

## ONCOLOGY

### EXPERIMENTS WITH HETEROGENOUS TRANSPLANTATION OF CHICKEN ROUS SARCOMA INTO DECEREBRATE AND NORMAL PIGEONS

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It is known from the literature that heterogenous transplants of tumorous tissues in adult animals are successful only in isolated instances, while transplanting into closely similar species.

In explaining the immunity of animals to heterogenous tumor transplants much significance is attached to the functional integrity of the reticuloendothelial system of the mesenchyme.

Blocking the reticuloendothelial system of the recipient by using intravenous injections of saccharated ferric oxide [3], splenectomy [7], generalized exposure to x-ray irradiation [19, 20], and even more - combining x-ray irradiation of the animals with introduction of cortisone [20] - reduces the resistance to heterogenous tumor transplants.

Insufficient mesenchymal development has been used to explain the lowered resistance of brain tissue, as well as that of the anterior chamber of the eye and the ovary. The possibility of the growth of heterophil transplants into these tissues has been demonstrated in the work of many authors [2, 4, 5, 8, 10-16, 18, 22].

In the investigations of K. P. Balitsky [1] there was set forth the task of demonstrating the role of the central nervous system in the resistance displayed by the organism to heterophil tumor transplants. To the possibility of growing chicken sarcoma in pigeons there is the testimony of the work by Duran-Reynals [17], who succeeded in growing Rous sarcoma in pigeons after preliminary culture of the tumor in ducks.

On the basis of the literature data indicating that pigeons possess a total resistance at all stages of growth to Rous sarcoma transplants, the authors decerebrated pigeons and after 3-4 weeks attempted to inoculate them with the chicken sarcoma.

In 15 out of 19 decerebrated pigeons, the chicken tumor transplants took root and grew, while in the 28 control pigeons growth occurred in only one. On the basis of this, it was thought that decerebration overcame the resistance of pigeons to chicken sarcoma.

We performed analogous experiments with the transplantation of chicken sarcoma to decerebrated and normal pigeons which led to somewhat different results.

#### EXPERIMENTAL METHODS

Experiments were done on mongrel pigeons - male and female - weighing 250-350 g. In each experimental bird both cerebral hemispheres were extirpated after which the pigeons recovered rapidly and lived when given appropriate care and artificial feeding for a prolonged period of time. Body stability was maintained, somewhat decreased as against the normal; they generally manifested the behavior usual in decerebrate birds.

Afterwards, at various time intervals after extirpation the Rous sarcoma was inoculated.\*

The characteristics of the sarcoma obtained may be summarized as follows.

The tumor, growing at site of inoculation, develops very rapidly from the acellular filtrate used. We continuously maintained it by transplanting every 10-11 days into the chest muscles of a chicken. Microscopic examination of the tumor established that it — a sarcoma of marked invasive ability — consists of spindle cells with rather comparatively large hyperchromic nuclei. The cells are polymorphic, scattered in rather irregular clumps, possessing a barely visible fibrillar structure. There are large areas of necrosis and necrobiosis; only in the infiltrating zone of a growth among the separating muscle fibers is there a rich cellular growth, lying tightly packed together. Within the areas of necrosis and at their borders there is marked edema and hemorrhagic infiltration. In places there is seen a rich vascular network packed with erythrocytes.

We injected 1 cc of the tumor (10-11 day old chicken sarcoma dissolved in physiological saline) into the right breast muscle of the pigeon in the thickest portion. Both the experimental and control pigeons were inoculated at the same time.

After this was done, observations were made on the appearance and rate of growth of the tumor.

In 3-4 weeks the experimental and control pigeons were sacrificed and autopsies gave macroscopic evidence of the rate of tumor development.

Altogether three series of observations were made.

In the 1st experimental series the tumors were inoculated on the 3rd postoperative day, in the 2nd series on the 24th and in the 3rd series on the 70th day after operation.

#### EXPERIMENTAL RESULTS

Observations on the experimental (decerebrate) and control (normal) inoculated pigeons showed that the culture used in our experiments, when inoculated, is capable of implantation and growth both in the decerebrate and normal pigeons. In approximately 70% of cases in both experimental and controls within 2-2½ weeks of inoculation the birds manifested at the site of tumor inoculation additional swelling which gradually enlarged and reached a maximum within 3½ - 4 weeks.

In pigeons killed at this time, we observed tumors of varying size, of a rather white color, solid, frequently demarcated from the surrounding muscle, sometimes infiltrating into it. In pigeons permitted to survive longer, the tumors gradually decreased and after an interval of one and one-half to two months would disappear; on autopsy the tumor could either not be seen at all or was observed as a small autolyzing, dissolving bit of tissue. In 24 control (normal) pigeons, into whom the chicken sarcoma had been inoculated, only one had a significant swelling by the 29th day.

Among 25 experimental pigeons not one death was caused by tumor growth; in addition, the size of the tumor in the experimental pigeons was less than in the control (see Figure), which must be due to the lowered metabolism after decerebrate surgery, since general nutrition is important in tumor growth as experimental oncology has shown.

The tumor inoculations in the controls showed vigorous growth in all three series of experiments.

Pigeons were sacrificed on the 27th and 30th day after transplantation.

Results of experiments (see Table) show that tumor growth was manifest in 18 of 25 pigeons, or 72%. The tumor did not take in 7 birds.

In the control (normal) pigeons the tumor took in 18 cases also out of 24, constituting 75%, not taking in 6 birds. Therefore, the percent of take in both groups was the same. Grouping the ill pigeons by size of take (experimental and control) into four subdivisions (see Table) gives parallel results to all practical purposes. It can be concluded, then, that antecedent decerebration has no influence on the degree of take or growth of these tumors.

\*The culture of the sarcoma was received from the laboratory under the supervision of the Active Member Acad. Med. Sci. USSR Prof. L. A. Zilber.



Rous sarcoma in pigeons. On left - experimental bird, on right - control. They were sacrificed on the 29th day after inoculation.

Influence of Decerebration on Heterophil Take of Rous Chicken Sarcoma

Experiments	No. of pigeons	Day after decerebration when tumor was inoculated	Day after inoculation when bird was sacrificed	Results of take		Size of swelling			
				yes	no	great	medium	small	resolved
Series No. 1									
Experimental	7	3	27	4	3	2	1	1	—
Control	7	—	27	4	3	3	1	—	—
Series No. 2									
Experimental	10	24	30	7	3	4	—	1	2
Control	9	—	30	7	2	3	1	2	1
Series No. 3									
Experimental	8	70	24	7	1	2	3	1	1
Control	8	—	24	7	1	3	3	—	1
Results: Experimental									
Control	25			18	7	8	4	3	3
	24			18	6	9	5	2	2

Histological studies of the tumors in the decerebrate and control pigeons revealed the infiltrating nature of this spindle-cell sarcoma. The tumor cells are polymorphic, containing large vacuolated nuclei, clearer when compared with the nuclei of chicken sarcoma. Along with this, large areas fail to show infiltrating growth, there being a preponderance of demarcation from the surrounding muscle tissue. At the border between tumor and muscle there are foci and even belts of plasma and lymphocytes. There are areas of necrosis and necrobiosis with a hemorrhagic infiltrate; in places, vessels are filled with erythrocytes.

In this way, there has been demonstrated a morphological similarity between the chicken sarcoma used in our work and the tumors growing in the pigeons, there being a tendency to their spontaneous resolution as manifested by their tendency to a diminishing infiltrative growth and a tendency for lymphocytes and plasmacytes to collect around the tumor.

Attempts to transfer the tumor into healthy pigeons were unsuccessful.

From the above considerations, it follows that in questions of immunity and final disposition of tumor transplants, it is of importance to consider the state of health of the organism and its resistance to transplantation of stem tumors, as growth will frequently not occur even within the same species but of a different strain.

Among the malignant, similar fowl tumors there exist variations, such as in regard to morphological form and biological qualities; in part they may be differentiated by their ability to resist acellular filtrates either by their eventual absorption or total rejection [16].

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\*In Russian.