THE INCIDENCE OF COLORECTAL TUMOURS IN THE MALTESE ISLANDS

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Colorectal neoplasm is one of the commoner forms of malignant disease; its incidence in England and Wales is second only to that of lung cancer (Annual Report Registrar General 1970). The morbidity due to this tumour shows a marked variation throughout the world (Table 1). It appears from the figures available for study that countries with a higher socio-economic status, and a better distribution of medical services have a higher incidence than other less affluent countries. In Poland eight per hundred thousand of the population are affected by this tumour; in contrast the incidence for the province of Manitoba with a much smaller population is five fold higher. In spite of this, this tumour accounts for a sizeable mortality in most areas.

To date the incidence of such tumours in the Maltese Islands has not been formally studied. A survey of the hundred and seventy three patients documented in the Tumour Registry as suffering from colorectal neoplasms between the years 1969-1972 (inclusive) was carried out. The local recorded incidence of colonic tumours is shown in figure one, and that for rectal tumours in figure two. The mean age of diagnosis of colorectal tumours was sixty years of age. Of particular interest in this survey is the incidence in the younger age group (i.e. those below forty five years of age). These patients numbered twenty four and their ages ranged from twenty to forty five years.

There is a great variation in the morbidity of colorectal tumours recorded in different countries. In Table 1, an attempt has been made to compare the incidence of these tumours in our Islands with that of other countries.

It is well known that a number of morbid anatomical lesions predispose to malignancy of the large intestine. There were only four recorded cases of adenomas in the survey, one of which was a two centimetre sessile adenoma; in spite of local excision this patient eventually died of extensive metastases. Some families are unduly prone to develop carcinoma of the colon (McSherry *et al* 1969). In this survey two patients stated that their parents died of a carcinoma of the colon. Carriers of the trait of familial polyposis will invariably go on to develop cancer. Nine cases of familial polyposis were found, six of whom already had a carcinoma supervening.

Longstanding colonic inflammation may also be complicated by the development of carcinoma of the colon and rectum. In the survey there were two cases of cancer complicating ulcerative colitis. One patient had a multifocal adenocarcinoma with secondary metastases, at the age of thirty three years, the other had a recto-sigmoid tumour with a caecal fistula at the age of seventy two years. Both these cases

TABLE 1

Age/sex incidence of colorectal tumours compared with other countries

Country	*Population in millions*	*ca. COLON morbidity*			*ca. RECTUM morbidity*		
		Male	*Female*	*Total*	*Male*	*Female*	*Total*
			/100,000			*/100,000*	
Malta 1972	0.32	4.0	4.4	4.2	3.5	2.0	2.8
Alberta 1968	0.80	14.3	17.7	16.0	9.3	7.5	8.4
British Columbia 1968	1.10	23.0	22.9	23.0	15.9	10.7	13.4
Manitoba 1968	0.76	28.7	33.5	31.1	15.2	8.5	11.8
N. Branswick 1968	0.50	27.4	31.2	29.3	19.8	10.3	15.1
Prince Edward Island 1968	0.10	14.4	34.9	24.5	10.8	3.7	7.3
Quebec 1968	0.18	15.5	19.7	17.6	10.2	7.5	8.8
Saskatchewan 1968	0.86	29.6	24.7	27.2	14.9	8.7	11.9
Connecticut 1968	2.0	20.4	14.4	17.3	4.3	5.0	4.7
Israel 1967	0.8	9.9	9.1	9.5	7.5	8.0	7.8
Bulgaria 1968	7.0	5.0	5.9	5.4	6.6	5.5	6.0
Finland 1967	3.9	7.2	10.2	8.8	6.7	9.5	8.2
Hungary 1969	9.2	7.0	8.6	7.9	10.0	6.9	8.4
The Hague 1969	0.6	16.9	19.3	18.2	13.8	10.3	12.0
Rotterdam 1969	0.66	18.7	27.8	23.3	17.5	12.0	14.7
Poland 1968	24.0	4.0	4.4	4.2	4.2	3.9	4.0
Sweden 1967	6.9	24.1	26.5	25.3	17.1	12.1	14.6
U.K. 1968	43.0	18.1	24.2	21.3	16.4	12.5	14.4
Yugoslavia 1969	15.8	5.6	7.0	6.3	12.8	10.0	11.4

had severe colitic symptoms of several years duration.

In only one hundred and eight cases was histology of the tumours available; the rest of the cases had a clinical diagnosis made at a laparotomy and necropsy confirmation was singularly lacking.

TABLE 2
Histological Classification

	Histological types	*Number of cases*
1.	Adenocarcinoma	104
2.	Argentaffin carcinoma	2
3.	Leiomyosarcoma	1
4.	Malignant lymphoma	1

Ninety five per cent of the tumours were carcinomas of variable degrees of differentiation. Both cases of argentaffin carcinomas died from metastases. A twenty three year old had a carcinoid tumour in the pelvic colon, and a sixty seven year old had an argentaffin carcinoma of the ascending colon. Neither had any clinical evidence of the carcinoid syndrome.

The distribution of these tumours in the large bowel is shown in figure three. The tumours in the rectum were equally distributed in the lower third of the rectum, the ampulla, and the upper third rectosigmoid colon.

Sixty five per cent of the tumours occurred in the rectum, a place easily accessible to investigation, namely palpation and endoscopy. The next commonest site for a carcinoma of the colon was the caecal region, which constituted sixteen per cent of all the tumours recorded. The other twenty per cent of tumours were equally distributed over the rest of the colon.

The classical way in which these tumours are said to present is a history of recent gross change in bowel habit, bleeding *per rectum,* weight loss and/or symptoms of dramatic large bowel obstruction. In the cases, reviewed, this could be no further from the truth. The commonest mode of presentation was lower abdominal pain. Overt bleeding was reported by about half the patients with tumours of the sigmoid colon; with the other colonic

Histogram to show the sex incidence in carcinoma of the colon

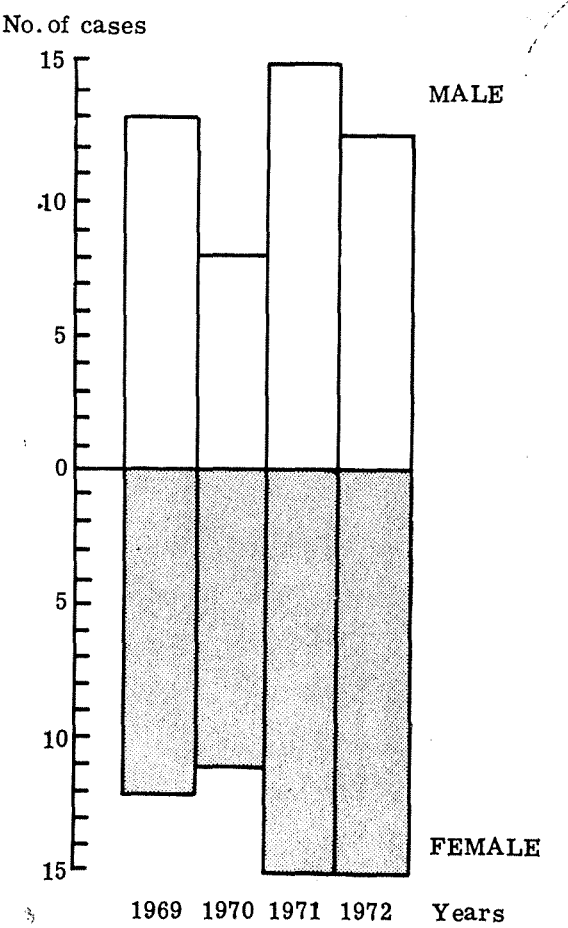

Figure 1

tumours bleeding occurred in less than a third of the patients, also infrequent were the changes in bowel habit.

An interesting finding was the presence of significant nausea and vomiting in fifty per cent of the patients with tumours of the left hemicolon and twenty per cent of cases with a tumour in the right hemicolon. This was associated with anorexia in a number of these patients. In some of the cases, investigation for an upper gastrointestinal tract lesion had already been in progress for some time thus delaying the diagnosis considerably. Episodes of acute obstruction superimposed on chronic

Histogram to show the sex incidence carcinoma of the rectum

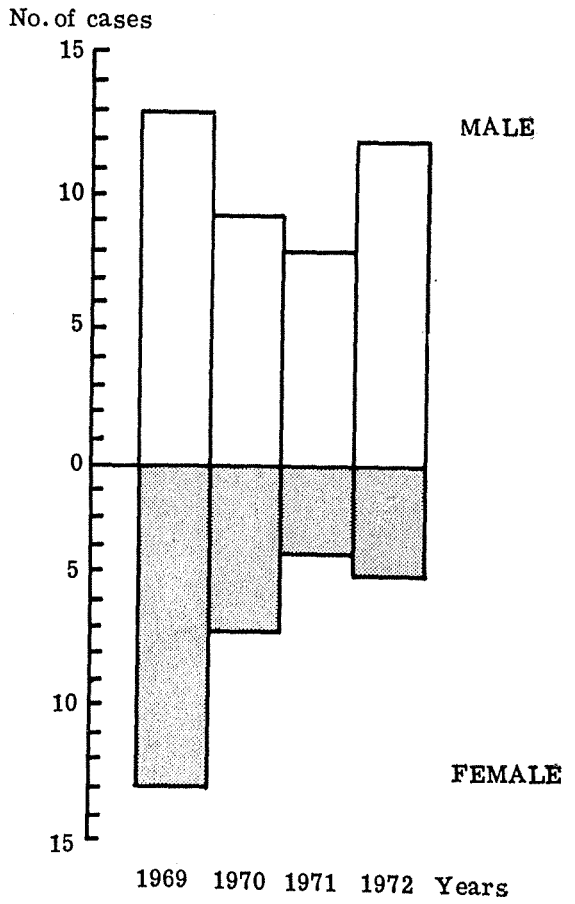

Figure 2

obstruction occurred in a quarter of the patients with sigmoid tumours. In tumours of other parts of the colon, obstruction only occurred as a late manifestation.

Another interesting observation was the presence of a pyrexia as one of the presenting features in a number of the tumours and some of these patients had undergone lengthy serological, radiological and bacteriological investigation for their pyrexia. Ulceration of the tumour, subsequent infection with endogenous coliform organisms and endotoxin absorption would account for the fever in such cases.

Pallor and the laboratory evidence of a microcytic hypochromic iron deficiency anaemia was another important clinical sign. The presence of associated bleeding haemorrhoids in such cases could be taken as a possible cause for the anaemia and this happened in two cases on record. The presence of complicated diverticular disease is yet another plausible explanation for abdominal pain, obstruction, bowel habit alteration and bleeding, and this may act as yet another red herring in the presence of a coexisting noeplasm: this occurred in six of the cases significantly delaying the diagnosis.

Four cases presented as an emergency with a picture of an acute appendicitis because of nausea, vomiting and abdominal pain. At laparotomy a tumour was discovered in the caecum and had caused the obstruction of the lumen of the appendix.

TABLE 3

Percentage incidence of Symptoms and Signs

Symptoms and signs	*Right colonic tumours*	*Left colonic tumours*	*Sigmoid tumours*	*Rectal tumours*
Abdominal pain	68	62	52	24
Bowel complaints	30	25	50	54
Bleeding	20	31	55	64
Vomiting and Nausea	27	50	?	?
Anorexia	6	12	?	?
Mucus in stools	2	—	2	4
Tenesmus	—	6	2	9
Palpable abdominal mass	54	25	—	—
Anaemia (Pallor)	34	6	12	4
Pyrexia	4	18	5	—
Mass felt P.R./endoscopy	—	—	20	100
Acute obstruction	9	18	25	1

Diagram to demonstrate tumor incidence in different parts of the caecum, colon and rectum

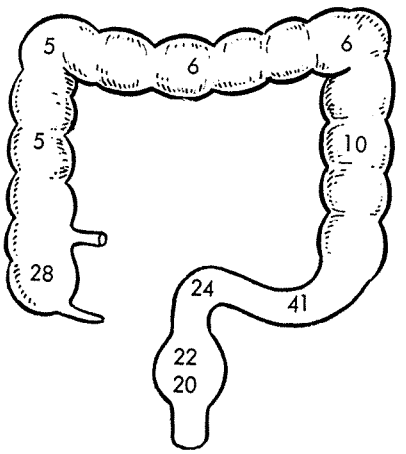

Figure 3

In all the tumours of the rectum recorded, a palpable mass was present. Bleeding occurred in almost two thirds of these cases in association with a change in bowel habit. The negative finding of a lack of alteration in bowel habit of about a half of the patients with such tumours was worth serious consideration. Also particularly significant were the absence of complaints of tenesmus and mucus admixed with the stools, both of which are popularly taught to be important diagnostic signs. Pain was also a late feature in rectal carcinoma, though ultimately it might give rise to great distress. There was an average delay of six months from the onset of symptoms to hospitalization.

Discussion

Over the past decade an increase in the incidence of colonic cancer has been recorded, but with no corresponding elevated incidence of rectal neoplasms (Stewart 1971). The incidence also appears to differ among countries. Both these features have led to epidemiological speculation as to its aetiology, with the diet coming under suspicion, as one of the factors responsible. Colonic tumours especially those of the right hemicolon often require radiological investigation which may not be universally available, and the inter country variation may just reflect the availability and the sophistication of the medical services provided. This alone does not fully explain the discrepancies in incidences.

Burkitt (1971) related the occurrence of tumours of the large intestine to diet on a goegraphical basis. Diets which are highly processed and refined and therefore deficient in fibre content are consumed in areas of a high incidence of colorectal cancer. Aries *et al* (1969) have shown that there is a striking variation in the bacterial flora in relation to the diet content. Hill *et al* (1971) proved that intestinal bacteria degrade bile salts differently and that the Bacteroides species among others, which are particularly abundant in the stools of individuals on a fibre-deficient diet can break down bile salts to possible colonic carcinogens. Recently beef consumption has been correlated with large bowel cancer (Haenszel *et al* 1974). The occurence of large bowel tumours in our Islands is very low in comparison with other countries in Europe (Table 1). Various explanations for this are possible, unfortunately no figures as to consumption *per capita* of the type of foods under suspicion are available from our Islands for comparison with those of countries with a high tumour incidence. It would be indeed interesting to carry out a prospective survey, looking into the dietary habits of the population and the faecal flora and attempt to correlate it with the 'low' incidence of colorectal carcinoma in the Maltese Islands.

Precancerous states of the colon were well represented in this survey. Polypoidal lesions of the large bowel are notoriously of sinister import. Spratt *et al* (1971) proposed that elective surgical intervention and resection should be undertaken of any intraluminal mass larger than ten millimetres seen either on barium studies or at endoscopy. This is interesting when one bears in mind that one of the cases reviewed had a twenty millimetre adenoma which was only locally resected and eventually gave rise to extensive metastases.

Macklin (1960) found that children of

parents with large intestinal cancer had a threefold increase in the expected date of colonic cancer and McSherry *et al* (1969) also conclusively showed that some families are unduly prone to develop carcinoma of the colon. Individuals with the 'familial polyposis' trait develop carcinoma of the colon as well and the tumour occurs in a much younger age group than is normally otherwise encountered. The incidence of this condition is said to be one in eight thousand three hundred births and is a dominant gene of variable penetrance (Reed *et al* 1955). These, polyps are rarely seen before the age of ten years; bleeding is said to herald the malignant transformation. The nine cases reported within the space of four years suggests a high incidence for our population and genetic counselling of these families in danger is strongly indicated.

Longstanding colonic inflammation as found in ulcerative colitis and schistosomal infestation can be complicated by the development of carcinoma of the colon and rectum. There is general agreement that cancer supervenes in three to five per cent of ulcerative colitis cases (Morson, 1969). The latter patients would have had symptoms of the chronic continuous disease, with a total colonic involvement for more than ten years; the distal forms carry an almost insignificant risk factor. The cancers which do develop are multiple, more invasive and less differentiated and are associated with a worse prognosis (Morgan 1971). The risk factors mentioned above necessitate six monthly colorectal biopsies and barium studies in such patients.

Histochemical studies of carcinomas of the large bowel have revealed features of both prognostic and aetiological value. The enzymatic patterns within the tumour cells become less specific as the tumour becomes more and more undifferentiated, and by an elaborate quantitative histochemical technique a working prognostic classification has been attempted (McGinty *et al* 1973). Mucosubstances produced by the neoplastic epithelium have also been similarly examined (Subbuswamy 1972). In the secretions of the normal colonic mucosa both sulphated and non-sulphated acid mucosubstances predominate. The mucosubstances produced by simple tumours are predominantly acid and non-sulphated and carcinomas produce scanty secretions with little sulphation of the mucopolysaccharides. These mucosubstances might therefore in some way regulate cell turnover and division, and a decrease in the concentration of sulphated mucopolysaccharides in bowel mucosal secretion may precede the actual development of the tumour. Mucosubstances are decreased in ulcerative colitis and are mainly non-sulphated acid in type but not in Crohn's disease, and the differing proneness to malignancy of these two diseases adds weight to the argument. The technical expertise involved in the study of these substances precludes their use as a routine procedure.

Over the last few years oncofoetal antigens, namely antigens present in foetal life but which normally disappear in extrauterine life until a tumour develops, have come to the forefront as possible early diagnostic aids for cancer. The carcinoembryonic antigen (C.E.A.) has been the most promising in this respect. Since Gold and Freedman (Thomson *et al* 1969) pioneered the sensitive Radioimmunoassay technique for the detection of this antigen extensive testing of large clinical series and controls has been undertaken in a number of centres (Miller *et al* 1974). The antigen is invariably present in concentrations exceeding 2.5 nanograms per millilitre in malignant large bowel tumours whether primary or secondary but may also be found in other tumours mainly of the foregut, haemopoetic system and from ectodermal origins, as well as in inflammatory conditions of the gastro-intestinal tract, alcoholic cirrhosis and chronic pancreatitis (Laurence *et al* 1972). Its value as a screening test has diminished (Miller *et al* 1974). Its use as a monitor of secondary tumour development is more promising, and in a number of cases the development of hepatic metastases could be predicted from several estimations of C.E.A. This would allow for an early radical approach to these tumours. Attempts at refining the estimation by making the assay more selective (Simmons *et al* 1973) may further increase

the diagnostic value of this test.

This survey has shown that there is an average delay of about six months from the time the patient first presents to his own practitioner until his hospitalization for investigation with yet further delays before surgery is attempted. The apparent cause for this is that all too often the patient presents with 'vague symptoms'; the classical textbook clinical picture appears much too late. Pain of any type is a particularly late symptom. In this respect 'piles' and colonic diverticular disease are often invoked as the cause of changes in bowel habit, gastro-intestinal upsets, anaemia and even bleeding *per rectum* in the middle-aged patient. Medical therapy is usually instituted for a few months, and the patient is only investigated when this has failed. Keeping in mind that the vast majority of large bowel tumours develop within the last twenty five centimetres of the large bowel, digital rectal examination and proctosigmoidoscopy will diagnose these neoplasms. Radiology of the large gut is also straightforward; the recent application of double contrast enemas have greatly improved the accuracy of diagnosis with special reference to polypoidal lesions and cancers of the right hemicolon (Martel 1971).

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