the extreme areas of the nuclei and nucleoli in carcinoma than there is in nonmalignant lesions. The average area of the nucleoli and the average nucleonucleolar ratio vary according to the degree of malignancy; the former in a direct and the latter in an inverse proportion. In carcinoma the average area of the nucleoli increases and the average nucleonucleolar ratio decreases from grade 1 to grade 2, from grade 2 to 3, and from 3 to grade 4. The increased amount of nucleolar substance in cancer cells is most probably attributable to the great cellular metabolism and cellular division characteristic of those cells. The increasing of nucleolar substance associated with the increasing in the grade of carcinoma is most probably attributable to the increase of cellular metabolism and cellular division from grade 1 to 2, from grade 2 to 3, and from grade 3 to 4.—Author's summary.


A lecture on the differentiation of carcinoma of the cervix uteri and reparative lesions.—H. G. W.


COMPARATIVE ONCOLOGY


Uterine fibroids can be induced in the guinea pig by prolonged treatment with estrogens, but spontaneous fibroids are extremely rare. One small pedunculated uterine fibromyoma was found in a group of 94 untreated, noncastrated adult females. Its microscopic structure was similar to that of fibromyoma in woman and different from that of experimental fibroid in the guinea pig.—H. G. W.
Reports of Experimental Research

Cancer Res 1941;1:825-832.

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