REGRESSION OF TRANSPLANTED LYMPHOMAS INDUCED IN VIVO BY MEANS OF NORMAL GUINEA PIG SERUM

I. Course of Transplanted Cancers of Various Kinds in Mice and Rats Given Guinea Pig Serum, Horse Serum, or Rabbit Serum*

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Plate 49

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In experiments undertaken for other purposes the observation has recently been made that subcutaneous lymphomas of two kinds promptly regress following the injection of normal guinea pig serum intraperitoneally into mice carrying them, the animals meanwhile remaining lively and fleshy and devoid of signs of illness, while the growths of untreated control animals, and those of mice given serum from rabbits or horses, enlarge progressively and kill their hosts. Furthermore, in control experiments two transplanted mammary carcinomas and a transplanted fibrosarcoma of mice did not regress but grew unimpeded following the injection of guinea pig serum into mice bearing them. The findings provide an example, unique thus far, of a naturally occurring substance that brings about regression of a single type of cancer cells in living animals without doing obvious harm to the latter. They are here reported in detail, while other observations related to the phenomenon are given in an associated paper.

Methods and Materials

General Plan of the Experiments.—Malignant lymphoma cells of one or another of three kinds—(Gardner's Lymphosarcoma 6C3HED (1), Lorenz's Lymphoma II (2), and the Murphy-Sturm lymphosarcoma (3)—were suspended in known numbers in saline solution, then implanted subcutaneously in both groins of experimental animals in which the cells were known to grow (C3H mice, A mice, and Wistar rats, respectively). After intervals varying from 1 hour to 19 days, some of the implanted animals were given guinea pig serum intraperitoneally, usually in repeated doses, while others were kept untreated as controls, and still others were given intraperitoneal injections of

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saline solution or of serum from rabbits or horses. The outcome of the implantations and injections was followed by repeatedly observing and gently palpating the groins of the injected animals, with careful and frequent chartings to show the size and course of every tumor that developed, and frequent weighings to provide an indication of the nutritional status and general condition of the hosts. In addition, postmortem examinations, including microscopic studies, were made of many of the animals that had been kept for long periods following regression of their subcutaneous lymphomas, to make certain that no residual tumor remained. After it was learned that regression of the murine lymphosarcomas regularly follows the injection of suitable amounts of guinea pig serum *in vivo*, similar tests were made with three additional transplanted growths (Sarcoma 180 and two transplantable mammary cancers of C3H mice).

The Experimental Lymphomas and the Control Tumors Used.—

The Gardner Lymphosarcoma 6C3HED (1), which originated a number of years ago in a C3H mouse given estradiol and has since been transplanted in series in mice of this inbred stain, was chiefly employed; it was generously provided by Dr. E. J. Foley of the Ciba Pharmaceutical Laboratory. In the present work, the implantation of 2 to 4 million 6C3HED cells subcutaneously in untreated young adult C3H mice generally gave rise to palpable growths within 4 to 7 days, and these enlarged steadily as a rule and brought about death of the animals with widespread metastases, usually between the 20th and 40th day following implantation. Occasionally, however, the growths enlarged for a time and then regressed spontaneously, while animals implanted with relatively small numbers of cells sometimes failed to develop palpable nodules.

Lymphoma II (2), which originated in an inbred stain A mouse in the laboratory of Dr. Egon Lorenz of The National Cancer Institute, Bethesda, was provided by him. When 2 million or more of the Lymphoma II cells were deposited in the subcutaneous tissues of the young adult A mice raised in this laboratory, palpable nodules usually appeared within 6 or 7 days, but the growths regressed spontaneously in about half the animals during the next 10 days, while in the rest they enlarged progressively and proved characteristically invasive, giving rise to widespread deposits of malignant lymphoma cells in lymph nodes, liver, and other organs and bringing about death within 20 to 30 days.

The Murphy-Sturm lymphosarcoma (3), made available by Dr. Kenematsu Sugiura of the Sloan-Kettering Institute, New York City, regularly gave rise to palpable growths within 7 days when sufficient numbers of its cells were suitably implanted in the subcutaneous tissues of young untreated Wistar rats of the Carworth Farms strain, and the tumors rapidly enlarged to kill their hosts, usually within 15 to 25 days.

Two C3H mammary carcinomas and *Sarcoma 180* were used in control tests. The mammary growths originated in C3H mice of this laboratory and grew readily when transplanted to the subcutaneous tissues of adult female C3H mice of the same inbred line. Dr. Chester Stock of the Sloan-Kettering Institute provided an animal carrying Sarcoma 180; this grew readily and progressively in the subcutaneous tissues of both the C3H and A strain mice here employed.

The Transplantation Technique.—Subcutaneous growths were procured with aseptic precautions, usually 7 to 14 days following implantation, and hashed with knives into pieces a millimeter or less across; these were pressed through a 40 mesh monel metal sieve into a buffered glucose Ringer's solution (hereinafter BGR) that had been buffered with dibasic

phosphate–citric acid mixture (0.002 M) at pH 7.4, and to which glucose had been added in a concentration of 500 mg. per cent. The suspension of tumor cells was then placed in a tall cylinder for 5 to 10 minutes to allow any clumps of tissue that might be present to settle out; when removed, the supernatant liquid contained individually suspended tumor cells, and in the case of the lymphomas, relatively few or no clumps of tissue, as the microscope showed. After the cells had been counted by means of an ordinary blood-counting chamber, the volume of the suspension was next adjusted with BGR so that it contained 4,000 to 10,000 or more cells per c.mm. 0.5 cc. of the suspension (containing, as a rule, 2 to 5 million or more cells) was then injected, by means of a tuberculin syringe and 25 gauge needle, into the subcutaneous tissues in each groin of the experimental animals. In every instance, cultures of the injected suspensions were made on agar and in enriched broth; these proved sterile without exception.

Experimental Animals.—The C3H and A mice were raised in this laboratory from stock provided initially by Dr. L. C. Strong of Yale University. Young adult animals weighing 20 to 22 gm. were employed for most experiments, though occasionally older and heavier animals were used. They were kept on sawdust, usually 4 together in half-gallon tin cans with wire mesh tops or 8 together in larger enamel pans; all had access constantly to laboratory pellets and water. The Lymphosarcoma 6C3HED grew equally well in male and female C3H mice, so that animals of the two sexes were used indiscriminately, though the males and females were housed separately.

Guinea pig serum was procured by bleeding from the heart with aseptic precautions but without anesthesia 12 to 36 or more hybrid, market-bought, adult guinea pigs, each weighing 350 gm. or more. 10 to 15 cc. of blood was taken from each animal and allowed to clot in a test tube partially coated inside with paraffin, the serum being removed and centrifuged 2 to 3 hours later. The various lots of serum were then pooled, and cultures were made on agar and in enriched broth; these too were regularly sterile in the experiments here reported. The pooled batches of serum—40 to 310 cc. in amount—were then stored in thick walled tubes, 10 cc. in each, in the deep freeze at −26°C., until used, usually within 3 or 4 weeks. Occasionally groups of guinea pigs were bled repeatedly, but never oftener than once a month. More than a dozen batches of pooled serum were employed during the work; within the limitations of the experimental observations, they all seemed to be approximately equal in potency.

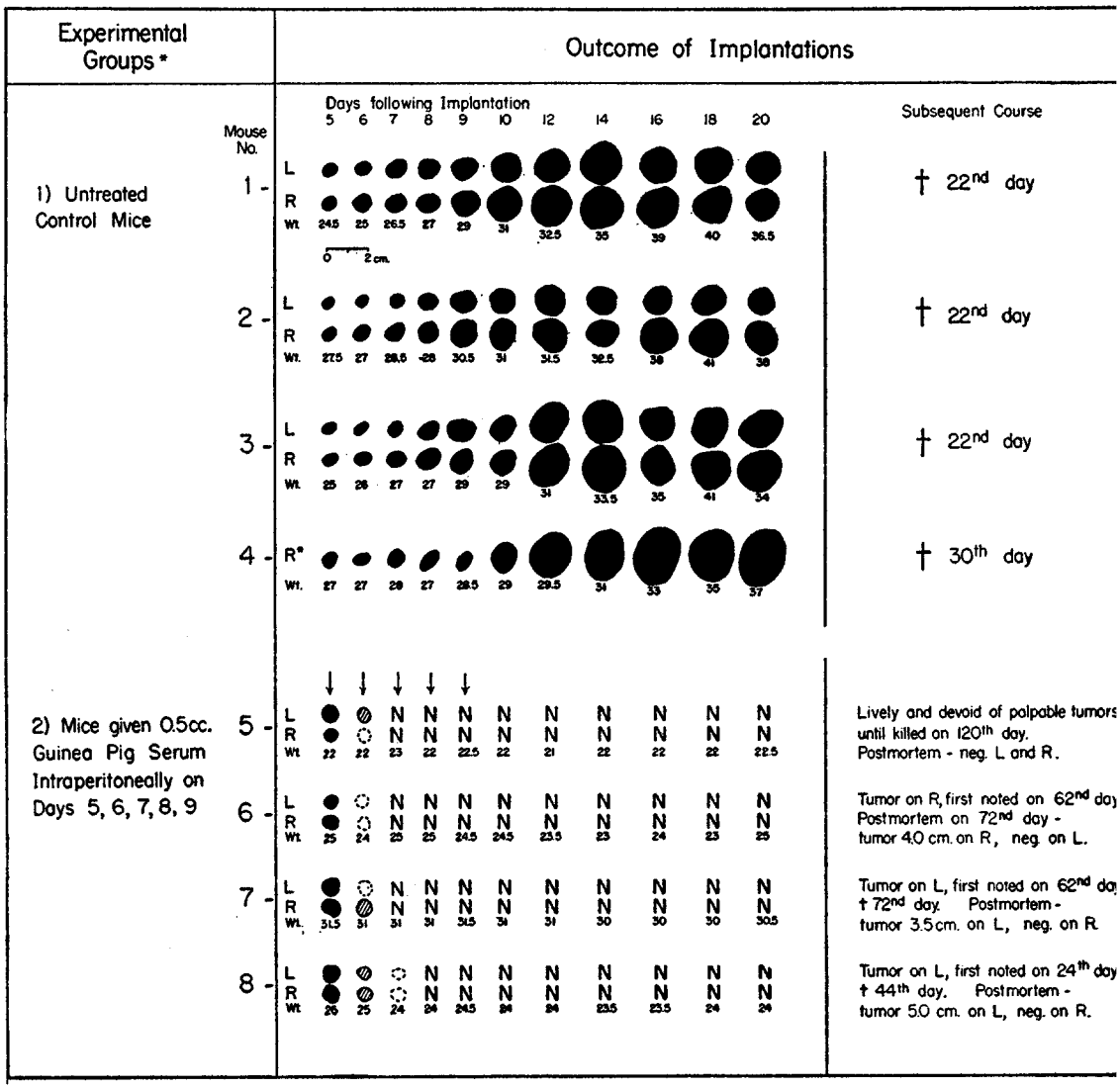
Regression of Subcutaneous Lymphosarcomas in Mice Given Guinea Pig Serum Intraperitoneally

In each of 9 experiments, subcutaneous 6C3HED lymphosarcomas 4 to 15 mm. across, growing as a result of implantations made 3 to 7 days before, promptly regressed following repeated injections of guinea pig serum intraperitoneally into the animals carrying them, while the growths resulting from identical implantations in untreated control mice, or in those injected with rabbit or horse serum, generally enlarged progressively. Charts 1 and 2 show in detail the findings of two of these experiments.

From Chart 1 it will be seen that the growths of 8 C3H mice in two experimental groups were 5 to 9 mm. across, as determined by careful palpation and charting, on the 5th day following the implantation of approximately 4 million Lymphosarcoma 6C3HED cells into their left and right groins. Immediately following the charting of the 5th day, and again on the 6th, 7th, 8th, and 9th days, 0.5 cc. of whole guinea pig serum, thawed and used as needed from a single lot of frozen material, was given intraperitoneally to the 4 mice comprising the

CHART 1

Regression of subcutaneous lymphosarcomas (6C3HED) in mice given guinea pig serum intraperitoneally



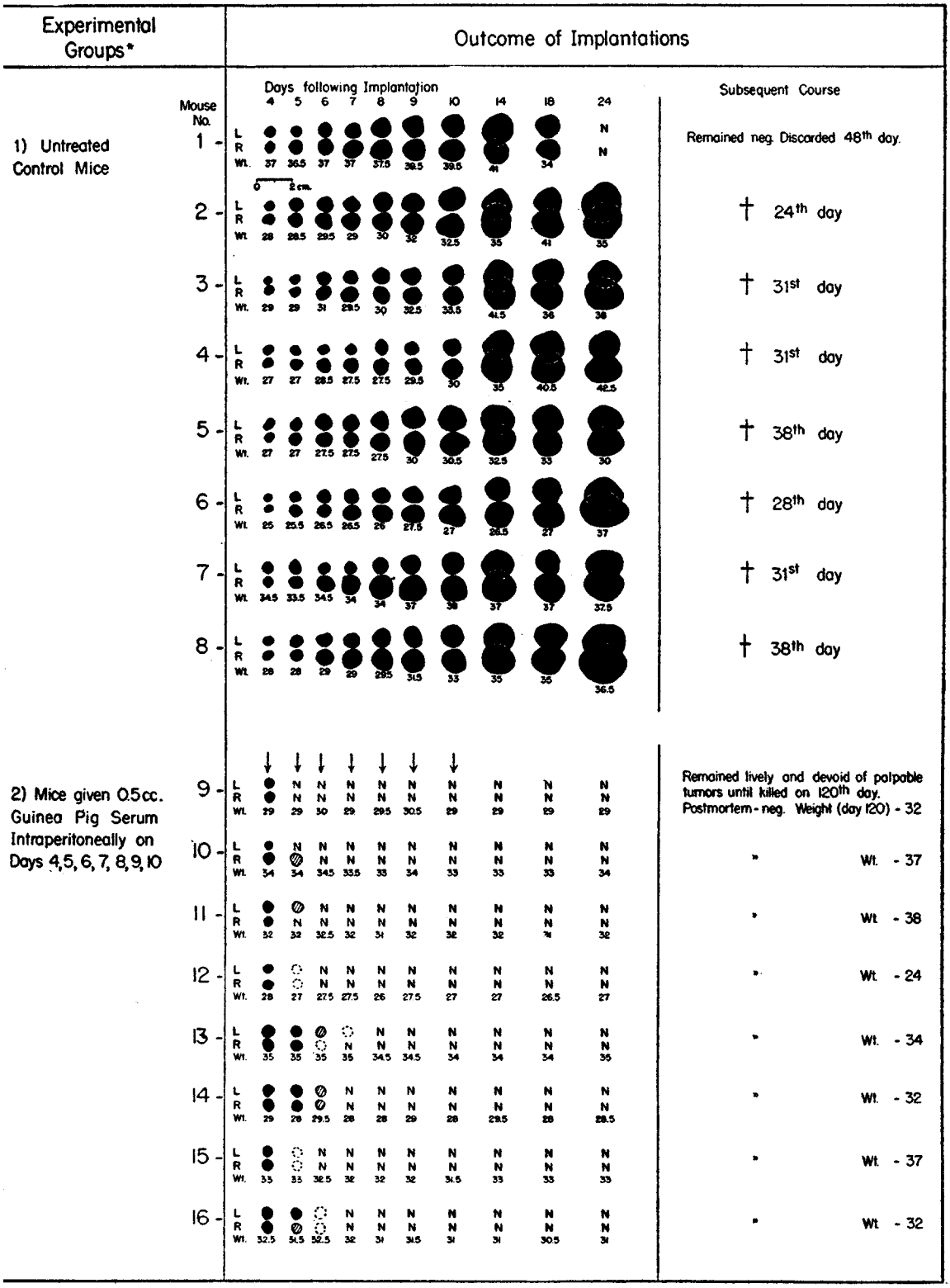
N = no palpable tumor. The hatched circles indicate growths that were much softer than those in the untreated animals, while the circles outl by broken lines indicate very soft, ill-defined swellings. L, R = left and right groins, respectively. Wt. = weight in grams of the animal. So, too, in charts that follow.

* Approximately 4 million 6C3HED lymphosarcoma cells implanted in left (L) and right (R) groins of all mice except No. 4, which was impla in R groin only.

Arrows indicate day guinea pig serum was injected intraperitoneally.

CHART 2

Regression of subcutaneous lymphosarcomas (6C3HED) in mice given guinea pig serum intraperitoneally



Approximately 4 million 6C3HED lymphosarcoma cells implanted in L and R groins of all mice.

treated group. On the 6th day, the growths of 2 of the control mice were charted as being slightly larger than on the previous day, while those of the other 2 were about as before; the growths of the 4 injected animals, however, were slightly smaller than they had been the day before, and they were now less turgid. On the 7th day the untreated mice all had tumors that were quite firm, and larger than they had been on the previous days, while 3 of the treated mice no longer had palpable growths and those in the 4th animal were small, ill defined, soft swellings. During the period 8 to 20 days the growths of the untreated mice continued to enlarge, and 3 of the mice were found dead with large tumors on the 22nd day, while the 4th animal, which had been implanted only in the right groin because of a slight wound in the skin of its left groin at the time of implantation, died on the 30th day with a single huge tumor.

The treated mice all remained free from palpable tumors during the period 8 to 20 days. Mouse 5 indeed remained lively and devoid of palpable tumors or other signs of illness until the experiment was terminated on the 120th day following implantation, at which time postmortem examination failed to disclose gross or microscopic evidence of lymphosarcoma. 2 other treated mice (Nos. 1 and 7) were negative when examined on the 44th and 54th days, but both had palpable tumors on the 62nd day, while mouse 8 developed a single palpable growth on the 24th day which brought about its death on the 44th day.

Frequent weighings showed that the untreated mice all gained a good deal of weight during the charted period, perhaps owing largely to the increase in mass of their tumors, and, in the end stages, to the edema fluid that accumulated in large quantities in the subcutaneous tissues of their flanks adjacent to the tumors. In mice 1, 2, and 3 much of the edema fluid dramatically disappeared, with concomitant loss in weight, during the 3 or 4 days before death occurred, and in mice 1 and 2 this loss in edema fluid was accompanied by a diminution in size of the charted growths—a result not infrequently seen during the terminal period in mice of other experiments in which postmortem examinations dislcosed widespread metastases. The weights of all 4 of the treated mice remained practically constant during the period 5 to 20 days, varying no more than 1.5 gm. from the mean for each animal, as the recorded figures show, the findings being similar in this respect to those obtained in several control experiments in which unimplanted and untreated C3H mice of comparable size were kept under identical conditions and weighed daily.

In the *experiment of Chart 2*, 16 female C3H mice that had been discarded from the breeding colony were divided into two groups of 8 animals each; these were all implanted in left and right groins with approximately 4 million lymphosarcoma cells suspended in 0.5 cc. of the buffered glucose Ringer's solution (BGR). Tumors 5 to 7 mm. across were palpable at all the implanted sites 4 days later, and on this day 0.5 cc. of guinea pig serum was injected intraperitoneally into 8 of the animals. The injections were repeated on days 5, 6, 7, 8, 9 and 10. From Chart 2 it will be seen that the tumors grew progressively in all except one of the mice of the control group, bringing about death between the 28th and 38th day. By contrast, the tumors in the injected mice promptly regressed, and they did not recur during the period of the experiment (120 days), their hosts remaining lively and devoid of palpable masses throughout the entire experiment, as the chart indicates; furthermore, the recorded figures show that the injected animals did not lose weight during the charted period, and careful postmortem examinations at the termination of the experiment failed to disclose either gross or microscopic evidence of residual lymphosarcoma.[1]

[1] Incidentally it may here be noted also that the animals, although given repeated injections of guinea pig serum, did not manifest any arteritis, nephritis, or other microscopic signs of reaction to the foreign material.

Guinea pig serum that had been concentrated by means of evaporation from a cellophane sausage casing suspended in front of an electric fan was employed in the next experiment. The results are illustrated in Chart 3 and in Fig. 1.

The findings set down in Chart 3 make it plain that subcutaneous lymphosarcomas 10 to 12 mm. across, were present in each groin of the 8 C3H mice of the experiment on the 6th day following the implantation of approximately 6 million lymphosarcoma cells at each site. The growths of 4 of the mice regressed following the intraperitoneal injection, on days 6, 7 and 8, of guinea pig serum that had been "fan-concentrated" to a strength approximately three times normal (see footnote of chart for further explanation), while the lymphosarcomas of the 4 untreated control mice continued to enlarge progressively throughout the period of observation.

One animal from each group was killed for photographic purposes on the 14th day following implantation, and another pair on the 15th day, the appearance of the latter being shown in Fig. 1. The two remaining untreated animals died with huge tumors on the 23rd and 25th day respectively, while both the treated mice remained lively and sleek and free from palpable tumors during 120 days' observation. Again the animals maintained practically constant weights during the period following regression of their tumors, as the chart shows.

To broaden the observations, lyophilized guinea pig serum was employed in the experiment of Chart 4, and lyophilized horse serum was used for control purposes.

12 female C3H mice, discarded from the breeding colony and weighing approximately 30 gm. each, were implanted in each groin with approximately 15 million lymphosarcoma cells in 1 cc. of the buffered glucose Ringer's solution. The resulting growths were charted on the 4th, 5th, and 6th days and on the last day, it can be seen from Chart 4, had reached diameters of 9 to 15 mm. 4 of the animals were kept untreated as controls, while 4 others were each given intraperitoneally 1.5 cc. of a distilled water suspension containing the lyophilized material from 5.0 cc. of horse serum, and the remaining group of 4 mice each received 1.5 cc. of a suspension containing the dried material from 5.0 cc. guinea pig serum. The injections were repeated on days 8, 12, and 16. Chart 4 shows that the lymphosarcomas grew progressively in the 4 untreated control mice, and so too in the 4 mice given lyophilized horse serum, while the growths of the 4 mice given lyophilized guinea pig serum promptly regressed, the animals maintaining their respective weights during the period immediately following the injections and 2 of them remaining lively and devoid of palpable tumors or other signs of illness during 120 days' observation.

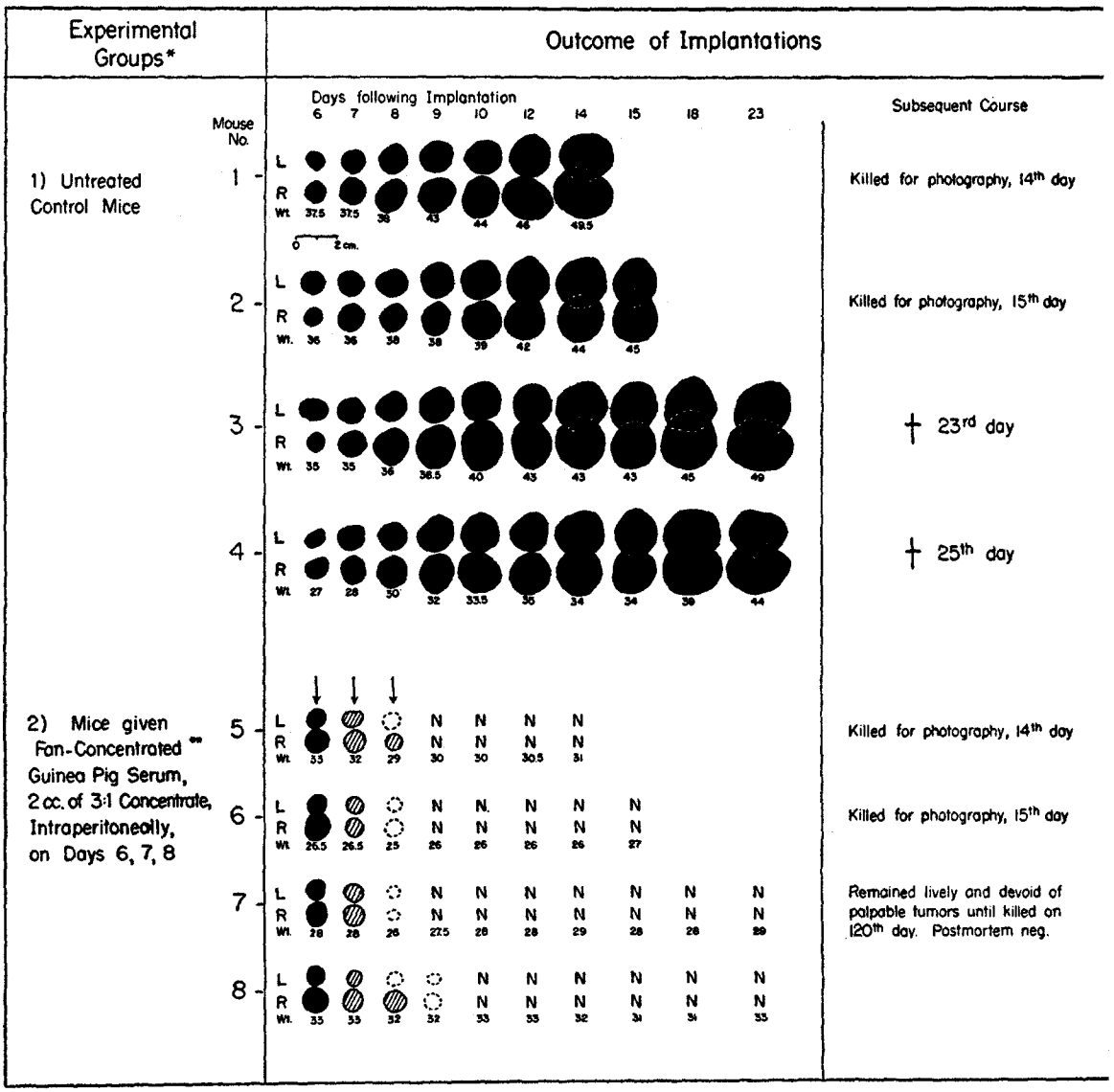
Effects of Guinea Pig Serum on Lymphosarcomas (Lymphoma II) in Strain A Mice

To broaden the findings further, tests were next made with a transplanted lymphosarcoma that had originated in another strain of mice, namely Lymphoma II of albino A mice (2). Chart 5 gives in detail the results of one of five experiments made with this growth.

From Chart 5 it may be seen that growths 8 to 14 mm. in diameter were present in each groin of 16 A mice that had been implanted 7 days previously with approximately 10 million Lymphoma II cells at each site. On the 7th day, and again on the 9th and 11th days, 8 of

CHART 3

Regression of subcutaneous lymphosarcomas (6C3HED) in mice given fan-concentrated** guinea pig serum intraperitonea

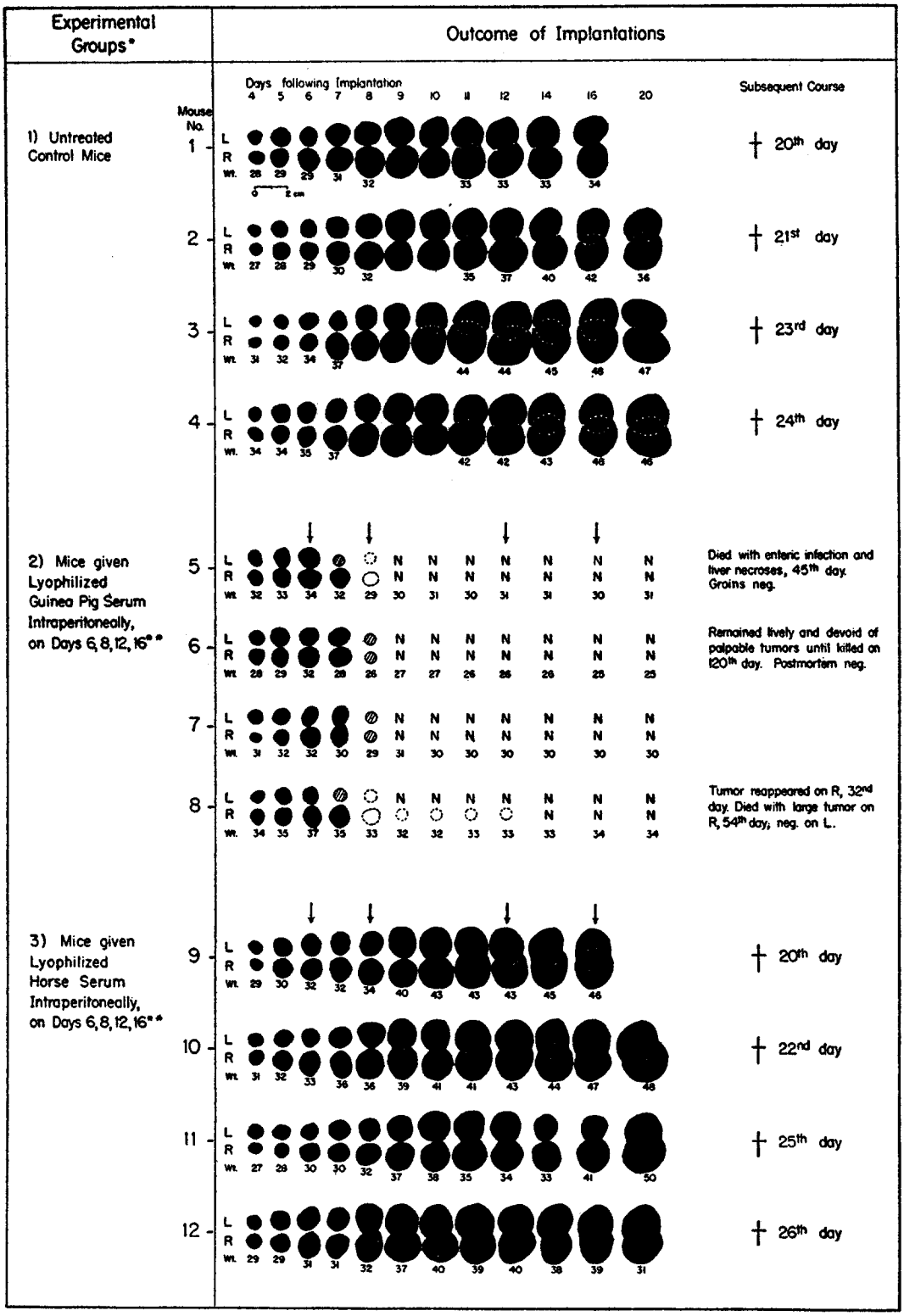


* Approximately 6 million lymphosarcoma cells (6C3HED) implanted in L and R groins of all mice.

** 60 cc. of guinea pig serum was placed in an 18 mm. cellophane sausage casing and held in front of an electric fan approximately 3 hours, the volu being thus reduced to approximately 20 cc. The concentrated material was then filtered through a Seitz Ek disc.

CHART 4

Regression of subcutaneous lymphosarcomas (6C3HED) in mice given lyophilized guinea pig serum intraperitoneally

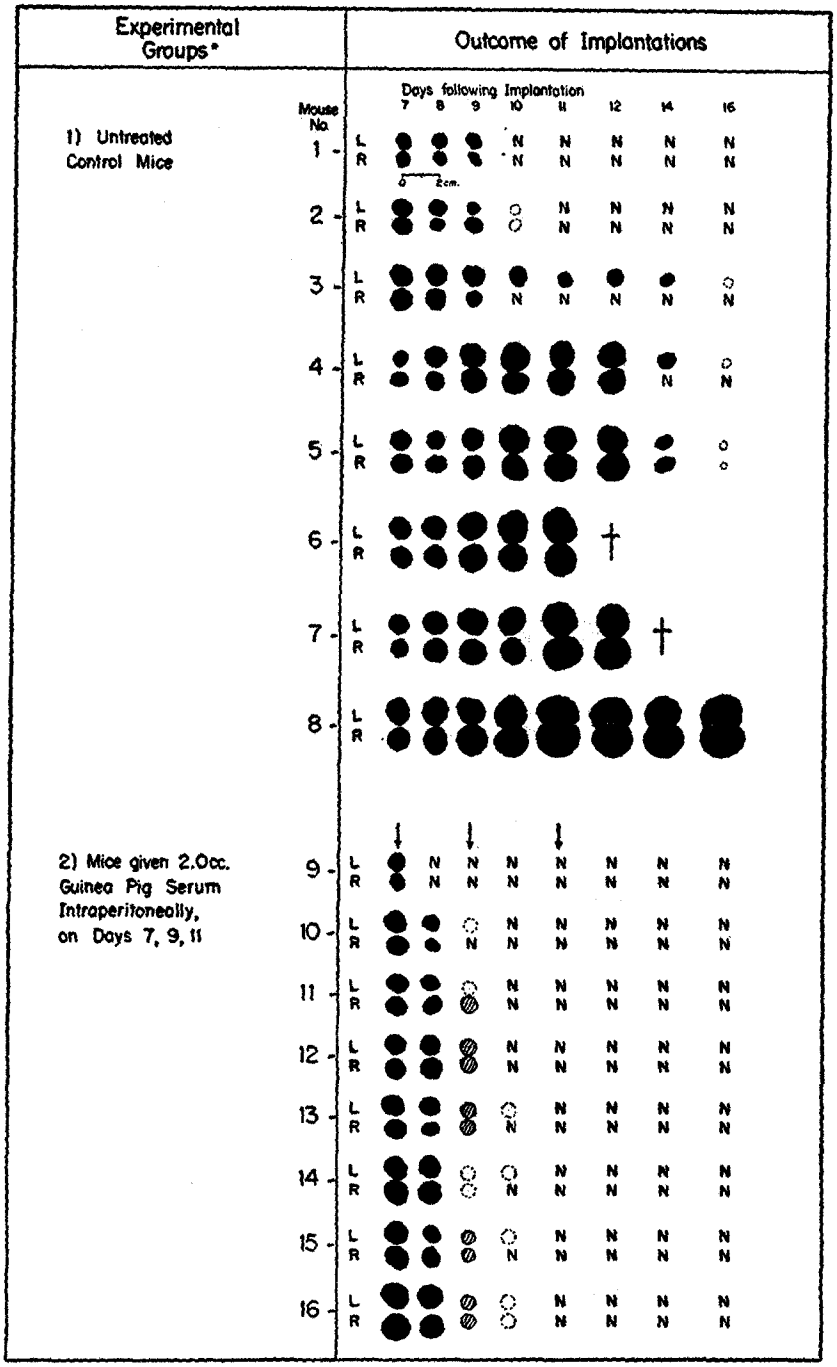


* Approximately 15 million (6C3HED) lymphosarcoma cells implanted in L and R groins of all mice.

** 1.5 cc. containing the dried material from 5.0 cc. serum given at each injection intraperitoneally.

CHART 5

Effect of guinea pig serum on subcutaneous (Lymphoma II) lymphosarcomas



* A-strain mice (Strong) were implanted with approximately 10 million Lymphoma II cells in each groin. The arrows indicate days on which serum injections were given.

the mice were given 2.0 cc. of guinea pig serum intraperitoneally, with result in prompt regression of the growths in all the treated animals. The growths of 5 of the untreated control mice also regressed, as the chart shows—this happening more or less regularly with this tumor in the A mice employed, as has already been mentioned, and not infrequently also with other tumors that have originated in one sub-line of an inbred strain of animals and subsequently been transplanted to hosts of another sub-line, as is well known. The regression was much less abrupt in 3 of the animals of this group, it may be noted, than it was in the animals given guinea pig serum; furthermore the lymphosarcomas grew progressively in the 3 remaining untreated mice, as the chart shows. In addition, 8 A mice implanted at the same time as were those of groups 1 and 2 of Chart 5 and having comparable growths on the 7th day, were given 2.0 cc. of horse serum intraperitoneally on days 7, 9, and 11. The outcome was again like that in the untreated control mice of Chart 5: lymphosarcomas grew progressively in 3 of the 8 mice and slowly regressed in the remainder. So too in still another group of 8 implanted mice which were given 2.0 cc. of rabbit serum on days 7, 9, and 11; the lymphosarcomas grew progressively in 4 of the mice and regressed in the others, the regression in 2 of the latter again being notably less abrupt than that taking place in the mice given guinea pig serum (Group 2 of Chart 5).

In a second experiment with this tumor the results were almost precisely like those shown in Chart 5, while in three additional experiments three injections of 1 or 2 cc. of fan-concentrated guinea pig serum were given intraperitoneally at intervals of 1 or 2 days to 5 mice with subcutaneous lymphosarcomas measuring 14 to 24 mm. across, which had resulted from the implantation of Lymphoma II cells 9 days before in one experiment, 12 days before in another, and 19 days before in the third. In all three experiments the large subcutaneous growths promptly and permanently regressed, the fact having special significance; for one of the mice—with a subcutaneous growth 18 mm. across on the 9th day following implantation, which regressed promptly and permanently following treatment with guinea pig serum—had been provided by Dr. Lorenz and implanted by him under conditions in which the Lymphoma II has usually metastasized widely throughout the body by the 9th day following implantation (2). In addition, palpation of the axillae of 4 of the 5 mice indicated that large lymph node metastases in each instance regressed as the subcutaneous growths did so.

Inhibition of Lymphosarcomas in Rats Following Injection of Guinea Pig Serum Intraperitoneally

Three experiments were next done to learn whether guinea pig serum would influence the growth of implanted Murphy-Sturm lymphosarcoma cells in susceptible rats. By this time much experience had shown that C3H mice, given a single injection of 1.0 cc. of guinea pig serum 1 hour after the implantation of 2 to 3 million 6C3HED lymphosarcoma cells, usually failed to develop palpable growths, and that they always failed to do so when a second injection of guinea pig serum was made the following day. Hence in the experiments with the rat lymphosarcoma the first injection was given 1 hour

after the implantations, and in two of the experiments additional injections were given at frequent intervals during the next several days.

In the first experiment, in which a single injection of guinea pig serum was given, the implanted lymphosarcoma cells grew almost as well in three young Wistar rats given 2.0 cc. of 3:1 fan-concentrated guinea pig serum as in 3 untreated control animals. But the outcome was quite different in the next two experiments in which repeated injections of concentrated serum were given. In these the lymphosarcomas of rats given repeated injections of guinea pig serum were inhibited, while those of rats given comparable amounts of horse serum appeared as promptly and grew as well as did the growths of untreated control animals. Chart 6 shows the results of one of these experiments in detail. It will be noted that the lymphosarcomas of the rats given guinea pig serum, while appearing considerably later than those of the control animals, grew quite rapidly once they had appeared, and brought about death of their hosts only a few days after the control animals had died. The limited supply of guinea pig serum available did not permit attempts to see whether still larger amounts of it would induce regression of large rat lymphosarcomas. More will be said further on about the implications of these findings.

Continued Growth of Sarcoma 180 and of Two Mammary Carcinomas in Mice Given Guinea Pig Serum Intraperitoneally

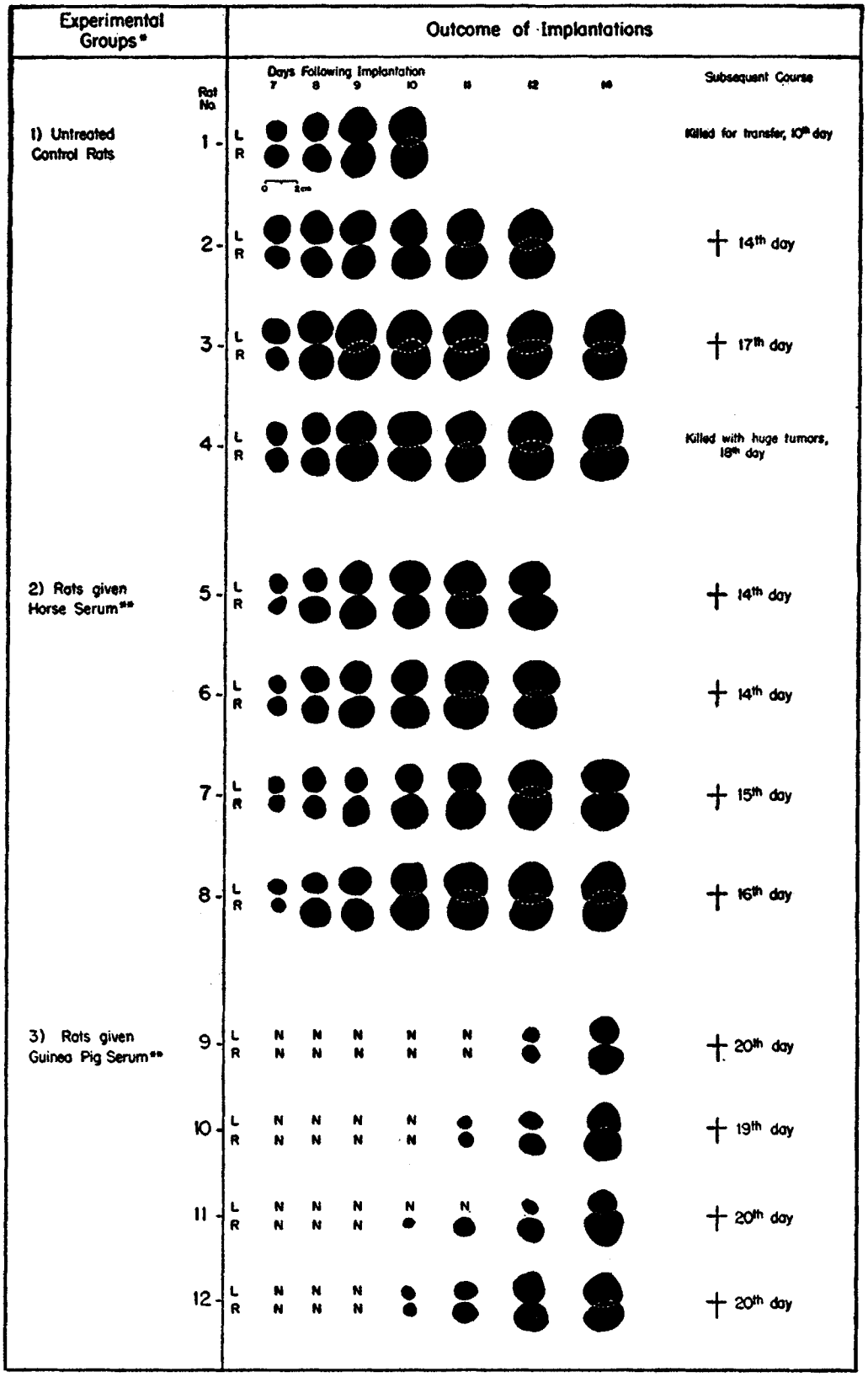
It was obviously of interest to learn whether guinea pig serum would influence the outcome of implantations with other types of tumor cells.

Chart 7 shows the results of an experiment in which approximately 1.8 million Sarcoma 180 cells were implanted in the left groins of 4 C3H mice and approximately 5 million Lymphosarcoma 6C3HED cells in the right groins, 2.0 cc. of guinea pig serum being given to each animal 1 hour after the implantations and again on each of the following 2 days. In the treated animals tumors appeared promptly and grew progressively at all the sites implanted with the Sarcoma 180 cells, the outcome being quite comparable to that in control, untreated animals concurrently implanted in both groins with the Sarcoma 180 cells. No growths developed, however, at the sites where the lymphosarcoma cells had been implanted in the treated animals, though 4 additional untreated control animals, likewise implanted with lymphosarcoma cells, all promptly developed lymphosarcomas. An additional test gave identical results: growths appeared as promptly and grew as well in 4 A-strain mice implanted with Sarcoma 180 cells and given 1.0 cc. of guinea pig serum intraperitoneally 1 hour afterwards as they did in 4 untreated control mice.

Two experiments were made with each of two mammary carcinomas of C3H mice, one of the growths being in its second and third serial transfers while the other was in its first and second, both growths having the morphology of adenocarcinomas. The outcome of implantations with the carcinoma

CHART 6

Inhibition of Murphy-Sturm lymphosarcomas in rats following injection of guinea pig serum intraperitoneally

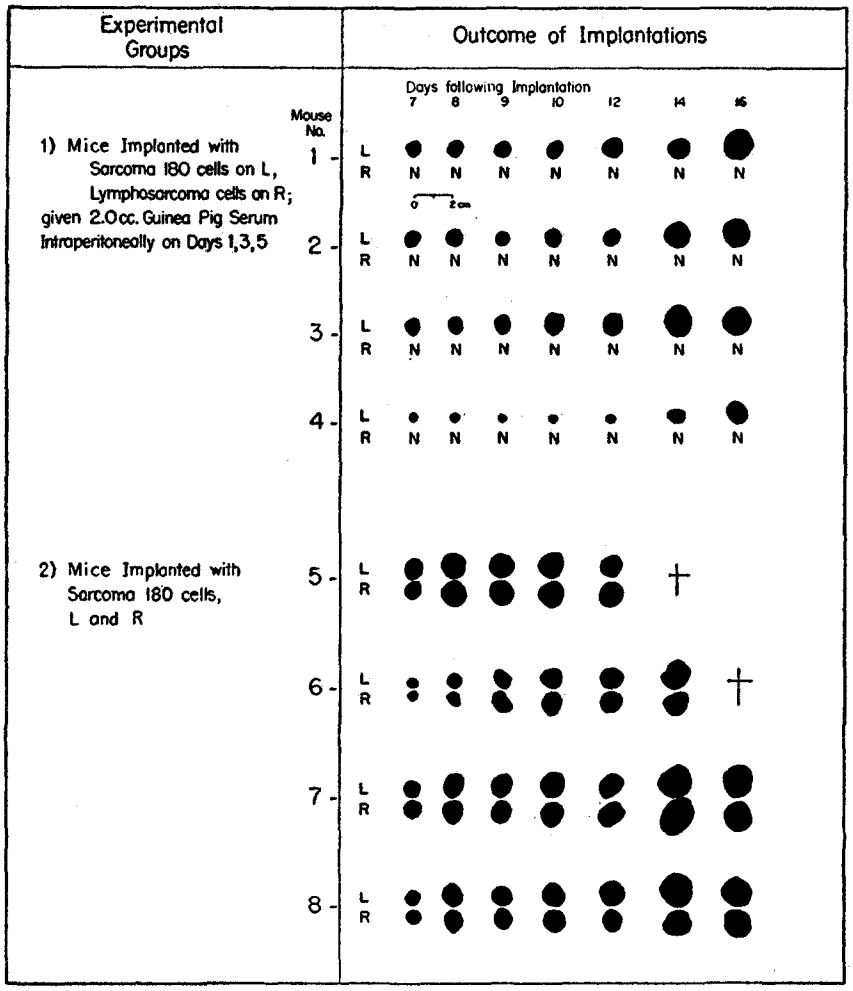


* All rats implanted with approximately 3.3 million Murphy-Sturm lymphosarcoma cells.

** 2.0 cc. of 3:1 fan-concentrated serum given intraperitoneally twice on the day of implantation and on each of the 3 following days.

CHART 7

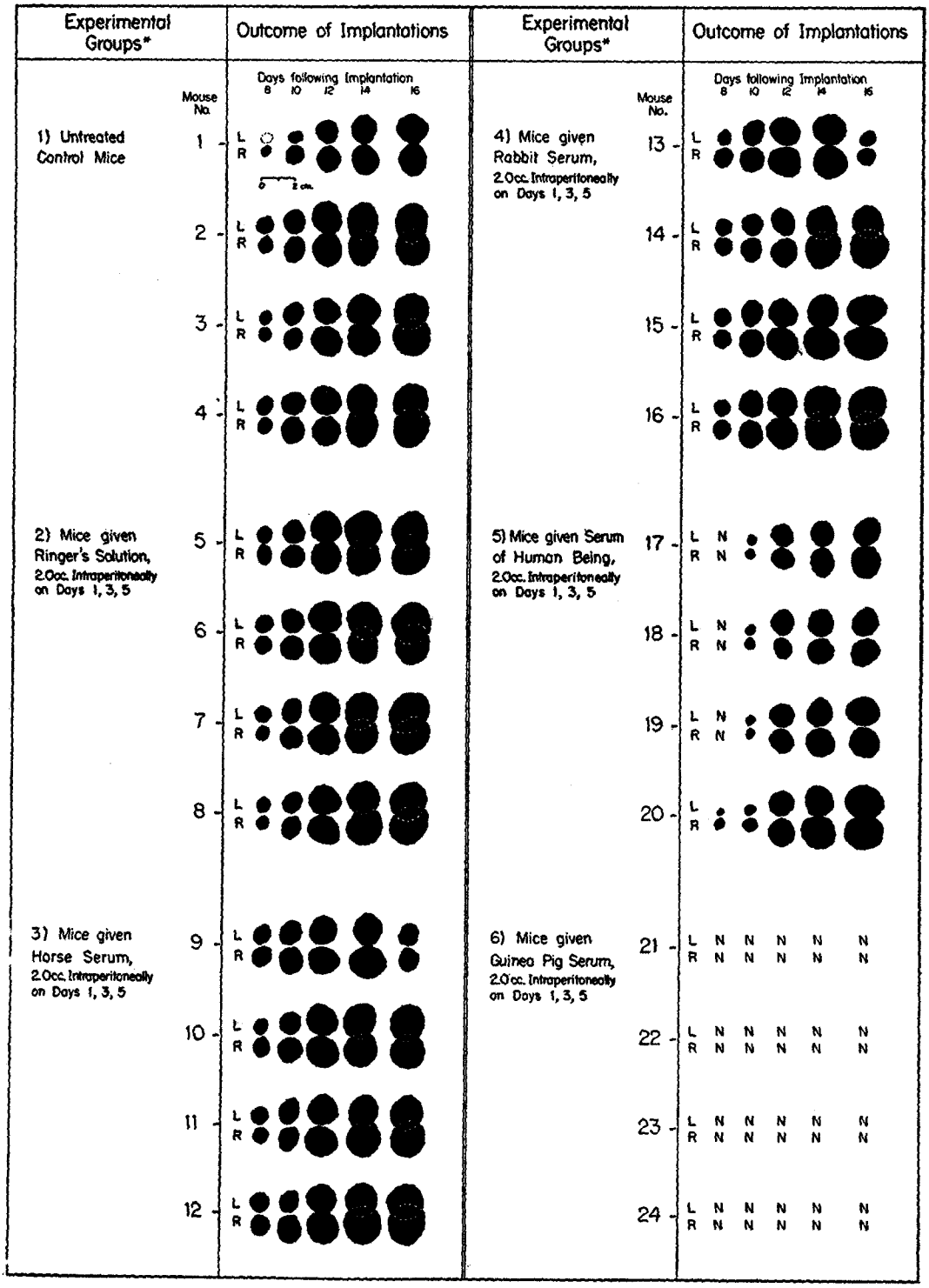
Continued growth of Sarcoma 180 cells in mice given guinea pig serum intraperitoneally



Mice of a 3rd experimental group were implanted in both groins with the (6C3HED) lymphosarcoma cells Palpable tumors were present at all sites on the 6th day, and these enlarged rapidly.

CHART 8

Tests with sera of other species



* All mice implanted in L and R flanks with approximately 2.5 million lymphosarcoma (6C3HED) cells.

The animals of 2 additional groups were given single injections of 2.0 cc. of human serum and guinea pig serum respectively, 1 hour after the implantations. Growth appeared in the animals given the single injection of human serum which, in time of appearance and course, were precisely like those of the control animals; no growths appeared in the mice given the single injection of guinea pig serum.

cells in the four experiments was uninfluenced by repeated injections of guinea pig serum given intraperitoneally, the animals receiving these, and the control untreated hosts as well, all developing irregularly bossed nodules after 7 to 14 days which enlarged progressively and comparably in the treated and untreated hosts. With both carcinomas experiments like the one illustrated in Chart 8 were next made, and with the same result: mammary carcinoma cells, implanted in one groin of C3H mice that were given three injections of guinea pig serum on the 1st, 3rd, and 5th days, formed palpable tumors precisely comparable to those of control untreated animals, while lymphosarcoma cells, implanted in the opposite groins of the same animals, regularly failed to grow, although others, implanted in additional control animals at the same time, grew as usual.

Will Serum From Other Species Induce Regression of Murine Lymphosarcomas in Vivo?

In the experiments of Charts 4, 5, and 6 the injection of serum from normal horses and rabbits failed to influence the outcome of implantations with three types of lymphoma cells in mice and rats, while guinea pig serum either inhibited growth of the cells or brought about regression of the tumors. Several additional tests were made to learn whether serum specimens procured from other mammalian species share with guinea pig serum the ability to induce regression of implanted 6C3HED lymphosarcoma cells *in vivo*. Three lots of rabbit serum, each containing pooled specimens from 3 or more rabbits, and three lots of horse serum, given by the Laboratories of the Board of Health of the City of New York, were tested in several experiments, as was the serum of a single human being. In every instance, the rabbit and horse sera were devoid of effect, while that of the human being exhibited only a relatively slight ability to inhibit temporarily the growth of the lymphosarcoma cells *in vivo*. Chart 8 shows the results of a typical experiment.

SUMMARY

In the experiments here described transplanted lymphomas of two kinds regularly regressed following repeated injections of normal guinea pig serum intraperitoneally into mice carrying them, the animals meanwhile remaining lively and devoid of signs of illness or wasting. The lymphomas of untreated control mice, by contrast, usually grew progressively and killed their hosts within 20 to 30 days, and the same was true of the growth of other mice given repeated injections of horse serum or rabbit serum.

In similar experiments, the cells of a transplanted lymphosarcoma of rats were temporarily kept from proliferating by repeated intraperitoneal injections

of guinea pig serum, though the cells of two transplanted mammary carcinomas of mice, and those of fibrosarcoma, grew unimpeded in hosts likewise treated.

Additional experiments related to the phenomenon here described, and a discussion of the findings as a whole, are given in an associated paper.

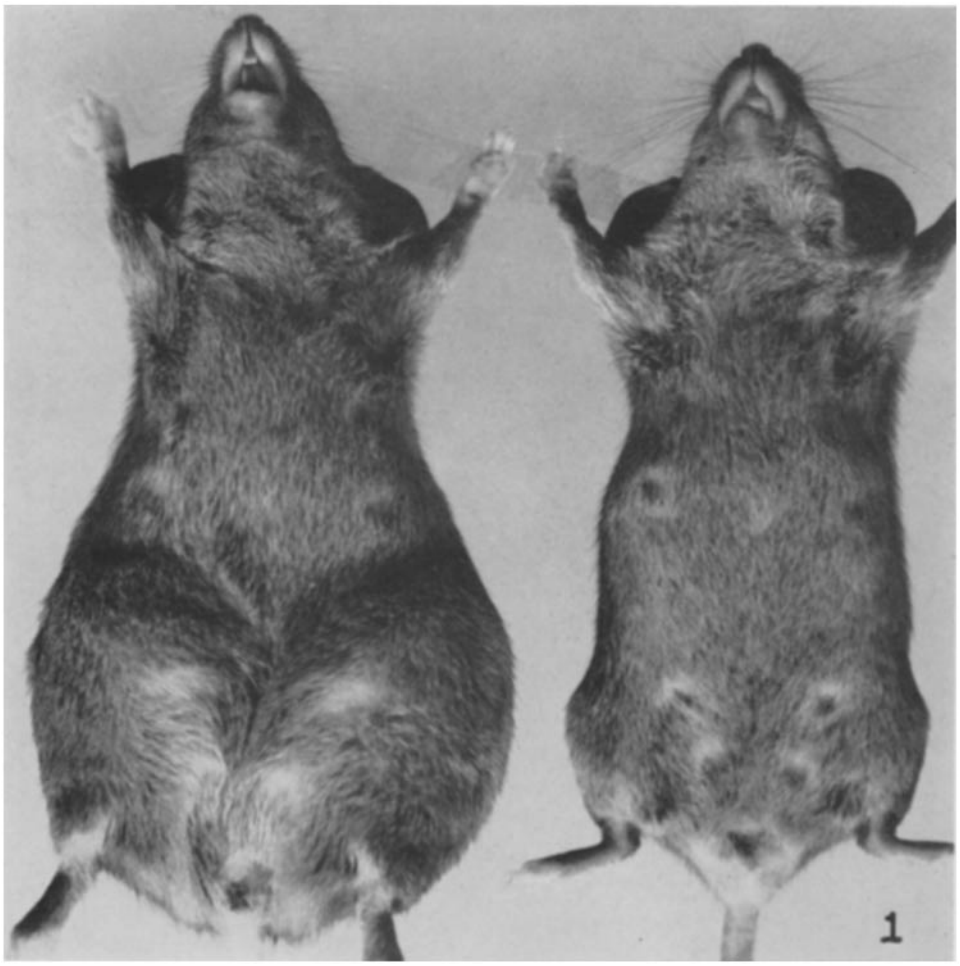
BIBLIOGRAPHY

(The references are given at the end of the associated paper)

EXPLANATION OF PLATE 49

The photograph was made by Mr. Julius Mesiar.

FIG. 1. To show large lymphosarcomas in the groins of a control untreated mouse (No. 2 of Chart 3) and their absence from the groins of a mouse given repeated injections of guinea pig serum intraperitoneally (No. 6 of Chart 3). Both animals were implanted with approximately 6 million lymphosarcoma cells in each groin, and both had growths 10 to 14 mm. across on the 6th day following implantation. On that day, and on the 7th and 8th days also, mouse 6 was given 1.0 cc. of a 3:1 concentrate of guinea pig serum intraperitoneally, with result in prompt regression of its growths (see Chart 3). On postmortem examination the growths of mouse 2 were large, characteristic lymphomas; no tumors could be seen or palpated in the groins of mouse 6. × 1½, approximate.



(Kidd: Induced regression of lymphomas. I)