THE PROBLEM OF SUSPECTED RECURRENCES IN CANCER OF THE ALIMENTARY TRACT

BY

K. CRONIN, F.R.C.S.

AND

H. ELLIS, M.Ch., F.R.C.S.

Surgical Registrars, the Radcliffe Infirmary, Oxford

In recent years important advances have been made in the treatment of recurrent and disseminated cancer, resulting both in prolongation of life and in palliation of symptoms.

Radiotherapy remains a well-tried and useful method of treatment for recurrences from a wide range of tumours, and to this has now been added the use of sex hormones and endocrine gland ablations for prostate gland and breast secondaries, radioactive iodine for thyroid metastases, and cytotoxins (Bodley Scott, 1958) for some cases of disseminated bronchial and testicular growths.

Unfortunately the adenocarcinomata of the alimentary tract are relatively insensitive to conventional radiotherapy, are not hormone-dependent, and show no response to any of the available cytotoxic agents. For this reason it is not unnatural to find a pessimistic attitude often taken by the patient's doctor when recrudescence of such a growth is suspected following removal of the primary tumour. Should a recurrence have in fact developed, any further attempt at cure depends on the possibility of excision of the secondary deposit.

The more aggressive surgical attitude which is developing to this problem of secondaries in the alimentary tract is engendered by modern advances in technique. Of particular importance are the use of relaxant drugs, chemotherapy, blood transfusion, and the possibilities of excising major vessels with graft restoration of continuity and of successful right or left hepatic lobectomy; all contribute to the possibility of adequate excision of intra-abdominal, body-wall, pulmonary, or even intracerebral secondary deposits.

In this paper we present a number of encouraging examples of later surgery carried out because of suspected recurrence of growth following resection of a primary tumour of the alimentary tract. Recurrences may be completely removable with hope of ultimate cure of the patient; a second operable primary growth may be encountered; or, most happy of all, the symptoms may be found to be due to a non-malignant condition such as adhesions, stricture, or intra-abdominal abscess. In many cases exploration unfortunately reveals a hopelessly incurable situation, but, even here, relief of symptoms may be achieved by short circuit, colostomy, or palliative resection.

Case 1. Repeated Excision of Abdominal Secondary Deposits Following Hemicolectomy for Carcinoma of Caecum

A civil servant aged 54 had a right hemicolectomy performed in December, 1953, for a carcinoma of the caecum 2 cm. in diameter. Histologically this proved to be a Broders grade II growth, and none of the eight lymph nodes examined contained secondary deposits.

He was readmitted in October, 1955, complaining of attacks of severe abdominal colic. Clinical examination was negative, but occult blood was present in the stools, and a barium follow-through examination showed dilated loops of upper jejunum.

Second Operation.—Laparotomy on October 12 revealed a stenosing tumour obstructing the mid small bowel. There were hard enlarged glands in the adjacent mesentery and nodules of growth on the serosa of both bowel and mesentery. A nodule 5 cm. in diameter was also found in the posterior rectus sheath near the umbilicus. This nodule, the small-bowel tumour, and the affected mesentery were removed together with 19 cm. of small intestine.

Microscopical examination showed this small-bowel tumour to be a secondary deposit from the original growth lying deep to but ulcerating through the mucosa. The lymph nodes, serosal nodules, and mass in the abdominal wall all proved to be secondary deposits.

In October, 1956, routine examination revealed a mass at the umbilicus; there was no clinical evidence of dissemination elsewhere.

Third Operation.—On November 8 the palpable mass was found to be a tumour 4 cm. in diameter adherent to the umbilicus, and this was excised widely. A further deposit 2 cm. in diameter was removed from the omentum. Numerous small nodules of growth were found in the mesentery of the terminal ileum, and a wide resection of mesentery together with about 50 cm. of ileum was performed. Again histological examination confirmed the malignant nature of all the involved tissues. The patient recovered smoothly and remained in excellent health, but in August, 1957, a small lump in the operation scar was detected at follow-up.

Fourth Operation.—On September 6 a wide excision of abdominal wall was carried out removing a 3-cm. deposit within the rectus abdominis. Laparotomy revealed no evidence of intra-abdominal malignant disease.

In April, 1958, his abdominal wall was soundly healed and he was very well, clinically free from disease more than four years from the date of the first operation.

Case 2. Resection of Solitary Secondary Deposit in Lung Two Years After Abdomino-perineal Excision for Carcinoma of Rectum

A solderer aged 49 had an abdomino-perineal excision performed for a carcinoma of the rectum in November, 1955. Histologically this proved to be a Dukes stage C, Broders grade III growth. He attended the follow-up clinic in August, 1956, complaining of a cough with blood-stained sputum; an x-ray film of his chest showed: "Some shadowing of the right lung." He was seen again in February, 1957, when the report on his chest x-ray examination was: "The shadow at the right base is getting bigger. This has the appearance of a neoplasm." In July, 1957, his chest x-ray film showed "further increase in the size of the right basal shadow." During the whole of the year, the patient's general condition remained excellent and there was no sign of any abdominal recurrence.

As the growth in the lung appeared to be very slowly growing he was referred to the thoracic surgical unit. A bronchogram confirmed the presence of a tumour in the right lower lobe of the lung, and in October, 1957, this lobe was resected. The histology showed that the growth was a secondary deposit from the original carcinoma of the rectum. At the time of writing the patient was alive and well.

Case 3. Anterior Resection for Carcinoma of Rectum. Abdomino-perineal Resection for Second Primary Growth in Rectum

A gas-fitter aged 65 had an anterior resection performed for a carcinoma of the rectum in November, 1953. Histologically this proved to be a Dukes stage A, Broders

grade III growth. The patient was seen regularly in the follow-up clinic, and in April, 1955, on rectal examination, a polypoid mass was felt at 3 in. (7.5 cm.). At this time the patient had no symptoms.

The growth was removed with diathermy, and the histology showed it to be adenocarcinoma of the rectum (Broders grade I). It was hoped that, as the tumour was of a low grade of malignancy, local excision would be sufficient. A recurrence, however, was soon evident, and an abdomino-perineal excision of the rectum was performed in August, 1955. Histologically, this new primary proved to be a Dukes stage A, Broders grade I growth. At the time of writing the patient is alive and well with no sign of recurrence.

The completely different histology of the two tumours strongly suggests that the second growth had arisen *de novo*.

Case 4. Resection of Pelvic Colon for Annular Carcinoma. Laparotomy for Suspected Recurrence, Small-bowel Obstruction Found to be Due to Adhesions: No Recurrence of Growth

A housewife aged 46 had a resection of the pelvic colon for an annular carcinoma in October, 1954. Histologically this proved to be a Broders grade II growth, and none of the lymph nodes examined showed secondary deposits. In July, 1956, she was seen in the follow-up clinic, where "some fullness" was noted beneath the scar in the left iliac fossa. At this time she was quite well, but admitted to having occasional attacks of abdominal colic and vomiting.

In January, 1958, she was admitted with a subacute intestinal obstruction. A straight x-ray film of the abdomen showed dilated loops of small bowel with some fluid levels, and a barium enema demonstrated some distortion at the site of the old anastomosis, possibly due to a growth.

At laparotomy a loop of ileum was found to be snared by a band running to the site of the colonic anastomosis. There was no sign of any recurrence of the original growth. The band was divided and the patient made an uninterrupted recovery. She remains alive and well.

Case 5. Chronic Abscess of Abdominal Wall Simulating Secondary Deposit

A man of 71 had an emergency ileo-transverse colostomy followed by a right hemicolectomy performed for an obstructing carcinoma of the ascending colon in June, 1953. He remained well until late in 1957, when he noted a lump in the abdominal scar. When seen at the follow-up clinic in February, 1958, there was a mass 7 cm. in diameter deep in the abdominal wall, which was hard and rather tender. He was afebrile. A confident diagnosis of a secondary deposit was made. At operation, however, this proved to be a chronic thick-walled abscess of the abdominal wall containing a length of nylon suture. Culture of the pus grew *Streptococcus pneumoniae*, and histological examination of the abscess wall showed a non-specific chronic inflammatory change only. He made a smooth recovery from this operation, over four and a half years after his original resection.

Comment

In the five years, 1953-7, 31 patients had laparotomies for suspected recurrent cancer; the operative findings are detailed in Table I. In 11 cases it was possible to remove the recurrence, and the case histories of these patients are summarized in Table II. Palliative procedures were done in four patients (one colostomy and three short circuits). One patient (Case 3) was found to have a new primary growth. In only four instances was it found impossible to do anything at operation.

It is a striking fact that in 11 patients, although a recurrence was suspected on clinical grounds, a benign condition was found at operation. One interesting feature of this last group is that in three patients the late appearance of a chronic abscess simulated a recurrence. Two patients had

TABLE I.—Patients Explored for Suspected Recurrences (1953-7)

Excision of recurrences	11
Palliative operations (1 colostomy, 3 short circuits)	4
Inoperable	4
Excision new primary growth	1
Non-malignant conditions discovered (3 deep abscesses, 1 anastomotic ulcer, 7 intestinal obstructions due to adhesions)	11

TABLE II

Sex and Age	Original Operation	Site of Excised Recurrence	Interval Between Original Operation and Excision of Recurrence	Length of Survival After Last Excision
F 67	Bilroth I gastrectomy for carcinoma of stomach	1. Scar 2. Scar 3. Both axillae	7 months 17 " 21 "	Alive and well, 4 months after last excision
F 53	Hartman's operation for carcinoma of sigmoid colon	Scar	25 "	Alive and well at present, 17 months after last excision
F 54	Abdomino-perineal resection for carcinoma of rectum	Scar	5 "	Dead. Survived 6 months
F 66	Right hemicolectomy for carcinoma of caecum	1. Umbilicus 2. Scar of above excision	26 " 29 " Also given deep x-ray therapy	Dead. Survived 4 months
F 65	Abdomino-perineal resection for carcinoma of rectum	Perineum	2 months. Also given deep x-ray therapy	Dead. Survived 26 months
M 54 (Case 1)	Right hemicolectomy for carcinoma of caecum	1. Small intestine, mesentery, and abdominal wall 2. Small intestine, omentum, and abdominal wall	22 months 35 "	Well, 10 months after last excision
F 67	Hartman's operation for carcinoma of recto-sigmoid junction	3. Scar Mass in left iliac fossa involving small bowel	45 " 39 "	Died in post-operative period
F 66	Anterior resection for carcinoma of rectum	Small bowel	22 "	" "
F 60	Resection for carcinoma of pelvic colon	Anastomotic line; abdomino-perineal excision performed	34 "	Dead. Survived 25 months
F 47	Resection for carcinoma of descending colon	Right Sylvian fissure	16 "	Dead. Survived 4 months
M 49 (Case 2)	Abdomino-perineal excision of carcinoma of rectum	Lung	24 "	Well, 6 months after last excision

deep abdominal-wall abscesses 18 months and four years (Case 5 above) after colectomy; both had had pre-operative and post-operative chemotherapy, and both had nylon suture material within the abscess cavity. The third patient developed an intra-abdominal abscess adjacent to the anastomosis of a right hemicolectomy, performed seven years previously, which was followed by a course of penicillin and streptomycin.

Such abscesses probably represent either flare-ups in foci of latent infection or sterilized collections of necrotic material which become secondarily infected. With extensive use of chemotherapy these delayed abscesses, presenting many months or even years after abdominal operations, will probably become more common (we have seen two following gastrectomy) and constitute an important differential diagnosis from secondary deposits in a laparotomy scar.

Discussion

A radical approach to the problem of recurrent abdominal cancer is the "second look operation" introduced by Wangenstein *et al.* (1954). He undertakes re-exploration of the abdomen six to eight months after the initial operation in cases where examination of the resected specimen shows that adjacent lymph-node involvement has occurred. At the second laparotomy any suspicious tissue is excised,

and, if this in turn proves to be involved, further explorations are undertaken at similar time intervals until no recurrences are found. He quotes one patient who had a total of five re-explorations following resection of a carcinoma of the caecum. At the last operation no malignancy was found, and the patient was well more than five years after the original hemicolectomy.

Although this scheme has been adopted by some other surgeons (Wilson, 1956), it is still admittedly in its trial stage. There are two disadvantages; first, it is necessary to explain to the patient the exact nature of his disease and its prognosis, a procedure which is inadvisable in a proportion (we would say a very high proportion) of cases; and second, in this country, the "second look" operation would impose a heavy strain on the available general surgical hospital beds. However, this procedure may well offer the possibility of improving the prognosis in relatively young and intelligent patients with intra-abdominal cancer.

Although the "second look" idea remains to be evaluated, there is no question that much can be gained from periodic careful clinical follow-up examination by the surgeon or general practitioner of all patients who have had resections of tumours of the alimentary tract. In some, evidence of recurrence will be found on clinical examination before symptoms have appeared.

Now that a standard technique has been devised for right hepatic lobectomy (Raven, 1947; Lloyd-Davies and Angell, 1957), as well as the comparatively simple resection of the left lobe for solitary or localized deposits, re-exploration can be undertaken with more confidence and with a greater chance of success than in the days when liver secondaries appeared to be a hopeless problem.

Pulmonary metastases were for long regarded as evidence of inoperable dissemination of malignant disease. Further research has shown that they may occur as a solitary deposit, and, where careful investigation reveals an isolated pulmonary secondary with no effusion and no evidence of spread elsewhere, surgery should be advised. The number of reports of successful removals of secondary pulmonary deposits is steadily increasing. Alexander and Haight (1947), for example, collected 24 cases, 12 of the patients being still alive (eight for more than a year after operation); one patient was well 12 years later. By 1956 Kelly and Langston reviewed 109 patients who had undergone surgery for lung secondaries: 19 (23.2%) had survived for two years or more without recurrence. Nelson *et al.* (1957) reported the resection of two successive pulmonary deposits from a patient who had had a resection of a carcinoma of the left colon, and collected 11 other cases where two lung secondaries had been removed.

Even cerebral secondaries are by no means always irremovable; Störtebecker (1954) reported a study of 158 resections of metastatic brain tumours, although only 13 of these came from primary carcinomata of the alimentary tract. The present series includes a deposit in the Sylvian fissure from a carcinoma of the descending colon.

Although our thesis is that recurrent growths are not necessarily irremovable, their prevention is better than cure. It will be seen that five patients in the present series had secondaries in the abdominal wall removed—one on two occasions and one on three. These deposits probably represent direct implants of malignant cells at the time of the original operation. Naunton Morgan (1958, personal communication) believes that conventional skin towels are inadequate to prevent inoculation of cancer cells at operation, and advocates the use of macintosh-reinforced towels over the raw wound surfaces and wrapped around the growth itself before this is handled extensively.

Recent cytological investigations have demonstrated cancer cells in the venous blood draining tumours of the large bowel in between 30 and 50% of cases examined (Fisher and Turnbull, 1955; Burns and Pfaff, 1956). Moore *et al.* (1957) have even detected tumour cells in the peripheral blood in 25 out of 57 patients with tumours of the alimentary tract.

It seems logical, therefore, that ligation of the vascular pedicle should be carried out before proceeding with manipulation of the tumour whenever possible, in an attempt to limit dissemination of malignant emboli into the blood stream (Cole, 1955).

Goligher *et al.* (1951) analysed the causes of recurrence following anterior resection of the rectum. Some are almost certainly second primaries (see Case 3), others result from inadequate resection, and others still from tumour-cell implantation at the anastomosis; an example of the latter occurred in the present series. Not only should excision be adequate (a 2-in.—5-cm.—clearance as the minimum distally) but the distal bowel should be washed out with 1:500 perchloride of mercury to kill off free cancer cells and prevent their implantation.

Unfortunately many patients will present with evidence of recurrences so hopeless that laparotomy is contraindicated; these will include the cases with ascites, a fixed mass in the pelvis, jaundice, and extensive liver secondaries. Pain in these sufferers can be controlled by analgesics and opiates, supplemented by chlorpromazine. Some selected cases may benefit from cordotomy, splanchnic blocks, and permanent local spinal blocks (Maher, 1955). Ascites and malignant pleural effusions may both be controlled in some measure by instillation of radioactive gold (MacKay, 1957), with relief from distension and dyspnoea. Above all, the "hopeless case" must not feel that he is being abandoned; attention to small details of nursing care will give considerable relief in the terminal stages of malignant disease.

Summary

Recurrence of symptoms after resection of a primary tumour of the alimentary tract may be due to secondary deposits, but these may be operable even if in lung or brain. In other cases the symptoms may be caused by the development of a fresh primary tumour or even by some non-malignant condition.

A more optimistic surgical attitude towards suspected recurrences is advocated and some encouraging examples are presented.

We thank the surgical consultant staff of the Radcliffe Infirmary, Oxford, for permission to study the patients recorded in this series. We are grateful to Mr. D. A. Abernethy and Mr. A. Elliot Smith for their advice and criticism.

REFERENCES

- Alexander, J., and Haight, C. (1947). *Surg. Gynec. Obstet.*, **85**, 129.
 Burns, F. J., and Pfaff, J. (1956). *Amer. J. Surg.*, **92**, 703.
 Cole, W. H. (1955). *Surg. Gynec. Obstet.*, **101**, 359.
 Fisher, E. R., and Turnbull, R. B. (1955). *Ibid.*, **100**, 102.
 Goligher, J. C., Dukes, C. E., and Bussey, H. J. R. (1951). *Brit. J. Surg.*, **39**, 199.
 Kelly, C. R., and Langston, H. T. (1956). *J. thorac. Surg.*, **31**, 298.
 Lloyd-Davies, O. V., and Angell, J. C. (1957). *Brit. J. Surg.*, **45**, 113.
 MacKay, N. (1957). *Lancet*, **2**, 761.
 Maher, R. M. (1955). *Ibid.*, **1**, 18.
 Moore, G. E., Sandberg, A., and Schubarg, J. R. (1957). *Ann. Surg.*, **146**, 580.
 Nelson, W. R., Brown, R. K., and Baer, S. (1957). *Ibid.*, **146**, 790.
 Raven, R. W. (1947). *Brit. med. J.*, **2**, 249.
 Scott, R. B. (1958). *Ibid.*, **1**, 1.
 Störtebecker, T. P. (1954). *J. Neurosurg.*, **11**, 84.
 Wangenstein, O. H., Lewis, F. J., Arhelger, S. W., Muller, J. J., and Maclean, L. D. (1954). *Surg. Gynec. Obstet.*, **99**, 257.
 Wilson, E. (1956). *Med. J. Aust.*, **2**, 292.

"To-day, we understand the means by which tuberculosis can be prevented, and we have the drugs through which, provided treatment is begun early and continued properly, the illness can be cured. . . . In 1957 there were 4,784 deaths, as against 23,076 ten years ago, though over 30,000 new patients are still discovered every year. Tuberculosis has been removed from among the great killers of men, and demoted to the position of a lesser—though still formidable—enemy. There are still 350,000 patients attending our chest clinics in Britain; and if we add their families (who are at risk) this means at least a million lives directly affected by a preventable disease."—From the *NAPT Annual Report, 1957–1958*.