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EXPERIMENTAL STUDIES AND ANIMAL TUMORS


A benzene extract of liver of persons with carcinoma of the stomach, lung, esophagus, and rectum, when dissolved in sesame oil, produced 13 tumors in 56 mice. The tumors were all spindle-cell or polymorphous-cell sarcoma. Extract from the liver of persons dying of disease other than cancer did not produce a single tumor in 53 mice. The author was not able to confirm Schabad's results (Compt. rend. Soc. de biol. 124: 213, 1937) with a benzene extract of the liver from a case of carcinoma of the stomach. These results were confirmed, however, on a considerable scale by Hieger (Am. J. Cancer 39: 496, 1940), who obtained 12 tumors in 367 mice. The tumors were produced by subcutaneous injection and were all spindle-cell sarcomas. What is most interesting in Hieger's results is that he obtained tumors from extracts of livers of non-cancerous persons. Des Ligneris (Am. J. Cancer 39: 489, 1940) also produced tumors in mice with extracts of both cancerous and non-cancerous liver. Similar results are reported in a paper by Kleinenberg, Neufach and Schabad (Am. J. Cancer 39: 463, 1940). These results show that no conclusions can be drawn at the present moment as to a carcinogenic substance being produced either in cancer or in the liver of cancer patients, or being absorbed in the liver from a cancer at a distance, but they show also that liver extracts of various types, composed chiefly of the non-saponifiable residues of human tissues, contain substances that exist both in normal and cancerous persons, which when administered to a highly susceptible animal may produce cancer.


Homologous, as well as heterologous blood of normal and cancer patients, human fetuses three to five months of age, and of guinea-pigs, was injected before or after transplantation of the Erhlich carcinoma or Besredka sarcoma in mice, the Flexner-Jobling carcinoma in rats, and the Brown-Pearce tumor in rabbits. The dose in mice was from 0.1 to 0.2 c.c., in rats 0.3 c.c., and in rabbits 0.5 c.c. Each animal received three to five injections.

The number of takes was 30 per cent less in animals receiving normal human blood or homologous blood than in controls, and tumor growth was retarded in treated animals after successful transplantation. Injection of homologous and heterologous blood after transplantation produced regressive changes and resorption of the tumors in 50 per cent of the animals bearing the Besredka sarcoma, in 66 per cent of the animals with the Ehrlich tumor, and in 37 per cent of the animals with the Flexner-Jobling carcinoma.

Injections of homologous and heterologous blood of animals and patients bearing spontaneous tumors increased the rate of growth of previously transplanted tumors.

M. Glasunow


By subjecting mice to a sudden low environmental temperature of -2° to -5° it has been found possible to reduce the body temperature below 20° for seven-hour periods on five successive days, or for a continuous twenty-four-hour period. Under these conditions a state resembling hibernation is produced. In the range of skin temperature 15-20°, the animals lose consciousness, respiration is diminished, the heart beat is reduced to about one-half the normal, and the blood sugar falls. If the environ-
mental temperature is lowered to 10–15° below room temperature (20°) for ten- to fifteen-day periods, no hibernation is produced.

No permanent effect on the growth of either a transplantable sarcoma (No. 180) or the spontaneous Marsh-Buffalo adenocarcinoma could be traced in mice subjected to these artificially induced conditions of hibernation. There was a temporary retardation in growth of the same order as that produced by caloric restriction.

[For clinical experience with hibernation in metastatic tumors, see abstract of a paper by Vaughn on p. 420].

A. F. WATSON

Effect of Methionine on Normal and Tumor Growth, H. P. MORRIS AND C. VOEGTLIN
J. Biol. Chem. 133: lxix, 1940.

Young normal mice and rats were maintained for periods of three and four weeks respectively on a methionine-deficient diet composed of arachin 15, starch 54.5, salts 4.5, Crisco 21.0, cod-liver oil 5.0, and growth vitamin concentrates. The animals were then divided into three groups. Group A was continued on the basal diet, Group B received in addition a supplement of 450 mg. of dl-methionine per 100 gm. of diet, while Group C received 362 mg. of l-cystine per 100 gm. of diet. Slow growth was obtained on the basal diet with both rats and mice. The cystine-supplemented basal diet induced slightly better growth than that obtained on the basal diet, while the methionine produced marked stimulation of growth in both rats and mice.

The average daily growth of spontaneous mammary tumors in the female C57 strain of mice maintained on the methionine-supplemented diet for three weeks was shown to be greater than the average daily growth of the tumors during a previous four-weeks period on the basal diet alone.

A. F. WATSON


By fractionation of broth culture filtrates of Bacillus prodigiosus, the substance which produces hemorrhage in mouse tumors, can be concentrated. By the method described previously (Shear and Andervont: Proc. Soc. Exper. Biol. and Med. 34: 323, 1936), a sixty times concentration by volume of the active substance has been effected.

Details are now given of a method for extracting the hemorrhage-producing substance from culture filtrates of the bacillus grown on a synthetic medium consisting of ammonium chloride, ammonium sulphate, potassium dihydrogen phosphate, sodium hydroxide, and glucose. These filtrates were treated with chloroform. The resulting emulsion contained practically all of the active material. After removal of the chloroform, an active water-soluble precipitate was obtained by treatment with alcohol. In this way a solution with a potency of 133,000 mouse tumour units per c.c. (compared with 330 units per c.c. of the original filtrate) and 26.4 mg. total solids per c.c. was obtained. The lethal dose of the various concentrates ranged from 100 to 1000 times the minimum effective dose. Neither in acid nor alkaline solutions was the active agent dialyzable through a cellophane membrane.

A. F. WATSON

Experimental Studies on Aniline Bladder Tumors, S. MORIGAMI AND I. NISIMURA. Gann 34: 146–147, 1940.

In view of the occurrence of bladder cancer among aniline workers, the authors attempted to produce the disease experimentally by o-toluidin and benzidine. Rabbits, guinea-pigs, and rats were used. A 1.0 per cent solution of o-toluidin in olive oil was injected subcutaneously six times a week in 0.1 c.c. doses. In other experiments o-toluidin and benzidine were dissolved in chloroform, in the ratio of 5 per cent, and the solutions were applied to the skin of the back every other day.

Bladder papilloma was produced in animals receiving injections of o-toluidin that survived over 100 days. Rabbits were especially resistant to the toxic action of the chemical and showed a high incidence of papilloma. Benzidine proved more toxic, but when animals withstood the treatment long enough this substance also produced atypical proliferation of bladder epithelium. Unfortunately, for the proper evaluation


Photo-oxides from a number of homologues of 1 : 2-benzanthracene have been prepared by passing a slow current of oxygen through a solution of the hydrocarbon in carbon disulphide exposed to the light from a 200-watt gas-filled lamp. The ability to form photo-oxides is widespread among anthracene derivatives but is not shown by any other group of polycyclic aromatic compounds. The relative stability of the photo-oxides is illustrated by the fact that 5 : 6 : 9 : 10-tetramethyl-1 : 2-benzanthracene photo-oxide, for instance, can be recovered unchanged after boiling for two hours in a solution of alcoholic potash.

These photo-oxides do not appear to be involved in the cellular changes which occur in the tissues under the influence of the carcinogenic hydrocarbons of the 1 : 2-benzanthracene group, since no tumors were produced by the injection into mice of suspensions in sesame oil of the pure photo-oxide of the highly carcinogenic 9 : 10-dimethyl-1 : 2 benzanthracene.

A. F. Watson


The details of the synthesis of a number of derivatives of 3 : 4 benzphenanthrene are given.

A. F. Watson


Syntheses of 6- and 22-methylcholanthrene and 6 : 20- and 6 : 22-dimethylcholanthrene are described. The new hydrocarbons are being tested for carcinogenic activity.

A. F. Watson


Briggs has succeeded in producing connective-tissue tumors of mixed-cell type in Rana pipiens tadpoles by means of methylcholanthrene-choleic acid. One hundred and fifty-four young tadpoles (20–30 mm. total length) were injected subcutaneously near the base of the tail or behind the ear with about 0.2 mg. of the carcinogenic agent either alone or in solution in lard. Ninety-four control tadpoles were injected with lard alone or with paraffin. All the surviving animals were autopsied from three to six months after the injections. None of the control tadpoles which retained the lard or paraffin showed any signs of tumor. Of the 154 experimental animals, only 12 retained the injected agent, and in 3 of these subcutaneous tumors had developed in tissue surrounding the carcinogen. In 2 animals, observed 95 and 158 days after injection respectively, the tumor remained localized, forming a firm, non-pigmented tissue mass. In the third case the induced tumor showed signs of malignancy, spreading subcutaneously and invading the body wall musculature and the posterior part of the lung. A photomicrograph of this tumor is shown.

The author draws attention to the recent work of Koch, Schreiber, and Schreiber, (Bull. de l'Assoc. franç. p. l'étude du cancer 28: 852, 1939), who have induced tumors in adults of Triton cristatis and Triton taeniatus by means of 1 : 2-benzpyrene and carcinogenic tar.

A. F. Watson


A special architecture of the colonies of fibroblastic sarcomatous cells during the in vitro cultivation of a tumor originally induced by 1 : 2 : 5 : 6 dibenzanthracene in
mice, is reported. When grown in Carrel flasks in hen plasma coagulum and fed with either heparin hen plasma or a mixture of hen serum, chick embryo juice, and Tyrode solution, in which the embryo juice concentration is kept low, the cells show a tendency to grow out in close association with one another, and to form ribbon-like strands or even broad sheets which resemble the epithelial type of growth in vitro. These ribbons frequently arborize, and their branches often join up with one another, forming loops and bridges enclosing the coagulum. The sheet-like growth is found especially at the interface coagulum-glass, whereas the cell ribbons occur also within the clot. These sarcomatous cells do not appreciably liquefy the hen plasma coagulum, although if the culture is supplied with embryo juice instead of the mixture described, the cells grow out in a more scattered way, forming long cell chains, each cell having a definite spindle shape.

It is suggested that the characteristic colony architecture described is related to the inability of the sarcomatous cells to liquefy the coagulum. The individual cell, unless aided by embryo juice enzymes, is unable to penetrate the coagulum to any extent but, when joined by fellow cells to form a ribbon or sheet, will do so at a relatively slow rate. Further details of the experiments are promised. A. F. WATSON


Experiments are recorded in which embryonic rat tissues, the leukocytes of rabbit blood, and the bone marrow of adult rats was treated *in vitro* with $1:2:5:6$-dibenzanthracene (6 experiments), methylcholanthrene (17 experiments), and $3:4$-benzpyrene (2 experiments).

$1:2:5:6$-Dibenzanthracene exerted only a slight toxic action; for even with concentrations of $1:1000$-$1:5000$ normal growth of the cultures occurred for more than a month.

Methylcholanthrene and $3:4$-benzpyrene were found to be very toxic. Only with low concentrations ($1:500,000$-$1:1,000,000$) was it possible to maintain the life of the cultures up to two or three months.

These carcinogenic substances did not exert, even in weak concentration and with prolonged treatment, any stimulating action upon the growth of the cultures, nor were any phenomena noted which would indicate a malignant transformation of the cells.

Subcutaneous inoculation into four rats of cultures treated with methylcholanthrene for one and a half to two months and then maintained from thirteen to thirty days in a normal medium gave a negative result. M. GLASUNOW


The intravenous injection of $3:4$-benzpyrene into the rat is followed by the elimination of fluorescent derivatives of the hydrocarbon in the urine and feces. The experiments recorded are an extension of those in which the author showed that $3:4$-benzpyrene was eliminated via the bile as a fluorescent derivative in the feces of the mouse (Biochem. J. 32: 271, 1938. Abst. in Am. J. Cancer 33: 129, 1938). The extraction and purification by chromatographic adsorption on aluminium oxide, of the fluorescent substance in rat feces are described. The pure substance is photolabile and soluble in sodium hydroxide with green-yellow fluorescence. Two diffuse fluorescence bands in the blue-violet region of the spectrum are shown by its alcoholic solution. A. F. WATSON

**Experimental Production of Skin and Lung Cancers in Mice by Painting with Quinones**, N. TAKIZAWA. Über die experimentelle Erzeugung der Haut- und Lungenkrebs bei der Maus durch Bepinselung mit Chinone, Gann 34: 158–160, 1940.


In view of the carcinogenic action of certain benzanthracene hydrocarbons and azo-compounds, the idea occurred to Asahina that quinones, which are produced by the oxidation and decomposition of these compounds with a benzene nucleus, might also produce cancer. Takizawa carried out animal experiments based on this idea.
Quinone, α-naphthoquinone, an equal mixture of quinone and α-naphthoquinone, anthraquinone, phenanthrenequinone, thymoquinone, chloroquinone, and β-naphthoquinone were used. These substances were dissolved in benzene and the solution, 0.1 or 0.25 per cent, was applied to the skin of the back of mice, the painting being repeated every day or every other day.

Papillomas were produced with quinone, with α-naphthoquinone, and with the mixture of the two, in about 15 or 20 per cent of the mice surviving over 200 days and in about a quarter or a third of the animals the papillomas progressed to epithelioma. Phenanthrenequinone produced papillomas in the same ratio as quinone and α-naphthoquinone, but none of the growths became malignant. A single example each of papilloma was produced by anthraquinone, thymoquinone, and chloroquinone.

Macroscopically, epilation and increased keratinization precede the development of papilloma, and in the case of α-naphthoquinone there may be severe epithelial necrosis. Single or multiple papillomas usually develop in about 200 days. In some animals the strong keratinization produces cutaneous horns; in others there is a gradual growth of the basal part of the tumor, with ulceration of the surface and finally infiltrative growth into the deeper tissue. Histologically the papilloma consists of proliferating squamous-cell epithelium, with but little proliferation of follicular epithelium. The growth of the epithelium is expansive, gradually invading the deeper tissue and producing degeneration of adjacent connective-tissue fibers. No metastasis was found in any of the cases, and none of the cancers was successfully transplanted.

In some of the mice, especially those with papillomas, lung cancer developed. These pulmonary tumors occurred most frequently in the quinone group, i.e. in 8 of 87 animals surviving over 200 days. The tumors had the morphology of adenocarcinoma in part, showing a tendency to grow infiltratively into the adjacent lung tissue and bronchial lumen. One of the lung cancers was successfully transplanted. W. Nakahara


After a historical survey of the subject of spontaneous lung tumors in mice, the authors report in detail their technical procedures. They found that pulmonary tumors induced in Strain A mice by the subcutaneous injection of carcinogenic hydrocarbons begin to appear as minute nodules in five to six weeks at the periphery of the lungs. As far as histologic examination goes, all these tumors seem to originate in the alveolar epithelium and not, as do human pulmonary cancers, in the bronchi. This may be due to the fact that the irritant producing the human carcinomas enters along the tracheobronchial tree, while in mice the carcinogenic substance is in the blood. Four plates show excellent photomicrographs of the lesion, and there is a bibliography of 30 references.

Reticulo-endotheliosis and Monocytic Leukemia due to Carcinogenic and Estrogenic Substances, T. Nonaka. Über Reticuloendotheliose und Monozytenleukämie nach der Darreichung der carcinogenen und der oestrogenen Substanzen, Gann 34: 148-149, 1940.

In rats receiving benzpyrene and "ovahormone" together sarcoma developed at the site of injection (uterus and subcutaneous tissue). Mice, under the same experimental conditions, died before the appearance of tumor. Reticulo-endotheliosis was found, however, in various organs, especially the liver, spleen, and kidney. The blood picture was that of monocytic leukemia. These changes occurred in 50 to 100 per cent of all the groups of mice used within a period of a month or less. W. Nakahara

On the Production of Cirrhotic Changes in the Liver by Furfural Feeding, W. Nakahara and K. Mori. Gann 34: 143-145, 1940.

Furfural (C₄H₄O·CHO) was mixed with rice in the proportion of 2.5 to 5 per cent and rats were allowed to feed on this mixture. Cirrhotic changes appeared in the liver regularly after 140 to 150 days. Localized cirrhotic changes developed in as little as 50 to 60 days. In typical cases the entire liver became cirrhotic, showing many
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hyperplastic and even adenomatous nodules. Microscopically there was a striking proliferation of fibrous connective tissue, generally showing the picture of annular cirrhosis. In the cirrhotic areas there was much proliferation of the so-called pseudo-bile-ducts. The results of four experiments involving 110 rats are tabulated. The investigation was still in progress at the time of the report. W. NAHARA


Full descriptions are given of preliminary experiments previously reported. Essentially the author's work is in the nature of confirmation and extension of that of Nishiyama, who discovered that repeated subcutaneous injections of concentrated solution of glucose engender sarcoma in rats. Takizawa confirmed this observation, using mice, and at the same time found that fructose and galactose injections also bring about sarcoma formation. Twenty-five per cent sugar solutions in distilled water were used, and doses of 0.75 c.c. were injected, either every day or every other day, into the same area of the subcutaneous tissue. In the glucose experiment 18 mice survived over 250 days and 5 of these developed sarcoma. With fructose, sarcoma was produced in 2 out of 16 mice surviving over 250 days, while galactose gave rise to sarcoma in 4 out of 13 mice surviving for an equal period. The sarcomas were all of the spindle-cell type, developing on the basis of a reactive fibrous connective-tissue proliferation. Many of the experimentally produced tumors proved to be transplantable.

In a control experiment with 0.9 per cent sodium chloride solution, only edematous swelling of subcutaneous tissue was produced, without marked connective-tissue increase.

Eighteen photographs, including 15 photomicrographs, illustrate the findings.

W. NAHARA

Experimental Production of Sarcoma in Rats by Injections of Concentrated Sodium Chloride Solution, Y. TOKORO. Über die artificielle Erzeugung des Sarkoms bei den weissen Ratten mittels konzentrierter Kochsalzlö sung, Gann 34: 149-155, 1940.

Solutions of sodium chloride, 5, 15, and 25 per cent, were repeatedly injected under the skin in a large series of rats. Sarcoma was produced in 2 out of 12 animals surviving 300 days, with 80 injections of the 15 per cent solution. In neither instance was metastasis observed, but the histologic character of the tumors was that of sarcoma, spindle-cell and polymorphous-cell. In the rats injected with 5 per cent and 25 per cent solutions the reaction was limited to fibrous hyperplasia and granulation tissue.

W. NAHARA

Production of Leukemia in the Albino Rat, S. ITO. Über die Entstehung der Leukämie bei Ratten, Gann 34: 133-137, 1940.

Methylene blue was administered to rats which had received o-amino-azotoluene in the diet for 250 days. In one of the rats so treated myeloid leukemia was demonstrated, with leukemic lesions in the liver, spleen, lymph nodes, bone marrow, kidney, and ovary. The author believed that the leukemia was experimentally produced, since he found no record of rat leukemia in the literature.

W. NAHARA

Effect of Liver Feeding on the Production of Malignant Tumors by Injections of Carcinogenic Substances, K. MORI AND W. NAHARA. Gann, 34: 48-59, 1940.

The authors previously reported that liver feeding inhibited the production of liver cancer by oral administration of the carcinogenic azo-compound, dimethylaminooazobenzol (Nakahara, Mori, and Fujiwara: Gann 33: 406, 1939). It is now demonstrated that liver feeding inhibits, also, the progress of tissue changes leading to the production of hepatic cancer following repeated intraperitoneal injections of dimethyl-
aminoazobenzol. On the other hand, no inhibiting effect was exerted upon carcinogenesis in tissues other than the liver in rats receiving subcutaneous injections of methylcholanthrene or in mice injected intraperitoneally with 3:4-benzpyrene. These results more or less agree with those of previous workers on the production of skin cancer in mice by coal tar painting, and indicate that the cancer-inhibiting action of liver feeding may be limited to the liver and not extend to carcinogenesis in other organs and tissues.

W. NAKAHARA


Having previously investigated the effect of ovariectomy on hepatoma production by o-amino-azotoluene (Gann 33: 446, 1939), the author has now studied the possible influence of prolan. Four groups of female rats were fed with o-amino-azotoluene so as to produce liver cancer. Two of the groups were castrated and of these one received injections of prolan; a third group was not castrated but was given prolan, while a fourth group was untreated. The highest incidence of liver cancer was in the castrated group which received no prolan (6 out of 7 rats which survived 365 days); the lowest in the groups receiving prolan injections (1 out of 7 rats in both the castrated and non-castrated group). Cancer appeared in 2 of the 7 untreated controls. From these results the author concludes that prolan has an inhibiting effect on the production of liver cancer by o-amino-azotoluene. In view, however, of the great variation among rats in their reaction to this chemical, the experiment should be repeated with a larger number of animals.

W. NAKAHARA


Repeated intravenous injections into rats of acacia solution produced remarkable changes in the liver, hitherto undescribed. The liver cells became transparent and showed no fat, glycogen, or starch. There was no sign of fibrous cirrhotic change around the masses of degenerative cells but nodular hyperplasia of the liver cells occurred, indicating a compensatory regeneration. The regenerated cells in their turn eventually underwent degenerative changes and regeneration again followed. Taking advantage of this method of inducing continued liver-cell regeneration, the author attempted to study the relation between regeneration and cancer production.

One hundred and sixty rats were fed with butter-yellow, and 103 of these received intravenous injections of 15 per cent acacia solution every week. Only 5 rats from each group survived as long as eighteen weeks. Liver cancer was found in 2 of those receiving acacia and in 3 of the control group. It is concluded that the increased cell regeneration did not affect carcinogenesis by butter-yellow feeding.

W. NAKAHARA

The Histology of the Rat's Liver during the Course of Carcinogenesis by Butter-Yellow (p-Dimethylaminoazobenzene), J. W. O'RR. J. Path. & Bact. 50: 393–408, 1940.

The primary effect of butter-yellow on the liver parenchyma was destructive, and the proliferative changes to be regenerative.

Wm. H. WogLOm


Histologic studies were made of spleen, bone marrow, and lymph nodes of rats so fed with butter-yellow as to produce liver cancer. The chief changes found were proliferation of myeloid tissue in the spleen and bone marrow, reduction of erythroblasts in the bone marrow, and proliferation of reticulum cells in the lymph nodes.

W. NAKAHARA

When rats receiving butter-yellow were also given anthranilic acid (a metabolic product of tryptophan generated in the liver) at the rate of 0.5 mg. per day, growth disturbances and mortality were reduced but no effect on the rate of liver cancer production was observed. W. Nakahara

Changes in the Liver of the Rat Caused by 4-Dimethylaminobenzene-1-azo-1-naphthalene, 4-Dimethylaminobenzene-1-azo-2-naphthalene, etc., R. Kinosita. Gann 34: 165–167, 1940.

Of the two derivatives of butter-yellow mentioned in the title, 4-dimethylaminobenzene-1-azo-1 naphthalene produced cancerous changes in the liver when fed to rats according to Kinosita’s standard method for butter-yellow; 4-dimethylaminoazo-benzene-1-azo-2-naphthalene, on the contrary, produced only a peculiar form of hepatic degeneration. W. Nakahara


A study of fine cytoplasmic structure of the cells of hepatoma produced by feeding rats with dimethylaminoazobenzene was made by means of the gelatin-silver impregnation method. Hepatoma tissue and normal fibroblasts were cultivated in vitro under identical conditions, and silver preparations were made after cultivation for twenty-four to seventy-two hours. The fibrillar structures of fibroblasts were as a rule thick and long and few in number, while those of hepatoma cells were fine and short, and rather profuse. In the cells which appeared to have lost their proliferative capacity the fibrillar structure was reduced to a granular form. W. Nakahara

Feeding Experiments with 4’-Amino-2 : 3’-dimethylazoxybenzene on Albino Rats, N. Nagao. Über die Fütterungsversuche mit 4’-Amino-2 : 3’-dimethylazoxybenzol bei weissen Ratten, Gann 34: 13–20, 1940.

4’-Amino-2 : 3’-dimethylazoxybenzene when fed to rats caused slight liver-cell hyperplasia and moderate proliferation of bile-duct epithelium, but did not produce liver cancer. This would indicate that the carcinogenic activity of o-aminazotoluene is lost when an oxygen molecule is introduced in the azo-position. The paper is illustrated with ten figures. W. Nakahara

Experimental Hepatoma Production in Rats by Feeding with N · N’-Oxalyl-o-aminazo-toluolene, N. Nagao. Gann 34: 161, 1940.

N · N’-oxalyl-o-aminazo-toluol, a derivative of the well known hepatoma-producing azo-compound, o-aminazo-toluolene, also induces hepatoma when fed to rats, with associated cirrhotic changes. W. Nakahara

Feeding Experiments on Rats with 4’-Methyl-4-N-dimethylaminoazobenzene and Other Azo Compounds, N. Nagao. Über die Fütterungsversuch mit 4’-Methyl-N-dimethylaminoazobenzol und anderen Azo-verbindingen bei weissen Ratten, Gann 34: 161–164, 1940.

Three derivatives of butter-yellow or dimethylaminoazobenzene, demonstrated by Kinosita to be highly carcinogenic to the liver, were fed to rats. Of these, 4’-methyl-4-N-dimethylaminoazobenzene alone retained the liver-cancer producing action of butter-yellow, although this action was not strong. The two other derivatives tested, which proved to be non-carcinogenic, were 2 : 4’-dimethyl-4-dimethylaminoazobenzene and 3 : 4’-dimethyl-4-N-dimethylaminoazobenzene. W. Nakahara

Since copper stands in important relation to the metabolism of the liver, and especially since it is said to play a rôle in the development of hepatic cirrhosis, the authors attempted to determine its possible influence on the production of liver cancer. Rats receiving α-amino-azotoluene and dimethylaminoazobenzene were given, also, copper sulphate, added to the food in amounts of 1, 3, 10, and 30 gamma. Doses of 1 to 3 gamma appeared to increase somewhat the incidence of cancer, but doses of 10 to 30 gamma produced liver necrosis.

W. Nakahara

Quantitative Changes of Thymo-nucleic Acid in the Course of Carcinogenesis, T. Masayama and T. Yokoyama. Verhalten des Gehaltes an Thymonukleinsäure beim Verlauf der Krebsentstehung. Gann 34: 174-175, 1940.

Having devised a method for the quantitative determination of thymo-nucleic acid, the authors investigated the changes in the amount present in the liver of rats under treatment with butter-yellow. The results showed that the amount of thymo-nucleic acid is doubled after thirty days of butter-yellow feeding, and that there is a sudden further increase as cancer develops.

W. Nakahara


A comparison was made of the phosphatase activities of liver cancer induced in the rat by butter-yellow and normal rat liver. β-glycerophosphoric acid and thymo-nucleic acid were used as substrates. It was found that the phosphatase activity of normal liver is strongest in acid media but that of liver cancer is most pronounced in alkaline media. It was also found that the reactivating action of magnesium is stronger on the alkaline side, that the inhibiting effect of sodium fluoride is more markedly manifested on the acid side, and that the enzyme is more stable in alkaline than in acid media. From these results the authors suggest that in vivo the enzyme has its optimum activity point on the acid side. The enzyme with its optimum point on the alkaline side was regarded as a "reverse" form. In liver cancer, according to the authors' interpretation, the unstable and active form of the enzyme is decreased in amount and the stable and inactive form persists.

W. Nakahara


It was previously shown by the authors (Gann 33: 332, 1939) that the cholesterol crystals isolated from a transplantable rat hepatoma contained provitamin D in a high concentration, i.e. about 7 per cent. In the present investigation cholesterol crystals were isolated from hepatoma nodules produced in rats by feeding with dimethylaminoazobenzene for 150 days, from the liver from which the hepatoma nodules had been removed, and from cirrhotic livers in which hepatoma had not yet developed as a result of dimethylaminoazobenzene feeding. For further comparison, cholesterol crystals were isolated also, from the necrotic tissue separated from the transplantable hepatoma previously used. All the cholesterol crystals were recrystallized from alcohol before determining their properties.

Spectrographically it was found that the hepatomas produced by feeding with dimethylaminoazobenzene do not contain provitamin D, thus differing fundamentally from the strain of transplantable hepatoma which the authors previously studied. This latter tumor contains provitamin D in a high concentration not only in actively growing areas but even in the necrotic parts. As in normal liver, provitamin D was absent from the non-cancerous areas of the livers examined and from the precancerous cirrhotic lesions.

Four spectrograms illustrate the paper.

W. Nakahara

Cholesterol crystals were isolated from transplanted rat hepatoma and normal rat liver and their properties were compared. Cholesterol from hepatoma tissue had a much higher iodine value than was theoretically expected, and also showed strongly positive Rosenheim and Tortelli-Jaffé color reactions. Spectrographic examination, demonstrated the five characteristic absorption bands corresponding to those of ergosterol or 7-dehydrocholesterol, i.e., provitamin D. From the intensity of the absorption bands it was estimated that about a fifth of the hepatoma cholesterol is made up of provitamin D. Cholesterol crystals isolated from normal rat liver were typical of pure cholesterol in every respect.

Studies on glutamic acid were carried out according to the method of Kogl, but the material used was the tissue residue from which the cholesterol fraction had been extracted with an organic solvent. The analytical values of glutamic acid isolated from hepatoma and from normal liver agreed well with the theoretical values, but the optical rotation was \( [\alpha]_D = + 31.1^\circ \) for normal liver glutamic acid, and +27.0° for hepatoma glutamic acid, showing that the latter contains 7.4 per cent of racemic or d(-)form. The authors believe that Kogl's work on the occurrence of d(-)form in cancer tissue is substantiated. [See, however, Absts. in Am. J. Cancer 39: 120, 266, 1940.— Ed.]

W. NAKAHARA


Evidence is submitted in this letter to the Journal of Biological Chemistry to show that the presence of d(-)-glutamic acid in hydrolysates of normal and cancerous tissues (see Kogl and Erxleben: Ztschr. f. physiol. Chem. 258: 57, 1939. Abst. in Am. J. Cancer 38: 116, 1940) is due to the racemization which takes place during the hydrochloric acid hydrolysis. Details are promised in a future paper. A. F. WATSON


The author found only a very small amount of d(-) glutamic acid in tumor tissue, not much more than was found in some normal tissues.


The authors previously made quantitative determinations of aneurin in liver cancer by means of the thiochrome and bradycardia methods and from the results assumed that the amount of co-carboxylase may be reduced. This assumption has now been verified by the direct determination of co-carboxylase. The co-carboxylase content of liver and muscle was also found to be reduced in tumor rats. W. NAKAHARA


The autolytic cathepsin of chicken sarcoma (the Fujinami strain of transplantable sarcoma) shows itself most active at pH 4.6; sarcomatous tissue removed one week after transplantation seems to have somewhat less activity than slightly older grafts. The autolytic activity is increased by the addition of cystein.

Similarly in thirty-day grafts of a transplanted rabbit sarcoma the cathepsin activity is found to be at its optimum at pH 4.6. The grade of activity is not greatly different from that of liver tissue. Younger grafts as, for example, fifteen days after transplantation, seem to be less active.

In grade of cathepsin activity, the tissues tested arrange themselves in the following order: liver, kidney, spleen, sarcoma, and muscle. The activity of spleen and of sarcoma is of about the same magnitude. In general, the autolysis of muscle is of the lowest
grade. The autolysis of rabbit sarcoma is activated by the addition of cystein but
the activation is not as marked as in the case of liver autolysis.

A comparison of the cathepsin activities of various organs (liver, kidney, spleen, and
muscle) between sarcoma-bearing and normal chickens and rabbits disclosed no per-
ceptible differences.

W. NAKAHARA

Rate of Turnover of the Lecithins and Cephalins of Rat Carcinosarcoma 256 as Measured

Rats bearing carcinosarcoma 256 were killed from four hours to twenty-six days
after receiving by stomach tube a solution of disodium hydrogen phosphate containing
radioactive phosphorus. Tumor phospholipids were isolated and the lecithin and
cephalin fractions separated by means of absolute alcohol. Up to thirty hours after
feeding, the radioactivity, expressed as percentage of dose per gram of phospholipid,
was significantly greater in the lecithin fraction than in the cephalin fraction. The
activities then became about the same and decreased at approximately the same rate.
The phospholipids of carcinoma 256 appear to resemble those of liver rather than those
of muscle.

A. F. WATSON

Cancer Cell and Growth-regulating System of the Body, L. DOLJANSKI AND R. S.
HOFFMAN. Nature 145: 857, 1940.

Fifteen years ago Cohn and Murray (J. Exper. Med. 42: 275, 1925) showed that the
period between the time that a fragment of embryonic tissue is removed and explanted
in vitro and the first appearance of new cells varies with the age of the embryo, the
latent period becoming progressively longer with the development of the embryo.
Doljanski and his colleagues have previously confirmed these early findings and in the
present communication they have extended their investigations to explants of tumor
tissue. Two tumors were used, one the Rous chicken sarcoma and the other a benz-
pyrene rat sarcoma. All explanted fragments of these tumors commenced to proliferate
in vitro following a latent period which was very much shorter than that of normal
adult tissue. Whereas in the latter, the latent period ranged from eighteen to twenty-
hours, in neoplastic tissue it never exceeded eight hours. In about half the
experiments, the first cells appeared on the margin of the tumor fragments in forty
to fifty minutes, i.e. practically without a latent period. This reduced latent period
placed tumor tissue, the authors contend, in a unique position compared with normal
adult and embryonic tissue, since even tissue from six- to seven-day-old embryos has
a latent period between one and a half and four hours. They find in their results
experimental proof for Cramer's conception that "what distinguishes a malignant cell
from a normal cell is its freedom from control by the organism to which the normal cell

A. F. WATSON

Specificity of Proteolytic Enzymes from Normal and Tumor Tissues, J. S. FRUTON.
J. Biol. Chem. 133: xxxiv, 1940.

The enzymatic action of extracts of tumors on synthetic peptides and peptide
derivatives is usually less than that observed with normal tissue extracts. Extracts
of the Brown-Pearce carcinoma of the rabbit, the Bashford mouse carcinoma, mouse
sarcoma 180, a human bone sarcoma, and human breast and thyroid carcinomas were
used and their action compared with that of extracts of beef spleen and beef and swine
kidney. In the case of two tumor extracts it was found that peptide linkages involving
d-amino acids (e.g. carbobenzyloxy-d-glutamyl-l tyrosine or d-leucineamide) were
hydrolyzed at rates similar to those for the corresponding l forms. Extracts of the
normal tissues as well as the other tumors hydrolyzed the l form of these substrates
more rapidly than the corresponding d forms.

A. F. WATSON

Inhibition of the Succinoxidase System of Extracts of Tumour and Normal Tissues,
K. A. C. ELLIOTT. Biochem. J. 34: 1134, 1940.

The very low "succinoxidase " activity of certain tumor tissues has previously been
demonstrated by the author and his colleagues (Biochem. J. 29: 1937, 1935 and 32:
1407, 1938). Having studied the possibility that this low activity might be due to the presence in the tumors of an inhibitor of the system, as well as to deficiency of the enzymes and carriers responsible for succinate oxidation, he reaches the following conclusions:

"(1) The aerobic oxidation of succinate with liver suspensions is strongly inhibited by suspensions or extracts of various tissues, especially of certain tumors, pancreas and spleen. The inhibitor is non-dialysable and, to some extent at least, thermostable. Commercial trypsin in small amounts is also inhibitory.

"(2) The succinic dehydrogenase (anaerobic reduction of methylene blue with succinate) and the cytochrome oxidase (oxidation of p-phenylenediamine in the presence of added cytochrome e) are both inhibited by tumor extracts, but not strongly enough to account for the main effect of the inhibitor on the complete succinoxidase system of liver. Cytochrome c appears not to be affected. It is concluded that the inhibitor acts particularly strongly on some other component of the succinoxidase system of liver, possibly cytochrome b.

"(3) Kidney suspensions are affected similarly to liver suspensions. The succinoxidase activities of brain and muscle suspensions are also inhibited. But the succinoxidase activity of heart suspensions is scarcely at all affected and tumor extracts actually provoke an acceleration of succinate oxidation with heart suspension in the presence of added cytochrome c. The oxidation of p-phenylenediamine with heart is considerably inhibited by tumor extract in the absence of added cytochrome c, but not in its presence."  

A. F. WATSON


The authors previously showed that the time of the first cleavage in the eggs of the sea-urchin is delayed when they are inseminated immediately after irradiation with roentgen, gamma, or beta rays (delay phenomenon), but that the delay is less when an interval is allowed to elapse between irradiation and insemination (recovery phenomenon) (Gann 33: 1, 117, 316, 323, 1939). The present paper describes later investigations, in which the delay was found to be due to the prolongation of a certain phase rather than all the phases of mitosis. Cytologic studies of irradiated eggs were made for this purpose.

The mitotic cycle of the first cleavage was divided into eight phases, according to Fry's method: (1) nuclei not touching; (2) nuclei touching; (3) nuclei fused, early; (4) nuclei fused, late (nuclear streak); (5) prophase; (6) metaphase; (7) anaphase; (8) telophase. The percentage of eggs coming under each of these phases was calculated for each period of time after insemination, ten to one hundred minutes. In this way it was discovered that the delay in cleavage following roentgen irradiation occurred essentially in the nuclear streak phase and prophase. In view of the previous finding that the radiological susceptibility of fertilized eggs is highest in the phase of nuclear streak, the authors suggest that this particular mitotic phase is of special importance in the injury of living cells by irradiation.

W. NAKAHARA

Histo-pathological Studies on Endemic Vesical Tumor in Formosan Yellow Cattle (Bos zebu indicus), I. WAKE AND J. GOTO. Gann 34: 127-132, 1940.

Spontaneous bladder tumors are sometimes found among cattle, horses, pigs, sheep, etc., but in no case has so high an incidence been recorded as occurs among the yellow cattle in certain districts in Shinciku province, Formosa, where the disease is associated with an endemic hematuria.

The frequency of bladder tumors is extremely high, amounting to 50 to 80 per cent in a given group of animals. The tumors occur in the female about twice as frequently as in the male. The predominant involvement of the trigone agrees well with the localization of bladder cancer in man and suggests a certain local predisposition. Histologic studies, based on 161 cases, indicate that the initial changes may be edema, hemorrhage, thickening, or polyp formation in the mucosa; these changes, character-
istic of chronic hemorrhagic cystitis, eventually lead to the formation of carcinoma, sarcoma, or carcinosarcoma. The authors suspect that certain geographical conditions prevailing in Shinchiku province may be responsible for the endemic occurrence of the tumor.

W. Nakahara


Economy in time and material can be effected by the use of desiccated chick embryo in tissue culture technic. Since November 1939 a variety of cultures of normal and malignant tissues have been maintained on fowl plasma clot to which the dried chick embryo dissolved in water has been added. The following tissues have been grown progressively in this way: (1) normal 17-day chick embryo heart muscle for four weeks; (2) normal 18-day chick embryo fibroblasts for four weeks; (3) Jensen rat sarcoma for five weeks, after which re-inoculated cultures grew in rats; (4) fowl-grown Fujinami filtrable sarcoma for four to six weeks, after which re-inoculated cultures grew in fowls; (5) GRCH/15 non-filtrable sarcoma for four to six weeks, after which re-inoculated cultures grew in some fowls.

A. F. Watson

GENERAL CLINICAL OBSERVATIONS


Mention has been made of the fact that the relationship of a person carrying a cancer is closer than the relationship of a mother to the fetus because of the presence in the fetus of protein elements derived from the father. This is the reason why the fetus produces certain reactions which tumors do not, for while it is possible that traces of the so-called proclams may follow the appearance of a tumor in the body, demonstration of this fact has not yet been had, with the exception of the various teratoid neoplasms, and in the presence of pregnancy. That the male does contribute protein substances which give rise to immune reactions in the mother is demonstrated by transfusion accidents which have occurred during the course of pregnancy where the husband donor belonged to the same blood group. A study of the bloods has shown that the phenomenon may be attributed to an agglutinin resulting from the immunization of the mother by the factors in the fetus inherited from the father, and not only have general reactions been noted in connection with this possibility, but a certain number of cases of erythroblastosis have been seen in infants and atypical agglutinins have been found in the blood. The concept of an antigen-antibody reaction as a basis for the etiology of erythroblastosis foetalis is not new, but the demonstration of atypical agglutinins is. The interesting fact has also been shown that after transfusion with the father's blood the agglutinins disappear owing to adsorption, and reappear only some days after the donor's blood has disappeared from the circulation.


Observations on the staining qualities of normal and malignant cells with rongalite white are recorded. Normal cells of animal and human origin are electively stained with this dye, in contrast to its failure to stain cells of the Flexner-Jobling rat tumor, a rat sarcoma, and the Ehrlich mouse adenocarcinoma. Of 64 human malignant tumors, 59 remained unstained. Cells of 10 of 13 benign tumors, however showed an affinity for the dye.

The negative staining quality of malignant cells is believed by the author to depend upon the absence of specific ferments. It is suggested that the rongalite white reaction,
ABSTRACTS

in combination with the method of MacCarthy (abnormality of the nucleus-nucleolus ratio), may be utilized in the differential diagnosis of malignant cells. M. GLASUNOW


By cauterizing the hypophysis of the common salamander (Hynobius lilhenatus Boulenger) of Hokkaido, Japan, the writers succeeded in producing an albino salamander in which they tried out the so-called "pituitary-melanophore reaction" of Allen, Swingle, Hogben and Winton. The melanophore dilated as soon as a small quantity of activating substance was injected, and the skin turned black, the change being easily observed against the pale yellow color of the animal. When urine from cancer patients was injected—0.2–0.3 c.c. subcutaneously in the back—a positive reaction usually followed, though a negative result was obtained in a small percentage of cases. Exceptionally some non-cancerous urines also gave a positive reaction. The writers believe that improvement of the technic may render this reaction useful in the diagnosis of cancer.

W. NAKAHARA


Four patients with metastatic carcinoma from the breast, one from the cervix, and one from the sigmoid, were exposed to hibernation, the lowest temperature attained being 83.2° F. by rectum. Two patients with primary carcinoma of the breast obtained marked relief of pain for two and three months, respectively, though the tumors progressed steadily. The others died shortly after the hibernation. The author's opinion is that the procedure is hazardous and unjustifiable in the treatment of hopeless metastatic carcinoma.

Cancer and Inflammation, J. M. NEIMAN. Arch. biol. sc. (Russ.) 54 (No. 3): 82-85, 1939.

The author suggests the use of granulation tissue extract for the treatment of tumors since some clinical observations, as well as experiments with transplantable tumors, show an inhibiting action of the inflammatory process upon the development of metastases and recurrences.


Relations between surgery and radiotherapy from the point of view of their respective representatives and the indications in certain malignant tumors are briefly discussed in both these papers. Schinz stresses again the need of radiotherapeutic clinics with beds. His article is illustrated with 23 pictures and 17 interesting statistical tables.

F. BURGHEIM


The determination of differences in the biological effects of radiation due to the rate of giving have been mostly carried out on human beings. Obviously the clinical results obtained in this fashion depend upon the sensitivity of the skin, if that is used as an indicator, or upon the disappearance of a tumor, and as tumors vary somewhat in their sensitivity it is evident that the indicator has a fluctuating value. It would be preferable if tumors could be treated in animals, but it is difficult to give these protracted doses in the small rodents which are ordinarily used and it is only in them that there exist homozygous strains which permit the elimination of resistance to inoculation.
The authors chose therefore to observe the effects on rabbits' ears of varying doses given at different rates. The right ear was irradiated with 400 r given in twenty minutes every other day, the left ear received 400 r in eighty minutes every other day, the rate of intensity being obviously 4:1. Nine rabbits were used, the ears of three of which received 4000 r, three 6000 r, and three, 8000 r. All the animals survived a satisfactory period.

The writers noted three stages in the reactions. The first occurs in the first months, with an erythema, then repair with wrinkling, scaling, and epilation. The second is from the third to the sixth month, with a new growth of hair, atrophy of the follicles, and disappearance of the skin pigment. The third stage occurs after six months, with hyperkeratosis, papillomatosis, and encrustation, followed by edema, cyanosis, and necrosis accompanied by mummification of the most severely damaged ears. A primary erythema usually appeared in one to two weeks, but the difference between the right and left ears was so small that no conclusions could be reached. Scaling was slightly less on the ears which were rayed at the lower rate. Epilation required 4000 r. It was most marked on the ear which had received radiation at 20 r per minute. The hair growth was less also on the ears which received 20 r per minute. Atrophy of the skin was always more marked on the side of rapid irradiation. Hyperkeratosis was rare in the ears rayed at the low rate. Necrosis due to endarteritis was less on the ears treated at a slow rate. The experiments may thus be summed up as giving good evidence that less permanent injury is inflicted on the tissues by radiating at 5 r per minute than at 20.


The paper is a short survey with two illustrations of the 60-inch cyclotron at the University of California. Among other matters of interest medically, is the fact that many patients with chronic leukemia are being treated by sodium phosphate containing the radioactive form of phosphorus, with frequent remissions of the disease. Patients suffering from cancer are now being treated regularly with neutrons from the new 60-inch medical cyclotron. Kruger has shown that mouse cancers placed in non-toxic concentrations of boric acid and irradiated with slow neutrons are killed with doses of irradiation which are harmless to tissues not in contact with the boron. When irradiated, the slow neutron is captured by the boron nucleus and the combination emits two heavy ionizing particles in opposite directions, an alpha particle and a lithium nucleus, which traverse a distance of about 7 microns in tissue and thus approximate an explosion within the cell. If the boron could be concentrated in a larger percentage of the tumor than in the healthy tissues, this discovery might be of practical interest.

A. F. Watson

THE SKIN


Ultraviolet light is quite as unnecessary for the production of experimental tar cancer as tar is for the production of ultraviolet light cancer. In the human subject, however, there is danger that in certain trades the activity of one may reinforce that of the other.

The article is appropriately illustrated and closes with a bibliography.

W. H. Woglom


A cancer of the leg caused by repeated burns of long standing is reported. The tumor was removed with the electric cautery, and the patient made an uneventful recovery. Microscopically the tumor was found to be a keratinizing squamous-cell cancer.

W. Nakahara
THE UPPER RESPIRATORY TRACT

Case of Reticulosarcoma of the Pharynx, S. Hanafusa and K. Kubota. Über einen Fall von Reticulosarkom des Rachens, Gann 34: 231-238, 1940.

A forty-three-year-old man had a primary tumor in the lymphadenoid tissue behind the wall of the right side of the pharynx. It was a relatively localized reticulosarcoma, with metastases limited to some of the lymph nodes of the neck and the kidneys. The histology of the tumor is described in detail, and photomicrographs are reproduced.

W. Nakahara

THORACIC TUMORS


A good deal of interest is being evinced at present in the study of tumors occurring in childhood. It has been traditional that they are extremely rare, but as material accumulates, it is found that quite a number of tumors ordinarily present only in adults may be seen in young children.

The authors' patient was a boy of eleven, with fever, pain in the right lower chest, and a non-productive cough of several weeks' duration. The pain and cough persisted, though the fever subsided. X-ray examination shortly after the fever had disappeared showed an opacity in the right superior mediastinum, about 4 cm. in diameter. Bronchoscopy showed occlusion of the right primary bronchus by a mass about 2 cm. below the carina. Microscopic study of a biopsy fragment revealed papillary adenocarcinoma. The administration of some 2700 r units of x-ray in the course of the next few months did not relieve the symptoms. Seven months after the diagnosis was made, therefore, a 100 mg. radium pack was applied to the right upper chest anteriorly and posteriorly and to the right axilla, for a total of 10,800 mg. hours. The boy was relatively well for the next eight months, his weight increased from 75 to 115 pounds, and he attended school and participated in athletic activities.

About two years after the diagnosis was made, the patient began to have occasional cough and blood-streaked sputum, and was given 720 mg. hours of radium over the same fields mentioned above, and about three months later another dose of the same amount. Seven years after the diagnosis had been made, he died. It had been noticed that he was growing rapidly and at death the body weighed 190 pounds and was 6 ft. 4 in. long. At autopsy, a pituitary adenoma of the anterior lobe was found, measuring some 2 cm. in diameter, which explains the excessive growth. Carcinoma was found in the lung, the lymph nodes, the kidneys, meninges, and the myocardium.

The authors believe that the heavy dosage with radium, totalling 25,200 mg. hours of therapy, gave more relief than they have usually noticed from treatment with roentgen rays. This is probably due to the great prolongation of the dose which results from a 100 mg. radium pack. The rate from the pack was presumably not over 4 to 5 r per minute.

THE DIGESTIVE TRACT


The author reports the extraction of estrogenic substances from six stomach cancers and from the stomach tissue of 4 of 13 non-cancerous patients. No tumors were observed in rats injected twice monthly for five months with the extracted estrogens.

M. Glasunow

THE FEMALE GENITAL TRACT


On the basis of 114 cases of carcinoma of the body and cervix of the uterus treated either surgically or by radiation, it is concluded that, other conditions being equal,
the mature types of carcinoma have a better prognosis when treated surgically, and the immature types when irradiated.

M. GLASUNOW


This is a cytologic study of uterine cancer based on 15 surgical specimens. The opinion is expressed that the large cells with large clear nuclei and small nucleoli are the true malignant elements. Photomicrographs illustrate this report. W. NAKAHARA


The authors report three cases of growth of glands resembling those of the cervix in the vaginal wall. In one case the squamous epithelium over these glands was healthy; in the other two there had been some ulceration of the vaginal mucous membrane. Such glands are not normal constituents of the vaginal wall, but probably arise from the müllerian epithelium which takes part in the formation of the vaginal epithelium. Hence these glands are not congenital abnormalities. A few cases of carcinoma have been described as arising presumably in such structures. Four excellent photomicrographs show the details of the lesion, which because of its rarity and the infrequency with which it becomes malignant may be regarded merely as a pathological curiosity. A bibliography of 46 references is appended to the paper.

**THE GENITO-URINARY TRACT**


Primary epithelioma of the ureter is a rather rare disease, not more than 200 cases being recorded. The predominant symptoms are hematuria and pain. Occasionally a palpable hydronephrosis has called the patient's attention to the lesion. The ureteral neoplasm itself rarely produces a palpable tumor. Backache is frequent. The diagnosis is best made by cystoscopic examination and roentgenography. The only effective treatment is complete extirpation of kidney, ureter, and uretero-vesical segment of the bladder, this last because of the tendency of the tumor to extend through the wall of the ureter to adjacent structures. All the peri-ureteral adipose tissue should be removed with the ureter. Only a few patients have remained cured, apparently about 5 per cent of the 200 recorded. Radiation therapy is useful for its palliative effect but has produced no cures nor has postoperative irradiation prevented the death of the patient in case the growth has not been entirely removed. The paper is well illustrated by good roentgenograms and contains a short bibliography.

**THE BONES**

**Solitary Granuloma of Bone Simulating Primary Neoplasm**, SADAO OTANI AND JOSEPH C. EHRLICH. Am. J. Path. 16: 479-491, 1940.

This is a report on a series of granulomatous lesions seen in three children and one adult thirty-five years of age. The ribs were involved in three patients, and the scapula in the fourth. The x-ray picture is that of a bone tumor, and the growth may form a fusiform swelling on the rib or be discovered solely because of localized pain. Two of the patients had a moderate elevation of temperature. The lesion is a granuloma. Bacteria are not present, and plasma cells are infrequently found. Giant cells may or may not be present. Some lipophages may be seen, but the fat is not double-refractile, so that it is probable that the lesion is not related to the Hand-Schüller-Christian disease.
The histology is not very characteristic. The lesion may be composed mostly of histiocytes and therefore resembles a reticulum-cell sarcoma to a certain degree. Other examples are purely granulomatous, with fibroblasts and eosinophiles. Some new formation of bone may occur. Silver stains were apparently not used. The treatment is surgical, and the authors' patients were all cured. Trauma seems to be the inciting agent.

Schairer (Centralbl. f. allg. Path. u. path. Anat. 71: 113–117, 1938) has reported two similar examples, in the skull, under the title "Osteomyelitis with Eosinophile Reaction." The authors did not find any other record of exactly the same lesion.

THE NERVOUS SYSTEM


A 33-page paper discussing intracranial tumors from the neuro-surgeon’s point of view. A statistical presentation of 1493 cases is followed by remarks on pathology, diagnosis, and surgical treatment. The paper reflects the generally known facts. Edwin M. Deery


An interesting discussion of the anatomical and clinical aspects of intracranial new growths, reflecting the generally known facts. The paper is sixty pages in length and includes numerous illustrations and a good bibliography. Edwin M. Deery


A detailed presentation, from the histopathologic point of view, of tumors arising from the neuroepithelium. Of a series of some 560 tumors involving the central nervous system studied by the writer, more than half [305] are considered to be of neuro-epithelial origin. The presentation includes some 48 illustrations. Edwin M. Deery


Investigations into the families of 30 patients having verified intracranial tumors revealed only one case in which there was a familial history of brain tumor. A high percentage of various other types of neoplasms was shown in this series, however, and the writer concludes that a tendency to tumor formation in general is hereditary. Edwin M. Deery


In an anatomical study the writers found various alterations in cerebral circulation in the presence of intracranial tumors. Besides increased vascularity about the neoplasm itself, other more remote circulatory changes occur within the brain. Edwin M. Deery


A statistical presentation of a series of 121 intracranial neoplasms in patients under twenty years of age. The various types of tumors found, their frequency, and location correspond with the well known facts. Edwin M. Deery

A statistical review of 128 operated and verified intracranial tumors. Types of tumors, location, and operability are shown and the generally known facts are reflected. There is a short bibliography.

Edwin M. Deery


This is a clinico-pathological presentation of two unusual cases. In each the brain tissue showed both inflammatory and neoplastic conditions. The histopathologic findings are described and illustrated. No definite diagnosis is made in either case.

Edwin M. Deery


A right-handed boy was found to have extensive involvement of the left occipital lobe by tumor. Removal of the lobe was followed by decided improvement in ability to read, write, and draw, and in many other faculties. The writers believe these functions had probably been taken over by the right cerebral hemisphere.

Edwin M. Deery

RETIWULM-CELL SARCOMA


This paper contains a description of 21 cases of reticulum-cell sarcoma. The clinical course in 8 cases was benign. Of this group, 5 patients had tumors in the nasopharyngeal region, 2 in the cervical, and 1 in the axillary lymph nodes. The growths were either localized or associated with regional metastases and responded well to surgical measures, irradiation, or combined therapy. Recurrences developed in 2 cases and these were likewise amenable to treatment. The symptom-free period varied from six to twenty-seven months.

Thirteen patients with more generalized involvement died despite attempts at operative treatment and radiotherapy. In some cases extensive disease precluded therapeutic measures. Of the 4 patients with a primary tumor in the nasopharynx, 2 had metastases in the skull, 1 in the lungs, and 1 in the regional nodes, abdomen, and inguinal region. A single malignant axillary growth produced pulmonary metastases. The primary focus was situated in the mediastinum in 1 case and produced general lymph node involvement and an isolated metastasis in the first lumbar vertebra. A relatively acute course in 5 cases was associated with generalized invasion of the lymphatic system, and all patients in this group died within one year after the onset of clinical manifestations.

Two patients had tumors of the wall of the intestine. One died two days following resection of the involved portion of the ileum and a mesenteric lymph node metastasis. The second died with evidence of intestinal obstruction, and autopsy revealed three distinct tumor foci in the ileum, adhesions to the abdominal organs, and metastases in the liver and lung.

The author stresses the extreme structural variability of the disease and the transitions in tumor morphology in different foci in a single case. In 2 cases of generalized involvement of the lymphatic tissues the process was difficult to identify as neoplastic or to distinguish from an atypical Hodgkin's disease. This form has been classified as the polymorphous-cell type of reticulum-cell sarcoma, its true nature being determined by the preponderant content of proliferating reticulum cells. In one instance a cervical lymph node metastasis of a pharyngeal growth appeared to have undergone
differentiation into a lesion resembling lymphatic leukemia, while in a second the process, although in the form of neoplastic nodules in the spleen, appeared as focal zones of uncomplicated hyperplasia in the lymph nodes. Two tumors when originally observed were composed of a syncytium of cells without intervening fibrils. A fibrillar structure, however, was apparent in the recurrences.

Photographs of gross specimens, photomicrographs, and references are included.

MILTON J. EISEN

EDUCATION, PUBLIC HEALTH


Johannes Müller's statement that cancer is cellular has remained since his day the foundation of cancer research. Almost everything we know about cancer, except its gross appearance, with which the ancient Greeks were familiar, has been gained in the single century since Müller's publication (Ueber den feinern Bau und die Formen der krankhaften Geschwülste) of 1838.

This quotation from Haggard and Smith's interesting account of the founder of microscopic pathology indicates the important place he holds in the study of neoplastic disease.


Godfrey, who is Commissioner of Health for the state of New York, discusses the question of improvement in the treatment of carcinoma in that state. He points out that New York has taken the lead in the development of tumor clinics, of which 23 are in New York City and 26 in upstate New York. Of the 49, 24 are fully approved by the American College of Surgeons. In the state exclusive of New York City there were 8,739 deaths, on the average, for the years 1935, 1936, and 1937. Eighty-two per cent of these patients died within five years. A careful study of the material has been made and the author thinks that the mortality could readily be reduced 60 per cent.