Second Transplantations of E 0771 Mouse Carcinoma and of Brown-Pearce Rabbit Tumor*†

ALBERT E. CASEY, GEORGE R. DRYSDALE, HOWARD H. SHEAR, AND JOANNE GUNN

(Laboratories of the Birmingham Baptist Hospitals, Birmingham, Ala., the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Me., and the Rockefeller Institute for Medical Research, New York, N.Y.)

When inoculations of long frozen or lyophilized tissue or fresh supernatant fluid from certain malignant tumors are injected into rabbits or mice, these hosts are rendered more susceptible to the subsequent transplant of the same tumor 1–3 weeks later (1–5, 8, 17, 25–25). This paper describes experiments designed to indicate whether a second transplantation of a fresh cellular suspension of the same tumor into a different site 1–3 weeks after a first transplant would alter the hosts’ total reaction to the neoplasm. Earlier experiments by various authors were concerned with estimates of acquired immunity to a second transplant in animals negative to or showing regression of a first transplant, or in animals bearing growing tumors (15–15, 22, 26, 27). The problem of whether the second transplant affected the eventual reaction was not specifically considered in controlled experiments. The experiments of Flexner and Jobling (15, 14), Jobling (15), and Rous and Murphy (22) were sufficiently extensive and well controlled so that rearrangement of their data and analyses by statistical methods made it possible to add information on the problem. Their data will be discussed later in this paper. Our material concerns the Brown-Pearce tumor in rabbits and mammary carcinoma E 0771 in mice.

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† Two of the experiments with the rabbits were done in the laboratories of Drs. Wade H. Brown and Louise Pearce at the Rockefeller Institute many years ago, and the experiments with the mice in the laboratories of Drs. George Snell and Nathan Kaliss at the Jackson Laboratory. The assistance of William Penn, R. R. Davis, M. L. Wrenn, Erma Salter, Gordon L. Ross, and Ward Talley of the Baptist Hospital Laboratory Staff and of Priscilla Smith, Freddy Gabrielson, Dianne Kelton, Joanne Byron, and Judy Fielder of the Jackson Laboratory is gratefully acknowledged.

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MATERIALS AND METHODS

Two parallel series of experiments were conducted: one involved the response of 166 mice given inoculations of C57BL mouse mammary carcinoma E 0771 (Table 1); the other involved the response of 79 rabbits inoculated with the Brown-Pearce rabbit tumor (Table 2).

Mice.—In the series with the mouse mammary carcinoma, 30 mice received subcutaneous inoculations in the groin of 0.1 cc. of a 1:4 saline suspension of viable E 0771 tumor cells, and 30 mice were similarly inoculated with a saline suspension of sedimented E 0771 tumor tissue (prepared by the centrifugation at 1,200 r.p.m. for 15 minutes of a saline suspension of tumor cells, followed by the removal of the resultant supernatant fluid and the resuspension of the resultant sediment in an equal volume of saline). Approximately 8 or 15 days later, these 60 mice were given injections of viable E 0771 tumor tissue subcutaneously over the right shoulder by means of a trocar (Table 1). With E 0771 tumor tissue from the same source (i.e., 10-day-old tumor E 0771 in C57BL/6 F1 mice from the Inbred Nucleus of the Jackson Laboratory), the 106 mice in the two control groups likewise received subcutaneous transplantations by trocar over the right shoulder by the same inoculation team. Of the 166 mice used, 60 were C57BR/cd and 106 were BALB/c (Jax subline) from the breeding rooms of the Jackson Memorial Laboratory at Bar Harbor, Maine. The 30 C57BR/cd and the 76 BALB/c controls were all the mice inoculated with C57BL subline 6 (C57BL/6) E 0771 tumor (from the Inbred Nucleus of the Jackson Laboratory) of which we have record. Mice receiving any other treatment were not included. The 60 experimental mice and 64 controls (except the last 42, marked SNCL in Table 1) were representative of some 600 mice (300 C57BR/cd and 300 BALB/c) from the same breeding rooms at the Jackson Laboratory, numbered and matched as to sex. All were 3–4 months of age when inoculated.

Rabbits.—In the Brown-Pearce tumor series,
sixteen rabbits in four experiments received, by intratesticular inoculation, 0.3 cc. of a 1:4 saline suspension of freshly excised Brown-Pearce tumor cells; and five others, Brown-Pearce tumor tissue (same site and dosage) which had been kept frozen for 18 hours at 24° F. Two weeks later the 21 experimental animals and the 22 previously un.injected controls (Table 2) were given inoculations, in the opposite testis, of 0.3 cc. of a 1:4 saline suspension of viable Brown-Pearce tumor tissue.

In four additional experiments (Table 2) nineteen rabbits received subcutaneous inoculations above the shoulder: five of 0.3 cc. of centrifugate of sedimented fresh Brown-Pearce tumor cells from which the supernatant fluid had been removed and replaced with saline, and fourteen others of a similar dosage of similarly prepared sedimented cells of Brown-Pearce tumor tissue which had been kept frozen 14 hours. Two to 3 weeks later the nineteen experimental rabbits and sixteen previously uninjected controls were given subcutaneous inoculations in the flank of 0.3 cc. of a 1:4 saline suspension of viable Brown-Pearce tumor cells.

There were originally 86 rabbits (34 chinchillas, sixteen New Zealand Whites, fourteen Brown-gray hybrids, eight Flemish, six English, four Dutch, and four miscellaneous, paired as to breed) utilized in the control and experimental series; but seven died of intercurrent disease before 21 days had elapsed following transplantation (Table 2). At post mortem examination it was possible to measure primary tumors and metastases by water displacement. The method of analysis of the rabbit tumor has been described (6).

Sections for histologic study were made of tumors used for transfer and of tumors and viscera of animals dying of tumor or having tumor at post mortem examination. After tumor transplantation the animals were examined at 5–7 days, 10–12 days, 14–15 days, 18–21 days, 28, 35, 42, 49, 56, and 63 days, when the surviving rabbits and mice were sacrificed (most of the mice without tumors at 30 days were sacrificed). Tumor growths were measured with calipers, and the product of the diameter of three dimensions in cm. was arbitrarily called the volume in cc. The error inherent in the method affected both controls and experimental animals. In the minimal lesion the product of the three dimensions was greater than 0.05 cc.

RESULTS

The results are presented in tabular form (Tables 1 and 2). It suffices to note that no statistically significant differences in the course of the Brown-Pearce or E 0771 tumors could be ascribed to the experimental series having had a second transplantation of tumor tissue, when compared to the controls.

Mice.—The occurrence of two deaths among the 60 experimental mice, each of which had two inoculations of tumor tissue, was not inconsistent with the two deaths among the 106 controls, which had a single inoculation. The four tumor growths at
21 days, in the subcapular area of the 106 controls, were not significantly less than the three growths in the subcapular area of the 60 experimental animals ($x^2 = 0.1, N = 4, P = 0.75$). The average volume of the five growths in both sites in the experimental series at 21 days was 1.0 cm. and for the four growths in the controls, 0.8 cm.—not significantly different (Table 1).

**Rabbits.**—The primary tumor from the 41 experimental rabbits averaged 20.1 cc. at necropsy, compared to 24.7 cc. among the 38 controls (difference, 4.5 ± 1.6 cc., $t = 0.8$—not significant); the metastatic foci, 7.4, compared to 6.3 among the controls (difference, 1.1 ± 0.8, $t = 0.6$—not significant); the total tumor, 79.2 cc., compared to 52.6 cc.—not significantly different (Table 1).

**Flexner and Jobling (13-15) used a slowly growing transplantable rat tumor (Flexner-Jobling tumor) which caused death by progressive local growth or by metastases to distant organs in 50 per cent of the rats, usually within 60-150 days. Tumors about 1 cm. in diameter were used for transfer. These growths were between 23 and 71 days of age (average, 47),**

### TABLE 2

**SECOND TRANSPLANTATION OF THE BROWN-PEARCE TUMOR INTRATESTICULARLY OR SUBCUTANEOUSLY IN RABBITS 12-28 DAYS FOLLOWING THE FIRST TRANSPLANTATION**

<table>
<thead>
<tr>
<th>Rab.</th>
<th>Br</th>
<th>Tr-S-I</th>
<th>B-S</th>
<th>RT-LT</th>
<th>MF</th>
<th>TT</th>
<th>Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1014</td>
<td>CH</td>
<td>BBRT14</td>
<td>BLT</td>
<td>24-2</td>
<td>21</td>
<td>64</td>
<td>23-10D</td>
</tr>
<tr>
<td>1017</td>
<td>BR</td>
<td>BBRT14</td>
<td>BLT</td>
<td>34-11</td>
<td>22</td>
<td>219</td>
<td>50-36D</td>
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<tr>
<td>1021</td>
<td>CH</td>
<td>BBRT14</td>
<td>BLT</td>
<td>0-0</td>
<td>0</td>
<td>75-61S</td>
<td></td>
</tr>
<tr>
<td>1022</td>
<td>EN</td>
<td>BBRT14</td>
<td>BLT</td>
<td>6-0</td>
<td>5</td>
<td>19</td>
<td>9-1 SD</td>
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**Means 41 EXP.**

<table>
<thead>
<tr>
<th>Days</th>
<th>M</th>
<th>810</th>
<th>825</th>
<th>840</th>
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<th>885</th>
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<td>41</td>
<td>43</td>
<td>45</td>
<td>47</td>
<td>49</td>
<td>51</td>
</tr>
</tbody>
</table>

### Means 41 EXP.

| 14-20 | 7.4 | 79 | D-16 | 38 | Control | 25 | 6.3 | 52 | D-16 |

**Notes:** Rab. = rabbit number; 1st digit = Exp. No.; Br = breed; TR-S-I = 1st transplant site and interval in days before 2d transplant; CH = chinchilla; BB = whole unfrozen Brown-Pearce tumor; BF = whole frozen Brown-Pearce tumor; BS = sedimented cells from frozen tumor fresh; BSC = sedimented cells from fresh unfrozen tumor; RT = right testis; LT = left testis; MF = number of metastatic foci; TT = total tumor, primary and metastatic, in cc.; Days = termination date after 1st and 2d inoculations; D = died from Brown-Pearce tumor; S = survived; F = paralyzed from tumor; M = moribund from tumor; SC = subcutaneous transplantation.
compared to 9–21 days for E 0771 mouse carcinoma transplants of comparable size. Jobling did not state which animals died from the tumor, only that the growths did or did not regress. Those growths which did not regress or stop growing are assumed to have killed the rat. Data on rats reinoculated 60–150 days after the first transplant were not used, since many rats died of the first transplant during this period. Jobling did not state that reinoculation within 60 days after the first transplant was ineffectual in changing host resistance, but we believe his data (his Tables 2, 4, 6) warrant this conclusion when rearranged and analyzed by the $\chi^2$ test.

Thus, of 193 rats reinoculated 0–60 days after the first transplant, 93 recovered, compared to 53 recoveries among the 108 control rats receiving one inoculation only. Thus, two transplants within 60 days resulted in the same mortality from the Flexner-Jobling tumor as occurred from a single transplant ($\chi^2 = 1.1, N = 2$—not significant).

Rous and Murphy (22) reinoculated 29 fowls with the same fowl tumor in a new site and with a different tumor in another site (chicken tumors I, VII, and XVIII were employed). The same tumor took in two of fourteen that were negative after the first inoculation; in three of eleven, regressing or stationary; and in two of four, with progressing tumor. The differences in the host-tumor reactions between the first and second inoculations with the same tumor were not statistically significant. In contrast, the fourteen fowls without tumors had ten positive growths of a different tumor among the fifteen animals with takes on the first inoculation ($\chi^2 = 6.6, n = 1, P = 0.01$, significant). This indicates that the chief factors of resistance to one tumor were both natural and different from those to another neoplasm.

DISCUSSION

The inoculation of Brown-Pearce or E 0771 tumor tissue which has been kept frozen for several weeks, or which has been lyophilized, resulted in a marked breakdown of the host’s resistance to the growth of the same tumor (1, 8, 24).¹ This is in contrast to the negative effect of a double transplantation of fresh whole tumor tissue or of sedimented cells. Recently, Shear et al. demonstrated that the supernatant unfiltered fluid of fresh unfrozen C3H tumor 8852 after prolonged low speed centrifugation contains an XYZ factor in full potency (23). In experiments paralleling those listed in Table 1, the supernatant fluid was poured off the sedimented E 0771 cells and injected (9). The result was a marked breakdown in the resistance of the C57BR/cd and BALB/c mice to the C57BL tumor E 0771, whereas the sedimented cells had no appreciable effect on host resistance.

Many years ago when the XYZ enhancing phenomenon was first observed with the Brown-Pearce tumor, the senior author observed similar results obtained by Jobling with heated emulsions of the Flexner-Jobling tumor (15). In a personal communication Dr. Jobling stated that he had had difficulty repeating the experiments, and several others had the same experience. The experiments of Chambers and Russ (10, 12) and Chambers and Scott (11) with the Jensen rat sarcoma, of Lepper (18), and of Rondoni (19) suffered a similar fate. It was concluded that heat was a poor way to demonstrate an XYZ factor in a given tumor, particularly since our emulsions of the Brown-Pearce tumor (7) seemed thermolabile (55°C., ½ hr.) and Jobling’s emulsion thermostable (55°C., ½ hr.). Recently, Snell¹ stated that the lyophilized material from mouse tumor 15091a which can induce the XYZ phenomenon is thermostable (55°C., ½ hr.), whereas we have found the XYZ factor (frozen but not desiccated) in mouse tumor E 0771¹ and that in the Brown-Pearce tumor to be thermolabile (7). It was postulated either that the XYZ factors differ in physical properties or that the thermostability is being affected by the medium or by the method of preparation. Both Jobling and Snell¹ and Kaliss, Jonas, and Avnet (14) used such fine emulsions (homogenates) of tumor that no tumor growth resulted from their injection, and their technics varied only in that the former authors heated for ½ hour at 55°C, whilst the latter lyophilized the material. Consequently, we have tabulated Jobling’s experiments with the 301 control rats ( singly and doubly inoculated animals), the 28 rats injected with unheated homogenate, and the 106 rats injected with heated (55°C., ½ hr.) homogenates.

<table>
<thead>
<tr>
<th></th>
<th>Died</th>
<th>Recovered</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>55</td>
<td>23 (12.3)</td>
<td>28</td>
</tr>
<tr>
<td>Heated</td>
<td>81</td>
<td>25 (47.5)</td>
<td>106</td>
</tr>
<tr>
<td>Total</td>
<td>136</td>
<td>148 (84.1)</td>
<td>284</td>
</tr>
</tbody>
</table>

¹ G. D. Snell, unpublished material.

² A. E. Casey, F. M. Schabel, Jr., and J. Gunn. Unpublished material.
Jobling's data indicate that the unheated emulsion set up a state of resistance when injected, only five animals so injected dying with the tumor ($\chi^2 = 21, P = 0.01$—significant), some 81 rats treated with heated material dying from the tumor. The injection of unheated emulsions of cytoplasm or of nuclei from the Brown-Pearce tumor prepared in a particular manner (Waring Blender, citric acid) induced a significant state of resistance in the rabbit, whereas the frozen or lyophilized tumor tissue induced a state of susceptibility (1–5, 8, 17, 23–25).

In the original experiments of Rous (20, 21), it would seem that an XYZ effect occurred with chicken tumor I. This neoplasm would not grow at first in any except a special line of Plymouth Rocks and in only 28 of the first 38 special fowls inoculated. At this point, ten special fowls were injected in one site with fresh tumor tissue and in another site with a supernatant fluid—a homogenate of fresh chicken tumor I tissue: (a) centrifuged 5 minutes at 2,800 r.p.m.; (b) the upper layers of the supernatant recently centrifuged 15 minutes at 8,000 r.p.m.; (c) the upper part of the second supernate used for injection. This method is almost identical with that used recently by Shear, Imagawa, Syverton, and Bittner (23). Progressive tumors grew in all the fowls (and in seven grew at the site of injection of supernate). This was a statistically significant enhancement of malignancy over the previous experience of 28 tumors among 58 fowls inoculated ($\chi^2 = 9.2, n = 1, P = 0.001$—significant). Casey noted that the XYZ effect could be obtained with the Brown-Pearce tumor in rabbits by simultaneous injections of the XYZ material at a different site from the tumor inoculum (1). From a fowl, injected by Rous (21) with the supernate plus tumor (as described above), tumor was excised and then inoculated into ten Plymouth Rocks not of the special line; and in five the tumor grew. The enhanced growth of chicken tumor I (associated with the supernate injection) was therefore transmissible serially, since, of 33 market Plymouth Rocks previously injected, the tumor grew in none ($\chi^2 = 18.9, n = 1, P = 0.001$—significant).

In another experiment (20, 21), Rous took the upper layer of the first supernate from chicken tumor I, filtered it through a coarse No. 2 Berkefeld filter, and injected nine market Plymouth Rocks with the supernate-filtrate alone (one growth resulted) and twenty market Plymouth Rocks with the supernate-filtrate at one site and the chicken tumor I tissue at another site. Of the seventeen free from intercurrent infection, thirteen died from progressive tumor growth (ten had metastases to distant organs), tumors grew in three and then regressed, and one had no tumors. This compared with 0 tumors among the 33 market Plymouth Rocks previously inoculated with the chicken tumor I alone, a statistically significant increase in malignancy compatible with the XYZ effect ($\chi^2 = 34, n = 1, P = 0.0001$—significant).

Of interest, therefore, are the observations that, with four malignant tumors in four animal species (the Brown-Pearce tumor of rabbits, E 0771 carcinoma of mice, chicken tumor I of fowls, and the Flexner-Jobling tumor of rats), reinoculation with the same tumor does not alter the host's reaction to the neoplasm, although potent XYZ factors are presumably present in the tumor emulsion.

**SUMMARY**

Mouse mammary carcinoma E 0771 of C57BL/6 origin, known to yield XYZ factors, was inoculated into 30 C57BN/cd as well as 30 BALB/c mice. Eight to 15 days later these animals, as well as an additional 30 C57BR/cd and 76 BALB/c mice, received an injection of viable E 0771 tumor cells. No significant difference in tumor development was noted when animals receiving only a single injection of E 0771 tumor cells were compared to mice receiving a double inoculation of the same tumor.

Similarly, the prior inoculation of fresh Brown-Pearce rabbit epithelioma cells failed to alter the malignant process in recipient hosts receiving a second implant of the same tumor administered at a different site 14–21 days later. This was made known in a series of experiments utilizing 78 rabbits of mixed breeds. Of these animals, 40 served as recipients of a double inoculum of viable Brown-Pearce tumor cells, while the remainder received only a single injection and served as controls. These results are in sharp contrast to the XYZ phenomenon observed when frozen Brown-Pearce tumor tissue is given prior to challenge transplantation with fresh homologous tumor tissue.

Thus, for these two mammalian tumors, the E 0771 mammary carcinoma of mice and the Brown-Pearce epithelioma of rabbits, the inoculation of test animals with fresh viable cancerous tissue, followed by a second implantation of the same tumor, does not alter significantly the malignant process in the recipient hosts, although potent XYZ factors are known to be demonstrable when these tumors are subjected to prolonged frozen storage, lyophilization, or centrifugation.

That this phenomenon may be applicable to
other experimental neoplasms is made apparent when the data of Jobling and Flexner concerning a rat carcinoma and the data of Rous and Murphy based on experiments with a fowl tumor are reviewed. Although the prior injection of heated rat carcinoma cells resulted in an enhancement of a subsequent transplant of tumor cells, the prior injection of fresh unheated tumor cells did not significantly alter the progress of a subsequent transplant with homologous cancer tissue. Similarly, although the Rous fowl sarcoma appears capable of exhibiting the XYZ phenomenon when supernatant fluid derived from the tumor is utilized, no enhancement of tumor transplant growth occurred when an injection of viable Rous tumor cells preceded challenge with the same tumor tissue.

CONCLUSIONS

The prior inoculation of homologous fresh whole tumor cells, known to yield demonstrable XYZ factors, did not significantly alter the incidence, growth, metastases, or mortality upon subsequent reinoculation of the E 0771 mammary tumor of mice and the Brown-Pearce tumor of rabbits. These results present a sharp contrast to the significant enhancement in the course of the malignant disease when XYZ factors, obtained by subjecting the cancerous tissue to freezing, lyophilization, or centrifugation are injected prior to implantation of the corresponding tumor.

A review of the literature reveals that similar results were obtained when a rat carcinoma and a fowl sarcoma were utilized experimentally in their respective hosts.

REFERENCES


ADDENDUM

Since this paper was submitted for publication, statistical analyses have been made of papers by Cloudman (Cloudman, A. M. Successful Interspecies Transplantation of a Mouse Tumor. Science, 78:625—26, 1932) and by Lewis and Lichtenstein (Lewis, M., and Lichtenstein, E. G. Breaking Down
the Resistance of Albino Mice to the Transplantation of Tumors Induced by 1:2:5:6-Dibenzanthracene in a Different Strain of Albino Mice. Am. J. Cancer, 27:246—56, 1936; Lewis, M. R., and Lichtenstein, E. G. Further Studies on the Breaking Down of Resistance of Mice of One Strain to the Transplantation of Tumors of Mice of Another Strain. Am. J. Cancer, 28:746—51, 1936) which bear on the subject of reinoculation with the same tumor. Cloudman transplanted Strain A mammary carcinoma 1509la (which was fatal in each of 150 strain A mice inoculated) into 485 mice of six foreign strains, the negative or recovered animals being reinoculated with the same tumor. Tumor 1509la killed 50 of 95 MD mice (W. S. Murray's dilute brown), 68 of 104 D mice (Strong's dilute brown), ten of 21 B mice (Little's blacks), seven of 46 Ld (J. M. Murray's leaden), one of 78 Z mice (Zavadakaia's albinos), three of 91 Mus bactrianus on the first inoculations; and 26 of 85 MD, 26 of 81 D, two of ten B, 0 of 39 Ld, 0 of 77 Z, and 0 of eleven Mus bact. negative or recovered mice on the second transplantation. The only statistically significant difference was in fewer reinoculations takes in the Ld strain, a strain naturally resistant on the first inoculation ($X^2 = 6.4$, $n = 1$, $P = 0.01$). In other words, "acquired resistance" could only be demonstrated in a strain with a high natural resistance to the neoplasm; or, it might be reasoned that high natural resistance could be even better demonstrated by reinoculation. Mice with little or no natural resistance showed no significant change in reaction upon reinoculation.

Lewis and Lichtenstein inoculated twenty CSH mice with BALB tumors Nos. 1, 3, and 6. From the 60 first transplants ten progressive tumors resulted; upon second inoculation of the same twenty mice with the same three tumors, thirteen of 60 transplants grew; with third and fourth inoculations of the same mice with the same tumors, twelve of 65 transplants grew (not sig.). The same authors inoculated 24 BALB mice with A strain tumors 9, 14, and 20; twelve growths occurred among the first 25 transplants; with the second inoculation of the same tumors, eighteen of 31 transplants grew; with the third and fourth inoculations of the same mice with the same tumors, there were nineteen growths in 62 transplants (not sig.). Again, 48 BALB mice were inoculated with CSH tumors 4, 8, 12, 13, 14, and 38; in the first inoculation one of 148 transplants grew; with the second inoculation two of 148 transplant grew; with the third and fourth inoculations five of 304 transplants grew (not sig.). Combining the three series, there were 23 tumors among 260 first inoculations with a given tumor; 38 of 259 second inoculations of the same tumors into the same mice; 36 of 381 third and fourth inoculations (differences not sig.).

Lewis and Lichtenstein attacked the problem of whether multiple inoculations of CSH tissue (CSH tumors) into BALB mice, or of BALB tissues (BALB tumors) into CSH mice, or of A tissues (A strain tumors) into BALB mice could break down the resistance of the mice of the foreign strain to the growth of inbred strain tumors. Their data were difficult to tabulate, but some 110 mice seem to have received 8—20 trocar implants (usually at 4-6-day intervals) of some 25 foreign mouse strain tumors. From the first seven inoculations (over a 30-day period) into each mouse 45 progressive tumors developed among 794 transplants; from the eighth to the twentieth inoculation (during second to fourth month) into the same mice 65 tumors developed among 801 transplants; the difference was probably significant in that more tumors occurred in the second series than in the first ($X^2 = 3.8$, $n = 1$, $P = 0.05$). Analysis revealed, however, that some tumors used in the first seven inoculations were not employed in the second series (Strain A tumors 4, 6, 7, 10, 11, 13; BALB tumors 5 and 7), and, vice versa, some tumors employed in the second series had not been employed in the first series (CSH tumors 11 and 23; BALB tumor 9). Thus, there were six growths among 901 transplants of tumors used only in the first seven inoculations and fourteen growths among 74 transplants of tumors used in the eighth to twentieth inoculation but not employed in the first to seventh inoculation; this difference was significant ($X^2 = 32.4$, $n = 1$, $P = 0.01$). As a further check on whether the observed increased incidence in the eighth to twentieth inoculation was due to the use of new tumors, an analysis was made including only tumors which were used in both the first to seventh and eighth to twentieth series. There were 39 growths among 503 transplants in the first as compared to 51 among 711 transplants in the second series of inoculations when the same tumors were used in both series; there were not only no significant differences, but the values were so nearly alike for the tumor incidence in the first as compared to the second series as to approach positive proof that no such differences existed ($X^2 = 0.144$, $n = 1$). In summary, it may be concluded that the data of Lewis and Lichtenstein (not the conclusions of the authors) show that seven to twenty transplantations of living BALB tumor tissues into CSH mice or CSH and A tumor tissues into BALB mice did not significantly break the resistance of the mice to either the same tumor or to different tumors of the same strain.
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