

A Brown-Pearce tumor, grafted into the wall of the transverse colon in rabbits, spreads along artificially created and spontaneously developing adhesions into the stomach, but not into the liver. Retrograde metastases are found in the wall of the intestine and stomach, the greater omentum, and the parietal peritoneum. The formation of new blood vessels in the adhesions is investigated.

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The object of this investigation was to examine the importance of abdominal adhesions in the spread of cancer cells.

#### EXPERIMENTAL METHOD AND RESULTS

Experiments were carried out on 37 rabbits. After laparotomy, a Brown-Pearce tumor was grafted into the wall of the transverse colon of 25 rabbits: 12 rabbits were injected with 0.5 ml of emulsion, 13 received pieces of tumor measuring  $9 \times 4 \times 4$  mm, in 13 rabbits (6 receiving emulsion and 7 receiving fragments) the wall of the intestine was sutured to an area on the greater curvature of the stomach denuded of its serous membrane. In the other 12 animals (6 with emulsion, 6 with pieces of tumor) the area of colon with the tumor was sutured to the liver after dissection of the fibrous capsule, and in 12 control rabbits no tumor was grafted but the intestinal wall was sutured to the stomach wall denuded of its serous membrane or to the liver after dissection of its capsule.

The rabbits were sacrificed and autopsied 5, 10, 15, 20, 25, and 30 days after the operation.

After 5 days adhesions were found between the colon and the sutured organs, while in some rabbits other spontaneous adhesions were discovered between various organs. In 13 experimental and 6 control animals the blood vessels of the adhesions were studied by injecting an aqueous suspension of ink into the thoracic aorta and then making histological investigations. In other animals the blood vessels were not filled with ink. The histological sections were stained with hematoxylin-eosin and by Van Gieson's method. In 6 control animals the acid phosphatase of the adhesions was investigated by Gomori's method, and the mean activity of the enzyme was determined. The fibrous framework and blood vessels of the adhesions were demonstrable 15 days after the operation. By the 25th day, many blood vessels  $13-72 \mu$  in diameter were found in the adhesions (Fig. 1).

In the remaining 6 control rabbits, into which ink was injected, the blood vessels of the adhesions were discovered 10 days after the operation.

In the experimental animals 5 days after the operation the tumor had spread from the submucosa to invade the muscular layer of the intestinal wall in some places. Ten days after suturing the colon to the stomach in one rabbit the tumor had invaded the intestinal wall and reached the muscular coat of the stomach along the silk suture closing the operation wound. In another animal the intestinal tumor had invaded another loop of large intestine. The tumor did not penetrate into the wall of the stomach sutured to the colon. The blood vessels of the organs joined by adhesions were appreciably filled with ink. A few vessels ran toward the tumor from the intestinal wall. Blood capillaries were visible in the adhesions.

After suture of the colon to the liver, penetration of the latter by the tumor was not observed. Blood capillaries were visible in the adhesions between the colon and liver. Blood vessels ran in a semicircle from the intestinal wall toward the tumor.

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Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 65, No. 4, pp. 93-97, April, 1968.  
Original article submitted June 10, 1966.

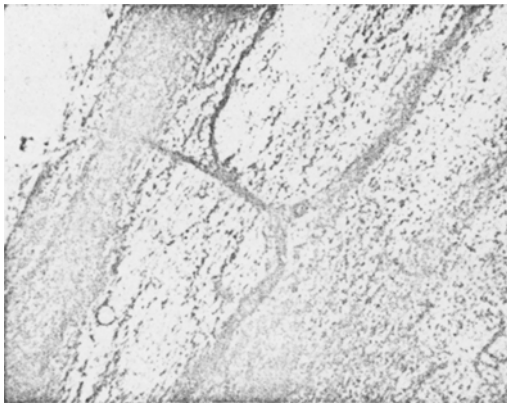


Fig. 1. Adhesions between transverse colon and stomach 25 days after operation. Total preparation. Blood vessels can be seen in an adhesion. Photomicrograph. Gomori. Objective 20, ocular 5.



Fig. 2. Penetration of tumor along adhesions 25 days after grafting a carcinoma into wall of transverse colon and suture of colon to stomach wall. Tumor visible between muscles of stomach wall. Blood vessels of tumor and of muscle coat of stomach filled with ink. Photomicrograph. Hematoxylin-eosin. Objective 20, ocular 7.

were found in the greater omentum and on the anterior wall of the stomach. The grafted tumor penetrated the stomach muscles mainly along the track of the silk suture.

After suture of the colon to the liver in one rabbit metastases were found in the mesentery and wall of the transverse colon, in the greater omentum, and near the hilum of the liver. The liver was joined by adhesions to the parietal peritoneum. The tumor had not penetrated from the colon into the liver. Blood vessels invaded the tumor from the colon and approached it closely from the adhesions.

After 15 days the tumor in one rabbit had not penetrated into the attached wall of the stomach. Tiny blood vessels filled with ink were visible in the adhesions. Three blood vessels were found in the adhesions of another animal. The grafted tumor began to penetrate from the colon into the adhesions.

Blood vessels were also found in the adhesions after suture of the colon to the liver. The tumor did not penetrate into the liver. The periphery of the tumor was stained unevenly with ink. The structure of the blood vessels in the tumor will ill-defined. In one rabbit spontaneous adhesions were formed between the liver and other loops of the large intestine. Few blood vessels were seen in these adhesions.

On the 20th day after suture of the colon to the stomach the tumor had penetrated into adhesions between the organs. The blood vessels in the adhesions were small. At the periphery of the tumor, blood vessels could be seen in the form of arcs of different sizes, and small vessels were present also in a spontaneous adhesion between the greater omentum and liver. Metastases had formed in a second rabbit in the transverse mesocolon. The tumor did not penetrate into the stomach wall sutured to the colon.

After suture of the colon to the liver, metastases were found in the serous membrane of the transverse colon of the first rabbit, and invasion of the whole intestinal wall by the tumor was discovered without penetration into the attached liver. Structureless areas were predominant in the tumor, stained with blood and ink. Blood vessels of the adhesion ran toward those of the tumor. In the mesocolon a metastasis could be seen. In the second animal the tumor had not penetrated from the colon into the liver.

On the 25th day after suture of the intestine to the stomach, in one rabbit the tumor had spread along the adhesion into the muscular layer of the stomach. Blood vessels filled with ink ran almost to the center of the tumor, and showed varices, which in some places appeared to have been cut off. Here and there between the tumor tissue were areas of stomach muscles with blood vessels (Fig. 2). In this same rabbit metastases had developed in the greater omentum and a vascularized adhesion had formed between a loop of large intestine and the peritoneum of the operation scar. In another animal metastases



Fig. 3. Metastasization of tumor in the presence of adhesions 25 days after grafting carcinoma into wall of transverse colon and suturing colon to liver. 1) Adhesions between transverse colon, liver, and stomach; 2) retrograde metastases in anterior wall of stomach; 3) retrograde metastases in wall of small intestine. Macrophotograph.

In another rabbit adhesions were found between the transverse colon and the anterior stomach wall near the pylorus and the large intestine. Metastases were visible in the serous membrane of these organs and the greater omentum (Fig. 3). The tumor did not spread from the colon into the liver along the adhesions.

Three rabbits were sacrificed 30 days after suturing the colon to the stomach. In the first animal the blood vessels were injected with ink. The tumor had spread from the colon into the stomach muscles. Blood vessels of the stomach had joined those of the tumor. Metastases were also found in a vascularized adhesion between the transverse colon near the grafted tumor and the peritoneum of the right hypochondrium. Metastases had also formed in the peritoneum around the adhesions. They were found in the greater omentum and in the wall and mesentery of the transverse colon. In the second rabbit the vessels also were filled with ink. The character of spread of the carcinoma was similar to that in the previous experiment. In the third rabbit metastases were predominant in the greater omentum, the anterior stomach wall, and the wall and mesentery of the transverse colon. The grafted tumor had penetrated the stomach muscles, and in some places its mucous membrane also.

Two rabbits were sacrificed 30 days after suture of the colon to the liver. Widespread carcinoma had developed in one animal. The greater omentum consisted of a mass covering the site of operation, adherent to the abdominal wall and to loops of intestine and invading the retroperitoneal space. Many metastases were found in the lesser omentum, the stomach wall, and the mesentery. The tumor did not penetrate from the colon into the liver. Blood vessels filled with ink were seen in the adhesion, and the liver contained metastases of the carcinoma with blood vessels entering them. In another rabbit the transverse colon was adherent to other loops of intestine. Metastases were found in the stomach wall, the liver, mesentery, wall of the intestine, parietal peritoneum, and greater omentum. The carcinoma had spread in the cranial portion of the abdomen. Several metastases were found in the right portion of the retroperitoneal space. The tumor grafted into the intestine had attained a large size but had not invaded the liver sutured to the colon.

Hence, blood vessels are formed by the 10th-15th day in adhesions produced artificially by operation, growing in from the sutured organs. A tumor grafted into the large intestine grows in its wall and spreads into the adhesions. After ten days blood vessels from the intestinal wall grow into the tumor. Vessels from the adhesions penetrate later. No appreciable difference is found in the times of formation of blood vessels in the adhesions with or without grafting of a tumor. Growth of the tumor is irregular. Foci of normal tissues with blood vessels penetrating them can be seen between different parts of the tumor. The fact that a tumor from the colon penetrated into the stomach wall but not into the liver may be explained by the compensatory powers of the liver cells [2]. Differences in the localization of identical tumors in the body lead to changes in their biological properties and in the structure of their blood vessels [1]. Metastasization began after the 20th day, and its less marked orthograde type in the mesocolon can be explained by the predominantly retrograde movement of the cancer cells along the adhesions. Metastases were commonest in the wall of the intestine and stomach, the greater omentum, and the parietal peritoneum.

#### LITERATURE CITED

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