

METASTASIS FORMATION OF BROWN-PEARCE TUMOR INOCULATED  
INTO DIFFERENT PARTS OF THE STOMACH UNDER NORMAL CONDITIONS  
AND AFTER EXPOSURE OF THE LIVER TO CARBON TETRACHLORIDE

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The liver is the organ which in cases of stomach cancer is most frequently affected by metastases. According to the findings of L. M. Nisnevich [10], metastases of stomach cancer in the liver are found in 28.3% of cases, and according to the data of F. I. Pozhariskii [15], in 36.4% of cases, a fact which puts the liver into the first place among those organs in which metastases of stomach cancer develop. This fact is also reported in the papers published by a number of other authors [2,12]. Cancer of the cardia part of the stomach is particularly dangerous, as it is difficult to recognize, a fact which prevents the early diagnosis [5,16].

Numerous clinicians and morbid anatomists [2,3,5,10,13] believe this form of cancer to be particularly malignant as far as the formation of metastases is concerned. There are also reports [4] according to which the lymphatic system of the cardia part of the stomach is connected with the efferent lymph vessels of the liver.

In view of the facts discussed above, study of the conditions enhancing the growth of metastases originating from a stomach carcinoma in the liver seems to be of particular importance.

There are reports in the literature according to which the development of precancerous conditions induced by the administration of carcinogenic substances, as well as the growth of the tumor in the liver, depends on the functional state of that organ [17,14].

N. P. Kochneva [8] transplanted Brown-Pearce tumors into the stomach wall of rabbits and observed the appearance of liver metastases after not less than two months. This author does not state the site of inoculation and the dose of tumor emulsion employed.



Fig. 1. The wall of the cardia part of the stomach of a rabbit to the mucosa site with a Brown-Pearce tumor on the 24th day after the inoculation.

In the present paper we set ourselves the task to study the metastasis formation of Brown-Pearce tumors transplanted into the stomach wall of rabbits in relation to the localization of the tumor in the stomach and to functional changes in the liver evoked by administration of a hepatotoxic substance.

#### METHOD

The experiments were carried out on male rabbits weighing 2500-2900 g. The Brown-Pearce tumor was inoculated on to the serous membrane of the stomach by injection of 0.4 ml of a 10% tumor emulsion. In the first series of experiments we used 16 rabbits which were distributed into four groups, each consisting of four animals. In the first group the tumor was inoculated into the pylorus, in the second group into the cardia, in the third group into the greater curvature and in the fourth group into the fundus.

In the second series of experiments the experimental animals (17 rabbits) were given for three subsequent days

carbon tetrachloride in a dose of 0.25 ml per kg weight by subcutaneous injection into the back. On the third day after the beginning of the experiments the tumor was inoculated into the cardia of all experimental and all 15 control rabbits. On the 13th day after the implantation of the tumor the experimental animals were again given an injection of carbon tetrachloride in the same dose.

The animals were sacrificed by air embolism on the 21st-23rd day after the implantation of the tumor. Autopsy revealed at the site of inoculation a tumor of circular shape, of 0.5 to 2-2.5 cm diameter, which infiltrated the gastric mucosa and formed on the mucosa surface ulcers with elevated rounded edges (Fig. 1). In some rabbits metastases were found in the stomach wall; more frequently remote metastases occurred on the peritoneum, the mesentery, in the intestine, omentum, kidneys, liver and lungs. The metastasis formation in the organs was studied according to an arbitrarily chosen fixed scheme, taking into account the number and size of the metastases expressed numerically. Metastases of 0.2 cm size were given one mark, metastases of 0.2-0.5 cm size were given two marks, and metastases over 0.5 cm three marks. These numbers were correspondingly increased depending on the number of metastases: up to ten metastases one more mark was given; between 10 and 30 metastases two more marks; if the number of metastases exceeded 30, three more marks were given. The numerical indices thus obtained were evaluated statistically: the coefficient of coincidence ( $X^2$ ) and the probability P were calculated with the aid of Fisher's tables [20].

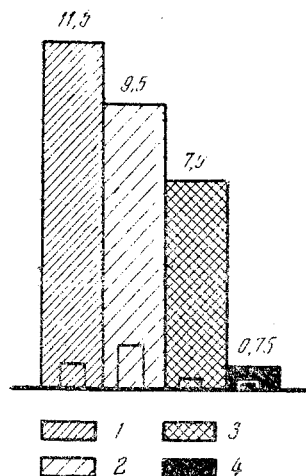


Fig. 2. The different degree of metastasis formation by a Brown-Pearce tumor in the organs of rabbits after inoculation of the tumor into various parts of the stomach. 1) Inoculations into the pylorus; 2) into the cardia; 3) into the region of the greater curvature; 4) into the fundus. The large columns illustrate metastasis formation in the internal organs, the smaller columns metastasis formation in the liver.

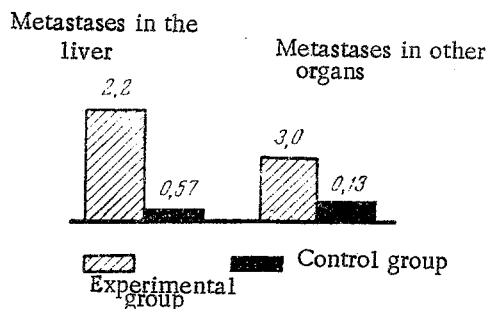


Fig. 3. Metastasis formation by Brown-Pearce tumor in the liver and other internal organs of rabbits after inoculation of the tumor into the cardia and injection of carbon tetrachloride.

## RESULTS

The results of the first series of experiments are set forth in Fig. 2.

Comparison of the findings concerning metastasis formation in the four groups of rabbits revealed that inoculation of the tumor into the pylorus and the cardia of the stomach were followed by the most intensive metastasis formation and inoculation into the fundus produced least of all metastases; results which more or less coincide with clinical observations [2].

The metastases in the liver were found after inoculation into all four localizations used by us, but the most intensive metastasis formation in the liver could be observed after inoculation of the tumor into the cardia.

The results obtained in the second series of experiments are set forth in Fig. 3. If one compares the metastasis formation in the experimental and control group, respectively, it appears that in those rabbits which had been given injections of carbon tetrachloride the metastasis formation was somewhat more intensive in the internal organs, but the number of metastases in the liver showed a particularly marked increase. The results of these experiments concerning the metastasis formation in the liver are statistically highly significant: the probability  $P < 0.01$ , with a coefficient of coincidence  $X^2=14.98$ . The findings concerning metastasis formation in other internal organs are less significant: P varies between 0.5 and 0.3, with a coefficient of coincidence  $X^2=5.15$ .

Numerous experimental data obtained in the laboratory of A. D. Speranskii and R. E. Kavetskii [1,6,7,9,18,19] have shown the importance of reflex influences in the process of metastasis formation, which influences may originate from the primary focus of tumorous growth as well as from various other parts of the body. These findings underline the importance of trophic changes in the tissues and organs in the metastasis formation, as these changes create conditions which may enhance or inhibit the tumorous growth.

Our experimental findings show that dystrophic disorders in the liver which develop under the influence of carbon tetrachloride create conditions favorable for the growth of metastases of stomach tumors in that organ, a fact which may be of importance in studies concerning the pathogenesis of metastasis formation in cases of stomach cancer.

#### SUMMARY

The author studied metastasization of Brown-Pearce tumor (inoculated into different portions of the rabbit stomach wall) into the liver and other internal organs. Observations were also made during the administration of carbon tetrachloride (hepatotoxin). The most extensive metastasization into the liver was observed when the tumour was inoculated into the cardia portion of the stomach. Hepatic functional disturbance intensified the metastasization of gastric tumours into the liver.

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