

when the 21-days serum is subjected to chromatography under the same conditions a considerable proportion (more than 50 per cent) of the neutralizing activity initially present in the serum is obtained in the 0.01 M phosphate fraction. It is evident that differences exist in the antibodies present in the two sera and these differences are being examined in more detail.

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Response of Newly Born Mice to a Chemical Carcinogen

MANY recent reports record that certain leukaemias and malignant lymphomas can be transmitted to newly born mice using cell-free extracts of tumour tissues^{1,2}. Under certain conditions, cell-free extracts of leukæmic organs also produced parotid gland tumours, sarcomas and other neoplasms³⁻⁵. Tissue culture extracts and extracts of tumour tissues⁶⁻¹⁰ have given rise to leukaemias and other tumours in rats and hamsters, following injection into the newly born animal.

Since all these studies have made use of newly born animals, it seemed to us that general studies of the pathological responses of the newly born animals were of considerable importance. We have investigated the effects of certain chemical carcinogens in this same biological system. This communication reports the effects of small doses of the purified carcinogenic hydrocarbon, 9,10-dimethyl-1,2-benzanthracene, administered subcutaneously as a colloidal suspension to newly born Swiss mice. The Swiss mice were originally obtained from the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine, and have been bred at random in this laboratory for the past nine years. The incidence of tumours occurring in these animals has been carefully followed in many untreated controls during this time; malignant lymphomas of different types have been found in 4 per cent of animals of more than one year of age but have not been seen prior to this time. A slightly higher incidence of malignant lymphomas (6 per cent) has been noted following a single dose of 9,10-dimethyl-1,2-benzanthracene given by various routes of administration to animals 8-10 weeks old. The earliest lymphomas seen in these animals occurred at 42 weeks of age.

In the present experiment 25 newly born Swiss male and female mice, less than 12 hr. of age, were given a single subcutaneous injection of 30 µgm. 9,10-dimethyl-1,2-benzanthracene as a colloidal suspension. The suspension was prepared by the rapid addition of 9,10-dimethyl-1,2-benzanthracene, dissolved in acetone to 1 per cent aqueous gelatin, kept at 56° C. in a water-bath. The acetone was then removed by slowly bubbling nitrogen through the suspension. Newly born mice were injected subcutaneously in the interscapular region (tuberculin

syringe, 26 gauge needle) with 0.015 ml. of the suspension, containing 30 µgm. 9,10-dimethyl-1,2-benzanthracene. The first animal was killed when moribund at the eleventh week from birth and showed a marked enlargement of the thymus which occupied a large part of the chest cavity, compressing the lungs. The spleen and peripheral lymph nodes appeared normal in size and colour. Three more animals were killed when moribund at the thirteenth week; one showed a marked enlargement of the thymus, the lymph nodes and spleen; the other two had an enlarged thymus and multiple lung adenomas less than 1 mm. diameter. Four additional mice, killed at the sixteenth, eighteenth and twenty-fourth weeks, all had enlargement of the thymus, lymph nodes, spleen and multiple lung adenomas. Histologically, these tumours are malignant lymphomas of the stem-cell type with early lymphocytic differentiation. Microscopic infiltrations of lungs, kidneys, skeletal muscles, spleen, lymph nodes, salivary glands and bone marrow were found; but not all these organs were involved in every animal. Thus, eight mice of a group of 25 have developed lymphomas in the short period of 11-24 weeks, at an average age of 15.3 weeks following injection (an incidence of 32 per cent). Control mice were given injections of a similar amount of colloid only; all survive and no tumours have occurred so far.

The finding that polycyclic hydrocarbon carcinogens can give rise to or enhance leukaemia has been reported many times using different strains of mice¹¹⁻¹⁴. The present study differs from prior investigations in that only a single, low dose of carcinogen has given rise to a high incidence of malignant lymphoma rapidly in a relatively unsusceptible mouse. It is emphasized, from this finding, that the development of this disease is dependent, to a great extent, upon factors inherent to the animals at this stage of development. The character of the response encountered in newly born mice with cell-free filtrates should be viewed not only in terms of virus concepts but also as a response of a sensitive biological system to carcinogenesis.

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