Clinical Experiences at St. Mark's Hospital with Multiple Synchronous Cancers of the Colon and Rectum*

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AT THE LAS VEGAS MEETING in 1971, Mr. H. E. Lockhart-Mummery presented a paper about the experiences at St. Mark's Hospital with metachronous cancers of the large intestine.[1] He and I wrote that paper jointly, and we have continued to pursue the question of multiple colonic cancers since that time. This further paper reviews the St. Mark's cases of synchronous cancer of the colon and rectum – *i.e.*, two cancers found at the same time, as opposed to metachronous cancer when the second growth manifests on another occasion, usually after one lesion has been cured.

First, what is the magnitude of the problem? Between 1928 and 1970 the St. Mark's records contain details of 4,884 survivors from operations for cancers of the large bowel apart from those associated with major polyposis or colitis (Table 1). Our previous paper showed that 83 of these operations (1.6 per cent) were for second growths. During the same period a second but synchronous growth was found at (or within a month of) operation in 157 patients, of whom 143 survived. This is nearly double the incidence of metachronous cancer in the same series – that is, 3 per cent, but the true incidence is slightly higher, since 18 of those classified as metachronous were certainly present at the time of the original operation. They were really "missed synchronous" growths which would, in a world of perfect surgeons, have been eligible for inclusion in this second paper. The true incidence is therefore about 3.5 per cent, which accords well with other previously published series. This happens to be almost exactly the same figure as the cumulative long-term risk of developing metachronous cancer. In other words, we can say that when we diagnose a colonic or rectal cancer, there is a 3.5 per cent risk that a second cancer is present at the same time, and if we cure the patient, there is a further 3.5 per cent risk that another cancer will develop over the years. It means, of course, that the detection of these second cancers is of considerable practical importance, since they are by no means extreme rarities. On the other hand, the value of their detection must depend upon the survival rate which can be achieved by their removal.

TABLE 1. *Clinical Material*

St. Mark's Hospital, 1928–1970, cancer operation survivors	
TOTAL	4,884
Number whose operation was for metachronous cancer, 83 (1.6 per cent)	
Number with synchronous cancer, 157	
Number with three growths, 9	
Percentage of survivors, 3.3	

* Read at the meeting of the American Proctologic Society, Detroit, Michigan, June 10 to 14, 1973.

For these purposes we have considered only those patients whose operations were performed before the end of 1967, so that five-year survival figures would be available. Of 168 patients, 11 (6 per cent) had inoperable cancers, 21 (12 per cent) had palliative operations, and the remaining 82 per cent had radical removals of both growths, either separately or in continuity. Of the patients treated by operation, 14 died (Table 2).

Before assessing the results it is important to appreciate that they go back to 1928. A truly comparable series of single cancers is not readily available, and we have therefore avoided spurious statistical comparison between imperfectly matched groups. However, certain trends are fairly clear. The operability rate of 82 per cent for radical resections is actually higher than the St. Mark's figure of 68 per cent quoted for single rectal cancers over the same period. Likewise, the crude uncorrected five-year survival figure for all resections is 49 per cent, which is very slightly better than the figure of 48 per cent found for single cancers during the same years (Table 3). There are other more familiar ways of presenting the same results; for instance, the corrected five-year survival rate for radical resection is 66 per cent. In round figures, one can say that four of five patients were operable, and that two out of three of these were cured of *both* growths by the operation. These figures are certainly no worse than those in most comparable series of single cancers, and may even suggest that a patient with *two* colorectal cancers fares slightly better than a patient with *one*.

TABLE 2. *Operability of Double Carcinoma*

Operations at St. Mark's Hospital, 1928–1970 (inclusive)	168
Inoperable (no resection)	11 (6 per cent)
Palliative removal	21 (12 per cent)
Radical	136 (82 per cent)

TABLE 3. *Five-year Survival with Double Carcinoma*

"Crude" uncorrected survival rate after all resections (including palliative) (=70 patients)	49 per cent
Corrected five-year survival rate after radical resections	66 per cent

TABLE 4. *Crude Five-year Survival by Stage*

Staging	Number of Patients	Per Cent
A + A	17	88
B + A	43	60
B + B	12	66
C + A	39	43
C + B	16	35
C + C	4	25

The nine cases of treble synchronous carcinoma in this series showed the same favorable trend. Four of the eight survivors lived for more than ten years, and the average survival time for all resections, including one classed as palliative, was seven years and eight months, which is almost exactly the average for single cancers.

These surprising facts merit closer scrutiny:

First, the patients themselves did not differ in any important way from patients with single cancers – their average age was 65 years and there was a slight male predominance in a ratio of 4:3.

Table 4 gives the five-year survivals by *stage* and demonstrates much the expected distribution of cures. It is interesting, particularly, that patients with two Dukes' B or C growths do not show the adverse effect that might be expected if the malignant potentials of the two were to summate. The comparable survival figures for patients with single cancers over the same years (1928–1967) are: Dukes' A, 82.8 per cent; B, 62.9 per cent, C, 27.8 per cent. This interesting fact may have wider implications in our

TABLE 5. *Association with Benign Tumors*

Number of patients	157
Number with associated adenomas or villous papillomas	116 (75 per cent)

TABLE 6. *Association with Benign Tumors*

Number of resection specimens	157
Number of carcinomas	323
Carcinoma arising in	
An adenoma	71 (22 per cent)
A villous tumor	16 (5 per cent)

TABLE 7. *Extent of Resection, 157 Cases*

Total colectomy	3
Excision of left colon, rectum and anus	103
Left-colonic resections with anastomosis	34
Right-colonic resections	4
Resection of two segments	12
Resection of one growth only	1

understanding of the immune response to malignancy.

Another feature of the series is shown in Table 5 — a remarkably high incidence of associated benign tumors. Metaplastic polyps are excluded, and the figure of 75 per cent for true adenomas or villous papillomas is even higher than that of 60 per cent which we published in our series of metachronous cancer. It is three times the incidence of such lesions in resection specimens for single cancers, and more than ten times that in the population as a whole. In a little more than a fourth of the cancers studied, we found the malignancy actually arising within a pre-existing benign tumor (Table 6). All of this is strong circumstantial evidence to link colorectal cancer, and particularly multiple malignancy, with benign tumors of large-bowel epithelium.

This leads to consideration of the extents of the resections, which may provoke some comment (Table 7). In only three cases was total colectomy undertaken; thus, 98 per cent of the patients were left with some colonic mucosa. In almost two thirds of the patients, the resection was of rectum and anus, together with various amounts of left colon. The remaining patients had restorative resections of colon or upper rectum, and the average length of excised large intestine in all patients was about 45 cm. In 12 patients two discontinuous segments of bowel were excised — *e.g.*, rectum and right colon, sigmoid and cecum, etc. Thus, the series contains 140 patients who had already had two colorectal cancers removed but still possessed the bulk of their colonic mucosa—patients whom many American surgeons would consider mandatory candidates for total colectomy. Table 8 shows the incidence of metachronous cancer in these patients to be 4.3 per cent, and the average time to develop the third growth was 12½ years; this is almost exactly the average interval in the series of metachronous growths after single first cancers, but the cumulative risk expressed as a percentage of survivors has more than doubled (from 3.5 per cent to more than 8 per cent).

Finally, we need to consider the way in which the second growth was discovered (Table 9). In a few cases both lesions were felt on routine clinical and rectal examination, and in a few more sigmoidoscopy revealed that two were present. In a smaller number of the more recent cases, both were detected on barium-enema examination. It is, however, salutary to note that, even in those cases where x-rays of the colon were undertaken, two thirds of the second growths were missed, although results have now improved greatly with double-contrast radiography. It is even more salutary to find that the second growth was palpable at operation in only 48 patients — that is, in less than a third of all cases. In 60 per cent of the entire series the second growth was discovered only when the resected specimen

was opened. It is this group of 84 missed lesions which provides the greatest challenge for the future. Many of them were early; 69, in fact, were Dukes' A growths, and some were very close together, but it is disturbing to report that 15 B's were also missed, which is more than half of those present as second growths, and even one C growth escaped detection.

Discussion

What message, then, does this series have for the practical surgeon? First, it is remarkable to report that the presence of a second growth, even a Dukes' B or C tumor, affects the prognosis very little. If, in round figures, we say that an average colorectal cancer will kill one patient in two, we might reasonably expect two cancers to kill three patients of four. For some reason which is not easy to understand, this is not so; two cancers at one time still kill only one patient in two. Less than one case in five, in fact, will be inoperable, and one can expect "cure" in two of three cases when resection appears to be complete. It is therefore very definitely worth the effort involved in detecting second growths, because they are eminently curable.

The experiences of the proctologic peers of Britain suggest, however, that second growths are astonishingly easy to miss. The only answer to this is a fixed routine that leaves nothing to chance. Every patient must have both sigmoidoscopy and a double-contrast enema study. One cannot repeat too often the value of an enthusiastic radiologist in this respect; there is all the difference in the world between a "barium enema" and a "good double-contrast enema," and it is unlikely that the colonoscope will ever be as useful as the latter, at least in this situation. It is vital that the colon be thoroughly emptied of feces before examination, and of barium after it, or the surgeon will be tempted to omit the x-ray when a large rectal cancer is present. This omission of one of the two essential investigations was overwhelmingly the most important cause of missing synchronous cancer. Table 10, reproduced from our first paper, underlines this point. It reconstructs the errors which led to failure of 18 cases of double cancer to be detected at the time of the original operation. These are the cases that should have been in this series but appeared with the metachronous growths because they were missed. In 12 of the 18 patients the relevant investigation had not been performed. In some the reason was local pain, a well-recognized pitfall that should alert the surgeon to the possibility of a malignant lesion in the anorectal region. However, it is abundantly clear that there is no substitute for a total colorectal investigation in all cases. The knowing hand

TABLE 8. *Risk of Developing Metachronous Cancer after "Conservative" Resection of Two Carcinomas*

Number of patients at risk with retained colonic mucosa	140
Number developing a third cancer	5 (4 per cent)
Average time interval 12½ years	

TABLE 9. *The Point at Which Diagnosis of Two Cancers Was Made*

Clinical examination — both felt	4
Sigmoidoscopy	16
Barium-enema study	5
Palpated at operation	48
Only found in resected specimen	84

TABLE 10. *Reasons for Missing Synchronous Cancer in 18 Patients*

Sigmoidoscopy relevant but omitted	5
Sigmoidoscopy performed but lesion missed	1
Barium-enema study relevant but omitted	7
Barium-enema study performed but lesion missed	3
No details available	2

on the abdomen and the passage of the "informed" digit into the rectum are simply not enough.

The extent of the operation when two growths have been discovered will be a matter for individual choice. St. Mark's surgeons over the years have elected to use a conservative approach, each growth being resected in a radical fashion but normal colon being retained where possible. More extensive colonic resections have many advocates in the United States, and it is interesting to report that the cumulative risk that survivors will develop a metachronous growth rises from about 3.5 per cent after resection of a single cancer to more than 8 per cent after removal of two growths. The time interval is around 13 years, and a strong argument could be put forward for conservative surgery, as in this series, backed by careful follow up. The increased morbidity and perhaps mortality of total colectomy must be weighed against the risk of developing a subsequent cancer which will have a very good chance of cure provided it is detected early. The St. Mark's approach to this situation is increasingly one of lifelong follow up combined with frequent exhortation of the patient to report suspicious symptoms at the earliest moment.

Summary

We have reviewed the experience of St. Mark's Hospital with double synchronous cancers of the large intestine. This occurs in 3.5 per cent of cancer resections, and in 75 per cent there are associated benign neoplasms. Patients with double or treble cancers fare much the same as those with single cancers, and the prognosis appears to be surprisingly favorable, even when the second growth is comparatively advanced. The second lesion, however, is usually not palpable at operation, and full clinical and radiologic investigation is therefore essential before any resection is undertaken for cancer of the colon or rectum.

Reference

1. Lockhart-Mummery HE, Heald RJ: Metachronous cancer of the large intestine. Dis Colon Rectum 15: 261, 1972

Announcement

The American Society of Colon and Rectal Surgeons will hold its 74th Annual Meeting at the Hilton Hotel in San Francisco, May 4-8, 1975. Information may be obtained from the Program Chairman, Stanley M. Goldberg, M.D., 1731 Medical Arts Building, Minneapolis, Minnesota 55455.