Studies on the Mechanism and Prevention of Recurrence of Carcinoma at the Suture Line

ARTHUR KENNETH WALTZER, M.D., WILLIAM A. ALTEMEIER, M.D., F.A.C.S.

From the Department of Surgery, University of Miami School of Medicine, Jackson Memorial Hospital and University of Cincinnati, College of Medicine and the Cincinnati General Hospital, Cincinnati, Ohio

Over a decade has passed since the work of Morgan,10 Goligher,6 and Cole et al.4 emphasized the frequency of recurrent tumor at the suture line following resection for carcinoma of the colon. As if in paradox, this definite rate of recurrence is found in dealing with a tumor that rarely extends more than 4 centimeters beyond its gross limits. Cole4 noted this fact and indicated that an inadequate resection is rarely the cause of recurrence. He demonstrated the presence of viable appearing tumor cells within the lumen of the bowel both proximal and distal to the primary growth.

Enemas, surgical manipulation, and the passage of the fecal stream over an ulcerated cancer account for these cells being desquamated from the primary growth and into the lumen of the bowel. Most investigators now agree that these cells can become implanted into the line of resection and anastomosis.

Many surgical clinics have reported a suture line recurrence rate of 10 to 20 per cent in patients having resection of the colon for carcinoma. The use of occluding ligatures, intraluminal anti-cancer agents, and iodized suture material5 have been recommended as a means of preventing this complication. Cohn and his group, using the Brown-Pearce tumor as a model, were able to demonstrate that a closed anastomosis did offer protection against suture line recurrence. Their method of anastomosis differs from the classical Halsted anastomosis in that a temporary basting stitch was used to seal the lumen of the bowel. After completion of the anastomosis this suture was removed.

The present study was undertaken to further evaluate if the two basic types of intestinal anastomosis, closed and open, differ in the protection offered against implantation of tumor cells at the line of resection and anastomosis.

Materials and Methods

Paired domestic rabbits weighing between 2.5 Kg. and 3.5 Kg. were used throughout this study. During the first 24 hours following surgery, they were given only water. Thereafter, they received a standard diet of Rockland chow and green leafy vegetables.

The tumor system used was the VX-2 carcinoma of rabbits. A suspension of tumor cells was prepared by mincing the freshly excised tumor and passing it through a stainless steel cytosieve with 10 meshes per square inch. This was then diluted to 25 cc. with chilled Ringer's solution. The suspension was then divided into two parts of 10 cc. each and one part of 5 cc. after an even distribution of the suspension had been obtained. Standard dilutions were not used and cell counts not done because of the clumped distribution of the cells. The animals were operated upon in pairs under intra-peritoneal pentobarbital sodium anes-
thea. After the peritoneum was entered through a midline incision, a non-crushing clamp was placed 2 cm. distal to the ileocecal valve and a second clamp 15 cm. distal to the first. Thus a portion of the ascending colon was isolated between the clamps. Through an #18 gauge needle placed within a pursestring suture 2 cm. from the proximal clamp, 10 cc. of tumor suspension was introduced into the isolated segment of each rabbit's colon (Fig. 1). Spillage of tumor cells was thus kept to a minimum. The experimental model is similar to that described by Cohn et al.3

Closed Anastomosis

In one of the paired animals, a closed anastomosis was carried out. The mid-point of the isolated segment of bowel was divided between crushing clamps using the cutting current of the electro-surgical unit. The ends were cauterized with the coagulating current of the same unit and the anastomosis was then accomplished using 4-0 silk sutures placed in a seromuscular fashion (Fig. 2).

Open Anastomosis

In the second of the paired animals, the bowel was divided with the scalpel, care being taken to prevent gross spillage. A one-layer 4-0 silk suture anastomosis was then performed using a running lock stitch on the posterior row and a Connell suture on the anterior (Fig. 3).

The remaining 5 cc. of tumor suspension was injected into the thigh of a third animal to ascertain tumor viability and maintain a supply of tumor. Uniform tumor growth occurred in all of these animals.

Animals were discarded if either member of the pair died in less than 14 days or if the tumor in the donor did not grow. If one member of the pair died after 14 days, the other was then sacrificed. Pairs living after 25 days were sacrificed. All suture lines were examined grossly and microscopically.

Results

This study is based on 30 pairs of animals that met the above mentioned criteria. Of the 30 animals treated with an open
Fig. 2. The closed anastomosis. A) The bowel is divided with the cutting current. B) Coagulation of the cut surface. C) Placement of seromuscular sutures. D) Placement of seromuscular sutures. E) The clamps are removed and the sutures are secured.

Fig. 3. Open anastomosis. A) The bowel is divided with the scalpel. B) Placement of silk sutures through all layers of the bowel wall. C) Anastomosis completed.
anastomosis, tumor was present in 17 or 57 per cent. However in the 30 rabbits in which a closed anastomosis had been done, there was tumor at the suture line in only 2 or 7 per cent.

Generally, widespread peritoneal implants were less frequent in the animals undergoing closed anastomosis, but the difference was not statistically significant. We believe this to be due to the method used of placing cells within the lumen of the colon as tumor nodules were frequently found about the pursestring suture.

The results of this experiment were subjected to statistical analysis. The value of "Z" was found to be less than 1 per cent.

Discussion

The VX-2 carcinoma of the rabbit is a poorly differentiated squamous cell carcinoma. It has certain properties similar to the carcinoma found in the human colon that make it ideal for use in suture line studies. Previous studies in our laboratory have indicated that this tumor will not grow on undamaged intestinal mucosa, but

Fig. 4. (Left) A suture is present in the center of the photomicrograph. Surrounding it are hyperchromatic cancer cells. (H + E X63.) (Right) Photomicrograph of the VX-2 carcinoma is shown. (H + E X100.)

Fig. 5. Note that in a closed anastomosis the sutures do not enter the lumen of the bowel.
will grow readily on peritoneal surfaces and within the wall of the bowel.

There is ample experimental evidence to explain the susceptibility of an open anastomosis to tumor cell implantation. Injured tissue forms a highly favorable medium for tumor growth.\textsuperscript{1, 5} The viable, divided end of bowel which is further traumatized during the performance of an anastomosis is an example of injured tissue. On the other hand, the end of bowel that has been divided by cautery and then coagulated presents a necrotic, nonviable surface which should not support tumor growth.

Haverback and Smith\textsuperscript{7} have shown that neoplastic cells can be transplanted from one tissue to another by contamination of suture material. Thus, when a suture is passed from the tumor contaminated lumen through all layers of the bowel wall as in the open type anastomosis, the possibilities of implantation are enhanced. In support of this contention was the frequent microscopic finding of tumor cells clustered about a suture (Fig. 4). In a well constructed closed anastomosis, however, the interrupted seromuscular sutures do not enter the lumen of the bowel, and tumor cell implantation is further prevented.

Some spillage of intestinal contents, however slight, accompanies an open anastomosis. With the closed anastomosis, the crushing clamps prevent tumor cells from spilling onto the adjacent serosa and peritoneum—membranes which offer an excellent milieu for tumor growth. Figure 5 summarizes these various factors.

The safety and structural integrity of the closed or aseptic anastomosis is well established after many years of clinical experience and usage. There is ample experimental evidence to recommend its use when dealing with carcinoma of the colon.

Summary

This study was undertaken to determine if the two basic types of intestinal anastomosis, closed and open, differed in the protection offered against implantation at the suture line.

A suspension of the VX-2 carcinoma was injected into an isolated segment of colon of each pair of rabbits. In one animal the bowel was divided and anastomosed in an open fashion. In the other a closed or aseptic anastomosis was done. Only those pairs in which both members survived 14 days are included in this study.

Of the 30 treated with an open anastomosis, tumor was present in 17 or 57 per cent. Of the 30 in which a closed anastomosis had been done, there was tumor at the suture line in only 2 or 7 per cent.

The results of this study offer experimental support to the concept that the closed method of intestinal anastomosis effects a protective influence in preventing recurrence of carcinoma at the suture line.

References