THE DURATION AND EXTENT OF INDUCED RESISTANCE TOWARD TUMOR TRANSPLANTATION IN MICE.*

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The extent and duration of the resistance which various tissues are able to evolve against the implantation of tumors has not yet been systematically examined and compared. The most complete experiments so far recorded in the literature are those of Ehrlich[1] which, however, concern themselves only with the immunity produced by tumors. Resistance was discovered from seven to fourteen days after the unsuccessful inoculation of spontaneous growths, and persisted for weeks or even months, while the immunity produced by transplantable tumors was distinct at the ninth day, and remained high for at least three months.

Bashford,[2] in discussing the resistance present after spontaneous absorption of Jensen's mouse tumor, said that it continued for at least six months.

As for the rat, Uhlenhuth, Haendel, and Steffenhagen[3] found that resistance was present for at least six weeks after the absorption of a spindle cell sarcoma, while Flexner and Jobling[4] estimated that the refractory condition initiated by the absorption of an adenocarcinoma was reduced by the mere lapse of time, but persisted for at least ninety days.

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[1] Ehrlich, P., *Ztschr. f. ärztl. Fortbild.*, 1906, iii, 211; *Arb. a. d. k. Inst. f. exper. Therap. zu Frankfurt*, 1906, No. 1, 90, 97.

[2] Bashford, E. F., *Brit. Med. Jour.*, 1906, ii, 209.

[3] Uhlenhuth, Haendel, and Steffenhagen, *Centralbl. f. Bakteriol., Ref., 1te Abt.*, 1910, xlvii, Suppl., 164.

[4] Flexner, S., and Jobling, J. W., *Monographs of The Rockefeller Institute for Medical Research*, 1910, No. 1, 54.

Bridré[5] investigated the resistance produced in mice by unsuccessful tumor inoculation, as well as that entailed by treatment with normal tissue, and concluded that it might endure for five months or more. That attendant upon the inoculation of mouse blood appeared after four days, according to Bashford, Murray, and Cramer,[6] but was more distinct after ten days, and continued for at least three weeks. In the experiments of Russell,[7] embryo mouse skin required twenty days to elicit the full refractory condition.

The occurrence of spontaneous tumors in mice which have become immune through unsuccessful tumor inoculation, as reported by Bashford, Murray, and Cramer,[8] Thorel,[9] and Clunet,[10] possesses a certain subsidiary interest in its relations to the duration of immunity. The sporadic growths recorded by these investigators occurred from ten days to nine months after immunization, but as the average duration of induced resistance is only three months, according to the authors previously cited, it may be questioned whether the refractory condition was still in existence in those mice which developed spontaneous tumors more than that length of time after immunization. Since, however, the conditions essential for the inception of malignant growth are in all probability distinct from those necessary for its continuation, as Bashford has repeatedly emphasized, the question whether or not tumors have ever arisen in artificially immunized mice can hardly be of more than academic interest, except in so far as it touches the hypothesis which would ascribe cancer to the invasion and growth of an exogenous cell.

[5] Bridré, J., *Ann. de l'Inst. Pasteur,* 1907, xxi, 773.

[6] Bashford, E. F., Murray, J. A., and Cramer, W., *Proc. Roy. Soc., Series B,* 1907, lxxix, 180; *Third Scientific Report of the Imperial Cancer Research Fund,* 1908, 333.

[7] Russell, B. R. G., *Third Scientific Report of the Imperial Cancer Research Fund,* 1908, 345.

[8] Bashford, E. F., Murray, J. A., and Cramer, W., *Third Scientific Report of the Imperial Cancer Research Fund,* 1908, 171, 322; Bashford, E. F., Murray, J. A., and Haaland, M., *ibid.,* 396.

[9] Thorel, *Verhandl. d. deutsch. path. Gesellsch.,* 1908, xii, 60.

[10] Clunet, J., Recherches expérimentelles sur les tumeurs malignes, Paris, 1910, 24.

EXPERIMENTAL PART.

The experiments about to be described are directed toward a contrast of the immunizing power of propagated growths and spontaneous tumors, all adenocarcinomata of the mouse and most of them hemorrhagic, with that of normal tissue, the latter represented by kidney or embryo skin. The immunizing dose of tumor, kidney, or embryo skin, except in the case of transplantable carcinoma 206, where 0.03 of a cubic centimeter was given, was 0.05 of a cubic centimeter of an emulsion, which was deposited in the left axilla by means of a syringe. The testing inoculation of tumor took place in the right axilla after an appropriate interval had elapsed, there being employed for this purpose carcinomata T and 91, each significant for its large percentage of takes, its uniform and progressive growth, and its inability to induce concomitant immunization. The inoculation yield with carcinoma T was estimated twenty-four days after inoculation, but with carcinoma 91 seventeen days, because of the more rapid growth of this tumor. On account of the proliferative activity of these two growths, it rarely happens that by the second or third charting the nodules are still so small as to render difficult an estimation of the result, and less than a dozen animals, therefore, among the sixteen hundred odd comprised in the experiment, had to be discarded because the outcome was doubtful. The small number of mice which died before the final charting were included if death had been postponed long enough to allow a definite decision to be reached. Otherwise they were eliminated from the experiment, as were those few in which the spontaneous growth employed for immunization had succeeded in gaining a foothold. All the mice used for controls were of the same age as the immunized animals, and were in every instance taken from the same batch and kept under identical conditions until the time for inoculation arrived.

The curves which follow show the degree of immunity as it was revealed at stated intervals. The ratio between the negative mice and the total number of mice in each group, expressed as a percentage, is taken as representing the extent of resistance, and the curves are, therefore, the obverse of those usually published to set forth the proportion of successful inoculations. The details upon which

they are founded are appended in a series of tables numbered to correspond with the charts (tables I to VI).

TABLE I.

Immunizing material.	Interval.	Testing inoculation.	Proportion of negatives.	Per cent. of immunity.
Embryo skin 0.05 c.c.	5 days.	*T*/36*B* 0.01 c.c.	8/13	61
Tumor 614 0.05 c.c.....	5 days.	*T*/36*B* 0.01 c.c.	1/13	8
Control (untreated).....		*T*/36*B* 0.01 c.c.	2/16	12
Embryo skin 0.05 c.c.	10 days.	*T*/34*I* 0.01 c.c.	17/17	100
Tumor 541 0.05 c.c.....	10 days.	*T*/34*I* 0.01 c.c.	7/9	78
Control (untreated).....		*T*/34*I* 0.01 c.c.	2/15	13
Embryo skin 0.05 c.c.	17 days.	*T*/35*A* 0.01 c.c.	16/17	94
Tumor 556 0.05 c.c.....	17 days.	*T*/35*A* 0.01 c.c.	7/23	30
Control (untreated).....		*T*/35*A* 0.01 c.c.	3/15	20
Embryo skin 0.05 c.c.	21 days.	*T*/35*C* 0.01 c.c.	18/19	95
Tumor 555 0.05 c.c.....	21 days.	*T*/35*C* 0.01 c.c.	3/14	21
Control (untreated).....		*T*/35*C* 0.01 c.c.	3/17	18
Embryo skin 0.05 c.c.	24 days.	*T*/34*G* 0.01 c.c.	19/19	100
Tumor 534 0.05 c.c.....	24 days.	*T*/34*G* 0.01 c.c.	3/18	17
Control (untreated).....		*T*/34*G* 0.01 c.c.	4/16	25
Embryo skin 0.05 c.c.	31 days.	*T*/34*H* 0.01 c.c.	5/11	45
Tumor 534 0.05 c.c.....	31 days.	*T*/34*H* 0.01 c.c.	2/17	12
Control (untreated).....		*T*/34*H* 0.01 c.c.	1/15	7
Embryo skin 0.05 c.c.	38 days.	*T*/34*J* 0.01 c.c.	13/17	76
Tumor 540 0.05 c.c.....	38 days.	*T*/34*J* 0.01 c.c.	3/17	18
Control (untreated).....		*T*/34*J* 0.01 c.c.	0/14	0
Embryo skin 0.05 c.c.	50 days.	*T*/41*D* 0.01 c.c.	15/24	62
Tumor 635 0.05 c.c.....	50 days.	*T*/41*D* 0.01 c.c.	10/27	37
Control (untreated).....		*T*/41*D* 0.01 c.c.	4/24	17
Embryo skin 0.05 c.c.	75 days.	*T*/44*E* 0.01 c.c.	7/28	25
Tumor 687 0.05 c.c.....	75 days.	*T*/44*E* 0.01 c.c.	4/23	17
Control (untreated).....		*T*/44*E* 0.01 c.c.	0/21	0

Although the configuration of the curves is of interest, showing as it does the rise and fall of resistance, these do not lend themselves for the exact mathematical analysis to which Ehrlich, and Arrhenius and Madsen have subjected their own curves illustrating the course of immunity in general. This is because, in the first place, the outcome of tumor inoculation, even when it is undertaken in normal untreated animals, is variable. Furthermore, it is not possible to read the result immediately, as it is in experiments which concern themselves with hemolysins, precipitins, or other bodies in-

TABLE II.

Immunizing material.	Interval.	Testing inoculation.	Proportion of negatives.	Per cent. of immunity.
Embryo skin 0.05 c.c.	5 days.	*T*/38*C* 0.01 c.c.	10/16	62
Tumor 665 0.05 c.c.....	5 days.	*T*/38*C* 0.01 c.c.	14/20	70
Control (untreated).....		*T*/38*C* 0.01 c.c.	3/18	17
Embryo skin 0.05 c.c.	10 days.	*T*/36*A* 0.01 c.c.	11/12	92
Tumor 550 0.05 c.c.....	10 days.	*T*/36*A* 0.01 c.c.	17/18	94
Control (untreated).....		*T*/36*A* 0.01 c.c.	1/14	7
Embryo skin 0.05 c.c.	17 days.	*T*/36*D* 0.01 c.c.	20/24	83
Tumor 587 0.05 c.c.....	17 days.	*T*/36*D* 0.01 c.c.	6/20	30
Control (untreated).....		*T*/36*D* 0.01 c.c.	0/12	0
Embryo skin 0.05 c.c.	21 days.	*T*/35*D* 0.01 c.c.	9/12	75
Tumor 533 0.05 c.c.....	21 days.	*T*/35*D* 0.01 c.c.	4/9	44
Control (untreated).....		*T*/35*D* 0.01 c.c.	0/8	0
Embryo skin 0.05 c.c.	24 days.	*T*/39*B* 0.01 c.c.	16/19	84
Tumor 521 0.05 c.c.....	24 days.	*T*/39*B* 0.01 c.c.	8/20	40
Control (untreated).....		*T*/39*B* 0.01 c.c.	2/22	9
Embryo skin 0.05 c.c.	31 days.	*T*/36*B* 0.01 c.c.	10/13	77
Tumor 541 0.05 c.c.....	31 days.	*T*/36*B* 0.01 c.c.	6/11	54
Control (untreated).....		*T*/36*B* 0.01 c.c.	3/11	27
Embryo skin 0.05 c.c.	38 days.	*T*/37*B* 0.01 c.c.	7/9	78
Tumor 549 0.05 c.c.....	38 days.	*T*/37*B* 0.01 c.c.	2/14	14
Control (untreated).....		*T*/37*B* 0.01 c.c.	2/17	12
Embryo skin 0.05 c.c.	50 days.	*T*/43*Q* 0.01 c.c.	10/17	59
Tumor 711 0.05 c.c.....	50 days.	*T*/43*Q* 0.01 c.c.	7/23	30
Control (untreated).....		*T*/43*Q* 0.01 c.c.	0/18	0
Embryo skin 0.05 c.c.	75 days.	*T*/45*A* 0.01 c.c.	15/27	55
Tumor 697 0.05 c.c.....	75 days.	*T*/45*A* 0.01 c.c.	4/14	28
Control (untreated).....		*T*/45*A* 0.01 c.c.	7/30	23

TABLE III.

Immunizing material.	Interval.	Testing inoculation.	Proportion of negatives.	Per cent. of immunity.
Embryo skin 0.05 c.c.	3 days.	91/37*B* 0.02 c.c.	4/23	17
Control (untreated).....		91/37*B* 0.02 c.c.	0/19	0
Embryo skin 0.05 c.c.	5 days.	91/37*D* 0.02 c.c.	14/20	70
Control (untreated).....		91/37*D* 0.02 c.c.	0/18	0
Embryo skin 0.05 c.c.	10 days.	91/37*C* 0.02 c.c.	18/23	78
Control (untreated).....		91/37*C* 0.02 c.c.	0/24	0
Embryo skin 0.05 c.c.	17 days.	91/37*G* 0.02 c.c.	22/23	96
Control (untreated).....		91/37*G* 0.02 c.c.	1/25	4

TABLE IV.

Immunizing material.	Interval.	Testing inoculation.	Proportion of negatives.	Per cent. of immunity.
Embryo skin 0.05 c.c.	3 days.	91/38*D* 0.02 c.c.	4/18	22
Control (untreated)		91/38*D* 0.02 c.c.	0/18	0
Embryo skin 0.05 c.c.	5 days.	91/38*F* 0.02 c.c.	10/17	59
Control (untreated)		91/38*F* 0.02 c.c.	2/16	12
Embryo skin 0.05 c.c.	10 days.	91/37*F* 0.02 c.c.	19/23	83
Control (untreated)		91/37*F* 0.02 c.c.	3/22	14
Embryo skin 0.05 c.c.	17 days.	91/38*C* 0.02 c.c.	12/14	86
Control (untreated)		91/38*C* 0.02 c.c.	2/19	10

TABLE V.

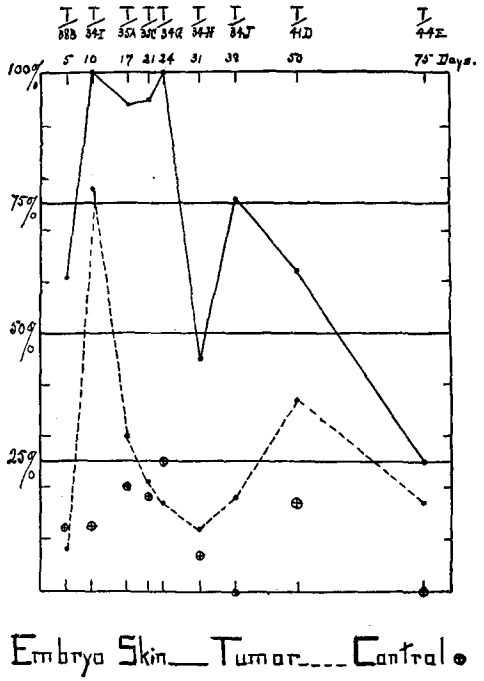
Immunizing material.	Interval.	Testing inoculation.	Proportion of negatives.	Per cent. of immunity.
Kidney 0.05 c.c.	5 days.	*T*/41*F* 0.01 c.c.	5/15	33
Control (untreated)		*T*/41*F* 0.01 c.c.	1/20	5
Kidney 0.05 c.c.	10 days.	*T*/41*G* 0.01 c.c.	14/21	67
Control (untreated)		*T*/41*G* 0.01 c.c.	2/24	8
Kidney 0.05 c.c.	17 days.	*T*/40*A* 0.01 c.c.	7/10	70
Control (untreated)		*T*/40*A* 0.01 c.c.	0/12	0
Kidney 0.05 c.c.	21 days.	*T*/42*A* 0.01 c.c.	9/21	43
Control (untreated)		*T*/42*A* 0.01 c.c.	3/21	14
Kidney 0.05 c.c.	24 days.	*T*/42*D* 0.01 c.c.	10/21	48
Control (untreated)		*T*/42*D* 0.01 c.c.	2/18	11
Kidney 0.05 c.c.	31 days.	*T*/43*O* 0.01 c.c.	10/20	50
Control (untreated)		*T*/43*O* 0.01 c.c.	3/24	12
Kidney 0.05 c.c.	38 days.	*T*/42*H* 0.01 c.c.	7/24	29
Control (untreated)		*T*/42*H* 0.01 c.c.	2/18	11
Kidney 0.05 c.c.	50 days.	*T*/43*G* 0.01 c.c.	11/35	31
Control (untreated)		*T*/43*G* 0.01 c.c.	5/31	16
Kidney 0.05 c.c.	75 days.	*T*/43*I* 0.01 c.c.	6/15	40
Control (untreated)		*T*/43*I* 0.01 c.c.	3/20	15

TABLE VI.

Immunizing material.	Interval.	Testing inoculation.	Proportion of negatives.	Per cent. of immunity.
Tumor 206 0.03 c.c.	12 and 80 days.	63/56*D* 0.02 c.c. and *T*/43*L* 0.01 c.c.	11/11 3/11	100 27
Control (untreated)		63/56*D* 0.02 c.c. and *T*/43*L* 0.01 c.c.	1/11 2/12	9 17

cluded in the province of the immunologist. On the contrary, there is interpolated between the testing inoculation and the ultimate estimation of the amount of resistance the length of time which is necessary for the tumors to obtain measurable proportions.

Text-figure 1 represents the onset and diminution of the immunity following the injection of embryo skin or spontaneous tumor. Even after five days there is resistance in something over



TEXT-FIG. 1. Curves showing the extent and duration of the resistance induced in mice with embryo mouse skin and spontaneous adenocarcinomata of the mammary gland of the mouse, respectively.

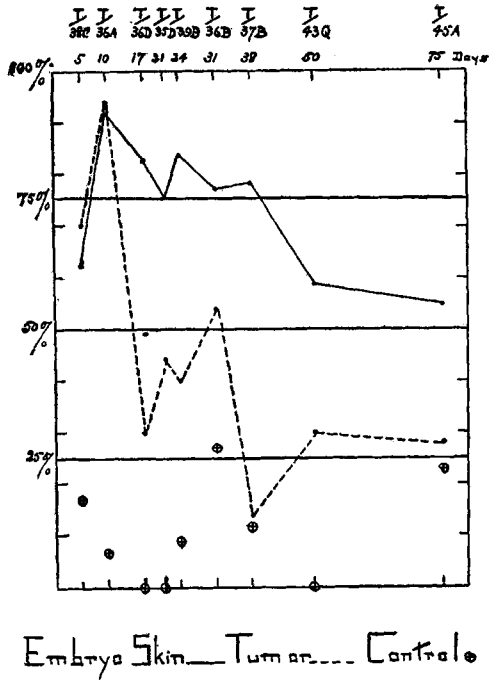
60 per cent. of the mice treated with embryo skin, while by the tenth day this immunity has risen to 100 per cent. Remaining at a high level until the twenty-fourth day, it then falls, until, at the seventy-fifth, it has reached 25 per cent., where it may be said practically to have vanished, since it falls within the resistance displayed by the control animals. The sharp drop at the thirty-first day is probably inside that margin of error for which allowance must be made in

biological experiments. By contrasting with this curve that which reproduces the immunity evolved by spontaneous tumors, it will be appreciated that the latter does not reach the high level attained by the former, and that it drops more rapidly. Why this should be so with spontaneous tumors, and, as will be seen later, also in the case of the kidney, is not clear. To ascribe it to the more rapid absorption of these two tissues in contrast to that obtaining with embryo skin, would be to refer immunity to the absorption of tissue. How unwarrantable this assumption may be, however, is suggested by the fact that animals with growing tumors in large part necrotic are not necessarily rendered resistant, although absorption of tissue may perfectly well be postulated; and that the failure of the absorbed material to produce immunity in such mice is not to be explained by the presence of a malignant growth is shown by the recent work of Russell,[11] who succeeded in conferring resistance even in the presence of a progressively growing transplanted tumor. For the present, then, one must be content merely to state that the resistance aroused by spontaneous tumor and by kidney is neither so intense nor of such long duration as that following treatment with embryo skin. The fact that the curve descends to a point where it is below the immunity exhibited by some of the controls, and rises again after having reached its lowest limit at the thirty-first day, is to be referred to experimental error. It is probable that under ideal conditions the immunity would disappear gradually, reaching 25 per cent. at about the fiftieth day.

Text-figure 2, depicting the outcome which ensued upon a duplication of the experiment under exactly parallel conditions, shows again the smaller degree of immunity evolved with spontaneous tumors as contrasted with embryo skin. The curve representing the immunizing power of embryo skin is, on the whole, a more level one, but suggests that more than seventy-five days may be required for the complete disappearance of the resistance following preliminary treatment with this material. Nevertheless, with an animal which, like the mouse, lives but a trifle more than two years, it would be injudicious to attempt an extension of the time element in

[11] Russell, B. R. G., *Fifth Scientific Report of the Imperial Cancer Research Fund,* 1912, 1.

such experiments as these, because mice which are immunized when they are about two months old have, at the expiration of seventy-five days, reached four months and a half, an age at which the comparative resistance displayed by older animals is likely to become a disturbing factor.

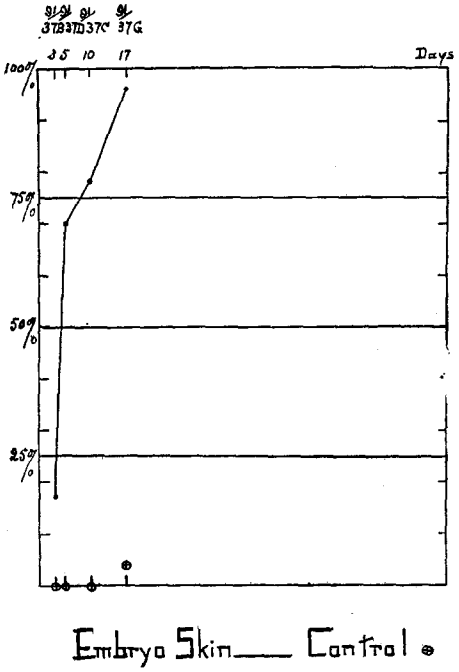


TEXT-FIG. 2. Curves showing the extent and duration of the resistance induced in mice with embryo mouse skin and spontaneous adenocarcinomata of the mammary gland of the mouse, respectively.

Because the rapid rise of the curve on these two charts might have been a result of the rather slow growth of adenocarcinoma T, and might not, therefore, correspond exactly with the rate at which resistance would develop against a tumor capable of establishing itself with more celerity, the first part of the experiment was twice repeated with adenocarcinoma 91, a neoplasm of such rapid proliferative energy as to yield within two weeks an amount of tissue varying between two and three grams, and this from an initial dose

of 0.02 of a cubic centimeter of emulsion. However, as text-figures 3 and 4 demonstrate, the curve is almost equally abrupt, and about 80 per cent. of immunity is obtained by the tenth day.

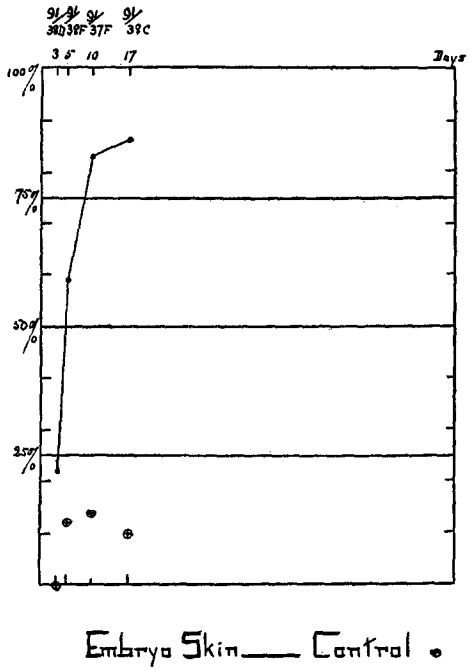
The salient feature in these two latter curves is the very rapid rise between the third and fifth days, a demonstration that within a period of but forty-eight hours the resistance has jumped from



TEXT-FIG. 3. Curve showing the abrupt rise of the resistance induced by embryo skin.

about 20 per cent. to 60 or 70 per cent. For this occurrence there are two possible explanations. As has been already pointed out, it is not possible to measure the amount of immunity actually present at the moment when the tumor was inoculated. Now, while the curves show that there is from 60 to 70 per cent. of resistance by the fifth day, this cannot be taken to mean that each of the mice in the experiment was from 60 to 70 per cent. immune, for it demonstrates, on the contrary, merely that six or seven mice out of ten

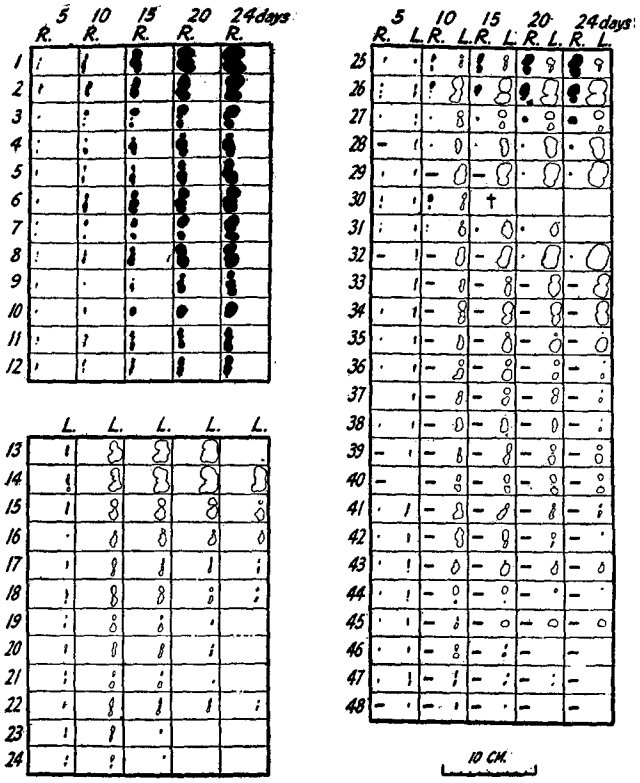
were immune. The two explanations turn upon the question whether the animals were partially or wholly immune. The first would assume that immunity was complete in 60 or 70 per cent. of the animals, and would state that this number of mice had become so resistant within five days after treatment as never to allow the tumor to gain a foothold at all. The second explanation, on the other hand, would suggest that the negative mice had not been



TEXT-FIG. 4. Curve showing the abrupt rise of the resistance induced by embryo skin.

absolutely resistant at the time of inoculation, but that a part of the refractory condition with which they were endowed had been conferred in the few days following the testing inoculation of tumor, to become operative against the graft several days after its introduction. As is well known, malignant cells upon their introduction into a new host force the tissues to provide them with a connective tissue scaffolding as well as a capillary blood supply, and this within

the first two or three days supervening upon their inoculation. The explanation now under discussion requires for its support, therefore, the subsidiary assumption that induced immunity may be valid even against a graft which is partially, or perhaps completely, vascu-

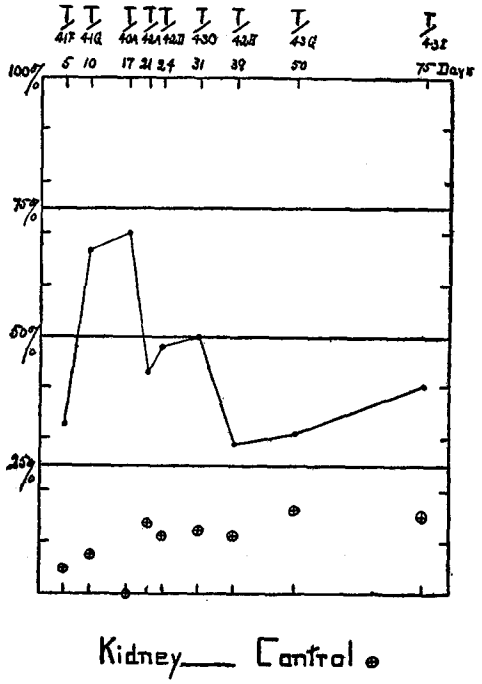


TEXT-FIG. 5. One tumor may immunize against a second, even though the two be implanted at the same time. Control mice 1 to 12 were inoculated with 0.01 c.c. of carcinoma 63, a tumor which does not immunize the host during its growth, while control mice 13 to 24 were injected with 0.01 c.c. of sarcoma 37, which does produce concomitant immunization. Mice 25 to 48 were inoculated simultaneously in the right and left axillæ with 0.01 c.c. of carcinoma 63 and sarcoma 37, respectively. Tumor 37 has been able to prevent the growth of 63.

Carcinoma 63 = black silhouette; sarcoma 37 = outline.

larized. That such a hypothesis cannot be categorically rejected is clear from the above chart (text-figure 5) accompanying Russell's article. It shows that a sarcoma endowed with the power of

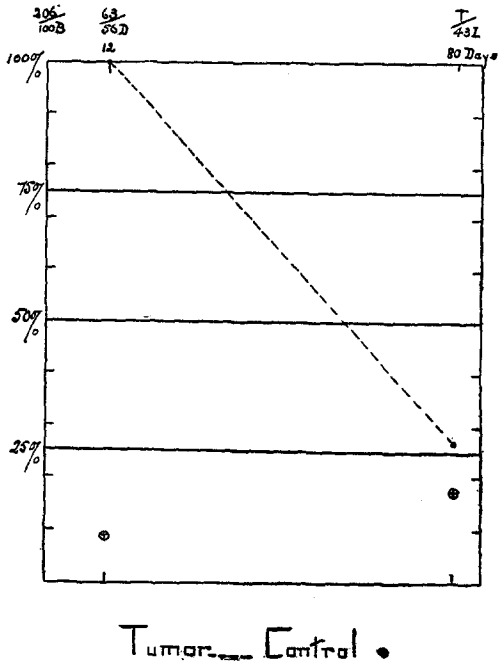
producing the refractory condition is able to do so against a carcinoma capable, under normal circumstances, of progressive growth, if the two be inoculated simultaneously; the author states, furthermore, that a certain carcinoma was discovered to be possessed of similar powers. For the present purpose, both tumors may be considered merely as mouse tissue able rapidly to evolve the refractory condition. As the carcinoma which was suppressed in Russell's



TEXT-FIG. 6. Curve showing the extent and duration of the resistance induced in mice by mouse kidney.

experiment had probably become vascularized by the third day after implantation, and as there is but little or no resistance present at this time according to text-figures 3 and 4, it is not improbable that immunity may be able to defeat a graft which has but recently become established. One accordingly inclines to accept the second explanation as the more satisfactory, reserving its application, however, to the first few days in the history of the graft, and to the

critical period between the third and fifth days when immunity is rising rapidly. This explanation does not nullify the objection brought forward in a previous paper[12] against confounding grafts which perish immediately in animals that have been immune for ten days or more, with those able to proliferate for a time before they are finally vanquished.



TEXT-FIG. 7. Curve showing the rate of disappearance of the resistance induced in mice by a transplantable carcinoma which undergoes spontaneous absorption in a large number of animals. These mice were relieved by operation of carcinoma 206, eleven days after inoculation, and on the following day were tested with carcinoma 63. Eighty days after the inoculation of 206, they were tested with carcinoma T. The controls were normal mice.

Text-figure 6 shows the extent and duration of the resistance resulting from immunization with kidney. The immunity does not occupy the high level attained by embryo skin, but more nearly approximates the curve for spontaneous tumor. It is more than

[12] Woglom, W. H., *Fifth Scientific Report of the Imperial Cancer Research Fund*, 1912, 43.

probable that, instead of rising, the curve would continue to fall after the thirty-eighth day, were exact conditions capable of attainment.

In order to test the duration of the refractory condition conferred by a transplantable tumor, certain mice which had been relieved by operation of carcinoma 206 (a growth producing a high degree of immunity) eleven days after its inoculation and of which 100 per cent. had proven themselves capable of resisting implantation with adenocarcinoma 63 on the day following operation, were inoculated with adenocarcinoma T eighty days from the beginning of the experiment. At this time, as text-figure 7 shows, the immunity had fallen to 27 per cent., at which point, allowing for experimental error, it may be said practically to have vanished. It is highly improbable that the unsuccessful inoculation with tumor 63 either increased or prolonged the resistance originally conferred by carcinoma 206.

As the percentage of resistance in the untreated control mice varied throughout the whole series between 0 and 27 per cent., the charts suggest the futility of drawing conclusions in cases where the difference between treated mice and their normal controls is less than 25 per cent.

CONCLUSIONS.

The foregoing experiments demonstrate that the immunity induced in mice by preliminary treatment with tumor or certain of the normal tissues reaches its maximum at about the tenth day, after which it gradually diminishes, probably to disappear after the lapse of about eighty days. It is significant that the curves with the three tissues, spontaneous tumor, kidney, and embryo skin, should parallel each other so closely, and the occurrence renders extremely probable the view, previously expressed by Russell[13] and by Woglom[14] after an examination of very young grafts in immune mice and rats respectively, that the resistance elicited in each case is similar. It is evident, however, that there is a difference in the degree to which it is developed.

[13] Russell, B. R. G., *Third Scientific Report of the Imperial Cancer Research Fund*, 1908, 341.

[14] Woglom, W. H., *loc. cit.*