The four leaks in parallel were sealed into the inlet system of a mass spectrometer. Several tests were made in which the rate of pressure change in a 10-liter reservoir behind the leaks was periodically measured, both by means of a McLeod gage and by detection of the appropriate ion with the mass spectrometer. The results indicated an effective area of 2.1×10^{-5} cm for the four leaks in parallel and a nitrogen flow of about 1.6 mg/day, agreeing with the calculated values within the estimated uncertainty.

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A New Influence on Chemically Induced Sarcomata[1]

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Many influences have been established as effecting the induction of sarcomata by chemical means. These influences may be classified into two groups, as follows: (1) the environmental and (2) the genetic. Under the environmental influences may be listed the specific carcinogenic compound, the amount used or dosage, the vehicle or solvent, the mode of introduction, the age of the experimental animal, and the species or subline of experimental animal employed. The genetic influence has always been inherited as a dominant multiple factor complex, although, in many cases, the susceptibility of the F_1 individual to the chemically induced tumor approaches the susceptibility of the dominant parent, but does not do so completely.

Examples of linkage between genes for susceptibility to induced neoplasms and the well-known color or morphological genes of mice have been demonstrated primarily by the work of Heston and of Strong. In an attempt to investigate further the nature of the genetic influence on the induction of tumors by methylcholanthrene, the following experiment was performed:

Mice of the NHO strain showing an intermediate degree of susceptibility to the subcutaneous development of sarcoma at the site of the injection of methylcholanthrene were outcrossed to mice of the C57 subline which showed a high degree of susceptibility to the same induced tumor. The outcross was made in both directions. Two hundred fifty-four F_1's were obtained. At 60 days of age the F_1 mice were injected with 1 mg of methylcholanthrene dissolved in 0.1 cc of sesame oil. The mice were periodically examined for tumors. Data obtained on the rate of appearance of tumors induced by methylcholanthrene are plotted in Fig. 1.

The mice were divided into three groups according to the litter in which they were born. Mice born in the first and second litters comprise group 1; mice born in the third and fourth litters of the same breeding parents were put into group 2; and mice born in the fifth and sixth litters of the same parents were classified as group 3. The three groups were approximately of the same

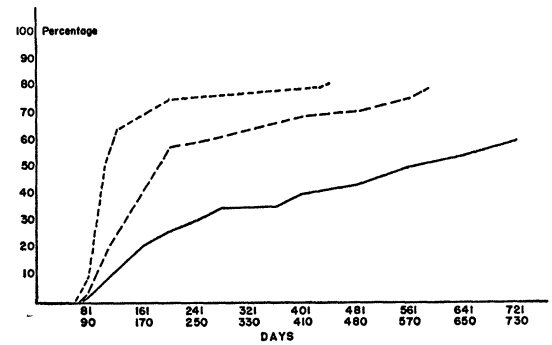

FIG. 1. Data obtained on the rate at which fibrosarcomata appear at the site of injection of methylcholanthrene in a series of F_1 mice. Time in days is given on the base line, the percentage of mice showing tumors along the vertical line. Group 1 consists of mice belonging to first and second litters (solid line); group 2, of mice of the third and fourth litters (long-dash line); and group 3, of mice from the fifth and sixth litters of the same breeding parents (short-dash line).

size (93, 80, and 81 mice, respectively). An examination of Fig. 1 discloses the fact that mice of the three groups develop sarcomata at the site of the injection of methylcholanthrene at significantly different rates. The rate for the appearance of tumors was slowest in group 1, intermediate in group 2, and highest in group 3.

All mice of the F_1 generation produced by an outcross of mice of two inbred strains are theoretically genetically alike. The difference of susceptibility to induced tumors obtained in this experiment is consequently not a genetic one. It is obvious that something which is increasing or decreasing in the mother's body is being handed down to her offspring. It is also possible that this principle varies in the father's contribution to progeny, although the evidence for this concept has so far not been indicated. This transmitted principle sensitizes or changes the progeny's susceptibility to a subsequent injection of methylcholanthrene, influencing the rate at which the offspring develop sarcoma in the presence of a given amount of methylcholanthrene. There are possible at least three modes of transmission for this principle. It may be (1) by cytoplasmic inheritance, (2) by transplacental transmission, or (3) through the mother's milk. These three were the modes of transmission regarded as possible for the transmission of susceptibility for spontaneous adenocarcinoma of the mammary gland in mice by the group at the Jackson Memorial Laboratory. In the spontaneous adenocarcinoma work it was subsequently conclusively demonstrated that the principle was transmitted through the mother's milk. This principle producing adenocarcinoma of the mammary gland is now sometimes referred to as the virus of Bittner.

[1] This experiment has been made possible by grants from The Jane Coffin Childs Memorial Fund for Medical Research and The Anna Fuller Fund.

In the present investigation it is extremely doubtful whether this new principle that influences chemically induced sarcomata is transmitted through the mother's milk, since there is ample evidence that foster nursing does not modify susceptibility or influence the rate at which the induced tumor appears following the injection of the carcinogen (unpublished data of author).

The present investigation is of significance, since it demonstrates that a new principle, presumably of a biochemical nature, has influenced the production of a malignant tumor. This agent varies in amount or potency with advancing age and is transmitted to the next generation. Perhaps when it is identified, other phases of the cancer problem, such as prevention and spontaneous regression, may be elucidated. Susceptibility to cancer is, of course, only the obverse of resistance to cancer. The present evidence indicates equally clearly the existence of a new *resistant* mechanism that is capable of changing the rate at which an offspring of a given female develops sarcoma in the presence of methylcholanthrene, that it is highest in young breeding females and diminishes in effectiveness with advancing age. It is in the young animal that this resistant mechanism for the control of some characteristics of cancer must be sought.

By the use of F_1 individuals that will grow the normal tissues of both ancestral stocks, the elucidation of this mechanism for resistance to cancer in young animals will be considerably aided.

Antibacterial Action of the Blood of the Large Milkweed Bug[1]

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The blood of the large milkweed bug, *Oncopeltus fasciatus,* contains an antibacterial agent active *in vitro* against *Staphylococcus aureus* and one strain of *Bacillus subtilis.* The active principle is water soluble, stable to boiling for 30 min but destroyed by autoclaving, and active at a dilution of at least 1 part in 10,000.

The large milkweed bug, a well-known laboratory insect, may be kept in culture throughout the year, with little care and expense, feeding on milkweed seeds and water (*7*). It is prolific and requires only about 3 weeks for development from egg to adult.

In our experiments two methods were used for obtaining blood from the bugs. For samples of pure blood, the legs and antennae were cut and the exuding droplets taken up in a pipette and diluted with physiological (0.85%) saline solution. This is a time-consuming procedure. For routine testing, therefore, the bugs were slit along the thorax and abdomen and the blood extracted by shaking in saline solution. This extract was filtered before use. When distilled water was substituted for saline solution, the extract was devoid of activity.

There are two possible objections to obtaining blood by the rapid extraction method: first, the solution thus obtained is heavily contaminated with bacteria; second, there is the possibility of contamination with feces of the bugs. With respect to the first objection, our observations lead us to believe that the bacteria thus introduced contribute nothing to the antibacterial action of the extract, since the extract may be put through a bacteriological filter or may be boiled up to 30 min without losing its activity. With respect to the second objection, it may be noted that tests with blood obtained without fecal contamination gave exactly the same results as those utilizing the extract. Further, if adult bugs were used, they either defecated on being slit, thus enabling removal of the feces, or usually they did not defecate at all. With nymphal bugs, which often defecated in the solution, fecal contamination was a factor, reducing the antibacterial activity. For this reason, adult bugs were used for all the experiments except those designed specifically to test the blood of nymphal bugs.

TABLE 1

Preparation	Diameter of ring of growth inhibition (mm)
1 part blood : 1 part saline	22
1 part blood : 49 parts saline	15
Filtered extract (1 bug/ml)	18–22
Same extract ether extracted, boiled, and refiltered	18–22
1 unit of penicillin/ml of dilute phosphate buffer	19–22

Antibacterial action was tested by the cylinder-plate method used in penicillin assay, using 10 ml of standard nutrient agar seeded with about 0.1 ml of a 24-hr broth culture of the test organism and incubating at 37° C for 16–18 hrs. When penicillin assay agar enriched with glucose and yeast extract was used, the zones of inhibition were smaller and not clear cut.

With *Staph. aureus* as test organism, the results presented in Table 1 were obtained. These show that, by the extraction method, the antibacterial activity from a single bug is the equivalent of above 1 Oxford Unit of penicillin. The actual content of the bug is undoubtedly greater, for this method does not extract all the blood. The blood of last instar nymphal bugs has antibacterial action like that of the adults.

The extract was active against *Staph. aureus* (F & D 209) and, to a lesser degree, *B. subtilis* (F & D 558-S),

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