COLORECTAL CANCER IN SINGAPORE: PRELIMINARY REPORT OF THE COLORECTAL CANCER PROJECT FROM THE UNIVERSITY DEPARTMENT OF SURGERY, NUS

H S Goh
T K Ti
A Rauff
W C Foong
Y S Lee

SYNOPSIS

The Colorectal Cancer Project was set up by the University Department of Surgery, National University of Singapore, in 1982 to establish a readily retrievable data-base on colorectal cancer. The aim is to provide a means for medical audit, and to have a system to collect data for specific studies. 109 cases of colorectal cancer seen in 1982 were analysed: the mode of presentation, operative and histological findings, treatment procedures and early results are presented. The common assumption that cases of colorectal cancer seen locally present at a late stage was not substantiated as 41% of our patients had localised disease (Dukes' A & B). 6.6% of patients with rectal cancer refused surgery when the possibility of a permanent colostomy was raised. The controversial role of adjuvant chemotherapy was discussed and a need for a controlled clinical trial was stressed.

INTRODUCTION

Colorectal cancer is one of the most common malignancies in the world. It has an approximately equal sex distribution but its geographical distribution shows a wide variation, from an incidence of 3.7 per 100,000 population in Dakar, Senegal to 87.5 per 100,000 population in Connecticut, USA. (1) This variation can be correlated with the amount of meat and fat consumed in the diet. (2).

The incidence of colorectal cancer in Singapore is 23.1 per 100,000 for males and 17.9 per 100,000 for females. These figures lie within the range seen in Europe. They are higher than those seen in eastern Europe and Finland, and slightly lower than those in the rest of Scandinavia and United Kingdom. They are higher than the rates reported in other Asian populations e.g. Bombay, Japan and Shanghai. (3).

In order of frequency, colorectal cancer in Singapore ranks fourth in males after cancers of the lung, stomach and liver, and it ranks second in females after breast cancer (statistics for 1968-1977). (3) In contrast to cancers of the oesophagus and stomach the incidence of colorectal cancer in Singapore is rising. The average number of cases was 410 annually for 1968-1977; the projected number based on current trends, are 675 for 1985, 954 for 1990 and 1343 for 1995. This would make colorectal cancer the second commonest cancer in males after cancer of the lung, and the commonest in females by 1985. (3)

well documented by the Singapore Cancer Registry. But there is little local clinical and pathological data available on this important topic. To date only four papers have been written on this subject: two were case reports and two were retrospective studies on personal series (4, 5, 6, 7).

In 1982, the University Department of Surgery of the National University of Singapore started the Colorectal Cancer Project to establish a readily retrievable data-base on colorectal cancer. The aim is to provide a means for medical audit, and to have a system to collect data for specific studies.

This paper presents an analysis of 109 new cases of colorectal cancer seen in 1982. The object of this preliminary report is to document the pattern of presentation, stage of disease and treatment procedures, as well as to compare these findings with those from other parts of the world.

University Department of Surgery
National University of Singapore
Singapore General Hospital
Outram Road
Singapore 0316

H S Goh, B Sc (Hon), FRCS
Lecturer,

T K Ti, MD, FRCS, FRACS
Associate Professor of Surgery

A Rauff, MS, FRCS
Associate Professor of Surgery

W C Foong, FRCS (E), FRCSZ
Professor of Surgery

University Department of Pathology
Singapore General Hospital
Y S Lee, MRCP, FRCPA, FCAP
Associate Professor of Pathology

PATIENTS AND METHOD

All new patients seen in our department were included in the project. A standard protocol was devised to enable prospective collection of clinical and pathological data for each patient. All the pathological specimens were reviewed by one pathologist (YSL). This information was then transfered into the main-frame IBM computer based at the Computer Centre, National University of Singapore. Data were analysed using the Statistical Package for Social Sciences (SPSS). (8)

RESULTS

A total of 115 cases were entered into the protocol for 1982. Six were excluded from analysis: Three of these were found to have benign adenomatous polyps after resection; two cases had bypass procedures done for unresectable carcinoma of the colon but no biopsies were taken and one patient had advanced caecal carcinoma but refused treatment. 109 cases with histological confirmation of colorectal cancer were analysed.

SEX AND AGE

The sex distribution were roughly equal with 58 males (53%) and 51 females (47%). The mean age at presentation was 61 years with a range of 31-86 years. The age distribution is shown in Fig. 1.

The mean duration of symptoms (from on-set of symptoms to hospitalisation) was 19 weeks with a median of 12 weeks. The distribution is shown in Fig. 2. There was no significant correlation between duration of symptoms and the size or pathological stage of the tumour.

Table 1 shows the presenting symptoms in order of frequency. Change in bowel habit was the commonest symptom (72%). Despite the many different dialect groups encountered there was no difficulty in eliciting the symptoms of change in bowel habit and bleeding per rectum. One of the authors (HSG) had personally interviewed most of the patients. Passage of mucus per rectum was difficult to elicit as most of the patients were not aware of the significance of this symptom. 43% of the patients felt that they had lost weight but this was difficult to document as most of the patient did not know their normal weight, in contrast to the weight-conscious populations in Western countries. Abdominal distension was a significant symptom; out of 26 patients who complained of abdominal distension, 24 had evidence of intestinal obstruction on X-ray.

SITE OF TUMOUR

Fig. 3 shows the distribution of tumours within the large bowel. 72% of the tumours occured in the rectum and sigmoid colon. Six cases had multiple tumours: two were cases of familial polyposis coli, while the remaining four (3.7%) had synchronous

Fig. 1   AGE DISTRIBUTION

MEAN 61 YRS
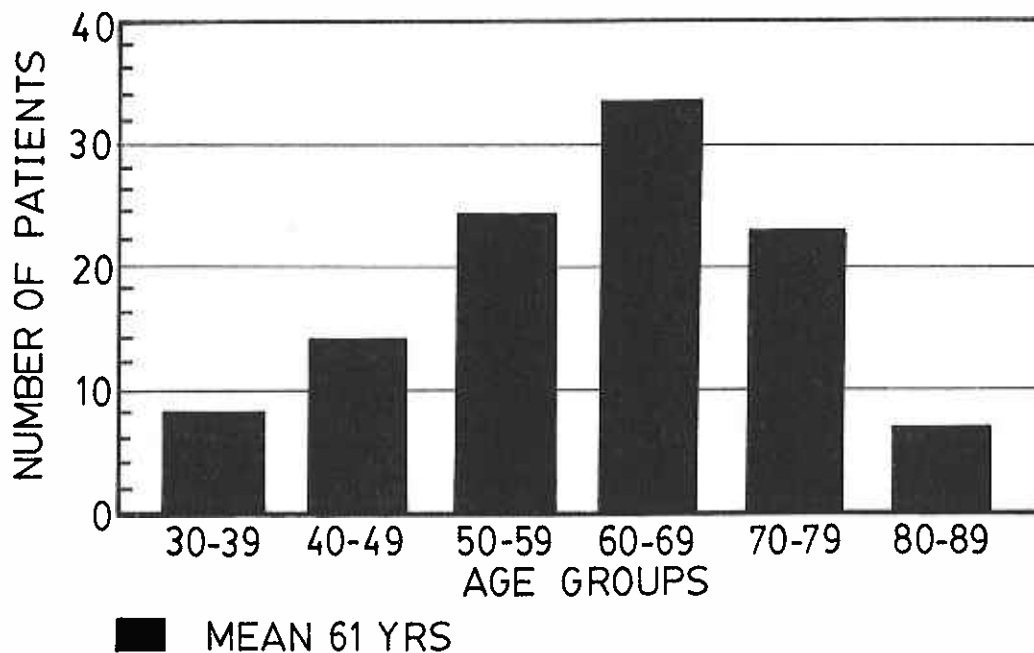
CLINICAL PRESENTATION

66 cases (60%) were elective admissions while 43 cases (40%) were admitted via the Accident and Emergency department. 41% of those admitted via the A & E department presented with intestinal obstruction against 9% of elective admissions (Chi Square p = 0.0003) and 62% against 40% stayed for three weeks or more on their first admission. (Chi square p = 0.025).

tumour.

POLYPS

17 patients out of 109 had associated polyps. Excluding the two cases of familial polyposis coli, only 15 out of 107 cases or 14% had associated polyps in the colon and rectum.
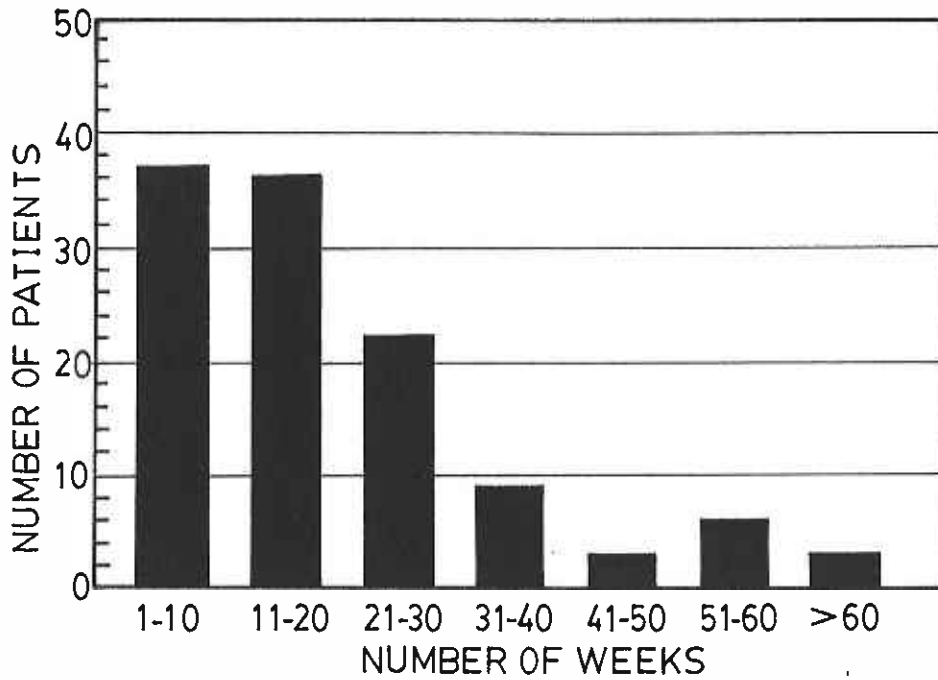
Fig. 2 DURATION OF SYMPTOMS IN WEEKS

TABLE 1: PRESENTING SYMPTOMS IN ORDER OF FREQUENCY

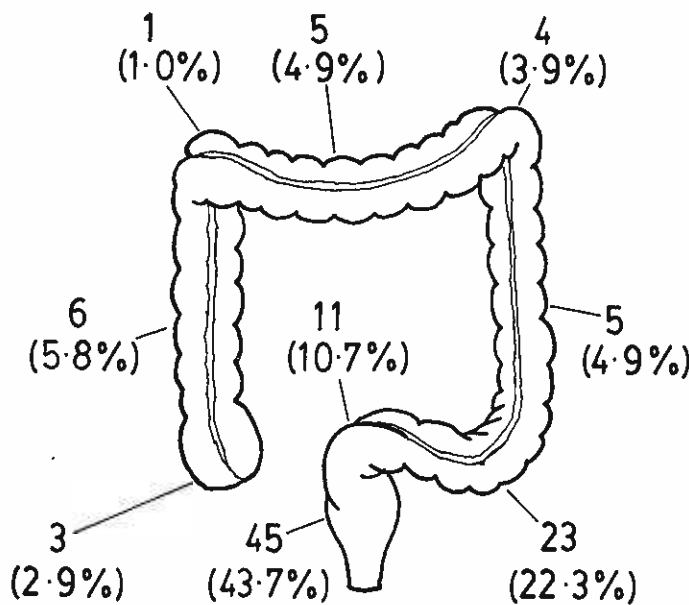| SYMPTOMS	% OF CASES
1. Change in bowel.habit	72
2. Bleeding per rectum	50
3. Abdominal pain	48
4. Loss of weight	43
5. Mucus per rectum	33
6. Loss of appetite	31
7. Abdominal distension	24

Fig. 3 TUMOUR SITE

TREATMENT

Surgery was carried out on 102 of the 109 patients. Of the seven who did not undergo surgery, three refused surgery because of an aversion to a permanent colostomy while the other four had obviously advanced disease. 91 out of 102 patients who underwent surgery had their tumours resected, a resection rate of 89%. Table 2.

TABLE 2: TYPES OF OPERATIVE PROCEDURES

PROCEDURES	NO.	%
1. Resection	91	83.4
2. Colostomy	6	5.5
3. By-pass	3	2.7
4. Laparotomy and biopsy	2	1.8
5. No. op. — advanced tumour	4	3.6
6. No. op. — refused surgery	3	2.7

RESECTION

Table 3 shows the types of resection performed. Anterior resection (33%) was the commonest resection performed. Two thirds of these were low anterior resection where the anastomosis were at or below the peritoneal reflection. The high number of this procedure was due to the introduction of the circular EEA stapler in March, 1982. Sigmoid colectomy and abdomino-perineal resection were two second commonest procedures at 15% for each. These three procedures made up roughly two thirds of all resections done in this series.

TABLE 3: TYPES OF RESECTION

TYPES	NO.
1. Right Hemicolectomy	9
2. Extended Right Hemicolectomy	1
3. Transverse Colectomy	5
4. Left Hemicolectomy	10
5. Sigmoid Colectomy	14
6. High Anterior Resection	10
7. Low Anterior Resection	20
8. A-P Resection	14
9. Total Colectomy	1
10. Panproctocolectomy	2
11. Polypectomy	1

ANASTOMOSIS

One layer, two layer and staple anastomosis were all represented in this series Table 4.

TABLE 4: ANASTOMOSIS

TYPE	NO.	%
One Layer	16	23%
Two Layer	39	56%
& Staple	15	21%

TABLE 5: OPERATIVE COMPLICATIONS

COMPLICATIONS	NO.	%
Mortality	2	1.9
Anastomosis leak (Clinical)	3	5
Wound infection	32	31

TABLE 6: HISTOLOGICAL TYPE

TYPE	NO.	%
1. Adenocarcinoma	91	83
2. Mucoid Adenocarcinoma	15	14
3. Signet-ring adenocarcinoma	2	1.8
4. Carcinoid	1	0.9

Out of 102 cases operated upon, there were two hospital deaths 1.9%. One patients died of a myocardial infarct three days after a laparotomy and biopsy. The other patient died of chest infection 34 days after a Hartmann's resection for an obstructing sigmoid carcinoma. Right-sided broncho-pneumonia associated with a concurrent occult bronchial carcinoma was found at post-mortem.

70 anastomoses were performed, and 11 had protective colostomies. Three anastomotic leaks were apparent (5% of unprotected anastomoses). 20 cases had limited barium studies and six of these had radiological evidence of leakage. 32 patients (31%) had wound infection.

HOSPITAL STAY

The mean hospital stay was 26 days; the median stay was 21 days with a range of 4-79 days. These figures were for the first admissions only, excluding the subsequent hospital stay of those who had staged operations or those who had subsequent complications. 25 patients had two-stage operations and five had three-stage operations.

PATHOLOGY

The distribution of tumour size is shown in Fig. 4. Only the greatest diameter of each tumour was recorded. All tumours were adenocarcinoma apart from one carcinoid tumour Table 6. 81.7 of the tumours were moderately differentiated and only 8% were poorly differentiated Table 7.

Dukes' A refers to cancer which have not spread beyond the muscularis propia, Dukes' B refers to cancer which has spread through the muscular wall of
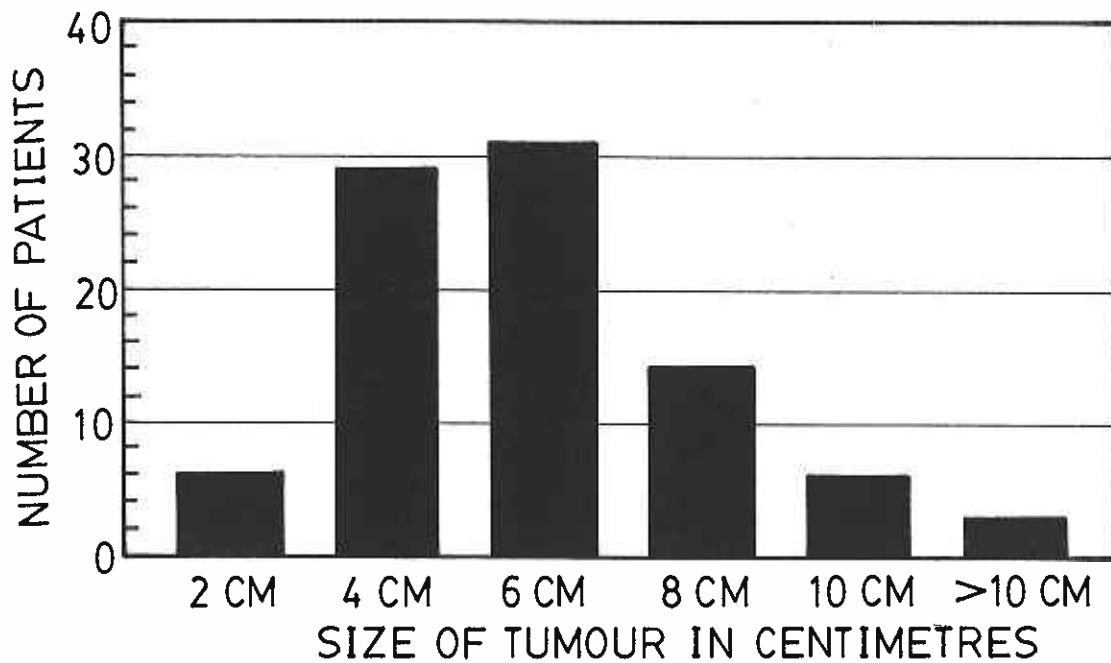
Fig. 4 TUMOUR SIZE

TABLE 7: GRADE OF TUMOUR

GRADE	NO.	%
1. Well differentiated	12	11
2. Moderately differentiated	88	81
3. Poorly differentiated	9	8

TABLE 9: PATIENTS WITH POST-OPERATIVE THERAPY

THERAPY	NO.	%
1. Radiotherapy	8	7
2. Chemotherapy	14	13
3. Both	12	11
	34	31

the bowel provided any local spread has been resected with the primary tumour, Dukes' C refer to cases with lymph node involvement but no distant mestastases, and Dukes' D refers to cases with distant metastases or extensive local spread beyond the limits of resection.

The modified Dukes' staging system was adopted. The findings are shown in Table 8. 56% of cases had either lymph node involvement or evidence of distant metastases. Of the 30 Dukes' D cases, 15 had their tumours resected and the other 15 did not.

POST-OPERATIVE THERAPY

31% of patients had post-operative radiotherapy, chemotherapy or both. Table 10. There are no standard policy on selection of patients for post-operative therapy. Some were referred for palliative treatment while others were sent for adjuvant chemotherapy in a bid to eradicate micrometastases.

TABLE 8: DUKES' CLASSIFICATION

STAGE	NO.	%
A	28	25
B	17	16
C	31	28
D	30	28
unknown	3	3

TABLE 10: COMPARISON OF MORTALITY BETWEEN POST-OPERATIVE TREATMENT GROUP WITH NON-TREATMENT GROUP

TREATMENT			NON-TREATMENT		
STAGE	DEATH	%	STAGE	STAGE	%
A	0	—	A	1	—
B	0	—	B	2	—
C	6(14)	43	C	2(17)	12
D	7(11)	64	D	15(19)	80

EARLY RESULTS

35 patients (32%) have died after a mean follow-up of 13 months, range 8-19 months. Table 11. This figure includes the two peri-operative deaths. In the 30 cases with distant metastases, there were no survivors amongst those with unresected tumours, while 40% of those with resected tumours are still alive. Of the 33 patients who died after initial discharge from hospital, 13 (39%) received post-operative therapy while 20 (61%) did not. Table 12.

DISCUSSION

The sex and age distribution, presenting symptoms and site of tumours in our series are similar to those reported in Western literature. (9, 10, 11) We have not analysed our data separately for colonic and rectal cancers because the clinical and pathological features are similar. However, in epidemiological studies, cancers of the colon and rectum are considered separately because of differences in sex ratio and in the distribution of age, geographical location and time. (12) This is exemplified by the influence of migration on the rates for cancer of the colon in both sexes and of cancer of the rectum in Chinese males: there is a gradual increase in incidence from the low incidence in Shanghai, though Singapore-Chinese born elsewhere, Singapore-born Chinese, Chinese in Hawaii to the high incidence in Chinese born in California. By contrast, the rates of rectal cancer in females in these five Chinese populations are similar. (3)

The mean duration of symptoms was 19 weeks with a median of 12 weeks. 80% of the patients presented within 30 weeks of their onset of symptoms. Reports from other parts of the world give a range of duration symptoms as 44% within 26 weeks in Italy (13) 45% within 39 weeks in Australia (14) and 75% within 35 weeks in New Zealand. (11) Our data support other reports that there is no correlation between the duration of symptoms and the stage of tumour at surgery. (13, 15) There is a suggestion that those with a longer history had better survival. (16) The duration of symptoms reflects the biological behaviour of a tumour rather than just an arithmetic spatial progression of that tumour. (17)

There is a local impression that tumours seen in South East Asian countries are much more advanced compared with those seen in Western countries. Our findings do not substantiate this assumption: 41% of our patients with colorectal cancer had localised disease (Dukes' A & B). This compares with 29.5% from an American national survey (18), 33% from Rome (13), 42% from New York (19), 45% from Pennsylvania (20) and 49% from London (21). 8% of our patients have poorly differentiated tumour while the figure from St. Mark's Hospital, London is much higher at 20%. (22)

Recent evidence has strongly suggested a sequential link between adenomatous polyps and colorectal cancer. (23, 24, 25) Gilbertsen (26. 27) has shown that it is possible to reduce the incidence of rectal cancer in a population by regular sigmoidoscopy and polypectomy. In Western series, about a third of cancer cases have associated polyps (28). In contrast to this only 14% of our cases have polyps, while an earlier Singapore series by Nambia and Lim (17) reported 3.7% and Wong and Ong (29) from Hong Kong reported 5% in their series. The low incidence of associated polyps in our cases could have been due to the lack of systematic search for polyps. We have therefore em-

barked on a study to determine the true incidence of associated polyps in our population by combining colonoscopy, double-contrast barium studies and a systematic search on resected specimens.

Our resection rate in patients who underwent surgery was 89%. This compares with 93% at St. Mark's Hospital, London (21), 87% at Princess Alexandra Hospital, Brisbane (14), 83% at a national survey by the American College of Surgeons (18), 78% at Queen Mary Hospital, Hong Kong (29) and 67% from Toa Payoh Hospital, Singapore. (7) Palliative resection was carried out in half of the 30 patients with distant metastases (Dukes' D). The aim of palliative surgery was to relieve symptoms, to prevent obstruction and to improve patient-wellbeing. (30, 31, 33) 40% of our patients who had palliative resections were alive after 13 months while none of the resected cases survived. This difference is probably because it was the more favourable cases who underwent resection. A point would probably be reached when the volume of metastatic tumour is so great that the risks of resection of primary tumour would out-weight any advantage.

The advent of the circular EEA staple had made' low anterior resection the commonest resection performed in this series. There is a fear that this might lead to an increase in local recurrence as reported by Hurst et. al. (34) The dilemma of sphincter preservation was most eloquently expressed by the late Harry E Bacon who said: "The avoidance of a colostomy when indicated may jeopardise the patient's chance of cure and this is an unfortunate mistake in surgical judgement. Equally tragic is the sacrifice of the patient's sphincter without increasing his chance of cure." (36) It must be emphasised that the surgical clearance of the pelvis in any of the sphincter-saving operation is no different from abdomino-perineal excision. But for a sphincter-saving operation, one must be aware of the extent of intramural spread distal to the tumour. The safe distal margin has been variously quoted as from 1-6 cm. (36, 37, 28, 29) A recent study showed that in specimens excised at AP excision, 76% had no distal intramural spread, 14% had distal spread of up to 1 cm, 4% between 1-2 cm and only 6% had distal spread of more than 2 cm. All the patients with distal spread of more than 1 cm, had poorly-differentiated had Dukes' stage C tumours and all were found at 3 year follow-up to be dead or dying from distant metastases. (40) There is no doubt that the quality of life of patients with intact sphincters compared to those who under-went AP excisions is far superior in terms of their dietary freedom, return to work, sexual function and psychological well-being. (41)

Many of our patients are averse to colostomies. 3 out of 45 patients (6.6%) with rectal cancer refused surgery while none of the colonic cancer patient did. In Hong Kong 10% of patients with rectal cancer and only 2% of those with colonic cancer refused surgery. (29) Those who refused surgery would invariably return months later with end-stage disease. Procedures like abdomino-transsacral resection used by Localio (42) or colo-anal anastomosis used by the late Sir Alan Parks (43) would give an additional option to patients who would otherwise have to choose between no treatment and a permanent colostomy. When properly selected a small but significant group of patients with low rectal tumours would be spared the fate of a permanent colostomy without sacrificing the chance of cure.

Our operative mortality last year was 1.9%. Most major series give a rate of 2% to 10% (44, 45, 46, 47) This mortality is influenced by the percentage of

emergency cases in the series as well as the period of reporting, improvement of results being seen in the more recent reports. None of our patients died of anastomotic breakdown, which is a significant cause of mortality. (48) However, 3 out of 59 patients (5%) had anastomotic leaks resulting in fistula formation. This compares with a 2% clinical leak rate reported by Matheson (49) and 15% reported by Goligher. (48) Only 20 anastomoses were subjected to radiological study and 30% of these showed a leak. Radiological leaks in Matheson's and Goligher's Series were 6% and 50% respectively. Some of these leaks were not evident clinically while others could have been suggested by a slightly prolonged ileus or a slight swinging temperature. Each of the three methods of anastomosis, one-layer, two-layer and staple anastomosis, had one case of leakage. The two-layer suture was used in palliative transverse colectomy and the other two were low anterior resections. The case of staple anastomosis was one of the first to be done using this technique. Leakage of anastomosis is determined not so much by the method of suturing, as by the basic requirements of a clean bowel, careful apposition, absence of tension and a good blood supply. (50)

The standard reporting results requires a minimum follow-up of five years. It would be inappropriate to publish results when the mean follow-up is only 13 months unless they could influence current management. One third of our patients had post-operative therapy. In Dukes' C disease, some patients received chemotherapy on an adjuvant basis. 6 out of 14 patients (43%) in the treated group died while only 2 out of 17 patients (12%) in the untreated group died. Although this is not statistically significant, it reaffirms that the role of adjuvant chemotherapy is controversial. Claims of therapeutic advantage (51, 52, 53) have not stood up to critical appraisals. (54, 55) This is not surprising as animal studies and clinical experience have shown that for a drug or drug combination to be significantly effective in the adjuvant situation, it must be able to induce complete remissions in 30% or more of individuals with clinically obvious metastases. (56)

5FU is the main chemotherapeutic agent used in colorectal cancer. (57) It produces an objective response in only 15-20% of patients. (58) The response produced is usually partial, lasting for a median time of four to five months. Because of this and of the cost and not insignificant side effects of chemotherapeutic agents, the place of adjuvant chemotherapy at present should be restricted to its use in well-designed controlled clinical trials.

ACKNOWLEDGEMENTS

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