Abstracts

Abstracts are grouped under the following main headings: Reports of Experimental Research, Comparative Oncology, Clinical and Pathological Reports, Statistics, and Cancer Control and Public Health. Subheadings are used in accordance with the subjects of papers abstracted.

The initials of the abstractor are placed at the end of each abstract. Contributors of abstracts published in this issue are: S. Bayne-Jones, E. Boyland, A. Haddow, E. L. Kennaway, A. A. Liebow, L. L. Waters, and H. Gideon Wells. It is a particular pleasure for Cancer Research to acknowledge the receipt of abstracts from Professor E. L. Kennaway and his associates. Professor Kennaway and Dr. W. E. Gye have kindly agreed to arrange for the abstracting of articles appearing in publications in the British Commonwealth.

REPORTS OF EXPERIMENTAL RESEARCH
CARCINOGENIC COMPOUNDS


Croton oil and croton resin, in various concentrations, were applied to the skin of mice in conjunction with painting with different amounts of 3,4-benzpyrene. Both the oil and the resin augmented the carcinogenic action of benzpyrene. The cocarcinogenic action of croton resin was stronger than that of the total oil from which it was derived. Turpentine and xylene applied in concentrations which produce comparable degrees of irritation to that of croton oil did not have cocarcinogenic action. The mechanism of cocarcinogenic action is discussed.—S. B. J.


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Photo-oxides of several homologues of 1,2-benzanthracene with substituents at positions 9 or 10 or both (namely 9-methyl-, 10-methyl-, 9,10-isopropyl-, 9,10-dimethyl-, 9,10-trimethyl-, 6,9,10-trimethyl-, and 9,6,9,10-tetramethyl-1,2-benzanthracene), and of 9,10-dimethyl-1,2,5,6-dibenzanthracene, were prepared by passing oxygen through solutions of the hydrocarbons in CS₂ during exposure to light. The structure of the photo-oxide of 9,10-dimethyl-1,2-benzanthracene was established as that of a peroxide involving both meso-carbon atoms. Derivatives of 1,2-benzanthracene with only one meso-substituent (9-methyl-, 10-methyl-, 10-isopropyl) gave photo-oxides less readily. The capacity to form these compounds appears to be unrelated to carcinogenic activity. Tumors were not produced by injection subcutem in mice of the photo-oxide of the highly carcinogenic 9,10-dimethyl-1,2-benzanthracene, and it has not been possible to isolate photo-oxides from 1,2,5,6-dibenzanthracene, 3,4-benzpyrene, or 1,2-dimethylchrysenec.—E. L. K.


With the addition of this review article to those appearing in the Am. J. Cancer, 29:219. 1937 and Am. J. Cancer, 33:550. 1938, the vast literature on chemical compounds as carcinogenic agents from 1933 to 1939 becomes available in summarized form. These reviews with their appended bibliographies of 86o titles are invaluable to anyone engaged in experimental cancer research.—L. L. W.
The malignant change must occur with sufficient regularity to establish a causal relationship to the experimental procedure.—H. G. W.


Ever since the structural similarity of some cancerogenic hydrocarbons and the sex hormones, bile acids, and cholesterol has been known, there has been much speculation as to whether or not the body is able within itself to produce substances capable of bringing about neoplastic changes in its own cells. It is to such, as yet hypothetical, "endogenic blastogenic substances" that the authors refer.

The existence of these substances has been investigated as follows:—Livers from human cancers and noncancerous patients were obtained at autopsy and benzene extracts of these made. After concentration of the extracts by removal of the noncancerous patients are explained by stating that either the body is able within itself to produce substances capable of bringing about neoplastic changes in its own cells. It is to such, as yet hypothetical, "endogenic blastogenic substances" that the authors refer.

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cultures of *Pseudomonas tenuifaciens* were injected into tumor-bearing mice. Hemorrhage and necrosis in the tumors was noted, but no regression.—L. L. W.


Ninety-nine mice of strain A and strain A backcross were given aqueous olive oil emulsions containing either 0.2 or 0.4 mgm. 1,2,5,6-dibenzanthracene or 20-methylcholanthrene per cc. in 0.2 cc of drinking water. On this regime, the daily dose per mouse varied from 0.5 mgm. to 0.88 mgm. of hydrocarbon per day. The experiment was continued from 7 to 13 months for some groups of animals. When the mice died or were sacrificed, their organs were studied for possible pathology, and spectrographically for content of carcinogenic hydrocarbon. Di-benzanthracene was found unchanged in the gastrointestinal tract proximal to the ileocecal valve. None was found unchanged distal to this point, and none could be detected in the blood, ascitic fluid, or in any of the body tissues. The most important pathological findings were 10 adenocarcinomas of the small intestine, multiple primary lung tumors in many animals, atrophy of the hematopoietic and genital tissues, and anasarca. Only 1 mouse showed cirrhosis of the liver. The intestinal tumors were first observed after 7 months and a total dosage of dibenzanthracene or methylcholanthrene ranging from 113 to 174 mgm. per mouse. The paper contains tables, charts, and photomicrographs.—L. L. W.


Young mice of the C57 black and C57 brown strains which show a low spontaneous incidence of skin tumors, were given biweekly paintings of a 0.5% solution of methylcholanthrene in benzene. Other groups of the same strains were given a single painting of the carcinogen, or were given a single painting on the back and additional paintings thereafter at other sites. A final group of C57 brown mice was painted once with methylcholanthrene and then given one intraperitoneal injection of 2.0 mgm. methylcholanthrene in sesame oil. The number and life histories of the papillomas arising in the various groups were compared. Papillomas produced by a single application of the hydrocarbon to C57 black mice disappeared spontaneously, but repeated applications resulted in papillomas that persisted and in many instances became malignant. Single applications of methylcholanthrene to the backs of C57 brown mice also produced a number of papillomas that regress but a few became carcinomatous. Additional painting at distant sites, or intraperitoneal injections of the carcinogen did not affect the incidence or behavior of the skin tumors arising at the primary site of application. The mice were studied in groups of 28 to 156 animals each.—L. L. W.


Liver feeding definitely inhibited the progress of tissue changes leading to the production of liver cancer induced by repeated intraperitoneal injections of dimethylaminoazobenzol. The inhibiting effect of liver feeding upon carcinogenesis in tissues other than liver was not demonstrable in 2 experiments based on subcutaneous injections into rats of methylcholanthrene and on intraperitoneal injections into mice of 3,4-benzpyrene. These results are in line with those of previous workers on the production of skin cancer in mice by coal tar painting, and indicate that the inhibiting action of liver feeding may be limited to the case of cancer production in the liver.—S. B-J.

NAKAO, N. (Basaki-Lab., Tokyo.) Über die Fütterungsvorsuche mit 4-Amino-2,3-dimethylaminoazobenzol bei weissen Ratten. The effect of feeding white rats 4-amino-2,3-dimethylaminoazobenzol, *Gann*, 34:18-20. 1940.

This compound administered in olive oil by mouth to white rats had a definite effect upon the liver but did not act as a carcinogen. The introduction of an oxygen atom in the azo-position in 0-aminoazobenzol causes a loss of the carcinogenic action of the compound upon the liver and the urinary bladder. Thrombosis and congestion of the liver were produced. The chemical method for preparing this compound is described. The lesions are illustrated in 10 figures.—S. B-J.


Tumors were produced in A strain mice by 3,4-benzpyrene, 1,2,5,6-dibenzanthracene, 20-methylcholanthrene, 10-methyl-1,2-benzanthracene, 9,10-dimethyl-1,2-benzanthracene, and 5-CONH2-10-methyl-1,2-benzanthracene. To the solutions of carcinogenic substances, varying percentages of the basic fraction of creosote oil were added except in the control groups. Then by comparing in this test and control animals the number of tumors produced and their times of appearance, the effect of the creosote oil could be determined. Painting with benzene solutions containing 0.05 to 0.02% 3,4-benzpyrene plus 1% basic fraction of creosote oil accelerated tumor development in female strain A mice. Single subcutaneous injections of 1% solutions of benzpyrene and the other hydrocarbons plus 5% of basic creosote oil fraction gave a similar accelerating effect in both male and female A mice if the carcinogen was not in too high concentration. Concentrations of hydrocarbons between 0.02 and 0.1% produced tumors slowly in about 50% of the controls and did not obscure the promoting effect of the creosote oil. Higher concentrations (3%) of the creosote substance apparently had a retarding effect.—L. L. W.


A uniform experimental procedure for the determination of relative potencies of carcinogenic hydrocarbons is described. The principles involved are: use of an inbred strain of mice, single injection of a pure substance in an innocuous solvent, the confirmation of the gross diagnosis of tumor by histological examination, and a comparison of the latent times. The method was demonstrated by testing the carcinogenicity of 20-methylylcholanthrene, 3,4-benzpyrene, and 1,2,5,6-dibenzanthracene on mice of the C3H strain. From 0.25 to 2.0 mgm. of each of these hydrocarbons was suspended or dissolved in 0.2 cc. of tricaprylin and injected subcutaneously into 20 C3H mice. Similar injections were given stock albino mice. Clear-cut differences in the latent periods of tumor production for the 3 substances were obtained. Methylcholanthrene produced tumors more rapidly than benzpyrene, and benzpyrene more rapidly than dibenzanthracene. The latent times of tumor production in non-homozygous mice and the numbers of tumors occurring were quite irregular and only grossly indicated the relative potencies of the carcinogenic substances. A supplementary experiment with dibenzanthracene showed that divided doses of hydrocarbon were no more efficacious than a single injection in eliciting sarcomas, providing the total dose was the same.—L. L. W.

The injection of 0.75 cc. of a 25% aqueous solution of glucose subcutaneously into mice, daily or every other day, for 250 days caused the development of spindle cell sarcoma at the site of injection in 5 out of 18 mice. This tumor was transplantable. Spindle cell sarcoma was produced also by subcutaneous injection of a 25% solution of fructose, in 2 out of 16 mice. In 4 out of 13 mice spindle cell sarcoma was produced by subcutaneous injections of 25% solution of galactose. The gross and microscopic appearance of the tumors are shown in 18 illustrations.—S. B.-J.


In an attempt to repeat Yoshida’s (Virchows Arch. f. path. Anat. 283:259-293) production of liver tumors in the white rat, 100 rats were given daily doses of 0.01 gm. of ortho-amidooazotoluol in olive oil. The chemical was added to a diet of wheat flour. At the end of a year no liver tumors were found in any of the animals. In a 2nd series of animals a weekly injection of thioracofos was given in addition to the ortho-amidooazotoluol with the idea of irritating the liver. Still no liver tumors were produced. In a 3rd series where the diet consisted solely of rice and dye substance, a large number of adenocarcinomas of the liver appeared, as Yoshida had previously observed.—L. L. W.

HORMONES


The paper describes the results of prolonged estrogen administration in male mice of 3 strains (R III, CBA, Strong A). Animals from the first 2 strains received triphenylethylene or estradiol dipropionate, while those from the 3rd received triphenylethylene only. The results were as follows:

Over 60% of R III males treated for 20 weeks or more with either estrogen developed mammary cancer, whereas no mice of the other 2 strains developed this type of cancer.

Herna appeared in 23 of 30 R III males treated with triphenylethylene, but in only 6 of 31 treated with estradiol dipropionate. Eleven of 23 Strong A males developed scrotal hernia. No hernias were observed in CBA males.

Advanced atrophy, with arrest of spermatogenesis, occurred in all R III and CBA males treated until the time of death. In no R III male was there any interstitial hyperplasia, but in 5/3 of the CBA males the interstitial cells were larger and more abundant than normal. This change was slight as compared with changes in Strong A males.

In Strong A males treated with triphenylethylene and examined before the expiration of 49 weeks of treatment (7 animals) the testes showed no gross diminution in size. In all the testes examined from treated Strong A mice (20 animals) interstitial hyperplasia was observed. Thirteen animals died or were killed between the 50th and 69th weeks of treatment, and all showed testicular nodules (bilaterial in 5 cases). Microscopically the process commenced as a focused densely packed polygonal cells, and in advanced stages appeared to be malignant. There was no conclusive evidence of invasion or metastasis. Attempts to graft the tumors were unsuccessful.

A progressive metaphasia, commencing in the coagulating gland and involving the seminal vesicles, was produced in both R III and CBA mice. In Strong A males, however, there was a striking absence of squamous metaplasia and keratinization in the pelvic organs.

The adrenals of 44 treated R III mice all showed brown degeneration. Of 30 CBA mice, 11 showed no brown degeneration, in 7 the lesion was very slight and in 2 it was fairly marked. Of 19 Strong A males, 6 showed no brown degeneration and in 13 it was very slight.

Gross pituitary enlargement was noted in 5 R III males (none of which bore a mammary cancer). Of 20 other males (15 of which had mammary carcinomas) the pituitary was of normal size in 19. Thirty of 32 CBA males had pituitaries of normal size. No pituitary enlargement was observed in 21 Strong A males treated with triphenylethylene.

The paper includes a full discussion of the significance of the testicular changes in relation to similar conditions in animals and man. The limitation of the development of experimentally induced testicular tumors to 1 strain of mice points to the importance of genetic constitution in determining the origin of these tumors.—A. H.


The influence of thyroid on tumor growth was proportional to its effect on the general metabolism, and the addition of 15% calcium carbonate to the diet had no significant effect on the growth of the host or of the sarcoma transplant.—H. G. W.


The author noticed previously that removal of the ovaries of rats developing hepatoma produced by o-amidooazotoluol restrained the malignant changes in the tumor. In experiments in which the animals were fed o-amidooazotoluol in olive oil for 365 days some groups of female rats were castrated; others were injected with prolact. Prolact definitely hindered the development of hepatoma.—S.-B.-J.


Of various estrogens promoting mammary gland proliferation, the most active, as judged by the mammogenic mouse unit technic, was found to be stilbesterol, which proved to be at least 400 times as effective as estrone. Next in activity, among the compounds studied, was estradiol benzoate, which showed 250 times the effectiveness of estrone, by weight. Anol and triphenyl ethylene compared favorably with aqueous estradiol, but were only 1/30 as effective as estrone. 1,2,5,6-Dihydrobenzphrene was only 1/75 as effective as estrone.—Author’s summary.


Lymphomatosis characterized by widespread tumor infiltration in viscera and skin occurred in 16 of 119 castrated S. C. white Leghorn cockerels. In none of the birds developing the disease could active testicular fragments be found at autopsy. On the other hand, in 55 birds in which the castrating operation was incomplete, no clear-cut case of lymphomatosis was encountered. A relationship between the development of the lymphomatous condition and a lack of male hormones was thus suggested.—L. L. W.

In a previous report (Arch. Path., 27:828-840. 1939) it was shown that injections of estrogen changes “the fitness of the animal host as an animated culture medium for supporting the continued growth of a small island of tumor consisting of cells already clearly malignant.” In the present experiments sarcoma 180 was implanted in mice of the C57 black and Bagg albino strains. Groups of the tumor-bearing animals were then injected with estrone, thyroxine, testosterone, and anterior pituitary growth hormone. The effects of castration also were studied. Under certain conditions estrone inhibited the growth of the implanted sarcoma. In this case, the sarcoma behaved as if benign in several respects. The inhibition is probably not a direct inhibition of tumor tissue, but the enhancement of a primary resistance mechanism. Androgen, anterior pituitary growth hormone, and thyroxine did not have this inhibitory effect. Castration of females may decrease slightly the resistance to tumor growth.---S. B.-J.


In view of the remarkable estrogenic activity of triphenylchloroethylenyl, which has been applied clinically, a number of new compounds related to triphenylethylenyl were synthesized, of one of which is much more active than triphenylchloroethylenyl, and which is shown in the following table:

<table>
<thead>
<tr>
<th>Compound</th>
<th>Dose mg.</th>
<th>Duration in days till intensity of estrus falls to 1/3</th>
<th>Proportion of mice showing full vaginal cornification</th>
</tr>
</thead>
<tbody>
<tr>
<td>na-[Di-p-methoxyphenyl]-\beta-phenylbromocyrenylene</td>
<td>100</td>
<td>68</td>
<td>3/3</td>
</tr>
<tr>
<td>Triphenylchloroethylenyl</td>
<td>20</td>
<td>9</td>
<td>10/10</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>Slight effect</td>
<td>0/5</td>
</tr>
<tr>
<td>Triphenylchloroethylenyl</td>
<td>100</td>
<td>12</td>
<td>11/15</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>No effect</td>
<td>0/10</td>
</tr>
<tr>
<td>Stiboeostrol</td>
<td>500</td>
<td>16</td>
<td>10/10</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>9</td>
<td>10/10</td>
</tr>
</tbody>
</table>

The triphenylethylenyl compounds have a prolonged action, although the threshold dose is comparatively high.---E. K.


Virgin female and male C3H mice were divided into groups of 5 or 10 animals, so that although the sexes were separate, litter mates were present in each group. The mice were then given weekly scubaeston injections of stilbestrol in sesame oil and estrone in peanut oil over a period of 24 weeks. The total dose of stilbestrol in 2 groups of males and females was 5 mgm., and 1.2 mgm. respectively. One group of males and females received 1.2 mgm. of estrone and 10 females were left untreated. The average latent period of the tumor development in the controls (untreated females) was 46.5 weeks, in the stilbestrol treated animals 34.8 weeks and in the estrone injected animals, 30.3 weeks. Eight of 10 male mice receiving a total dose of 5.0 mgm. of stilbestrol developed mammary carcinoma as definite evidence of the carcinogenicity of this substance. Histological observations on the tumors produced, the endocrine organs, and the genital tissues are presented.---L. L. W.


Investigations were made of the influence of potassium salts of the \beta-hydroxyisomer (heterocuixin), potassium \beta-indololactate on the growth of Bashford’s carcinoma. The lethal dose of this compound per 10 gm. of body weight for mice weighing 15 gm. was 15 mgm., by subcutaneous injection and 10 mgm. by intravenous injection. Three groups of mice were injected subcutaneously respectively with 0.03 mgm., 0.3 mgm., and 3.0 mgm. of potassium \beta-indololactate 10 days after subcutaneous implantation of the carcinoma. The tumors grew in all animals but were smaller in the animals injected with this compound than in the controls. It is concluded that potassium \beta-indololactate hinders the growth of this transplanted carcinoma in mice. Reference is made to similar inhibitory effects of indole, skatole, and tryptophane.---S. B.-J.


The effect of low concentrations of estrin, progesterone, and testosterone on the growth of mouse embryo fibroblasts in tissue cultures was studied. Estrin in a dilution of 10^-2 had a slight stimulatory effect, but higher concentrations were inhibitory as were all concentrations of progesterone and testosterone.---L. L. W.


Thyroxin in concentrations of 10^-2 and 10^-1 increased slightly the growth of fibroblasts from mouse embryo hearts as compared to the Tyrode controls. Insulin added to flask cultures produced a 100% increase of the original explant within 7 days with a large rise in the mitotic index. Concentrations of 0.001 unit and 1 unit per cc. were used. With insulin it was noted that lipid droplets accumulated in the fibroblasts, making them nearly indistinguishable morphologically from fat cells. Adrenalin and cortin in all dilutions used proved inhibitory to the growth of fibroblasts. Cortin, however, was found to prolong the life of the culture.---L. L. W.

VIRUSES


Humoral antibodies against the Rous chicken sarcoma develop with maturation. The sera of chickens 6-10 months old reduced the activity of tumor extracts, diluted from 1:20 to 1:200, when incubated together for 3 hours at 24°C. The incidence of takes was lower and the size of the tumors smaller at 21 days in comparison with control extracts similarly incubated with saline. The tumor growth rate was greater in chicks than in mature animals. Mature animals exhibited marked variations in susceptibility. The sera of 2 resistant chickens had a greater inhibitory effect than 1 from a known susceptible. That the action of the inhibiting sera was directly on the virus was demonstrated by the use of virus material purified by ultracentrifugation. Furthermore the capacity of the sera to flocculate extracts of the tumor as well as normal mouse liver bore no relation to inhibiting potency. The sera of adult chickens also inhibited the virus of the Fugwani sarcoma and that of Mill Hill 2 endothelioma.---A. A. L.

Among the determinants of the tissue response to the Rous and Fujinami agents are the host's age and the dose and activity of the virus. Intrajugular injection of tumor extracts diluted from 1:20 to 1:2000 in amounts proportional to the body weight, produced generalized hemorrhagic, necrotic, or mixed lesions. The 1st, which was rapidly fatal, predominated in the youngest chicks (in whom no viral antibody was present), the 3rd was characteristic of mature animals, and the 2nd occurred in those of intermediate age. The hemorrhagic changes, most often observed in the liver and spleen, sometimes occurred in the absence of demonstrable tumor tissue and were interpreted as resulting probably from damage to the endothelium directly. It was concluded that the hemorrhagic disease was not due to an adventitious virus, since after 8 passages through chicks typical neoplastic lesions were still elicited in adults. When subcutaneous lesions developed at the site of intravenous inoculation they were most often of the same type as the generalized. In the more susceptible animals of all ages in which the tumor grew rapidly, the lungs and other metastatic sites tended to contain hemorrhagic tumors.—A. A. L.


Intracardiac injection of fresh saline extracts of the Shope fibroma produced in newborn rabbits a generalized disease characterized by vacuolization, and rarely necrosis, chiefly of the cells of the kidney and liver. Sometimes these were associated with discrete hemorrhages and cell proliferation, particularly in the spleen. Virus was demonstrated in the viscera. Adult animals injected intravenously with proportionate doses developed no noticeable disease. Subcutaneous inoculation of newborn rabbits produced large invasive tumors which exhibited a tendency to form satellite nodules, together with generalized degenerative changes as after intracardiac injection. Virus previously stored in glycercine induced similar changes in some newborn rabbits. Others developed multiple vesicular as well as local tumors, in one instance together with degenerative renal change. Some rabbits showed local tumors which regressed, or no tumors or visceral lesions. In contrast, in adult rabbits, subcutaneously introduced fresh virus elicited merely local fibromas, and glycercinized virus none at all.—A. A. L.

Consistent effects of colchicine upon the Yale carcinoma 1 were obtained by basing the dose of colchicine upon the animal's weight. Single injections of from 0.0089 to 0.0012 mgm./gm. produced a progressive accumulation of cells in an atypical metaphase characterized by contraction of the chromosomes into a compact central mass; this was maximal at about 9 hours. With doses greater than 0.0014 mgm./gm. necrosis was observed in the central portions of the tumor. Single injections as high as 0.0035 to 0.0040 mgm./gm. of colchicine were administered repeatedly at intervals of from 3 to 5 days most of the animals died and none of the tumors regressed. With the smaller dose, however, in some instances retardation of tumor growth and prolongation of life were observed. The percentage of cures was higher than with x-ray alone when the dose is increased. The effect of colchicine and x-ray on tumors or no tumors developed. Offspring of these mice were then selectively bred according to the type of tumor they had produced. In the F3 and F4 generations, litter mates began to develop similar types of tumors, that is, began to show the effects of the selective breeding. Thus a selection line for spindle cell sarcoma, carcinoma of the skin, and for no tumor became well established. Two other selection lines have not yet become pure. The author concludes that the directional path taken by the individual in specific tumor induction is determined by genetic factors.—L. L. W.

The mechanics of growth of adenocarcinoma of the frog kidney have been studied by transplanting it into the anterior chamber of the frog eye. The form of the growing tumor depends on the immediate physical environment, the growth taking place according to well defined structural patterns. Temperature affects the rate and character of cancerous growth in much the same general way as it affects the growth of normal tissues. Metastasis occurs more often and is more extensive at high temperature than at low.—H. G. W.


Crystalline carboxypeptidase and partly purified polyphenoloxidase are inactivated by x-rays. The rate of inactivation varies with the enzyme concentration. Inactivation does not occur if carboxypeptidase is acting on a substrate during irradiation.—E. B.


A lecture discussing the effect of radiation on mouse sarcoma, and the enhancing of this effect by subsequent injections of distilled water.—H. G. W.


Consistent effects of colchicine upon the Yale carcinoma 1 were obtained by basing the dose of colchicine upon the animal's weight. Single injections of from 0.0009 to 0.0012 mgm./gm. produced a progressive accumulation of cells in an atypical metaphase characterized by contraction of the chromosomes into a compact central mass; this was maximal at about 9 hours. With doses greater than 0.0014 mgm./gm. necrosis was observed in the central portions of the tumor. Single injections as high as 0.0035 to 0.0040 mgm./gm. of colchicine were administered repeatedly at intervals of from 3 to 5 days most of the animals died and none of the tumors regressed. With the smaller dose, however, in some instances retardation of tumor growth and prolongation of life were observed. The percentage of cures was higher than with x-ray alone when the dose is increased.
Abstracts

CHEMOSURGERY


This paper describes a method for using a paste containing zinc chloride for the fixation of a neoplasm in situ, under microscopic control. The formula of this preparation (Z-184a) is:

- Sulfate (80 mesh sieve) .......................... 40.0 gm.
- Sanguinaria canadensis ............................. 10.0 gm.
- Zinc chloride, saturated (4:1 soln.) ......... 34.5 cc.

In rats, growths of transplanted Philadelphia sarcoma, mammary carcinoma MS-2, Flexner-Jobling carcinoma, and carcinoma C-256 were removed by applications of this paste, followed by excision of fixed tumor tissue. Treatment of cancer in rats by fixative chemicals did not increase metastasis even when this was purposely attempted by prolonged subcurative dosage.—S.B.-J.

Biochemistry and Nutrition—Chemotherapy


Groups of rats were fed the same amounts of o-amidoazo-toluid in the following different diets: polished rice, unpolished rice and yest, wheat, and barley. The animals in the barley group died in 231 days without cancer of the liver. All 6 animals in the polished rice group developed carcinoma of the liver; 5 had hepatoma and 1 had cholangioma. Of 6 rats on the rice-yest diet 3 developed hepatoma. None of the 6 animals on the wheat diet developed carcinoma of the liver. The results show the important influence of diet upon the production of carcinoma of the liver by o-amidoazotoluid. Certain cereals, particularly wheat, inhibit the development of tumors after feeding this compound. This coincides with knowledge of the incidence of cancer of the liver in man, the disease being more prevalent among people who have a rice diet than among those living on a wheat diet.—S.B.-J.


Compounds were administered by mouth daily to dilute brown mice grafted with the homologous sarcoma M. C. D. B. 1 and to mice bearing spontaneous mammary carcinomas. The growth of the sarcomas was compared with that of control tumors grafted at the same time. The growth under treatment of the carcinomas was compared with the growth of the same tumor during a period immediately preceding treatment. The results have been examined statistically. Heptaldehyde (Strong. Am. J. Cancer, 35:461. 1939), phloroglucinaldehyde (Boyland and Mawson. Biochem. J., 32:1982. 1938), and acrolein were all equally effective in checking carcinoma growth. It is possible that heptaldehyde is metabolized by way of pimelic acid, glutaric acid, and malonic acid. Malonic acid markedly inhibited the growth of sarcomas and carcinomas. Citral was much more effective than other aldehydes tested but the known metabolism product “Hildebrandt Acid” was not so active.—E. B.
painted with it on alternate days with methylviolethrene, but
has no effect on papillomas and carcinomas that have started to
grow.—H. G. W.

CHALKLEY, H. W., and C. VOEGTLIN. (National Cancer
Inst., Bethesda, Md.) The effect of variation in oxygen tension
and sulfhydryl concentration on nuclear growth and fission in

Studying Amoeba proteus it was found that both nuclear
growth and fission can be retarded by either increasing or de-
creasing the O2 tension for a period of 24 hours. The retarding
effect of an increased O2 tension was unchanged by the addition
of M/100,000 SH glutathione to the medium, but the retarding
effect of a decreased O2 tension was enhanced by its addition.
Recovery of nuclear growth and fission took place when the O2
tension was returned from low to normal but not from high to
normal. Amoebae studied in cultures containing SH glutathione
at 1/100,000 at normal oxygen tension showed acceleration of
both nuclear growth and fission rate. These phenomena were
accentuated when O2 tension was increased for a short period
(3 hours) and then returned to normal. The authors suggest
that the SH group and oxygen may act upon intracellular en-
yymes concerned with nuclear growth, which in turn is corre-
lated with fission.—L. L. W.

CRABTREE, H. G. (Imperial Cancer Research Fund, Mill
Hill, London, England.) Retardation of the rate of tumour
induction by substances which inhibit glycolysis. J. Path. &
Bact., 51:303-309. 1940.

A series of mono-chlor-compounds reacted with cystine with
increasing velocity in the following order: monochloracetal,
c-tetrahydroxyl, a-chloroethylketone, methyl-a-chloropropylketone,
mercaptoacetic acid. The ability to inhibit the anaerobic glycolysis
of tumor tissue in vitro also increased in the same order. Mixed
stock mice were painted with carcinogenic compounds (either
3,4-benzpyrene dissolved in ether and liquid paraffin or 1,2,5,6-
dibenanthracene dissolved in acetone and liquid paraffin) twice
weekly and with a chlor-compound (0.1% in ether) thrice
weekly. The chlor-compounds inhibited tumor induction to a
degree varying with their chemical reactivity and their power of
inhibiting glycolysis.

Berenblum, Kendal, and Orr (Biochem. J., 30:709, 1936)
had shown that ββ'-dichlorodiethylsulphide, ββ'-dichlorodiethyl-
sulphane and cantharidin inhibit tumor glycolysis and the induc-
tion of tar tumors while ββ'-dichlorodiethylsulphoxide, thioli-
glycol and croton oil did not reduce glycolysis or the formation
of tar tumors.—E. B.

CRABTREE, H. G. (Imperial Cancer Research Fund, Mill

Benzpyrene and mono-chloracetal were applied to the skin
of mice in various amounts, and at various time intervals.
The effect of mono-chloracetal on the rate of tumor induction by
3,4-benzpyrene in mice is a function of the concentration used.
Low concentrations caused marked inhibition, but higher con-
centrations appeared to be innocuous, since the net effect on the
average induction time is negligible. Higher concentrations may
prove to be slightly stimulatory in mice more susceptible to
tumor development. The discussion includes a concept of stimu-
lation in which a residual tendency to carcinogenesis is enhanced
by the cooperation of a disturbance of cell metabolism. This
metabolic disturbance may be complex. The analogy between
the checking of glycolysis in vivo and the action in vitro may
not be sufficiently comprehensive.—S. B-J.

CRABTREE, H. G. (Imperial Cancer Research Fund, Mill
Hill, London, England.) Retardation of the rate of tumor
induction by hydrolyzing chlor-compounds. Cancer Research,

The effect of a series of aliphatic, and one aromatic, acid
chlorides (stearyl, acetyl, valeryl, palmityl, myristyl, and benzene
sulfochlorides) upon the rate of tumor induction in mice by
3,4-benzpyrene was investigated by the use of local cutaneous
applications of the compounds in various concentrations and
at various intervals of time. All proved inhibitory. The degree
of inhibition varied with the molecular size and rate of hydrolysis,
but did not run parallel with any single physical or chemical
characteristic. The most effective was benzene sulfochloride
which hydrolyzes less rapidly than the aliphatic acid chlorides.
It is concluded that the acid chlorides impair the activities of
enzymes nonspecifically due to the liberation of HCl, and that the
apparent inhibition of glycolysis is merely one expression of this
generalized damage.—S. B-J.

ELLIOTT, K. A. C. (Biochemical Research Foundation of
the Franklin Inst., Philadelphia, Penn.) Inhibition of the
succinoxidase system by extracts of tumour and normal

Suspensions and extracts of Walker 256 carcinoma, Phila-
delphia 1 sarcoma, spleen, and kidney extracts increased the oxygen
uptake of liver suspensions in the presence of succinate. Suspen-
sions of Jensen rat sarcoma had much less effect. Tumor extracts
did not inhibit the reduction of methylene blue by succinic
dehydrogenase to the same extent. The effect is possibly due to
action on the cytochrome part of the oxidase system.—E. B.

GREENSTEIN, J. P., with the technical assistance of W. V.
JENNETTE. (National Cancer Inst., Bethesda, Md.) Chemi-
cal studies on the components of normal and neoplastic tissues.
I. Viscosity and streaming birefringence of sodium thymo-

This study relates the structural viscosity of solutions of
sodium thymonucleate to their streaming birefringence (double
refraction of flow) as evidenced by parallel decreases in the
presence of certain salts. The most effective action in this respect
is iodide and the most effective cation is guanidinium. The
magnitude of the viscosity and intensity of birefringence of the
thymonucleate solutions depended largely on the method
of preparation. Although the addition of salts to thymonucleate
solutions apparently destroyed viscosity and double refraction of
flow, these properties returned when the salts were removed.
The viscosity of rat serum albumin was increased and that of
sodium thymonucleate decreased when the same salts were added
to each.—L. L. W.

GREENSTEIN, J. P., with the technical assistance of W. V.
JENNETTE. (National Cancer Inst., Bethesda, Md.) Chemi-
cal studies on the components of normal and neoplastic tissues.
II. The nucleoprotein fraction of normal animal liver. J. Nat.
Cancer Inst., 1:91-106. 1940.

A method of separation of nucleoproteins from the livers of
rabbits, rats, calves, and cows is described. Analyses of the prep-
ervations were made for total N, amide N, P, total S, cystine-
cysteine, methionine, tyrosine, and tryptophane. No significant
differences between species were found in the values obtained
for these substances. However, very great species differences
were found in the -SH group values as estimated by por-
phyridin titration. Nucleic acid was isolated from 1 of the cow
liver nucleoprotein preparations and its viscosity and streaming
birefringence compared with those of thymonucleic acid. Further
viscosity studies on cow liver nucleoprotein showed that this
substance behaves like serum albumin in that its viscosity
increases in the presence of salts.—L. L. W.

JACOBI, H. P., and C. A. BAUMANN. (Coll. of Agriculture,
Univ. of Wisconsin, Madison, Wis.) The effect of fat on tumor

Groups of 20-25 C albino or stock mice were given high fat
diets (20-25%) and were painted with carcinogenic hydro-
carbons in order to determine the effect of the fat on the rate of
tumor production. The fats used were Crisco, lard, coconut oil,
and butter fat. The carcinogens were 3,4-benz-
pyrene, methylviolethrene, and 1,2,5,6-benzanthracene. Con-
cancer cells as distinguished from normal fibroblasts. The fibrillar structures of the fibroblasts were usually thick, long, and tissue culture 48 hours old gave characteristic appearances of hepatoma, produced experimentally in rats by administration of dimethylaminoazobenzol, was studied by means of the gelatin-silver impregnation method of Fujita and Fukuda. Cells from a the treatment of transplanted and spontaneous malignant Osaka Kais. Univ.) Feinere Zytoplasmastruktur der experi-

KISHI, S. and W. NAKAHARA. (Lab. of the Japanese Foundation for Cancer Research, Tokyo.) On provitamin D in experimentally produced rat hepatoma. Gann, 34:258-255. 1940. Cholesterol crystals were isolated from hepatoma nodules produced in rats by feeding butter yellow, dimethylaminoazobenzol, for 150 days, according to the method of Kinosita. The crystals were examined for their chemical properties, and ultraviolet absorption spectra of their solutions were compared with absorption spectra of solutions of cholesterin crystals from organs and tumors. Four of these absorption spectra are shown in illustration. Hepatomas experimentally produced in rats by feeding with dimethylaminoazobenzol do not contain provitamin D. In this respect they differ from the Ikubu strain of transplantable hepatoma of the rat. The latter tumor contains provitamin D in a concentration of 7%. Noncancerous parts of hepatoma liver and precancerous cirrhotic liver, like normal liver, do not contain provitamin D.—S. B-J.

LEWISohn, R., R. LEUCHTENBERGER, and D. LASZ-

Low, (Mt. Sinai Hosp., New York, N. Y.) Spleen extract in the treatment of transplantable and spontaneous malignant tumors in mice. Surg., Gynec. & Obst., 71:274-285. 1940. Since transplanted sarcoma could be healed by injection of splenic extracts, which produced considerable enlargement of the spleens, the effect of injection of extracts of these enlarged or “healed” spleens was tried. Of 57 animals with transplanted sarcoma, 39 were cured by injections of the healed splenic extract, which produced considerable enlargement of the spleens, the effect of injection of extracts of these enlarged or “healed” spleens was tried. Of 57 animals with transplanted sarcoma, 39 were cured by injections of the healed splenic extract, 7 by concentrated purified spleen extract.—H. G. W.

MORIGAMI, S., and N. KasIWABARA. (Path. Inst. der Osaka Kais. Univ.) Feinere Zytoplasmastruktur der expe-

mentell erzeugten Hepatomasellen. Die lineare cytoplasma structure of experimentally produced hepatoma cells. Gann, 34: 297-301. 1940. The cytoplasmaic structure of explained cancer cells from hepatoma, produced experimentally in rats by administration of dimethylaminoazobenzol, was studied by means of the gelatin silver impregnation method of Fujita and Fukula. Cells from a tissue culture 48 hours old gave characteristic appearances of cancer cells as distinguished from normal fibroblasts. The fibrillar structures of the fibroblasts were usually thick, long, and few in number. In contrast, the hepatoma cells contained numerous delicate and short fibrils. Cells which had stopped growing lost this fibrillar structure and became granular. These appearances are shown in 4 figures.—S. B-J.


SUGIURA, K., and C. P. RHOADS. (Memorial Hosp., New York, N. Y.) Experimental liver cancer in rats and its inhibition by rice-brain extract, yeast, and yeast extract. Cancer Research, 1:3-16. 1941. The authors investigated various factors which influence the production of liver cancer in rats by feeding butter-yellow, p-dimethyl-amino-azobenzene. Albino rats of the Sherman and inultars exceeding the lives of the animals and influenced the type of tumor. Rice bran extract (ether soluble) exerted a transitory inhibition on the development of liver cancer. Ether extract of yeast also inhibited tumor development, but to a less extent than the ether extract of rice bran. Butter-yellow did not produce liver cancer in rats fed on a diet of unpolished rice containing 15% of brewer’s yeast. The paper is a detailed report of experimental tests of the protective action of dietary constituents derived from rice bran and yeast.—S. B-J.

TANNENBAUM, A. (Tumor Research Lab. of Michael Reese Hosp., Chicago, Ill.) Relationship of body weight to cancer incidence. Arch. Path., 30:509-517. 1940. A study of the incidence of tumors in mice kept on different diets, and study of insurance statistics, supports the conclusion that both animals and men who are overweight are more likely to develop tumors than those who are average or underweight.—H. G. W.

TENNANT, R., and A. A. LIEBOW. (Yale Univ. Sch. of Med., New Haven, Conn.) The actions of colchicine and of ethylcarbylamine on tissue cultures. Yale J. Biol. & Med., 13: 38-49. 1940. By correlating mathematically the accurately determined expansion ratios in Carrel flasks of colonies of cells from a mouse breast carcinoma (Yale carcinoma 1) with the mitotic counts it was found that colchicine, even in concentrations as low as 1.64 million, diminished the rate at which cells entered mitosis. This was true despite the apparently remarkable accumulation of karyokinetic cells. Morphological studies of normal cells from the breast of the newborn mouse showed that following mitosis under the influence of colchicine cells may attain chromosome and of the diploid. This results from dispersion of chromosomes longitudinally split during prophase and subsequent reconstitution of the cell without division of the cytoplasm. Despite profound nuclear changes the cells remain alive as demonstrated by successful growth upon transplantation into animals or fresh media. The effect upon mitosis of ethylcarbylamine, known to inhibit the Pasteur phenomenon (Warburg), is similar to that of colchicine but occurs over a narrower and higher range of concentrations.—A. A. L.


cische Kathepsinwirkung des Särgongewebes. The autolytic kathespin activity of sarcoma tissue. Gann, 34: 215-220. 1943. The autolytic kathespin activity of the Fujinami chicken sarcoma was greatest at pH 4.6. It was weaker in the earlier
stages after inoculation; stronger in the later stages. The addition of cysteine to the tumor emulsion increased the autolytic activity of the sarcoma. Significant autolytic activity was found in a rabbit sarcoma 30 days after inoculation. This approached the activity of the liver. The degree of autolytic activity of organs was in the following order: liver, kidney, spleen, sarcoma, and muscle. Spleen and sarcoma had approximately the same autolytic activity. Cysteine increased the autolytic activity of rabbit sarcoma, but to a less degree than it aided autolysis of the chicken sarcoma. There was no significant difference between the autolytic activity of tissues and organs from normal rabbits and from sarcomatous rabbits.—S. B-J.

IMMUNOLOGY


Rabbits were inoculated intrathecally and intradermally with the Brown-Pearce carcinozma. After regression of tumors tests of immunity were made by reinoculations into the testis. Serological tests were made for the demonstration of humoral antibodies. It was observed that nonspecific tissue factors might induce a state of resistance to the growth of tumor cells, rabbit embryo skin was injected intradermally into adult rabbits. In confirmation of Reserlek's reports, it was observed that over 90% of intradermal Brown-Pearce carcinozmas regressed spontaneously, and that rabbits with intracutaneous tumors, in which these tumors had regressed, were refractory to subsequent inoculations of the tumors. No evidence of humoral antibodies was obtained. Pathological and immunological studies did not explain the fundamental nature of the immunity. The possibility of its being a nonspecific tissue reaction is discussed.—S. B-J.


Among 350 tumors induced by dibenzanthracene in mice of pure inbred strains there were 6 spindle celled sarcomas that grew when transplanted into mice of certain strains, although they regressed later except in animals of the same strain in which the tumor originated. The growth of a graft of any one of the 6 tumors for as long as 4 days in mice of a strain different from that of the graft's origin brought about in the alien strain host an immunity from the growth of the autograft or another graft of the same tumor, but not from the graft of another tumor. Complete removal of the 1st tumor before the implantation of the 2nd showed that this type of tumor immunity was already established by the 5th day and was not dependent upon the continued presence of the 1st tumor nor upon its regression. When the 1st tumor was not removed, it continued to grow for a number of days in those mice which its own growth for 4 days had rendered unfavorable for the growth of another graft of the same tumor. The development of immunity proved to be dependent upon the growth of tumor cells in the host. The absorption of tumor proteins and of other proteins by mice of susceptible strains failed to bring about immunity. The growth of a graft in mice of the strain in which the tumor originated failed to bring about immunity. Mice of each pure inbred strain could be rendered immune from the growth of all tumors that originated in mice of other pure inbred strains, but these mice remained susceptible to the growth of a graft of those tumors that originated in mice of their own strain. Treating tumors with heat, pressure, and chemicals before implantation failed to cause regression in mice of their strain of origin.—H. G. W.


Antiserum was prepared against human carcinoma (gastric, cervical) proteins by injecting rabbits intramuscularly with the tumor tissue adsorbed on albumin cream according to the principles of Hektoen and Wellker (J. Infect. Diseases, 53:309-333, 1933). By this method precipitins for the blood serum proteins necessarily included in the tumor tissue disappeared from the rabbits' sera in from 1 to 6 months. Antiserums so prepared gave positive precipitin reactions with autolysates of malignant tissues in high dilutions whereas negative reactions were recorded with normal tissue autolysates and also by normal rabbit serum on malignant tissue. The serum of carcinomatous patients was set up against the precipitin sera and of 7 patients with clinical gastric cancer, 4 gave positive reactions. Seven of 8 patients with carcinoma of the cervix were also positive. Serum from normal controls or from noncancerous patients with various disorders were negative. The authors conclude that the proteins of carcinoma tissue have specific antigenic qualities and may be detected in the blood stream of patients by the appropriately prepared antiserum.—L. W. L.

LEUKEMIA


The offspring of 18 pregnant mice with transmissible leukemia (Akh 5 or Akh 106) failed in utero, in the neonatal period, or at the age of 3 months to show leukemia. This finding is in accord with the literature on human leukemia complicated by pregnancy, which reports no authentic case of transmission of the disease from mother to fetus.—L. W. F.


Leukemia was produced by the administration of carcinogenic chemicals in mice of a leukemic stock (AK), in mice of a stock (RF), in which spontaneous leukemia is rare, and in hybrids of these stocks. The genetic structure of neoplastic blood cells from induced leukemias was tested in transmission experiments using purebred mice of these stocks. Previous experiments have shown that the spontaneous leukemias arising in these hybrids are, in transmission experiments, similar to the spontaneous leukemias arising in leukemic stock. The present experiments have shown that the induced leukemias differ among themselves. Only 1 of 6 transmissible leukemias induced in hybrids resembled closely those arising spontaneously. Two were nonspecific and could be grafted on both parental leukemic and nonleukemic stock, and 2 could be readily grafted on hybrids but not on either parental stock. It is concluded that cells from spontaneous and induced leukemias may differ genetically. This difference may be explained by assuming that the cells of the induced leukemias are mutants.—S. B-J.


Extensive myeloid leukemic metaplasia was found in the liver, kidneys, lymph nodes, spleen, and ovaries of a rat which had been used in experiments made to study the inhibitory effect of methylene blue upon the formation of hepatorium o-aminozotol. The rats were fed for 250 days a diet of unpolished rice containing 2.5% o-aminozotol in oil. After the 250th day 11 rats were living, of which these were then given unpolished rice, to 100 g., of which was added 5 g. of 0.1 to 0.5%
aqueous solution of methylene blue. One of the rats in this group developed myeloid leukemia and died on the 32nd day of the experiment. The findings at autopsy with a description of the cells are reported. The author comments on the extreme rarity of spontaneous leukemia in the rat and concludes that the occurrence of the disease in this animal was directly related to the feeding of o-aminoazotoluol followed by feeding with methylene blue. The paper is illustrated with 15 figures.—S. B-J.


The agent of fowl leukosis (Furth strain 1) was studied in relation to its properties in the ultracentrifuge, and with regard to host susceptibility. Sedimentation of potent material from diluted heparinized plasma of leukemic animals at 30,000 r.p.m. for 1½ to 1 hour was incomplete. At 6,000 r.p.m. no sedimentation was demonstrable. Aggregation of particles in the sediment was indicated, first by the observation that the centrifugate was always less active than the crude extract or plasma (contrary to Claude's experience with the agent of chicken sarcoma), and second by the fact that the sedimented agent was not filtrable through candles that readily allowed the passage of particles in the original leukemic plasma. Animals less than 10 weeks of age were found more susceptible than older birds to leukemic whole blood, plasma, crude marrow extracts, and to ultracentrifugates of the last. With whole blood the breed of the fowl also was found to determine susceptibility. When unfiltered leukemic plasma was inoculated into the amniotic sac at the 7th (lay, some of the animals developed leukemia after hatching, but inoculations into the albumin were never successful before the 10th day (the time when the bone marrow develops). This suggested either that the hemopoietic elements of the yolk sac can be the site of introduction of the leukemia, or that the virus can survive in certain parts of the embryo for at least 3 days. In animals after hatching the bone marrow always gave the second histological evidence of leukemic change.—A. A. L.

GENERAL REVIEWS


A general review of the differences between cancer cells and normal cells. Chief of these are a loss or lack of polarity, a wide range in variation of nuclear and cytoplasmic structures, a decrease in structural differentiation and dependent specific functional activity, a decrease in dependence on oxygen supply, a decrease in organism control over cell division and an increase in autonomy of cell division, an increase in transplantability and an increase in invasiveness and ability to outlive cells of invaded tissue.—H. G. W.


The author discusses fundamental problems of malignant neoplastic growth and outlines some of the approaches of cancer research.—L. L. W.

COMPARATIVE ONCOLOGY


A spontaneously occurring carcinoma of the prostate without metastasis is reported in a very old rhesus monkey.—L. L. W.


This is a description of an embryonal adenocarcinoma of the kidney of a rabbit. There were no metastases.—S. B-J.


This is a description of a transplantable, nonfilterable lymphosarcoma which arose spontaneously in a Leghorn chicken.—S. B-J.


The published accounts of spontaneous and induced tumors in guinea pigs are reviewed. The authors report their observations on 1 spontaneous tumor in guinea pigs and on 2 liposarcomas and 2 fibrosarcomas induced in guinea pigs by subcutaneous injection of 3,4-benzpyrene in glycerine. The guinea pig appears to be resistant to the development of spontaneous tumors, to transplantation of spontaneous and induced tumors, and to the production of induced tumors other than that of the gall bladder. Carcinogenic hydrocarbons are of potent guinea pigs than in mice.—S. B-J.

CLINICAL AND PATHOLOGICAL REPORTS


General considerations, with particular reference to food deficiencies.—H. G. W.

DIAGNOSIS—GENERAL


Of 30 patients injected with Evans blue, 20 showed selective concentration of the dye in and about the neoplastic foci, with no correlation between the histologic type and ability to localize the dye, which is deposited in the fibroblasts and macrophages and not in the tumor cells themselves. Benign neoplasms did not localize the dye.—H. G. W.


Fractionated urinary solutions from patients with far advanced cancer were found to cause loss of weight, stupor, vaginal bleeding, resorption of the embryos when injected intravenously into pregnant rats and mice. Similar but less pronounced results were produced by the urine of a healthy subject. The method of preparation of the urine fraction is given.—L. L. W.


General review.—H. G. W.


The melanophore pituitary reaction, using the so-called "albino-salamander," whose hypophysis is cauterized, was applied to various cases of cancer, other tumors, pregnancy, diseases of internal secretion, and inflammation. The test was made by injecting 0.2 to 0.3 cc. of morning urine from a patient sub-
Reports of Experimental Research

Cancer Res 1941;1:75-85.

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