

METASTASIZATION OF INDUCED AND TRANSPLANTED TUMORS
IN RATS FOLLOWING IMMUNIZATION WITH HOMOLOGOUS
AND HETEROLOGOUS ANTIGENS

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Before the problem of metastasization of malignant tumors can be solved, a correct explanation must be given of the causes of this process. Metastasization is observed in those parts of the body which are injured by various biological or physicochemical factors [1, 5-12].

The authors' previous investigations [2] showed that immunization of rats with antigens from homologous and heterologous tissues, mixed with Freund's complete adjuvant, leads to the appearance of antibodies reacting with the recipient's own organs. Meanwhile destructive changes were observed in the liver and kidneys of the immunized animals.

The object of the present investigation was to study the effect of immunization of animals with antigens from homologous and heterologous tissues on the process of metastasization of experimental tumors.

EXPERIMENTAL METHOD

The investigation was conducted on 240 Wistar rats of both sexes aged 5-6 months. The following tumors were used: a rhabdomyosarcoma of rats (second passage), induced with 9,10-dimethyl-1,2-benzanthracene in the region of the left hind limb, and a transplanted carcinoma of the kidney, strain PA.

The rats were immunized with homologous kidney and liver, and also with rabbit's kidney and liver, both with and without Freund's adjuvant, in accordance with the scheme described in the previous paper [2]. On the 12th day after the last immunization a suspension of the tumor in physiological saline (1:4) was transplanted into the spleen of the rats in a dose of 0.2 ml per animal. This method of transplantation was chosen because, as previously demonstrated [3-4], the most rapid growth and metastasization of experimental tumors is observed when they are transplanted into the spleen.

The development and localization of the metastases were investigated in rats dying from the tumors. The metastases were counted and measured on the surface of the organ and then in slices cut to a thickness of 2-5 mm. The numerical results obtained were analyzed by statistical methods and differences were regarded as significant when $P < 0.01$.

EXPERIMENTAL RESULTS

Altogether two series of experiments were carried out. In 120 rats of series I the effect of immunization on the process of metastasization of the induced rhabdomyosarcoma was studied, and in the 120 animals of series II its effect was studied on metastasization of carcinoma of the kidney, strain PA. The results of these experiments are given in the table.

The results of the experiments of series I showed that following immunization of the rats with homologous and heterologous antigens, both with and without Freund's adjuvant, the metastasization of the induced tumor in the kidneys and liver was intensified. However, a statistically significant increase in the degree of metastasization of this tumor was observed only in the liver after immunization of the rats with antigens from rat's and rabbit's liver with Freund's adjuvant, and also with antigens from rabbit's liver without adjuvant ($P < 0.01$). After immunization of the animals with antigens from rat's and rabbit's kidney, whether with or without Freund's adjuvant, the increase in the intensity of metastasization in the liver by comparison with the control figure was not significant ($0.2 < P < 0.5$).

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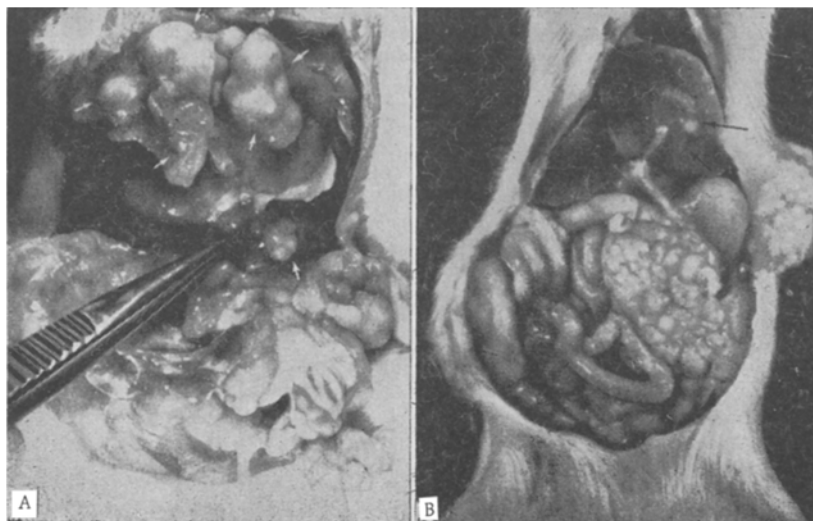
Effect of Immunization of Rats with Homologous and Heterologous Antigens with the Process of Metastasization of Induced Rhabdomyosarcoma and Carcinoma of the Kidney "PA"

Tissue of immunization	No. of animals	Tumor used	Metastasization			
			in liver		in kidney	
			Freund's adjuvant	Without Freund's adjuvant	Freund's adjuvant	Without Freund's adjuvant
Rat's kidney	20	Induced rhabdomyo-sarcoma	$\frac{8}{4}$	$\frac{8}{3}$	$\frac{8}{3}$	$\frac{8}{2}$
	20	Carcinoma of the kidney "PA"	$\frac{10}{5}$	$\frac{10}{3}$	$\frac{10}{3}$	$\frac{10}{1}$
Liver	20	Induced rhabdomyo-sarcoma	$\frac{8}{7}$	$\frac{7}{4}$	$\frac{8}{1}$	$\frac{7}{0}$
	20	Carcinoma of the kidney "PA"	$\frac{10}{7}$	$\frac{10}{5}$	$\frac{10}{1}$	$\frac{10}{0}$
Rabbit's kidney	20	Induced rhabdomyo-sarcoma	$\frac{8}{5}$	$\frac{8}{4}$	$\frac{8}{4}$	$\frac{8}{3}$
	20	Carcinoma of the kidney "PA"	$\frac{10}{1}$	$\frac{10}{1}$	$\frac{10}{0}$	$\frac{10}{1}$
Control No. 1 (physiological saline + Freund's adjuvant)	20	Induced rhabdomyo-sarcoma	$\frac{9}{8}$	$\frac{8}{7}$	$\frac{9}{2}$	$\frac{8}{0}$
	20	Carcinoma of the kidney "PA"	$\frac{10}{8}$	$\frac{10}{6}$	$\frac{10}{2}$	$\frac{10}{1}$
Control No. 2 (no treatment)	20	Induced rhabdomyo-sarcoma	$\frac{7}{2}$	$\frac{7}{2}$	$\frac{7}{0}$	$\frac{7}{0}$
	20	Carcinoma of the kidney "PA"	$\frac{10}{2}$	$\frac{10}{1}$	$\frac{10}{0}$	$\frac{10}{0}$
	20	Induced rhabdomyo-sarcoma	$\frac{8}{2}$	$\frac{7}{1}$	$\frac{8}{0}$	$\frac{7}{1}$
	20	Carcinoma of the kidney "PA"	$\frac{10}{2}$	$\frac{10}{2}$	$\frac{10}{0}$	$\frac{10}{0}$

Note: Numerator – number of rats with transplanted tumors; denominator – number with metastases in organ.

In the case of immunization of rats with antigens of rat's and rabbit's liver, especially with Freund's adjuvant, the size of the metastases in the liver differed considerably from their size in the animals of the other groups and the controls. Whereas in the controls the medial lobe of the liver was usually affected by metastases (3-5 metastases with a mean diameter of 0.2×0.5 cm), in the experimental series the medial lobe was solidly invaded with tumor tissue and metastases were present also in the other lobes of the liver, their mean diameter 0.7×1.5 cm (see the figure a and b).

The degree of metastasization in the kidney following immunization with the antigens described above was slightly higher, although it was not significantly different from the control figure ($0.2 < P < 0.5$). The kidneys were usually affected by 2 or 3 metastases, situated on the surface and not spreading deep into the tissue.



Metastasization of an induced rhabdomyosarcoma in a rat. a) In an animal immunized with antigen from rabbit's liver, mixed with Freund's adjuvant; b) in an unimmunized animal (control). The metastases are indicated by arrows.

In all cases of immunization the intensity of metastasization into the omentum, diaphragm, peritoneum, mesentery, perinephric tissue and other parts of the body showed no significant difference from the control figure.

Similar results were obtained in the experiments of series II to study the effect of immunization with homologous and heterologous antigens on the process of metastasization of a transplanted carcinoma of the kidney, strain PA, in rats.

A statistically significant increase in the intensity of metastasization of carcinoma of the kidney was observed only in the liver after immunization with antigens of rat's and rabbit's liver together with Freund's adjuvant ($P < 0.01$). Immunization of the rats with antigens from rabbit's liver without adjuvant also led to a definite increase in the degree of metastasization in the liver ($P < 0.05$).

Following immunization of the rats with antigens of rat's and rabbit's kidney, both with and without Freund's adjuvant, the increase in the degree of metastasization in the liver and kidney was not significant by comparison with the control figure ($0.2 < P < 0.5$).

In all cases of immunization the intensity of metastasization of the carcinoma of the kidney in other parts of the body was the same as in the control series.

Injection of physiological saline mixed with Freund's adjuvant into the rats caused no increase in the intensity of metastasization of either the induced rhabdomyosarcoma or the carcinoma of the kidney, strain PA, in the liver, kidneys or other parts of the body.

The results obtained thus show that immunization of rats with antigens from homologous and heterologous tissues, mixed with Freund's complete adjuvant or without it, stimulates metastasization of an induced rhabdomyosarcoma and a transplanted carcinoma of the kidney, strain PA, in rats. The greatest increase in the intensity of metastasization, especially in the liver, was observed when the rats were immunized with antigens from rabbit's and rat's liver.

The results described are in agreement with those of a previous investigation [2] in which it was found that immunization of rats with any one antigen (for example, from the liver) leads to the appearance of antibodies against the corresponding autologous organ, and also against other tissues (the kidneys). The destructive processes developing in these circumstances are observed to a greater degree in the corresponding organ, although other tissues in the body may also be affected. Consequently, the destructive changes developing in the organs of rats following immunization with homologous and heterologous antigens facilitate the increase in the intensity of metastasization of experimental tumors.

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