Capsule Implantation: Method for Establishing Simulated Colon Carcinoma in Rats. (24754)

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There are many surgical problems relative to colon cancer which could be further clarified if a laboratory animal bearing a simulated human colon cancer were available for experimentation. For example, problems such as the relationship of tumor manipulation and incidence of liver metastasis; importance of pre- and post-operative peritoneal cavity care (with regard to free and spilled cancer cells); usefulness of peritoneal cavity treatment by isotopes, chemotherapeutic agents or both. An insight into these problems and many others could be gained if such a tool were available. Recognizing this need, the authors attempted to create a simulated human colon tumor by injecting under the serosa of the rat colon about 5 x 10^7 tumor cells of the ascitic form of the Walker carcinosarcoma 256. Also small bits of the solid form of this tumor were implanted under the serosa *via* trocar. Despite efforts to prevent peritoneal seeding both methods failed because carcinomatosis peritoneii developed before the intended tumor became large enough for experimentation. To circumvent this difficulty, the following technic was devised.

Method. A solid Walker carcinosarcoma 256 tumor is excised from a donor rat, placed in a sterile Petri dish containing 10 ml of 0.9% NaCl and diced into approximately 2 mm fragments. A fragment is inserted into a 5-0 gelatin capsule and the capsule placed in 95% ethyl alcohol (Fig. 1a). The alcohol kills any cancer which may be clinging to the outside of the capsule and hardens it. The cecum of a Nembutal-anaesthetized rat is exposed by a mid-line incision. A purse string suture is placed around the cecum about 1 cm from its tip and the serosal area inside the purse string suture is scarified with a surgical knife to create a tumor bed (Fig. 1b). The hardened capsule is removed from ethyl alcohol with forceps and placed in the barrel of a tuberculin syringe, modified by cutting off the tip. The cecum is then invaginated with the syringe barrel and the capsule delivered into the serosal pouch (Fig. 1c). The barrel of the syringe is then removed with a gentle rotating motion and the purse string suture secured (Fig. 1d). The cecum is then dropped into the peritoneal cavity and the wound closed in a conventional manner.

Results. Fifty animals were treated as described, and growth of tumor resulted in all. After 7-8 days one can palpate the tumor through the abdomen. In 12-14 days it had grown to 2 cm in diameter.

We elected to operate on the experimental animals at 14 days for observation and surgical removal of the tumor. At operation, all animals were grossly free of disease except for the tumor growing in the cecal tip. However, peritoneal washings taken before the surgical removal of the tumor were found positive for free floating tumor cells in 34 of 50 animals.

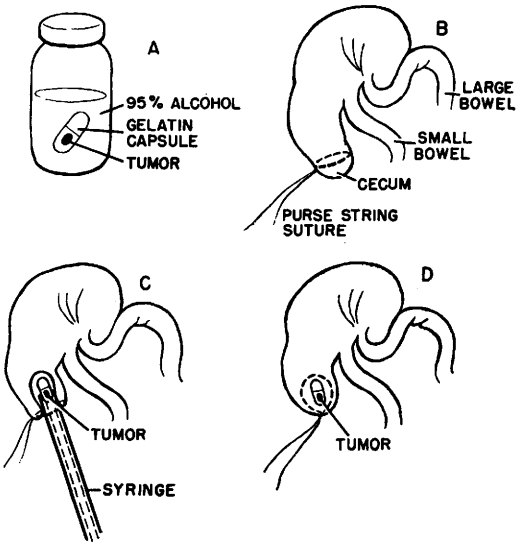

FIG. 1. Operative technic for tumor implantation.

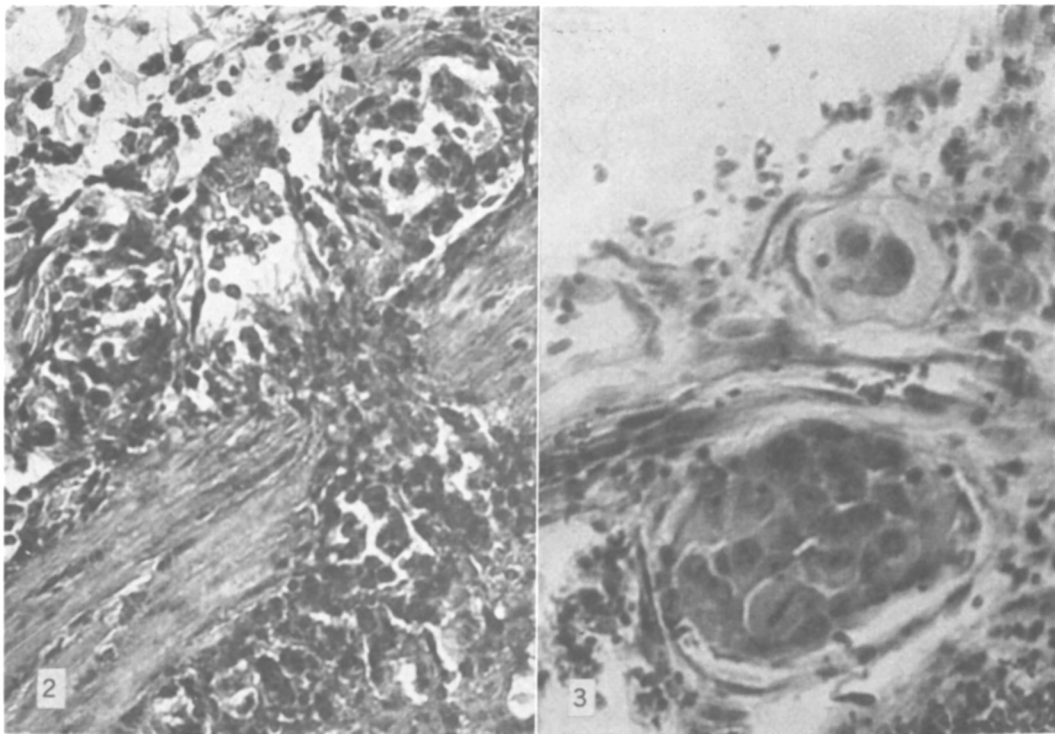

FIG. 2. Tumor invading bowel wall.
FIG. 3. Tumor in vascular channel. Note mitosis figure.

A recent clinical study revealed that 80% of patients with recto-sigmoid or colon cancer have free floating cancer cells in their peritoneal cavity prior to definitive surgery (S. H. Seal, unpublished).

Surgery consisted merely of placing a ligature around the base of the cecum, care being taken not to incorporate any of the small intestine or colon in the ligature. The cecal portion bearing the tumor is severed distal to the ligature.

Eighteen of the 50 animals thus operated died within the first 2 weeks after operation. On autopsy, they were found to have carcinomatosis peritoneii, ascites and recurrences in the operative site. Seven had liver metastasis. The remaining 32 animals survived 9 weeks and were then sacrificed. At autopsy 11 were found to have recurrences at the surgical site and of these 11, 6 also had carcinomatosis peritoneii. None had liver metastasis. Twenty-one animals were free of disease.

Discussion. It is felt that this tumor fulfills many of the criteria required to simulate a human colon cancer. Early in the tumor's history, it invades rapidly from the serosa penetrating through the muscle layer, submuscularis, muscularis and into the mucosa (Fig. 2). Like the human colon cancer it tends to be well circumscribed rather than run under the submucosa once it has broken into the bowel lumen. The tumor also invades the vascular channels (Fig. 3) and this invasion is detected not only histologically but also by the presence of tumor cells in the circulating blood.

Conclusion. A method is presented for implantation of Walker carcinosarcoma 256 into the tip of the cecum of the rat. The technic results in 100% take of the tumor and this tumor parallels many of the characteristics of a human colon carcinoma.

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