
In view of the inhibitory action on tumor growth of some polycyclic compounds containing nitrogen atoms in the ring system, 6-azachrysene, 1-azaperylene, 5-methyl-4,6-diazachrysene, 3,4-benz-5-azaphenanthrene, and 3,4-benz-5,7-diazaphenanthrene were synthesized.—E. L. K.


Medawar, Robinson, and Robinson (Nature, London, 151:195. 1943) previously described the isolation, from a commercial malt extract, of small quantities of a steam-distillate. It seemed probable that the material was some polycyclic compounds containing nitrogen atoms that permitted the free growth of epithelial tissue. It seemed probable that the material was an unsaturated lactone, and it was found that synthetic specimens of d,l-2,4-hexenolactone exhibited similar inhibitory properties. A new synthesis is described whereby this lactone can be obtained in about 35% overall yield from propylene oxide; the new method has the advantage of being readily adaptable to the preparation of related lactones.—A. H.


Each series of mice was painted with a different mixture of 2 compounds consisting of a strong and a very feeble carcinogen (i.e., methylcholanthrene+1,2,5,6-dibenzfluorene; 1,2,5,6-dibenzanthracene+1,2,5,6-dibenzacridine; methylcholanthrene+methylenechrysan; methylcholanthrene+six methyl derivatives of benzacridine). Controls were painted with the strong carcinogen alone. Carcinogenicity of the solutions was assessed by noting the latent period of papilloma formation and of malignancy; lung adenomas, weight of spleen and liver, and body weight were recorded.

The authors are satisfied that addition of a feeble carcinogen inhibits the activity of a powerful carcinogen and explain this result by appealing to some such mechanism as competition between the 2 compounds for a substrate essential for cellular multiplication. The methyl acridines showed no inhibitory power, but no statement is made about their carcinogenicity.

The mechanism of the phenomenon of inhibition of carcinogenis is discussed.—I. H.
It seems evident from the results of these experiments that the variation in tumor formation observed when different lipids are used as solvents for a carcinogen cannot be attributed to any single characteristic of the oils. Instead, it appears that a variety of factors concerning the chemical and physical characteristics of the lipid, and the differences in tissue response to the solvent, all play an important role in carcinogenesis.—Authors' abstract.


Previously, intraperitoneal injections of urethane had been found to induce lung tumors in A strain mice. The present investigation indicates that the subcutaneous implantation of crystalline urethane in 1 mgm. pellets and its oral administration as a 0.1% solution for drinking water are both effective means of inducing lung tumors at an early age in this strain of mice, and that the number of tumors per lung is increased by increasing the total dose of drug. Also, by giving urethane intraperitoneally at different periods during the life of the animals evidence was obtained indicating that most, though not all, of the lung nodules arise within 1 to 2 months after treatment, and that lung tissue that was not susceptible to tumor induction early may become so later on.—R. A. H.


In the insect Leucophaea maderae (Orthoptera) transection of the recurrent nerve resulted in the appearance of tumors in the organs normally innervated by this nerve. The tumors appeared within 10 days to several months after the operation and were found most frequently in the anterior portion of the midgut and in the salivary reservoir. In the foregut and salivary glands well developed tumors were relatively rare. Various types of control operations (allatectomy, castration, etc.) failed to produce tumors.—R. B.


One section of this review summarizes the statistical, geographical, and experimental evidence, now considered quite conclusive, that sunlight is a major factor causing skin cancer in man. Experiments with animals have shown that the ultraviolet portion of the spectrum is responsible for the development of the tumors. The mechanism by which the irradiation produces the tumors is unknown. Various hypotheses have been put forward and are summarized by the author.—R. B.


Compared with the 3 causes so far known, the constant presence of a mild irritant (black silk thread) in the mamma of RI1I virgin female mice was of no importance in determining the site or accelerating the initiation of mammary carcinoma.—Author's summary.


It is well known that epidermal warts in mice, produced by painting with tumor-producing agents, often show periods when their growth rate is reduced or their size diminished, and they may even disappear temporarily. During observations on the growth of hair near warts produced by benzpyrene, it was noted that diminution in growth of the warts occurred, whereas in black mice the surrounding skin, normally pale, became pigmented as it does when the hair bulbs cause a diversion of blood towards themselves and away from the overlying epidermis and warts; hence the blanching, the lowered growth rate, and the diminution in size of the warts.—A. H.


The role of calcium as a factor in the age difference seen in the response of epidermis of old and young mice of the New buffalo and CBA strains of mice to methylcholanthrene was investigated. Old mice of both strains were found to contain more epidermal calcium than the young. The epidermis of both age groups of the New Buffalo strain responded similarly when treated with methylcholanthrene; that is, they underwent a nearly 50% decrease in the calcium content. However, the diminution in the calcium content of the CBA strain was less than that of the New Buffalo, and the young group showed about 50% less drop than did the old.—Authors' summary.


Patients with gastric carcinoma were among the subjects tested. The results have been published elsewhere (J. Nat. Cancer Inst., 5:360. 1945; abstr. in Cancer Research, 5:604. 1945).—E. E. S.


The proteose levels of rabbit sera were studied by determining the polarographic activity of sulfosalicylic acid filtrates. The activity was found to vary considerably in normal rabbits from animal to animal and in the same animal at different times. After intratesticular injection of normal-rabbit-testis mash, no change in serum proteose was noted. There was generally, however, a gradual increase in polarographic activity after intratesticular inoculation of the Brown-Pearce tumor. Although this increase usually did not occur until the tumors were palpable, the degree of increase could be correlated with...
the size of the tumor only in extreme cases. Intercurrent respiratory infections also increased the activity of the filtrates. No qualitative differences were noted in the polarographic waves of the sera from normal and tumor-bearing animals.—R. A. H.


A discussion.—E. F. S.


Thiourea was added to the diet of virgin C3H mice when they were 11 months of age. The animals were maintained on this regimen until they developed spontaneous mammary cancer, when they were killed and the ovaries, uteri, adrenals, and thyroids studied histologically. The thyroids showed the expected hyperplasia, red blood cells were found within their follicles, and a granular, greenish yellow pigment appeared in the cytoplasm in the distal portion of the follicular cells. No changes were seen in the uterus, but a general degeneration of the follicles and ova was noted in the ovaries, and there was a decrease in the osmiophilic material of the adrenal cortices.—R. A. H.


In female mice of the Marsh-Buffalo strain, the maximum amount of estradiol which could be administered without producing toxic symptoms or significant losses in body weight was without effect on the development of mammary tumors in intact mice and without appreciable effect on the development of lymphoid tumors in both intact and castrated mice. Mammary tumors were produced in castrated female mice, but the incidence was less than that produced by toxic doses and less than that in intact controls. Lymphoid tumor formation was not significantly different in controls, whether intact male or female mice or castrated males. Lymphoid tumor formation was significantly increased by nontoxic dosage of estrogen in the castrated male. A comparison made upon litter mates castrated at 30 days of age and receiving identical treatment as to housing, food, and dosage with estradiol, revealed 23% development of tumors of the mammary gland in the castrated females against 3% in the castrated males.—Authors' abstract.


In 48 mice of the Marsh-Buffalo strain, breeding was without influence upon the onset and accumulative incidence of cancer of the breast. This observation was in contrast to the experience of Marsh. The observations of Marsh in regard to tumor incidence in virgins were confirmed.—Author's abstract.


The estrus cycles of virgin C3H and A strain mice were followed for a period of 150 days in order to determine whether the difference in the incidence of mammary tumors in virgin females of these two strains was reflected in the estrus cycles. No differences in regularity or duration were found, but it was noted that the vaginas opened significantly later in the A strain than in the C3H strain or F1 hybrids between A and C3H. The authors conclude that, "These findings contribute evidence that the difference between the strain C3H virgin females with a high tumor incidence and the strain A virgin females with a low tumor incidence, . . ., is manifested in part at least through the hormonal mechanism."—R. A. H.


The relationship of the carcinogen-induced to the spontaneous neoplasm can be studied in the case of mammary cancer by using the dba strain, which is susceptible to both types of tumor. The present experiments were designed to test the role of the milk influence in governing the response of the mammary gland to methylcholanthrene applied to the skin 2 to 3 times weekly as a 0.25% solution in benzene.

Strain dba males (sublines 12 and 212) were crossed with C3H females possessing the milk influence (Z stock) and with C3H females lacking the milk influence (ZB stock). Their hybrids were observed either as virgin or as forced-bred females during treatment with methylcholanthrene. Breeding females of the genetic constitution (ZB × dba) × dba were also skin-painted with the carcinogen. These backcross animals lacked the milk influence but carried genetic susceptibility and hormonal influence.

Mammary cancer was induced in the absence of the milk influence. However, if breeding females, treated with methylcholanthrene, carried the milk influence, they developed mammary cancer earlier, in greater numbers, and with more rapid growth of the cancer than did genetically identical animals without this influence.—M. B.


Mice of the low mammary cancer strain C (1.4% in breeding females) were nursed by C3H foster mothers and then bred brother to sister for 11 generations without further foster nursing. Of the 20 foster-nursed C females, 70% developed mammary cancer, and in the subsequent generations the incidence of mammary tumors varied from 83 to 96%. (1 × C3H) F1 hybrid females fostered by these C mice also developed a high incidence of mammary...
cancer. These data indicate that female mice of the low cancer strain C can transmit the milk influence through 11 successive generations or passages.

Two female mice of the low mammary cancer C57 black strain were also foster nursed by C3H females and then bred brother to sister. Neither of these females developed mammary cancer, but of 13 (C x C3H) F1 hybrid mice fostered by them, 12 developed mammary cancer. One of 9 C57 black females of the so-called F2 generation (from the inbred fostered females) but none of 11 hybrid mice fostered by them had mammary gland tumors. No mammary cancer developed in the 3 subsequent generations of C57 black females nor in genetically susceptible hybrid mice fostered by them.

This would indicate that, unlike the C strain, the C57 black strain is unable to propagate or transmit the milk influence through successive generations in sufficient amounts to incite cancer in susceptible hybrids. Apparently, then, the genetic constitution of inbred mice determines not only their susceptibility to the milk influence but also their ability to propagate or transmit it.—R. A. H.


Female mice of the low cancer strain C were bred to male mice of the C3H strain. Each litter was born, the males were discarded and 1 to 3 young (1 x C3H) F1 hybrid females added to serve as test animals for the presence of the milk influence in the C mothers. The resulting (C x C3H) F1 and fostered (1 x C3H) F1 females were bred at 2 months of age and each bore 3 litters in rapid succession, not being allowed to nurse the young. Fifty-two per cent of the (C x C3H) F1 females developed mammary cancer as compared to 8% of the (1 x C3H) F1 mice nursed by the same C strain females. Extracts and extract concentrates were made from 11 of the (C x C3H) F1 tumors and fed to 79 young “test” females none of which developed mammary tumors.

The author concludes that, “The results show that mammary tumors arose in hybrid mice derived from strain C females and strain C3H males and suggest but do not prove that a milk influence was not involved in the occurrence of the tumors.”—R. A. H.


The tumor rates of 4 groups of virgin mice, the Marsh albino (M) stock, the Bittner albino (A), and the reciprocal crosses of the 2 strains were compared. The A ? M males showed a higher tumor rate (98.0%) than either of the parent stocks (A stock, 29.0% and M stock, 63.5%), and approximately double that of the reciprocal cross (53.0%). It was concluded that: (1) the extrachromosomal, or milk, agent is more concentrated in the A than in the M stock; (2) the M stock is genetically more susceptible to the milk agent than the A stock; and (3) the inherited susceptibility of the physiological system is of greater importance than the milk agent in the development of mammary tumors in these 2 strains of mice.—Authors’ abstract.


The 2 mice reported came from a line (XXX) in which no mammary tumor had been observed for 11 years.—G. H.


A general review of experimental and statistical investigations, with an extensive bibliography.—W. A. B.


Further experiments are reported on the effect of antigen treatment upon the incidence of tumors induced by a depot of 1 to 2 mgm. of benzpyrene in mice, and upon the growth of transplanted mouse tumors. In the animals treated with benzpyrene, the antigen treatment consisted either in cautization of the skin of the mice by a drop of concentrated H2SO4 at the beginning of the carcinogenic treatment and repeated 4 weeks later, or in injections of pure serum albumin (horse). Mice with 76% tumor incidence after benzpyrene treatment showed only a 15% incidence after cautization of the skin. Injection of 10y of serum albumin into mice of the Swiss or dilute brown strain that received 2 mgm. of benzpyrene was without significant effect; however, a decrease in the rate of tumor incidence was observed in dilute brown mice that received only 1 mgm. of benzpyrene, indicating a correlation between dosage of the carcinogen and success of the antigen treatment. It is suggested that the concentrated H2SO4 contributes antigens by denaturing the tissue proteins or by favoring infection by antigen-producing bacteria.

Transplanted tumors (Ehrlich’s adenocarcinoma and Lettré’s ascites tumor) were not influenced even by injections of up to 50y of serum albumin.—Z. D.


To find out whether the antigenic properties of artificial antigens depend on the presence either of a carbohydrate or of tyrosine or of both, 3 series of compounds were synthesized by coupling pectin azide directly to proteins (gelatin and globulin), or first to the tyrosine ethyl ester and the ethyl ester of glucosaminic acid and then to the protein molecule. Only the compounds containing both pectin and tyrosine proved to be antigenic (precipitin test). Their influence on tumors could not be tested, because of their high toxicity. The nonantigenic pectin-gelatin compounds were without influence on tumors (15y injected twice a week during 28 to 30 weeks into mice bearing benzpyrene depots.)—Z. D.