### Abstracts

#### Reports of Research


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


Medlawar, Robinson, and Robinson (Nature, London, 151:195, 1943) previously described the isolation, from a commercial malt extract, of small quantities of a steam-volatile substance that inhibited the growth of fibroblasts at concentrations 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 dl-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 + chrysene; 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 carcinogenesis is discussed.—I. H.


Five compounds, whose structural relation to active carcinogens resembles that of stilbestrol to estrone, were tested for carcinogenic activity. Slight activity was demonstrated in one of them—2-ethyl-β-sec-butylsalbene—which is regarded as a benzpyrene analogue. The other compounds tested were: 2,2,β,β-tetraphenyl-α-butylen, 2,2,β-diphenyl-β-ethyl-α-amylen, 2,2,β-diphenyl-β-ethyl-α-butylen, and 1,4-dityryl-benzene.—Authors' abstract.


The effect of various lipids on sarcogenesis, when used as solvents for 3,4-benzpyrene, was compared with certain chemical and physical characteristics of the lipids. The vehicles used were ethyl stearate, ethyl oleate, ethyl linolate, ethyl palmitate, methyl caprate, tricaprylin, lecithin, "mouse fat," corn oil, cottonseed oil (largely freed of antioxidants), "lard filtrate," and "lard residue." A pronounced retardation of tumor formation was observed with methyl caprate, ethyl linolate, lecithin, lard residue, and a petroleum ether extract of mouse carcasses.

With some lipids there was an indication that their effect on sarcogenesis could be correlated with their susceptibility to autoxidation in vitro and with the corresponding destruction of the dissolved hydrocarbon. Thus the addition of α-tocopherol to ethyl linolate, ethyl oleate, or cottonseed oil (largely freed of antioxidants) decreased the rate of destruction of 3,4-benzpyrene and favored the formation of tumors. However, tocopherol also enhanced the genesis of sarcomas when added to the saturated fatty acid ester, methyl caprate, a substance that is not susceptible to autoxidation. Furthermore, there was relatively little destruction of benzpyrene in vitro when it was dissolved in lard residue, yet this solvent had a striking inhibitory influence on the development of tumors.

No relationship was observed when the rate of disappearance of hydrocarbon from the tissues was compared to the incidence of tumor formation. Thus when 3,4-benzpyrene was dissolved in ethyl linolate or ethyl oleate (with and without added tocopherol), lard residue, or lard filtrate and the mixtures were injected subcutaneously, the carcinogen disappeared at the same rate from the tissues of all the groups, but the final incidence of sarcomas varied from 3 to 77% depending on the solvent used.

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 hairs 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 that 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 f) × dba g 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.
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 fostered by C3H females and then bred brother to sister. Neither of these females developed mammary cancer, but of 13 (I × 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. As each litter was born, the males were discarded and 1 to 3 young (1 × C3H) F1 hybrid females added to serve as test animals for the presence of the milk influence in the C mothers. The结果 (C × C3H) F1 and fostered (1 × 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 × C3H) F1 females developed mammary cancer as compared to 8% of the (I × C3H) F1 mice nursed by the same C strain females. Extracts and extract concentrates were made from 11 of the (C × 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 hybrids showed a lower 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.
Reports of Research

Cancer Res 1945;5:661-664.

Updated version Access the most recent version of this article at: http://cancerres.aacrjournals.org/content/5/11/661.citation

E-mail alerts Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.