

# CHANGES IN THE BIOLOGICAL PROPERTIES OF THREE TRANSPLANTABLE TUMORS WHEN INOCULATED SIMULTANEOUSLY DURING PASSAGE THROUGH INBRED MICE

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In the course of passage of 3 transplanted tumors through inbred mice, we transplanted all 3 tumors into the same animal. By means of this method we were able to compare the rate of growth and to study the effect of the tumors on each other from one passage to the next.

## EXPERIMENTAL METHOD

Three mouse tumors were studied: Ehrlich's adenocarcinoma, Crocker sarcoma, and acridine sarcoma. Ehrlich's carcinoma was inoculated into the left side of the neck, Crocker's sarcoma under the skin of the right flank, and the acridine sarcoma under the skin of the left flank. This order of inoculation was adhered to constantly. Passage was carried out every 15-18 days into mice of line A. When this time had elapsed, all the tumors were excised in toto, weighed, and then transplanted into the next animals. Ten mice of the same sex, weight, and age were used for each passage.

## EXPERIMENTAL RESULTS

In the first passages all the tumors grew equally well. Starting with the 15th-18th passage, a perceptible difference appeared in the rate of growth: the development of Ehrlich's adenocarcinoma was slowed and its weight gradually began to fall behind that of the Crocker's and acridine sarcomas (Table 1).

We know from the literature [1] that the rate of growth of tumors is greatly influenced by the site of inoculation and by the innervation of that part of the body. We accordingly modified the scheme of passage and began to transplant the Ehrlich's adenocarcinoma into the place of the acridine sarcoma or the Crocker's sarcoma. The experiments showed that this had no effect on the rate of growth of the tumors; the growth of the Ehrlich's adenocarcinoma was retarded still more strongly, and ultimately, at the 33rd passage, it ceased to be transplantable.

The experiments were repeated. The same tumors were again taken and we started their passage through inbred mice of line A. The scheme according to which they were inoculated simultaneously into the same mouse remained as before, except that in a parallel series we began to determine the rate of growth of the same tumors by transplantation singly into mice. Each tumor was transplanted into the same place as when the 3 tumors were transplanted at the same time. We found that the previous results were repeated. Starting with the 20th passage the rate of growth of the Ehrlich's adenocarcinoma began to fall appreciably by comparison with that of the other two tumors, and after the 42nd passage it ceased to be transplantable. However, the results of the experiments in which each tumor was transplanted separately did not agree with these findings. Ehrlich's adenocarcinoma developed much better than when the 3 tumors were transplanted simultaneously. Nevertheless, its growth was appreciably retarded by comparison with the ordinary transplantation of the tumor before passage (Table 2).

The facts described above suggest that when 3 tumors was transplanted simultaneously into the same recipient, definite immunological relationships are formed between them. It cannot be regarded as fortuitous that growth of Ehrlich's adenocarcinoma was depressed, for the passage of the tumors was repeated twice. Nor, in this case, can we speak of the importance of the site of inoculation, for when this was altered it had no effect on the development of the tumor.

TABLE 1. Weight of Tumors (in mg) at the 1st and 20th Passages when Inoculated Simultaneously into the Same Animal

Mouse No.	1st passage			20th passage		
	Ehrlich's carci- noma	Crocker's sarcoma	acridine sarcoma	Ehrlich's carci- noma	Crocker's sarcoma	acridine sarcoma
1	1 230	1 450	1 560	200	1 360	1 250
2	1 210	1 340	690	370	720	1 360
3	420	870	1 320	60	1 280	980
4	1 400	1 230	870	80	1 130	750
5	1 380	1 400	890	90	680	860
6	1 200	1 120	1 400	140	930	420
7	560	680	1 200	210	870	1 180
8	670	920	1 320	20	1 440	1 520
9	630	490	1 280	30	900	1 200
10	1 450	480	580	50	930	1 180
Total	10 150	9 980	11 010	1 250	10 240	10 700
Average weight	1 015	998	1 101	125	1 024	1 070

TABLE 2. Weight of Tumors (in mg) at the 1st and 25th Passages when Inoculated Separately into Animals

Mouse No.	1st passage			25th passage		
	Ehrlich's carci- noma	Crocker's sarcoma	acridine sarcoma	Ehrlich's carci- noma	Crocker's sarcoma	acridine sarcoma
1	1 300	1 480	1 300	420	1 250	980
2	740	1 320	1 280	380	1 350	990
3	880	1 220	790	450	1 400	1 200
4	1 200	980	680	450	990	1 400
5	1 000	870	1 010	420	970	720
6	560	620	1 450	370	640	780
7	670	530	820	420	580	820
8	720	500	560	540	600	620
9	730	690	580	390	720	860
10	800	810	690	350	780	870
Total	8 600	9 020	9 160	4 190	9 280	9 240
Average weight	860	902	916	419	928	924

In a paper by Andervont [2], who studied the natural resistance of different lines of mice to the transplantation of tumors, it is reported that the serial passage of transplanted tumors (sarcomas 180 and 37) in mice of the same line (in particular, line D) has a definite effect on their capacity for growth in other strains of mice. Many authors emphasize that a change in the rate of growth depends on an increase in the virulence of the tumors during passage, by which the tumor may be transplanted successfully in the line through which it has been taken by passage, but loses its ability to grow in its original conditions. In our experiments, on the other hand, the Ehrlich's adenocarcinoma lost its virulence during the prolonged passage of the 3 tumors simultaneously through mice of line A. Meanwhile the passage of this one tumor alone resulted in only a slight decrease in its virulence.

It is thus quite obvious that a change took place in the biological properties of the Ehrlich's adenocarcinoma, in the form of a lowering of its virulence during passage through line A mice. It may be postulated that during the

development of 3 tumors simultaneously in the same animal, each has a mutual biological effect on the others. In particular, Crocker's sarcoma and the acridine sarcoma depress the growth of Ehrlich's adenocarcinoma. Two factors are evidently important here: the biological interrelationships between different types of tumors growing in the same animal, and the natural resistance of mice of line A to the strain of Ehrlich's adenocarcinoma. This tumor is known to be nonstrain-specific, and it grows successfully in different lines. However, by prolonged passage it was possible to detect some biological properties of the tumor which hitherto had passed unobserved.

#### LITERATURE CITED

1. O. I. Epifanova, Byull. Éksper. Biol., 11, 55 (1956).
2. H. B. Andervont Pub. Health. Rep., 52, 1885-1895 (1937).

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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