Abstracts

Reports of Experimental Research

Carcinogenic Compounds


Single subcutaneous injections of 0.2 mgm. quantities of 3,4,5,6-dibenzoazepine dissolved in lard, sesame oil, or olive oil were made into the right axillary region of mice from strains C3H, C5, 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-dibenzoazepine than are the females. Pulmonary tumors were produced in strain A female mice as early as the 10th week. An incidence of 60 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 biliary 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 to be 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-methylcholanthrene are reported. The derivatives were classified in 6 groups. These groups were: 1. alkyl derivatives, 2. oxygen-containing derivatives, 3. chloro, bromo, and cyan compounds, 4. anthracene derivatives, 5. bile acids and choleic 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, cholangrene, 15,20-
dimethyl, 20-ethyl, 16,20-dimethyl, 20-10-propyl, and
20,!, butylochloranthrene. Two of the seven oxygen-contain-
ing 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-acenanthrene. 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. Desoxy-
cholic acid of group 5 was found to be toxic when
administered to 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 carci-
nogenic were 6-methylchrysene and 4,9-dimethyl-1,2-
benzanthracene.—R. C. R.

Bethesda, Md.] EFFECT OF CARCINOGENS ON SMALL
ORGANISMS. III. CELL-DIVISION RATE AND POPULA-
ITION LEVELS OF METHYLCLOLANTHRENE-ADAPTED

Paramecium multimicronucleatum has been shown to
survive partial starvation for longer periods of time after
prolonged exposure to carcinogens than do normal para-
meccia 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 155 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 di-
vision in both the controls and adapted paramecia.
Caladium pantothenate markedly increased the cell popu-
lations 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 mar-
kedly 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 im-
plausibility 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.

STEWART, H. L., and E. LORENZ. [Nat. Cancer Inst.,
Bethesda, Md.] INDUCTION OF ADENOCARCINOMA OF
THE PYLORIC STOMACH IN MICE BY METHYLCLOLAN-

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 in 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 methyl-
cholanthrene. 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.

IMMUNOLOGY

ROCH-LIGETI, C. [The Roy. Cancer Hosp. (Free), Lon-
don] STUDIES ON THE EFFECT OF CARCINOGENIC HY-
DROCARBONS ON IMMUNITY REACTIONS. Brit. J. Exper.

Rabbits which had received colloidal polycyclic hy-
drocarbons (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 noncar-
cinogenic 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. \textit{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 lateral-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 metastasis 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 lateral-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.

\textbf{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 autonolysed growth then does normal stomach mucosa, liver, or kidney.—R. C. R.

NAGAYO, M. [Labs. of the Japanese Foundation for Cancer Research, Tokyo] \textbf{ON HETEROPLASTIC TRANSPLANTATION OF MOUSE SARCOMA. Gann, 35:223-246. 1941.}

A sarcoma produced by daily injection of fructose into a mouse for 296 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 polymorphic 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 filtrates 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.

\textbf{Clinical and Pathological Reports}

\textbf{Radiation—Diagnosis and Therapy}


A new principle and technic of external irradiation gives a more pronounced effect on the more radioresistant mucosa of strain I mice possesses a greater capacity for autonomous growth than does normal stomach mucosa, liver, or kidney.—R. C. R.


Two transmissible 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.
Reports of Experimental Research

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