Abstracts
Reports of Research


Potential differences (p.d.) were measured, by a vacuum tube microvoltmeter, between positions on the surface of tumor tissue and neighboring normal tissue in the skin of MRC mice (from the Medical Research Council), the tumors being produced by painting with the carcinogen 9,10-dimethyl-1,2-benzanthracene in acetone. P.d. alone showed an electrical asymmetry (left side of animal changes during carcinogenesis were compared with similar measurements in control mice painted with acetone.

In individual animals a statistical analysis of measurements showed only one significant result, i.e., at "clinical" stages distinguished during carcinogenesis, p.d.'s tended to remain at a given level, although there was diversity about this level at certain other stages.

For all animals taken together it was found that there was no change in p.d. due to painting with acetone or with carcinogen in acetone. The mean p.d.'s in the animals before painting or in those painted with acetone alone showed an electrical asymmetry (left side of animal positive) that increased with age, as did the variance and standard deviation of these p.d.'s. The animals painted with carcinogen in acetone showed a maximum variance of the p.d. during the hypertrophic stage, and a smaller variance of p.d. during the malignant stage, than during the rest of the experiment. There was also some evidence that the mean p.d. is more negative (with reference to normal skin) in the period immediately preceding and during the early stages of development of a papilloma than during the rest of the experiment, and there was a greater variance and a change in the level of the p.d. during this period. There was no such change in the mean p.d. or in the variance in the period immediately preceding and during the early stages of malignancy, although there was a definite change in the level of p.d. in this period.—Authors' abstract.


The tumor used in this experiment was the Bagg-Jacksen mammary mouse cancer 755, grown in an inbred strain of mice, C57"V" black. X-radiation was applied to the tumor fragments in vitro and in situ. With a dose of 3,500 r in air at high voltage (h.v.l. 0.9 mm. Cu) in vitro there were 58.6% "takes," while with 4,500 r growth of the irradiated implants was prevented. The dose required to destroy tumor in situ does not appear to differ greatly from that necessary to prevent an implant from producing a tumor when an inbred strain of mice is used.—R. E. S.


The cholesterol-free residues of the unsaponifiable fraction from livers of persons dying of cancer and of non-neoplastic disease, respectively, have been separated into 5 fractions by chromatographic adsorption, and slight differences have been found in the percentage composition of the cancer and non-cancer residues. (The "cancer livers" themselves contained no tumor tissue, or were only slightly involved.) One fraction was found to be mainly saturated hydrocarbon, and another fraction was considered to be largely hepane. Further investigation of the residues is reported to be in progress.—H. J. C.


In these studies a transplantable squamous cell carcinoma was employed that was originally produced in the epidermis of a Swiss mouse by the application of methylcholanthrene. This tissue was found to contain less calcium than hyperplastic epidermis, which in turn contained less calcium than normal epidermis; the potassium content of the carcinoma likewise was less than that of hyperplastic and normal epidermis. The precautions necessary in the selection of tissue are noted.—H. J. C.


A single application of methylcholanthrene to mouse epidermis produced a rapid and extensive decrease in the calcium and iron content of the tissue. Continued treatments had little effect on the calcium content but did cause a further decrease in the iron content. It was found that the amounts of potassium, sodium, magnesium, and ascorbic acid were not decreased significantly by single or repeated methylcholanthrene applications. The transplantable skin carcinoma resulting from methylcholanthrene, when it was small, solid, and practically free of necrotic tissue, contained less of all the minerals than did...
normal and hyperplastic epidermis. However, necrotic tumor tissue had more calcium and sodium, and less potassium and magnesium, than did the small, solid tumors.—H. J. C.


The results presented in this paper indicate that the theory that "the fundamental cause of increased division rate and malignancy is the excess amount of nucleic acid in the nuclei" may be unsound. It was observed that the nuclei of Walker carcinosarcoma 256 in the resting stage have nearly the same concentration of desoxyribonucleic acid as the nuclei of cells of normal rat liver in the resting stage and that the nuclei of hepatoma 31 have a lower content of the acid. Nuclei from bird erythrocytes and fish spermatozoa have a higher content of desoxyribonucleic acid than the nuclei of the tumors that were studied.—H. J. C.


Thymonucleic acid from hepatoma 31 shows a phosphorus and a nitrogen content equal to that of thymonucleic acid from normal tissues. The turnover of thymonucleic acid phosphorus, as measured by the uptake of radioactive phosphorus, is very slow in non-growing liver, intermediate in hepatoma 31, and rapid in regenerating liver. The implications of thymonucleic acid metabolism with regard to cell growth and nuclear stability are discussed.—H. J. C.


A deficiency of cytochrome c cannot be regarded as exclusively characteristic of malignant neoplasms because certain tissues (of the rat and of man) subject to spontaneous neoplasms were found not to differ significantly in cytochrome c content from the neoplasms derived from these tissues. It was found that the concentration of cytochrome c in the same epithelial tissues from different species in many cases was approximately an inverse function of body mass. In man, all the normal epithelial tissues studied were found to be low in cytochrome c.—H. J. C.


From the urine of a boy with an adrenocortical carcinoma there was isolated a new steroid, which was identified as \( \Delta^\circ \)-androstenetiol 3(\( \beta \),16,17).—H. J. C.


Crystalline acetates of \( \Delta^\circ \)-pregnenediol-3(\( \beta \),20(\( \alpha \)), \( \Delta^\circ \)-androstenediol-3(\( \beta \),17(\( \alpha \)), and 3 unidentified compounds have been obtained from the urine of a boy with adrenocortical carcinoma. The parent substances of these acetates have not been encountered previously in human urine. Pregnenediol and androstenediol may be derived at least in part from substances formed in the adrenal tumor.—H. J. C.


A compound with an oxygen atom at C 11 of the steroid nucleus has been isolated from the urine of 7 patients with tumors or hyperplasia of the adrenal cortex. It is suggested that the compound is androstanediol-3(\( \beta \),11(\( \beta \))-diol-17-one.—H. J. C.


The concentration of urinary and fecal estrogens was studied in 10 ovariectomized mice of the NIH strain bearing spontaneous adrenal tumors and compared to the estrogen excretion of 11 intact normal females of the same strain. The tumors-bearing ovariectomized mice excreted 0.19 I.U. daily in the urine and 0.10 I.U. in the feces, while the normal females excreted 0.03 I.U. in urine and 0.04 I.U. in the feces. Thus the tumor-bearing mice excreted about 4 times as much estrogenic material as the intact normal females.—C. A. P.


Feminizing tumors of the testis of dogs are rich in lipids and estrogen. They are growths of the sustentacular cells of Sertoli; these cells in the testicular tubule produce estrogen.—Authors' abstract.


Lipschitz and his co-workers reported recently that estradiol and equilin, when absorbed from pellets implanted in the spleen, had relatively little fibromatogenic effect. This result indicated to them that the hormones were inactivated in the liver. However, Cantarow and his associates think that this conclusion is unwarranted, since estrogens were previously shown by them to be excreted in the bile and thus may be removed from the circulation without being activated in the liver.—R.B.
Induction and Prevention of Fibromyoepithelioma of the Utricular Bed in Male Guinea Pigs.


Tumorous growths attaining in some cases a diameter of 2 cm., or more were elicited in the prostatic region of male guinea pigs by the prolonged action of various estrogens (±estradiol, estradiol dipropionate, stilbestrol, and hexestrol) absorbed from subcutaneously implanted tablets. The earliest tumor appeared 108 days after their implantation. The incidence increased greatly with the greater length of estrogenic action. In experiments lasting from 7 to 11 months the incidence reached more than 40% in castrated animals and seemingly less in intact ones.

The tumors were fibromyoepitheliomas, and resulted from further hyperplastic growth of the fibromuscular pre-utricular tissue and metaplastic growth of the mucosa of the utricle and a limited area of the vasa deferentia. The fibromyomatous part of the pre-utricular tumor was structurally different from the estrogen-induced abdominal fibroid of peritoneal origin. Whereas fibroblasts originating from the peritoneum prevailed in the latter, bundles of smooth muscle fibers originating from the utricular bed prevailed in the former. The proliferative, and especially the metaplastic, changes of the utricular mucosa started not at its extreme caudal end, but a certain distance cephalad.

The estrogen-induced fibromyoepitheliomas of the utricular bed were prevented when, after a few weeks of action of the subcutaneously implanted estrogenic tablets, tablets of antifibromatogenic steroids, such as progesterone, deoxycorticosterone acetate, and testosterone propionate, were implanted. However, when the antifibromatogenic steroids were added 5 to 6 months after the implantation of the estrogenic tablet and allowed to act for another 4 months, fibromyoepitheliomas of the utricular bed were present in a number of cases, and their structure was the same as that of tumors arising from estrogen alone. But the incidence of these tumors was lower and their size smaller than after estrogens only. The question is discussed whether there are quantitative differences of response to antifibromatogenic steroids between the two types of estrogen-induced mesodermal tumors, i.e., peritoneal fibroid and the pre-utricular fibromyoma.—Authors' summary.


A transplanted lymphosarcoma that takes (practically 100%) in 10 to 14 days and kills within 14 to 18 days after the tumor is palpable was treated with compound E. Mice that received 0.3 mgm. of compound E in the drinking water daily failed to grow the tumors during 23 days of treatment and for 13 days afterward. However, following this period, 4 of 7 mice began to grow the tumor. Well developed tumors also underwent a rapid regression when the mice received compound E in the drinking water. Injection of 1 to 2 mgm. of compound E caused regression of the tumors in varying degrees; regression was faster and more consistent in females than in males. Castration of male mice or treatment with estradiol propionate appeared to increase the effect of compound E. In both sexes the effect of compound E was enhanced by simultaneous administration of phlorhizin. The influence of compound E appeared to depend on stimulation of the rate of the catabolism of proteins to a degree that resulted in the death of the malignant cells. The normal tissue cells of the animal, although perhaps placed under severe strain, did not appear to undergo permanent injury.

Although dramatic and apparently complete cures were produced, they were only temporary in a majority of the animals. After an interval of a few days or weeks the tumors usually recurred, and this time they were completely refractory to treatment, and in every case eventually caused the death of the animal. The refractory state was apparently inherent in the tumor cell and did not depend on the host.—C. A. P.


Two testicular interstitial cell tumors, one that arose in a mouse of the A strain that had received triphenyl-ethylene and one that arose in a hybrid mouse (A¥× C3H£) that had received stilbestrol, were transplanted subcutaneously into other mice for 9 and 4 generations respectively. The tumors consisted predominantly of cells of "generation two," as described previously.

The tumors failed to grow in all 34 genetically susceptible and untreated mice into which they were implanted. Seventeen mice of the A strain received transplants, and no growth occurred during the subsequent 51 to 204 days. Estrogens given at this time resulted in the growth of 16 of the "tumor rests." The rests grew as rapidly as recently transplanted tumors. The transplanted tumors that developed in estrogen-treated mice continued to grow, or persisted, when treatment was discontinued for periods of 14 to 188 days. The tumors persisted for 10 to 28 days in hypophysectomized mice although the hosts lost weight. The rate of growth and the structure of the tumors did not change appreciably during a period of 3 years of successive transplantation. The testicular tumors failed to grow in estrogen-treated mice of unrelated strains.—Author's summary.


This article is devoted principally to the physiology of the normal prostate in man and the lower animals. A short section on benign prostatic hypertrophy describes the salient features of this condition. The main part of the evidence indicates that the hypertrophy is due in part to androgen stimulation even though androgenic hormones are produced in smaller amounts in older men, in whom the condition is common, than in young men, in whom it is rare. To account for this set of facts it is suggested that the threshold for stimulation by androgen is lowered in the part of the prostate becoming hypertrophic, so

A method is described for the concentration of biologically active materials from the urine and feces of patients with leukemia and related diseases. The concentrates produce specific myeloid or lymphoid proliferation in guinea pigs. The factors responsible for the two types of hyperplasia are interchangeable by oxidation or reduction involving hydroxyl and carbonyl groups respectively.—H. J. C.


Myeloid hyperplasia and metaplasia in guinea pigs have been reported as following the injection of extracts and adsorbrates of human urine obtained from patients with chronic myeloid leukemia. The present report deals with some chemical and physical properties of a further purified fraction.

The benzoic acid adsorbate was extracted with acetone, and the insoluble residue leached with sufficient M/2 boric acid buffer (pH 8.3) to produce an extract of pH greater than 7. The solution was acidified with acetic acid (pH 4.3) and treated with 1.25 volumes of acetone in the cold. The resulting precipitate was dissolved in saline solution containing phosphate buffer (final pH 7.5). Assay of this material in guinea pigs gave an adequate biological response for testing its stability.

Activity was partly lost after heating on the steam bath for 1 hour at pH 7.5 or after exposure to a solution of pH 1.1 at 27.5°C for 24 hours. Most of the activity was lost in a solution of pH 11.2 at 27.5°C within 24 hours. Potency was retained after dialysis against distilled water from 50 to more than 100 times. These tumors bore a striking resemblance to the granulosa-cell tumors of the ovary produced by transplanting one ovary to the spleen and removing the other. The cellular components apparently derived from the tubules and the interstitial cell mass in the testicular tumor are indistinguishable from the granulosa-cell and theca-cell components, respectively, of the ovarian tumor. Also, portions of the testicular tumor were reminiscent of the structure seen in arrhenoblastoma.—M. B.


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**Abstracts**


Two groups of strain a mice were studied. The groups consisted of: (a) 23 castrated male mice and (b) 16 intact male mice. Castration was performed when the mice were 1 to 3 days of age. The animals were autopsied when they were from 13 to 29 months of age. Adrenal cortical carcinomas were found in 100% of the castrate mice and in none of the intact mice. The condition of the accessory sex organs of the castrate mice indicated that they were being subjected to influences similar to sex hormones, that these were multiple, and that the amount and nature of these varied from individual to individual.—Authors' abstract.


Thirteen spontaneous tumors occurred during 7 years among 1,000 Syrian hamsters descended from a single family. These tumors were: (1) a polymorph sarcoma transmissible by graft or by heart blood but not by filtrate; (2) a polymorph sarcoma transmissible by graft; (3) a carcinoma "embedded in pancreatic tissue," graftable; (4) cortical hypernephromas in the adrenals in 10 hamsters (sex not stated), only 2 transmissible by subcutaneous or intraperitoneal graft.—E. L. K.


A short discussion, with bibliography, of recent advances in cytology, virology, enzymology, and genetics, as they influence our ideas of the nature of cancer, with special reference to the author's enzyme-virus theory of cancer (Cancer Research, 3:358. 1943; abstr. in 3:490. 1943).—R. B.

**Conference on Gastric Cancer**

This conference was held Nov. 11, 1944, at Memorial Hospital, New York, N. Y., under the auspices of the Committee on Cooperation in Cancer Research, National Advisory Cancer Council, U. S. Public Health Service. Abstracts of the papers follow:


A general discussion of certain aspects of gastric physiology and their possible relationship to gastric carcinoma. Special emphasis is given to: (1) mucus secretion, its physiology and protective significance; (2) chronic gastritis, its occurrence and relationship to malignant disease; and (3) achlorhydria and pernicious anemia, their relation to atrophic enteritis and carcinoma. There is a comprehensive review of pertinent literature, with critical comments, showing the present state of our knowledge of these subjects and pointing out lines of future investigation. The bibliography contains 103 references.—R. A. H.


By tandem crossing of 3 inbred strains of mice a heterozygous population was obtained. For 5 generations every individual was given a subcutaneous injection of methylcholanthrene, and breeding with selection away from local tumors was carried out. This produced sublines of mice that developed a great variety of neoplastic lesions. These lines have now been continued by brother to sister inbreeding for 9 to 11 generations without further treatment with carcinogen. Observations on gastric neoplasms in one of these sublines are presented in this discussion.

As the degree of homozygosity has increased, the incidence of spontaneous glandular neoplasms of the stomach has also increased, until, of the last group observed, 53% of the animals autopsied when 551 to 600 days of age showed these lesions. Three types have been noted: (1) adenocarcinomas, 80.5% of lesions, (2) adenomas, 8.2%, and (3) adenomatous hyperplasias, 11.2%. The adenocarcinomas are histologically malignant, metastasize to regional lymph nodes, and invade contiguous tissues. Animals with these adenocarcinomas were found to be hypochlorhydric and moderately anemic, as compared to normal mice of the same age.

Preliminary experimentation indicates that the main gene determining the tendency for gastric carcinoma development is dominant and carried in the chromosome for brown coat color. The author advances the theory that the injection of methylcholanthrene in the original heterozygous population caused: (1) a somatic mutation of the gastric mucosa giving rise to gastric carcinoma in the treated animals, and (2) a hereditary germinal mutation increasing the susceptibility of subsequent untreated generations to spontaneous gastric neoplasms.—R. A. H.


A study of 23 cases of superficial spreading carcinoma of the stomach indicates that this type of carcinoma metastasizes to the regional nodes less frequently than do other types and, therefore, appears to be more amenable to resection. Six of the patients under observation have already passed the fifth postoperative year, and 11 others are still alive less than 5 years after operation.—R. A. H.


The author advocates massive resection of the stomach and contiguous organs for palliation in cases of far advanced carcinoma of the stomach. Two techniques are reviewed. In all, 8 such massive resections, with 2 postoperative deaths, have been performed by the author.—R. A. H.


Gastric mucus secretion was stimulated by mild chemical...
irritants; the pH and histology of the secretion were studied. Several stimuli including 50 to 85% ethyl alcohol and a saturated aqueous solution of ether, applied to the mucosa of gastric corpus pouches not secreting acid at the time, called forth a secretion the pH values of which varied widely but clustered about pH 7. This was interpreted as indicating the presence of transudate and inflammatory exudate, as well as mucus, in the specimens. Clove oil, on the other hand, gave a secretion with a narrow pH range and a clearly defined peak at pH 8.4. The buffer capacity of the mucus, between the initial pH and 3.5, ranged as high as 84 mN with the chloride concentration between 57 and 186 mN, neither of these characteristics being correlated with the pH value. The mucus secreted contained large amounts of columnar cells. The significance of the observations in relation to gastritis and cancer is discussed.—R. A. H.


Sodium salts of sulfadiazine and sulfapyridine were given intravenously to human subjects, and the rate of excretion into the gastric juice was studied. The ratio of the concentration of sulfadiazine in the gastric juice to that in the blood was usually 0.45 or less for normal persons, and for patients with atrophic gastritis, peptic ulcer, and, less extensive gastric cancer, while for 7 patients with extensive gastric carcinoma the mean ratio was 0.69. No correlation could be demonstrated between this concentration ratio and free or total acidity or pH of the gastric contents. In the case of sulfapyridine, however, the concentration ratio was usually between 4 and 8 in the normal pH range, but was found to approach 1 as the pH of the gastric contents approached 7 to 8. By postulating a simple diffusion mechanism for the gastric secretion of sulfonamides, the concentration ratios could be predicted with accuracy from the dissociation constant of the sulfonamide administered.—R. A. H.


In order to study the abnormal carbohydrate metabolism of patients with gastric cancer under more controlled conditions, subjects were maintained for 3 to 4 weeks on an experimental diet, and intravenously, as well as oral, glucose tolerance curves were studied. Under these conditions the curves showed the aberrations that have been described as typical for patients with gastric cancer, i.e., a somewhat elevated fasting and maximum blood glucose concentration with a noticeably slow return to the fasting level. To determine if this slow disappearance of glucose from the blood was due to a decrease or loss in the effectiveness of insulin, 0.1 unit of insulin per kgm. body weight was given intravenously to normal subjects and to patients with gastric cancer. As this produced the same drop in blood sugar levels in the two groups, it was concluded that the presence of cancer does not affect the insulin hypoglycemic reaction.

The relation of adrenal cortical hormone to carbohydrate metabolism was then investigated. The fasting liver glycogen content was determined in 27 patients with gastrointestinal cancer and in 9 with nonneoplastic gastrointestinal disorders. The results demonstrated no differences in the two groups. Liver glycogen was then determined in similar groups of subjects, after the administration of large doses of glucose. The results suggested that patients with gastrointestinal cancer have an impaired ability to form or store glycogen in the liver. When adrenal cortical extracts were given along with the glucose, evidence was obtained suggesting that the adrenal hormone promotes glycogen storage in the liver under these conditions.

Although a good deal of confirmatory evidence must still be obtained, these data indicate that the liver-adrenal cortex mechanism is a factor in the disturbed carbohydrate metabolism of patients with gastrointestinal cancer.—R. A. H.


Multiple cancers occur in about 6% of cancer cases, according to necropsy observations in 3,974 cases of malignant disease. "This is tenfold or even tenfold the expected incidence and may be assumed to represent a susceptibility to cancer in certain persons." Nine per cent of persons with gastric cancer were found to have multiple malignant growths; in no case were the multiple lesions confined to the stomach. Fifteen per cent of persons with cancer of the large intestine had multiple malignant lesions; this higher figure illustrates the effect of premalignant multiple polyposis, which is known to be more frequent in the large intestine than in the stomach. In 29% of the cases of multiple cancer of the large intestine, the lesions were restricted to that organ.—R. A. H.


From a histological study of 200 stomachs surgically removed it was concluded that the average severity of chronic gastritis, if present, is no greater in patients with gastric cancer than in those with gastric or duodenal ulcer.—R. A. H.

Discussions were held after the first and second papers and at the conclusion of the conference. The original should be consulted for comments on such topics as the significance of cell desquamation during mucus secretion, intestinal metaplasia of gastric mucosa in relation to gastric neoplasia, the negative results in attempts to induce tumors of the glandular stomach in mice, the possibility that selection (without mutation) could account for the development of the "stomach cancer" strain of mice, and hepatic dysfunction in cases of cancer in human subjects.—R. A. H.
history of intermittent right lower quadrant pain with nausea and vomiting, and the finding of a palpable mass under McBurney's point, suggested an appendiceal abscess. The lesion proved to be a lymphosarcoma. Twenty-three previously reported cases are reviewed.—W. A. B.


Report of 3 cases in which a localized lymphoma was found in an appendix that had been removed after the development of symptoms simulating those of acute appendicitis.—J. G. K.


Early total colectomy in cases of polyposis is needed if the almost certain eventual occurrence of malignancy in the colon or rectum is to be avoided. A case is presented in which 4 carcinomas of the colon arose in a young man as a result of malignant transformation in congenital polyposis.—M. E. H.


Case report. The removed colon showed diffuse polyoid adenomatosis with extensive precancerous changes.—W. A. B.


A case report.—J. G. K.


The use of the Devine colostomy as a preliminary procedure for resection of a tumor of the left side of the colon, rectosigmoid, or rectum is described. No deaths followed the procedure in 30 cases.—W. A. B.


The surgical treatment of 198 cases of carcinoma of the rectum in which radical resection was performed is discussed. A 5 year cure rate of 30% was obtained. A single-stage abdominoperineal resection is recommended, the operative mortality in such cases having been 10% compared with an over-all mortality of 13%.—C. W.

LIVER


A review, and report of experience at Cincinnati General Hospital, with 3 detailed case histories.—J. G. K.


A case report. A classification of these tumors as cholangiomatous, parenchymatous, or mixed is suggested.—M. E. H.


A case report.—G. J. K.

BONES, JOINTS, TENDONS


Osteogenic sarcoma of the skull is a relatively rare tumor, comprising only about 1% of all osteogenic sarcomas. Garland reports a case in a 17 year old male, treated palliatively by surgery and x-ray.—R. E. S.


Synovial sarcomas are composed of two types of cells, those resembling fibrosarcoma cells with accompanying reticulin fibers, and synovial elements that often contain mucicarminephilic droplets and may line slits in the tissue. An analysis of 9 new cases and 95 from the literature is presented, and in only 3 was there survival for 5 years without evidence of metastases. The neoplasm occurred more frequently in males, the average age of appearance was 32 years, and almost half of the tumors were found in the knee. Metastases were disseminated usually by way of the blood vessels but occasionally were found in regional nodes. Although a fatal disease, the average course lasted 5.7 years. Treatment advocated is a limited, incisional biopsy with high amputation immediately after the diagnosis has been made from permanent sections. Dissection of regional nodes may be desirable as a separate procedure. No beneficial effects from irradiation were found.—W. J. B.

Corrections

Volume 5:602. (Abstracts) 1945. Column 2: line 31-32: for "in the stomach of the host" read "in transplanted stomach tissue"; line 34: for "carcinomas and sarcomas developed" read "carcinomas and sarcomas developed apparently from the transplants." [Editorial errors.]
