cells as Lyt-2 antigen, the only suggestion which remains is that it is Lyt-3 antigen. This hypothesis is confirmed by the fact that presence or absence of reaction of F9 MCA (Table 1) correlates precisely with the presence or absence of Lyt-3,2 antigen, but not of other antigens, on the thymocytes of mice of this particular line.

Since two groups of determinants were discovered [7] on Lyt-2 antigen with the aid of MCA it can be tentatively suggested that the same groups of determinants exist on Lyt-3 antigen, which is linked with Lyt-2. In that case the F9 MCA which we obtained evidently reveal a determinant of the second group of Lyt-3 antigen, expressed on a relatively smaller proportion of T cells of lymph nodes and spleen.

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CHANGES IN HOST RESISTANCE TO CANCER DURING CHEMICAL CARCINOGENESIS

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After a single injection of a chemical carcinogen (9,10-dimethyl-1,2-benzanthracene — DMBA) into noninbred rats a long time elapses before the appearance of a tumor. The duration of the latent period depends on the dose and site of administration of the carcinogen. The writer has shown [1, 2] that after peroral administration of 20 mg DMBA to rats weighing 90-100 g it is 5-9 months, whereas after subcutaneous injection of 0.6-4 mg into rats of the same weight it is only 2-4 months.

The aim of this investigation was to study the resistance of rats at different stages of growth of a tumor induced by subcutaneous injection of DMBA as reflected in the successful taking of tumors with different levels of transplantability.

EXPERIMENTAL METHOD

An injection of 4 mg of DMBA in 0.2 ml of peach oil was given subcutaneously into the left side of female rats weighing 90-100 g. Three months later, 30 animals from this group were selected, in which foci of induration no bigger than a lentil (tumor anlage) could be

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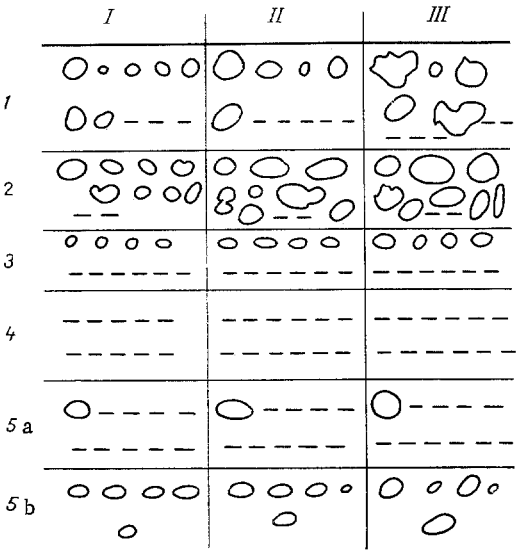

Fig. 1 Fig. 2

Fig. 1. Mammary gland adenocarcinoma induced by peroral administration of 20 mg DMBA: a) general view (120 ×); b) numerous division figures, considerable polymorphism of cells (450 ×).

Fig. 2. Results of inoculation of transplantable and DMBA-induced mammary gland carcinoma in rats 3 months after receiving injection of DMBA. Numbers on left indicate groups of animals. I) 11 days; II) 17 days; III) 21 days after transplantation of tumor.

palpated at that time at the site of injection of DMBA. The selected rats were divided into three groups (10 animals in each group).

The rats of group 1 received an injection of 0.5 ml of a 25% suspension of a mammary gland tumor, induced by peroral administration of 25 mg DMBA, in physiological saline. The tumor was inoculated alongside the focus of palpable induration at the site of subcutaneous injection of DMBA. During histological investigation the induced mammary gland tumor was found to be an adenocarcinoma. The ducts were lined with several rows of epithelial cells which exhibited considerable polymorphism, and mitotic division figures were visible (Fig. 1).

The rats of group 2 were inoculated alongside the palpable induration at the site of injection of DMBA with 0.5 ml of a 25% tissue suspension of a transplantable mammary gland adenocarcinoma in physiological saline (MGC-1), obtained and fully described by Konoplev et al. [3].

Rats of group 3 served as the control for growth of tumors induced by subcutaneous injection of DMBA, and no other tumor was transplanted into them.

Since the rats weighed 250-280 g at the beginning of the transplantation experiment two further control groups were used: group 4 (10 rats) — control for successful taking of induced mammary gland carcinoma in healthy rats of the same weight, group 5a — the control for successful taking of the MGC-1 in rats weighing 250-280 g, and group 5b (rats weighing 60-70 g) — the control for transplantation of MGC-1 into young rats.

In 11 rats in which 5 months after subcutaneous injection of 4 mg DMBA, well-formed tumor nodules measuring from the size of a large pea to a large walnut could be palpated at the site of injection, 0.5 ml of a 25% suspension of an induced mammary gland carcinoma (nine

rats) and a transplantable mammary gland carcinoma (MGC-1) in the same dose (two rats) were transplanted. Tumors were transplanted on the side opposite to the site of injection of the carcinogen.

Nine rats with tumors at the site of injection of DMBA, similar in size to tumors in rats of the experimental group, and into which nothing was transplanted, served as the control.

EXPERIMENTAL RESULTS

Tumor nodules varying in size from a pea to a plum were found 11 days after transplantation of the first generation of induced mammary gland carcinoma in seven of the 10 rats of group 1 at the site of transplantation. In two rats the tumors which appeared were subsequently absorbed, whereas in the rest they continued to grow and reached a large size (Fig. 2).

In the animals of group 2, tumor nodules were found at the site of transplantation of MBC-1 in eight of the 10 rats. The tumors varied in size from a pea to a large plum, and in one rat they reached a size of 4.7 × 3.0 × 1.7 cm.

During this period, in the control group (group 3) tumor nodules not larger than a pea could be palpated in only four of 10 rats at the site of injection of DMBA. In the remaining six rats, foci of induration that were palpable at the site of injection of 4 mg DMBA at the time of selection, were absorbed by this time.

In group 4 (control for transplantation of induced mammary gland carcinoma) no tumors were found in any of the 10 rats. From 10 animals weighing 250-280 g, MGC-1 was transplanted into only one rat, whereas growth of the tumor was noted in all five rats weighing 60-70 g.

DMBA-induced mammary gland carcinoma which, as a rule, did not grow after transplantation even in young noninbred rats, thus took successfully in 50% of rats weighing 250-280 g, in which foci of induration measuring up to the size of a lentil were present at the site of injection of DMBA toward the time of transplantation of the tumor. The transplantable strain of mammary gland carcinoma (MGC-1) gave 85% of successful takes in these animals, whereas in healthy animals of the same weight, it took in only 10% of cases.

In the later stages of carcinogenesis, when well-formed tumors ranging in size from a pea to a large walnut were palpated at the site of subcutaneous injection of DMBA, the first generations of induced mammary gland carcinoma took successfully in eight of nine rats, and in three of the nine rats metastases measuring from the size of a millet seed to a small pea were found in the lungs. Simultaneously with successful transplantation of mammary gland carcinoma, rapid growth of the tumor at the site of injection of DMBA also was observed. In 1 month the tumors grew to an enormous size, occupying the whole of the lumbosacral region, and sometimes merging with the tumor at the site of inoculation.

In the nine control rats into which the tumor was not inoculated, by this time the tumors at the site of injection of DMBA had only doubled in size, and in most rats they varied in size from a large haricot bean to a large plum.

Two rats with well-formed tumors at the site of injection of DMBA, into which MGC-1 was transplanted, died 12 and 22 days later respectively. In both rats enormous tumors were present at the site of transplantation of the tumor and at the site of injection of DMBA, metastases were present in the lungs, and one rat also had metastases in the lymph nodes of the left and right axillary regions.

These results are evidence that even in the early stages of chemical carcinogenesis, during the period of tumor formation, antitumor resistance declines. This fall becomes more marked in stages of carcinogenesis, when well-formed tumor nodules appear. This was manifested not only as the successful taking of tumors of varied degrees of transplantability, but also as the appearance of distant metastases after transplantation both of first generations of induced mammary gland carcinoma and also of transplantable mammary gland carcinoma (MGC-1) which, as we know, under ordinary conditions does not metastasize after transplantation into normal rats.

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