
Single subcutaneous injections of 0.2 mgm. quantities of 3,4,5,6-dibenzcarbazole dissolved in lard, sesame oil, or olive oil were made into the right axillary region of mice from strains C3H, C57, and A. Tumors produced at the site of injection and livers were examined grossly and microscopically.

Male mice of these strains were found generally to be less susceptible to liver damage than female mice. Females of all 3 strains showed liver damage when sesame oil was used but strain A mice showed liver changes only when lard was used. Castration of the male strain A mice increased the percentage of cases of liver damage from a control figure of 14.3% to 47% in the castrates. Thirty-eight per cent of castrated males receiving stilbestrol developed liver damage.

Lard solutions were less active in producing subcutaneous fibrosarcomas than solutions of the carcinogen in sesame oil. Male mice are more susceptible to subcutaneous tumor production by lard solutions of 3,4,5,6-dibenzcarbazole than are the females. Pulmonary tumors were produced in strain A female mice as early as the 10th week. An incidence of 66 to 70% of pulmonary tumors occurred. The type of solvent did not materially vary the occurrence of these tumors.

Regardless of the strain or hybridization, the sex susceptibility to liver damage due to 2-amino-4-azotoluene in 10 mgm. doses per month for a period of 10 months is demonstrable. It is suggested that the rather high urinary protein excretion in male mice may enable them to excrete more of the carcinogen. The influence of sex was more pronounced in determining the degree of susceptibility to induced hepatic changes than to induced subcutaneous growths.—R.C.R.


Of 143 male C3H mice fed 23 or more 0.1 cc. feedings of a 40% olive oil solution of carbon tetrachloride given 2 to 3 times a week, 126 or 88.1% developed hepatomas. In a similar experiment with 54 mixed sex strain A mice, 100% of the mice developed hepatomas. No hepatomas were found in 17 C3H controls. A group of mice fed olive oil without carbon tetrachloride showed an incidence of hepatoma in 4.3% of the cases. Whether the tumors themselves are directly due to the effect of the carbon tetrachloride or to the hepatic damage awaits further study.—R.C.R.


One hundred and six 1-month-old rats of the Osborne-Mendel strain were fed basal diets and butter yellow supplements. All animals were autopsied between 2 and 52 weeks of butter yellow feeding and microscopic sections were obtained. Sixty-six of these animals developed hepatomas and 20% of these tumors metastasized.

The gross pathology of the liver, peritoneum, kidney, spleen, lungs, lymph nodes, and gastrointestinal tracts of these rats is described. Microscopic examination of the hepatomas divides them into two general classes, the hepatoma and the adenocarcinoma. The hepatoma was subdivided again into two subclasses; namely, a type which was well differentiated and at times encapsulated resembling normal liver parenchyma, and a second type composed of less differentiated cells but still maintaining the general structural pattern of liver tissue. Concerning the origin of the adenocarcinoma, the authors consider functions and anatomic relationships of hepatic and bile duct cells. It is concluded that the adenocarcinoma probably originated from the hepatic parenchymal cells.

The occurrence of bone was noted in several of the hepatic tumors. It was considered probably due to the stimulation of metaplasia of fibroblasts to osteoblasts by the regenerating transitional epithelium.

There were three types of pigment observed in these animals. They were: 1. an iron-containing, granular, brown pigment found in the liver, spleen, and lymph nodes; 2. one found in the tubular cells and macrophages of the renal cortex was brown and granular and gave no test for iron; and 3. one deposited in the liver and lymph nodes as a canary yellow material. It was lipoidal in nature. The tumor cells themselves were not observed to contain pigment nor glycogen.—R.C.R.


Data obtained following the injection of 22 compounds related structurally to 20-methylcolchicine are reported. The derivatives were classified in 6 groups. These groups were: 1. alkyl derivatives, 2. oxygen-containing derivatives, 3. chloro, bromo, and cyano compounds, 4. anthracene derivatives, 5. bile acids and cholic acids, and 6. a miscellaneous group. Carcinogenic potency for mice was determined by gross and microscopic observations on tissues at the site of injection and by the occurrence of multiple tumors of the lungs. A total of 475 mice of inbred strains, chiefly strain A, was used. Crystalline derivatives were moistened in glycerol and injected. When
too small a quantity of material was available lard was used to dissolve the crystals. Lard and glycerol were used in preference to sesame oil because of the carcinogenic action of certain products of this oil. Carcinogenic potency for compounds in group 1, reported in order of decreasing activity, was: methylcholanthrene, cholanthrene, 15,20-dimethyl, 20-ethyl, 16,20-dimethyl, 20-10-propyl, and 20-t-butylcholanthrene. Two of the seven oxygen-containing derivatives displayed carcinogenic activity. These were 15-hydroxy- and 15-keto-20-methylcholanthrene. Group 3 showed no carcinogenic activity. The only anthracene derivative shown to be carcinogenic was 1,2-cyclopenteno-5,10-aceanthracene. This conforms to the fact that the angular benzene ring of 1,2-benzanthracene is not essential for activity. Its presence however confers a high order of activity on anthracene derivatives. Desoxycholic acid of group 5 was found to be toxic when injected in glycerol and in water. Small amounts of crystals of the acid had no such effect. This acid was shown to be noncarcinogenic. The compounds 1,2,5,6-dibenzanthracene-cholic acid and 20-methylcholanthrene-cholic acid both showed carcinogenic activity. No tumors were produced with cholic acid or acenaphthene-cholic acid. Miscellaneous other compounds found to be carcinogenic were 6-methylchrysene and 4,9-dimethyl-1,2-benzanthracene. —R. C. R.


Paramecium multimicronucleatum has been shown to survive partial starvation for longer periods of time after prolonged exposure to carcinogens than do normal paramecia of the same species.

The population curve of these microorganisms after the 44th transfer in methylcholanthrene was seen to reach a maximum of nearly 600 organisms in 15 days whereas the normal organisms reached a level of 165 in 2 days and then declined. This phenomenon was not observed until the above number of transfers was reached.

Several amino acids were found to stimulate cell division in both the controls and adapted paramecia. Calcium pantothenate markedly increased the cell populations in both controls and methylcholanthrene-adapted organisms. If Staphylococcus albus was added to the organisms as food, increases occurred in the population curve in both controls and methylcholanthrene-adapted organisms. Fluorescein-adapted organisms failed to show as marked a change as the normals after staphylococcus feeding. Testosterone propionate was found to be markedly toxic to both the adapted and the normal controls. A mild inhibitory effect was caused in both types by colchicine. This potentiality for prolonged survival is retained in considerable degree even after the species is removed from the methylcholanthrene for 5 to 10 transfers. No structural changes have been noted to date in the methylcholanthrene-adapted group.

These findings seem to throw some light on the implausibility of the tissue tension theory of cancer. In these tests, a free-living organism relieved of all growth-restraining influences seemed to be endowed with more than the ancestral power of cell division and survival when the species was exposed to a blastogenic hydrocarbon for many generations. These carcinogens seem actually to enhance certain vital functions rather than decrease them. —R. C. R.


Four cases of induced adenocarcinoma of the stomach in C3H mice are reported. This strain of mice has never developed spontaneous adenocarcinoma of the stomach in the author's laboratory. The tumors were produced by direct injection into the wall of the pyloric chamber of the stomach of C3H mice. The material injected was a horse serum dispersion of methylcholanthrene. It was injected in amounts varying between 0.03 to 0.05 cc. This represented about 0.6 to 1.0 mgm. of the methylcholanthrene. If 100% pellets or mineral oil solutions of methylcholanthrene were used, the tumors produced were mixed with sarcoma. Adenoacanthoma of the stomach has also occurred in this group of mice. —R. C. R.


Direct evidence is provided for the existence of both soluble and insoluble phases of neutralized virus and for the dissociation of both with dilution when the 2 phases are separated. An estimate is afforded of the distribution of virus between the 2 phases separated in this way by centrifugation. This distribution however can be considered only for the special region of serum-virus amounts employed. The reduction in free virus in the supernatant fluid could not have been due to sedimentation of free virus since it could not be found in the pellet suspension. The possibility of a shift in chemical equilibrium is suggested to explain this phenomenon. —M. B.

IMMUNOLOGY


Rabbits which had received colloidal polycyclic hydrocarbons (methylcholanthrene, 1,2,5,6-dibenzanthracene, 1,2-benzanthracene, phenanthrene) sub cutem during one year were immunized with horse serum. All the animals developed a strong immunity. There was no difference between the amounts of precipitin produced in the blood of the animals treated with carcinogenic and noncarcinogenic hydrocarbons.

Rabbits were immunized with horse serum, and then received injections of colloidal hydrocarbons sub cutem. Forty-eight hours after injection of 1,2-benzanthracene or anthracene the optimal proportion was unchanged or slightly lowered; in 7 out of 9 animals receiving methyl-
cholanthrene a sudden drop occurred and the time of precipitation was generally prolonged. Estimation of the nitrogen precipitated showed a smaller difference between the effects of the two classes of hydrocarbons.—E. L. K.


After some considerations of the influence of the lymphatic system on the genesis and evolution of cancer, the author describes experiments carried out on the rat in order to prove the defensive role of the lymphatic nodes against the dissemination of the tumor. The aortic nodes of 16 rats were removed and a spontaneous sarcoma of the same animal was inoculated in the left posterior limb. Some days later 81% of the operated animals showed intra-abdominal metastases whereas in the controls no metastasis developed. At the same time the operated animals were more sensitive to the tumor which had a shorter evolution, was larger and more invasive of the neighboring tissues. In order to see if the anticancerous power of the nodes depended on the presence of this tissue or was in proportion to its degree of development half of the aortic nodes were left intact in some animals, and the results were the same as in the experiment mentioned above. Other experiments showed that the defensive power of the nodes is manifest only when they are connected with the lymphatic vessels.—M. D.-R.

Transplantation


Strain I mice develop spontaneous adenomatous lesions in the glandular region of the stomach. This is found in most of these mice living to be 8 months old or more. It is more pronounced in animals eating roughage. It appears to be a recessive hereditary character. Histologically, the lesions appear malignant, but grossly they are benign. They do not appear in F1 hybrids of strain I mice.

An attempt to transplant this lesion was made. It was minced and suspended in saline and injected intravenously into strain I and strain I hybrid mice. Pulmonary takes similar to the original lesion were found in a large percentage of cases. Strain I hybrids were found to be less susceptible than the pure strain I mice. These pulmonary tumors were found not to be subcutaneously transplantable. Control mice injected with normal stomach mucosa were negative in most cases after 6 months' time. Minces of liver and kidney injected in a similar manner into strain C mice produced no pulmonary lesions.

These results tend to indicate that the hyperplastic mucosa of strain I mice possesses a greater capacity for autonomous growth than does normal stomach mucosa, liver, or kidney.—R. C. R.


Two transplantable tumors originated in adenomas of the lung of mice. One grew in the subcutaneous tissues and assumed a sarcoma-like appearance in the course of the first two subpassages. Histological studies suggest that this change is due to a modification in appearance of the tumor cells. This modification is fixed and is not altered by different environment or conditions. The second strain could at first be transmitted only by the intravenous route. It is characterized by affinity for lungs and by a very long incubation period. Areas not changed in the course of four successive passages during which the neoplastic cells retained their adenoma carcinoma-like character. It is unchanged by growth in the subcutaneous tissues.—Authors' abstract.


A sarcoma produced by daily injection of fructose into a mouse for 250 days was successfully transplanted to rats. The tumor was first grown for 38 generations in mice, during which time it changed histologically. The tumor originally contained characteristic slender spindle cells with many collagenous fibers and occasional hyalinized areas, but after the 30th transplant the predominant cells were short, closely packed spindle and polymorphous cells. The transplantation from mice to rats was successful more than a dozen times, and the tumors resulting were identical with the mouse tumors. After growing in rats for several generations the tumors could be transplanted back to mice without any evidence of histological change. Attempts to transplant the tumor to rabbits, guinea pigs, and chickens failed. Desiccated tumor tissue of Berkefeld filters failed to induce tumors in mice. The incidence of takes was 80 to 100% in mice, and about 40% in rats. Careful histological studies at short intervals after transplantation of small bits of tumor from mice to rats revealed that the rat tumors arose from the cells of the transplanted tumors. In contrast to mice, which showed no regression once the tumor started to grow, 13 out of 141 rat tumors showed regression. It was observed that preliminary injections of mouse blood or spleen emulsion to rats 3 to 16 days before transplantation of the mouse tumor resulted in a lower percentage of takes. According to the author this represents an acquired immunity.—P. P. C.

Clinical and Pathological Reports

Radiation—Diagnosis and Therapy


A new principle and technique of external irradiation gives a more pronounced effect on the more radioresistant forms of cancer of the mouth, pharynx, and larynx than the methods of external irradiation now in use. This technique has been called the method of concentration. It can be applied daily and continuously or in two cycles interrupted by a rest period of 11 to 15 days. Since this method has been used but 3½ years nothing can be said of the permanence of the results, but certain carci.
Reports of Experimental Research

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