Section of Proctology

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President's Address

Intestinal Polyposis: The Present Position

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There has been no dramatic change in our knowledge of intestinal polyposis since it was the subject of a Presidential Address from my friend and senior colleague, Henry Thompson (1958). Our approach to the treatment of this disorder has now become standardized and the present operations, their limitations and indications were well reviewed in that address of nine years ago. However, since that time further experience has added to our knowledge and enabled us to classify more accurately some of the less common forms of polyposis. So it might be useful, first, to review as a result of our experience at St Mark's Hospital some of the points of clinical interest and importance in relation to familial adenomatosis coli; second, to review our present knowledge of other forms of gastrointestinal polyposis and their associated disorders. What in the 1920s was regarded as one condition we now know to be several disorders characterized by polypi within the gastrointestinal tract, many of them associated with other manifestations (Table 1). Though rare, these conditions are of great clinical interest and importance, for early accurate diagnosis may lead to prevention of much illness, disability and death. There has been confusion in the past among these various forms of polyposis but recent literature has clarified the position considerably and the time now seems opportune for a further brief review.

Let me start on some aspects of familial adenomatosis coli, for it is the commonest of these conditions and the one with which we mostly have to deal; it is, moreover, the one of which I can speak with most experience, both personal and as a result of reviewing all the cases at St Mark's Hospital. My active practice began in the early 1950s when colectomy and ileorectal anastomosis had become a standard treatment for most patients with this disorder; it is now our policy to carry out this operation at a relatively early age, we hope before any carcinoma will have developed in the large bowel. Experience has taught us all that, if any part of the colon is left behind, a carcinoma will sooner or later form therein and may well be beyond the hope of cure before it is detected. In the pre-war years at St Mark's some limited excisions of the colon or excisions of only the rectum were done for multiple polyposis and there have been several cases known to us where a further carcinoma did develop in the retained bowel.

Table 1
Forms of intestinal polyposis

Adenomatosis coli
Adenomatosis coli – Gardner's syndrome
Juvenile polyposis
Peutz-Jeghers syndrome
Cronkhite-Canada syndrome
Others
Lymphomatous – benign, malignant
Metaplastic
Inflammatory
Lipomatous
Neurofibromatous

If any part of the retained large bowel is liable to form cancers, then obviously one danger of colectomy and ileorectal anastomosis is the formation of a further carcinoma in the rectal stump. According to various reports, the incidence of this complication is between 5% and 8%; at St Mark's Hospital, so far, it has occurred in only 2 patients out of the 65 who have undergone this operation. One of these patients had not had a sigmoidoscopic inspection of the retained rectal stump for eighteen months because he had had a gastrectomy for a duodenal ulcer at another hospital and had attended that hospital for follow-up. When he did attend again at St Mark's Hospital a small carcinoma in the retained rectum was found and this proved after excision

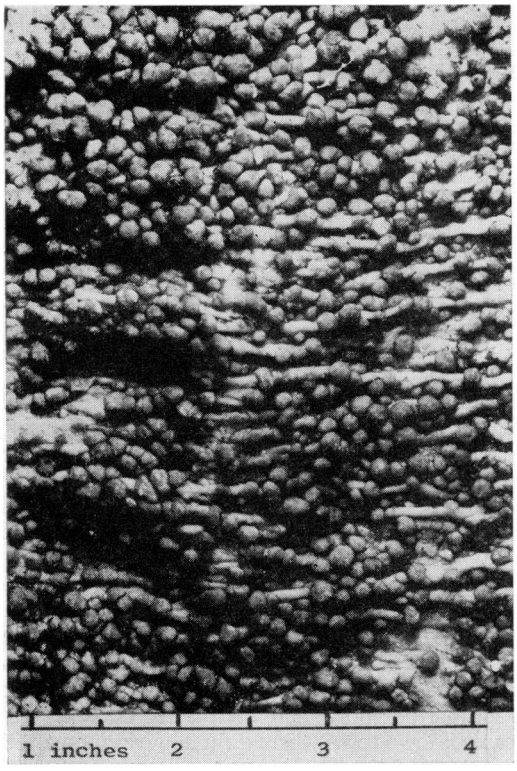

Fig 1 *Extensive and severe adenomatosis coli. This patient's mother had adenomatosis and died of carcinoma of the colon*

of the rectum to be an A case.[1] The other patient had attended regularly and between an attendance in December and one the following March a small carcinoma formed in the rectal stump and this again proved to be an A case. We have no proof, of course, that in this disease all carcinomas in the bowel are preceded by adenomas and we may be deceiving ourselves in thinking that a careful follow-up inspection of the rectal stump and destruction of any adenomas that form will be successful in preventing cancers. However, it seems to be a reasonable working hypothesis and, unless further follow up of the many cases that have been so treated shows a high incidence of other carcinomas forming in the rectal stump, I feel that we should continue with the policy of colectomy and ileorectal anastomosis as the main line of treatment for this disease. In this connexion one further case may be of interest. Fig 1 is from a young man of 18 on whom I did a colectomy and ileorectal anastomosis. The colon was carpeted with polypi and the rectum had much the same appearance, and it was only after many fulgurations of the polyps in the rectum that the main operation was carried out. For some years after the operation the rectum remained free of polyps but then many small ones began to form throughout the whole of the retained rectal mucosa and last year a biopsy of some of these showed very active epithelial proliferation. It seemed likely that a carcinoma was going to form in the rectum and accordingly I carried out a 'prophylactic' excision of the rectum. There were multiple adenomas throughout, all showing active epithelial proliferation but no actual carcinoma. Whether this was the right policy I shall never know but complete destruction of all the rectal polyps would not have been technically possible. It is essential that all patients who have a retained rectum should be examined periodically and it may well be that biopsy will give us some guide to what active treatment is required. As these patients who are mostly still young get older, it will be interesting to see whether more polyps form and whether these polyps show a greater tendency to malignant change.

[1]Dukes' classification

There have been papers recently about the tendency of polyps in the rectum to regress and even disappear following ileorectal anastomosis (Cole & Holden 1959, Cole *et al.* 1961). A review of our own cases seems to confirm this: in many of our patients who had several polyps in the rectum before operation very few more have formed in the years following a colectomy and ileorectal anastomosis. However, my impression from reviewing the notes of these cases is that this abeyance is a temporary one and that after a few years polyps tend to form as much as before. It would certainly be unwise to assume that the rectum is in some way protected from the risk of carcinoma by having the colon removed and the ileum joined on instead.

The immediate mortality after this operation has been gratifyingly low; only one patient has died, from intraperitoneal hæmorrhage occurring on the night of the operation.

However, there is a later morbidity, with some mortality, which is disturbing: the main complication seems to be intestinal obstruction and, of our series of 65, 17 have suffered from this trouble, 2 of them on two occasions; 3 of those who have had a total proctocolectomy or other operations have also had an intestinal obstruction. Of these 20 patients with 22 intestinal obstructions, 3 have died as a result of the obstruction (Table 2). The interval between the operation and the obstruction has varied from five days to twenty-three years, with an average of four years; in most of these patients the obstruction occurs within the first two years. This incidence of post-

Table 2
Intestinal obstruction following 112 operations for polyposis (St Mark's Hospital series, 1966)

	No. of cases
Colectomy and ileorectal anastomosis	65
Laparotomy for obstruction	17●
Other operations	47
Laparotomy for obstruction	3
Deaths as result of obstruction	3

●on two occasions in 2 cases

operative obstruction of about 20% is disturbingly high and seems to be greater than the incidence for the same operation carried out for other conditions. Although not all these obstructions were due to adhesions it may well be that there is in these patients an increased tendency to form fibrous tissue and adhesions which, in its more overt form, becomes a definite Gardner's syndrome which I shall be discussing below.

Before leaving the subject of adenomatosis coli, I would like to make three points, summarized under 'sigmoidoscopy as a guide to treatment':

(1) The size of the polyps in the rectum as seen on sigmoidoscopy is no certain guide to the state of the rest of the colon; a patient may have only a few small and scattered polyps in the rectum but more numerous or larger ones at a higher level, so it is unwise to assume on sigmoidoscopic findings alone that there is no risk of cancer developing. We have, however, as yet seen no patient in whom sigmoidoscopy showed a rectum absolutely free of polyps who was found to have polyposis on barium enema. There has always been evidence of polyposis on sigmoidoscopy also.

(2) I would suggest a possible danger of pre-operative fulguration and removal of polyps in the rectum as a preliminary to colectomy and ileorectal anastomosis: the danger of implantation of malignant cells from a carcinoma at a higher level on to a granulating surface in the rectum may be theoretical; but we know that this does occur occasionally in other conditions and there is no reason why it should not occur in familial polyposis. Carcinoma has developed in several patients under the age of 25, the youngest in our series being 20; it may be completely symptomless. So to do a pre-operative fulguration in any patient over 20 is running a possible risk of implantation. Many of the polypi in the rectum regress and may even disappear following colectomy and ileorectal anastomosis; if they do not, it is an easy matter to fulgurate them at a later stage when the main operation is completed, which is probably the wiser course.

(3) It has been assumed that any patient whose parents had polyposis, who does not develop polyps in the rectum by the age of 40, can be regarded as clear of the disease: unfortunately we now have one patient at St Mark's Hospital who was clear at the age of 42 but later developed polyposis and had a carcinoma of the cæcum at the age of 53, so it is difficult now to lay down any limit at which a patient can be regarded as completely free from the chance of developing polyposis.

Gardner's Syndrome

Intestinal adenomatosis may sometimes be associated with other rather unusual features. In 1952 and 1953 Gardner, Professor of Genetics in Salt Lake City, first described a family with colonic adenomatosis associated with sebaceous cysts and mesodermal tumours (Gardner & Richards 1953). Since then over 120 cases of this syndrome have been reported, some with more complex manifestations than Gardner first described. This association between adenomatosis coli, skin cysts and mesodermal tumours is now generally accepted and is best referred to as Gardner's syndrome. It may be dependent on the inheritance of a single dominant gene, as first postulated by Gardner, which, however, may show variable penetrance so that not all the features of this syndrome occur in every case.

The incidence of this condition is difficult to assess as there are few large series and no criterion is defined of what constitutes the syndrome. Smith (1958) reports from the Mayo Clinic a series of 201 patients with adenomatosis coli, 17 of whom had one or more manifestations of the syndrome; that is an incidence of 8·5%. He also (1959) quotes the incidence of desmoids as 3·5% in operated cases and mentions that this is several hundred-fold the incidence of desmoid tumours complicating any other known disease. Our own figures at St Mark's Hospital show that 23 patients out of 140 (16·4%) had one or more manifestations of this syndrome, a considerably higher figure than that from the Mayo Clinic. However, most of our patients have not had routine skull X-rays, nor was the possible relevance of sebaceous cysts realized some years ago and their presence may not have been recorded in the clinical notes, so the actual incidence may be even higher than this.

The syndrome as now recognized may have all the features described by Weary *et al.* (1964) (Table 3), but it is more usual for only one or two of them to be associated with polyposis and, in all reported series, cystic lesions of the skin seem to be the most common. These can be either

Table 3
Features of Gardner's syndrome

Intestinal adenomatosis
Cystic lesions of the skin
Osteomas
Fibrous tissue tumours
Dental anomalies
Miscellaneous lesions

epidermal inclusion cysts or sebaceous cysts, and are most commonly found on the scalp or face, though they may be anywhere. A point of particular clinical interest is that these cysts may be present at birth or arise in early childhood; they may appear, therefore, well before the polyps in the bowel and indicate in an affected family the children who are going to develop intestinal polyposis. Of our series of patients with polyposis at St Mark's, 17 had cystic lesions in the skin, of whom 4 had other manifestations of Gardner's syndrome and 3 had other miscellaneous tumours.

Osteomas seem to occur mainly on the face and cranium; the long bones may have osteomas or irregular cortical thickening revealed only by X-ray studies. These osteomas grow very slowly and seem to stop growing after a time, and rarely require treatment: no case of malignant change in an osteoma has ever been reported. Of our patients, 4 have had clinically recognized osteomas but, as we have not done facial and skull X-rays routinely, the actual incidence may well be higher.

Perhaps the most important and notable feature of Gardner's syndrome is the tendency to proliferation of fibrous tissue, leading in many cases to the formation of fibrous tissue tumours. I have already mentioned the disturbingly high incidence of post-operative obstruction in patients with adenomatosis. The adhesions in some of these patients may be particularly severe and tough. Similar reports have come from other centres and it has been suggested that this high incidence is due to an abnormal tendency in some of these patients to form fibrous tissue and may be an expression of Gardner's syndrome. Fibrous tissue tumours in these patients have been reported in the skin and retroperitoneal tissues but the two most important sites from a clinical point of view are the desmoid tumours of the abdominal wall and the mesenteric fibromas.

Desmoid tumours may arise in these patients *de novo* but are seen more often in the scars of abdominal incisions. Six of our 112 operated patients have had one or more desmoids; the Mayo Clinic reports 7 patients in a series of 150 operated cases. So they occur rarely but may cause diagnostic difficulty for, if a patient has had a cancer in the colon removed, it may be impossible to differentiate clinically between an implant of secondary carcinoma and a desmoid tumour.

Two of our patients with desmoid tumours of the abdominal wall have had multiple tumours in the mesentery of the small bowel and large tumours of retroperitoneal tissues. Such mesenteric tumours are well recognized and are usually associated with other signs of Gardner's syndrome (Shiffman 1962, Simpson *et al.* 1964). They can present an alarming appearance with the small bowel mesentery packed with hard tumours but it is worth emphasizing that they do not necessarily progress, that too gloomy a prognosis should not be given and that too vigorous treatment may be unwise.

As an example of this curious slow progression I quote some details of a patient under my own care:

Case History
A woman aged 35 when I first saw her in 1957 gave a six weeks' story of diarrhœa with blood and mucus; sigmoidoscopy and barium enema showed multiple adenomatosis coli and there was a family history of rectal cancer. She was admitted in early 1958 and found to have an adenoma of the thyroid and two desmoid tumours of the abdominal wall. In March I did a laparotomy, removing one of the abdominal wall desmoids in the main incision. I found a right pelvic kidney but no further intra-abdominal disease other than the polyposis of the colon, so I did a colectomy with ileorectal anastomosis; in the subsequent weeks the remaining polypi in the rectum were fulgurated. Pathological examination of the specimen showed adenomatosis coli and no carcinoma; the abdominal wall tumour was confirmed as a desmoid. Six months later I excised the desmoid from the right rectus muscle. Nine months later, in the summer of 1959, she returned to hospital because she had noticed that both the tumours on the abdominal wall had recurred and she also complained of a large suprapubic tumour. I again excised the one in the left upper rectus muscle and in so doing opened the abdomen and to my distress found multiple fibromas throughout the small gut mesentery and a large retroperitoneal tumour in the left upper quadrant of the abdomen. I closed the abdominal wall with a tantalum replacement for the upper left rectus muscle but took a very gloomy view of the prognosis, though luckily I did not tell the patient that. In 1960 she returned again with all the tumours much larger and with a few attacks of abdominal colic: there was a very large suprapubic tumour which was quite fixed and multiple fibromas were easily palpable in the abdomen. In 1961 the suprapubic tumour had got considerably larger and was causing her some distress, so I did a purely local excision of the bulk of that

prominent tumour but, in so doing, cut through the middle of the tumour, leaving most of it behind as it was quite irremovable. She then remained in good health until August 1966, when she had a spontaneous perforation of the small bowel; a laparotomy was done at a hospital in the West Country and she has made a good recovery but I do not yet know what was the state of the intra-abdominal tumours at that laparotomy.

The suprapubic tumour has never re-formed nor enlarged, though it is now over five years since the palliative partial excision of the protuberant tumour because it was unsightly and causing distress; she has had no other treatment because there did not seem to be anything one could usefully do; clinically there seems to have been no increase in the size of the tumours in the last five years nor any decline in her general health.

The other patient, who had two abdominal wall desmoids excised with tantalum replacement, returned with a large intra-abdominal mass which was treated by radiotherapy but with little objective response. It is doubtful whether desmoids are radiosensitive and they seem to have a natural tendency to spontaneous arrest of growth; moreover, small bowel is easily harmed by ionizing radiation. Fibrous tissue formation in these patients and the best treatment, of which we know little, would make a fruitful field for further research.

Before leaving the subject of Gardner's syndrome I should mention two other features that are reported, namely the dental anomalies and the occurrence of other miscellaneous tumours. Dental anomalies reported include supernumerary teeth, unerupted teeth, follicular odontomas and dentigerous cysts. We have no record at St Mark's of such anomalies among our patients, but they have not had routine dental checks nor dental X-rays, so a negative report on this subject is of little value. However, several of our patients have had other tumours (Table 4). This incidence of a variety of tumours would seem to be well within the bounds of chance in a small series and it will need follow up of several much larger series to know if patients with polyposis are more likely to develop tumours other than those of fibrous tissue.

Table 4
Miscellaneous tumours associated with adenomatosis coli (St Mark's Hospital series, 1966)

Carcinoma of uterus
Malignant melanoma
Lymphatic leukæmia
Hepatoma
Mixed parotid tumour
Ovarian cystadenoma
Thyroid adenoma
Lipoma (3 cases)

Other Types of Intestinal Polyposis

I want now to discuss some other types of intestinal polyposis. While occasional cases of these other types have been reported for many years, it is only in the last fifteen that definite syndromes have been described and recognized and their essential differences tabulated and recorded. Hence many reports are not only confusing but, in the light of modern knowledge, misleading.

Juvenile Polyposis

Juvenile polyposis has been clearly described and separated from other forms of polyposis by Veale and his colleagues from the Research Department at St Mark's Hospital (Veale *et al.* 1966). There had been many reports in previous years of polyposis in the colon occurring in children; hence there had been some disagreement about the age at which polyps appear in intestinal adenomatosis. However it now seems clear that most of these were cases of juvenile polyposis and that it is rare if not unknown for intestinal adenomatosis to occur under the age of 10 or 12.

Juvenile polyps differ from adenomatous polyps in that they are hamartomas, i.e. malformations rather than neoplasms. The word 'juvenile' is perhaps unfortunate, for it implies that they occur exclusively in young people; though they are certainly more common in young people and children they may continue to form well into adult life and even middle age. They differ from adenomas both in their gross and in their microscopic appearances, though the differences may not be so great as to be always obvious to the clinician on sigmoidoscopy. In contrast to the lobulated appearance of adenomas, they are smooth in contour and may vary in size from a few millimetres to one or two centimetres in diameter; as a result of infarction they may be red and hæmorrhagic, which may suggest to the clinician a very active epithelial growth; sometimes the stalks may be seen without the tumours, which have fallen off and been passed as a result of infarction. Microscopically these juvenile polyps consist of a few epithelial tubules, some of them dilated, widely separated by a loose areolar connective tissue. There is no increased epithelial activity or over-growth and no sign whatever of neoplastic proliferation.

Juvenile polyposis is rare (only 6 cases have been seen at St Mark's, in contrast to 140 cases of intestinal adenomatosis) but they are of great interest for their clinical features and for their curious genetic association with adenomatosis.

The first point of interest in Veale's series was the age of onset of symptoms, at an average age of 6 years, the youngest patient being only 18 months old when she first had bleeding per rectum. In contrast, the average age for onset of symptoms in adenomatosis coli is 30 years and it is rare, if not unknown, for polyps to form under the age of puberty. Secondly, the symptoms of juvenile polyposis differ from those of adenomatosis in that bleeding is an early and usually the most prominent symptom and may sometimes lead to anæmia. Prolapse of polyps from the anus and the passage of polyps in the stool are also seen, and these symptoms have never to my knowledge been found in adenomatosis. A third clinical feature, rare in adenomatosis, is abdominal pain; this is almost certainly due to recurrent minor intussusceptions and a few of these patients have actually undergone laparotomy during childhood for an intussusception. Again, these symptoms have never been found in adenomatosis. Thus the clinical features of juvenile polyposis coli are so different from those of adenomatosis that they enable a clear diagnosis to be made on clinical and sigmoidoscopic grounds alone in most cases. A further feature of interest is that some of the patients with juvenile polyposis have other congenital abnormalities, which have not been seen in association with adenomatosis.

The genetic aspect is interesting in that at least one case in the St Mark's series has arisen in a family with proven adenomatosis; another has arisen in a family with known polyps, and cancer in the family background, but the pathological nature of those polyps has never been satisfactorily proven; two others have arisen in families with a definite history of large bowel cancer without adenomatosis. Yet it appears from follow up of the patients with juvenile polyposis, who presented when young and are now in middle life, that there is a tendency for the polyps to diminish and disappear as the patients get older and for very few new ones to form; there is no tendency for cancer to develop. This is in keeping with the microscopic appearance without epithelial activity, which is not pre-malignant.

Veale and his colleagues consider that the occasional occurrence of juvenile polyposis in children of a family with adenomatous polyposis could arise from the inheritance of a modifying allele from the normal parent. If that is so, then patients with juvenile polyposis may pass on juvenile polyposis to some of their children and adenomatous polyposis to others, as well as having some children with neither. However, many years of further follow up will be necessary before we know whether this genetic hypothesis is correct.

Peutz-Jeghers Syndrome

I want now to discuss a different form of polyposis in which polyps may form throughout the entire gastrointestinal tract. This is now known as the Peutz-Jeghers syndrome, so called because of a case report by Peutz in 1921 and a masterly analysis of 10 cases by Jeghers *et al.* in 1949. Dormandy reviewed the syndrome in 1957, described further cases and, in an excellent historical review, quoted earlier reports than those of Peutz, the first case apparently being described in 1881.

Table 5

Features of Peutz-Jeghers syndrome

Gastrointestinal polyposis
Mucocutaneous pigmentation
Inheritance through a mendelian dominant gene

The essential features of this syndrome are gastrointestinal polyposis, mucocutaneous pigmentation and mendelian-dominant inheritance (Table 5) but the responsible gene may not always express itself completely, so that pigmentation has been reported without polyposis and vice versa. Before completely accepting the absence of polyposis in patients with the characteristic pigmentation however, direct examination of the small bowel is necessary because micropolyps may occur, undetectable by any clinical method. Moreover, cases may arise, as in adenomatosis, without any previous family history and these are presumably due to gene mutations.

The pigmentation may be present at birth or may arise in infancy or early childhood; the pigment is melanin and the spots are darker than freckles. It affects particularly and characteristically the buccal mucosa, usually the lips and rarely the tongue. The spots also usually occur on the face, mainly around the eyes, the mouth and over the bridge of the nose, and many patients also have spots on their fingers and toes but there is never generalized pigmentation. The spots may fade from the skin in later life but not from the buccal mucosa.

The polyps may be present throughout the gastrointestinal tract but are particularly common in the small bowel and it is from these that symptoms and disabilities usually arise. The polyps are not adenomas but have the appearance of malformations, though they differ from the hamartomas of juvenile polyposis. There is an excess of normal intestinal epithelium covering

arborizing strands of muscularis mucosæ. Although there is apparently no epithelial overgrowth there are several well-proven reports of bowel carcinoma arising in patients with Peutz-Jeghers syndrome and it is curious that most of these have arisen in the duodenum (Reid 1965, Horn *et al.* 1963, Williams & Knudsen 1965). However, the risk of malignancy seems to be slight. The polyps usually arise in childhood and cause recurrent attacks of abdominal colic, borborygmi and usually recurrent intussusception. They may also cause melæna and sometimes hæmatemesis and nearly always a chronic anæmia from the constant minor blood loss. However, the most serious effect of these small bowel polyps is recurrent intussusception, because it not infrequently leads to gangrene and gut resection, so that these unfortunate patients may have undergone several laparotomies and have a dangerously shortened small bowel by the time they reach their late teens.

Table 6
Features of Cronkhite-Canada syndrome

Gastrointestinal polyposis
Generalized pigmentation
Alopecia
Onychotrophia

Treatment is obviously difficult because polyps continue to form into adult life, though this tendency may decrease with age. But it is apparent that, if possible, resection of small bowel should be avoided and that the polyps should be removed through multiple enterotomies, if necessary. Naturally this treatment is unlikely to cure the patients, as further polyps will probably form which may well require further laparotomies and enterotomies but, as Dormandy says, however much both the patient and the surgeon may deplore 'nibbling' operations, such a policy is preferable to a state where no small gut is left to be nibbled away. He also points out that the rate of growth of these polyps is irregular, periods of quiescence which may last months or years intervening between spurts of growth. If the patients are told to report any recurrence of colic or borborygmi and to have regular blood counts, a fresh crop of polyps can be suspected and confirmed by radiology, by which any large ones can be demonstrated. Perhaps in this way intervention to remove the polyps can be undertaken before intussusception, with its possible risk of gangrene and loss of small bowel, occurs. This is of course mere speculation. The syndrome is rare and there does not seem to be any centre that has yet had enough experience of sufficient cases to offer much guidance. There had been no case known at St Mark's until 1965 but 3 cases, two of them siblings, have now been seen and treated by Mr O V Lloyd-Davies. They will be carefully followed up, for they are all young and many years of observation and care will be necessary.

Cronkhite-Canada Syndrome

I want to deal now with a rare syndrome known as the Cronkhite-Canada syndrome. In 1955 Cronkhite & Canada reported two cases of intestinal polyposis associated with certain other clinical features. Since then further similar cases have been reported and one, rather similar but lacking certain of the features, was reported recently in *Proceedings* (Ryall 1966) and a further one in *Gut* (Manousos & Webster 1966); but as far as I can determine that still only makes nine cases in the world literature to date. We have had no such case at St Mark's Hospital nor have I seen one elsewhere.

The essential features of this syndrome seem to be those shown in Table 6. In no reported case was there any family history and the condition appears to have arisen after middle age in previously healthy people, most cases being in women. All the patients had diarrhœa, leading in most cases to hypoproteinæmia, œdema and cachexia, with a low serum calcium and potassium; 5 of the 7 cases collected from the literature by Jarnham & Jensen (1966) were fatal within eighteen months of onset. Polyps have been found in the stomach, duodenum and colon in all reported cases but not apparently in the small bowel in every case, which sounds rather odd in view of the cachexia and fatal termination. In most of the literature of this condition the polyps are reported as adenomas but, from the illustrations in Jarnham & Jensen's paper, this pathology is somewhat dubious. Although this must be a very rare condition, all the cases are sufficiently alike to make it appear that this is a definite syndrome, though its pathology is still little known. The polyps from the case reported by Ryall (1966) were examined by my colleague, Dr Basil Morson, who regarded it as colitis cystica superficialis; the illustrations in the papers by Jarnham & Jensen and by Manousos & Webster appear to be of a similar nature. Colitis cystica superficialis is a histological appearance found in the gastrointestinal tract in pellagra – a disease due to vitamin B deficiency. It is possible that the Cronkhite-Canada syndrome is caused by some similar mechanism. This syndrome therefore appears to be different in many ways from the other conditions with gastrointestinal polyposis I have discussed, particularly in the lack of family history, the onset in middle life and the rapidly fatal course in many cases; however, as some of these patients may have

polyps that can be detected sigmoidoscopically, it is of some clinical interest to this Section and this must be my excuse for discussing a condition of which I have no personal experience.

This brings me to the final phase of my review, that is a mere mention of those other forms of intestinal polyposis listed at the foot of Table 1. All these conditions are rare but all have been known to form multiple tumours in the gastro-intestinal tract, thus clinically and on sigmoido-scopy constituting polyposis. Probably the only one seen often in this country is the inflammatory type of polyposis that occurs in the severer cases of ulcerative colitis but, in other parts of the world, inflammatory polyposis may be seen in bilharzia and certain other infectious diseases.

It is not always easy to distinguish on sigmoid-oscopy between inflammatory and neoplastic forms of polyposis and it may be impossible to distinguish the different neoplastic forms from each other and from the hamartomas: so it is important that we should all recognize that other forms of polyposis than multiple adenomas do exist and that pathological diagnosis by adequate biopsy should always precede decisions on treatment.

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