

Abstracts

Reports of Research

The Pathological Effects of an Instantaneous Dose of Radiation. WARREN, S. [(MC) USNR] *Cancer Research*, 6:449-453. 1946.

This is the address of the president of the American Association for Cancer Research given at the 37th annual meeting of the society and concerns the biological effects of the atomic bombs on the inhabitants of Nagasaki and Hiroshima. The injuries experienced by these persons could in general be classified into those occurring immediately after the explosion and those occurring after a delayed period. The immediate injuries were mainly those due to the intense heat, flash-burns frequently being 2nd or 3rd degree, as well as thermal injuries due to induced fires. It was an interesting fact that frequently parts of the body were protected from flash-burns by the upraised hand or arm, or the reflecting properties of a piece of clothing. Also there were injuries which were not peculiar to this type of bomb due to the blast itself. Some of the inhabitants suffered from all types of injuries and it was difficult in others to determine the real cause of death. Short-wave irradiation and neutrons were likewise responsible for some immediate effects, as weakness, general malaise, fever, and sometimes death. The delayed effects due to radioactivity were anorexia, weight loss, epilation, and changes in the cellular elements of the blood and bone marrow. Leukopenia was an outstanding effect, the white cells sometimes being reduced to 200 per cubic mm. during the first few days after the exposure. This was interpreted to mean that the cells of the circulating blood were destroyed as well as their precursors in the hemopoietic centers. Three to 5 weeks after the blast some of the natives showed a thrombocytopenia, some dying of acute hemorrhage, while others had ecchymoses, purpuric patches and petechiae. The late blood changes were mainly those of anemia of the aplastic type. The effects of this irradiation on the gonads were also noted, the testes being more severely affected than the ovaries, and showing in some cases suppression of spermatogenesis with subsequent atrophy. However, the interstitial cells were not damaged. It is pointed out that it will be necessary to follow the population of these two communities for a long time in order to determine the full effects of these atomic bomb explosions.—E. W. S.

The Carcinogenic Activity of Some New Derivatives of Aromatic Hydrocarbons. II. Compounds Related to 1,2-Benzanthracene. DUNLAP, C. E., and WARREN, S. [Harvard Cancer Commission, and Harvard Med. Sch., Boston, Mass.] *Cancer Research*, 6:454-465. 1946.

Thirty-eight substitution products of 1,2-benzanthracene were tested for carcinogenic activity by subcutaneous in-

jection in mice. Each of 12 of the compounds produced one or more sarcomas at the site of injection while the remaining 26 were inactive. Among the new compounds, those which showed the greatest activity were 5-bromo- and 5-cyano-9,10-dimethyl-1,2-benzanthracene. The results of these tests permit no new generalizations as to the relationship between the chemical structure of hydrocarbons and their carcinogenic activity.—Authors' abstract.

Association d'hydrocarbures polycycliques et mécanisme de la cancérisation. [The Association of Polycyclic Hydrocarbons and the Mechanism of Carcinogenesis.] LACASSAGNE, A., BUU-HOI, H.-P., and CAGNIANT, P. [Pasteur Inst., Institut of Radium Annex, and Polytechnic Sch., Paris, France] *Compt. rend. Soc. de biol.*, 138: 16-17. 1944.

This work was based on the following hypothesis: It is known that the cumulative action of small doses of a carcinogenic substance induces, after a certain lapse of time, a tumor. The change in the properties of the cell seems to be due to an accumulation of small insults to the mechanism which controls division of that cell. By introducing a mixture of 2 very similar substances, the one carcinogenic, the other non-carcinogenic, it is reasoned that the latter material should occupy some space in the cell, thus preventing the entrance of the carcinogenic material. Hence the tumor formation should be delayed.

Two groups of 10 mice of the same strain and age received the same amount of methylcholanthrene subcutaneously. The second group received, in addition, dibenzofluorene in equimolecular concentration. Substantial differences were noted. There was considerable delay in the appearance of the tumors in the second group; only 6 animals developing growths, whereas cancer appeared in all the 10 animals of the first group.—R. J.

Production de tumeurs du type éléidome à la suite d'injections d'oestrone. [Production of Tumors of the Eleidoma Type after Injections of Oestrone.] CHEVREL-BODIN, M. L., and CORMIER, M. [Lab. of Hôtel-Dieu, Rennes, France] *Compt. rend. Soc. de biol.*, 138: 30. 1944.

Injections into 7 rabbits of oestrone in an oil suspension, at doses varying from 18 to 300 mgm. induced subcutaneous and visceral fatty infiltration of the liver, kidneys, and lungs. Subsequent injections of folliculin in an oil suspension resulted in the appearance of tumors at the site of the injection. The opinion is given that the production of tumors in such animals is connected with the presence of free fatty acids due to faulty metabolism.—R. J.

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Serial Transmission of the Milk Agent of Mouse Mammary Carcinoma. GREEN, R. G., MOOSEY, M. M., and BITTNER, J. J. [Univ. of Minnesota Med. Sch., Minneapolis, Minn.] *Proc. Soc. Exper. Biol. & Med.*, **61**:362-363. 1946.

Mice of the hybrid ZBC strain, which are susceptible to but do not carry the milk influence, were given serial inoculations of filtrates of mammary tumor from C3H mice and normal lactating mammary tissue. The procedure was to inject 30 mice with filtrates, 15 of the animals being held indefinitely and forced-bred to induce maximum mammary cancer production. The other 15 mice were permitted to raise one litter and then were sacrificed to yield lactating mammary tissue to be inoculated into another group of 30 mice. In a similar manner 15 of the second group were forced-bred and 15 allowed to have but one litter, the latter furnishing the lactating mammary tissue for the third batch of animals. This was repeated 4 times.

In the first group of mice receiving mammary tumor filtrate all 15 females developed tumors. In the group of females receiving suspensions from the first transfer of mammary glands, the number of tumors fell to 11; in the second transfer 6 tumors appeared, and in the third and fourth transfers no tumors developed. The disappearance of cancer in the later transfers may be due to the fact that a hybrid strain was used, to a loss or modification of the virus, or to a change in immunologic relationships.—M. B.

Bone Tumors in Fowls Injected Intravenously with Causative Agent of Rous Sarcoma. PIKOVSKI, M., and DOLJANSKI, L. [The Hebrew Univ., Jerusalem, Palestine] *Proc. Soc. Exper. Biol. & Med.*, **61**:246-248. 1946.

White leghorn chicks of both sexes, and *in vitro* cultures of the Rous-Fischer strain of filterable fowl sarcoma agent were used. Fragments of a Rous cell colony were planted into a Carrel flask containing 1 part of chicken plasma diluted with 2 parts of Tyrode solution. After cultivation for 1 to 3 weeks the flasks were overlaid with Tyrode solution and incubated for 30 minutes; the supernatant fluid was pipetted off and centrifuged 3 times at 3,000 r.p.m. for 15 minutes each.

Twelve chicks, aged 4 to 10 weeks, were each injected intravenously with 1 cc. of washings from tissue cultures of Rous sarcoma cells, 2 or 3 injections being given at weekly intervals to each bird. Individuals died in 21 to 42 days after the initial inoculation. Autopsies showed growths in the liver, lungs, heart, and kidneys in 9 of 12 chicks. The visceral tumors were always associated with a sarcoma at the inoculation site. The outstanding feature observed in 11 of 12 chicks was the extensive neoplastic bone changes (sternum, femur, tibia, tarso-metatarsus, radius, ulna, humerus). Histologically, the tumors were typical invasive osteoid sarcomas. No explanation for this phenomenon is offered, although the repeated intravenous injections of the agent or a modification of the agent during passage *in vitro* are mentioned as possibilities.—M. B.

Cancer du foie apparu chez un lapin irradié par neutrons. [Appearance of a Cancer of the Liver in a Rabbit after Irradiation by Neutrons.] LACASSAGNE, A., and JOLIJOT, F. [Coll. of France and Inst. of Radium, Paris, France] *Compt. rend. Soc. de Biol.*, **138**:50-51. 1944.

A young male rabbit weighing 1,350 gm. was exposed for 3 days to a bombardment by neutrons. Considerable alterations in blood picture were especially marked on the ninth day (800 white blood cells). Nevertheless, the count returned very rapidly to normal and remained so for several months. Nine and one-half months after the exposure the general condition of the animal became poor, and death occurred in the 17th month. The autopsy revealed the existence of a large carcinoma of the liver. There was no doubt in the minds of the authors but that the neutron bombardment caused the appearance of the tumor. Spontaneous cancer of this type is entirely unknown in rabbits.—R. J.

Creatine Metabolism in Relation to Pituitary Tumours. CUMINGS, J. N. [Nat. Hosp., London, England] *Brain*, **67**:265-269. 1944.

The urine of 8 patients with chromophobe adenoma of the pituitary contained slightly more creatinine than that of control subjects, and on some days also contained small amounts of creatine when kept on a meat-free and fish-free diet. The urine of 16 patients with acidophil adenoma of the pituitary contained an increased quantity of creatinine and a definite but variable amount of creatine. In a creatine tolerance test, made by giving 1 gm. of the compound orally and examining the urine and blood during the next 3 hours, 3 patients with chromophobe adenoma gave a response that differed considerably from that of 2 patients with acidophil adenoma; the test is recommended for differential diagnosis.—M. H. P.

The Effect of Diets Containing an Abundance of Milk, Liver, Riboflavin, and Xanthine on Methylcholanthrene Carcinogenesis. STRONG, L. C., and FIGGE, F. H. J. [Yale Univ. Sch. of Med., New Haven, Conn.] *Cancer Research*, **6**:466-469. 1946.

A diet of liver supplemented by combinations of raw, unpasteurized milk, riboflavin, and xanthine had little or no influence on the latent period or growth rate of tumors induced in C3H mice by the subcutaneous injection of 1 mgm. doses of methylcholanthrene. In general, the diet supplements stimulated tumors at first and later seemed to have a slight inhibitory effect. This effect was most pronounced in the group of mice receiving raw milk and riboflavin in addition to the basic dried liver, milk, Nurish-mix diet. In any case, the effect of diet was so slight that its significance was questionable. This is in contrast to the remarkable inhibition of the carcinogenic action of *p*-dimethylaminoazobenzene observed by other investigators when adequate amounts of yeast, liver, or milk are added to the diet.—Authors' abstract.

Sur la croissance des tumeurs spontanées chez des souris recevant des injections d'acide ascorbique (vitamine C). [Action of Vitamin C on the Growth of Spontaneous Tumors in Mice.] DOBROVOSKAIA-ZAVADSKAIA, N. [Inst. of Radium, University of Paris, France] *Compt. rend. Soc. de Biol.*, **137**:689-691. 1943.

Ascorbic acid, in solutions of 1 and 5%, was injected

subcutaneously or intravenously into 55 tumor-bearing mice. The results were not conclusive. This was due, perhaps, to the fact that the mouse's ability to synthesize vitamin C varies with each animal. As a result the amount of vitamin C supplied by the mouse cannot be controlled and comparative studies become difficult. Injections of high concentrations of vitamin C seemed to have a curbing action on the tumor growth in certain cases, but in several other instances the growth was accelerated.—R. J.

Cytotoxic Property of Mouse Cancer Antiserum.

GREEN, R. G. [Univ. of Minnesota Med. Sch., Minneapolis, Minn.] *Proc. Soc. Exper. Biol. & Med.*, **61**:113-114. 1946.

In a study concerning the milk influence associated with mammary gland carcinoma of mice, an antiserum prepared from rabbits has been tested for its toxicity for cancer cells. Mouse cancer tissue was homogenized and fractionally centrifuged. The first sediment, obtained by centrifugation for 1½ hours at 14,000 × gravity, was discarded. The supernatant was again centrifuged 1 hour at 100,000 × gravity. The second sediment was collected, suspended in 0.9% saline solution and injected intraperitoneally into rabbits in 5 weekly doses totaling 2 gm. of original tissue. The rabbits were bled for serum 14 days after the fifth injection of centrifugate. An antiserum against normal lactating mouse mammary tissue was prepared in an identical manner, the normal mammary tissue coming from mice susceptible to but not carrying the milk influence. Normal rabbit serum was used as an additional control. To test these sera, cancer tissue was macerated, suspended in saline, and allowed to settle for 30 minutes. This cell suspension was then diluted 10 times and divided into 4 portions. To each of these aliquots 5 volumes of cancer antiserum, normal tissue antiserum, normal rabbit serum, and 0.9% saline were added respectively. All the mixtures were held at room temperature 3 hours, and then in the refrigerator at 7° C. for 3 hours. A sixteenth of a cc. of each preparation was injected intraperitoneally into separate groups of 10 mice each.

The cancer antiserum completely inhibited the growth of cancer cells. Both the normal rabbit serum and normal mammary tissue antiserum caused a delay in tumor development. The normal rabbit serum inhibited slightly the tumor growth since only 7 of the 10 injected mice showed tumors at the end of 60 days.

Tumors developed more rapidly than in the other groups in all mice injected with tumor cells in saline solution.—M. B.

Antigenic Character of the Cancer Milk Agent in Mice. GREEN, R. G., MOOSEY, M. M., and BITTNER, J. J. [Univ. of Minnesota Med. Sch., Minneapolis, Minn.] *Proc. Soc. Exper. Biol. & Med.*, **61**:115-117. 1946.

The milk agent used in this study was obtained from high-speed centrifugates, collected between a first run at 15,000 × g. and a second at 95,000 × g. of mammary cancers. These sediments were injected into rabbits and white rats to produce antisera. Five doses of the materials obtained, each the equivalent of 4 gm. of spontaneous mouse tumor suspended in 3.5 cc. of saline, were injected into

rabbits at 5 day intervals. The rats were similarly immunized, but each dose was 2 cc., equivalent to 1 gm. of tumor. Seven to 10 days after the last injection the animals were bled.

Ninety mice of the ZBC strain were separated into 3 groups of 30 animals each. Group 1 of mice received a centrifugate equivalent to 0.25 gm. of tumor tissue suspended in 0.5 cc. saline solution. At the end of 11½ months, 25 of the 30 mice had developed mammary cancer. Group 2 individuals were injected with a centrifugate equivalent to 0.25 gm. of tumor tissue suspended in 0.5 cc. of rabbit immune serum after the mixture had stood at room temperature for 2 hours. At 11½ months, 2 of the 30 mice had developed tumors. The mice in group 3 were injected with similar amounts of centrifugate suspended in 0.5 cc. of normal rabbit serum. Of these, 14 developed mammary cancer at 11½ months. After inoculation all animals were forced-bred to stimulate cancer development.

In a second experiment, antisera against spontaneous mouse tumor tissue, transplanted tumor tissue, and from normal mouse liver, heart, spleen and kidney, were prepared in laboratory rats as already described. In addition, normal rat serum was obtained. ZBC mice, 1 month old, were injected with tumor sediments mixed with the various antisera following incubation for 2 hours. One control group received active sediment suspended in 0.9% saline solution.

Of the 48 mice that received spontaneous tumor antiserum mixtures (24) and transplanted tumor antiserum mixtures (24) none developed cancer at 13½ months. Twenty-one mice of the 24 receiving normal tissue antiserum developed tumors, as did 13 of the 24 that received the normal rat serum. Of the 24 control mice that received the active material without the addition of serum, 18 became cancerous.

The authors feel that 3 basic criteria of a virus are now known to be met by the milk agent, and the evidence also indicates that the agent is a virus of exogenous origin.—M. B.

Essai d'immunisation contre un épithélioma de l'utérus du Rat par 'injection de filtrat tumoral. [Tentative Immunization against an Epithelioma of the Uterus of the Rat by Injections of Tumor Filtrate.] ROUSSY, G., GUÉRIN, M. and GUÉRIN, P. [Cancer Inst., Univ. of Paris, Paris, France] *Compt. rend. Soc. de biol.*, **138**: 121-123. 1944.

Ground tumor tissue filtered through a bacterial filter was used as a vaccine. The tumor was a transplantable epithelioma of the rat's uterus. Different experiments involving a total of 95 rats, did not show any significant difference between experimental and control animals in the growth of tumors grafted. A very limited immunity existed in animals inoculated 2 months previously with vaccine, but it was completely lacking in animals vaccinated 3 or 4 months earlier. Other experiments were done using a mixture of the filtrate plus an attenuated suspension of tumor, the results here were likewise negative.—R. J.

Tests for Specificity of Tumors and Sera of Rats. BAILEY, G. H., and GARDNER, R. E. [Sch. of Hyg. and Pub. Health, Johns Hopkins Univ., Baltimore, Md.] *Am. J. Hyg.*, **40**:212-223. 1944.

Guinea pigs were passively sensitized to autoclaved extracts of rat carcinoma 256 and sarcoma 10 by intraperitoneal injection of antisera from rabbits immunized with vaccines of *Pasteurella bovisseptica* grown in infusion broths made from the tumors. Such antisera showed little if any specificity for autoclaved extracts of the tumors, but gave many cross reactions in passive anaphylactic tests in guinea pigs. The sensitized guinea pigs showed considerable anaphylactogenic specificity for unheated sera of rats bearing the tumors. Rabbit antisera against autoclaved extracts of the 2 tumors mentioned or of normal rat tissues, were very toxic on intravenous injection in rats. The sera of the tumor-bearing rats showed greatly increased amounts of the complement but no increased specific or nonspecific hemolytic action on sheep red blood cells. Positive precipitin tests were obtained with the fresh sera of tumor-bearing rats when the sera were mixed with fresh guinea pig serum and the specific carbohydrate complex of *Salmonella enteritidis*. Essentially negative results were obtained in an attempt to apply precipitin and anaphylatoxin tests to differentiate the sera of human patients with and without tumors.—M. H. P.

Studies in Hodgkin's Syndrome. II. A Search for Brucella in Hodgkin's Syndrome. HOSTER, H. A., DOAN, C. A., and SCHOMACHER, M. [Ohio State Univ., Columbus, Ohio] *Proc. Soc. Exper. Biol. & Med.*, **57**:86-88. 1944.

The coexistence of Brucella infection and Hodgkin's syndrome has previously been reported. In this investigation, a series of 71 patients were studied; 35 with histologically verified Hodgkin's granuloma and 36 with miscellaneous diseases involving the reticuloendothelial system. Bacteriological studies included cultures from nasal and throat secretions; from urine and blood; from aseptic surgical specimens of liver, spleen, lymph node and bone marrow; from postmortem samples of spleen, lymph node and liver; and from other miscellaneous sources. No organisms identified as belonging to the Brucella group were isolated. Three patients with Hodgkin's granuloma had brucellergin skin tests which were positive after 48 hours. None, however, showed a significant agglutinin titer for Brucella and none developed an elevation of the opsonocytaphagic index which was considered significant.—M. B.

Significance of the Age Factor and Sex Glands in Experimental Leukemia in Mice. SILBERBERG, M., and SILBERBERG, R. [City Hosp. and Jewish Hosp., Saint Louis, Mo.] *Proc. Soc. Exper. Biol. & Med.*, **58**:347-348. 1945.

This investigation deals with the influence of age and sex glands on the development of leukemia in strain D mice in which the incidence of spontaneous leukemia is 2%. Of the 141 males and 117 females used, 73 males and 57 females were castrated at the age of 2 to 3 weeks, and 68 males and 60 females served as noncastrated controls. All mice were injected subcutaneously once a week for 5 months with 200 rat units of estradiol benzoate in sesame oil. The animals were divided into 2 groups. In group A, estrogen was injected about a week after opera-

tion, the mice being 3 to 4 weeks old; in group B, estrogen treatment was begun 6 weeks or 3 months after castration. After estrogen treatment was stopped, the mice were permitted to live until their natural deaths.

The incidence of leukemia of the intact, estrogen-treated males was 30%; of the castrated, estrogen-treated males, 50%. Leukemia developed in 45.8% of the intact females, whereas ovariectomized, estrogen-treated females showed a 40% incidence. These differences are probably not significant. The same number of castrated males and females developed leukemia, whether injected immediately after castration or at a later date. In females with intact ovaries, leukemia was somewhat more frequent in animals injected at 3 to 4 weeks of age (45.8%) than in those injected at the age of 2 to 3 months (36.1%). The age of non-castrated males at the onset of treatment had a decided influence on the incidence of leukemia. Those mice receiving estrogen after sexual maturity had an incidence of 57.9% while only 30% of the younger animals developed leukemia. The presence of the testes in sexually immature males seemed to inhibit the development of the leukemia which would have usually occurred under the influence of estrogen.—M. B.

Nouvelles recherches sur la transplantation de tissus au cours de leur cancérisation par le benzopyrène. [New Research on Transplantation of Tissues during the Process of Carcinogenesis by Benzopyrene.] ROUSSY, G., GUÉRIN, M., and GUÉRIN, P. [Cancer Inst., Univ. of Paris, Paris, France] *Compt. rend. Soc. de biol.*, **138**:25-27. 1944.

A small amount of benzpyrene was introduced under the skin of 50 rats; using 10 rats as control, the nodule of benzpyrene plus surrounding tissue were removed from 40 of the animals and reintroduced, in 6 different groups using different technics. The conclusions were that the process of carcinogenesis by benzpyrene seems to be due to the result of a local action rather than a general one on the whole organism. The chemical reaches not only the cells in direct contact, but also cells which are at a certain distance from the benzpyrene. After transplantation of the tissue surrounding the benzpyrene pellet, a certain antagonism is observed between the cells of the new host and those which are in the tumor. Trauma to the cells favors malignant change.—R. J.

Failure of Homozygous Embryo Skin to Prevent Growth of Autogenous Tumor-Grafts in the Rat. GOLDFEDER, A. [New York City Cancer Inst. and New York Univ., New York, N. Y.] *Proc. Soc. Exper. Biol. & Med.*, **60**:338-340. 1945.

Several investigators have reported the induction of resistance to malignant growths, including leukemias, in hybrid animals by injecting normal homologous tissues, such as liver, spleen, blood and homologous skin. However, similar results have not been obtained when inbred strains of animals were used, and it has been concluded that the degree of induced resistance that can be produced depends upon the genetic relationship between the host and the immunizing agent; and that no resistance to tumor growth can be produced either with normal or malignant tissues in animals of pure line.

In this investigation, an attempt was made to produce

immunity to a reticulum cell lymphosarcoma, which arose in an inbred strain of rats by the use of normal embryo skin of the same strain. The skins of rat embryos were removed under strict asepsis, finely minced, and a concentrated suspension prepared in a small amount of 0.85% saline. Portions of 0.3 cc. of this suspension were injected into the right flank of 15 male rats. Twelve days later, the left sides of the same rats were injected by trocar with grafts of 3 to 4 mgms. of the reticulum cell lymphosarcoma which arose in this strain. As controls, 6 male rats of the same strain were implanted with the same tumor. Criteria for evaluating results were: percentage of takes, latent period of takes, and initial and maximum tumor sizes. There were no significant differences in tumor behavior between experimental and control groups, and no evidence of induced resistance to the grafts.—M. B.

Transplantability of Induced Granulosa Cell Tumors and of Luteoma in Mice. Secondary Effects of These Growths. FURTH, J. [Cornell Univ. Med. Coll., New York Hosp., New York, N. Y.] *Proc. Soc. Exper. Biol. & Med.*, 61:212-214. 1946.

A single exposure of x-rays in dose of 87 r given over the entire body to 44 mice about 6 weeks old produced ovarian tumors in 31. These growths were of 3 main histological types (a) tubular adenomas (b) luteomas and (c) granulosa cell tumors. Thirteen of 21 attempts to transfer these tumors were successful. Tubular adenomas of 3 mice proved transplantable. This is a very slow-growing tumor, becoming palpable (about 2 mm. in diameter) after about 6 months. Two induced luteomas were readily transplantable. Luteomatous cells proliferate by mitotic division retaining the morphological characteristics of lutein cells in mice of both sexes. Mice bearing one of these luteomas (Strain IX) do not show evidence of hyperestrinization, but the adrenal cortex undergoes profound atrophy. These mice gained considerable weight. A granulosa cell carcinoma (Strain III) arose in an F_1 mouse that received 175 r when 6 weeks old, followed by a painting with 0.5% methylcholanthrene in benzene. Histological changes indicated that cells of this tumor secreted estrogens. Mice carrying tumors of this strain also exhibited a cavernous dilatation of the sinusoids of the liver, spleen and adrenals.—M. B.

The Invasive Character of Cancer Growth. COMAN, D. R. [Univ. of Pennsylvania Med. Sch., Philadelphia, Pa.] *Am. J. M. Sc.*, 211:257-260. 1946.

The author, finding that cancer cells are less firmly attached to one another than are normal or benign tumor cells, suggests that this fact offers a physical basis for invasive growth. The question is raised whether the decreased cohesiveness of cancer cells depends either upon the local calcium deficiency that is known to exist in cancer tissue or upon a local increase in spreading factor or both.—M. T.

Nitrogen Mustards in the Treatment of Neoplastic Disease. RHOADS, C. P. [Committee on Growth of the National Research Council, New York, N. Y.] *J. A. M. A.*, 131:656-658. 1946.

The present therapeutic status of the nitrogen mustards is summarized. Methyl-bis (β -chloroethyl) amine hydro-

chloride has been used more extensively than tris (β -chloroethyl) amine hydrochloride and on the basis of this experience the methyl-bis compound seems to be preferable as venous thrombosis is not so likely to follow at the injection site. Thus far a total of 160 patients suffering from neoplastic disease (chiefly lymphoma, leukemia, and allied conditions) has been treated with these agents. The dosage of the methyl-bis compound recommended as a single course is 0.1 mgm. per kgm. of body weight intravenously on 4 successive days.

The nitrogen mustards in large enough doses are injurious to many types of tissues, and appear to exert their greatest effects on rapidly dividing cells, presumably either normal or neoplastic. The predominant toxicologic effect of these compounds is to damage the normal hemopoietic system of the body. The tumor regressions induced by these compounds are temporary and no cases of the neoplastic diseases studied have been observed. The effects of the nitrogen mustards are in many respects similar to those of x-rays. The great advantage of radiation therapy is that it can be given locally. The agents are available for experimental purposes only by qualified institutions through the Committee on Growth, National Research Council, Washington, D. C. Members of the Committee on Growth are listed.—M. E. H.

An Experimental Evaluation of Methionine in the Therapy of Liver Injury from Carbon Tetrachloride. SHAFFER, C. B., CARPENTER, C. P., and MOSES, C. [Mellon Inst. and the Sch. of Med. of the Univ. of Pittsburgh, Pittsburgh, Pa.] *J. Indust. Hyg. and Toxicol.*, 28:87-93. 1946.

Liver damage was produced in 28 normal dogs by the intraportal injection of undiluted carbon tetrachloride in dosages ranging from 0.05 to 0.252 cc./kgm. Fifteen of these animals received 0.3 gm./kgm. of methionine postoperatively by the intravenous route, and in some cases, a second therapeutic dose of equal size 18 hours later. On the basis of gross and histopathological observations, liver function tests, and length of survival of methionine-treated and control animals, no consistent beneficial action of methionine in the prevention or repair of liver damage due to carbon tetrachloride was found. Moderate amounts of carbon tetrachloride given intraportally were absorbed almost completely by the liver with little pathologic change resulting elsewhere. Larger doses caused tubular and some glomerular damage in the kidney, and hemorrhage in the other abdominal viscera as well as in the lungs. The maximum injury to the liver occurred in the caudate and right lateral lobes.—F. L. H.

Effect of Bacterial Toxins on Tumors. VII. The Tumor-Hemorrhage Factor in Bacteria. ZAHL, P. A., STARR, M. P., and HUTNER, S. H. [Haskins Lab., New York, N. Y.] *Am. J. Hyg.*, 41:41-56. 1945.

Seven day old implants of mouse sarcoma 180 in white male Rockland mice became hemorrhagic 8 hours after the intraperitoneal injection of killed suspensions of various gram-negative bacteria, including plant pathogens of the groups *Agrobacterium*, *Bacterium*, *Pseudomonas*, and *Xanthomonas*. Contrary to previous reports species of the gram-negative genus *Rhizobium* and of the gram-negative photosynthetic genera *Rhodobacillus* and *Phaemonas* like-

wise possessed this ability. In *Salmonella choleraesuis*, but not in *Hemophilus influenzae*, smooth strains were much more potent than rough for the production of hemorrhage in tumors. No tumor hemorrhages were produced by streptococci or (with few exceptions) other gram-positive bacteria, or by protozoan flagellates. Apparently the hemorrhagic factor of the gram-negative bacteria is bound in the complex O antigen. The mode of action of "Coley's toxin" is discussed.—M. H. P.

Number of Peyer's Patches in Mice Belonging to High and Low Mammary Tumor Strains. KELL-SALL, M. A. [Roscoe B. Jackson Memorial Lab., Bar Harbor, Me.] *Proc. Soc. Exper. Biol. Med.*, **61**:423-424. 1946.

Mice used in this study were of both sexes, varying in age from 4 weeks to 1.5 years. The animals were starved for two days prior to death, killed with ether, and the small intestine as well as the cecum removed, fixed in 10% formalin solution for 2 days, and then thoroughly washed. This procedure enabled the patches to be easily seen macroscopically. The 5 different strains used included C57 black, having a low average of 6.3 Peyer's patches and in which spontaneous mammary tumors are very rare, strain C, Swiss mice and dba, with an intermediate number of patches averaging 8 to 9. These latter strains have a higher incidence of spontaneous tumors (up to 85% in dba breeding females). Finally C3H mice were also

studied and were found to have the highest number of patches (mean being 10.7); the incidence of mammary cancer in this strain is about 95%. The correlation between the number of Peyer's patches and the incidence of spontaneous mammary tumors is significant.—M. B.

The Experimental Production of Extraskelatal Bone-Forming Neoplasms in the Rat. DUNNING, W. F., and CURTIS, M. R. [Wayne Univ. Coll. of Med. and Detroit Inst. of Cancer Research, Detroit, Mich.] *Radiology*, **44**:64-76. 1945.

Bone-containing neoplasms having no connection with the skeleton were experimentally produced in rats. In one group of 7,500 neoplasms induced in rats' liver by *cysticercus fasciolarus*, 49 were bone-forming tumors. The tumors varied from benign to highly malignant growths and showed extreme variability. Sixty-six bone-forming neoplasms were observed in 2,351 tumors induced by subcutaneous injection of paraffin containing 3,4-benzpyrene. Three concentrations of benzpyrene were used: 1.0, 0.25, and 0.1% giving rise to tumors in the proportion of 1, 7, and 20% respectively. The most favorable incitant of heteroplastic bone-forming neoplasms was 0.1%, the weakest concentration used.

It was noted that the osteosarcoma induced had a greater average daily increase in diameter than the bone-containing neoplasms which were primarily fibrosarcomas.—R. E. S.

Clinical and Pathological Reports

Clinical investigations are sometimes included under Reports of Research

DIAGNOSIS—GENERAL

The Significance of Tumor Cells in Serous Effusions. HONIGMAN, A. H. [Sch. of Med., Univ. of Md., and Univ. Hosp., Baltimore, Md.] *Surg., Gynec. & Obst.*, **81**:295-301. 1945.

An examination for malignant cells was made of 172 samples of fluid aspirated from 142 patients, and the results are tabulated and discussed. Malignant cells were found in nearly 60% of the fluids from patients with confirmed carcinoma.—J. G. K.

The Vaginal and Endometrial Smear as a Diagnostic Procedure in Cancer of the Uterus. PAPANICOLAOU, G. N. [New York Hosp., New York, N. Y.] *N. Y. State J. M.*, **45**:1336-1338. 1945.

The author believes that although this method is still incompletely explored and should not be expected to compare in accuracy and dependability with the long tested and well standardized methods of biopsy and curettage, its clinical test in various laboratories has proved its validity as a source of reliable information. It presents some distinctive and advantageous features, which are enumerated. Two case histories are reported.—J. L. M.

II. The Value of the Vaginal Smear in the Diagnosis of Uterine Cancer. A Report of 1015 Cases. MEIGS, J. V., GRAHAM, R. M., FREMONT-SMITH, M., JANZEN, L. T., and NELSON, C. B. [Vincent Memorial Hosp., and Harvard Med. Sch., Boston, Mass.] *Surg. Gynec. & Obst.*, **81**:337-345. 1945.

The authors conclude that the vaginal smear technic is an accurate method of diagnosis of cancer of the uterus and that its most important contribution may be in the field of cancer control, since large numbers of women may be screened and those with positive smears studied further by biopsy.—J. G. K.

THERAPY—GENERAL

Results in the Treatment of Skin Cancer. GOLDMAN, L. B. [Queens Gen. Hosp., Jamaica, N. Y.] *N. Y. State J. M.*, **45**:2186-2189. 1945.

The two varieties of skin cancer, basal and squamous, are presented with illustrations before and after treatment. The author points out that any skin ulceration, small as it may be, if persistent, should be suspected of malignancy unless repeated biopsies are negative. Three methods of treatment, irradiation, electrocoagulation, and surgery, are utilized in skin cancer. The results, however, depend not so much upon the choice of a modality as upon its proper use. The common skin lesions should be treated with irradiation rather than with surgery or electrocoagulation. Surgery is indicated in skin carcinomas of the extremities, being of special advantage in cases of ulcerations that do not heal under ordinary care.—J. L. M.

Hormone Treatment of Cancer. DODDS, E. C., ET AL. [Discussion at Med. Soc. of London, Dec. 10, 1945] *Lancet*, **249**:817-818. 1945.

E. C. DODDS said that a small proportion of breast cancers are undoubtedly benefited by estrogen. TERENCE MILLIN