Abstracts
Experimental Research, Animal Tumors

Production of Subcutaneous Sarcomas in Mice with Tars Extracted from Atmospheric Dusts.

Nine specimens of atmospheric dust were obtained from various locations by three methods of collection. Subcutaneous injection, into male C3H mice, of 20 mgm. of unextracted dust (6 specimens) in saline, or of 0.25 cc. of tricaprylin alone, did not produce sarcomas at the site of injection in 12 months. A single subcutaneous injection of about 50 mgm. of tar, extracted from these dusts by benzene and by ethyl ether and dispersed in tricaprylin, produced sarcomas at the site of injection in 18 of an effective total of 291 mice (strain C3H males and strain A mice of both sexes) in 12 months.—F. L. H.


A new type of dust collector and two others provided specimens of black dust from various cities. Extraction of these dusts with benzene yielded black tars which were then dispersed in tricaprylin and injected subcutaneously into male mice of the C3H strain. A single injection of about 50 mgm. of tar dispersed in 0.25 cc. of tricaprylin was given. The first sarcoma appeared at the site of injection after 5 months. By the end of 16 months the incidence of sarcomas was 8%.—F. L. H.


The carcinogenic hydrocarbons, 20-methylcholanthrene, 3,4-benzpyrene, and 1,2,5,6-dibenzanthracene, were introduced by specified technics into the wall of the pyloric stomach of mice of both sexes of strains C3H, A, C, C57 black, I, and dilute brown. At autopsy the following tumors of the stomach were found: involving, singly or in combination, the intestine, mesentery, pancreas, or pancreatic lymph nodes developed and metastasized to the liver and the lung.

Pulmonary tumors were induced in both strains of mice, with the higher incidence in the strain C mice.—F. L. H.


One hundred and twenty-four mice of the inbred strains dba, C57 black, and I, and of the first generation hybrids derived by reciprocal matings of the dba and C57 black strains, were painted on the skin of the back twice weekly with a 0.06% benzene solution of 5,9,10-trimethyl-1,2-benzanthracene. Of these, 102 were suitable for pathologic study.

The first papillomas appeared at 39 days in 2 strain I mice. Seventy-nine animals developed malignant tumors as follows: squamous cell carcinoma, 77; fibrosarcoma, 10; mixed carcinosarcoma, 3. Squamous cell carcinomatous metastases to the lymph node or lung occurred in 21 mice.

Pigmented foci in the painted area occurred in 61 mice. None of these lesions was considered to be a definite neoplasm. Their morphologic characteristics, nature, and significance are described and discussed.—Authors’ summary.

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A single cutaneous application of a 0.6% (weight/volume) solution of methylcholanthrene in benzene reduced the total iron content of the epidermis of mice within a few days to approximately 50% of the normal content. Multiple applications of the carcinogen made on alternate days produced a further lowering. Ascorbic acid, on the other hand, was not significantly altered during the course of epidermal carcinogenesis.—F. L. H.


The total lipid material extractable from the epidermis of mice was found to be much lowered a few days after even a single topical application of methylcholanthrene in benzene. Mice treated with benzene alone showed no such reduction. Protein nitrogen was used to indicate the amount of tissue involved.—F. L. H.


One application of methylcholanthrene reduced the calcium content of mouse epidermis within a few days to approximately 50% of the normal content. Multiple applications of the carcinogen on alternate days produced only slight further lowering. On the other hand, the epidermal sodium content was not significantly affected by similar treatment with the same carcinogen. Nucleoprotein phosphorus was used as a base of reference representing the amount of tissue involved. Three tables are appended.—Authors' abstract.


It has been observed that N,N-dimethylaminoazobenzene causes hematuria in rats when incorporated in a diet of rice and oil but does not cause hematuria in a diet containing casein, lard, sugar, corn starch, salt mixture, cod liver oil, thiamin, riboflavin, pyridoxin, and pantothenic acid. However the latter diet became procarcinogenic when croton or butter fat was substituted for lard and brown or white rice was substituted for the corn starch and sugar. The authors assume that the diet became procarcinogenic, for these substitutions preserved the incorporated N,N-dimethylaminoazobenzene. It was found that unsaturated fatty acids, linoleic, arachidonic, and oleic acids, have a destructive effect on N,N-dimethylaminoazobenzene and that rice contains a stabilizer or antioxidant for this dye. Therefore, since replacement of lard in the diet by a more saturated fat, butter or croscro, decreases the rate of destruction of N,N-dimethylaminoazobenzene, and replacement of sugar and starch by rice prevents the destruction of the dye, the diet became procarcinogenic.—D.S.


The creatine and creatinine content of various normal and tumorous hepatic tissues was determined by the specific enzymatic method of Dubos and Miller. No difference was found in the true creatine content of transplanted rat hepatoma 31, of the livers of rats bearing transplanted hepatoma 31, of normal and of regenerating rat liver, all values being between 10 and 12 mgm. per 100 gm. of tissue. Similarly, transplanted mouse hepatomas 587 and 7A/77, the livers of mice bearing these tumors, and the livers of normal mice of the same strain showed no significant differences in creatine content. The values for the mouse tissues were 5 to 6 mgm. per 100 gm., or one-half those for the corresponding tissues of rats. The true creatinine content of all these tissues was vanishingly small. The total creatine chromogen of all the hepatic tissues of both rats and mice was 32 to 36 mgm. per 100 gm., and the total creatine chromogen was 1.2 to 1.6 mgm per 100 gm. Thus, while a species difference was found in true creatine, none was found in total chromogen.—H. Q. W.


A mediastinal neurilemmoma was successfully grown in vitro, and reticulin fibers were demonstrated in connection with the Schwann cells by means of Foot's silver impregnation method. The reticulin formation was slow, sparse, and sporadic in cultures of the neuromioma, and much less conspicuous than in cultures of the stroma of an adenomatous human parathyroid gland grown under comparable conditions. Six figures illustrate the Schwann cells growing in cultures and the association of reticulin therewith.—J. G. K.


The myxoma and fibroma viruses appear to be basically related, since infection of the rabbits with one virus creates an immunity against the other. In the present work, an attempt was made to evaluate the antigenic relationship between the two viruses in terms of the complement fixation reaction. Specific complement-fixing antibodies against the myxoma and fibroma viruses were produced in sera of rabbits recovered from actual infection with the diseases or after injection of heat-inactivated virus suspensions. Stronger reactions were found when an antigen was tested against its own antiserum but cross-fixation reactions were obtained in all cases, indicating a close relationship between the virus antigens. The presence of soluble, closely related, heat-labile, complement-fixing bodies in myxoma and fibroma virus suspensions was demonstrated, in addition to a heat-stable complement-
fixing fraction in unfiltered viral suspensions. There is evidence that the presence of measurable fixing bodies in the serum is not necessary for immunity to myxoma.

--A.C.


The V2 carcinoma, a transplanted rabbit cancer derived originally from a virus-induced papilloma and carrying in masked form the virus primarily responsible for it, was propagated in 5 successive groups of rabbits all previously hyperimmunized against the papilloma virus. It was found that the cancer grew as well in the hyperimmunized rabbits as in normal animals. In addition, serological tests showed that not only did the virus remain associated with the carcinoma cells but it also increased as the tumor grew in the hyperimmune animals. This latter result differed from the finding that during the propagation of the V2 carcinoma certain extraneous viruses were eliminated.

--D.S.


It was found that a few preliminary applications to rabbit skin of tar, benzpyrene, or methylcholanthrene greatly enhanced the susceptibility of the skin to papilloma infection. However, these carcinogenic agents were employed for so short a time that they themselves elicited no tumors. Inoculation of the papilloma virus into skin that had been treated with these agents produced papillomas earlier and in greater numbers than on normal skin, and much higher dilutions gave rise to growths. This enhanced susceptibility was brought about by noncarcinogenic agents also; a mixture of turpentine and acetone greatly enhanced the susceptibility of the altered skin. The author suggests that this increased susceptibility of the altered skin may be due to an increased number of young susceptible cells and to a richer vascularization caused by the agents employed.

--D.S.


Rabbit papilloma virus protein isolated in phosphate buffer by ultracentrifugation was photographed with the electron microscope at a magnification of 29,000 diameters. The preparations of the papilloma virus protein appeared to be of considerable homogeneity with respect to particle size and shape. The mean diameter of the papilloma virus images was 44.0 m. They were circular in shape and usually single, although grouping occurred in preparations of virus concentrations higher than 0.1 mgm. per cc.

--M. B.


Transplants of the mammary carcinoma of the dba and C3H strains were used. Tumor tissue, free of necrosis and infection, was squeezed through muslin. The resulting material was diluted with saline so that each milliliter of suspension contained about 0.2 gm. of tumor tissue. Fertile eggs incubated for 4 or 5 days at 38° C. were used for inoculation; 0.25 ml. of the tumor suspension was injected into the yolk, and the eggs were then incubated at 37° C. for 12 days or more. The injected tumor tissue became attached to the inner wall of the yolk sac from which it derived its blood supply. The bulk of the tumor grew down into the yolk. These tumors grew readily when transplanted back into mice. Tumor cells appeared also to be dispersed diffusely through the yolk substance. Histological sections showed healthy cancer cells with numerous mitoses. The supporting stroma was supplied by the yolk sac membrane.

--M. B.


Yolk sacs of chick embryos were implanted on the fifth day of incubation with saline suspensions of fresh tissue from a mammary carcinoma that had arisen spontaneously in a dba mouse. The eggs were then incubated for 12 days more, after which yolk was collected from those eggs bearing comparatively large tumors (1 gm. or more). The viscous yolk was diluted with an equal amount of saline solution, the material centrifuged, and the supernatant liquid passed through an N size Berkefeld filter. All operations were kept aseptic. Mice of the dba strain were injected subcutaneously with the filtrate (0.33 cc. per mouse).

Tumors developed at the site of injection, and smaller growths were found in the liver and in the visceral peritoneum of the digestive tract. The induced tumors were transplanta, grew rapidly, and histologically were composed of malignant cells of epithelial and connective tissue types.

The evidence indicates that the tumor cells constantly gave off the virus substance which was caught and preserved by the surrounding yolk. Whether the tumor factor is able to grow independently in the yolk medium has not been definitely determined.

--M. B.


An experimental study of the effect of environmental temperature upon tumor genesis and growth. The study includes: (1) methylcholanthrene-induced tumors and (2) a transplantable tumor of induced origin. Induced tumors arose earlier in C3H mice kept at 92° F. and 50% relative humidity than in litter mates kept at 65° F. and variable humidity. When injected subcutaneously the transplantable sarcoma grew rapidly in animals in the hot room and slowly or actually regressed in those in the cold room. When injected intramuscularly the sarcoma grew equally well in both hot and cold room animals.

--G. W. W.

Studies on the Effect of Hypothermia. I. Acute Physical and Physiological Changes Induced by the
abstracts


The body temperature of the rabbit can be reduced to very low levels by immersing the rabbit upright and chest high in ice and water. The rectal temperature can be lowered to 10°C but the ability of the rabbit to recover spontaneously after it is removed to room temperature diminishes rapidly in the low body temperature ranges. Recovery is greatly accelerated by the application of external heat. A pseudohibernating state can be produced when the rectal temperature is lowered and maintained in the range between 23°C and 28°C. Spontaneous recovery from this state can be brought about by exposing the animal to room temperature with the hair dry. The extent of the narcotic effect of the low temperature increases as the body temperature falls, producing at the low levels lack of movement and almost complete cessation of the cardiac and respiratory rhythm. Complete spontaneous recovery from this inactive state is rare but may be assisted by the application of external heat. Sudden death from convulsive seizures may occur at any stage in the reduction of the body temperature, but in the dormant state exitus may be so gradual that it cannot be well defined. It should not be regarded as final until all resuscitative efforts have failed. The reaction of the individual animal varies considerably in the time required to reduce the temperature, the lowest temperature level attained, the capacity for recovery, etc. The presence of a 2 week old Brown-Pearce epithelioma did not change the reaction of the animal to the hypothermia.—Authors' abstract.


Short periods of low body temperature (6 hours at a rectal temperature of 18°C, 8 hours at 20°C, 24 hours at 30°C) have a definite effect upon testicular transplants of the young Brown-Pearce rabbit epithelioma. An analysis of the averages of the growth curves indicates a definite retardation of growth during the first week, with restoration of the normal growth rate by the second week. The reaction of the individual tumor transplant may vary tremendously. Its growth rate may be increased, unchanged, or decreased. The occurrence of metastases seems to be definitely increased. In the gross and histologically, the tumor and the tumor site show congestion, edema, and focal hemorrhage with extensive diffuse necrosis. One week after treatment collars of rapidly growing tumor cells could be seen around the blood vessels. This offers an explanation for prompt recurrence. No definite "cures" were obtained by the experimental periods and technics used although a destructive effect was demonstrated.—Authors' abstract.


By the use of the spectrochemical method, it was found that the serum magnesium showed a rise of 24% above the control value after 2 to 5 hours in the hypothermic state. There did not seem to be any correlation between the serum magnesium levels and the extent or duration of the hypothermic state. There may be some relationship between the serum magnesium and the depressed thyroid activity, and the soporific state, corresponding to the findings in a normally hibernating animal. The serum sodium values fluctuated widely; no explanation can be given for this finding.—Authors' abstract.


The results of a considerable number of experiments on the induction of tumors by ultraviolet radiation are examined statistically to determine the accuracy to be expected in such studies. The logarithm of the induction time is normally distributed among individual male strain A albino mice. The distribution does not vary systematically with dosage of radiation, interval between exposures, intensity of the radiation, or age. The accuracy to be expected when experimental groups are compared is considered, and different methods of comparison are evaluated. The variation among mice is very wide, making it necessary to use large numbers of animals and to
gives particular attention to methods of comparison if a reasonable degree of accuracy is to be achieved. Strictly, these findings apply only to induction of tumors by ultraviolet radiation, but it is probable that the wide variation found here is not unique in the field of cancer. If comparable latitude is found elsewhere, certain types of comparison in common use may prove unreliable.—Authors’ summary.


The time required to induce tumors in 50% of a series of mice exposed to ultraviolet radiation was studied. The induction time was shorter when the same weekly dose was given in 5 or 7 exposures than when it was given in a single exposure. For a given schedule of exposures there was a minimum induction time that was not reduced by increasing the weekly dose, but below a certain dosage the induction time increased rapidly with decrease in dose. For a given dose the induction time was longer for older animals than for younger ones. It is pointed out that cells that are only slightly injured by ultraviolet radiation may recover between exposures and undergo no permanent change; cells severely injured may die and slough off. The cells receiving intermediate injuries are probably those which become cancerous. The authors are unable to describe the quantitative relationships found in terms of any one mechanism.—H. Q. W.


Considered in terms of surface dosage, wave length 2.537 Å is much less effective than longer wave lengths of the carcinogenic spectrum in inducing tumors and in producing other tissue changes. This is best explained by the fact that wave length 2.537 Å is absorbed principally in the stratum corneum before it reaches the viable cells. Thus it appears evident that photochemical changes taking place in the stratum corneum play no part in carcinogenesis and that the locus of carcinogenic action of ultraviolet radiation is the living cell itself.—F. L. H.


The histopathology of tumors induced by a wide variety of dosages of ultraviolet radiation was studied. Spindle cell sarcomas arising from connective tissue elements predominated. Some polymorphous cell sarcomas occurred which possibly originated from muscle cells. Squamous carcinomas that arose in the epidermis or its appendages and that often occurred with sarcomas made up a small group of tumors. A few hemangioendotheliomas, one osteochondrosarcoma, and one sebaceous carcinoma were also found. Hemangioendotheliomas and spindle cell sarcomas of the eye are described. The authors conclude that ultraviolet radiation may induce tumors in a variety of tissues depending upon the susceptibilities of the latter and limited by the penetration of the radiation.

The ratio of carcinomas to sarcomas was not affected by dose per se but increased slightly with increase in tumor induction time. The ratio increased greatly with frequency of exposure, thus demonstrating a difference in response of epidermal and connective tissue elements.—F. L. H.


Tumors were produced by exposure of mice to the wave length band 2,800-3,400 Å. A filter is described for the isolation of this band with the least possible loss of energy. Carcinogenesis could be effected with these wave lengths, but more energy was needed than when the whole mercury arc spectrum was employed, an implication that certain other portions of the spectrum can influence carcinogenesis. Small amounts of energy applied over a long period of time appeared to be more efficient for tumor production than large doses given during shorter periods. This indicated that there was a waste of energy when large doses were employed, or that the high levels had an additional retarding influence.—Authors’ abstract.


A method is described for isolating nuclei in quantity from liver and tumor tissues with 5% citric acid. Radioactive phosphorus administered in the form of disodium phosphate was taken up rapidly by nuclei in the living animal, but not in tissue slices.

Nuclei of tumor cells accumulated more radioactive phosphorus than those of normal liver. This was shown to be due to mitotic activity and not to a form of metabolism peculiar to tumor cells.

As early as 1 hour after the administration of radioactive phosphorus, 60 to 70% of the total radioactivity of liver nuclei was found in the nucleoprotein fraction. This radioactivity was as great then as it was several days after injection, suggesting that conversion of phosphorus to nucleoprotein must be quite rapid. In rapidly growing lymphoma tissue the nucleoprotein fraction was found to contain 90 to 95% of the total nuclear radioactive phosphorus. From the rate of radioactive phosphorus uptake by nuclei it was calculated that a new lymphoma nucleus was synthesized on the average once every 12 hours.

Irradiation with 200 r x-rays altered the distribution of P32 in the lymphoma cell, increasing the concentration in the nucleus shortly after irradiation. The P32 concentration in the cytoplasm decreased with time after irradiation. The altered distribution may have resulted from the inhibition of mitosis produced by the x-rays.—J. L. M.


If the mammary tumor-producing substance in the milk
of high tumor strain mice is similar to the estrogens or known synthetic carcinogenic hydrocarbons, it should be demonstrated by a comparison of the ultraviolet absorption spectra of the milk and mammary glands of high and low tumor strain mice. Milk and tissue from nontumorous mammary glands from lactating high tumor strains A, C3H, and dba, and from the low tumor strain C57 black were studied. Freshly excised mammary glands were minced in a frozen state and extracted with acetone, ether, alcohol and isooctane. This procedure permitted study in the ultraviolet region down to 2,300 Å. The alcohol-soluble and alcohol-insoluble fractions were examined independently. Comparison of the ultraviolet absorption spectra of the milk and mammary gland tissue of these high and low tumor strain mice showed no significant differences. Ultra-centrifugation data recently published by other investigators have indicated that the active agent is primarily in the non-fat fraction.—M. B.


Milk, pieces of spleen, and minced mammary gland from lactating strain C3H mice were administered to fostered strain C3H females. The oral administration of 0.1 to 0.8 cc. of milk to mice 7 to 10 days old produced mammary tumors. The subcutaneous injection of lactating mammary gland, splenic tissue, or 0.1 to 0.2 cc. of milk to mice 7 to 10 days old also produced tumors. The subcutaneous injection of 0.15 to 0.25 cc. of milk to nursing mice produced tumors in 11 of 16 mice, whereas 0.5 cc. of milk to mice 30 to 57 days old produced tumors in 2 of 14 animals. The oral administration of 0.5 to 1.0 cc. of milk to mice 3.5 to 4 months old produced tumors in 3 of 24 mice. Older mice are apparently more resistant to the agent than are animals 7 to 10 days old.

Mice 7 to 14 days of age, derived from a cross of strain 1 females and C3H males, are suitable test animals for quantitative studies on the mammary tumor inciter of mice. They are highly susceptible to the agent and do not obtain it from their strain 1 mothers.—F. L. H.


As noted by Anderson, and as previously stated by the writer, the average age at which spontaneous mammary tumors appear in females of the C3H strain may decrease with continued inbreeding. The incidence of mammary tumors for the mice of groups with different average tumor ages remains the same when the incidence is based on animals living to the respective average tumor ages.

That foster nursing does not alter the inherited susceptibility for the development of spontaneous mammary cancer is demonstrated by the incidence of tumors appearing in the hybrids derived by mating unfostered (high tumor) and fostered (low tumor) C3H mice.

The active mammary tumor milk influence may appear at any time in the life of individual females. If the milk becomes active after the mice have given birth to young, the females usually die without cancer. The active milk influence is transferred to the progeny and the young that receive it usually die with cancer. This may indicate that the active mammary tumor milk influence must be present when the mammary glands start to develop if it is to play a role in the genesis of mammary cancer in mice.—Author's abstract.


This is a genetic analysis in which susceptibility to induced pulmonary tumors is measured by the time at which the tumors arose and by the number of nodules found in each mouse. Crosses were made between strains A (highly susceptible) and L (highly insusceptible), and F1, F2, and backcross generations were raised. Intravenous injections of 0.5 mgm. of 1,2,5,6-dibenzanthracene dispersed in 0.5 cc. horse serum were given to mice of the 6 groups. The results confirm the conclusion that genetic as well as environmental factors are involved. It is also shown that genetic factors influencing susceptibility are multiple in number. A rough estimate shows that strains A and L differ by at least 4 pairs of factors and probably more.—G. W. W.


Data on the incidence of spontaneous pulmonary tumors in mice at different age periods are presented. Mice of strain A (susceptible) and strain L (insusceptible to pulmonary tumor) were mated and the F1 generation was produced as well as backcross hybrids resulting from mating the F1 to the parent strain L. The data reported tend to run parallel to those published for induced pulmonary tumors. The results suggest that susceptibility to spontaneous pulmonary tumors in mice, like susceptibility to induced pulmonary tumors, is inherited on a multiple factor basis. It is pointed out that multiple factor inheritance offers an explanation for the variation in spontaneous pulmonary tumor incidence between the different inbred strains of mice.—G. W. W.


A genetic investigation of the transplantable melanoma of the mouse, S91, with special reference to the F2 albino hybrids of reciprocal crosses between mice of the A and dba strains is reported. The melanoma grows regularly and successfully in strain dba and fails to grow in the strain A mice. Results of transplantation into a large number of colored F2 hybrids suggests that one mendelizing gene is involved in the growth of this tumor. Transplantation gives a different ratio with the albino F2 animals. A tentative hypothesis which fits the experimental figures is advanced. It is suggested that further physiologic and genetic studies of melanotic tumors transplanted into albinos under various conditions of modification might well prove to be important.—G. W. W.

The number of lung nodules per mouse, following intravenous injections of 20-methylcholanthrene dispersed in horse serum, was taken as a measure of susceptibility. It was found that yellow F1 hybrid mice resulting from mating A strain females to Y strain males were more susceptible to induced pulmonary tumors than were their brown litter mates. Since the hybrid test animals can be considered isogenic except for this 1 pair of chromosomes, it is indicated that this increase in susceptibility is due to the A' gene per se. It is suggested that the physiologic process that is associated with the A' gene and that lead to increased body weight of the yellow mice over their brown litter mates may also lead to the increased susceptibility to induced pulmonary tumors of the yellow mice.—G. W. W.


Reciprocal crosses to secure F2 hybrids were made between strain F mice (high leukemia) and mice of 3 low leukemia strains (CBA, C57, and A). F1 hybrids were backcrossed to the high (F) and low (A and CBA) leukemia strains in such a manner that strain F influence was supplied entirely by the male or entirely by the female parents in the 2 generations of the experiment. Observations were made also on F2 hybrids where the female influence was provided by either high or low leukemia females. In addition, strain F mice were foster-nursed by animals of several low leukemia strains (CBA, I, A, C3H, NH). Transfer of the young to foster mothers was effected within 24 hours after birth.

Results from the breeding experiments listed above did not indicate that a specific milk influence (as for mammary cancer) is concerned in the development of leukemia in strain F mice. The incidence of leukemia in a group of 48 strain F mice fostered by low leukemia strain mice was, however, somewhat lower than in unfostered controls of the same strain.—M. B.


Leukemia was produced in mice by repeated percutaneous applications of methylcholanthrene. The animals were killed at intervals, blood-forming organs examined microscopically, and transmission experiments made with suspensions of cells from spleen and lymph nodes. Numerous transmission experiments made before the eighth week of painting were uniformly negative, although hyperplastic changes were evident in lymphoid tissues. Three cases of leukemia were first demonstrated by transmission experiments. A subsequent microscopic review showed the presence of collections of atypical cells in the splenic pulp and in lymph nodes, while the bone marrow and liver showed no change. The numerous transmission experiments made from histologically definite cases of leukemia failed in only 1 of 46 injected mice. Of the tests used to determine the presence of leukemia, gross examination is the least reliable, microscopic examination next in order, and inoculation experiments are the most decisive. The type of leukemia produced was lymphoid or atypical, with the exception of a few myeloid or monocytic leukemias. Evidence is presented suggesting that the atypical cells originate in lymphoid tissues. The onset of induced leukemia is sudden when judged by the criteria studied. The incidence of leukemia was slightly higher among the x-rayed and painted mice than among the mice painted but not x-rayed. A preliminary study of blood smears indicates that the majority of leukemias are accompanied by specific blood changes recognizable at least 2 weeks before the death of the animals.—Authors’ summary.


A study was made of the metabolism (Q values) and derived quotients of lymphoid, myeloid, monocytic, and atypical leukemias induced in mice by methylcholanthrene with or without x-irradiation. Lymph nodes, spleens, and livers were analyzed metabolically, examined histologically, and often tested for ability to transmit leukemia. In general, the results obtained with the two stocks of mice employed were similar, and no decided effects of sex, age, or x-irradiation were observed. The anaerobic glycolysis of lymph nodes and spleens with induced leukemias showed no definite metabolic distinctions (>20%) between control, preleukemic, or leukemic mice, irrespective of type or extent of infiltration in the leukemic mice. The anaerobic glycolysis of leukemic livers, however, showed, depending upon the extent of infiltration, a twofold to eightfold increase over controls that took place simultaneously with histopathologic indication of onset of disease and successful transmission. All three types of analysis, metabolic, histopathologic, and transmission, concurred in indicating, after several months of painting, a sudden onset and rapid development involving but a few days.

The respiratory quotients of all tissues examined were well below unity, which is typical of both adult normal and malignant tissue. The oxidative metabolism (QO2) and QO2 of RF lymph nodes and spleen showed a definite difference between normal and preleukemic organs on the one hand, and leukemic and leukemoid organs on the other, values for the latter groups being increased 25 to 75%. The aerobic glycolysis values (QO2) of preleukemic, leukemic, and leukemoid lymph nodes, spleens, and livers were 50 to 100% above normal. Chemical lactic acid determinations (QO2) agreed in general with the manometric glycolysis values (QO2) under anaerobic conditions, but there were differences under aerobic conditions, especially in liver. No evidence was obtained for the existence of any preleukemic metabolism different from normal metabolism, except possibly for a small increase in aerobic glycolysis that developed some weeks.
prior to the onset of leukemia. In general, the metabolism of the induced leukemias, while qualitatively characteristic of malignancy, quantitatively probably represents, together with certain chicken erythroleukoses, the lowest limit for any type of malignant tissue reported up to the present time.—Authors’ abstract.


Unfiltered suspensions of the spleen cells, leukocytes, and plasma of leukotic fowls induced leukosis in chick embryos when placed on the chorioallantoic membrane after the eighth day of incubation of the egg. Berkefeld filtrates of leukotic tissue and plasma failed to produce the disease in eggs similarly inoculated, though they gave rise to leukosis when injected intravenously into young fowls. The question whether the chorioallantoic membrane is unsuitable for growth of the virus is discussed. Seven illustrations.—J. G. K.


A histological search was made for preleukemic changes in mice of the C58 strain, of which 90% die with some form of leukemia after the age of 6 months.

Of the C58 mice, 157, all clinically nonleukemic and aged between 176 and 382 days, were killed and the tissues examined: 59 of the animals exhibited reticulum cell hyperplasia, which was not seen in young C58 mice or in old mice of nonleukemic strains (total number of animals in the latter categories not given). In general the hyperplasia, which is described and illustrated in 7 figures, was confined to the reticulum of the medullary regions of lymph nodes or to the perivascular regions of the livers. The spleen seemed to be involved in only 3 animals. The distribution of the hyperplasia was limited, and in no case was there a generalized systemic reaction. When it occurred in lymph nodes, only 1 or 2 nodes were usually affected. In livers the lesions were not widely spread but were confined to a few foci.

In another group of 24 mice of strain C58, successive biopsies of lymph nodes were made at monthly intervals. Ten of the animals manifested leukemia at autopsy (eighth to twelfth months), which was preceded without exception by reticulum hyperplasia and lymphopoiesis, this appearing usually by the sixth month. In a further study a number of C58 mice were killed before and at 6 months of age and the tissues examined. Of the 24 animals less than 6 months old, none showed reticular hyperplasia, whereas of the 16 mice killed at 6 months, 7 showed reticular hyperplasia identical with that reported above in either lymph nodes or liver. Three Storrs-Little mice (a nonleukemic strain) showed no reticular hyperplasia when killed at 6 months.

The authors conclude that the restricted areas of reticulum hyperplasia in the lymph nodes and liver become the sites for primary malignant lymphocytosis in C58 mice. Following the production of a population of free malignant lymphocytes, invasion accounts for the majority of the widespread lesions common to the terminal stages of leukemia.—J. G. K.


The history and pathologic features of a spontaneous transplantable fibrosarcoma involving the foreleg and paw of a virgin female C3H mouse are reported.—F. L. H.


The article reviews the pathology of spontaneous neoplasms in mice with emphasis on the more common varieties such as those arising in the lung, mammary gland, liver, and the region of the salivary gland.—F. L. H.


Observation of a large colony of rabbits over a period of 14 years disclosed 4 instances of embryonal nephromas. Study of the growths in both original and experimental hosts showed a morphological identity with similar human neoplasms, but because of the extreme variation in biological behavior in the two species it was concluded that the rabbit tumors are not analogous with the well-defined clinical and pathological entity of Wilms’ tumor in man.—Author’s abstract.

**Clinical and Pathological Reports**

**Diagnosis—General**


The results of peritoneoscopy in 75 patients are reported. The gross pathologic lesions were identified and a correct diagnosis returned in 55 cases. In 25% of these, the findings fundamentally altered the treatment. The portion of the abdominal cavity seen by means of the peritoneoscope was found to be normal in 18 cases. Examination was unsatisfactory in 2 instances because of adhesions. The authors feel that peritoneoscopy is essential in order to avoid needless laparotomies.—G. H. H.

**Skin and Subcutaneous Tissues**

Melanogepithelioma (Malignant Melanoma) of the Extremities. Beckel, W. H., Meyerding, H. W., and Broders, A. C. [Mayo Clinic, Rochester, Minn.].
Experimental Research, Animal Tumors


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