ASPECTS OF GASTROINTESTINAL TUBERCULOSIS AT KING EDWARD VIII HOSPITAL

by

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ABSTRACT

Evidence from post mortem studies and the radiological investigations of sanatoria patients suggest a significant association between pulmonary and intestinal tuberculosis.

This study explored this association and examined the contribution of modern techniques to the diagnosis of intestinal tuberculosis in patients studied in the medical wards of King Edward VIII Hospital, Durban.

Upper gastrointestinal endoscopy, double contrast small and large bowel radiology and colonoscopy were utilized to investigate 50 patients with open cavitating pulmonary tuberculosis. No evidence of tuberculosis was encountered in the upper gastrointestinal tract. In the small bowel, disease of the terminal ileum was suspected in one patient, but not proved despite multiple biopsies. In the large bowel, however, 14 proven cases of tuberculosis were identified, together with 9 further possible ones. Of the proven cases, 92,9% had caecal lesions, 50% had colonic involvement and in 28,6% a segmental colitis was present. The lesions encountered were small, being in the main, single or multiple 3-5 mm nodules (found in 78,6%) or 1-2 mm superfical ulcers (present in 44,4%).

Diagnosis was achieved by colonoscopy in all cases and by a combination of colonoscopy and radiology in 2 cases. This series confirmed the unreliability of the double contrast barium enema in the detection of small mucosal lesions.

This series is notable for the detection of early tuberculous enteritis, the paucity of ileal lesions and the high frequency of detection of acid fast bacilli in biopsy specimens.

An analysis of the abdominal physical signs and symptoms in the patients studied indicated that these were of no value in the detection of those patients with early gastrointestinal tuberculosis.

Scintigraphy with both Gallium 67 and Indium 111 was performed in 8 patients diagnosed in the present series, and a further 6 patients who presented with intestinal tuberculosis. Results indicated that both isotopes could detect tuberculous enteritis, and that Gallium 67 was superior to Indium 111. Scintigraphy with Gallium 67 may be of particular value in the assessment of patients too ill to tolerate endoscopy or barium studies and in children.

In this research, the statistical planning has been done in consultation with the Institute for Biostatistics of the Medical Research Council.

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'Υπὸ φθίσιος ἐχομένῳ

διάρροια ἐπιγενομένη, θανατῶδες.

Hippocrates

For Joy

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CHAPTER 1

INTRODUCTION

King Edward VIII Hospital:

In 1986, the year that the clinical work for this thesis was completed, King Edward VIII Hospital, Durban, celebrated its Golden Jubilee. The hospital is situated in the southern Durban suburb of Umbilo, occupying a site of some 28 acres. At any one time, it accommodates over 2,000 inpatients, although for approximately 150 of these, their beds are mattresses placed on the floor (1). Caring for both inpatients and the 1,500 outpatients, who are seen on an average day, are over 500 doctors and 2,000 nurses (1). The hospital caters mainly for African patients, although Indians are also treated. During 1984 and 1985, the years when the majority of the clinical work for the thesis was performed the ratio of African to Indian admissions was 13,7:1.

The patients are accommodated in a mixture of purpose-built outpatient and ward blocks and prefabricated "huts", the latter dating from the second world war. The Medical Faculty of the University of Natal was established on an adjacent site in 1951. This led to the development of the hospital as a teaching centre, and despite its many problems of overcrowding and inadequate facilities, it remains one of the major training hospitals in Africa for both undergraduate and postgraduate medical students.

At King Edward VIII Hospital, nutritional diseases and infections are among the most frequently encountered medical problems and it is therefore not surprising that the many manifestations of tuberculosis are frequently seen.

Pulmonary and Intestinal Tuberculosis: Historical Aspects

Evidence of tuberculosis in Sumarian and Egyptian skeletons, dating from 4000 years B.C., probably represents the earliest indication of the disease in man (2). Hippocrates' pronouncements on the natural history and treatment of tuberculosis suggest this was a disease with which he had more than a passing acquaintance. His aphorism, quoted on page 7 is translated by WHS Jones as "if diarrhoea attacks a consumptive patient, it is a fatal symptom" (3). Pathological descriptions of intestinal tuberculosis are, however, of much more recent origin - the most famous being the report of a post mortem examination on Louis XIII of France in 1643 (4). This describes a large pulmonary cavity and ulcerating intestinal lesions. Despite this, much information about intestinal tuberculosis at that time remained in the realms of folk lore. Thomas Sydenham (5), writing in 1685, described the fatal outcome of tuberculosis thus:

> "lastly to close the scene a looseness succeeds occasioned partly by corrupt humours... and thus the patient perishes at length the following summer by a distemper occasioned by the foregoing winter."

By the early 1700's, the pathology of intestinal tuberculosis was put on a firmer footing by more detailed necropsy descriptions. In 1715, Brunner (6) described 60 separate intestinal ulcers, probably tuberculous, many originating in Peyer's patches, in a patient who had died of pulmonary tuberculosis. In 1731, intestinal stenosis, probably tuberculous in origin, was described by Walther and Krisch (7).

One of the earliest writings to detail the association between intestinal and pulmonary tuberculosis was that of G.L. Bayle (8), who, in 1810, published his observations on the post mortem examination of 100 cases of pulmonary tuberculosis.

> "...33 had a healthy alimentary canal and 67 presented ulcerations in the intestinal canal."

This was followed in 1825 by the detailed studies of anatomical pathology in 123 patients by Louis (9). Ulceration was present in half of them in the small or large bowel, or both. With few exceptions, the ulcers were small and few in number. In the small bowel, he noted ulcers increasing in number and severity as the caecum was approached. In the large bowel, he found the caecum and ascending colon to be the most frequently affected sites. Twenty five per cent of his cases had diarrhoea from 5 - 20 days before death.

The relationship between pulmonary and intestinal tuberculosis was also stressed by Rokitansky (10), who published his classic descriptions of intestinal tuberculosis in 1845.

> "With us, the affliction rarely occurs in the idiopathic form ... it is commonly by consequence of pulmonary tuberculosis".

He also described the site of submucosal infection, the typical circumferential ulcers and the occurrence of stricturing with healing.

> "Thus the cure of a tuberculous intestinal ulcer is always accompanied by a diminution of intestinal calibre."

Rokitansky also noted that the colon may be the initial site of intestinal disease.

> "Sometimes it is much advanced in the colon and then appears to have been first developed at this point and subsequently to have extended to the small intestine."

Austin Flint (11) in 1875, returned to the theme of Hippocrates' aphorism which was quoted earlier.

> "There are no facts which show that recovery ever takes place in cases of phthisis when the prominence and persistence of diarrhoea warrants the conclusion that intestinal ulceration exists".

He also noted some of the complications of intestinal tuberculosis.

> "Perforation of the intestine is an occasional accident in connection with intestinal ulceration."

> "Haemorrhage incident to intestinal ulceration may occur and the loss of blood may be the immediate cause of death."

In addition, in one of his 31 cases, the stool contained copious liquid fat. By the end of the century, Hartman and Pilliet (12) had described the first case of surgery for caecal tuberculosis.

The Relationship between Pulmonary and Intestinal Tuberculosis:

In the first half of the 20th Century, several further necropsy studies examined the relationship between pulmonary and intestinal tuberculosis. In 5 published series involving 1971 patients, (13,14,15,16,17), the incidence of intestinal tuberculosis, in the presence of pulmonary disease, ranged from 22% - 80% with a mean of 53,1%. In the largest of these series, Cullen (14), reported a study of 1,042 necropsies. He found that in patients with mild pulmonary disease, the incidence of intestinal lesions was low, whereas it was encountered in 72,7% of patients with severe pulmonary disease. Moreover, in patients with severe pulmonary tuberculosis, there was a preponderance of patients with the most extensive forms of intestinal involvement.

Following Crohn et al's (18) description of regional enteritis in 1932, a number of studies on the separation of Crohn's disease, from intestinal tuberculosis were made. Some workers in areas with a high prevalence of pulmonary tuberculosis, even began to doubt the existence of ileocaecal tuberculosis (19,20). The possibility that such views could

be held, rested on the difficulty in distinguishing between the two conditions on clinical, radiological and even histological grounds. This requires that much of the earlier literature on intestinal tuberculosis should be accepted with reservation.

In life the relationship between pulmonary and intestinal tuberculosis has been studied principally in Sanatoria patients, in whom Blumberg (21) described the situation as follows:

> "In far advanced active (pulmonary) cases it may be present in from 70 - 80%. In moderately advanced active cases, it may be present in from 14 - 18%, while in the early cases it may exist in 5 - 9%".

However, he gives no indication of the origin of his data. Probably, the largest study is that of Mitchell and Bristol (22), who analysed their results covering a 25 year period ending in 1949, and involving 5,529 patients admitted with pulmonary tuberculosis, to the Trudeau-Saranac sanatorium, New York. Patients were investigated only by barium meal and follow through and intestinal tuberculosis was identified in 346 (6,26%). Once again, the incidence of intestinal tuberculosis was found to increase with the severity of the pulmonary disease. It occurred in 1% of patients with minimal pulmonary disease, 4% with "moderately advanced disease" and 24,7% with "far advanced disease". Follow-up by serial barium studies was possible in 204 of the 346 patients. It was possible to document improvement in the

intestinal lesion in 47,7% of cases and progressison in only 1,7%. They also documented a marked decline in the incidence of intestinal disease during the period of the study, from 10% per annum in 1924 to approximatley 1% in 1949. This decline was present in all grades of severity of pulmonary disease and cannot be accounted for by a reduction in the relative number of patients with the severest forms of pulmonary involvement.

Mortality Trends:

The poor prognosis of tuberculosis, with gastrointestinal involvement that was recognized by Hippocrates, changed little over the subsequent 2000 years (11). To John Bunyan, tuberculosis was "the captain of all these men of death" (23). However, since this was written, there has been a dramatic decline in the mortality from the disease in Europe.

In the first half of the present century, the decline has ranged from 31% in Spain to 88% in Sweden (24). In the United Kingdom, for example, the rate fell from 140 per hundred thousand to less than 30 per hundred thousand (24). Although this trend is based on crude death rates and takes no account of the changing structure of populations, its magnitude is so great that its reality seems certain.

By contrast, there is much evidence that South Africa is experiencing an epidemic of tuberculosis - perhaps its first (25). In the 1980's, the mortality approximates to that in the United Kingdom in the 1940's (before the introduction of anti-tuberculous chemotherapy), that is about 50 per hundred thousand (26). This relates to 5,5 million people infected with tuberculosis (27) in a country with a population of approximately 25 million.

Tuberculosis in Natal:

While the author could trace no published work relating to the history of tuberculosis in Natal, it seems likely that the disease was brought into the Province, as into other parts of Southern Africa, by European settlers (25), and during much of the early part of this century remained almost unknown in Zulu Kraals (27A). It seems likely that the other major immigrant group, the indentured Indians, who arrived in Natal from 1860 brought little tuberculosis with them, as health checks on entry into the country resulted in the return to India of those with clinically evident disease (27B).

Other Demographic Features:

Intestinal tuberculosis is a disease of young adults diagnosed most frequently in the second, third and fourth decades (28,14,29,30). An analysis of 1,017 cases of

intestinal tuberculosis in 6 published series (28,22,32,32 33,34) shows a male to female ratio of 1 : 1,05, although a more definite female preponderance of 2 : 1 (29) or higher (33) has been described from India and a male preponderance from the U.S.A (15). In the United Kingdom, intestinal tuberculosis is predominantly a disease of Asian immigrants. This group accounted for 56,9% of the total notifications of abdominal tuberculosis in a Medical Research Council survey, (35) although comprising less than 4% of the population. In South Africa, it is predominantly a disease of the non-white population, being reported from Cape Town in only 6 white patients out of a total of 105 with tuberculous enteritis collected over 20 years (36,31).

Aetiology of Intestinal Tuberculosis:

The relationship between the extent of pulmonary disease and the presence of intestinal tuberculosis, supports the view that intestinal lesions may develop as a result of swallowed infected sputum. This presupposes that tubercule bacilli can penetrate into intestinal mucosa. There is some experimental evidence to support this. In 1935, Carnot et al (37) were able to induce intestinal tuberculosis in guinea pigs by the innoculation of blood withdrawn from the dog following the installation of human tubercle bacilli into a Thiery Vella fistula. In 1944, Medlar and Sasano (38) were able to

produce intestinal lesions in rabbits, by ingestion of tubercle bacilli. A mechanism for intestinal infection, involving mucosal penetration of tubercule bacilli has been proposed by Boyde (39). He suggests that massive doses of bacilli are swallowed and pass into the intestinal mucosal glands where an inflammatory exudate is produced. The bacilli are then carried through the epithelial lining by phagocytic cells and thus reach the submucosa where they give rise to the usual tuberculous lesions. The overlying mucosa may be shed and an ulcer formed, or remain intact. The bacilli may be carried from the submucosa to the mesenteric lymph nodes and there produce caseous lesions.

Recent studies from the United Kingdom (32,34) emphasize that in less than half the patients with intestinal tuberculosis, is evidence found of active pulmonary disease. In those patients without active pulmonary tuberculosis, it is only possible to speculate on the origins of the infection, although other routes of infection include the blood stream, lymphatics and by direct spread from adjacent organs. Certainly the ingestion of bovine tuberculosis (M. Bovis) can only be implicated in a small minority of cases of isolated intestinal involvement, due to the virtual elimination of infected cattle (40). Moreover in India, where attempts have been made to isolate the infecting organism from lone intestinal lesions, only the human strain has been recovered (41,42).

Anatomical Pathology:

1. Gross Pathology: Four pathological varieties of bowel involvement have been described (40) - ulcerative, hypertrophic, a mixed variety - ulcerohypertrophic and a stricturing form. In the ulcerative form (29), the diseased segment is indurated and the circumference studded with nodules of varying size. The ulcers are usually superficial, not penetrating the lamina propria, and arranged in an annular form. They may completely encircle the bowel although this is not invariable (43). The mucosal folds may be ironed out and replaced by a mamillated surface or scattered with irregular mucosal erosions (29). In the hypertrophic variety (44,41) the thickening of the bowel wall is mainly due to subserous fibrosis, fat and mucosal hypertrophy (44). The lesion is normally located in the ileocaecal region and the thickening may result in extensive narrowing of the colonic lumen. The serosal surface of the bowel may show small tubercles and the ileum may be dilated.

Previously the ulcerative type was considered secondary to pulmonary tuberculosis, while the hypertrophic variety occurred in the absence of pulmonary involvement. However, the correlation now appears to be poor (45,46,47). The mixed form, showing features of both hypertrophic and ulcerative types, was present in 10 of Hoon's 58 cases of ileocaecal tuberculosis (43) and 16 of Anand's 50 cases (41). The

stricturing form is less common (48,43) and consists of single or multiple fibrous strictures. This form may in many cases represent a healing phase of the disease (29). It is probable that the form of the disease encountered, depends upon factors such as the number of infiltrating bacteria, their virulence, the immunological response of the host and the effects of chemotherapy (40,21).

2. Histology: The characteristic cell type is the epithelioid cell, oval or spindle shaped with abundant cytoplasm and a faintly staining nucleus. Collections of these cells surrounded by lymphocytes, plasma cells and Langhan's giant cells form the typical granuloma, the central cells of which may undergo caseation necrosis. The granulomata tend to become confluent and show a marked variation in size. They may occur first in the mucosa or submucosa (29). However, lesions due to tuberculosis, may lack specific features such as these and consist of non-specific inflammatory tissue with a varying degree of hyalinization (29,49,41). In particular, the specific findings of acid fast bacilli and caseating granulomata, may be undetectable in intestinal lesions, while they may be recognized in adjacent lymph nodes (32,43,29). All 50 cases of ileocaecal tuberculosis studied by Anand (41) had positive mesenteric lymph nodes, while intestinal caseating granulomata were only found in 5 cases.

Distribution of Intestinal Lesions:

The relative paucity of intestinal granulomata may contribute to the poor diagnostic yield of colonoscopy in previously published series (49,50,51). This is particularly unfortunate, since the majority of tuberculous intestinal lesions are within the reach of the colonoscope. Shown below is the distribution of lesions compiled from 4 series (33,31,34,32) involving 268 patients described since 1978.

Oesophagus	1	(0,4%)
Gastroduodenal	9	(3,3%)
Small bowel	77	(18,1%)
Ileocaecal area	122	(44,5%)
Caecum alone	9	(3,3%)
Colon	45	(16,4%)
Anorectal region	8	(2,9%)

These figures emphasize the rarity of upper gastrointestinal tract lesions and caecal lesions in the absence of ileal disease. They also demonstrate the predominance of small bowel and particularly ileocaecal tuberculosis. It is of interest that a similar pattern of distribution was observed by other workers, notably Cullen (14), before the advent of anti-tuberculous chemotherapy.

Colonoscopic Features

Despite easy accessibility of the majority of these lesions to the colonoscope, the colonoscopic diagnosis of intestinal tuberculosis has been sufficiently rare to justify case reports (53,54). Larger published series have originated mainly from Japan, India and South Africa. Indeed, one of the earliest colonoscopic series reporting tuberculous

colitis emanated from King Edward VIII Hospital. Moshal et al described in their first hundred patients examined in this manner, 9 patients with tuberculous colitis (50). The typical appearance of the lesions encountered was the presence of one or more large bowel strictures with adjacent stellate ulceration. This report emphasized the poor yield of colonoscopic biopsies in obtaining a histological diagnosis of tuberculosis. None of the patients had positive biopsies in this respect. Only 4 patients were subsequently proved to have had tuberculous colitis, the diagnosis being made in each case at laparotomy. Two other series are available which deal with the colonoscopic appearances of tuberculous colitis. Aoki et al (51) described their findings in 9 proven and a further 5 suspected cases of tuberculous colitis. They found ulceration in 6 patients and described the size of these ulcers as "from very small one to a very large one". The ulcers were irregular in shape and orientation (although circumferential ulcers were described in the ileum). "Active inflammation and erosions" were found in 6 patients. The ileocaecal valve was deformed in 4 cases, while inflammatory polyps and strictures were each found in 8 patients.

The largest series of colonoscopically diagnosed tuberculosis so far published, is that by Bhargava et al (52). They described their findings in 11 patients with ileocaecal

disease. The ileocaecal valve was deformed in all patients and the caecum narrowed in 10, while 8 patients had multiple mucosal nodules 2 - 6 mm in diameter. These were most frequent near the ileocaecal valve. Pseudopolypoid oedematous mucosal folds were seen in 2 patients and caecal ulceration in a further 2 patients. The ulcers ran transversely with irregular, swollen and red margins. They measured 3,5 x 3 mm and 1,5 x 3 mm. The smaller ulcer was found between mucosal nodules. Of note is the fact that in this series histological evidence of tuberculosis was obtained by colonoscopy in only 3 of the 11 patients. In 2 of these 3 patients the diagnosis was based on the finding of confluent granulomata without acid fast bacilli or caseation, and would not be considered to have proven intestinal tuberculosis in the present series. In only one patient was tissue from the submucosa, included in the biopsy.

Radiographic Features:

Radiographic observations of intestinal tuberculosis date from 1911, the time of Stierlin's (55) description of the sign that bears his name.

> "In infiltrating and ulcerative involvement of the caecum and ascending colon, there is absence of the normal shadow of this part of the colon, as shown in the striagram 6 or 7 hours after the barium meal, while the terminal ileum and transverse colon are filled. Consequently, the early as well as the later stages of the so-called caecal tuberculosis can be diagnosed by this means even in cases undiagnosable by the ordinary clinical methods."

The early radiological signs of intestinal involvement in tuberculosis, relate to bowel motility and tone (56,57). Acclerated transit of barium, together with areas of spasm or decreased tone, lead to separation and flocculation of the barium column in the standard barium follow through. Early infiltration of the mucosa produces stiffening and later nodularity, particularly in the distal small bowel (56). These changes of motility and tone are present particularly at the ileocaecal valve, where spasm renders reflux filling of the terminal ileum much less frequent in tuberculosis, when compared with other conditions (58). Later changes of the ileocaecal valve include incompetence due to induration and fibrosis and deformity due to ulceration and the presence of granulation tissue (56,58). If the edges of the valve are ulcerated, the inverted umbrella defect described by Fleischner may occur (58).

In the colon, the hyperplastic type with a long segment of narrowing and rigidity was the commonest abnormality in the 50 patients studied by barium enema by Kolawole et al (57). In that series, a carcinoma-like variety was uncommon (3 cases), whereas it occurred in 7 out of 10 patients with colonic tuberculosis reported by Werbeloff et al (59). The appearance of the lesion is of a constant filling defect, sometimes annular, with overlapping edges (57,60). The

ulcerative type shows single or multiple ulcers which may be superficial or deep, but which typically run transversely. A segmental colitis has also been described in which multiple skip lesions may occur (59,60). This pattern is one of segmental inflammation and stenosis with or without inflammatory mass formation (56). In the 7 cases described by Balthazar et al (60), the lesions were generally short (5-7cms) and showed no predilictions for any particular part of the colon.

Many of the radiographic abnormalities associated with tuberculous enteritis have been known for over 60 years. It is therefore surprising that little use has been made of this knowledge to investigate the frequency of the disease particularly in high risk groups. In South Africa where pulmonary tuberculosis is not infrequent, the prevalence of the intestinal involvement is totally unknown. In other countries studies on the subject relate to a time before the introduction of anti-tuberculous chemotherapy, a time when the best available investigative techniques would appear crude by today's standards. It, therefore, seems timely at least to begin an assessment of intestinal tuberculosis in a prospective study employing modern imaging techniques.

CHAPTER 2

INTESTINAL AND PULMONARY TUBERCULOSIS AT KING EDWDARD VIII HOSPITAL: THE BACKGROUND

The majority of patients in the present study were enrolled during 1984 and 1985. As a background to this investigation, a retrospective study was also undertaken to determine the observed frequency of intestinal tuberculosis both as a clinical diagnosis and as a post-mortem finding at King Edward VIII Hospital during these years.

Retrospective Clinical Study:

Statistics from the medical records department of the hospital were examined to determine the number of patients discharged with the diagnosis of tuberculosis in general (International Classification of Disease No. 010-018) and specifically with pulmonary (011) and abdominal (014) disease.

From 1st January 1984 until 31st December 1985, 202,582 people were admitted to King Edward VIII Hospital. During this period 3,170 patients (1,6%) were discharged with a diagnosis of tuberculosis. Pulmonary tuberculosis was present in 2,198 cases that is in 69,3% of all patients with tuberculosis and 1,1% of total discharges. In 563 of these, pulmonary disease was associated with tuberculosis in other organs.

Excluding those patients detected in the prospective series described in Chapter 3, a diagnosis of abdominal tuberculosis was made in 134 patients, that is 4,2% of patients with tuberculosis and 0,066% of total discharges. The classification "014" used for abdominal tuberculosis includes intestinal and peritoneal tuberculosis, tuberculous fistulae and sinus tracts and tuberculosis of abdominal lymph nodes.

The inpatient notes of all 134 cases of abdominal tuberculosis were available for study. Table I (opposite page 33) shows the findings in this group analysed according to abdominal disease site. Sixteen patients were considered to have intestinal tuberculosis. This represents 0,5% of all patients discharged with a diagnosis of tuberculosis and 0,008% of total discharges. In six cases the diagnosis was not confirmed on the basis of accepted criteria (Page 44). In 4 of the latter the diagnosis was based on the presence of an intestinal stricture and in two on the presence of an abdominal mass. Two patients in this group had a normal chest x-ray while pulmonary fibrosis was found in one patient, features suggesting active tuberculosis in two and a pleural effusion in one.

Ten patients were identified as suffering from proven intestinal tuberculosis. This represents 0,3% of all patients discharged with the diagnosis of tuberculosis. This group of

10 patients comprised 3 females and 7 males with ages ranging from 6-74 years (mean 38,8 years), three cases being below the age of 18 years. The criteria for diagnosis of intestinal tuberculosis were:

Acid fast bacilli in biopsy material	6
Caseating granulomata in biopsy material	4

All patients had abdominal symptoms, 7 of whom gave a history of chronic disease (greater than 2 weeks) while in the remaining 3, symptoms were of acute onset. The clinical presentation in the patients with intestinal tuberculosis was as follows:

Diarrhoea	3
Small bowel obstruction	3
Rectal bleeding	1
Gastric outlet obstruction	1
Large bowel obstruction	1
Acute abdominal pain	1

A mass was palpable in the right iliac fossa in 2 patients.

Available endoscopic and radiological evidence indicates that in the patient with gastric outlet obstruction, the presentation was due to intestinal tuberculosis rather than primarily the result of disease in lymph nodes.

Fourteen sites of disease were identified and these were distributed thus:

Duodenum	2
Jejunum	1
Ileum alone	1
Ileocaecal area	3
Transverse colon	3
Ascending colon	1
Rectum	3

The diagnosis of intestinal tuberculosis remained unsuspected prior to the definitive diagnostic procedure in 3 patients. The favoured diagnosis in these cases was carcinoma (2 patients) and appendicitis (1 patient). Even at surgery, the diagnosis was thought to be a large colonic neoplasm in one of these 3 patients. Five of the 10 patients underwent intestinal resection.

Not all of the patients with intestinal tuberculosis had evidence of pulmonary involvement.

The chest radiograph was normal in 3 of the patients, showed unilateral hilar lymphadenopathy in 1, apical fibrosis in 1 and features suggesting active tuberculosis in 2. Neither the radiographs nor reports could be traced in the remaining 3. The diagnosis was established as a result of surgery in 6 patients and sigmoidoscopy and/or colonoscopy in 4 patients.

Retrospective Necropsy Study:

Further information concerning pulmonary and intestinal tuberculosis was sought from the necropsy records of the Department of Pathology, Faculty of Medicine, University of Natal, Durban. The reports of all available post mortem examinations conducted in 1984 and 1985 were scrutinized and details of pulmonary and intestinal disease noted.

During the 24 month period from 1st January 1984, there were 9,146 deaths at King Edward VIII Hospital and 1,581 post mortem examinations were carried out. Forty five reports were not available for study. In the 1,536 necropsy reports studied evidence of tuberculosis was found in 112 (7,3%) and pulmonary disease in 96 (6,2%). Abdominal tuberculosis was present in 42 cases, that is 37,5% of cases with tuberculosis and 2,7% of necropsies studied. Table 2 (opposite page 36) shows this group analysed by disease site.

Thus 18 necropsies showed evidence of gastrointestinal tuberculosis, i.e. 1,2% of all necropsies studied and 16,1% of those with evidence of tuberculosis.

Of the 13 patients with both pulmonary and intestinal tuberculosis, bilateral cavitating disease was found in 4, bilateral non-cavitating disease in 3, unilateral non-cavitating disease in 1 and miliary tuberculosis in 5. The figures quoted in Table 2 include the results of all necropsies studied involving patients dying with abdominal tuberculosis at King Edward VIII Hospital, during the period under discussion.

Table 3 (opposite page 37) shows the figures relating to patients 18 years old and above, that group which corresponds more closely with that of the prospective clinical series described in subsequent chapters. When these figures are considered, the number of cases of abdominal tuberculosis falls by 9 and those of intestinal tuberculosis by 4 when compared with those for all necropsy examinations. In patients 18 years old and above, abdominal tuberculosis was present in 4,1% of necropsies and intestinal tuberculosis in 1,8%.

Necropsy reports at King Edward VIII Hospital state an anatomical diagnosis rather than the cause of death. However, inspection of the available evidence suggests that in the 112 patients with tuberculosis the disease contributed significantly to the patients' death in approximately 88 cases (78,6%) and was an incidental finding in approximately 23 cases (20,5%).

Being a retrospective study, both in the clinical and necropsy series, evidence of intestinal tuberculosis was not specifically sought at the time the records were made. Small lesions may have been overlooked. In addition, the necropsy group contains more African than Indian subjects (ratio 97,6:1) compared with the general hospital population (ratio

13,7:1). Tuberculosis is more frequent in the African than the Indian population (ratio for King Edward VIII Hospital, 1984-1985, 21:1) and hence the findings of the post mortem series may, in this way, over-estimate the prevalence of intestinal tuberculosis if applied to the hospital as a whole.

Conclusion:

Thus pulmonary tuberculosis remains an important inpatient diagnosis at King Edward VIII Hospital. It is especially true in the medical wards where, over a 25 year period in one Unit, the disease accounted for 7% of all admissions of African patients (Mayet, F.G.H. Personal Communication).

Intestinal tuberculosis is, however, comparatively rare, being identified from the necropsy and medical records in 34 cases during 1984 and 1985. In 10 patients (29,4%) there was no post mortem or radiological evidence of pulmonary tuberculosis. In only 10 cases was the diagnosis of intestinal tuberculosis proven in life.

The analysis shows a significantly higher rate of diagnosis of intestinal tuberculosis in the necropsy group (1,2%) as compared with the retrospective clinical study (0,008%). This may be due to a number of factors. Firstly, in patients

presenting with pulmonary tuberculosis at King Edward VIII Hospital, abdominal signs and symptoms are only infrequently investigated unless there is an inadequate response to antituberculous therapy. Thus even symptomatic cases may be undiagnosed. Secondly, gastrointestinal tuberculosis is often associated with the more severe forms of pulmonary disease and hence patients with intestinal tuberculosis are more likely to come to post mortem. In addition, one may expect that a well conducted post mortem examination may detect mild disease without physical signs or symptoms.

The findings of both the clinical and necropsy series should, however, be viewed with some reserve. Their accuracy will suffer from the same fault inherent in any retrospective analysis. That is, the evidence in question was not being specifically sought at the time the records were made. Some degree of underdiagnosis seems almost inevitable. However, the figures do provide a background against which a prospective investigation may be considered.

CHAPTER 3

THE AIMS AND DESIGN OF THE PRESENT STUDY

Definition of Intestinal Tuberculosis:

Intestinal tuberculosis for the purpose of the present study is defined as tuberculosis of the oesophagus, stomach and small and large bowel. Tuberculosis at these sites is included in the International Classification of Diseases, Categories 014 and 107.8. This definition excludes anal and perianal tuberculosis, tuberculosis of mesenteric and retro-peritoneal lymph nodes and tuberculous peritonitis.

Aims of the Present Study:

The aims of the present study were:

1. To determine the value of small and large bowel radiology in the diagnosis of intestinal tuberculosis.
2. To determine the value of upper and lower gastro-intestinal endoscopy in the diagnosis of intestinal tuberculosis.
3. To determine whether gastrointestinal tuberculous lesions can be identified by radioisotope methods using Gallium 67 and possibly Indium 111.
4. To compare the above techniques in the evaluation of intestinal tuberculosis.
5. To determine the prevalence of intestinal tuberculosis in the patients studied at King Edward VIII Hospital.

Patients:

The study was to be based on 50 patients. The population chosen consisted of patients with open cavitating pulmonary tuberculosis admitted to the medical wards of King Edward VIII Hospital. This group of patients was chosen because it was expected, on the basis of the evidence previously discussed, to provide a sufficiently high yield of patients with tuberculous enteritis, in whom to study the contributions of radiology, endoscopy and nuclear medicine. Selection was based on sampling using random tables. Informed consent to the proposed investigation was obtained. Patients who were considered too ill to tolerate all the proposed investigations or who declined consent were excluded.

Methods:

Those patients accepted for the study were assessed clinically with special reference to gastrointestinal symptoms and abdominal physical signs. Thereafter, patients were investigated by upper gastro-intestinal endoscopy, colonoscopy, small bowel contrast radiology and double contrast barium enema. The method of choice for the radiographic investigation of the small bowel was the small bowel enema. This investigation was performed by Dr. C. Larsen of the Department of Radiology, University of Natal.

Other radiographic examinations were performed routinely by various members of the Department. Radiographs were reviewed by the author, the radiologist performing the investigation and subsequently by an independent radiologist. Neither the radiologist nor the endoscopist was aware of the findings of the other. Differences in assessment between radiologists were reconciled by discussion and no attempt was made to assess inter-observer variation.

Those patients with proven intestinal tuberculosis were in addition, investigated where possible, scintigraphically with Gallium 67 and/or Indium 111 to determine if these isotopes could be used to detect areas of tuberculous enteritis. Scintigrams were reviewed by the author and by the physicist and radiologist in charge of the investigation. They were subsequently reviewed by an independent radiologist with an interest in nuclear medicine. The radiologists were unaware of the sites of intestinal tuberculosis in each case. Once again differences in interpretation were resolved by discussion and no attempt was made to assess inter-observer variation.

At the time of endoscopy and colonoscopy biopsy specimens were taken of any abnormality found and the specimens submitted for histological examination. It was originally intended to submit specimens for culture and for guinea pig innoculation, but this was subsequently abandoned because all patients were receiving antituberculous chemotherapy.

This decision was based on a pilot study which showed no positive results in any patient receiving anti-tuberculous treatment, although positive results were obtained in patients not receiving such treatment. In this study biopsy specimens from 8 patients with histologically proven intestinal tuberculosis were submitted for guinea pig innoculation and culture. Only one positive result was obtained, and that in one of the 2 patients not receiving anti-tuberculous chemotherapy at the time biopsies were taken. No specific references could be traced concerning the relationship between positive culture and guinea pig innoculation and the duration of anti-tuberculous chemotherapy. However, the advice from the staff of the local centre specialising in the treatment of tuberculosis, King George V Hospital, was that these results were attributable to the prior anti-tuberculous treatment.

In August 1988 the author learnt that investigations by the MRC Tuberculosis Research Unit had shown sputum culture, though not necessarily the Ziehl Neelsen strain for tubercle bacilli become negative from between 2-4 weeks after the start of chemotherapy in patients who were initially culture positive (Prof. Kleeberg, Personal Communication). This information had not yet been published and was not available at the time the decision was made to discontinue the

biological investigations. However, the results of these investigations may not be incompatible with the results of the pilot study. The success of culture and guinea pig innoculation depends in part on the number of viable organisms innoculated. It is probable that the numbers of tubercle bacilli available in the sputum of patients with open cavitating pulmonary tuberculosis greatly exceeds that available from the one or two small colonoscopic biopsies that were submitted for innoculation and culture.

Diagnostic Criteria:

Any one of the following criteria was used for the diagnosis of intestinal tuberculosis (Adapted from Marks et al, 40).

1. Histological evidence of caseating granulomata.
2. Histological demonstration of acid fast bacilli in the lesion.
3. Good therapeutic response to chemotherapy in patients with radiological and/or endoscopic evidence of intestinal tuberculosis, associated with proven tuberculosis elsewhere.

These strict criteria were employed to reduce any possible doubt concerning the accuracy of diagnosis in this series. The protocol for the study was passed by the Ethical Committees of the University of Natal and the South African Medical Research Council.

Sixty nine patients were randomly selected for inclusion in the study. Thirteen of these were excluded, 6 having refused consent and 7 being considered too ill to tolerate the proposed investigation. A further 6 patients were subsequently withdrawn after they withdrew their consent during investigation. Because of the comparative rarity of Indian patients with any form of tuberculosis at King Edward VIII Hospital, the group selected included only African patients.

Thus the results of a comprehensive investigation of the gastrointestinal tract are available in 50 patients with open cavitating pulmonary tuberculosis. This group compared 44 men and 6 women within an age range of 18-67 years and a mean of 39,7 years. These results will be discussed in subsequent chapters.

CHAPTER 4

THE UPPER GASTROINTESTINAL TRACT AND SMALL BOWEL

1. Oesophagus, Stomach and Duodenum:

Introduction:

The upper gastrointestinal tract is one of the least common sites of intestinal tuberculosis, and hence no attempt was made in this area to compare the accuracy of diagnosis of radiology and endoscopy. However, the region was surveyed endoscopically in order to reduce the risk of a rare case being missed and hence error occurring in the prevalence data. Fiberoptic endoscopy was chosen as the only method of investigation because of the greater accuracy of this technique (61,62) and the opportunity it affords for biopsy. The fiberoptic endoscope was pioneered by Hirschowitz and his colleagues at the Ann Arbor University and was first employed diagnostically in February 1957 (63). Its development hinged on the production of the glass-coated glass fiber achieved by Curtis working in the same Institution in 1956 (63).

Upper Gastrointestinal Endoscopy:

Method:

Endoscopies in this series were performed using the Olympus GIF-K2 or GIF-Q endoscopes. Topical pharyngeal anaesthesia with 10% lidocain spray (Xylocaine Astra) and diazepam 5 -10mg (Valium; Roche) intravenously, or midazolan 2,5 - 5 mg (Dormicum; Roche) intravenously were used for premedication. Biopsies were attempted of all lesions found. Specimens obtained were mounted in paraffin wax and sectioned routinely. The sections were then stained with hematoxylin and eosin, periodic acid Schiff and Ziehl Neelsen stains. Histological reports of the biopsies were made routinely by various members of the Department of Anatomical Pathology, University of Natal and subsequently reviewed by a Senior Pathologist, Dr. D. Pirie.

Results:

Upper gastrointestinal endoscopy revealed no abnormality in 32 patients and was abnormal in 14. It was not performed in 3 patients - 2 of these withdrew consent before the examination and in the third, intubation was unsuccessful, due to severe micrognathism. The patients who withdrew consent acceded to the other required investigations. In one further patient, an examination although attempted was not complete due to a recent meal.

The abnormalities encountered are detailed below:

Non-specific gastritis	3 patients
Oesophageal candidiasis	3 patients
Sliding hiatus hernia plus ulcerative oesophagitis.....	2 patients
Non-specific duodenitis	2 patients
Uncomplicated sliding hiatus hernia...	1 patient
Hiatus hernia plus oesophageal candidiasis	1 patient
Non-specific mucosal irregularities...	1 patient
Gastric submucosal haemorrhages	1 patient

In no patient was histological evidence of tuberculosis obtained. Duodenitis, gastritis and ulcerative oesosphagitis have all been attributed to tuberculosis (64,65). However, no lesion encountered was sufficiently typical to allow the diagnosis to be made even on the basis of a successful response to anti-tuberculous chemotherapy. The frequency with which these non-specific mucosal abnormalities occur in the absence of tuberculosis, together with the rarity of the disease in the upper gastrointestinal tract, makes the diagnosis of tuberculosis in these cases unlikely.

2. <u>The Small Bowel:</u>

The small bowel is one of the most difficult parts of the gastrointesinal tract to examine. Apart from its extreme ends, it is out of the reach of conventional endoscopes and hence barium contrast studies remain the primary diagnostic tool.

Standard Barium Follow Through Examination:

The standard method of examining the small bowel at King Edward VIII Hospital is the barium follow through examination. With this technique the patient swallows 200-300ml of barium sulphate suspension (85% w/v). Gastric emptying may be accelerated by metaclopramide, 10mgs (Maxolon; Beecham) given by intramuscular injection. Abdominal radiographs are then taken with the patient supine at half-hourly intervals until barium reaches the colon. If any abnormality or suspicious area is detected on these films, further spot films are obtained of the area, using abdominal compression to separate bowel loops (Shapiro, B. Personal Communication).

Unfortunately this technique has several problems, which often result in inadequate studies, particularly of the distal ileum, where the majority of pathology is expected (66,67). Interruption of barium flow by the pylorus, often results in poor distension of the bowel and hence strictures may be overlooked. In addition, since the passage of barium is dependent on peristalsis, the time taken for the contrast to reach the caecum is unpredictable in individual patients. The radiographs often show multiple overlying loops and the terminal ileum may be further obscured by contrast in the caecum.

The Small Bowel Enema:

During 1983, we were privileged to have as a guest in the Department of Radiology, Dr. S. Somers of Ontario, Canada, who demonstrated to us the methyl cellulose double contrast small bowel enema (68). In its earliest form, the small bowel enema was described by Schatzki (69) in 1943 and it is an adaptation of this technique that has been adopted as the method of choice for examining the small bowel in the present study.

In the 24 hours before the examination, the patient receives a low residue diet (Ensure; Abbott). At 18.00 hrs the day preceding the examination, 60 ml of castor oil are administered and at 22.00 hrs an oral laxative is taken (Bisacodyl 5mgs: Dulcolax; Boehringer Ingelheim). Nothing is given by mouth from 06.00 hrs on the day of the examination. The small bowel enema is performed as follows: the small bowel is intubated beyond the ligament of Treitz by a soft flexible tube that can be passed nasally or orally and positioned with the aid of a flexible guide wire. Intubation is facilitated by the application of a local anaesthetic spray to the throat and, if required, the nose (Lidocain 10%; Xylocaine Astra).

Following intubation, 150-200 ml of high viscosity barium suspension (liquid polybar), is infused into the small bowel. This is followed by 1,5 - 2 litres of methyl cellulose, introduced at approximately 80 mls/min by a constant infusion pump. The methyl cellulose propels the barium towards the colon, leaving behind a barium coating on the mucosa, which is preserved for 15-20 minutes. A double contrast is produced between the high density mucosal barium and low density methyl cellulose, in the lumen on one side and the soft tissue density of the bowel wall, on the other side. The progress of the barium column and the methyl cellulose is observed fluoroscopically. Abdominal palpation is used to separate overlying loops and spot films are taken at the discretion of the radiologist who is present throughout the entire examination.

With this technique, optimal distension of the small bowel is achieved and a high quality double contrast examination of its entire length, is made in the majority of patients.

The accuracy of the small bowel enema has been well documented (70,71,72). However, it remains an under-utilized method of small bowel examination (70) perhaps because it is time consuming for the radiologist and can be uncomfortable for the patient unless the radiologist is skilled at small bowel intubation.

Barium Enema:

In addition to the small bowel studies, some detail of the terminal ileum may be obtained during a barium enema examination when contrast refluxes into the ileum. However, it is not always possible to achieve reflux and there is often less than optimum distension of the ileum. Both factors limit the usefulness of the procedure in examining the distal small bowel. Nevertheless, information from this source has been used in the study where ileal reflux occurred. The technique is discussed more fully in Chapter 5.

Comparison of Radiological Techniques:

One study is available by Gurian et al (70) which compares retrospectively the accuracy of diagnosis of the small bowel enema, barium enema and small bowel follow through examination in 88 patients. It concluded that, of documented diagnoses made by small bowel enema, 96% were correct as compared with 65% of the small bowel follow through studies. Only one small bowel enema was shown to be incorrect - a false negative result in a patient with Crohn's disease of the ileum found at laparotomy.

Incorrect barium follow through studies were mostly false negatives. Missed pathology included Crohn's disease, radiation enteritis, intestinal obstruction and lymphoma. The barium enema failed to achieve ileal reflux in 26% but had an accuracy of 84% when reflux occurred.

Colonoscopy:

Endoscopic visualization of the small bowel is possible with conventional instruments only at its extreme ends. Entry into the second part of the duodenum can be achieved in nearly every patient during upper gastrointestinal endoscopy in the absence of an obstructing lesion such as stenosis or tumour. Intubation of the ileum at the time of colonoscopy is achieved less frequently. One published series suggests that it can be achieved in 66% of examinations (73), but few colonoscopists can make that claim (74). Colonoscopy is discussed more fully in Chapter 5.

Results:

Small Bowel Enema:

Forty-six patients were examined by small bowel enema and 4 by barium follow through, following the failure of small bowel intubation. Despite careful positioning and palpation of the abdomen, detailed visualization of the terminal ileum during the small bowel enema examination, was not achieved in 4 patients. What was seen of the small bowel in these cases was normal. Results of the 46 small bowel enema examinations were as follows:

Normal.....	37
Mucosal oedema	3
Multiple round worms	4
Possible adhesions	1
Mucosal nodularity	1

Mucosal oedema was attributed to hypoproteinaemia in these patients. However this could not be confirmed retrospectively as serum protein estimates were not made in these and the majority of patients in this series. The patient in whom the small bowel enema showed ileal mucosal nodularity (Case 41) was subsequently suspected to have tuberculous enteritis on the basis of the endoscopic appearance of the large bowel and terminal ileum although positive biopsies of the ileum or elsewhere were not obtained. This is discussed on page 65.

Barium Follow Through:

The barium follow through examination showed no abnormality in the 4 patients examined by the method. The terminal ileum was not well shown in 1 patient.

Barium Enema:

The terminal ileum was filled by reflux in 27 patients (54%) and appeared abnormal in 1 patient (Case 41), where a mucosal nodularity and irregularity was found. This is illustrated in Figure I (following page 54). These abnormalities were also identified by small bowel enema and colonoscopy.

Colonoscopy:

The terminal ileum was entered in 16 patients (32%) and found to be abnormal in 2 (Cases 28 and 41).

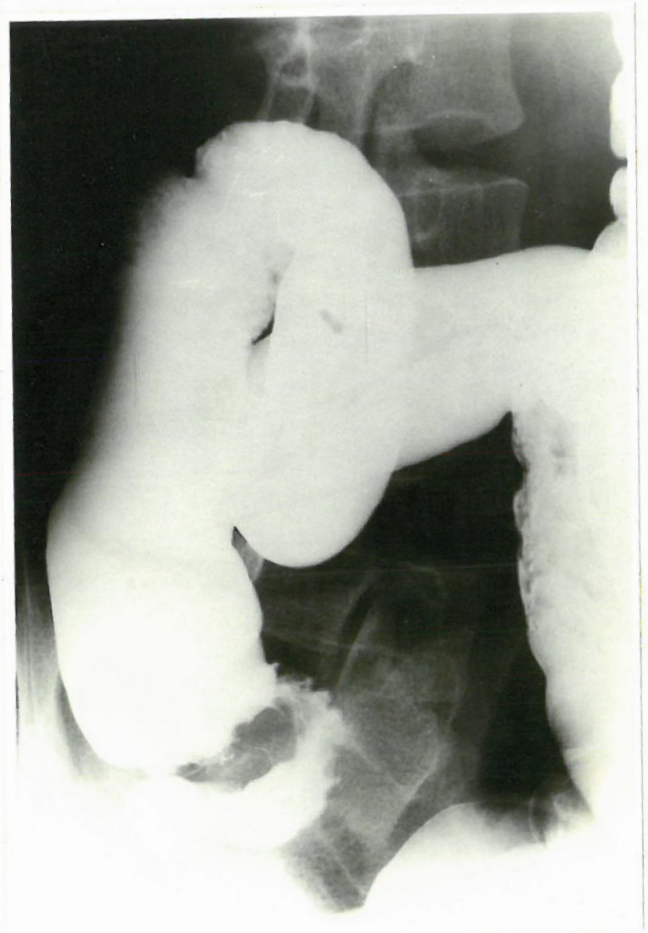


FIG. 1:

BARIUM ENEMA SHOWING NODULAR FILLING DEFECTS IN THE ILEOCAECAL AREA. CASE 41

a) Case 28: the ileum was entered to a length of approximately 7 cm. The mucosa appeared finely granular with loss of the normal vascular pattern. Biopsies showed a mild increase in chronic inflammatory cells in the mucosa. Granulomata or acid fast bacilli were not identified. Acid fast bacilli, however, were identified in colonic biopsies. The cause of the ileal mucosal granularity is unclear. It may represent tuberculous enteritis in view of the fact that acid fast bacilli were identified in the colon, but such an endoscopsic appearance is not typical of tuberculosis. Another explanation is lymphoid hyperplasia which may produce exactly the mucosal changes observed, although it is uncommon in those of this patient's age, (50 years) (20).

b) Case 41: the ileum was entered to a length of 10 cm. It appeared nodular and ulcerated. No histological evidence of tuberculosis was obtained. However, the macroscopic appearances were suggestive of tuberculosis. This case is further discussed on pages 60 and 65.

Ileal Intubation:

The frequency of ileal intubation in the series is low, and this must bias the results against the detection of ileal lesions, particularly as, in the colon at least, colonoscopy is considered more sensitive than barium studies in the detection of small mucosal lesions. Several factors may have

resulted in the low frequency of ileal intubation. In 5 cases swollen mucosa of the ileocaecal valve may have been partly responsible for failure of intubation. In 2 cases solid faeces obstructed the valve. However, the most important factor was probably the colonoscopist's lack of experience with the technique.

The frequency of ileal disease encountered in the present study will be discussed more fully in the light of the results of the large bowel studies described in the next chapter.

Conclusion:

Thus, in the examination of the upper gastrointestinal tract and small bowel, two possible case of tuberculous enteritis was identified. The abnormalities encountered were demonstrated by colonoscopy, barium enema and small bowel enema in one case (Case 41) and by colonoscopy alone in the other (Case 28).

CHAPTER 5

THE LARGE BOWEL

The large bowel was examined by radiology and colonoscopy.

Radiology:

Introduction:

The first radiographic examination of the colon by radio opaque enema was performed in 1904 by Schule (75). However, it was not until fluoroscopic control, first described by Haeniseh in 1911 (76), became readily available that the contrast enema examination of the colon became a dependable method of diagnosis. The double contrast technique using air insufflation was not described until 10 years later (77), although it was subsequently to become the preferred method for demonstrating colonic mucosal detail.

Methods:

The technique of the double contrast barium enema examination performed at King Edward VIII Hospital generally, and for the purpose of this study, is similar to that described by Samuel and Laws (78). A liquid diet is administered 2 days prior to the examination and catharsis achieved by a combination of sorbitol (150 mls of 70% solution) and Bisacodyl 10 mgs (Dulcolax; Boehringer Ingelheim) given orally on the day preceding the examination. A high bowel washout is performed on the morning of the procedure.

Results:

A double contrast barium enema examination was performed on 50 patients. This was normal in 38 patients, abnormal in 8 and judged not to be of diagnostic quality in 4 due to inadequate bowel preparation. The abnormalities encountered were as follows:

Rectal polyp	Case 3
Mucosal nodularity	Case 4
Stricture and ulceration of descending colon	Case 9
Shrunken caecum	Case 24
Aphthous ulceration of descending colon	Case 33
Right-sided diverticula and contracted caecum	Case 39
Nodular filling defects in ileocaecal region	Case 41
Right-sided diverticula	Case 46

Case 3:

A polyp measuring 0,5 cm diameter was noted in the lateral rectal wall. No stalk was visible and the appearance may have been due to faeces. At colonoscopy no polyp was found.

Case 4:

Mucosal nodularity encountered in this case extended throughout the large bowel and was thought to represent lymphoid hyperplasia. The mucosa appeared normal colonoscopically.

Case 9:

A short 2 cm stricture involving the distal aspect of the descending colon was found, associated with a 1 cm diameter ulcer with a depressed crater. The appearance is shown in

Figure 2 (following page 59). There was spiculation proximal to the stricture suggesting further ulceration. The caecum was judged to be normal. Tuberculosis was considered a possible cause. At colonoscopy, the presence of a solitary ulcer in the descending colon was confirmed. However, no stricture was recognized. Mucosal nodularity and ulceration were encountered in the caecum. Biopsies of the lesions confirmed the diagnosis of tuberculous colitis.

Case 24:

The caecal pole appeared shrunken and drawn upwards although no mucosal lesions were identified. Tuberculosis was considered a possible cause for the abnormality. At colonoscopy, multiple caecal aphthous ulcers were found together with a solitary mucosal nodule. Caecal anatomy was thought to be otherwise normal. Biopsy specimens confirmed tuberculous colitis.

Case 33:

Multiple aphthous ulceration thought to be present in the descending colon was not confirmed colonoscopically. The mucosa appeared normal and the findings of the barium study were thought to be an artifact.

Case 39:

Diverticula were demonstrated in the caecal pole which was thought to be slightly contracted though distensible. Diverticula were also found at colonoscopy. Biopsies revealed non-specific inflammatory change.

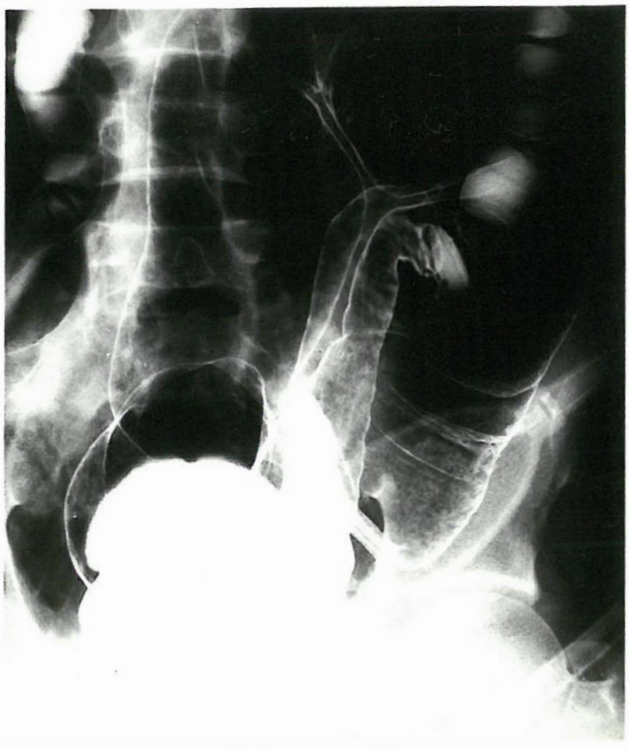


FIG. 2:

BARIUM ENEMA SHOWING (a) AN AREA OF NARROWING AND ULCERATION IN THE DISTAL SIGMOID COLON. CASE 9.

Case 41:

Nodular filling defects were present in the ileocaecal area though the mucosa appeared intact. This is shown in Fig. 1 (following page 54). Tuberculosis was considered a possible diagnosis. At colonoscopy a nodular and ulcerated ileum and transverse colon were found, together with a granular caecal mucosa and a rectal ulcer. The macroscopic diagnosis was tuberculosis, however, biopsies failed to confirm this and showed only non-specific changes.

Case 46:

Right-sided diverticula were noted, but no diverticular openings were noted at colonoscopy.

Thus, although no patient was found with typical changes of tuberculosis on double contrast barium enema, 3 possible cases of tuberculous colitis were identified (6%).

Colonoscopy:

Introduction:

Fiberoptic colonoscopy was pioneered by Japanese workers in the early 1960's (79,80). By 1970 progress in instrumentation had made possible the passage of a colonoscope to the caecum without resorting to the use of an orally passed guide wire. With further refinements in design, including greater tip control and flexibility, the entire colon can now be visualized and is accessible for procedures such as biopsy and polypectomy in the majority of patients (81).

Methods:

Colonoscopy in this series was performed using the Olympus CF-LB3 and CF-LB3W colonoscopes. Bowel preparation was achieved with the use of a sodium sulphate solution, "Golitely" (82), administered 3-4 hours before the procedure. Possible nausea was minimized by metaclopramide 10 mg (Maxolon; Beecham) given by intramuscular injection and by using Golitely, chilled from a refrigerator. Sufficient Golitely was administered (usually 3-4 litres) to produce a clear effluent. Patients received a normal diet on the day prior to the investigation and then nothing by mouth from midnight. The procedure was performed in the morning and assisted by fluoroscopy when necessary. Biopsies were taken for histological examination, of any abnormality detected, and were processed and reported in the manner described previously (page 47). Biopsy forceps were used as a guide for the measurement of any lesions found (83).

Results:

Colonoscopy was performed in 50 patients. The caecum was reached in 48 patients (96%). In the remaining 2 patients the examination was incomplete for technical reasons. It was not possible to progress beyond the mid-transverse colon in one patient and the splenic flexure in the other. Both these incomplete investigations revealed no abnormality. The examination was normal in a further 21 patients. Of the remaining 27 patients, tuberculous colitis was confirmed in 14 and suspected in a further 9. Other abnormalities were found in 4 patients.

The 14 cases of tuberculous colitis comprised 13 males and 1 female with an age range of 24-59 years and a mean of 37,6 years. The diagnostic criteria used were as follows:

Acid fast bacilli detected in biopsies.....	12 patients
Caseating granulomata identified in biopsies (Case No. 9).....	1 patient
Colonic lesion suggestive of tuberculous colitis healed after 6 months' chemotherapy (Case No. 7).....	1 patient

A minimum of 2 biopsies was taken from each site of disease.

The morphology of the lesions encountered was as follows:

Multiple nodules.....	8 patients
Superficial ulcers.....	6 patients
Solitary nodules.....	3 patients
Swollen and erythematous ileocaecal valve	3 patients
Deep ulceration	1 patient
Erythema only.....	1 patient

The nodular lesions consisted of 0,2-0,5cm diameter mucosal nodules, single or multiple, usually situated on the crest of a swollen and red mucosal fold. They occurred in 78,6% of patients with proven intestinal tuberculosis and those found in Case 7 are shown in Figure 3 (following page 62). In two patients areas of multiple nodularity produced a mass extending approximately 1 cm longitudinally and bulging into the lumen. One moderately deep ulcer was also encountered (Case 9). This was ovoid, 1 cm long, with rounded edges and occurred in the descending colon. This is shown in Figure 4 (following page 62). Superficial ulcers consisted of aphthous ulcers, that is, 0,1-0,2cm diameter white-based superficial ulcers on red and swollen mucosa. These were multiple in 5 patients and solitary in 1. Examples are illustrated in Fig.

FIG. 3: NODULAR LESION: THE CAECUM. CASE 7.

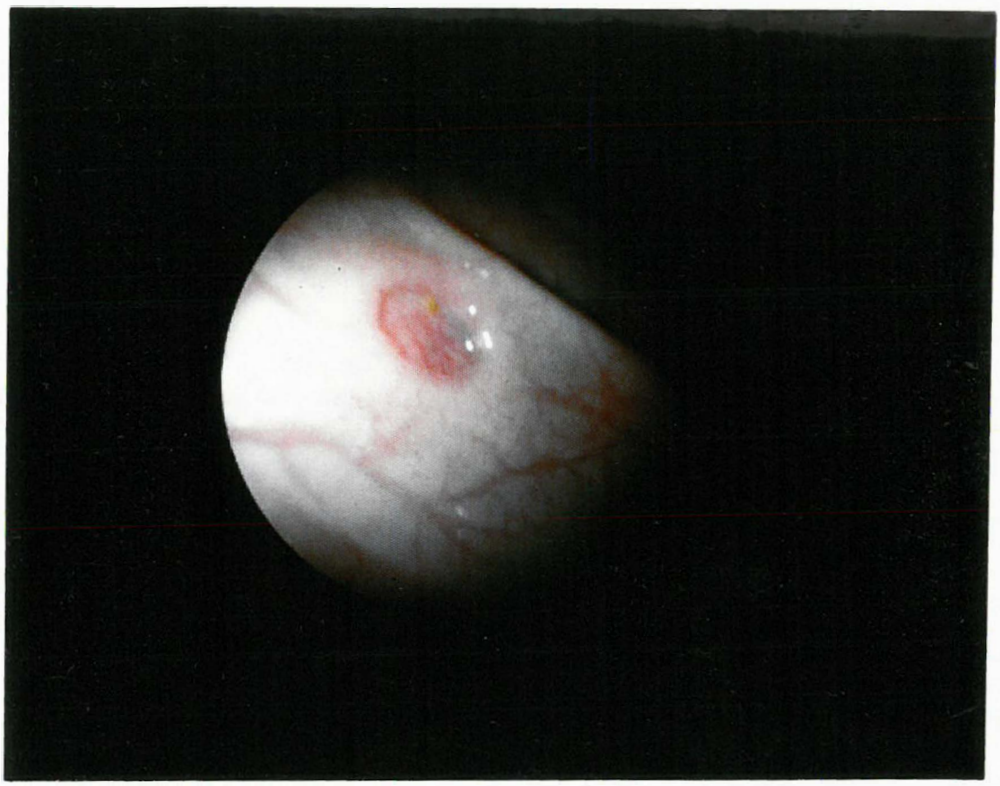


FIG. 4: DESCENDING COLON ULCER. CASE 9.

5 and Fig. 6 (following page 59). Erythema alone in the caecal pole was found in 1 patient and yielded granulomata and acid fast bacilli on biopsy. The distribution of these lesions is shown below:

Caecum.....	13 patients (92,9%)
Transverse colon.....	4 patients (18,6%)
Ascending colon.....	2 patients (14,3%)
Descending colon.....	1 patient (7,1%)
Rectum.....	1 patient (7,1%)

In 5 patients more than one site was involved and in 4, the lesions were discontinuous, i.e. a segmental colitis was present. The extent of the disease encountered was as follows:

Caecum alone.....	8 patients (57,1%)
Transverse colon alone.....	1 patient (7,1%)
Caecum and ascending colon.....	1 patient (7,1%)
Caecum and descending colon.....	1 patient (7,1%)
Caecum and transverse colon.....	1 patient (7,1%)
Caecum, ascending colon and transverse colon.....	1 patient (7,1%)
Caecum, transverse colon and rectum	1 patient (7,1%)

Nine further patients were identified with colonoscopic abnormalities that may have been due to tuberculosis. In these cases, however, histology showed non-specific inflammatory changes only. These patients were:

Case 3:

The ileocaecal valve appeared red and swollen.

FIG. 5:

SUPERFICIAL ULCERS ON A NODULAR MUCOSAL FOLD.
CASE 9.

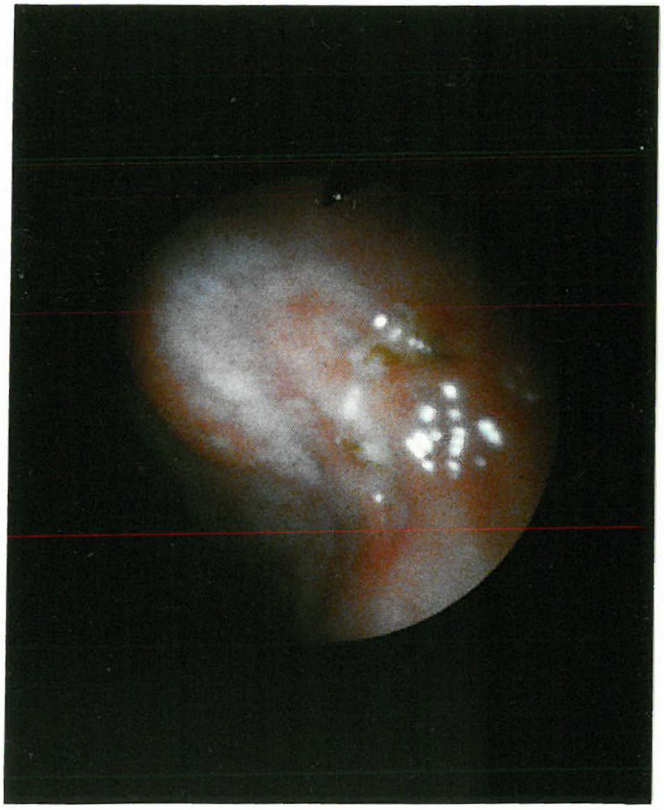


FIG. 6:

SUPERFICIAL ULCERS ON RED AND SWOLLEN MUCOSA.
CASE 8.

Case 4:

A single 0,3 cm nodule was found in the caecal pole. The large bowel was otherwise normal.

Case 10:

This was a diffuse mucosal erythema and swelling in the caecum, colon and rectum. In addition, two longitudinal superficial ulcers (0,3 cm) were present in the rectum.

Case 12:

The mucosa of the ascending colon and caecum appeared erythematous.

Case 17:

A 0,3 cm shallow circumferential ulcer was present in the transverse colon, together with similar ulceration in the upper ascending colon. There the surrounding mucosa appeared irregular.

Case 19:

Multiple superficial 0,1 cm ulcers on red and swollen mucosa were encountered in the caecal pole.

Case 26:

In the mid-transverse colon an area of swollen and irregular mucosa 1 cm diameter was present within which was a 0,3 cm nodule. The ileocaecal valve appeared normal but with a 1 cm diameter patch of erythema below its inferior lip. In addition, an adenomatous polyp was present in the rectum.

Case 41:

The ileocaecal valve was fixed open. The distal 10 cm of ileum contained multiple nodules and superficial ulcers running both circumferentially and longitudinally. The caecal mucosa was granular with contact bleeding. At the splenic flexure, multiple 0,1 cm superficial ulcers were present with multiple 0,3 - 0,5 cm nodules. In the rectum, an ovoid 0,5 cm moderately deep ulcer was also present.

Case 51:

Multiple 0,1 cm superficial ulcers on red and swollen mucosa were found in the caecum and ascending colon, together with a single large 0,5 cm superficial ulcer in the transverse colon.

The evidence of tuberculosis is perhaps strongest in Case 41. However, all these patients are regarded as possible cases of tuberculous enteritis.

The ileum was entered in 8 of the 23 patients with proven or possible tuberculous colitis (34,8%) and only two possible case of tuberculous ileitis was found. This is discussed on page 55.

Colonoscopic abnormalities were also encountered in a further 4 patients. These abnormalities comprised:

Multiple right-sided diverticula..... 1 (Case 39)
Areas of telangiectasia..... 3 (Cases 52,2,27)

Case 39 showing diverticula has been mentioned previously (page 59). In cases 52, 2 and 27, the areas of telangiectasia were not biopsied, but an adjacent site in 1 case yielded bilharzial and Trichuris ova.

Comparison with Previous Colonoscopic Descriptions:

Previous published colonoscopic descriptions of tuberculosis have already been discussed. Table 4 (opposite page 66) shows the features as described by Bhargava (52) and by Aoki (51) and those encountered in the present investigation. Strict comparison between these series is difficult however, because the composition of the different series is not uniform. Bhargava's series of 11 patients is taken from a group of 14 patients with "a possible diagnosis of ileocaecal tuberculosis". How these 14 were selected is not stated. Moreover although the 11 patients discussed are described as proven cases, only 7 cases were diagnosed as the result of colonoscopic biopsy and in 2 of these the granulomas encountered were non-caseating and without associated acid fast bacilli. The criteria for the diagnosis in the remaining 4 patients is not stated.

Aoki's series appear to contain all the suspected and proven cases of intestinal tuberculosis diagnosed by colonoscopy in his Unit from June 1969 to May 1974, the cases being referred routinely for the investigation of abdominal symptoms. Eight of the cases were regarded as proved by the finding of caseating granulomata. The remaining 5 patients were diagnosed on the basis of the colonoscopic appearances, a history of pulmonary tuberculosis and positive stool cultures for tubercle bacilli.

In Table 4 (opposite page 66), Aoki's description of inflammatory polyps is equated with mucosal nodularity, and erosions equated with aphthous ulceration. Proven and suspected cases in the series of Aoki et al and Bhavgava et al are not separated as this is not possible from the information provided.

Bearing in mind these reservations, it can be seen that the present series differs from the published colonoscopic descriptions of tuberculous disease in the low frequency of ileocaecal valve involvement, and luminal narrowing and by the presence of solitary nodules and erythema alone as manifestations of tuberculous colitis - features not previously described. These features support the view that the lesions described in the present series represent an

early phase in the development of tuberculous enteritis. A further striking feature of the present series is the frequency with which acid fast bacilli were detected in biopsy specimens. Even when the 9 possible cases of tuberculous colitis are added to the 14 proven cases, acid fast bacilli were identified in 52,2% of patients. The success of the present series in identifying acid fast bacilli cannot be attributed merely to the number of biopsies taken. In Bhargava's colonoscopic series (52), 10 biopsies were taken from each patient and in another study by the same author, (84), 6-8 biopsies were taken and here the yield was zero in 10 patients. In the present study, a minimum of 2 biopsies was taken from each lesion, and the total number obtained from each patient was between 4 and 10, with a mean of 6. The authors of the other series (51,52) emphasize the difficulty of obtaining granulomata, let alone caseating granulomata or acid fast bacilli in colonoscopic biopsy specimens, on the grounds that the lesions are located submucosally, and hence inaccessible to endoscopic biopsy.

Such difficulty was not apparent in the present series. Moreover, acid fast bacilli were found in the mucosa of 4 patients and the submucosa of 6. In addition, acid fast bacilli or granulomata were present in the lamina propria of 3 cases. Thus both the mucosal situation of acid fast

bacilli in some cases and the depth of biopsy specimens in others were together possibly responsible for the high histological yield in the present series. It is possible that in early cases of intestinal tuberculosis such as these, mucosal hypertrophy is less than that in advanced disease and, therefore, more readily permits access to tissue containing acid fast bacilli or granulomata.

It is probable that the acid fast bacilli identified in the present series were Mycobacterium tuberculosis. Due to the absence of evidence from cultures however, it is not possible to exclude entirely the possibility that some at least were atypical Mycobacteria. Nevertheless this is thought unlikely, particularly in view of the rarity with which such organisms are isolated locally. At the laboratory of King George V Hospital, which acts as the reference laboratory for the greater part of Natal, the isolation rate for atypical mycobacteria is approximately 30 cases per year out of approximately 25,000 specimens examined. Mycobacterium bovis is even rarer, no isolates of the organism have been made in the past five years. Moreover, in other published series where attempts have been made to isolate the infecting organism in cases of intestinal tuberculosis, only human strains have been recovered (41,42).

Colonoscopy versus Barium Enema:

In considering the different diagnostic yields of colonoscopy and double contrast barium enema in this series, it is appropriate to examine some previously published evidence relating to the diagnosis of polyps and inflammatory bowel disease by these methods.

In one of the earliest papers on the subject, Loose et al (85) examined the results of their first 700 colonoscopies and correlated the findings with radiology. In the diagnosis of ulcerative colitis, they reported an agreement between barium enema and colonoscopy in 68% of patients studied. However, in 18%, radiology substantially underestimated the extent of the disease and in 14% a normal barium enema was obtained in patients with a mild total colitis. In addition it was found that the double contrast enema missed 12% of polyps which were less than 1 cm in diameter, subsequently identified at colonoscopy. A similar finding regarding missed polyps was recorded by Thorni et al (86) who found that 11,7% of small polyps found at colonoscopy were undetected by double contrast barium enema. Aldridge et al (87), found a benign polyp or carcinoma in 32% of 37 symptomatic patients with a normal barium enema. The influence of polyp size on radiological accuracy is stressed by Wolf et al (88) who noted that in 146 patients, 166 polyps

were diagnosed by barium enema (of which the majority were of double contrast type), but an additional 118 radiologically unrecognized polyps were found at colonoscopy. Of these 118 polyps 97 were less than 1 cm and 53 less than 0,5 cm in diameter. Thus these studies indicate that the detection of small mucosal lesions by double contrast barium enema examination is unreliable. However, in none of these studies was a valid comparison of the accuracy of colonoscopy versus radiology made. In each case, the colonoscopist had the results of the barium study available to him and hence was at a considerable advantage. Colonoscopy is certainly not infallible in the detection of polyps and this is emphasized by Lauffer et al (89) who reported that 6 out of 56 polyps detected by double contrast barium enema had been missed at an initial sigmoidoscopy or colonoscopy, but later confirmed when the procedure was repeated. These comparisons with respect to colonic polyps are particularly relevant since 11 of the 14 patients with proven intestinal tuberculosis had single or multiple colonic nodules which resembled small sessile polyps. Nevertheless, except in areas of tight angulation such as the rectum, and hepatic and splenic flexures (89) the impression remains that colonoscopy is superior in the detection of small mucosal lesions. In the present study, both colonoscopist and radiologist were

unaware of the findings of each other, and the expertise of the various operators performing the two procedures, were comparable. As described previously, the barium enema examination was abnormal in 8 patients. Colonoscopy failed to confirm the abnormalities in 6 patients. These were: right-sided diverticula (Case 46), extensive mucosal nodularity (Case 4), a 5 mm polyp (Case 3), multiple aphthous ulceration (Case 33), a contracted caecum (Case 24), and a colonic stricture (Case 9). None of these 6 patients consented to a repeat colonoscopy or radiographic examination and hence the correct interpretation of these conflicting findings remains a matter of conjecture. In Case 33, following a totally normal colonoscopy of the relevant region and a further review of the barium studies, the findings of the latter investigation were thought to be due to an artifact. However, it is considered that in Cases 46, 24, 9, 4 and possibly 3, colonoscopy missed significant additional abnormalities diagnosed by barium enema. In two patients (Cases 24 and 9), biopsies suggested that these abnormalities were due to tuberculosis.

Colonoscopy identified abnormalities in 27 patients. In 5 patients these were of a vascular nature (telangiectasia in 3, erythema in 2), and would not be detected radiologically. In each of the remaining 22 patients, lesions were detected

by colonoscopy but not radiologically. The nature of these lesions is shown in Table 5 (opposite page 73) Of the 14 patients with proven tuberculous colitis, the barium enema was of diagnostic quality in 13 and normal in 11. This is perhaps not surprising in view of the small size of the lesions encountered. In the 2 remaining patients, with good quality barium enemas, the areas of abnormality identified were also noted colonoscopically. Thus in the diagnosis of small tuberculous lesions, double contrast barium enema gives unreliable results and significantly underestimates the frequency of disease.

Colonoscopic Follow-Up:

Follow-up colonoscopy was performed in 6 patients. One case of proven tuberculosis (Case 7) was diagnosed by the finding of colonic lesions suggestive of tuberculosis which healed after chemotherapy. The initial colonoscopy showed swollen mucosal folds in the caecal pole studded with multiple 3 mm nodules and on one mucosal fold, a solitary 2mm superficial ulcer. The ileum was entered and found to be normal. Biopsies revealed only non-specific inflammatory changes.

Follow-up colonoscopy after 7 months' anti-tuberculous chemotherapy showed the caecum to be drawn up and the ileocaecal valve relatively vertical. However, the caecal mucosa was entirely normal with no evidence of the nodularity or ulceration previously noted. Colonoscopic follow-up after a minimum of 6 months' anti-tuberculous treatment was obtained in a further 5 patients.

In 3 patients (Cases 29, 25 and 21) there was complete resolution of the lesions previously seen and the repeat colonoscopy was entirely normal. In Case 21, after an initial colonoscopy showing two 3 mm mucosal nodules in the caecal pole, the patient absconded from hospital but returned 4 months' later with a worsening of respiratory symptoms and a deterioration in the radiographic appearance of his pulmonary tuberculosis. Colonoscopy at this time showed the original nodules unchanged, together with nodularity of caecal mucosal folds and of the mucosa below the ileocaecal valve. Following 7 months of treatment, the caecum appeared normal at colonoscopy.

In 2 patients (Cases 9 and 46), colonic mucosal lesions persisted. In Case 9, initial colonoscopy showed a 1 cm moderately deep ulcer in the descending colon with swollen and nodular caecal mucosal folds and superficial ulceration. At follow-up, the descending colon was normal and no nodularity of the caecal mucosa was present. However, there was one 0,3 cm irregular superficial ulcer present in an area of previously normal mucosa. Biopsies revealed a mixed inflammatory reaction and candidiasis, but showed no specific evidence of tuberculosis. In Case 46, the initial colonoscopy showed an area of nodularity in the mid-transverse colon producing a mass lesion that extended for 1cm longitudinally.

At follow-up, the same area showed three 3 mm nodules. Biopsies again revealed a mixed inflammatory reaction with no evidence of tuberculosis. The erythrocyte sedimentation rate in both these patients was 6 mm per hour. Further features of the follow-up obtained in this series are discussed in Appendix B. Thus, this limited follow-up has demonstrated that complete resolution of intestinal mucosal lesions after a minimum of 6 months' anti-tuberculous chemotherapy is not invariable. This conclusion is supported by other workers (32, Wright, J. Personal Communication). The significance of the residual mucosal abnormalities is not known but persisting tuberculous infection has not been entirely excluded.

The Relationship between Pulmonary and Intestinal Tuberculosis:

The relationship between pulmonary and intestinal disease has been discussed previously. In the present series, although all patients studied had cavitating disease, different grades of severity of pulmonary disease were present, viz. unilateral cavitating pulmonary tuberculosis, bilateral tuberculosis with unilateral cavitation and bilateral tuberculosis with bilateral cavitation.

In the 50 patients studied, 8 had unilateral cavitating disease and 2 (25%) of these were found to have proven or

possible intestinal tuberculosis. Twelve patients had bilateral tuberculosis with unilateral cavitation, four (33,3%) of these had possible or proven intestinal disease. Thirty patients had the severest grade of pulmonary disease with bilateral cavities and 16 of these (53,3%) had possible or proven tuberculous intestinal lesions.

Thus in this series, intestinal tuberculosis was associated predominantly with the severest form of pulmonary disease encountered among the patients studied. Indeed 12 out of the 14 patients with proven intestinal tuberculosis, that is 85,7%, had bilateral pulmonary tuberculosis with bilateral cavitation.

Conclusion:

In the examination of the large bowel in 50 patients by colonoscopy, 14 proven and 9 possible cases of tuberculous colitis were identified. These 23 patients comprised 20 men and 3 women, with an age range of 18-60 years and a mean of 38,5 years. Except for the presence of a deep 1cm ulcer in the descending colon encountered in one patient (Case 9), the proven tuberculous lesions were small and probably represent the earliest changes in the development of tuberculous colitis so far recorded. These changes range from erythema alone, through single nodular lesions and aphthous ulcers to

areas of multiple mucosal nodularity. Mucosal nodules occurred in 78,6% of cases, whereas ulceration occurred in the absence of mucosal nodules in only 2 patients (14,3%). The majority of the lesions were present in the caecum. In the 34,8% of the patients with proven or possible tuberculous colitis in whom the ileum was inspected at colonoscopy, two possible cases of tuberculous ileitis were found. The presence of such early lesions may in part be due to the criteria used for patient selection, in that patients were chosen without regard to the presence of abdominal signs or symptoms.

CHAPTER 6

SCINTIGRAPHY AND TUBERCULOUS ENTERITIS

The two isotopes used in this study for imaging tuberculous enteritis were Gallium 67 and Indium 111. Although both isotopes have been employed in the imaging of inflammatory bowel disease, no studies have been reported on their use in tuberculous colitis.

Gallium 67:

Introduction:

Gallium is a metallic element in Group 3A of the Periodic Table. Two isotopes of Gallium, Gallium 68 and Gallium 67, have been used clinically. Gallium 67 emits 4 gamma photons and has a half life of 72 hours. It is usually administered, as in this series, as the citrate which remains soluble at a neutral pH. In the first 24 hours, 10-30% of administered activity can be recovered in the urine (90,91), thereafter the only important route of excretion is in the faeces (91). Following intravenous injection, Gallium 67 is localized in a wide variety of neoplastic and inflammatory lesions. The mechanism of localization has been reviewed by Tsan (92). In normal plasma, Gallium 67 is almost exclusively bound to transferrin. This large molecule does not readily diffuse from normal capillaries. However, the increased vascular permeability at sites of inflammation may itself be

responsible for some localization of Gallium. Other factors involved are the take-up of Gallium by neutrophils in which it is bound to the plasma membrane and by bacteria at the site of inflammation.

Clinical Studies in Inflammatory Bowel Disease:

Gallium 67 citrate was first used extensively in the investigation of tumours (93,94,90). However, following the observation of Gallium uptake in a lung abscess in 1971 (95), its use was extended to include the detection of inflammatory processes and abscesses, particularly in the abdomen (96,97). Gallium 67 was first used to image the inflamed bowel by Tedesco et al in a case of pseudomembranous colitis (98). Thereafter, reports of its use in the investigation of ulcerative colitis and Crohn's disease soon followed.

In ulcerative colitis, Gallium scintigraphy is usually positive in active disease. In the series of Rheingold et al (99), all 9 patients with ulcerative colitis had positive scans. No false positive results in 9 control patients was observed. Bronwyn Jones et al reported positive scans in each of 6 patients with active disease, and negative scans in 2 patients with inactive disease (100). In the former series, no attempt was made to compare scintigraphy with barium enema or colonoscopy. Bronwyn Jones, however, recorded a good correlation between extent and activity of disease as assessed by scintigraphy and colonoscopy or barium enema. No

false negative results were found in these studies but in a smaller study by Sarkar et al (101) of 4 patients with active ulcerative colitis, one false negative result was obtained.

In Crohn's disease, Gallium uptake is less constant. Six of Rheingold's 7 patients with active disease had negative scans (99). In 11 studies performed by Goldenberg et al (102), 6 were also negative.

Patients:

In the present study, Gallium 67 scans were performed on 11 of the 14 patients with tuberculous colitis. Only three positive scans were obtained. However, this low positivity is not surprising, when one considers the small mucosal lesions which the study detected. The distribution of activity recorded on these scintigrams suggests intestinal disease. However, a definite distinction between this and uptake by abdominal lymph nodes is not possible on the evidence available.

It was, therefore decided to study isotopically six consecutive patients with more florid tuberculous enteritis identified as a result of routine investigations for abdominal symptoms and diagnosed by the finding of acid fast bacilli in biopsy specimens. Each of these patients was receiving anti-tuberculous chemotherapy for periods between 3 days and 6 weeks prior to scintigraphy.

Methods:

After an intravenous injection of 2,5 - 3 mCi (120 MBq) of Gallium 67 citrate, (Amersham), scintigrams were obtained at 24 and 48 hours. Additional scans at 72 hours and 120 hours were made in some cases. Abdominal scintigraphy was performed using an Elscint 415 collimated gamma camera.

Scintigraphy was performed within two weeks of diagnosis and scintigrams reported by a radiologist with an interest in nuclear medicine, unaware of the results of previous investigations. The extent of the disease defined scintigraphically was compared with the results obtained by endoscopy (either upper gastrointestinal endoscopy or colonoscopy). The Kappa statistic was employed to measure the degree of agreement beyond chance between the diagnostic methods. The analyses were performed by Dr. P.S. Becker of the Institute of Biostatistics, Johannesburg.

Results:

Results are shown in Table 6 (opposite page 81) analysed by the site of intestinal involvement detected. For the purpose of analysis, the combination of distal ileal involvement with caecal involvement is considered as one site since it was not thought possible to separate these areas scintigraphically. In the 6 patients, 15 sites of disease were detected endoscopically, and 12 of these sites were detected by Gallium 67. An example of a positive scintigram is shown in Figure 7 (following page 81). Thus when

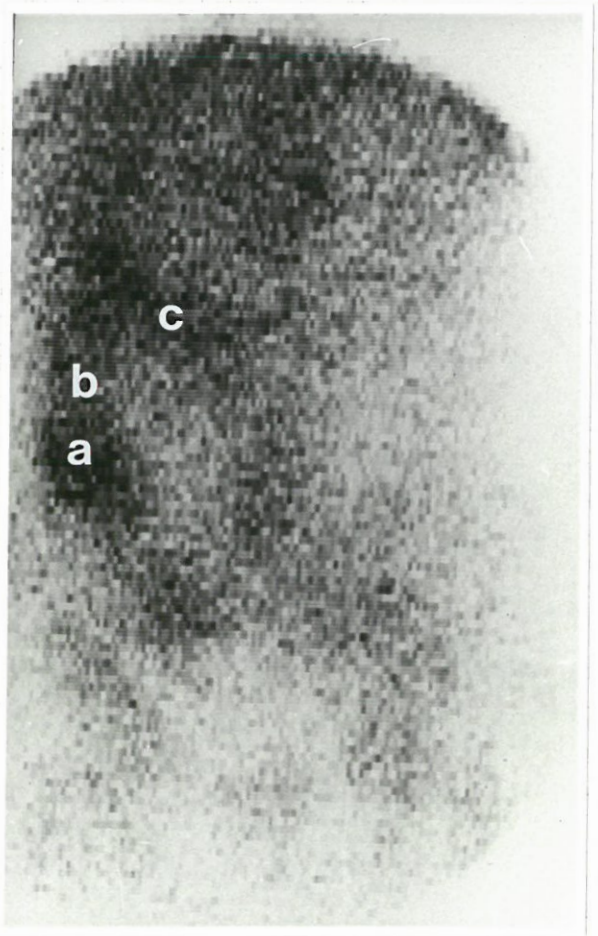


FIG. 7:

GALLIUM SCAN SHOWING INCREASED UPTAKE IN (a) ILEOCAECAL AREA, (b) ASCENDING COLON, (c) PROXIMAL TRANSVERSE COLON AND NORMAL UPTAKE IN THE LIVER, SPINE AND PELVIS. CASE D.

endoscopy is taken as the gold standard, Gallium scintigraphy has a sensitivity of 80% and a specificity of 100%. Agreement between the two imaging techniques is regarded as excellent (Kappa = 0,838, see Table 8).

Indium 111:

Introduction:

Like Gallium, Indium is a metallic element in Group 3A of the Periodic Table. Two isotopes have been used clinically - Indium 111 and Indium 131m. Indium 111 emits 2 gamma photons and has a half life of 2,8 days. In this study, Indium III has been used as a complex with oxine, a chelating agent.

The complex readily penetrates cellular membranes (103). Once intracellular, the complex disassociates, oxine remaining diffusible and the cells stably labelled with the radionuclide (103). If leucocytes are labelled in vitro with Indium 111 and re-injected, the leucocytes migrate to areas of inflammation, permitting scintigraphic detection of the lesion (104).

Clinical Studies in Inflammatory Bowel Disease:

The first report of the use of this method in the detection of inflammatory bowel disease appeared in 1981 (105), and three subsequent studies have compared the results of scintigraphy with those of radiology and colonoscopy.

Saverymuttu et al (106) found scintigraphy to be as accurate as radiology in the assessment of both ulcerative colitis and Crohn's colitis. Buxton-Thomas et al (107) found less than perfect agreement between Indium scintigraphy and the results of colonoscopy, radiology and the study of resected specimens. However, the agreement was good in 4 of the 6 patients with Crohn's disease and 5 of the 9 patients with ulcerative colitis that he studied. A separate comparison of the results of Indium scintigraphy with colonoscopy, radiology and surgery was not made.

Stein et al (108) in the study of 15 patients, found an excellent to good agreement between scintigraphy, radiology or colonoscopy in 4 of the 5 cases of Crohn's disease and 8 of the 10 cases of ulcerative colitis. In this study, the comparison was with colonoscopy in the majority of cases, and also in some instances with radiology but separate comparisons were not made.

Patients:

In the present study, Indium labelled leucocyte scans were performed on 8 of the 14 patients with tuberculous colitis identified prospectively and no positive scintigrams were obtained. However, when the techcnique was applied to the 6 patients with more florid symptomatic disease, the ability of Indium labelled leucocytes to detect tuberculous enteritis was demonstrated.

Method:

The method of labelling leucocytes has been adapted from the method described by Amersham the suppliers of Indium 111-oxine. Aseptic procedures were used throughout.

Whole blood (45 mls) is drawn from the patient in 15 mls ACD. To this is added 27 mls of 0,5% Methocell-saline solution which is gently mixed and allowed to stand for 1 hour at room temperature. (To minimize red-cell contamination air bubbles are removed by means of a syringe). The supernate is then taken off, avoiding the settled red blood cells, and transferred to sterile conical vials. The vials are centrifuged for 10 minutes at 80 - 90g to form a pellet of white cells. The supernate is withdrawn and discarded. 500 uCi In-III oxine are added and the cells gently mixed, and left to label at room temperature for 30 minutes. After re-injection into the patient, scintigrams are obtained at 2 - 4 and 24 hours.

Scintigraphy was performed within 2 weeks of the diagnosis using as an Elscint 415 collimated gamma camera.

Results:

The results, reported and analyzed in the same way as for Gallium 67, are shown in Table 7 (opposite page 84).

Of the 15 sites of disease detected endoscopically in the 6 patients, Indium labelled leucocyte scintigraphy detected 9 sites and, in addition, gave one apparent false positive

result. An example of a positive Indium 111 labelled leucocyte scintigram and the corresponding endoscopic appearance are shown in Figures 8 and 9 (following page 85). Thus when endoscopy is taken as the gold standard, Indium leucocyte scintigraphy has a sensitivity of 60%, and specificity of 96%. The agreement between the two imaging techniques is regarded as fair to good (Kappa = 0,607).

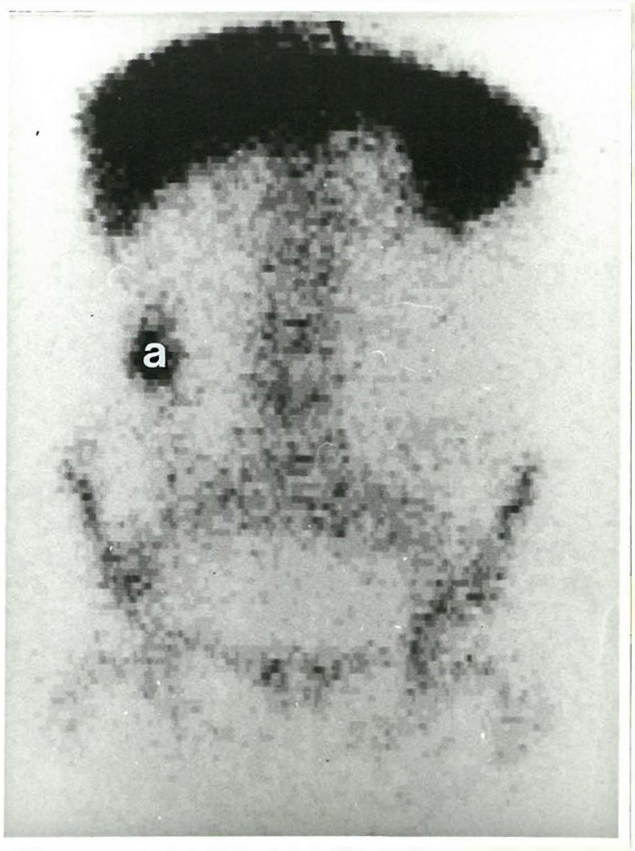
Although for the purpose of analysis the positive scintigram indicating disease in the ileocaecal area of Case B is regarded as a falst positive, it is possible that the scan detected submucosal inflammation not visible endoscopically.

Relative Merits of Indium Leucocyte and Gallium 67 Scintigraphy:

Although Gallium 67 has the advantage of a short in vivo preparation time, interpretation of scintigrams may be complicated by the excretion of the isotope into the bowel lumen. In addition, scintigrams taken at 72 hours or longer may be required for adequate assessment. Indium 111 labelled leucocyte scintigraphy has a shorter scan time, 24 hours, and a higher target to background ratio of activity, however in vitro preparation time is 2-3 hours in our hands and the procedure more complex. Thus it is important to obtain information of the relative sensitivity and specificity of the two isotopes in the detection of disease.

FIG. 8:

INDIUM SCAN SHOWING INCREASED UPTAKE IN (a) ILEOCAECAL AREA.
NOTE NORMAL UPTAKE IN LIVER AND SPLEEN. CASE A.



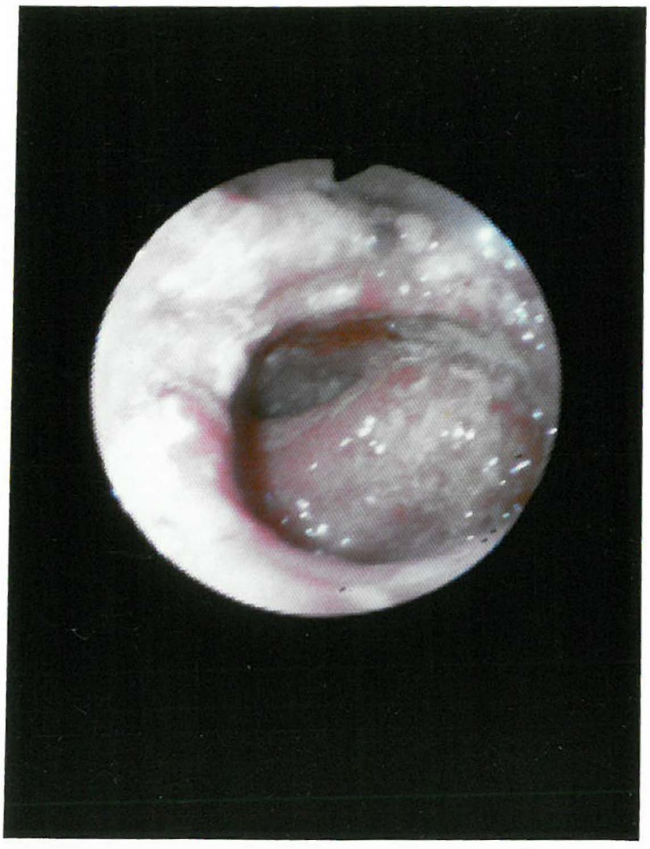


FIG. 9:

CAECAL TUBERCULOSIS.
CASE A.

Information concerning the relative yields of Gallium 67 and Indium 111 scintigraphy in intestinal disease is not available. However, two studies have been reported comparing the use of these isotopes in extraintestinal sites. Sfakianakis et al (109), in a prospective study of 32 patients with suspected focal infection, investigated the sensitivity and specificity of Indium 111 labelled leucocyte scintigraphy compared with Gallium 67 scintigraphy performed 24-48 hours later. One hundred and ninety two sites of possible infection were evaluated and 26 foci of infection were subsequently proved by other diagnostic techniques. The overall sensitivity and specificity for Indium scintigraphy was 73% and 98% respectively, and that for Gallium 81%, and 91% respectively. The results obtained in the present series have been expressed in a similar way to permit comparison.

Of particular interest was the fact that 27% of the false negative Indium scintigrams involved infection of more than 2 weeks' duration and 19% of the Gallium 67 false negative studies were in patients with infection of less than 1 week's duration. The authors suggest, therefore, that Gallium 67 may be the isotope of first choice in chronic (over 2 weeks) infection, while Indium 111 may be the agent of first choice in more acute infections.

McHillop et al (110),in a smaller study of possible infection around prosthetic joints, also confirmed the superiority of Gallium 67 over Indium 111 in chronically infected hips. Abnormal Gallium scintigrams were found in 5 of the 6 patients with subsequently proven infection, whereas the Indium scan was abnormal in only 3. The results of both series although involving small numbers, are in agreement, as pointed out by Sfakianakis et al, with the theoretical consideration that acute sepsis with vigorous leucocyte migration should have a rapid and clear visualization with Indium leucocyte scintigraphy, while those with insufficient white blood cell migration, as in the case of chronic encapsulated abscesses, may have a slow and poor visualization with these scintigrams.

Comparison in Tuberculous Enteritis:

The present study, although involving small numbers enables, for the first time, a comparison to be made between Indium 111 labelled white blood cells and Gallium 67 in the detection of intestinal disease. The results of both isotope series are shown in Table 8 (opposite page 87) where they are related to the findings at endoscopy (either upper gastrointestinal endoscopy or colonoscopy).

The agreement between the isotope techniques is poor (Kappa 0,25) and the results suggest that Gallium 67 is significantly superior to Indium 111 labelled leucocytes in the detection of tuberculous enteritis. In each of the six patients studied, symptoms were present for more than 2 weeks at the time of diagnosis, supporting the contention of Sfakianakis et al that Gallium 67 may be superior to Indium 111 for the assessment of chronic disease defined in their terms.

Conclusion:

Thus both Indium 111 and Gallium 67 have been shown to image tuberculous enteritis and provide evidence of its extent. In addition, it appears thatGallium 67 may be the isotope of choice. This conclusion is, however, based on a very limited number of investigations and must be treated with caution. Although a consecutive series of symptomatic patients was investigated, patient selection may have biased the results. Nevertheless the results obtained are in agreement with theoretical considerations and the conclusions of others. They represent the only information so far available on the comparative use of the isotopes in intestinal disease in general and intestinal tuberculosis in particular.

CHAPTER 7

CLINICAL FEATURES

Signs and Symptoms:

Introduction:

There are no pathonomonic symptoms or syndromes in any form of intestinal tuberculosis (112). Indeed, it is one of the great mimics of many medical, surgical and gynaecological conditions. Some early series even cast doubts as to whether patients with intestinal tuberculosis have gastrointestinal symptoms. Schwatt and Steinbeck (13) in 1923 reported that in 61,5% of 127 patients who had autopsy proven gastrointestinal tuberculosis the disease was not diagnosed in life due to the absence of intestinal symptoms. Granet in 1935 (113) found that only 29% of 800 patients with radiologically diagnosed intestinal tuberculosis had intestinal symptoms and that in 17,5% of those with no evidence of intestinal disease, similar symptoms were present. More recent studies, however, suggest a much better correlation between symptoms and diagnosis (111).

Recent Observations

Two of the largest recent series originate from opposite sides of the globe. Novis et al (36) and Gilinsky et al (31) together analysed the Groote Schuur Hospital, Cape Town, experience of 105 patients with tuberculous enteritis collected over 20 years. Klimach et al (34) performed a similar analysis on 109 cases collected in Blackburn, Lancashire, over 15 years. Results of these studies are shown in Table 9 (opposite page 90).

Both series record other non-specific features such as fever, weight loss and malaise. However, as both series contained patients with co-existing extra-abdominal disease it is not possible to say from the published data to what extent the symptoms occurred in intestinal disease alone. Klimach et al did not detail the abdominal physical signs in their patients.

The Present Series:

In the present series, the abdominal signs and symptoms in the patients with and without intestinal tuberculosis is shown in Table 10 (opposite page 91).

For the purpose of this analysis, the 14 proven cases of gastrointestinal tuberculosis and the 9 further suspected cases are taken together. No significant difference in gastrointestinal symptoms or signs were found in those patients with and without gastrointestinal tuberculosis. This is hardly surprising when one considers the small mucosal lesions that make up the majority of intestinal pathology detected in this series and the fact that symptoms become more frequent as the severity of the intestinal involvement increases (14).

The high incidence of hepatomegaly and diarrhoea found in both groups of patients is unexplained. Stool examination was not included in the protocol of the study and was only

performed in 8 patients by the Clinician in charge of the cases. No bacterial pathogens were isolated. In only one patient in this series was a liver biopsy requested. The histological diagnosis in this instance was one of schistosomiasis. However, of interest is the findings of Maharaj et al (114) in a survey of causes of hepatomegaly at King Edward VIII Hospital, in which 9,2% of clinically unexplained hepatomegaly in a sample of 240 patients was subsequently shown by liver biopsy to be due to hepatic tuberculosis.

Conclusion:

The presence of abdominal symptoms and physical signs is of no help in the identification of those patients with early tuberculous enteritis in a group with severe pulmonary disease.

CHAPTER 8

CONCLUSION

Thus in the present series of 50 patients with open cavitating pulmonary tuberculosis, the presence of intestinal tuberculosis was identified in 14 patients (28%) and suspected in a further 9 patients. The prevalence of proven and suspected cases (46%) is higher than described by Mitchell and Bristol (22) in their cases of "far advanced" pulmonary disease. However, it is doubtful if many of the present cases would have been detected by the single contrast barium follow through examination used by them. Hence the findings in the present series may in fact reflect a lower prevalence when judged by their criteria. Certainly the intestinal disease encountered in the present series, being undetected for the most part by high quality small and large bowel barium studies, is much less severe. The population studied in the present series is so different from that of Mitchell and Bristol that it is not possible to draw any conclusions concerning the overall trend in the prevalence of intestinal disease in the presence of pulmonary tuberculosis. However, a reduced prevalence of intestinal tuberculosis would not be out of keeping with the findings of Mitchell and Bristol, who documented a decline in intestinal tuberculosis from 10% in 1924 to approximately 1% in 1949. In this connection, it is of interest that the rate of intestinal

tuberculosis in the presence of pulmonary tuberculosis at necropsy at King Edward VIII Hospital (13,5%) is lower than comparable figures obtained elsewhere in the first half of the century.

In the present series, proven and suspected intestinal tuberculosis was most frequently encountered in those patients with the severest form of pulmonary disease, being found in 53,3% of patients studied with bilateral pulmonary cavities. In proven cases the majority of the lesions encountered were in the caecum alone (57,1%), while the remainder of the colon was involved in 6 patients (42,9%). In only 1 patient was the colon involved in the absence of caecal involvement. In 4 of the 5 patients with more than one site of large bowel disease, the lesions were discontinuous, i.e. a segmental colitis was present. Small bowel and particularly ileal involvement was striking by its rarity. Two possible examples were diagnosed and only one in the presence of proven tuberculous colitis (Case 28). The reason for this is not clear. It is possible that small ileal mucosal lesions of the type encountered in the large bowel could have been overlooked radiologically. However, the ileum was entered during colonoscopy in 8 of the 23 patients (34,8% with proven or suspected intestinal tuberculosis and apart from the granular mucosa detected in Case 28, this technique confirmed the normal appearances where this was described radiologically.

Nevertheless in the majority of patients with proven intestinal tuberculosis the ileum was not inspected. Even where this was possible, it is conceivable that small nodules could have again been missed. On balance, however, it seems unlikely that the majority of cases of ileal disease would have escaped diagnosis. Thus even allowing for some false negative diagnoses the occurrence of combined ileocaecal involvement in early cases of intestinal tuberculosis would appear to be less frequent than in more advanced disease. This implies that in some cases at least, ileal disease occurs separately from and later than co-existing caecal disease or the infection spreads proximally from the caecum. In this regard it is interesting to recall the work of Rokitansky (10) quoted in the Introduction (page 18) "sometimes it is much advanced in the colon and then appears to have been first developed at this point and subsequently to have extended to the small intestine ".

What then is the reason for this delayed development of ileal compared with caecal involvement ? One possibility is that ileal contents in some way retard the growth and multiplication of tuberculous bacilli. It would, therefore, be of interest to examine the effects of ileal contents on tuberculous bacilli in culture, perhaps looking specifically at some constituents of ileal fluid such as bile salts, comparatively little of which pass on into the large bowel.

The manifestations of intestinal tuberculosis in this series, were mainly small mucosal lesions, consisting of single or multiple mucosal nodules 0,2 - 0,5 cm diameter, resembling sessile polyps, and superficial ulcers. Such nodules were found in 78,6% of patients with proven intestinal tuberculosis. These features probably represent the earliest changes in the development of tuberculous enteritis, so far recorded. Of particular interest, was the recovery of acid fast bacilli, from areas of colonic erythema, where no other lesion was visible macroscopically. In addition, this series differs from those reported previously in the low frequency of ileocaecal valve involvement and luminal narrowing. An important feature in the present series, was the demonstration of acid fast bacilli in colonic biopsy specimens, in 12 patients. One reason for this success was the inclusion of tissue, deep to the mucosa in colonic biopsy specimens. Acid fast bacilli were found in the submucosa, or, lamina propria, in 7 of the 12 cases and caseating granulomata in the lamina propria of a further case. Intestinal tuberculosis in this series was most frequently encountered in those patients with the severest form of pulmonary involvement, being found in 43% of patients with bilateral pulmonary cavities. This finding is in keeping with that of other studies and supports the belief that intestinal lesions have resulted from the ingestion of infected sputum.

This is supported by the comparatively frequent finding, unique to this series, of tubercle bacilli in the mucosa of biopsy specimens (4 of the 12 patients in whom acid fast bacilli were identified). These bacilli may have been detected en route to the submucosa in the manner proposed by Boyde (39) and discussed on page 23. Clearly such a mode of intestinal infection cannot explain the origin of the intestinal lesions in the 3 patients discussed on page 35 and the many like them who have no evidence of pulmonary disease. Thus the mode of infection of patients with intestinal tuberculosis does not appear to be uniform.

Biopsy facilities are one of the principal advantages of fiberoptic endoscopy, when compared with radiographic imaging. It is interesting that in 2 recently published series, those of Klimach et al (34) and Palmer et al (32), involving 151 patients with intestinal tuberculosis, collected since 1973, originating from the United Kingdom, colonoscopy was employed for diagnosis in only 4 patients. Indeed in a letter from the Department of Surgery at the All India Institute of Medical Sciences, Kapoor et al (115), replying to Palmer's paper, claim that the diagnosis of intestinal tuberculosis can only be confirmed at laparotomy. The present series has shown otherwise.

The superiority of colonoscopy over double contrast barium enema has been emphasized by the present series, in which mucosal abnormalities, were identified colonoscopically, in 27 patients, but missed, by double contrast barium enema. Specifically in the 13 patients with proven large bowel tuberculosis and a barium enema examination of good quality, the lesions encountered at colonoscopy, were missed by the barium enema examination, except for the presence of one ulcer, in the descending colon (Case 9). Although barium enema provided additional information about the gross anatomy of the colon in 2 patients with colonic tuberculosis, in no case, was the diagnosis of intestinal tuberculosis, made only by barium enema.

Although colonoscopy and barium enema, may together provide the most complete assessment of large bowel pathology, colonoscopy is undoubtedly, the more accurate technique and no assessment of a patient with suspected intestinal tuberculosis can be regarded as adequate, without it. Moreover, a laparotomy for the purpose of diagnosis in this condition, can only be justified, when colonoscopy has failed to provide the answer. The follow-up of patients with proven and suspected intestinal tuberculosis was poor, but the rate (34%) was comparable to that achieved by other workers at King Edxward VIII Hospital (cf. Appendix A). Complete resolution of the intestinal mucosal lesions, after 6 months

anti-tuberculous chemotherapy, did not occur in 2 of the 6 patients followed up. The significance of these residual mucosal abnormalities, is not known and the patients concerned, are being kept under review. However, residual tuberculous disease cannot be excluded at this stage.

Radionuclide imaging of tuberculous enteritis and a comparison between Indium 111 and Gallium 67 isotope techniques applied to intestinal disease have been described in the present series for the first time. Both Indium 111 and Gallium 67 were shown to detect tuberculous enteritis although the latter isotope was found to be significantly superior, having an excellent correlation with endoscopy. Although the series is small the results obtained agree with theoretical considerations and the outcome of other studies. The technique of Gallium scintigraphy is simple, however, it has the relative disadvantage that the examination may need to be performed over a period of up to three days. The method nevertheless may be of particular value in the assessment of patients too ill to tolerate endoscopy or barium studies and in children where non-invasive techniques may be the methods of choice.

With regard to the symptoms and signs of early gastrointestinal tuberculosis, this series failed to show any

significant difference in those patients with intestinal tuberculosis compared with those without the disease. Thus abdominal symptoms and signs cannot be relied upon to detect early intestinal disease in patients with pulmonary tuberculosis.

It has been recommended that for overt intestinal disease, chemotherapy should be continued for 9 - 12 months, although no controlled trials are available to support this view.

However, with the trend towards shorter periods of anti-tuberculous chemotherapy for pulmonary disease - trials of a 4 month regime have been undertaken - it is uncertain whether early intestinal lesions, will continue to be adequately treated. This point must be borne in mind by those designing and undertaking trials of short term anti-tuberculous chemotherapy. Perhaps more important than this, there is an urgent need for more information on the effect of modern anti-tuberculous chemotherapy on intestinal tuberculosis. This would be provided by an adequate controlled trial. The trial would probably need to be of a multicentre type with long term follow-up to detect possible relapses. This extensive undertaking may need to be co-ordinated and financed by a body such as the Medical Research Council. However, there can be few countries better placed

to initiate such a study than South Africa, a country where "third world" disease goes hand in hand with "first world" expertise. Furthermore, what better Institution could there be to head the list of participating centres than King Edward VIII Hospital ?

APPENDIX A

In the 14 patients with proven intestinal tuberculosis and 3 of the possible cases, attempts were made to see the patients again at 6 months from the date of their original colonoscopy, and to repeat the colonoscopy and any of the radiological or scintigraphic examinations that were previously abnormal. Of the 17 patients, 15 were transferred from King Edward VIII Hospital to the King George V Hospital, Durban, where they received inpatient treatment for periods ranging from 4 - 6 months. Of the remaining 2 patients, 1 patient received inpatient treatment at the Charles Johnson Hospital, while the other patient was treated at the Local Authority Health Clinic in Umlazi, as an outpatient.

Each of the patients received on discharge from King Edward VIII Hospital, a written appointment with a proposed time and date for follow-up, together with a verbal explanation of the importance of keeping the appointment. Each patient treated at King George V Hospital, was visited there either by the author or by the Social Worker attached to the Gastrointestinal Unit at King Edward VIII Hospital, to ensure that he remained aware of the need for follow-up and the arrangements for it that had been made. Despite these efforts only 2 patients attended for follow-up on the appointed date (Cases 7 and 46). Attempts were made to get

into touch with the remaining patients by telephone or telegram at their contact address given at the time of their original admission. These attempts were unsuccessful. Notices were then placed in the press and messages broadcast on the radio. Two broadcasts were made on Radio Zulu during July and August 1986 and two notices appeared in Ilanga, the local Zulu language newspaper, October 1986. Each of the patients who had not at that time been followed up, were identified by name and asked to contact the Gastrointestinal Unit of King Edwdard VIII Hospital. These efforts resulted in a further 4 patients attending for follow-up.

Thus follow-up information is available in 6 patients. In only 1 patient (Case 9) was an initial radiological examination of the gastrointestinal tract found to be abnormal. The findings in this case are discussed on page 54 and involve stricturing and ulceration of the descending colon found on barium enema. However, this patient would not consent to a repeat of this examination and hence follow-up in all cases was restricted to colonoscopy.

All patients were treated for a minimum period of 6 months by one of the Department of Health's approved rifampicin-containing regimens, and showed radiological evidence of healing of their pulmonary disease. The interval between the initial and follow-up colonoscopy ranged from 6-11 months with a mean of 8 months.

A follow-up rate of 35,3% is disappointing, but it is generally agreed that follow-up of outpatients at King Edward VIII Hospital is usually poor. This, however, is not inevitable. In a recent trial of non-steroidal drugs conducted by Rheumatologists in the Department of Medicine, a follow-up of 100% in 20 patients at 6 months was achieved (Naidoo, P.D. Personal communication). These patients with a chronic painful disease required continued treatment, for symptomatic relief, a factor which did not apply in the present study. A more reasonable comparison is provided by a study of amoebic liver abscesses performed in the Gastrointestinal Unit. In this trial after a period of curative treatment, follow-up of asymptomatic patients at 6 months was attempted. This yielded a follow-up rate of 31% (Nel, J. Personal communication).

APPENDIX B

CASE SUMMARIES

CASE NO. 1: AGE: 59 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Multiple filling defects throughout distal small bowel in keeping with ascaris lumbricoides
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal ileum not entered
CONCLUSION:	Ascaris lumbricoides infestation of the small bowel

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CASE NO. 2: AGE: 24 SEX: F

SYMPTOMS:	Constipation, 5 days
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Multiple linear filling defects in distal small bowel in keeping with ascaris lumbricoides
BARIUM ENEMA:	Normal
COLONOSCOPY:	Multiple areas of telangiectasia from rectum to mid transverse colon. Terminal ileum normal. HISTOLOLGY: Scattered degenerate bilharzial ova in lamina propria and trichuris ova on luminal surface.
CONCLUSION:	Infestation with ascaris lumbricoides schistosoma and trichuris sp.

CASE NO. 3: AGE: 48 SEX: M	
SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	5 mm diameter polyp on lateral rectal wall. Otherwise normal
COLONOSCOPY:	No rectal polyp seen. Swollen and red mucosal folds around ileocaecal valve. HISTOLOLGY: Superficial mucosa showing foci of regeneration and mixed inflammation. No evidence of tuberculosis.
CONCLUSION:	Non-specific inflammation of the ileocaecal valve. Ileum not entered
CASE NO. 4: AGE: 51 SEX: M	
SYMPTOMS:	Upper abdominal pain, 3 months
SIGNS:	4 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Red and swollen mucosal fold in duodenal cap. HISTOLOGY: Mild increase in mixed inflammatory cells in lamina propria
SMALL BOWEL RADIOLOGY:	Normal. Good views of terminal ileum not obtained
BARIUM ENEMA:	Normal
COLONOSCOPY:	3mm sessile nodule in caecal pole. No other abnormality seen. Ileum not entered. HISTOLOGY: Mild increase in mixed non-specific inflammatory infiltrate. No evidence of tuberculosis.
CONCLUSION:	Probable caecal tuberculosis

CASE NO. 5 AGE: 28 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Films not of diagnostic quality. Poor bowel preparation.
COLONOSCOPY:	Normal. Ileum not entered.
CONCLUSION:	No intestinal pathology detected.

CASE NO. 6 AGE: 39 SEX: M

SYMPTOMS:	Diarrhoea 1 week, upper abdominal pain 2 months
SIGNS:	3 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum normal
CONCLUSION:	No intestinal pathology detected

CASE NO. 7 AGE: 24 SEX: M	
SYMPTOMS:	Nil
SIGNS:	4 cm hepatomegaly, smooth, firm consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Swollen and nodular caecal mucosal folds with a 2mm superficial ulcer. Ileum entered and normal. HISTOLOGY: Mixed inflammatory cells in lamina propria. No evidence of tuberculosis.
FOLLOW-UP COLONOSCOPY: (after 7 months' treatment)	Caecum drawn up and ileocaecal valve relatively vertical. Normal caecal mucosa
GALLIUM SCAN:	Increased uptake ileocaecal area.
CONCLUSION:	Caecal tuberculosis

CASE NO. 8 AGE: 38 SEX: M

SYMPTOMS:	Diarrhoea and lower abdominal pain, 1 month
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Not diagnostic quality due to poor bowel preparation
COLONOSCOPY:	From splenic flexure to caecal pole multiple areas of red and swollen mucosa with central 1 mm ulceration. Red and swollen ileocaecal valve. Ileum not entered. HISDTOLOGY: Caseating granulomata with acid fast bacilli present in the lamina propria.
GALLIUM SCAN:	Negative
CONCLUSION:	Tuberculosis of caecum, ascending and transverse colon

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CASE NO. 9 AGE: 30 SEX: M

SYMPTOMS:	Nil
SIGNS:	5 cm hepatomegaly, smooth, firm
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Barium follow-through examination normal.
BARIUM ENEMA:	2 cm stricture in descending colon with a single adjacent 1 cm diameter ulcer and spiculation proximal to stricture suggesting further ulceration.
COLONOSCOPY:	1cm ovoid ulcer in descending colon. Swollen and nodular mucosal folds in caecum with superficial o,3 cm ulcers. Ileum not entered. HISTOLOGY: Caseating granulomata in lamina propria
FOLLOW-UP COLONOSCOPY: (after 6 months' treatment)	One irregular superficial ulcer in caecal pole (0,3cm). No evidence of tuberculosis on repeat biopsy.
GALLIUM SCAN:	Increased uptake in ileocaecal area
CONCLUSION:	Tuberculosis of descending colon and caecum

CASE NO. 10 AGE: 44 SEX: M	
SYMPTOMS:	Abdominal pain, central, 3 months
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Diffuse mucosa erythema and swelling in caecum, colon and rectum. In rectum 2 longitudinal superficial ulcers 0,3cm. Ileum normal. HISTOLOGY: Mild increase in chronic inflammatory cells. No evidence of tuberculosis.
CONCLUSION:	Non-specific inflammatory changes in large bowel with rectal ulceration
CASE NO. 11 AGE: 48 SEX: F	
SYMPTOMS:	Abdominal pain, right upper quadrant, 2 months
SIGNS:	3 cm hepatomegaly, small, firm consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis and bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal
CONCLUSION:	No intestinal pathology detected

CASE NO. 12 AGE: SEX:	
SYMPTOMS:	Diarrhoea 1 week
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADISOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Erythematous mucosa in ascending colon and caecum. Ileum not entered. HISTOLOGY: Mild increase in plasma cells in lamina propria. No evidence of tuberculosis
CONCLUSION:	Mild non-specific inflammatory changes in caecum and ascending colon

CASE NO. 13 AGE: 35 SEX: M	
SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Possible adhesions in pelvis. No other abnormality found.
BARIUM ENEMA:	Normal
COLONOSCOPY:	Large bowel enema normal. Ileum entered and normal
CONCLUSION:	No intestinal pathology detected

CASE NO. 14 AGE: 24 SEX: M

SYMPTOMS:	Diarrhoea and central abdominal pain, 3 weeks.
SIGNS:	1 cm hepatomegaly, smooth, firm (biopsy showed bilharzial ova)
CHEST X-RAY:	Unilateral pulmonary tuberculosis, unilateral cavitation
UPPER G.I. ENDOSCOPY:	Red and swollen mucosa and superficial ulceration in duodenal cap. HISTOLOGY: Acute inflammatory exudate with no evidence of tuberculosis.
SMALL BOWEL RADIOLOGY :	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum entered and normal
CONCLUSION:	Duodenitis with no other intestinal pathology detected

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CASE NO. 15 AGE: 25 SEX: M	
SYMPTOMS:	Diarrhoea, 1 week
SIGNS:	2 cm hepatomegaly, firm, smooth, 2 cm splenomegaly
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Oesophagus: multiple adherent white plaques suggesting candidiasis. Stomach and duodenum normal. Biopsy not taken due to technical difficulty
SMALL BOWEL RADIOLOGY:	Some dilatation of small bowel with prominence of mucosal folds in keeping with oedema
BARIUM ENEMA:	Poor bowel preparation. Radiographs not of diagnostic quality.
COLONOSCOPY:	Normal large bowel. Ileum entered and normal.
CONCLUSION:	Oesophageal candidiasis and dilation and mucosal swelling in the small bowel attributed to oedema.
CASE NO. 16 AGE: 33 SEX: M	
SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Proximal mucosal thickening attributed to oedema.
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum entered and normal
CONCLUSION:	No intestinal pathology demonstrated apart from proximal mucosal thickening attributed to oedema

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CASE NO. 17 AGE: 45 SEX: M

SYMPTOMS:	Diarrhoea, 3 months
SIGNS:	3 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Antral erythema and solitary pre-pyloric 5 mm ulcer. HISTOLOGY: Chronic inflammatory cells in lamina propria. One area of ulceration with adjacent regenerative granular activity
SMALL BOWEL RADIOLOGY:	Normal. Terminal ileum not well seen
BARIUM ENEMA:	Normal
COLONOSCOPY:	3 mm shallow circumferential ulcer in transverse colon. Further similar ulcer in upper descending colon with surrounding irregular mucosa. Ileum not entered. HISTOLOGY: Mucosa with minimal inflammatory changes. No evidence of tuberculosis.
CONCLUSION:	Non-specific colonic ulceration and antral gastritis.

CASE NO. 18 AGE: 36 SEX: M

WITHDRAWN DUE TO INCOMPLETE INVESTIGATIONS

CASE NO. 19 AGE: 29 SEX: M	
SYMPTOMS:	Diarrhoea, 3 months
SIGNS:	3 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Areas of submucosal haemorrhage in upper gastric lesser curve. Otherwise normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	In caecal pole, multiple 1 mm superficial ulcers on red and swollen mucosa. Ileum not entered. Remainder of large bowel normal. HISTOLOGY: Mild increased inflammatory cells in mucosa with regenerating surface epithelium and glands. No evidence of tuberculosis.
CONCLUSION:	Non-specific caecal ulceration and gastric submucosal haemorrhages
CASE NO. 20 AGE: 27 SEX: M	
SYMPTOMS:	Diarrhoea, 2 weeks
SIGNS:	Nil
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum entered and normal
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 21 AGE: 36 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
COLONOSCOPY:	Two 5 mm nodules in caecal pole. Ileum entered and normal. HISTOLOGY: Granulomata with acid fast bacilli present in mucosa.
FOLLOW-UP COLONOSCOPY: (1) After 4 months' without treatment	Two 5 mm nodules in caecal pole plus nodularity of a caecal mucosal fold and area below ileocaecal fold. Terminal ileum normal.
FOLLOW-UP COLONOSCOPY: (2) After 7 months' treatment	Normal
GALLIUM SCAN:	Negative
INDIUM SCAN:	Negative
CONCLUSION:	Caecal tuberculosis

CASE NO. 22 AGE: 51 SEX: M

SYMPTOMS:	Nil
SIGNS:	4 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Thickened irregular ileocaecal valve. Single 5 mm nodule in caecum and similar nodule in ascending colon. Ileum not entered. HISTOLOGY: Non-caseating tuberculoid granulomata with acid fast bacilli in submucosa and lamina propria.
GALLIUM SCAN:	Negative
INDIUM SCAN:	Negative
CONCLUSION:	Tuberculosis of caecum and ascending colon

CASE NO. 23 AGE: 53 SEX: M

CASE WITHDRAWN

CASE NO. 24 AGE: 30 SEX: F

SYMPTOMS:	Nil
SIGNS:	Lower abdominal tenderness
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	5 mm white nodule at oesophago-gastric junction, otherwise normal. HISTOLOGY: Mild superficial inflammation and spores of candida.
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Caecum shrunken but mucosa normal
COLONOSCOPY:	One x 5 mm nodule and 2 groups of 1 mm superficial ulcers on red and swollen mucosa in caecum. Terminal ileum normal. HISTOLOGY: Increased numbers of chronic inflammatory cells in lamina propria. Non-caseating tuberculoid granulomata with acid fast bacilli present in the submucosa
GALLIUM SCAN:	Negative
INDIUM SCAN:	Negative
CONCLUSION:	Caecal tuberculosis and oesophageal candidiasis

CASE NO. 25 AGE: 30 SEX: M

SYMPTOMS:	Diarrhoea, 1 week
SIGNS:	2 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Mucosal irregularity at oesophago-gastro junction HISTOLOGY: Normal
SMALL BOWEL RADIOLOGY	Coarse mucosal folds throughout the small bowel in keeping with mucosal oedema.
BARIUM ENEMA:	Normal
COLONOSCOPY:	Two nodular mucosal folds in upper caecum. Ileum not entered. HISTOLOGY: Caseating granulomata with acid fast bacilli present in mucosa.
FOLLOW-UP COLONOSCOPY: (after 6 months' treatment)	Normal
GALLIUM SCAN:	Negative
INDIUM SCAN:	Negative
CONCLUSION:	Caecal tuberculosis and non-specific oesophageal mucosal changes.

CASE NO. 26 AGE: 60 SEX: M

SYMPTOMS:	Diarrhoea, 1 week
SIGNS:	3 cm hepatomegaly, smooth, normal consistency
UPPER G.I. ENDOSCOPY:	White polymorphic plaques on red mucosa in middle and lower third of oesophagus. Otherwise normal. HISTOLOGY: Focal transmural acute inflammation with hyphae and conidia of candida species in superficial layers.
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	3 mm sessile polyp in rectum. In mid-transverse colon, 1 cm diameter area of mucosal irregularity and swelling and 1 x 3 mm nodule within it. 1 cm diameter patch of erythema below ileocaecal valve. Ileum not entered. HISTOLOGY: Rectum polyp biopsy showed features of an adenoma. Caecum and transverse colon showed mucosal congestion in lamina propria
CONCLUSION:	Probable tuberculosis of transverse colon and oesophageal candidiasis.

CASE NO. 27 AGE: 52 SEX: M

SYMPTOMS:	Nil
SIGNS:	5 cm hepatomegaly, smooth, firm
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Patchy areas of telangiectasia scattered throughout large bowel. Ileum not entered. HISTOLOGY: Mild increase in chronic inflammatory cells in lamina propria. Normal vasculature
CONCLUSION:	Non-specific colonic telangiectasia

CASE NO. 28 AGE: 50 SEX: M

SYMPTOMS:	Right upper quadrant pain, 2 weeks
SIGNS:	6 cm hepatomegaly, firm, smooth
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Mild erythema and scattered white plaques in distal oesophagus plus 2 cm sliding hiatus hernia. HISTOLOGY: Normal squamous epithelium.
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Solitary 3 mm nodules present in caecal pole, transverse colon, rectum. Ileum showed granular mucosa. HISTOLOGY: Ileum, increase in chronic inflammatory cells in mucosa. No evidence of tuberculosis. Large bowel, mixed acute and chronic inflammation within mucosa and submucosa with granulomata and acid fast bacilli present in submucosa
GALLIUM SCAN:	Negative
INDIUM SCAN:	Negative
CONCLUSION:	Tuberculosis of caecum, transverse colon and rectum.

CASE NO. 29 AGE: 39 SEX: M	
SYMPTOMS:	Constipation, 2 weeks
SIGNS:	2 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Nodular mucosal fold in caecum with two 2 mm superfical ulcers on red and swollen mucosa. Ileum entered and normal. HISTOLOGY: Non-caseating granulomata and acid fast bacilli present in submucosa.
FOLLOW-UP COLONOSCOPY: (after 10 months' treatment)	Normal
GALLIUM SCAN:	Negative
INDIUM SCAN:	Negative
CONCLUSION:	Caecal tuberculosis
CASE NO. 30 AGE: 61 SEX: M	
SYMPTOMS:	Right upper quadrant, abdominal pain 1 month
SIGNS:	5 cm hepatomegaly, smooth, firm
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavity
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 31 AGE: 33 SEX: M

SYMPTOMS:	Right iliac fossa pain and diarrhoea, 3 weeks
SIGNS:	2 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal terminal ileum not well shown
COLONOSCOPY:	Nodular ileocaecal valve. In ascending colon, an area 2 cm x 1 cm of irregular mucosa and a nodular mucosal fold. Ileum not entered. HISTOLOGY: Granulomata with acid fast bacilli were present in mucosa.
GALLIUM SCAN:	Negative
INDIUM SCAN:	Negative
CONCLUSION:	Tuberculosis of the caecum and ascending colon

CASE NO. 32 AGE: 66 SEX: M

SYMPTOMS:	Nil
SIGNS:	4 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
CONCLUSION:	No intestinal pathology detected

CASE NO. 33 AGE: 20 SEX: M	
SYMPTOMS:	Diarrhoea, 2 months
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Small aphthoid type ulcers present in descending colon
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated
CASE NO. 34 AGE: 32 SEX: M	
SYMPTOMS:	Nil
SIGNS:	Tender right iliac fossa. 2 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Films not of diagnostic quality due to inadequate bowel preparation
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 35 AGE: 35 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	To splenic flexure only, normal
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 36 AGE: 50 SEX: M

CASE WITHDRAWN

CASE NO. 37 AGE: 55 SEX: M

SYMPTOMS:	Diarrhoea, 1 month
SIGNS:	3 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 38 AGE: 22 SEX: F	
SYMPTOMS:	Nil
SIGNS:	2 cm hepatomegaly, normal consistency
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Progression to hepatic flexure only. No abnormality found.
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 39 AGE: 55 SEX: M	
SYMPTOMS:	Diarrhoea, 2 weeks
SIGNS:	3 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Multiple right-sided diverticula
COLONOSCOPY:	Right-sided diverticula HISTOLOGY: Mixed inflammatory cells in lamina propria with regenerative activity in glands.
CONCLUSION:	Right-sided colonic diverticula

CASE NO. 40 AGE: 32 SEX: M	
SYMPTOMS:	Diarrhoea, 2 weeks
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Not diagnostic due to poor bowel preparation
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 41 AGE: 36 SEX: F

SYMPTOMS:	Diarrhoea, 2 months
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Distal ileum was ill defined with loss of normal mucosal coating. Nodularity of terminal ileum, together with ill defined mucosal irregularity.
BARIUM ENEMA:	Nodular filling defects present in ileocaecal region, although mucosa appeared intact.
COLONOSCOPY:	Distal 10 cm of ileum, nodular and ulcerated with transverse and longitudinal superficial ulcers. Caecum was granular with contact bleeding and ileocaecal valve fixed and open. Mucosa of the ascending colon was red. In the splenic flexure an area of mucosa nodularity and multiple 5mm superficial ulcers. In lower rectum a 5 mm moderately deep ulcer. HISTOLOGY: Biopsies from ileum, rectum, caecum and splenic flexure showed ulceration and a non-specific mixed inflammatory infiltrate in the lamina propria. No evidence of tuberculosis.
CONCLUSION:	Probable tuberculous ileocolitis

CASE NO. 42 AGE: 38 SEX: M	
SYMPTOMS:	Nil
SIGNS:	4 cm hepatomegaly, smooth, firm
CHEST X-RAY:	Bilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Longitudinal ulceration in distal oesophagus with 2 cm sliding hiatus hernia. HISTOLOGY: Ulcerated mucosa with mixed inflammatory cell infiltrate and fungal spores and hyphae consistent with candida sp.
SMALL BOWEL RADIOLOGY:	Normal. Terminal ileum not well seen.
BARIUM ENEMA:	Normal
COLONOSCOPY:	Large bowel and terminal of ileum normal
CONCLUSION:	Hiatus hernia and oesophageal candidiasis.
CASE NO. 43 AGE: 67 SEX: M	
SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation.
UPPER G.I. ENDOSCOPY:	Intubation unsuccessful due to micrognathasm
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 44 AGE: 24 SEX: F

CASE WITHDRAWN

CASE NO. 45 AGE: 66 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Not performed due to withdrawal of consent
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 46 AGE: 33 SEX: M

SYMPTOMS:	Diarrhoea, vomiting, central abdominal pain, 1 week.
SIGNS:	2 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Right-sided diverticulae.
COLONOSCOPY:	Caecum normal. In mid-transverse colon, an area of multiple nodules extending for 1 cm longitudinally and bulging into the lumen. HISTOLOGY: Non-caseating tuberculoid granulomata and acid fast bacilli present in the submucosa
FOLLOW-UP COLONOSCOPY:	In transverse colon at previously abnormal site, 3 mm diameter nodules. Large bowel otherwise normal.
GALLIUM SCAN:	Area of increased uptake in ileo-caecal area.
INDIUM SCAN:	Negative
CONCLUSION:	Tuberculosis of transverse colon

CASE NO. 47 AGE: 38 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY :	Mild erosive antral gastritis., HISTOLOGY: Intestinal metaplasia and neuropathy in the lamina propria and glands
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	Erosive antral gastritis

CASE NO. 48 AGE: 48 SEX: F

CASE WITHDRAWN

CASE NO. 49 AGE: 50 SEX: M

CASE WITHDRAWN

CASE NO. 50 AGE: 27 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Oesophagus: Distal linear superficial ulcers and 2 cm sliding hiatus hernia HISTOLOGY: Superficial squamous epithelium with adjacent non-specific acute and chronic inflammation
SMALL BOWEL RADIOLOGY:	Linear intraluminal lucencies compatible with multiple round worms. Small bowel otherwise normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	Oesophagitis with sliding hiatus hernia and round worm infestation of small bowel

CASE NO. 51 AGE: 18 SEX: M

SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Unilateral pulmonary tuberculosis with unilateral cavitation
UPPER G.I. ENDOSCOPY:	Not performed due to withdrawal of consent
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Distal ileum normal. Multiple aphthus ulcers in caecum and ascending colon with a single 5 mm superficial ulcer in transverse colon. HISTOLOGY: Mixed acute and chronic inflammation and oedema in lamina propria. No evidence of tuberculosis.
CONCLUSION:	Non-specific colonic ulceration

CASE NO. 52 AGE: 50 SEX: M

SYMPTOMS:	Abdominal pain 2 days, diarrhoea 4 days
SIGNS:	1 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation.
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Multiple round worms noted in small bowel, otherwise normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Multiple areas of telangiectasia in caecum and ascending colon. Ileum not entered HISTOLOGY: Non-specific superficial inflammatory infiltrate
CONCLUSION:	Non-specific colonic telangiectasia and round worm infestation of the small bowel

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CASE 53 AGE: 59 SEX: M

SYMPTOMS:	Nil
SIGNS:	1 cm hepatomegaly, smooth, normal consistency
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
COLONOSCOPY:	Multiple 2mm - 3mm mucosal nodules in caecum and one similar nodule in transverse colon. Ileum not entered HISTOLOGY: Acute inflammation in mucosa together with caseating granulomata and acid fast bacilli.
CONCLUSION:	Tuberculosis of caecum and transverse colon

CASE NO. 54 AGE: 41 SEX: M	
SYMPTOMS:	Nil
SIGNS:	Nil
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	2 cm hiatus hernia
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Normal. Ileum not entered
CONCLUSION:	No intestinal pathology demonstrated

CASE NO. 55 AGE: 39 SEX: M	
SYMPTOMS:	Nil
SIGNS:	Nil
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Patchy erythema with multiple 1 mm superficial ulcers in caecum. Ileum not entered. HISTOLOGY: Non-caseating granulomata in lamina propria with acid fast bacilli present.
CONCLUSION:	Caecal tuberculosis

CASE NO. 56 AGE: 40 SEX: M	
SYMPTOMS:	Nil
SIGNS:	5 cm hepatomegaly, smooth, firm
CHEST X-RAY:	Bilateral pulmonary tuberculosis with bilateral cavitation
UPPER G.I. ENDOSCOPY:	Normal
SMALL BOWEL RADIOLOGY:	Normal
BARIUM ENEMA:	Normal
COLONOSCOPY:	Patchy erythema in caecum with adult Trichuris worms. HISTOLOGY: A non-caseating tuberculoid granulomata in the submucosa with acid fast bacilli present, plus cross section of worms resmebling Trichuris.
CONCLUSION	Caecal tuberculosis and Trichuris infestation of the large bowel

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