Table 2

Results of treatment of Stage II carcinoma of cervix uteri

	Method of treatment			*Survival*			*Causes of death*	
Year	*Caesium and Wertheim hysterectomy*	*Caesium and external irradiation*	*Hysterectomy and external irradiation*	*Three years*	*Five years*	*Alive and well March 1974*	*Carcinoma of cervix*	*Other*
1965	2	—	1	3/3	1/3			Pneumonia, 1 Carcinoma of lung, 1
1966	2	5	1	7/8	7/8		1	—
1967	3	4	2	5/9	4/9		4	Coronary thrombosis, 1
1968	—	10	2	9/12	8/12		4	—
1969	—	9	—	4/9		4/9	3	Heart failure, 1 Pneumonia, 1
1970	4	6	—	8/10		8/10	2	—
1971	2	2	—			3/4	1	—
1972	1	2	—			2/3	1	—

Results

In Stage IIA, 11 out of 14 patients treated by intracavitary ^{137}Cs and Wertheim's hysterectomy were alive and well in March 1974 (78%); in Stage IIB, treated wholly by irradiation, 23 out of 38 cases (61%) were alive and well in March 1974 (uncorrected figures).

In Stage IIA and B, 5 patients died from causes other than recurrent disease: one survived carcinoma of the cervix with no recurrence to die 3½ years later of carcinoma of the bronchus; 2 died of pneumonia, one of coronary thrombosis, and one, who had had valvular disease of the heart for many years, of heart failure. The others died of local recurrence of disease (Table 2).

Of the 8 patients who had wide-field irradiation to the para-aortic strip as well as the pelvis, 6 are alive and well five years after their initial treatment with no sign of recurrence.

Although these numbers are small it does seem worth while to treat all the known disease in these patients who, although clinically they can only be staged as II, really have Stage IV disease outside the pelvis. Until lymphography becomes a routine investigation, patients will be lost due to inadequate coverage of their disease.

The corrected figures for patients with Stage IIA and B disease with all treatments are 76.8% three-year survival and 72% five-year survival (Table 3).

Table 3

Carcinoma of cervix: 'life table' survival rates (%), 1965–1972

Term (years)	*Stage I*	*Stage II*	*Stage III*	*Stage IV*	*All Stages*
1	100.0 (0.0)	91.4 (3.7)	84.4 (4.8)	45.5 (12.3)	87.8 (2.4)
2	98.2 (1.8)	82.6 (5.0)	53.8 (6.7)	24.5 (11.1)	73.7 (3.2)
3	92.2 (3.8)	76.8 (5.7)	45.2 (6.8)	24.5 (11.1)	67.5 (3.5)
4	87.2 (4.9)	72.0 (6.3)	36.8 (7.1)	16.3 (9.9)	61.4 (3.8)
5	87.2 (4.9)	72.0 (6.3)	33.6 (7.2)	16.3 (9.9)	60.5 (3.8)
No. of cases initially at risk	57	58	58	17	190

Figures in parentheses are the standard errors of the survival rates (Greenwood's method)

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Bowel Damage from Radiation

This paper reviews a series of 52 patients with chronic bowel damage developing as a complication of pelvic radiotherapy and then poses three questions and comments on each: (1) Why do some patients develop intestinal complications after pelvic radiotherapy? (2) How can the diagnosis of bowel damage be more easily made? (3) How should patients be treated once the diagnosis is made? The clinical details of 38 of the series were obtained by a retrospective review of patients attending St Thomas' Hospital between the years 1961 and 1971 inclusive. The other 14 patients have been seen personally since January 1973.

Clinical Details

There were 36 women and 16 men in the series, their ages ranging between 39 and 76 years at the

Table 1

Diseases for which pelvic radiotherapy was given in 52 patients with irradiation bowel damage

Original disease	*No. of cases*
Carcinoma of cervix	25
Carcinoma of bladder	13
Carcinoma of endometrium	5
Carcinoma of ovary	5
Carcinoma of prostate	2
Seminoma of testis	1
Menorrhagia	1

Table 2

Type of radiotherapy given in 52 patients with irradiation bowel damage

Treatment	*No. of cases*
External radiotherapy in hyperbaric oxygen	16
Intracavitary and external radiotherapy	19
External radiotherapy alone	15
Intracavitary radiotherapy alone	2

time of presentation with intestinal symptoms. Table 1 shows the disease for which the radiotherapy was given and Table 2 shows the type of radiotherapy. In all cases the treatment was to the pelvis with carcinoma of the cervix accounting for nearly one-half of the series (48%). Eleven patients (21%) had received what would now be regarded as a high, or in some cases a very high, dose of radiation during the development of a new dose fractionation technique for use with hyperbaric oxygen (Table 3). The incidence of preradiotherapy operations or pelvic sepsis which could result in pelvic adhesions was 31%, but the incidence was the same in both the group of patients with large bowel complications and in the group with small bowel complications. Generalized arteriosclerosis was present in 12% of the series.

The large bowel complications are seen in Table 4: 25 of 35 patients (71%) had a stricture and 19 patients (54%) had chronic proctocolitis; rectal ulcer, fistula, necrosis and impaired healing of anastomoses were less common complications. A similar range of complications, with the addition of malabsorption, involved the small bowel (Table 4). As with the large bowel complications, stricture formation accounted for a majority of these complications, 14 of 26 patients (54%).

Table 5 shows the time intervals between the radiotherapy and the onset of intestinal symptoms. Chronic proctocolitis and ulceration in the large bowel tended to occur earlier than stricture formation, which in turn tended to occur earlier than necrosis or fistula. Similarly, stricture formation tended to occur earlier than necrosis or fistula in the small bowel also. Commonly, one

Table 3

Possible etiological factors in 52 patients with intestinal complications of pelvic radiotherapy

Possible etiological factors	*No. of cases*
High radiotherapy dosage	11 (21%)
Preradiotherapy operation or pelvic sepsis	16 (31%)
Generalized arteriosclerosis	6 (12%)
No apparent factors	19 (37%)

intestinal complication was the precursor of another, and the disease was often progressive. Colorectal stricture was associated with subsequent necrosis and perforation of the rectum in 2 patients, and with the development of spontaneous rectovesical fistula in 2 other patients.

Many of the patients with large bowel complications presented with typical colonic symptoms such as rectal bleeding, alteration of bowel habit or mucous discharge from the rectum enabling early diagnosis to be made. Those patients with stricture formation and rectal ulcers, however, usually presented with colicky lower abdominal pain which was often misdiagnosed as recurrent tumour. In some cases the true diagnosis of radiation damage was delayed until further complications such as a perforation or fistula developed several months after the symptoms first

Table 4

Large and small bowel complications of pelvic radiotherapy

Large bowel complications	*No. of cases (n=35)*	*Small bowel complications*	*No. of cases (n=26)*
Stricture, colorectal	21	Stricture	14
Stricture, anal	4	Malabsorption	10
Proctocolitis	19	Necrosis	8
Rectal ulcer	8	Impaired healing	8
Fistula	5	Fistula	2
Necrosis	3		
Impaired healing	2		

Table 5

Time interval between pelvic radiotherapy and onset of bowel symptoms

	No. of cases	*Time interval*			
		Less than 6 months	*6–12 months*	*1–5 years*	*More than 5 years*
Large bowel complications					
Proctocolitis or rectal ulcer	27	14	9	3	1
Colorectal stricture	21	6	9	4	2
Anal stricture, necrosis or fistula	12	0	3	6	3
Small bowel complications					
Stricture	14	7	3	4	0
Necrosis or fistula	10	1	2	4	3
Steatorrhœa	7	4	2	0	1

began. Similarly, diagnosis was often unduly delayed in patients with small bowel strictures. Colicky abdominal pain caused by an ileal stricture was misdiagnosed as being caused by recurrent tumour in 2 patients. Another patient was referred for psychiatric treatment of her abdominal symptoms. Three patients developed acute intestinal obstruction, all of whom gave a typical history of intermittent colicky abdominal pain and weight loss for several months preceding the acute episode. Eight patients with small bowel strictures progressing to necrosis were diagnosed only at emergency laparotomy after they had developed either peritonitis or a pelvic abscess. In all these examples the patients concerned were attending a regular follow-up clinic, either gynæcology or radiotherapy or both, and had reported their symptoms.

Small bowel anastomoses failed to heal after surgical operations in 8 patients, and large bowel anastomoses broke down in 2 patients. In each case the cut ends of bowel had bled freely and had appeared macroscopically normal before anastomosis. Further resection of small bowel was undertaken in 4 of these patients, but the new anastomosis also became necrotic and the patients died.

Evidence of malabsorption of fat, vitamin B_{12} and calcium was found in some patients. The fæcal fat (39 g per 24 hours) exceeded the daily intake (30 g per 24 hours) in one of 7 patients with steatorrhœa, causing a 'fat-losing enteropathy'. The Schilling test indicated defective vitamin B_{12} absorption in 6 patients. Of 2 patients with calcium deficiency one presented with tetany two months after the resection of a small bowel stricture.

The outcome of the intestinal complications of pelvic radiotherapy was as follows: 19 patients (37%) died, 13 of whom had no sign of recurrent tumour; 24 (46%) had residual symptoms or disability; only 9 (17%) became completely asymptomatic after treatment of their bowel disease.

Why do Some Patients Develop Intestinal Complications after Pelvic Radiotherapy?

The factors which may predispose to the development of intestinal complications have been suggested by several authors, including Bloedorn *et al.* (1962), Graham & Villalba (1963) and DeCosse *et al.* (1969). The dose of radiation is generally agreed to be an etiological factor in some patients, but in this series a minority (21%) had high doses of radiotherapy. Pelvic adhesions which may anchor a loop of bowel in the irradiated field have also been suggested as a factor in small bowel disease, but the equal incidence of pre-radiotherapy abdominal operations (or pelvic sepsis) in patients with small bowel complications (15%) and in those sustaining damage to the already immobile rectum (15%) suggests that adhesions were not of etiological importance in this series. Calame & Wallach (1967) and DeCosse *et al.* (1969) believe that the development of chronic intestinal complications is caused by ischæmia of the bowel. Certainly vascular sclerosis was prominent in the histology of specimens obtained in the present series, and was associated with excessive deposition of dense fibrous tissue in the submucosa producing an appearance similar to that seen in ischæmic colitis. It is possible that some patients with atheroma and an already precarious intestinal blood supply may develop frankly ischæmic bowel in response to standard doses of radiotherapy, but only 12% of patients in the present series had evidence of generalized arteriosclerosis.

Thirty-seven per cent of the patients in this series had no recognized predisposing factors of any sort, and the cause of their bowel disease remains obscure.

How can the Diagnosis of Bowel Damage be More Easily Made?

A notable feature of this series is the frequent delay in the diagnosis of bowel damage caused by radiotherapy. The diverse manifestations of bowel complications may develop insidiously, are often progressive, and may be fatal. All too often the symptoms are wrongly ascribed to recurrent tumour. On the other hand one patient was referred to and treated by a psychiatrist for eight months before perforating her small bowel stricture and presenting with generalized peritonitis.

I believe the keynote of early diagnosis is to have a high index of suspicion. All patients who develop rectal or colonic symptoms, and especially those who develop colicky abdominal pain, should be suspected of having developed bowel complications and investigated without delay. Investigations should include sigmoidoscopy, rectal biopsy and a barium enema in those patients with large bowel symptoms. Examination under anæsthesia to assess more accurately any rectal ulceration or lesion of the rectosigmoid area may also be indicated. Patients with unexplained abdominal pain should also have small bowel contrast studies performed, as characteristic abnormalities may often be observed (Wellwood & Jackson 1973). If a diagnosis is not reached after full investigation, then careful and regular follow-up assessment is necessary with repeat investiga-

tions if symptoms continue. In this way the incidence of perforation and intestinal obstruction should be reduced and the mortality lessened.

Tests for malabsorption should be performed if radiation damage is suspected. It is of interest that Newman *et al.* (1973) investigated 17 consecutive patients who had received pelvic radiotherapy for gynæcological malignancy, none of whom was complaining of specific bowel symptoms: 16 out of 17 had abnormal cholyl-glycine-1-(^{14}C) breath test, suggesting dysfunction of ileal resorption, and 8 out of 11 had abnormal small bowel radiographs. Similarly, McBrien (1973) investigated 14 symptomless patients for evidence of vitamin B_{12} deficiency after pelvic radiotherapy, and found impaired Schilling tests in 8. It seems possible, therefore, that subclinical malabsorption after pelvic radiotherapy is more common than is generally realized.

How Should Patients be Treated Once the Diagnosis of Radiation-damaged Bowel is Made?

Clearly, the detailed management will vary depending on the condition of the patient and only general principles can be suggested here. Furthermore, this paper is confined to the principles of surgical management in those patients with strictures, perforations, fistulæ and leaking anastomoses. I must stress that both in my experience, and in the experience of others, resection and anastomosis of radiation-damaged bowel may be both technically extremely difficult and also exceedingly hazardous for the patient. The pelvis may be 'frozen' with dense fibrosis as a result of the radiotherapy. Pelvic dissection in this situation, when there is obliteration of the normal anatomical planes, is difficult, with a high risk of damage to the bowel itself, the urinary bladder or the lower ends of the ureters. Not only may the lower ends of the ureters be damaged directly, but they may be rendered partially ischæmic with subsequent necrosis and ureteric fistulæ developing some days later. In general, therefore, deep pelvic dissection should be avoided. Several of the deaths in the present series were directly attributable to complications of pelvic surgery performed in these circumstances.

Even if mobilization of the diseased bowel is straightforward, there may still be hazards. Although there is often no clinical evidence of intestinal damage a few centimetres distant from the damaged area of bowel, sclerotic vessels in the intestinal wall may be unable to provide the increased blood supply necessary for reparative processes, and postradiotherapy intestinal anastomoses may fail to heal. In other words, the microscopic extent of the radiation damage may be much greater than is detectable macroscopically; therefore, if resection is to be performed safely, it must be done widely. Even so, there is still a risk of anastomotic breakdown and all anastomoses should be covered by a proximal stoma. It has been suggested that frozen section examination of the bowel ends may be of value before an anastomosis is performed (Higgins *et al.* 1966), but I have no personal experience of this technique.

Some authors have advocated bypass procedures in the treatment of small bowel damage (Graham & Villalba 1963, Lindahl 1970), but this does not prevent later spontaneous perforation of the irradiated segment which remains *in situ*, and the bypassed bowel may also cause a blind loop syndrome. For these reasons I prefer to resect widely small intestinal lesions and to cover the anastomosis with a temporary loop ileostomy. For large bowel lesions I resect and restore continuity with a covering colostomy when the pelvis is free of fibrosis. If the lesion is low in the rectum and dissection is difficult, however, a Hartmann type of operation is recommended. In this way, anastomotic breakdown is prevented and poor healing of the irradiated perineum which may be seen after abdominoperineal resection is avoided.

Conclusion

The intestinal complications of pelvic radiotherapy may occur after a variable latent interval ranging from a few months to over five years, may be progressive, and are potentially fatal. A high index of suspicion is needed if diagnosis is to be made at an early stage. Surgery is often necessary, but may be hazardous, and failure to observe simple surgical principles may lead to postoperative complications or death.

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