Transmission to Adult Pigeons of Several Variants of the Rous Sarcoma of Chickens*

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Previous studies have shown that both cell suspensions and filtrates of the Rous sarcoma grown in adult chickens were entirely inactive when injected into even newborn pigeons (2). On the other hand, it was also shown that the Rous virus can be adapted to ducks and other species as well, provided the recipient host be a young or a newborn individual (1, 2) and the donor host be endowed with a certain degree of resistance linked with age (4).

In the present publication, we report the fact that the Rous sarcoma after adaptation to ducks can be easily transferred to pigeons with little or no age limitations on the part of the recipient host. The duck variants of the Rous sarcoma studied were strains HV obtained in 1941 (1), 14(e), and 14(d)7 obtained in 1945 (5), and another duck tumor strain 55(e), the origin of which is rather uncertain. The pigeons employed were of the common varieties found in markets.

Additional attempts to transfer the Rous sarcoma to pigeons. About 15 pigeons, from a few weeks to 4 months of age, were injected in the breast muscles with various amounts of cell suspension and filtrates of the Rous sarcoma from chickens of different ages. Again, no success was achieved. In one case only a tumor nodule 0.3 cm. in diameter was found in the injected site 40 days after inoculation of 2 cc. of cell suspension at 1:5. This tissue grafted into 3 more pigeons induced no growths.

Strain 14(e).—Three pigeons 2 months old were injected in the muscles of each breast with 1 cc. of cell suspension of a duckling tumor of the third passage. Tumors developed which attained a sizable growth after 30 days, but regressed in 2 of the pigeons. The bird bearing the third tumor measuring by now 4 X 3 X 2 cm. was killed 73 days after injection and was passed by means of cell suspensions into 2 other pigeons. Growth followed in 3 with regression in 2 of them.

Strain HV.—At the 42nd passage of the strain, 2 pigeons about 5 months old were injected in each breast with 1 cc. of cell suspension at 1:5. Both animals developed tumors, one of which attained a size of 2.5 X 2.5 X 2 cm., while the other was smaller. The first animal was killed 22 days after inoculation and cell suspensions from the tumor were injected into 2 pigeons, while filtrates were injected into 2 others. The cell suspensions induced growths which were followed by regression, while filtrates were ineffective.

The tumor in the second pigeon remained stationary for several weeks and the bird was killed 3½ months after inoculation. A few small nodules of tumor tissue were still present. A cell suspension of this tissue inoculated into 2 pigeons induced no growth.

The same experiment was repeated with a tumor of the 44th passage of the duck strain and the same results were obtained.

The tumors in pigeons were lobulated, translucent, soft, and viscid, well circumscribed from the adjacent tissues, and they never induced generalized lesions. No microscopic examinations were carried out. The loss of the duck tumor strain prevented further studies.

Strain 55(e).—A brief description of how this strain was obtained has been given elsewhere (3). A cell suspension from a tumor induced in a pigeon by means of methylcholanthrene was inoculated into 4 ducklings with the result that tumors developed rapidly in all the animals injected. These tumors were easily transmitted to other ducklings in 12 successive passages by means of cell suspensions or filtrates. Although on the one hand, strain 55(e) offered many analogies with several

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duck variants of the Rous sarcoma, which, by that time, were kept in the laboratory, on the other hand, it had characteristics of its own, and at the present moment we are unable to state how the strain originated. Of interest in the experiments to be described is the fact that the primary tumors both grossly and microscopically were practically identical to those of strains A, HV, and HC (1).

In 10 different passages in the course of transplantation of this strain, each of 25 pigeons about 6 weeks old was injected in the breast muscles with 1 cc. of cell suspension of the duck tumor grown in young hosts. Growth followed in 17 cases, in 8 of which regression occurred. In 4 other pigeons injected with filtrates, no lesions developed.

The tumors grew at a moderate rate, but steadily, and attained in some cases a size of $6 \times 4 \times 3$ cm. after 2 or 3 months before regression or the death of the host. These tumors in pigeons resembled very much the duck-grown tumors. They were lobulated, translucent, resilient, or soft (Fig. 1). Microscopically they proved to be largely collagenous with many extremely loose areas. However, they were very well circumscribed from the adjacent tissues and generalization never occurred. Death occurred in 3 cases, while in the other cases the pigeons were killed for transplantation or other purposes.

A second passage was attempted on 3 occasions by injecting cell suspensions into other young pigeons. In one instance, growth followed by regression was observed in all of the 4 pigeons inoculated, while no lesions developed in the other two cases. However, the same cell suspensions injected into ducks produced the customary disease with large primary tumors followed by

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FIG. 1.—Tumor induced in 24 days in pigeon injected at age of 6 weeks with cell suspension from duck tumor of strain 55(e).

FIG. 2.—Metastases in lungs, liver, and one rib following primary tumor in 1 year old pigeon injected in breast with cell suspension from duck tumor of strain 14(d17). The bird died 27 days after inoculation.
generalized neoplastic and hemorrhagic lesions, and filtrates of these tumors were also active in other ducks, thus proving that free virus was present in them.

Strain 14(d)7.—At the seventh passage of the strain, 3 pigeons 12 months old were injected in the muscles of each breast with 2 cc. of cell suspension at 1:5 from a large tumor 7 days old grown in a duck 15 days old at death. Growth followed in the 3 pigeons. In one of them the tumor remained stationary for about 3 months and finally regressed. The second pigeon died in 27 days with a rather necrotic but very infiltrating primary tumor filling the whole breast, and hemorrhagic metastases in lungs, liver, and one rib (Fig. 2). Filtrates from the primary tumor of this bird proved ineffective in 4 young pigeons. The third pigeon was killed 14 days after injection. There was a tumor 3 × 3 × 3 cm. in each side of the breast and many minute metastases in the liver. A second passage by cell suspension into 2 pigeons resulted in 2 tumors, one of which regressed. The remaining bird was killed 27 days after injection and was found to have a large, firm tumor wholly free of necrosis. This tumor produced in a third passage a growth followed by regression in 1 of 3 pigeons inoculated with cell suspensions, but filtrates of the same growth induced no tumors in 2 pigeons 6 weeks old. At both the first and second passage a total of 6 ducklings and 2 chicks were inoculated with cell suspensions. Large primary tumors followed by generalization such as is usually found in the routine passage of strain 14(d)7 were induced in all animals.

Another line was started with a duckling tumor at the 21st passage of the tumor strain. In a first passage, 4 pigeons from 2 to 10 months old were injected with 1 cc. of cell suspension in each breast. Growth followed in all, but regressed only in the 10-month-old pigeon. Another of the pigeons died in 15 days with a large breast tumor and no metastases, while the other 2 died in 27 days with large primary tumors and many metastases in the spleen, lungs, and liver. In a second passage, cell suspensions of the tumors of one of these birds and filtrates from the tumors of another were inoculated into 7 pigeons. The cell suspensions produced temporary growths, while the filtrates were ineffective.

Microscopically, both the primary and metastatic tumors derived from strain 14(d)7 kept many of the characteristics present in ducks. The growths, in general, were loose and rather pleomorphic (Fig. 3). Other times they consisted of large cells arranged in a syncytiot fashion and containing many nuclei. Mitoses were rare. The tumors, especially in the first passage, were very invasive—this characteristic being especially conspicuous in the metastases in the liver, lungs, and spleen. Here, the tissues were so diffusely invaded by the large tumor cells that this trait, together with the conspicuous lymphoid and myeloid cell reaction either close to the tumor tissue or distant from it, and the subsequent necrosis and vascular alterations, frequently gave the impression that one was dealing with inflammatory lesions. Some of the tumors of the second passage were almost unrecognizable on account of the heavy cell reaction. Another feature also encountered with tumors derived from strain HV was the presence of tumor nodules consisting of a collagenous matrix from which cells were practically absent.

DISCUSSION

The results described are of interest in what concerns the problem of species-specificity in relation to cell growth. It is well known that no restrictions to progressive growth of alien cells are present in embryos (8), newborn and young individuals (1, 2), or in certain locations of the adult, such as the brain (8) and the anterior chamber of the eye (6, 7). But with the duck variants of the Rous sarcoma here studied the case is entirely different, for tumor cells from strains 14(e), 55(e) and HV grew well locally in the breast of pigeons several months old, and on occasions the tumors thus induced also grew in pigeons in another passage. Results with another variant, strain 14(d)7, were far more interesting. Here, suspensions of tumor cells caused...
fast-growing tumors to develop, followed by widespread metastases and death in pigeons as old as 12 months—the whole picture being one of an extremely malignant disease.

True, these pigeon tumors could not be maintained beyond a second or third passage, and growth in these passages was far less malignant than in the first, but as a long experience on transplanting avian tumors has shown, attempts to obtain stable lines of pigeon tumors have not been numerous enough to justify the conclusion that such lines cannot be obtained.

Concerning the results obtained with strain 14(d)7, one has to keep in mind that this is the most malignant of all avian tumors so far observed.

There would seem to be little doubt that the pigeon tumors, at least to a certain extent, are the result of multiplication of the injected cells, for filtrates of these growths tested under the same conditions as the cell suspensions failed to induce tumors. However, virus was plentiful in the growths as inoculations into ducks proved. Further experiments will show whether filtrates can also be active for pigeons under certain conditions.

SUMMARY

Suspensions of tumor cells of 2 duck variants of the Rous sarcoma and another duck tumor of uncertain origin injected into the breast of pigeons several months old induced local growths never followed by generalization, while tumor cells from another variant induced even in pigeons 12 months old large local growths often followed by generalized metastases and causing death of the host in a few weeks. These tumors have been maintained in 2 or 3 successive passages through pigeons.

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