

THE HEALTH OF ILEOSTOMISTS

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ABSTRACT

The aims of the present study were to survey the general state of health of a group of ileostomists, including social, psychological and sexual aspects, and to investigate a range of metabolic functions in the same patients.

The patients studied consisted of 39 subjects who had previously suffered from ulcerative colitis and 12 who suffered from Crohn's disease. A control group of 39 healthy volunteers matched for age and sex with the ulcerative colitis patients had various similar investigations.

The general state of health of the ileostomists was very good. Virtually all were pursuing their normal occupations and recreations. An appreciable number considered that they had received inadequate explanation and guidance before and after the institution of the ileostomy. Psychological abnormalities, as judged by responses to standard inventories, were minor. There was little evidence of physical impairment of sexual activity but psychological problems were not unusual.

The dietary habits of the ileostomists were essentially normal but they consumed more fluid and more salt than the control subjects.

The ileostomists showed evidence of mild dehydration and aldosteronism. Possible methods for correcting these abnormalities are discussed.

There was a mild degree of iron deficiency which was correctable by oral iron supplements. Vitamin B₁₂ absorption was enhanced in the ileostomists who had had ulcerative colitis and possible mechanisms are discussed. There was no evidence of folate depletion.

The ileostomists had increased retention of calcium. This suggests that they were probably deficient in calcium at the time of operation and were slowly correcting the deficit.

Male ileostomists had a high incidence of urinary stones, possibly related to a low pH and volume of the urine and a high level of plasma uric acid.

The ileostomists had a high incidence of gallstones and possible mechanisms are discussed.

The gastrointestinal hormone profile in the ileostomists showed significant differences from normal in the values of motilin, enteroglucagon and neurotensin.

This thesis is dedicated to my father,
the late Dr. Robert Kennedy, who has
been a constant source of wisdom and
encouragement throughout my life. He
died suddenly when the thesis was in
the final stages of preparation.

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STATEMENT OF ORIGINALITY

The work contained in this thesis was undertaken between 1978 and 1981 whilst a MRC Research Fellow in the Nuffield Department of Clinical Medicine, John Radcliffe Hospital, Oxford. This thesis represents a definite contribution to the study of the social, psychological and metabolic consequences of a permanent ileostomy. The large group of ileostomists who took part in the present study were investigated in much greater detail than in any previous study and the use of a group of healthy subjects matched for age and sex to the patients has revealed many metabolic abnormalities not previously detected.

Due to the diversity of the investigations that were carried out it was necessary to collaborate with medical scientists in several centres. The part they played is covered in the Acknowledgements and otherwise all the work was my own.

ACKNOWLEDGEMENTS

I am greatly indebted to Dr. Sidney Truelove for his guidance, help and inexhaustible patience. He has constantly encouraged me and his skill in the art of editing has been an invaluable help during the preparation of this thesis.

I am most grateful to Professor David Weatherall for his advice and support and for my attachment as a research fellow to the Nuffield Department of Clinical Medicine. Dr. Gerry Warner has also helped to supervise the work embodied in this thesis and has been a great source of kindness and encouragement. In particular, he has supervised the studies using the Total Body Counter and given me guidance on the analysis of the data.

Professor Harding Rains kindly agreed to act as my Supervisor for the University of London and I am very grateful to him for his advice.

I should like to thank Mr. Emanuel Lee and Mr. Michael Kettlewell for their interest and co-operation. They had operated on all the patients who were investigated and without their skill and enthusiastic participation the present study could not have been undertaken.

Dr. Wattie Fletcher and the staff of the Radiology Department in Oxford carried out all the radiological and ultrasound examinations. I am very grateful to them.

Dr. Richard Wilkinson has allowed me free access to the Department of Clinical Biochemistry. Many of the investigations undertaken in the present study have involved biochemical analyses and I should like to thank all the staff in the department who have helped me and in particular, Mr. Bill Penfold, Mr. Allen Walker, Miss Angela Giles and Mr. Denis Quantrill.

Dr. Gordon Claridge of Magdalen College, Oxford instructed me in the use of the standard psychological matrices and I am most grateful for his help.

The assays of plasma renin and aldosterone were carried out in the laboratory of Dr. Chris Edwards at St. Bartholomew's Hospital. Dr. David Sarson arranged for the plasma levels of the gastrointestinal hormones to be determined in Professor Stephen Bloom's Laboratory at the Hammersmith Hospital, London. The plasma levels of ferritin were measured at the University Hospital of Wales in Cardiff under the guidance of Dr. Mark Worwood. Dr. John Kanis arranged for Dr. Guy Heynen to measure the plasma levels of parathyroid hormone and calcitonin at the University of Liège, Belgium. Finally, Dr. Juliet Compston measured the plasma levels of 25-hydroxy vitamin D at St. Thomas's Hospital, London. I should like to thank all the doctors mentioned for their help, efficiency, and great enthusiasm. In addition, I am most grateful to the staff of these laboratories for undertaking the assays.

Many thanks are due to Miss Elizabeth Todd for her expert assistance with the dietary study and to Mrs. June Warner

for entering the dietary records into the computer. I am greatly indebted to Mr. Tony Stark for his skill and patience in organising the retrieval of this data from the computer. Mrs. Tessa Fox gave valuable technical assistance with the studies involving the Total Body Counter.

Our secretaries, Miss Rebecca Darnell and Mrs. Shelagh Brooks were always most kind and helpful. I am greatly indebted to Mrs. Zena Jennings for her constant encouragement and in particular for typing the manuscript of this thesis with such skill and dedication.

Finally, my most sincere thanks are due to the patients who have taken part in the many studies that are incorporated in this thesis. They have participated with enthusiasm and have often gone to great lengths to organise their lives to attend for the investigations. They have all earned my greatest respect and have made the period of the study a particularly happy time for me.

The work on which this thesis is based was supported by a project grant from the Medical Research Council, for which I am very grateful.

ETHICAL CONSIDERATIONS

Permission to use the isotopes Ca-47, Fe-59 and Co-58-B₁₂ for absorption studies in the ileostomists being examined on the Oxford total body counter was obtained from the Isotope Advisory Panel at the Department of Health and Social Security

BB

LP2



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Dr S C Truelove
Nuffield Dept of Clinical Medicine
The Radcliffe Infirmary
Oxford OX2 6HE

Your reference

Our reference

H/I68/8-5

Date

31 July 1978

Dear Dr Truelove

Thank you for your letter of 29 June concerning the use of Ca-47, Fe-59 and Co-58-B₁₂ for a research project to study metabolic functions.

The Isotope Advisory Panel are prepared to accept for this purpose your proposal to administer orally, 5µCi of Ca-47, 2µCi of Fe-59 and 0.5µCi of Co-58-B₁₂ to a maximum of 160 adult non-pregnant patients who are living with permanent ileostomy and who apart from the research aspects of the project may themselves benefit from the investigations.

Yours sincerely

A J WHITEBY

The use of these isotopes to measure absorption in healthy subjects was not thought to be justified for the

purposes of the present study because the absorption of calcium, iron and vitamin B₁₂ had all previously been measured in healthy subjects using the Oxford total body counter. The results obtained in these subjects were used as the normal control values for comparison with the results obtained in the ileostomists taking part in the present study.

In addition, the study was approved by the local Ethics Committee and informed consent was obtained from all the subjects before they entered the study.

telephone: Oxford 64811
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OXFORDSHIRE AREA HEALTH AUTHORITY (TEACHING)

Our Ref: RS/HE
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The Nuffield Orthopaedic Centre
Headington
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24th July 1978.

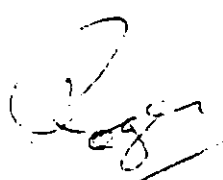
Dr.S.C.Truelove,
Nuffield Department of Clinical Medicine,
Radcliffe Infirmary,
Oxford.

Dear Sidney,

Metabolic Consequences of a Permanent Ileostomy.

I am glad to say that the ethics committee have now considered and approved this study.

Yours sincerely,



R. SMITH.
Chairman,
Ethics Committee.

The Ethics Committee consists of a chairman, consultant surgeon, consultant physician, lay member and nursing

representative. Research projects submitted require answers to the following questions:
responsible investigator, title of project, hypothesis to be tested, design of study, whether informed consent is to be obtained, details of subjects and control groups, details of substances and routes of administration, samples to be taken and possible discomfort to the patients.

CHAPTER 1

GENERAL INTRODUCTION

Proctocolectomy with the formation of a permanent ileostomy is the main operation performed in Oxford, where the work for this thesis has been undertaken, when surgery becomes necessary for the treatment of ulcerative colitis. This procedure is also required in the management of some patients with severe Crohn's disease involving the large bowel. Nearly 200 patients have had this operation carried out in Oxford during the past fifteen years. It is estimated that there are, currently, between 15,000 and 20,000 people with an ileostomy living in Great Britain and Ireland. Taking the world as a whole, there are many thousands of people living with a permanent ileostomy.

The major emphasis of the work carried out in this thesis has been the study of patients who have a well established ileostomy after surgery for ulcerative colitis. These patients are cured of their bowel disease and have an intact small intestine. However, a small number of patients who have had an ileostomy for Crohn's disease have also been studied. These subjects are not cured of their disease and form a less homogeneous group. Therefore, throughout this manuscript, the main results and discussion concern the patients who have had a proctocolectomy with permanent ileostomy for ulcerative colitis. Nevertheless, where appropriate, mention is made of the different problems that may arise when patients with Crohn's disease have an ileostomy.

THE HISTORY OF ILEOSTOMY

Ulcerative colitis used to be a very serious disease because it caused many deaths in previously healthy young adults and created much invalidism. For example even as recently as the period between 1939 - 1949, patients admitted to hospital in Oxford in their first attack had a 20 per cent chance of dying in the first year (Rice-Oxley and Truelove, 1950). It was with the background of this serious prognosis for patients suffering from ulcerative colitis that surgical intervention began to be more widely used for some patients suffering from this disease.

One of the earliest suggestions that surgery might be helpful in the treatment of ulcerative colitis was made by C.B. Keetley of the West London Hospital in 1895. He suggested that appendicostomy should be carried out so that the inflamed bowel could be irrigated through the stoma. However, the first appendicostomy was not performed until 1902 by R.F. Weir, in New York, whose paper was entitled "A New Use for the Useless Appendix in the Surgical Treatment of Obstinate Colitis".

The first operation to create an ileostomy, as part of the treatment for ulcerative colitis, was performed by J.Y. Brown of St. Louis in the United States of America (Brown, 1913). Several years elapsed before this operation became widely used in the treatment of ulcerative colitis. Logan (1919), Stone (1923) and Strauss and his colleagues (1924) were amongst the first to use this procedure in the United States. Its acceptance in Britain took longer despite

Sir Humphrey Rolleston writing in the surgical section of the Proceedings of the Royal Society of Medicine in 1923 that "the radical means of providing physiological rest to the colon is complete transverse ileostomy to exclude the colon". Hurst (1940), Ogilvie (1940), Corbett (1940, 1945) and Maingot (1942) were the main early advocates of this operation in the United Kingdom.

At the same time as Brown was demonstrating the value of ileostomy, Sir Arbuthnot Lane attacked the problem in a different way. In the period between 1909 and 1913 he performed 52 ileosigmoidostomies, followed by a colectomy at a second stage, with only five inpatient deaths. However, the surgical treatment of ulcerative colitis in the first half of this century consisted largely of creating an ileostomy and leaving the colon in place. Unfortunately it was found that the mortality associated with this surgical approach was considerable (Bargen et al, 1932; Cattell, 1935; McKittrick and Miller, 1935; Cave and Thompson, 1941).

It became evident that ileostomy was often being performed in moribund patients and the increasing importance of earlier surgical intervention for ulcerative colitis was stressed by Stone (1929), Jones (1938) and Lahey (1951). In addition, various surgeons, including Cattell (1948), found that closure of the ileostomy was followed by a high incidence of reactivation of the disease, a finding that prompted the aphorism "Once an ileostomy, always an ileostomy".

Peritonitis, haemorrhage, dehydration and embolism were found to be the principal causes of death in ileostomy patients, and it was gradually realised that better results were achieved by resecting the diseased colon. Finally, it was found that there is a greatly increased risk of malignant change in the chronically inflamed colon (Bargen, 1928; Cattell, 1948; Counsell and Dukes, 1952; MacDougall, 1954). Bargen and his colleagues (1954) found that the risk of carcinoma of the colon is approximately 30 times greater in patients with ulcerative colitis than in the general population. As a result of these considerations, it became accepted that a permanent ileostomy should be followed by elective removal of the colon and rectum, which was usually performed as a two-stage procedure.

Gradually the stages were eliminated and finally MacGuire described a one-stage total colectomy and abdominoperineal resection of the rectum in 1940. Ravitch and Handelsman (1951) reported that they had carried out this operation in 12 patients without mortality. The trend towards completing surgery in ulcerative colitis as soon and as completely as possible is typified by the remarks of Counsell and Goligher (1952): "All cases are proceeding to colectomy and ileostomy as a routine and all patients who have had an ileostomy some years ago are being recalled for colectomy and excision of the rectum". Also in this paper Counsell and Goligher report their experience with a one-stage proctocolectomy and ileostomy in four patients all of whom made a rapid recovery. This procedure has since been widely accepted due to the greatly reduced mortality and morbidity that can be achieved.

While these substantial improvements were occurring in surgical technique, a major advance took place in ileostomy care. In 1944 Koenig and A.A.Strauss developed the first adherent rubber appliance (Strauss and Strauss, 1944). Koenig, who was a chemistry student and a patient of Strauss and Strauss, then collaborated with Rutzen to produce the Koenig-Rutzen appliance on a commercial basis. Before this appliance was developed, simple bags and boxes were used which were pressed firmly against the skin. This arrangement sometimes worked fairly well while the patients were up and about during the day but at night, while they were lying down, the ileostomy fluid came into contact with the skin and leakage was common. Further important steps have been taken in stoma care since 1944. Amongst these advances were the introduction of Karaya gum powder and later Karaya rings (Sparberg et al ;1966,) the introduction of Stomahesive (Sircus, 1964; Kyte and Hughes, 1970); and the development of opaque, light weight and odour-proof bags. The formation of ileostomy associations, such as that in the USA in 1951 (Lyons, 1952) and in Britain in 1956, was an important factor in encouraging proper care of an ileostomy. Finally, the realisation of the importance of stoma therapy, with nurses being trained specifically to help stoma patients, is making an important contribution to the care of these patients and their families.

Surgical advances continued to take place. Brooke (1952) described the technique of eversion of the whole thickness of the terminal ileal wall with primary suture of the mucosa to the skin. This simple technique has considerably reduced the morbidity that previously occurred as a result of

scarring and fibrosis of the stoma. In 1969 Kock described his operation of "continent ileostomy", in which an intra-abdominal reservoir is fashioned from the terminal ileum and obviates the need for an external appliance. This procedure is now performed in various specialist centres and Kock (1980) has recently reported on his extensive experience.

Two important aspects of modern care have been advocated by workers in Oxford. The first of these was the introduction of the 'five day intravenous regimen' for acute severe ulcerative colitis which incorporates definite criteria for proceeding to urgent proctocolectomy (Truelove and Jewell, 1974). There is no doubt that a well defined programme for medical treatment, with precise indications for proctocolectomy and ileostomy if the medical regimen fails, has greatly improved the prognosis of patients with a severe attack of acute ulcerative colitis. For example, in a subsequent study of the outcome in 100 severe attacks of ulcerative colitis, there were no medical or surgical deaths (Truelove et al, 1978). This is mainly because the patients came to surgery in relatively good physical and psychological condition.

The second contribution from Oxford was the development of the technique of dissecting the rectum in the perimuscular plane from above and in the intermuscular plane from below (Lee and Dowling, 1972). This has virtually eliminated the bladder and sexual dysfunction which are liable to follow a proctectomy.

Finally, two groups of surgeons have reported their results of an operation which combines an ileal reservoir with an ileo-anal pull-through anastomosis, initially covered by a loop ileostomy (Ferrari and Fonkalsrud, 1978; Parks and Nicholls, 1978; Parks et al, 1980). This procedure is in its infancy and has to be fully assessed but it may be possible for these patients not to have an abdominal stoma if this operation proves to be successful. However, the metabolic consequences of a proctocolectomy are likely to be similar whichever surgical technique is used.

The foregoing discussion has concerned patients suffering from ulcerative colitis. As has already been mentioned it is sometimes necessary to perform proctocolectomy and ileostomy in some patients with severe Crohn's disease of the colon and rectum. Most of the advances in the formation and care of an ileostomy that have been mentioned, also apply to the group of patients with Crohn's disease but there are some differences.

Crohn and his colleagues (1932) established granulomatous enteritis as a clinical entity and the condition is now usually called Crohn's disease. However, the same condition had previously been described by Moynihan (1907), Mayo-Robson (1908) and Dalziel (1913). In the original paper of Crohn and his colleagues (1932) they described the disease as involving the terminal ileum and they called it regional ileitis. However, it was soon realised that the disease could involve any part of the alimentary tract and that small bowel disease could be accompanied by colonic disease (Colp, 1934;

Crohn and Rosenak, 1936). It was later established, especially as a result of the work of Lockhart-Mummery and Morson (1960, 1964), that colonic involvement is quite common in Crohn's disease and that the disease could be confined to the colon, when it is frequently known as primary Crohn's disease of the colon. It is sometimes necessary, particularly when there is severe rectal disease, for a proctocolectomy and ileostomy to be carried out in these patients. It is the practice in Oxford to perform a 'split ileostomy', that is to make an ileostomy but leave the colon in place with a proximal colostomy, on some patients with colonic disease (Truelove et al, 1965). The principles behind this are similar to those previously suggested in the management of ulcerative colitis, namely to rest the bowel and to apply treatment locally to the colonic mucosa. These principles may apply better to Crohn's disease than to ulcerative colitis and it is more important to preserve as much bowel as possible in Crohn's disease in case substantial resections are subsequently necessary. However, some workers have not obtained satisfactory results using this technique and it is not widely used (Oberhalman and Kobutsu, 1971, McIlrath, 1971).

An important factor to mention in this context is that the newer procedures of Kock (1969) and Parks and his colleagues (1978, 1980), are not suitable for patients suffering from Crohn's disease. This is simply because of the substantial risk of granulomatous enteritis occurring in the distal small bowel and particularly in the 'continent pouch'.

MORTALITY

The mortality related to ileostomy surgery has fallen sharply during the course of this century. The improvement in mortality has occurred for several reasons. First, the medical management has improved and the indications for surgery are now well defined. Secondly, surgical techniques have improved as has already been discussed. Finally, general advances have taken place in medicine during the past 50 years, such as the development of clinical biochemistry, the introduction of antibiotics and improved anaesthetic techniques.

When considering mortality related to ileostomy surgery it is best to divide it into immediate mortality, defined as death occurring before the patient leaves hospital, and late mortality defined as death occurring after the patient returns home.

Immediate Mortality

In 1954 Goligher demonstrated that it was possible to reduce the immediate mortality to 2.7% (Table 1.1). The results recorded in this report, when immediate colectomy or proctocolectomy was the operation performed, were in contrast to the results of the previous study of Counsell and Goligher (1952) when the early mortality was 21.6% . In this earlier study, ileostomy alone without immediate colectomy had been the operation performed. Unfortunately, as is shown in Table 1.1, more recent reports have recorded

Table 1.1 Mortality related to ileostomy surgery

1. Immediate:	Date	%Mortality	Authors
	1952	21.6	Counsell and Goligher
	1954	2.7	Goligher
	1966 (a)	11.9	Watts et al
	1968	10.4	Daly
	1972	8.4	Ritchie
	1974	23.7	Ritchie
	1980	6.7	Goligher
2. Late:	Date	%Mortality	Authors
	1968	9	Daly
	1971 (b)	8	Ritchie
	1980	4.6	Goligher

a higher mortality. Ritchie carried out two studies which showed an early mortality of 8.4% in St. Mark's Hospital and a 23.7% mortality in 34 non-teaching hospitals in the North East Metropolitan Hospital Region. These figures are particularly disturbing when it is realised that it is possible to have an immediate mortality as low as the 2.7% reported by Goligher and which corresponds to the mortality in Oxford. However, Goligher (1980) states that "comparison of achievements in different centres where criteria for acceptance of cases for operation may vary significantly is open to fallacy". Nevertheless, by laying down well defined criteria for proceeding to surgery, accepted by both physicians and surgeons, a very low mortality can be achieved.

Goligher (1980) demonstrates another factor in the operative mortality, that is the urgency of the operation. In his personal series of 504 cases he had a 2.8% mortality in elective cases, a 10% mortality in urgent cases and a 23.3% mortality in emergency cases. In Oxford there has been no difference in mortality between the emergency and elective cases.

Late Mortality

The late mortality is also significant, as is shown in Table 1.1. This mortality may be related either to the surgical morbidity (which is discussed later), or to the original disease. There are also some deaths which occur that are not related to the disease or operation. The most common causes of late deaths associated with the disease or

operation include metastases from carcinoma in colitis, widespread Crohn's disease when proctocolectomy has had to be carried out for severe Crohn's disease of the colon (see below), small bowel obstruction or perforation, liver failure, pulmonary embolism and cardiovascular complications. As with immediate mortality, it is possible to reduce late mortality to low levels by good medical and surgical management.

Mortality in ileostomy patients with Crohn's disease

The mortality relating to proctocolectomy and ileostomy in patients with Crohn's disease includes all the problems discussed in the previous section, as well as the intrinsic problems associated directly with this disease. Consideration of these potential complications, particularly co-existent or recurrent small bowel disease, is very important when surgery becomes necessary for disease of the large bowel. There have been few series reporting the prognosis of patients undergoing proctocolectomy and ileostomy for Crohn's colitis. Roy and his colleagues (1970), reporting on their experience with ileostomies found a high mortality in their 110 patients who survived operation for granulomatous colitis. Ritchie and Lockhart-Mummery (1973) and Goligher (1980) reported recurrent disease as a frequent sequel in their patients, although no precise long-term prognosis was determined. There is little doubt that mortality is worse in these patients than in patients having proctocolectomy and ileostomy for ulcerative colitis.

EXPECTATION OF LIFE

Two studies have investigated the long-term prognosis of patients given an ileostomy as treatment for ulcerative colitis (Daly, 1968; Ritchie, 1971b). The findings of these two studies are not the same. Daly (1968) had 358 patients who survived at least one year from the date of the operation and who did not have cancer of the bowel. Nineteen of these patients died subsequently, whereas, using an age and sex matched group of the general population drawn from the Registrar General's Tables, 17.66 people would have been expected to have died. He concludes "I would suggest that this proves that surgery can restore a full life expectancy to a patient suffering from ulcerative colitis". However, in the subsequent survey by Ritchie (1971b), which also excluded the first postoperative year and patients who had had cancer of the bowel, there was a 50 per cent excess mortality over the expected rate. Ritchie's survey did include a few patients with Crohn's disease but only one of these patients subsequently died, so that this inclusion did not account for the excess mortality. In eight out of the 18 patients who made up the observed deaths in Ritchie's survey, the cause of death was considered to be certainly or possibly related to the original disease or its complications, or to the surgery carried out. It seems likely that the excess mortality can be reduced to negligible proportions by the application of modern medical and surgical management.

The long-term prognosis of patients given an ileostomy

for Crohn's disease has already been briefly discussed. Suffice it to say that the expectation of life of these patients is not as good as that of the general population or that of patients with ulcerative colitis treated by proctocolectomy and ileostomy.

GENERAL STATE

Various aspects of the general state of patients living with an ileostomy have been investigated in four main surveys (Watts et al, 1966b; Daly, 1968; Roy et al, 1970; Ritchie, 1971b). They found that the general health of their patients was good but there were differences between the various studies in the findings relating to such aspects as surgical morbidity associated with the formation of an ileostomy and the impact of the ileostomy on the quality of life. In addition, the most recent of these surveys was published ten years ago and there have been considerable changes both in surgical technique and ileostomy care during the last decade.

Four studies have all dealt with the sexual problems that may be experienced by ileostomists but they differ in both their mode of questioning and in the results obtained (Watts et al, 1966b; Daly, 1968; Burnham et al, 1977; Grüner et al, 1977). Finally, there are no reports in the literature of formal psychological testing of patients with an ileostomy.

METABOLIC STUDIES

There is no report in the literature of a detailed metabolic study of a large group of well documented patients.

As has been mentioned, there have been several large surveys of the general health of patients with an ileostomy (Watts et al, 1966b; Daly, 1968; Roy et al, 1970; Ritchie, 1971b). None of these studies included a detailed metabolic survey although Daly collected data on general haematology and biochemistry in 100 patients. Other metabolic studies have dealt with isolated aspects of metabolism, such as water and electrolyte balance (Clarke et al, 1967; Turnberg et al, 1978), or the incidence of nephrolithiasis (Maratka and Nedbal, 1964; Bennet and Hughes, 1972). These and other limited studies are useful contributions and will be considered in detail in the appropriate chapters of this thesis. However, none of them provides a general view of metabolism in a single group of patients. Another limitation of most previous studies is the small number of patients studied and a total lack of data on age- and sex-matched healthy control subjects.

CHAPTER 2

AIMS OF THE PRESENT STUDY

Ileostomy surgery has been undertaken for most of this century but the consequences in terms of both the social and psychological effects and the metabolic changes have not been subjected to much detailed research. As we have seen, there are probably between 15,000 and 20,000 people living with an ileostomy in the British Isles. One of the reasons for the lack of detailed studies has been an understandable preoccupation with trying to reduce the considerable mortality and morbidity that has occurred in these patients. These problems can now be reduced to a minimum and therefore any social, psychological and metabolic problems that occur take on a relatively greater significance. Possibly another reason for the lack of detailed information was the sense of security engendered by the finding of Daly (1968) that the long-term life expectancy of ileostomists approximated to that of the general population provided that they survived the first year after the operation and that they did not have a cancer of the bowel. However, as has been mentioned, Ritchie (1971b) found a 50 per cent excess mortality over the expected rate in her survey of ileostomists.

Surgery to form an ileostomy is being carried out on many people who have a large part of their lives ahead of them. Social and psychological effects may play a significant role during this time and it is possible

that changes in metabolism might manifest themselves by increased morbidity, and possibly even mortality, after a number of years. It is also conceivable that the social and psychological consequences might be minimised by expert care and advice and that the metabolic changes might be reversible at an early stage by simple corrective measures.

The main aims of the present study were as follows:

1. To investigate the general state, social, psychological and sexual aspects of a randomly selected group of ileostomists. These patients were all being cared for in Oxford and details of the history, operation and subsequent course were all available for careful investigation.
2. To attempt to determine the underlying cause for any general, social, psychological or sexual affects and to consider ways in which these might be minimised.
3. To determine the long-term metabolic consequences of proctocolectomy and ileostomy in patients who have had this operation for ulcerative colitis. These subjects are cured of their disease and have had a minimal resection of terminal ileum. It is known that there are early metabolic changes and that it takes some time for the body to adapt to the absence of the colon. For example, 1.5 to two litres of fluid normally passes into the colon from the small intestine but in a patient with a well established ileostomy the volume of ileostomy effluent is about 600 ml (Chapter 7).

It was the aim of the present study to consider the long-term metabolic changes that might occur, and therefore all the subjects taking part had had their operation performed at least one year before entering the study and all were apparently well adapted to life with an ileostomy.

Some functions of the colon are well known. The aspects of metabolism that have been investigated in the present study include some that might be expected to alter after removal of the colon, such as fluid and electrolyte balance. Various other metabolic aspects have been studied such as iron and calcium metabolism. In addition, other fields of interest have been investigated such as the gastrointestinal hormones. The full range of metabolic studies that have been carried out is given in detail in the following chapters.

4. To attempt to determine the cause of any metabolic changes that were found and to consider ways in which these might be corrected.

5. To attempt to shed further light on the normal functions of the colon by studying any metabolic changes that occur in patients who have had a proctocolectomy for ulcerative colitis. This was possible because, as has been mentioned already, these subjects are apparently normal individuals apart from the absence of their large intestine.

6. To study a smaller group of patients who have had an ileostomy performed for Crohn's disease to determine whether their metabolic changes are different from those in ileostomists who originally suffered from ulcerative colitis.

CHAPTER 3

SUBJECTS STUDIED

PATIENTS

Fifty-one patients have taken part in this study. Proctocolectomy with ileostomy was performed in 38 of these for ulcerative colitis, in one for polyposis coli and 12 had an ileostomy for Crohn's disease involving the colon. Three of the 12 patients with Crohn's disease have had the colon left in place and have a 'split' ileostomy; these patients have a terminal ileostomy with the proximal end of the colon brought to the surface as a mucous fistula, so that no faeces pass into the colon. The patient who had polyposis coli is included in the ulcerative colitis group for all the metabolic and some of the general studies.

All the patients taking part in this study were cared for in Oxford and all but two had had all their surgery carried out in the Oxford hospitals. It was therefore possible to obtain histories both from before and after the operation and to acquire accurate information concerning the medical and surgical procedures that had been undertaken. Every patient was leading an apparently normal life with a well established ileostomy that had been formed at least one year before entering the study. The aims and practical requirements of the study were carefully explained to all the patients before they were invited to volunteer to take part.

The patients were chosen at random from the total group of ileostomists, the only factor which influenced their selection being that they were living in Oxford or reasonably close to it, as all of them were required to attend the hospital on at least six occasions. A total of 70 patients were contacted; five of these replied that they could not take part with no reason being given. The remaining 14 patients who could not attend enclosed a covering letter stating that they would have liked to take part but six of them had difficulties with transport, six could not take sufficient time away from work, one was pregnant and one was disabled due to rheumatoid arthritis. This left the 51 patients who subsequently took part in the study. It appears likely that these 51 patients are a truly representative sample of the Oxford group of ileostomists.

All except four of the ulcerative colitis group had less than 10 cm of ileum resected. These four patients had the following lengths of terminal ileum removed: 12cm, 15cm, 20cm and 28cm respectively. The length of small intestine resected in the Crohn's disease group ranged from less than 10cm in six patients to 67cm in the patient who had the longest resection. It was thought that the remaining small bowel was 'normal' in the patients selected for the Crohn's group. The remaining small intestine had been judged to be normal by the surgeon at the time of operation and the subsequent clinical course and investigations (such as radiological examination of the small intestine) were also compatible with this view. However, during the course of the study, two of them were found to have developed recurrent

small-intestinal lesions.

CONTROLS

Thirty-nine healthy control subjects were studied. They were age and sex matched to the patients in the ulcerative colitis group. Twenty-nine of the 36 controls were either the spouse or a first degree relative of one of the patients. Of the remaining ten subjects, five had attended the hospital for minor surgical procedures such as a hernia repair, four were members of the hospital staff and one was a friend of one of the patients. The aims and practical requirements of the study were carefully explained to all the controls before they were invited to volunteer to take part. Each control subject had a medical history taken and was given a full physical examination. All of them were found to be clinically normal.

Table 3.1 summarizes the age and sex data of each group and also records the duration of the ileostomies. It shows that the healthy control subjects were well matched by age and sex with the ulcerative colitis patients. It also shows that the mean duration that the patients had been living with an ileostomy was more than five years, so that they were highly suitable for examining the long-term consequences of this form of life.

LENGTH OF HISTORY AND INDICATIONS FOR SURGERY

The length of history of ulcerative colitis before proctocolectomy with ileostomy was very variable, ranging from a few weeks to 23 years (mean 10.9 ± 7.6 years).

Table 3.1 Age and Sex Data for the patients and normal controls.
Duration of Ileostomy also included.

	MALE	FEMALE	TOTAL
<u>Normal Control Group</u>			
No: of subjects	23	16	39
Age Range	26 - 77	32 - 67	26 - 77
Mean Age $\pm$ 1 standard deviation (SD)	50 $\pm$ 14	48 $\pm$ 11	49 $\pm$ 13
<u>Ulcerative Colitis Group</u>			
No: of patients	23	16	39
Age Range	23 - 80	32 - 65	23 - 80
Mean Age $\pm$ 1 SD	49 $\pm$ 12	46 $\pm$ 12	48 $\pm$ 13
Duration of Ileostomy Range	1 - 15	1 - 13	1 - 15
in years Mean $\pm$ 1 SD	5 $\pm$ 3.7	6 $\pm$ 3.7	5.5 $\pm$ 3.7
<u>Crohn's Group</u>			
No: of patients	5	7	12
Age Range	27 - 74	34 - 66	27 - 74
Mean Age $\pm$ 1 SD	47 $\pm$ 20	45 $\pm$ 16	46 $\pm$ 16
Duration of Ileostomy Range	2 - 9	1 - 11	1 - 11
in years Mean $\pm$ 1 SD	5 $\pm$ 2.5	5 $\pm$ 3.5	5 $\pm$ 3.0

The average length of history in the men was somewhat shorter than that in the women but the difference was not significant (Men 9.11 ± 7.7 years, Women 12.8 ± 7.0 years). There was no appreciable difference between the sexes in the proportion of urgent operations (40% of the men having an urgent operation and 43% of the women).

The indications for surgery in the ulcerative colitis patients are recorded in Table 3.2. There was a much shorter history of colitis in the urgent group, 7.4 ± 6.1 years as opposed to 13.5 ± 7.7 years for the elective group ($p < 0.02$). Forty-two per cent of the operations were classed as urgent. Only five (13%) of these were truly emergencies.

The length of history in the Crohn's disease group was shorter, being 5.2 ± 2.9 years. Four of these operations fall into the urgent category, two of these being emergencies (both toxic dilatation).

STATISTICAL METHODS

Throughout this thesis Student's t test has been used to compare the results obtained in the patients with those in the control subjects.

Table 3.2 Indications for proctocolectomy with ileostomy in patients with ulcerative colitis

			<u>Number of patients</u>
Urgent and Emergency	Early complication	{ Toxic dilatation	2
		{ Perforation	2
		{ Haemorrhage	2
		{ Abscess	1
	Failed Medical Regimen		9
	Total:		16
Elective	Troublesome Symptoms	< Alone	4
		< + long history	11
	Frequent Attacks		2
	Complication	{ Stricture	2
		{ Dysplasia	2
		{ Cancer	1
Total:		22	

CHAPTER 4

GENERAL PHYSICAL STATE

INTRODUCTION

This chapter gives details of the surgical morbidity experienced by the patients who took part in this study. It also includes a section giving the conditions mentioned in the medical history of the patients both before and after the formation of the ileostomy and another section giving the findings of a physical examination carried out on each of them. Finally there is one section recording the standard measurements such as height and weight and another recording the results of routine biochemical and haematological tests.

Surgical morbidity following proctocolectomy with the formation of an ileostomy can be considered under several headings: problems with the stoma itself; failure of the perineal wound to heal; and the development of intestinal obstruction (Table 4.1). Impairment of sexual function may also be a result of surgery but this is discussed in the next chapter. The results shown in Table 4.1 indicate the considerable morbidity that has been reported following proctocolectomy with the formation of an ileostomy. In this chapter, the surgical morbidity found in the ileostomists who took part in the present study is analysed and subsequently compared to the results given in Table 4.1.

Two studies have reported the incidence of general medical conditions following the formation of an ileostomy (Daly, 1968;

Table 4.1 Surgical morbidity following proctocolectomy with the formation of an ileostomy

1.	<u>Ileostomy requiring refashioning</u>	<u>Date</u>	% <u>Morbidity</u>	<u>Authors</u>
		1967	6.0	Daly and Brooke
		1970	9.7	Roy et al
		1971(a)	10.8	Ritchie
		1980	5.0	Goligher
2.	<u>Perineal wound not healed six months after operation</u>			
	(1) Open management	1966(a)	25	Watts et al
		1972	50	Ritchie
	(2) Primary suture	1975	30	Irvin and Goligher
		1978	30	Marks et al
3.	<u>Obstruction</u>	1966(b)	8.4	Watts et al
		1967	9.0	Daly and Brooke
		1971(a)	9.3	Ritchie

Ritchie, 1971b). In this study all the diseases occurring both before and after the operation were recorded. In addition, each patient had a clinical examination and standard measurements were made on all of them; these studies have not been undertaken by other workers. Finally of the four large surveys reviewing the general health of ileostomists (Watts et al, 1966b; Daly, 1968; Roy et al, 1970; Ritchie, 1971b), only that of Daly included the results of routine haematological and biochemical tests. Two small studies involving 14 and 10 patients respectively, have included haematological and biochemical tests (Clarke and McKenzie, 1969; Jagenburg et al, 1971). Singer and his colleagues (1973) studied the biochemistry of 20 patients. In only one of these studies, that of Singer and his colleagues, was there an age- and sex-matched healthy control group. In the present study, routine haematology and biochemistry have been carried out on all the patients and on an age- and sex-matched healthy control group.

SURGICAL MORBIDITY

As mentioned in the introduction, this may be divided into three parts; problems with the stoma, failure of the perineal wound to heal and the development of intestinal obstruction.

Morbidity related to the stoma

Five of the 39 patients in the ulcerative colitis group had had problems requiring refashioning of their ileostomy, that is 13 per cent. Three of these patients had had some stenosis of the stoma, one had had a prolapse and one had

had two episodes of ileostomy recession. Three of the 12 Crohn's patients (25%) required further surgery to their stoma. One of these was for recurrent disease and the other two were for stenosis of the stoma.

Morbidity related to the perineal wound

Twenty-six patients in the ulcerative colitis group healed their perineal wound by primary intention (66.7%). Of the remainder, eight developed an abscess, one (who was a haemophiliac) had a haematoma, and four developed small sinuses. Thirty-six patients (92%) had healed their perineal wound within six months of the operation. The remaining three patients had some minor trouble for more than a year but in all of them the wound finally healed. Nine of the patients with Crohn's disease had a proctocolectomy. Seven of these healed by primary intention. Two patients developed a perineal abscess. One of these healed within six months but the other caused some trouble for more than a year, although the patient's general health and activity were not impaired.

Morbidity related to intestinal obstruction

Two of the ulcerative colitis patients (5%) developed intestinal obstruction secondary to intra-abdominal adhesions. These adhesions were divided at laparotomy with no recurrence. One of the patients with Crohn's disease had a similar problem.

ASSOCIATED DISEASES

Included under this heading are all the conditions mentioned in the medical history of the patients with the

exception of childhood illnesses, minor trauma, appendicitis and tonsillitis. The diseases are divided into two groups depending on whether they were diagnosed before or after the operation. The results are shown in Table 4.2.

The arthritis mentioned was always in association with the history of colitis, although it is interesting that six patients suffered from mild arthralgia after their operation. These six patients were not all the same as those who had arthritis before their operation. Of the patients developing arthritis after the proctocolectomy, two complained of back pain which may have been related to their previous corticosteroid therapy. Gout had been diagnosed in two patients and this is considered in detail in Chapter 10. Three of the ulcerative colitis patients and one of the patients with Crohn's disease had a past history of tuberculosis. Three patients had eczema and one of these has problems with the peristomal skin.

Physical Examination

Each patient had a detailed physical examination but this did not reveal any abnormal findings that had not been diagnosed already. For example, the three patients with a history of hypertension were all found to be mildly hypertensive despite being on anti-hypertensive therapy. Of the six patients who complained of arthralgia after the proctocolectomy, none had overt inflammation of their joints and there was no joint swelling or deformity. One of the three patients who has eczema had inflammation of the peristomal skin but with meticulous stoma care this was kept to a minimum.

Table 4.2 Diseases diagnosed in ileostomists before and after proctocolectomy for ulcerative colitis and Crohn's disease

	Ulcerative Colitis Group 38 Patients		Crohn's Disease Group 12 Patients	
	Pre	Post	Pre	Post
'Arthritis'	6	6	-	-
Gout	2	-	-	-
Ankylosing Spondylitis	1	-	-	-
Eczema	1	2	-	-
Tuberculosis	3	-	1	-
Hypertension	3	-	-	-
Renal Stones	1	-	-	-
Duodenal Ulceration	1	-	1	-
Myocardial Infarction	-	1	-	1

STANDARD MEASUREMENTS

The standard measurements taken and the results obtained are shown in Table 4.3. The span was measured to determine whether the height/span ratio was altered in patients with an ileostomy as compared to healthy control subjects. There are two possible reasons why there might be a reduction in height in patients with an ileostomy. They might have become osteoporotic as a result of corticosteroid therapy for the colitis before the operation, which was carried out on average about 11 years after the onset of the disease, and therefore might have developed crush fractures of their vertebrae. Alternatively, if the ileostomy resulted in a persistent reduction in total body water, this might reduce the fluid content of the intervertebral discs and hence the length of the vertebral column. Neither of these conditions applied to the patients who took part in the present study. There was no significant difference between the heights, spans or height/span ratios of the subjects in the three groups.

The patients with Crohn's disease had a lower mean weight than the normal controls but this difference does not reach statistical significance. The mean weight of the patients in the ulcerative colitis group and the control subjects was very similar. Finally, blood pressure measurements were taken during the physical examination using a standard mercury sphygmomanometer. Measurements were made with the subjects lying and again after standing for one minute. It was thought that, if there were a reduction in the

Table 4.3 Standard measurements in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease, compared with those in a group of healthy control subjects who were age- and sex-matched to the patients in the ulcerative colitis group. The values given are the arithmetic means $\pm$ 1 standard deviation

Variable		Ulcerative colitis group 39 patients	Healthy control group 39 subjects	Crohn's disease group 12 patients
Height	cm	169.7 $\pm$ 10.2	169.7 $\pm$ 8.9	166.1 $\pm$ 10.3
Span	cm	173.1 $\pm$ 10.1	172.3 $\pm$ 10.3	168.0 $\pm$ 10.6
Weight	kg	70.0 $\pm$ 11.9	71.3 $\pm$ 14.5	62.5 $\pm$ 12.3
Blood Pressures mm Hg				
Systolic lying		133 $\pm$ 23	133 $\pm$ 19	132 $\pm$ 21
Systolic standing		124 $\pm$ 20	126 $\pm$ 15	126 $\pm$ 20
Diastolic lying		83 $\pm$ 11	82 $\pm$ 11	82 $\pm$ 14
Diastolic standing		82 $\pm$ 10	81 $\pm$ 9	82 $\pm$ 11

intravascular sodium and water volume in ileostomists, there might be a larger postural drop in blood pressure in the patients with an ileostomy than in the healthy control subjects. As is shown in the Table, there was no significant difference in the blood pressure readings between any of the groups.

ROUTINE BIOCHEMISTRY AND HAEMATOLOGY

Biochemistry

A routine twelve channel biochemical profile was carried out on a blood sample from each patient. The equipment used for this purpose in Oxford is a Vickers M 300 discrete analyser. The results obtained from this analysis are shown in Table 4.4. These measurements were broadly similar between the three groups but there are several interesting observations that may be made. There is no statistically significant difference between any of the values normally referred to as the urea and electrolytes (that is the top six variables in Table 4.4). This finding corresponds with the results obtained by other workers. In particular, it is worth noting that the serum potassium and bicarbonate values were normal. These findings are discussed in more depth in Chapter 7 in which water and electrolyte balance is considered in detail.

Referring again to Table 4.4, the calcium and phosphate levels were similar in the three groups and the metabolism of these substances is discussed in Chapter 9. Both the total protein and albumin values were significantly higher

Table 4.4 A 12 channel plasma "Biochemical Profile" in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to that in a group of healthy control subjects age- and sex-matched to the patients in the ulcerative colitis group. The values given are the arithmetic means $\pm$ 1 standard deviation

Variable	Ulcerative Colitis Group 39 Patients	Healthy Control Group 39 Subjects	Crohn's Disease Group 12 Patients
Sodium mmol/l	141.9 $\pm$ 3.0	141.2 $\pm$ 2.4	141.2 $\pm$ 2.9
Potassium mmol/l	3.90 $\pm$ 0.70	4.00 $\pm$ 0.71	4.02 $\pm$ 0.52
Chloride mmol/l	102 $\pm$ 3	102 $\pm$ 2	100 $\pm$ 3
Bicarbonate mmol/l	26 $\pm$ 5	25 $\pm$ 5	28 $\pm$ 4
Urea mmol/l	5.7 $\pm$ 1.1	6.3 $\pm$ 1.9	5.3 $\pm$ 1.5
Creatinine μ mol/l	83 $\pm$ 21	84 $\pm$ 17	75 $\pm$ 18
Calcium mmol/l	2.45 $\pm$ 0.14	2.40 $\pm$ 0.09	2.40 $\pm$ 0.13
Phosphate mmol/l	0.98 $\pm$ 0.20	0.88 $\pm$ 0.16	0.99 $\pm$ 0.16
Total protein g/l	74.8 $\pm$ 4.8 ^{***}	70.1 $\pm$ 4.3	71.5 $\pm$ 4.0
Albumin g/l	44.2 $\pm$ 2.9 [*]	42.7 $\pm$ 2.2	41.3 $\pm$ 3.0
Bilirubin μ mol/l	10.15 $\pm$ 3.98	11.41 $\pm$ 4.98	12.58 $\pm$ 8.35
Alkaline phosphatase iu/l	211.7 $\pm$ 64.1 [*]	181.9 $\pm$ 40.1	232.0 $\pm$ 55.2 ^{**}
Aspartate transaminase iu/l	26.1 $\pm$ 10.5	22.4 $\pm$ 8.4	24.8 $\pm$ 10.7

* = $p < 0.02$

** = $p < 0.01$

*** = $p < 0.001$

in the ulcerative colitis group than in the healthy control subjects. It is said that a raised serum albumin is only found in patients who are dehydrated, although it may be raised artefactually if the blood sample is taken after prolonged venous stasis (Zilva and Pannall, 1979; Varley et al, 1980). In the present study, the blood samples were taken without prolonged stasis and, in any case, they were collected in an identical manner from the patients and the control subjects. The raised total protein and albumin values are considered further in the discussion at the end of this chapter and also in Chapter 7.

Two of the last three substances in Table 4.4, namely the plasma bilirubin and aspartate transaminase levels, were not significantly different between the patients and control subjects. However, the mean plasma alkaline phosphatase level was significantly raised in both the ulcerative colitis and the Crohn's disease groups as compared to the healthy control subjects ($p < 0.02$ and $p < 0.01$ respectively). One patient in the ulcerative colitis group and one of the control subjects were excluded from this analysis as they both were found to have considerably raised plasma alkaline phosphatase levels due to Paget's disease. With the exception of this one patient there were no others who had a level above the upper limit of normal. It is uncertain whether the source of this generalised rise in plasma alkaline phosphatase is the liver, the bones, or the bowel.

There is a well-known association between ulcerative colitis and chronic liver disease. Apart from the raised alkaline phosphatase, which may be coming from the liver, the mean values of the other liver function tests measured as part of the biochemical profile (bilirubin, aspartate transaminase and albumin) show no evidence of liver disease. However, in this context, it is important to consider the results in individuals in addition to the overall mean values for the group. No patient either in the ulcerative colitis group or in the Crohn's group was found to have abnormal liver function tests. In addition, the prothrombin time, which is frequently prolonged in chronic liver disease, was normal in all the patients, except for the one patient with haemophilia.

Haematology

A routine full blood count and ESR were carried out on a sample of blood from each patient and healthy control subject. Serum and red cell folates were measured in all the patients, as was the prothrombin time. Iron metabolism, vitamin B₁₂ metabolism and folate levels are dealt with in detail in Chapter 8. Table 4.5 gives the mean values for the full blood count and ESR in the three groups. The male and female subjects are considered together in each group for the sake of clarity as it was found that similar changes were occurring in both male and female ileostomists. It may be seen that there was no significant difference between the measured mean haemoglobin value of the ileostomists who had had ulcerative colitis and the healthy

Table 4.5 The mean results of a full blood count and ESR carried out on a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the patients in the ulcerative colitis group. The values given are the arithmetic means $\pm$ 1 standard deviation

Variable	Ulcerative Colitis group 39 patients	Healthy Control group 39 subjects	Crohn's Disease group 12 patients
Haemoglobin g/dl	14.4 $\pm$ 1.5	14.1 $\pm$ 13.1	12.9 $\pm$ 1.4**
Corrected haemoglobin g/dl	13.4 $\pm$ 1.4*	14.1 $\pm$ 13.1	12.1 $\pm$ 1.3****
Mean corpuscular volume fl	86.1 $\pm$ 4.4****	89.6 $\pm$ 3.8	89.1 $\pm$ 6.2
Mean corpuscular haemoglobin pg	29.5 $\pm$ 2.0***	30.7 $\pm$ 1.5	30.1 $\pm$ 2.6
Mean corpuscular haemoglobin concentration g/dl	33.9 $\pm$ 1.1	33.8 $\pm$ 0.9	33.6 $\pm$ 1.0
Erythrocyte sedimentation rate mm in one hour	7.5 $\pm$ 6.5	6.3 $\pm$ 5.1	19.3 $\pm$ 14.5***

* = $p < 0.05$

** = $p < 0.02$

*** = $p < 0.01$

**** = $p < 0.001$

controls; whereas the mean value for the patients with Crohn's disease was significantly low. However, if the haemoglobin values are corrected for the apparent haemoconcentration demonstrated by the higher total protein in ileostomists who had had ulcerative colitis as compared to the healthy controls (a factor of 6.81%), then both groups of ileostomists are found to have a significantly lower haemoglobin concentration than that found in the healthy control group. In addition, the ileostomists who had had ulcerative colitis had a significantly lower mean corpuscular volume (MCV) and mean corpuscular haemoglobin (MCH) than the control group. This indicates that the red cells in these patients are small and contain less haemoglobin than in health. However, the concentration of haemoglobin within each cell appears to have been normal, as there was no significant difference in the mean corpuscular haemoglobin concentration (MCHC) between the ileostomists and the healthy controls. These findings all suggest that the ileostomists were mildly iron deficient.

If the haemoglobin values in individual patients are studied then two men but no women in the ulcerative colitis group were anaemic (taking a lower limit of normal for haemoglobin concentration as 13.0 gm/dl in men and 12.0 gm/dl in women and not allowing for haemoconcentration). If allowance is made for haemoconcentration then three of the women would also be considered to be anaemic. One of these women said that she had required intermittent courses of oral iron because she periodically did become anaemic.

The final result shown in Table 4.5 is the erythrocyte sedimentation rate (ESR), which may be considered as an indicator of inflammation. The ESR was not raised in the ulcerative colitis group which helps to confirm that the disease has been cured and the minor arthralgia reported by some patients (see the section dealing with associated diseases) was probably not directly related to the colitis.

As has been mentioned already, the prothrombin time was found to be normal in all the patients. This was measured partly to assess liver function (see section on biochemistry) and partly because it is known that the colonic bacteria synthesise vitamin K and that a substantial part of the normal body requirements are obtained from this source. Vitamin K plays an essential role in the synthesis of clotting factors II, IX and X. It was thought possible that, in the absence of the colon, vitamin K might become deficient. This was not established in these ileostomists. However, it is possible that under conditions of 'clotting stress', such as after a major injury, vitamin K might become deficient sooner than in a normal individual.

Referring back to Table 4.5 to consider the results obtained in ileostomists with Crohn's disease, three of the seven women were anaemic on direct measurement and, if correction is made for dehydration, this number rises to five. None of the men were anaemic on direct measurement but two were anaemic if haemoconcentration is taken into account. The measured mean value shows these subjects to have a significantly lower haemoglobin than the controls and

the difference is even more significant after allowing for haemoconcentration. The cause of this anaemia will be considered further in Chapter 8. The mean value of the ESR is significantly raised ($p < 0.001$) in these patients as compared to the healthy controls. Four of the patients had a value over 20mm/hour (being 21, 30, 43 and 50 respectively). All of these four patients had had a proctocolectomy and apparently had no residual disease. However, one of them has subsequently had to have an ileal resection for a recurrence of her Crohn's disease. The other three patients remain well. The prothrombin time was normal in all the ileostomists with Crohn's disease.

DISCUSSION

Surgical morbidity following proctocolectomy with the formation of an ileostomy remains a considerable problem as may be seen from the results already presented in Table 4.1. Problems related to the stoma itself have become much less frequent since the introduction of the technique of full-thickness eversion of the ileostomy stump (Brooke, 1952). However, problems still arise, as is shown in the present study in which 13 per cent of the ulcerative colitis group patients and 25 per cent of the Crohn's group patients have required refashioning of their ileostomy. Nevertheless, if this degree of morbidity occurs with a conventional stoma, it seems possible that there will be an even greater morbidity associated with the more complicated Kock and Park's procedures.

Referring again to Table 4.1, even in the most recent report from St. Mark's Hospital, 30 per cent of the patients

had not healed their perineal wound six months after the operation. The results obtained in the patients who took part in the present study are encouraging; 92 per cent of these patients had healed their perineal wound by six months after the operation; however, only 66.7 per cent of the patients healed this wound by primary intention, the remainder having minor perineal abscesses, haematomas or sinuses. The morbidity associated with this wound may be reduced to low levels by good surgical technique and the modern use of suitable antibiotics to control both aerobic and anaerobic organisms.

Finally the morbidity occurring from intestinal obstruction was only five per cent in the patients who took part in the present study. Table 4.1 gives figures of 8.4, 9.0 and 9.3 per cent respectively. Once again, this complication continues to be an appreciable risk. If the morbidity associated with the stoma, perineal wound and intestinal obstruction are added together, the overall morbidity suggested by the results given in Table 4.1 is considerable. Mainly due to the good results obtained with the perineal wound, the overall surgical morbidity in the patients who took part in this study was less than that suggested in the Table. With good medical, surgical and nursing care it is now possible to reduce the surgical morbidity to low levels.

In a detailed survey of the medical histories of 100 patients, Daly (1968) found no associated diseases apart

from cirrhosis of the liver, which was found in three patients and was thought to be related to the previous colitis. Ritchie (1971b) also found no associated disease with the exception of a 4.3 per cent incidence of renal calculi. Two other groups of English ileostomists have been surveyed for the incidence of renal stones and no increased incidence was found in either group (Alexander, 1970; Goligher, 1980). In the present study, no definite associated disease emerged from interviewing the patients and examining their case notes. However, in this context, the number of patients is small. The six patients who were troubled by 'arthritis' only had minor intermittent arthralgia with the exception of the two with back pain. Subsequent chapters will demonstrate that associated conditions can be found in ileostomists when detailed investigation is undertaken.

Both the physical examination and standard measurements carried out on each patient showed that they were all in good physical condition. The ileostomists who had had their operation for ulcerative colitis were of normal weight and in fact a number of them complained that they had to be careful not to become overweight. The blood pressure measurements did not demonstrate an abnormal postural blood pressure drop. This may be because the haemoconcentration, suggested by the high plasma protein levels, is mild and the reflex mechanisms for blood pressure control can probably compensate for this small change. It is possible that the increased incidence

of postural hypotension experienced by the elderly in the general population will be even more marked in elderly ileostomists.

The results of the routine biochemical and haematological tests were very interesting as has been shown earlier in this chapter. The raised plasma protein levels and abnormal haematological indices correspond well to the findings of more detailed studies and will be discussed more fully in Chapters 7 and 8. The main point of interest is the demonstration of the value of an age- and sex-matched healthy control group. Without these subjects none of these abnormalities would have been detected.

CHAPTER 5

SOCIAL, PSYCHOLOGICAL AND SEXUAL ASPECTS

INTRODUCTION

The general health of patients surviving ileostomy surgery for ulcerative colitis has been thought to be very good. This is exemplified by the results of three studies all of which found that patients assessed their own general health as being good or excellent in 87 to 96 per cent of cases (Watts et al, 1966b; Daly, 1968; Roy et al, 1970). The patients taking part in the present study have also been asked for an assessment of their own general health. The social consequences of having an ileostomy have been studied in the same three surveys (Watts et al, 1966b; Daly, 1968; Roy et al, 1970). The most recent of these was published ten years ago, and so it was thought that a further detailed review of the social consequences of an ileostomy would be valuable.

As has been mentioned previously, there are no reports in the literature of formal psychological testing of patients with an ileostomy. It was considered important as part of an overall study of ileostomists that a formal psychological assessment should be made. The results of this assessment are recorded in this chapter. In addition, a survey of the sexual function of this same group has been undertaken; the results are discussed in conjunction with those of several previous studies which have shown considerable sexual problems in ileostomists (Watts et al, 1966b; Daly, 1968;

Dlin et al, 1969; Burnham et al, 1977; Gruner et al, 1977).

PATIENTS' OWN ASSESSMENT OF THEIR STATE OF HEALTH

Thirty-four (87%) of the patients in the ulcerative colitis group reported that their general health was good or excellent. Four (10%) said that it was fair and the remaining patient claimed that her health was poor. Two of the four patients who said that their health was only fair had other medical problems; one had osteoarthritis of the spine and the other had diabetes mellitus. The remaining two patients were both women who found it very difficult to accept life with an ileostomy. The woman who considered herself to be in poor health also found life with an ileostomy difficult. On physical examination, all three were in good general condition and have experienced few physical problems with their stomas.

All except one of the patients with Crohn's disease said that their general health was good or excellent. The one patient who said that her health was only fair had had considerable problems with her disease prior to her proctocolectomy and she was the one who had had the largest small-intestinal resection. Nevertheless, since her proctocolectomy she had not experienced any major problem and, at the time of examination, she had no evidence of residual or recurrent disease.

PATIENTS' OWN ASSESSMENT OF THEIR OPERATIVE PERIOD

It has been realised for a long time that the preoperative

and early postoperative medical and nursing care is an important factor in the successful adaptation of patients to life with an ileostomy. This view has been accepted in Oxford for many years and the medical and nursing staff have attempted to give this type of care despite great pressures of general medical and nursing work. However, it is only in the past 18 months that a stomacare nurse has been appointed in Oxford. All the patients taking part in the present study were operated on before the stoma care nurse took up her post. As part of the questionnaire, each patient was asked for their assessment of the preoperative or early postoperative care that they received. All the patients said that they were very grateful for the help that they had been given and did not wish to complain. However, it was explained to them that it was important to study this aspect of care so that any necessary improvements could be made in the future. It must be stressed that nearly all the patients were seriously ill at the time of their operation and that some of the answers given may be inaccurate as a result.

Each patient was asked if a doctor had explained what an ileostomy is and how it works. Thirty-six out of the 51 patients said that a doctor had explained. (One of them was upset at the time as she had been told about the operation and the formation of the ileostomy in front of several medical students). Seven patients judged that they were too ill for a proper explanation to be comprehended and eight patients thought that no explanation had been given. In reply to the question "Do you think that the doctor gave

you a true idea about the problems of having a permanent ileostomy" ? Only 19 patients said "Yes". Thirty-one patients thought that the ileostomy had been discussed with members of their family before the operation. Five of these thought that the explanation given to their families had been inadequate. Three patients said that they did not have a close relative available for explanation, but that still leaves 17 patients who thought that no explanation had been given to a close relative.

It has been the policy for many years in Oxford for patients about to have a proctocolectomy and formation of an ileostomy to meet an ileostomist before the operation. This is not always possible if the patient is very ill and the operation is being performed as an urgent procedure. Only 22 patients said that they had met an ileostomist before the operation. Of these patients, one was upset by such a meeting; one was introduced to another patient on the ward who had complications; but the remaining 20 patients thought that this meeting was very helpful.

The patients were then questioned about their postoperative care. Thirty-two patients thought that the care during this period had been very good. Eight said that they had not changed their own appliance while in hospital and three more said that they had had to change it for the first time without help. Two of the men have never changed their own appliance because their wives do it for them! Four patients said that, although the nurses tried hard to help, some of them did not seem to know how to change an ileostomy bag; this led to a bag bursting on one occasion. Four

patients said that they were frightened to look at the stoma when they first woke up after the operation.

On returning home, many patients said that they were anxious and seven found it particularly difficult. Comments such as "it was like taking home a new baby", "I took well over an hour to change my bag when I first got home", "I just broke down and cried" and "I found that neither my general practitioner nor the district nurse really knew about ileostomies". Many said that a home visit by a stoma nurse soon after they had arrived home would have been most helpful. Many others found no difficulty when they left the hospital. A summary of these findings is given in Table 5.1.

The overall impression given by the patients was that they thought that everyone who had cared for them had tried hard under difficult circumstances. Nevertheless, these findings are far from ideal and they are considered further in the discussion at the end of this chapter.

OCCUPATION

Thirty-four of the 38 patients (89.5%) who had had ulcerative colitis were fully employed. Three were retired because of age and one man had not returned to work as a packer because of osteoporosis of the spine. It must be said that his general health was otherwise good and he could have sought a lighter job. He was an Italian with a large supportive family who preferred that he should stay at home to "direct operations"! The women were regarded as being fully employed if they were carrying out

Table 5.1 A summary of the patients' own assessment of their operative period

Questions asked (Question 6 is a summary of several questions)	Patient replies expressed as percentages	
	Yes	No
1. Did the doctor explain what an ileostomy is and how it works ?	71	29
2. Did the doctor give you a true idea about the problems of having a permanent ileostomy ?	37	63
3. Did anyone discuss the ileostomy with your family before having the operation ?	61	39
4. Did you meet anyone with an ileostomy before your operation ?	43	57
5. Did you practice changing the bag before you went home ?	84	16
6. Was every part of your postoperative care satisfactory ?	63	37

their housework and caring for their families. In addition to this, five out of the 16 women were engaged in either full or part-time employment.

Twenty-seven out of the 34 working people said that the surgery and resulting ileostomy made it easier to do their work than it had been when they had ulcerative colitis. Six of the patients said that there was no change and one patient said that the ileostomy made his work more difficult. He was an executive who had lost some of his self-confidence. He found his frequent journeys abroad difficult because he was constantly worried that customs officers would find his ileostomy appliances and equipment in his baggage. Seven of the patients thought that their chances of promotion had been adversely affected by the ulcerative colitis but nobody had lost their job due to the disease. Except for the executive already mentioned, all the patients thought that their ileostomy did not affect their chances at work. Nobody had had to change jobs because of the ileostomy; in fact, two of the patients had heavy manual jobs and one was a lorry mechanic.

It is interesting at this point to mention one aspect of the psychological assessment, which is otherwise dealt with later. Several of the patients with high intelligence quotients are carrying out jobs which require only limited intelligence. There are no control data for this finding but there is no doubt that a similar situation also occurs in the general population. For example, the winner of the Mastermind contest on BBC television (1980) was a London taxi driver.

Ten of the 12 patients with Crohn's disease were fully employed and the remaining two had retired because of age. Seven out of the ten working people thought that the surgery had made it easier for them to do their work while the other three found no difference. Three out of the ten working people thought that the Crohn's disease either had adversely affected their chances of promotion or would have done so if the operation had not been performed. None of these patients thought that having an ileostomy affected their chances of promotion

SOCIAL AND SPORTS ACTIVITIES

Most of the patients thought that their social life was improved compared to the life that they had been able to lead with their inflammatory bowel disease. Thirty of the 38 patients (78.9%) who had had ulcerative colitis considered that they led a normal social life. The remaining eight people felt uneasy in public places due to their stoma, most of them being worried by the noise it might make. Four of the 12 patients with Crohn's disease had similar apprehensions.

Sporting activities were very variable, ranging from squash and badminton to deep sea fishing. One man was building himself a new house. None of the patients was still taking part in contact sports, such as soccer or rugby football (this is the one type of activity that they are advised to avoid). Sixteen people in the ulcerative colitis group liked to swim but four of them had stopped completely because of their ileostomy. Five out of the

six swimmers in the Crohn's group had stopped swimming for the same reason.

Three patients had not told their children about the ileostomy; three had not told their employer and five had not told their colleagues at work. Most of the patients said that some of their friends know about the stoma; however they tended to tell only the people whom they knew well. Several patients said that it would be helpful if there were greater public knowledge and acceptance of stomas.

Twenty-four of the 51 patients used a black rubber appliance, the remaining 27 used the more modern plastic disposable bags. The patients using the rubber bag claimed that they felt more secure using this appliance and that the outlet was better. One female patient said that she preferred the rubber appliance but wished that it was white rather than black. It must be remembered that several of these patients had their ileostomy formed many years ago when the disposable plastic bags were not available. It seems that ileostomists get used to one type of appliance and tend to continue using it. Most of the new ileostomists in Oxford now immediately start using one of the disposable plastic appliances. Two patients said that they preferred the non-disposable rubber bags when travelling abroad because plastic appliances were sometimes hard to obtain and their disposal was sometimes difficult.

ATTITUDE OF THE PATIENTS AND THEIR FAMILIES TO THE ILEOSTOMY

The attitude of the patients to their ileostomy was

assessed by asking the question shown in Table 5.2. Each patient was asked to say yes or no to all the statements listed. Ninety per cent of the patients in the ulcerative colitis group and all the patients in the Crohn's disease group said that they had got used to it. However, 41 per cent and 25 per cent respectively found that their stoma was a nuisance. In addition, 18 per cent of the patients in the ulcerative colitis group and one of the patients with Crohn's disease (8%) stated that they actually hated their stoma. One patient wondered whether she would have preferred to have died rather than have a stoma. This particular patient seems to be very similar to the patient described by Daly (1968) who "appeared to gain satisfaction from regarding herself as an invalid".

The number of patients may be insufficient to draw firm conclusions about the different attitudes of the men and women (28 men and 23 women took part in the study). In any case it is interesting to find that a higher percentage of women said that they hated their stoma and also that they did not want anyone to know about it. A larger number of men than women stated that their stoma smelt; this may have been either because they take less trouble looking after it or because the appliance is more liable to become detached from the skin in men as more of them are carrying out heavy manual tasks.

Attitude of the family to the ileostomy

All the married ileostomists, with the exception of one, found that their spouse was most supportive and helpful

Table 5.2 Attitude of the patients to their ileostomy

The question asked was as follows:

How would you categorise your current attitude to having a stoma ?

	Ulcerative Colitis Group	Crohn's Disease Group	Total Group	
	%	%	Male %	Female %
1. I hate it	18	8	11	22
2. Its a nuisance	41	25	39	35
3. It smells	13	8	18	4
4. I have got used to it	90	100	93	91
5. It stops me from doing important things	10	-	7	9
6. I do not want anyone to know about it	18	-	7	22
7. I wish that I had never had the operation	23	-	-	24

over the operative period and particularly when the patient first returned home. The first few days at home seem to be one of the most difficult periods and there is no doubt that a supportive spouse at this time is of great help. The one patient who said that her husband did not help was about to be divorced at the time of operation and it seems likely that neither the ulcerative colitis nor the ileostomy affected the home situation. Nearly all the other patients said that their spouse accepted the stoma well and that they were all very pleased that the patient should be well after suffering from a severe illness. It seemed that the chronic colitis had put some of the marriages under considerable stress and that the improvement in health resulting from the ileostomy actually helped many of these marriages.

With regard to the patients' children, all of them without exception appeared to accept the stoma readily and several of them had said that they would like to try one for themselves. In one family the stoma was known as "Ossy".

"MY IDEAL BATHROOM"

Each patient was asked whether there were any improvements that could be made to their house or whether there were any features of their home that they particularly valued. The replies were almost totally confined to the toilet and washing facilities. The following section sets out what seems to be an ileostomist's "dream bathroom", based on the ideas of the 51 ileostomists who took part in the

present study.

The bathroom needs to be of reasonable size so that there is room to move about but it should not be too large to be heated easily. It needs a good background heat from central heating and a wall-mounted electric heater for rapid additional heat. It needs an extractor fan and good ventilation to allow odour to be removed quickly and to remove humid air after a bath, so that the skin is not too damp for a clean appliance to be fastened. The bathroom requires a good sized bath so that it is possible to lie flat and it also requires a good shower. Several patients said that they preferred to take a shower now that they had an ileostomy. The room also needs to contain a toilet and ideally an additional modified toilet attached to the wall at an appropriate height, so that the appliance can be easily emptied. Failing this, the floor needs to be carpeted around the lavatory so that it is possible to kneel to empty the bag. The toilet paper needs to be of a soft and strong variety as this is much preferred for cleaning around the stoma and the bag exits. In addition, there needs to be a basin with a surrounding flat surface so that the new appliance, cleaning materials and other equipment can be laid out. It is also most helpful to have a mirror placed at a suitable height so that the stoma can be seen while the patient stands in front of it. There needs to be good cupboard space in which to keep the spare bags and equipment. A number of patients said that they would like a bathroom en suite with their bedroom as this would make emptying and changing the appliance more

convenient. Several patients thought that a bidet would be useful and nearly all of them said that it was important to have two lavatories in the house. One patient who preferred the rubber non-disposable type of appliance found that her utility room was the ideal place for hanging a cleaned bag up to dry. Finally, the bathroom needs a good pedal-bin containing a polythene bag to facilitate disposal of plastic bags and waste material.

Mention should be made of one unfortunate patient who lived in a council house with only an outside lavatory. He developed severe Crohn's colitis which necessitated many nightly visits to the outside lavatory in both summer and winter. He asked his council to provide a lavatory inside his house but failed to get any help. In the end, he managed to save up sufficient money to have a lavatory put into the house. He now has an ileostomy and remains very pleased that his washing and toilet facilities are inside his home.

PSYCHOLOGICAL ASSESSMENT

Three tests were employed for this assessment. Raven's Progressive Matrices test and Raven's Mill Hill Vocabulary test were used to measure performance and verbal intelligence quotients (IQ) respectively. Eysenck's Personality Questionnaire was used to assess various aspects of personality (Eysenck and Eysenck, 1975). For the analysis of these results it was decided to consider both the patients who had had ulcerative colitis and those who had Crohn's

disease as a single group of patients. However, the results were analysed separately according to sex. One woman was not willing to complete either the IQ or the personality questionnaires, and so the group is comprised of 28 men and 22 women, making a total of 50 patients. There was no control group for these observations. The results obtained are compared to those found in large samples of the general population.

Intelligence Quotients

The results of the intelligence tests are recorded in Table 5.3. It may be seen that both the men and the women performed well in the performance IQ but both groups had only an average verbal IQ. It is interesting to note that the IQ of several of the men did not match up well with their occupation. One man who was a manual labourer on a fruit farm had a performance IQ of 121; another with a performance IQ of 130 was a carpenter, and another who was a delivery man had a performance IQ of 119. All three of these men had verbal IQ scores of between 90 and 100. The only person in the whole group who thought that he had definitely not attained as much academically as he might have done was a young man who had a place at University. He was unable to take up the place because at the time he was ill with Crohn's disease. His verbal IQ score was 102 and performance IQ was over 130. He was employed as a draughtsman in a local government office. This point is also mentioned earlier in this chapter in the section dealing with occupation.

Personality Characteristics

The results of the personality questionnaire are

Table 5.3 Mean Intelligence Quotients (IQ) obtained in fifty patients with an ileostomy using Raven's Progressive Matrices and Raven's Mill Hill Vocabulary Tests

Test	Males 28 subjects	Females 22 subjects	Totals 50 subjects
Progressive Matrices (Mean Performance IQ) ± 1 SD	119.96 ± 12.86	114.59 ± 11.52	117.6 ± 12.46
Mill Hill Synonyms (Mean Verbal IQ) ± 1 SD	102.82 ± 11.91	100.91 ± 9.84	101.98 ± 10.98

summarised in Table 5.4 The first point of interest is that there is a marked difference between the male and the female patients when compared to the results obtained by age- and sex-matched groups of the general population. The female patients show no significant difference in personality traits from the normal sample. However, the male patients showed some marked abnormalities. As may be seen in the Table they had a low psychoticism score ($p < 0.05$) but a significantly raised "lie" score ($p < 0.001$) They tended to be introverted ($p < 0.01$) but their neuroticism rating was not significantly different from that of the general population. The "lie" score in this context, can be said to measure social conformity on the one hand and a tendency of the subjects to "fake good" on the other. The low P scores fit in well with this finding as a P scale measures the tendency to reject socially acceptable norms of behaviour, a high P score indicating a high tendency to reject these norms of behaviour. In addition, the low E score for these male patients indicates a tendency towards introversion. This finding also correlates well with the high L and low P scores. Details of the background and use of the personality test used in this study may be found in the "Manual of the Eysenck Personality Questionnaire", (Eysenck and Eysenck, 1975).

SEXUAL FUNCTION

This aspect of life with an ileostomy was also carefully assessed by interviewing all the patients after they had been taking part in the study for some time. A detailed questionnaire was completed for each patient. Twenty

Table 5.4 An assessment of personality characteristics of fifty ileostomists using Eysenck's Personality Questionnaire. The values given are the arithmetic means $\pm$ 1 standard deviation

Personality Characteristic	MALES			FEMALES		
	Patients Score 28 subjects	Gen.Pop. Score 327 subjects	Significance	Patients Score 22 subjects	Gen.Pop. Score 416 subjects	Significance
P (Psychoticism)	2.07 $\pm$ 1.44	3.09 $\pm$ 2.59	$p < 0.05$	1.91 $\pm$ 1.69	2.35 $\pm$ 2.11	NS
E (Extraversion)	9.36 $\pm$ 4.70	12.38 $\pm$ 5.14	$p < 0.01$	11.00 $\pm$ 5.97	12.24 $\pm$ 4.92	NS
N (Neuroticism)	10.07 $\pm$ 4.97	9.17 $\pm$ 5.06	NS	14.04 $\pm$ 4.66	12.63 $\pm$ 5.38	NS
L (Lie Score)	11.00 $\pm$ 4.33	8.07 $\pm$ 4.08	$p < 0.001$	10.32 $\pm$ 3.41	8.86 $\pm$ 3.87	NS

Statistical comparison is made between the mean scores of the patients and the mean scores for the general population in the age range 40 - 49; as this corresponds to the mean age in both the male and female sub-groups (Eysenck and Eysenck, 1975)

of the 23 men in the ulcerative colitis group reported normal sexual function. One man was 80 years old and no longer had a sexual relationship and one man was impotent although he attributes this to an intervertebral disc lesion and not to the proctocolectomy. The remaining patient can perform satisfactorily, indeed his wife became pregnant during the study, but his erection deviates towards the left side. Therefore it appears that the proctocolectomy has not rendered any of these male patients impotent. However, five of the men did admit to having some psychological difficulty. One of these men found that the appliance was a nuisance and the remaining four, including the only two young unmarried men (aged 21 and 26), said that they were shy as a result of having the ileostomy. The two unmarried men found it difficult to become intimately involved with a woman in case they were rejected. One of them had a stable relationship with a girlfriend, who attended as a normal control. She was very understanding and wished that he would worry less. The two married men who reported difficulty said that they found intercourse less enjoyable and spontaneous because the bag always had to be emptied first. They were also continuously worried that the appliance would become loose. This type of difficulty was mentioned by other patients but seemed to be less of a problem for them.

Four of the women in the ulcerative colitis group had not had a sexual relationship since their operation. One was a spinster and another was a widow. A third had a "poor marriage" and the operation was the "last straw"; although she was not divorced, she and her husband slept

in separate rooms. The fourth woman was the patient previously mentioned who regards herself as an invalid. Leaving out the spinster and the widow, only six of the remaining 14 women (43%) said that their sexual relationship was entirely satisfactory. Three of the others had some dyspareunia and one found that her husband kept on asking her if she was alright. The remaining two were shy, not liking to get undressed in front of their husbands and not feeling fully feminine. This problem was also mentioned in passing by some of the other women and they probably all experience it to some extent. All the women who had intercourse said that they were "turned on" by sex play and that they were able to have normal orgasms. The Crohn's disease group is very small but a similar pattern emerged. All the men were potent; one 23 year old unmarried man said that he found it difficult to make a close relationship and one young married woman did not like her husband to see her undressed.

Finally, each patient was asked how soon after the operation did they begin to have intercourse. The results are confined to those patients who were in a position to have intercourse on returning home. The mean time interval between the operation and first sexual intercourse was 11 weeks. The range of time was large; the shortest time was ten days, as the patient left hospital on the tenth day and had intercourse the same night. This fact was later confirmed by his wife. The longest period was just over a year; this delay was due to recurrent minor problems with the perineal wound.

DISCUSSION

Eighty seven per cent of the patients who took part in the present study said that their general health was good or excellent. This correlates well with the results of other workers who found that the general health of their patients was reported as being good or excellent in 87 to 96 per cent of their patients (Watts et al, 1966b, Daly, 1968; Roy et al, 1970). There are always a small percentage of patients who have other medical conditions and a few others who do not adjust well psychologically to the stoma.

It is not possible to compare the results obtained in this study concerning the patients' opinion about the help and care that they received during the operative period with those of other centres, because there are no reports in the literature of investigations into this aspect of care. As has already been mentioned the importance of this aspect of proctocolectomy and the formation of an ileostomy has been realised for many years in Oxford. However, despite having attempted to explain to each patient about the operation, to discuss it with members of their family, to arrange a meeting with an ileostomist and to have efficient and sympathetic postoperative care, it seems that in practice this policy has not been completely fulfilled. It is important to stress again that some of the replies may well have been inaccurate, particularly as many of the patients were very ill at the time of operation. It is known that patients, even if they are relatively well and attending outpatients, forget about

half of the verbal information given to them (Ley,1972). Nevertheless, it is apparent that at each stage of this period there was a substantial percentage of patients who were not entirely satisfied with their care.

The reasons for this failure of communication were probably first attributable to doctors; it is often just prior to the operation that the patient is transferred from the care of a physician to that of a surgeon. Each of these doctors may think that the other has explained more than actually is the case. The second factor was undoubtedly the absence of a stoma care nurse at the time when the ileostomists of the present study had their operation. This nurse performs a vital role in the management of these patients and the situation has been transformed since such a nurse has been appointed in Oxford. Despite this, it is still very important that the doctors concerned should talk carefully to each patient and their families about the operation and its consequences. As a result of the present findings, it is suggested that a check list should be included in the case notes of every patient who is about to have a proctocolectomy, so that no important aspect of care is forgotten. The check list that is being suggested for use in Oxford is given in the Appendix.

Besides the one man who did not really wish to return to work, all the patients carried on with their previous full-time employment. As previously mentioned, several of the men were able to continue with their heavy manual jobs. These findings correlate well with those of Watts et al (1966b); Daly (1968) and Roy et al (1970). In all these

studies it seemed that the ileostomy was no bar to returning to the same full-time employment. Indeed, many patients who took part in the present study said that their ability to work had greatly increased after their operation. In addition, the time spent off work due to ill health and attending clinics had markedly reduced since the operation in every patient who took part in this study. These results also correlate closely with the findings of other studies. It is of much more concern as to whether the ulcerative colitis or Crohn's disease affects the education and employment prospects particularly of young patients. One of the patients who took part in the present study had a place at university but was unable to take it up because he was ill with Crohn's disease at the time.

Most of the patients returned to their normal social lives although there was a minority who felt uneasy in public places. This uneasiness was mainly due to the noise that the stoma might make. This finding also confirms the results of the three studies mentioned in the last paragraph. However, in the present study there were a high percentage of patients who liked to go swimming but were inhibited from doing so because of the ileostomy. This arose mainly because they were embarrassed for other people to see their appliance rather than any fear about the bag coming loose. This problem can be overcome by choosing a suitable type of swimming costume. However, there may be some difficulty while changing as there are often no private cubicles in the changing rooms of modern swimming pools.

It is this type of circumstance which tends to make patients with an ileostomy avoid situations where they may be 'discovered' in public.

Ninety-two per cent of all the patients said that they had got used to their stoma. However, it was disturbing to find that 11 per cent of the men and 22 per cent of the women said that they hated their stoma. It seemed to be the existence of the stoma that the patients hated rather than any particular complication associated with it. It is difficult to suggest any remedies for this problem besides the use of a different operation. Nevertheless, it is possible that efficient help and advice during the operative period may help. The introduction of each patient to a well-adjusted ileostomist is particularly helpful in this respect. In addition, involvement of the spouse and close family is an important aspect of an ileostomist's care. However, caution has to be exercised, even with this recommendation, because two of the men relied totally on their wives to change the appliance. It was discovered that at least one of these two wives was unhappy with the task.

Both the male and female patients were found to have a high performance IQ. However, a group of patients drawn mainly from the Oxford area may not represent a random sample of ileostomists with respect to intelligence because this area of the country probably contains an excess of academic and research establishments. It would be interesting for similar studies to be undertaken with ileostomists in other areas of the country.

In general, the personality characteristics of the female patients all fell within the normal range whereas the men tended to be introverted and appeared to conform closely to the socially acceptable norms of society. The male patients also exhibited a tendency to 'fake good'. These findings fit in well with the impression left after interviewing all the patients. The women were able to express their problems well and not be afraid of discussing their difficulties. However, the men tended not to admit to many problems and said that they were able to continue with their lives normally. It is probable that the males had as many problems as the female patients but they were less willing to admit these either to themselves or to anyone else. These findings may be important in the help and advice that is given to patients. A different approach may need to be taken in the management of patients depending on whether they are male or female. In addition, when considering the results of questionnaires and interviews, a straightforward interpretation of the findings may be misleading.

There have been a number of studies investigating the sexual aspects of life with an ileostomy (Stahlgren and Ferguson, 1958; Watts et al, 1966b; Daly, 1968; Burnham et al, 1977; Gruner et al, 1977). The results of the four European studies of the sexual function of patients with an ileostomy are summarised in Table 5.5. The way in which the questions are asked is an important factor in any research investigating sexual function. It can be seen in the Table that, in three out of the four studies, each patient was personally

Table 5.5 Sexual aspects of life with an ileostomy

Number of patients	Form of questions	Male % impaired	Female intercourse % impaired	fertility
100m 62f	interview	11.0	-	reduced Daly 1966
41m 67f	interview	27	7.5	- Watts et al 1966b
118m 165f	questionnaire	29	33	- Burnham et al 1977
67m 40f	interview	22	1.75	reduced Gruner et al 1977

m = male

f =female

interviewed, whereas, in the remaining study the patients were sent a questionnaire. The mode of questioning may be very important in determining the results of the research. For instance, in the study in which patients were sent a questionnaire it can be seen in the Table that a high incidence of sexual difficulties was found, particularly in female patients. It is difficult to be certain which form of questioning gives the more accurate information in this sensitive field. Nevertheless, there are some important points which emerge from the results of both the present study and the studies included in Table 5.5. Another important consideration is whether any abnormality found in sexual function is the result either of damage to the autonomic nerve supply to the sexual organs at the time of operation or of psychological difficulties arising from the presence of the stoma.

In the male, erection mainly occurs as a result of stimulation of parasympathetic nerves (nervi erigentes) supplying the penis. Ejaculation occurs as a result of stimulation to the sympathetic nerves supplying the seminal vesicles, ejaculatory ducts and prostatic septa. Surgical damage to either of these nervous pathways can result in failure of male sexual function. Similarly, intact parasympathetic and sympathetic nerves are required for a normal female orgasm.

Table 5.5. shows the proportion of male patients who have either total or partial loss of sexual function. This very high rate of sexual impairment is of great concern, particularly as many of the patients are young. In two of

the studies, sexual potency in male patients who had had a proctocolectomy with formation of an ileostomy was compared with the potency in patients who either had an ileostomy with the rectum remaining or had had an ileo-rectal anastomosis (Burnham et al, 1977; Gruner et al, 1977). In both of these studies it was found that the sexual function of male patients was normal when the rectum was left in place. Therefore, the high rate of sexual impairment in males appears to be directly related to the removal of the rectum. However, in the present study, none of the male patients had become impotent following their proctocolectomy. It is believed that this is because of the technique of perimuscular excision of the rectum which was discussed in Chapter 1. Nevertheless, 23 per cent of the male patients in the present study did mention that they had some psychological difficulty in their sexual relationships. This was particularly apparent in the young unmarried men who were frightened of admitting that they had an ileostomy to their girlfriends. Burnham and his colleagues (1977) also mention some psychological difficulties in the ileostomists that they studied.

The information concerning female sexual function is less precise. Table 5.5 shows the markedly different results in relation to female sexual dysfunction found in the various studies. Some of the patients in these studies complained of loss of libido because they had lost normal sensation in the perineum. However, the common cause of sexual dysfunction in the female patients was dyspareunia. In the present study only 43 per cent of the sexually active women, with an ileostomy as a result of ulcerative colitis, were entirely satisfied with their sexual relationship. All the sexually

active women had normal perineal sensation but three of them had dyspareunia and the others who were dissatisfied with their sexual relationship had psychological difficulties. These difficulties seem to result mainly because the patients feel less feminine and less attractive. Similar results were obtained by Burnham and his colleagues (1977).

Fertility is probably reduced in female ileostomists (Daly, 1968; Gruner et al, 1977). This may result either from inflammation in the pelvis due to the diseased colon and rectum or from adhesions and scarring following surgery. Two of the female ileostomists who took part in the present study had had children after their proctocolectomy. However, due to the small number of patients no comment can be made about fertility in the female patients who took part in this study.

The main points to note as a result of the findings of this sexual survey of ileostomists operated on in Oxford are that it is possible to avoid sexual dysfunction as a direct result of surgery but that there may be a considerable psychological problem, particularly in young patients. If it is at all possible to postpone proctocolectomy and ileostomy until after the young people are married and settled, then this may be of considerable help to the individuals concerned.

CHAPTER 6

DIET

INTRODUCTION

Ileostomists were questioned about their diet in two large surveys dealing with their postoperative course (Daly, 1968; Roy et al, 1970). Most of the ileostomists taking part in these studies were found to enjoy a normal diet without restrictions. However, some patients avoided foods containing much dietary fibre, as these tended to cause partial intestinal obstruction. It has been usual to advise ileostomists that they may eat anything they wish but that poorly digested foods should only be taken in moderate quantities and should be chewed thoroughly before swallowing (Truelove and Lee, 1973).

Two studies have investigated the dietary habits of ileostomists in more detail (Thomson et al, 1970; Gazzard et al, 1978). Both groups concluded that no item of food should be excluded from the diet of an ileostomist without an adequate trial by each individual. This advice was reinforced by a Leading Article in the British Medical Journal (1970) which expressed essentially the same opinion.

A detailed survey of the diets of the ileostomists taking part in the present study was thought to be important. Moreover, apart from an analysis of the food items avoided by the ileostomists, it was judged essential to analyse the individual nutrients being consumed by the ileostomists compared to those being taken by age- and sex-matched healthy

control subjects. This was necessary to determine any deficiencies in the diets of the ileostomists, and also to evaluate the results of the detailed metabolic investigations that were being undertaken as part of the present study. Therefore, the patients and the healthy control subjects were invited to make a careful record of their diet for one week. In addition, each patient was interviewed to determine which items of food they tended to avoid. This chapter describes the results of these interviews and gives the data obtained from a computer analysis of the dietary records.

PATIENTS AND METHODS

All of the 51 ileostomists took part in the dietary study. Every patient was interviewed and questioned as to whether they avoided taking any food item in their diet or if they ate an entirely normal diet. The results of these interviews were recorded. After considering the various methods that have been tried for assessing dietary intake, it was decided to ask the patients to record everything that they ate and drank for seven consecutive days (Marr, 1971). This method of assessing dietary intake has been shown to give more accurate results than those obtained by taking a dietary history (Young et al, 1952). During the period of study the ileostomists were encouraged to remain on their usual diet. They were not asked to weigh every item of food because it was thought that this would alter their eating habits and make good compliance with the study less likely. Instead they were given the instructions shown in Table 6.1 together with a careful explanation about how to use the

Table 6.1 Instructions given to each patient and healthy control subject about how to record the quantity of food and fluid consumed during a seven day period

Food Diary

Record all food and drink consumed for 7 consecutive days.

Please state how food is cooked - whether grilled, boiled, fried, stewed, roast, with or without oil

Record foods in handy measures

Fluids - cup/glass/mug/tankard

Cereals, rice, vegetables and fruit stews, gravies, sauces, puddings, custard, cream etc, can all be measured as heaped or level tablespoons

Sugar, salt, jams and preserves, salad cream, bottled sauces, cocoa, butter, can all be measured as heaped or level teaspoons

Cheese - matchbox size pieces

Meat - number of thin hand size pieces

Potatoes - number the size of an egg

Bread - state large/small thick/thin

Please give as detailed a description as possible - e.g. coffee - 1 mug all milk + 2 sugars

or 1 large slice bread $\frac{1}{4}$ " thick with 1 level teasp. butter

standard measures which was given by a senior dietitian. When the patients returned the completed food diaries, the same dietitian estimated the weight or volume of each individual item and coded them according to the McCance and Widdowson food codes (Paul and Southgate, 1978). The information on the paper type version of the McCance and Widdowson tables is held in the University of Oxford Computer, an ICL 2980. Therefore, the data obtained from the present study were entered into the computer and an estimate of the nutrient consumption was obtained for each patient.

Thirty nine healthy control subjects also took part in the dietary study. These subjects were age- and sex-matched to the 39 ileostomists who had had ulcerative colitis. Twenty seven of these healthy subjects were the spouses of patients involved in the study and two more were first degree relatives. The remaining ten control subjects were either friends of the patients or hospital personnel. All these subjects were asked to record their food and fluid intake in the same way as the ileostomists. They were given the instructions shown in Table 6.1 and a careful explanation about how to use the standard measures was given by the same dietitian who instructed the ileostomists. When both the husband and wife were taking part in the study, the records of their diets were made during the same period of seven days. This removed many possible underlying inaccuracies such as the exact nutrient content of a food or the amount of salt used in cooking because both the husband and wife were eating food from the same source and cooked in the same manner.

RESULTS

The results obtained from the interviews with the ileostomists are given in Tables 6.2 and 6.3. Table 6.2 lists each food item that was avoided by one or more of the ileostomists and the reason why it was avoided. Table 6.3 gives the percentage of ileostomists who had no food restrictions and also lists the food items avoided by at least ten per cent of the patients.

Table 6.4 gives the results of the computer analysis of the seven day dietary records. The results given in this Table show that there are few significant differences in food and fluid intake between the three groups. The ileostomists who had had ulcerative colitis were found to be drinking significantly more fluid than the healthy subjects ($p < 0.001$). The patients with Crohn's disease were also drinking more than the control subjects, but the difference was not statistically significant. However, the mean 24-hour output of urine in the ileostomists with Crohn's disease was significantly less than that in the healthy subjects as is shown in Chapter 7 ($p < 0.01$). The sodium intake in the patients who had had ulcerative colitis was higher than that in the control subjects but the difference was not statistically significant. However, the sodium intake in the group of ileostomists with Crohn's disease was significantly increased compared to that in the control group ($p < 0.01$).

As a result of the findings shown in Tables 6.2 and 6.3 it might be expected that the ileostomists would eat less dietary fibre than the control subjects, but although

Table 6.2 Foods avoided by one or more of the ileostomists

Foods avoided because they tended to cause either discomfort passing through, or obstruction of the stoma

General	:	Nuts, peels, skins, pips, coconut
Fruits	:	Currants, raisins, sultanas, raspberries, strawberries, blackberries, oranges, grapefruit, pineapples, apples
Vegetables	:	Mushrooms, sweetcorn, lettuce, tomatoes, broad beans, runner beans, peas, uncooked cabbage, brussels sprouts, cauliflower, celery, onions, chinese meals

Foods avoided because they tended to cause odour, noise or excess fluid output through the stoma

Onions, mushrooms, curries, spicy food, red wine

Table 6.3 Dietary precautions taken by ileostomists who had had ulcerative colitis and those with Crohn's disease

Variables	Ulcerative colitis group n = 39 Values in percentages	Crohn's disease group n = 12 Values in percentages
No dietary restriction	41	33
Items of food avoided by 10% or more of the patients:		
Nuts	41	33
Peels:skins	15	33
Pips	15	8
Raspberries	21	17
Broad beans	10	8
Mushrooms	3	25

Table 6.4 Mean daily intake $\pm$ 1 standard error of the mean of energy, fluid, electrolytes and nutrients in the two groups of ileostomists compared to that in the healthy control group

Variable	Ulcerative colitis group n = 39	Healthy control group n = 39	Crohn's disease group n = 12
Energy value kcal	2635 $\pm$ 115	2501 $\pm$ 103	2548 $\pm$ 147
Fluid volume ml	1919 $\pm$ 60**	1568 $\pm$ 78	1750 $\pm$ 132
Protein g	90 $\pm$ 4	89 $\pm$ 3	86 $\pm$ 5
Carbohydrates g	304 $\pm$ 15	284 $\pm$ 15	283 $\pm$ 23
Fat g	119 $\pm$ 6	115 $\pm$ 5	114 $\pm$ 6
Simple sugars g	144 $\pm$ 9	122 $\pm$ 8	124 $\pm$ 14
Dietary fibre g	17 $\pm$ 1	18 $\pm$ 1	14 $\pm$ 1
Cholesterol mg	329 $\pm$ 20	295 $\pm$ 21	366 $\pm$ 47
Sodium mg	4098 $\pm$ 208	3614 $\pm$ 154	4823 $\pm$ 631*
Potassium mg	3216 $\pm$ 113	3229 $\pm$ 118	3101 $\pm$ 170
Calcium mg	1126 $\pm$ 51	1097 $\pm$ 42	978 $\pm$ 94
Magnesium mg	295 $\pm$ 13	296 $\pm$ 13	260 $\pm$ 9
Phosphorous mg	1474 $\pm$ 57	1470 $\pm$ 53	1343 $\pm$ 67
Iron mg	16 $\pm$ 2	17 $\pm$ 2	13 $\pm$ 1
Retinol μ g	1053 $\pm$ 189	1141 $\pm$ 182	1143 $\pm$ 366
Vitamin D μ g	3.2 $\pm$ 0.3	3.3 $\pm$ 0.4	2.4 $\pm$ 0.1
Thiamin mg	1.4 $\pm$ 0.1	1.3 $\pm$ 0.1	1.2 $\pm$ 0.1
Riboflavin mg	2.1 $\pm$ 0.1	1.9 $\pm$ 0.1	1.7 $\pm$ 0.1
Nicotinic acid mg	18 $\pm$ 1	18 $\pm$ 1	16 $\pm$ 1
Vitamin C mg	63 $\pm$ 6	62 $\pm$ 5	54 $\pm$ 7
Vitamin B12 μ g	6.1 $\pm$ 0.7	6.7 $\pm$ 0.8	7.1 $\pm$ 1.4
Total folic acid μ g	185 $\pm$ 10	185 $\pm$ 8	165 $\pm$ 12

* $p < 0.01$

** $p < 0.001$

both groups of ileostomists did eat less fibre than the control group, the differences were not statistically significant. The metabolism of many of the other variables shown in Table 6.4, such as calcium, magnesium and iron were investigated in detail in the present study. Therefore, it was of interest to find that the intake of all these variables was not significantly different in the ileostomists from that in the control subjects.

DISCUSSION

Many of the ileostomists who took part in the present study ate a normal diet without any restriction. All the patients were in good general health and were well nourished. As was demonstrated in Chapter 4, the mean body weight of the ileostomists was not significantly different from that of the control subjects. Moreover, several of the patients said that they needed to limit their intake of calories because otherwise they gained excessive weight. Soon after proctocolectomy with ileostomy, many patients suddenly felt hungry for the first time after experiencing anorexia for years as a result of their disease. In addition, with the removal of a chronically inflamed colon, it is probable that the body utilises food more efficiently. When a large part or the whole of the colon is inflamed, the patient is often in a catabolic state, partly as a direct result of the inflammation and partly because of heavy losses of protein and other substances. As a result, a rapid increase in weight often occurs after the operation. It is worth warning new ileostomists of this possibility, particularly as obesity can make the management of the stoma and the

ileostomy appliance difficult.

The food restrictions reported by 59 per cent of the patients were minor and this result is in general agreement with the findings of previous workers (Thomson et al, 1970; Gazzard et al, 1978). As is demonstrated in Table 6.3, the restrictions reported in the present study were mainly confined to nuts, skins and pips. It should be mentioned that some of the patients had been told to be very careful of these food items; this advice, in itself, had made several of the ileostomists wary of eating any nuts or foods with skins or pips. The finding, as shown in Table 6.4, that the dietary fibre, vitamin C and folate intakes in the ileostomists were not significantly different from those in the control subjects demonstrates that only minor changes in the fruit and vegetable consumption had taken place as a result of the ileostomy.

The great majority of the ileostomists who took part in the present study were only concerned about the possible obstruction of their stoma by undigested fibrous foods. Only a few patients mentioned that they avoided a food item because it caused odour, noise or excess fluid output through the stoma. Indeed, several patients claimed that odour and increased fluid output were of less concern to an ileostomist than they were to a normal subject because the appliance contained any such odour or excess fluid.

A number of the ileostomists said that additional fluid intake did not alter the volume of their ileostomy effluent.

This is in agreement with the results of two groups who found that the volume of the ileostomy effluent did not increase after an oral fluid load (Kramer et al, 1962; Hill et al, 1976). This is an interesting observation because many centres ask their patients to drink large quantities of fluid as part of the preparation for a barium enema in the belief that this helps to clear the colon. From the results mentioned above it is probable that this belief is unfounded.

The results shown in Table 6.4 demonstrate that the ileostomists who took part in the present study were eating an adequate and near normal diet. It could be argued that the spouses of the patients might modify their own eating habits to take a similar diet to that of the ileostomists, and therefore should not be used as a control population. However, 12 of the control subjects were not spouses of the ileostomists and when their consumption of nutrients was compared with that of 12 age- and sex-matched subjects who were spouses of the ileostomists, no statistically significant difference was found.

Several other points of interest emerge from the results presented in Table 6.4. The fluid consumption of the group of ileostomists who had had ulcerative colitis was significantly increased to compensate for the additional loss from the intestine and the mean 24-hour urine volume in these patients was not significantly different from that of the control subjects. However, there was not an increase in the intake of fluid in the ileostomists with Crohn's disease and their mean 24-hour urine volume was significantly less than

that of the healthy subjects ($p < 0.01$), The reverse is true when the intake of sodium is considered. The ileostomists with Crohn's disease ate significantly more sodium in their diet than the control subjects. By contrast, although the ileostomists who had had ulcerative colitis ate more sodium than the healthy subjects, the increase in intake was not statistically significant. There is no obvious explanation for these differences between the two groups of ileostomists but it seems that all patients with an ileostomy should be encouraged to drink plenty of water and to eat at least the additional salt that seems natural to them (Chapter 7).

The metabolism of iron, vitamin B₁₂, folate, calcium and magnesium are all discussed in other chapters. However, at this point it is worth noting that there was no statistically significant difference in the intake of iron, vitamin C, vitamin B₁₂, folate, calcium, vitamin D, magnesium and phosphate between either group of ileostomists and that of the control group.

In conclusion, the results of the present study confirm that ileostomists should be encouraged to eat all forms of food. It is wise for them to chew poorly digested food thoroughly and to eat only moderate quantities of fibrous foods at any one time. All patients should be encouraged to drink plenty of fluid and possibly to take some additional salt, sodium citrate or glucose electrolyte mixture. The question of the best type of supplement is considered at the end of Chapter 7.

CHAPTER 7

WATER AND ELECTROLYTE BALANCE

INTRODUCTION

For many years salt and water depletion has been a recognised complication of the early postoperative period in patients with an ileostomy. There was a further development when, in 1962, Gallagher and his colleagues described episodes of salt and water depletion occurring in patients with well-established ileostomies. Later work suggested that even apparently healthy patients with an ileostomy have persistent depletion of sodium and water (Clarke et al, 1967; Hill et al, 1975a). However, in 1978, Turnberg and his colleagues reported that their patients had normal extracellular and total body water volumes, although they did find that total exchangeable sodium and potassium were reduced. As the serum electrolytes were normal in these subjects, they concluded that there must be an intracellular depletion of sodium and potassium.

Another feature of sodium and water balance in patients with an ileostomy is the finding that they probably have an increased potential difference across their ileal mucosa (Isaacs et al, 1976). It is possible that this indicates increased sodium absorption by the mucosa. However, despite evidence for sodium conservation by the kidney and intestine in patients with an ileostomy, plasma aldosterone levels have been found to be normal in almost all the small number of patients studied (Isaacs et al 1976; Turnberg et al, 1978). As yet, there is no adequate explanation for these conflicting

observations and so the present study was designed to investigate the water and electrolyte balance and acid:base status of a large group of ileostomists, using a group of normal subjects matched for age and sex as controls.

PATIENTS AND METHODS

All of the 51 ileostomists took part in the investigations related to water and electrolyte balance and acid:base status. The studies that were made on samples of blood, urine and ileostomy fluid were as follows:

Blood

Every patient had samples of venous blood collected to measure the plasma levels of sodium, potassium, chloride, bicarbonate, urea, creatinine, calcium, phosphate, total protein and albumin. These variables formed part of the biochemical profile measured on a Vickers M300 Discrete Analyser. The plasma magnesium was measured using a Perkin-Elmer Atomic Absorption Spectrophotometer. Blood pH was determined by taking a sample of arterialised venous blood from a vein on the dorsum of a hand. Before the sample was taken, the hand was held in hot water for five minutes and no tourniquet was used in order to avoid venous stasis. The samples were placed in ice and analysed within 15 minutes using a Radiometer ABL2 Acid-Base Laboratory. This technique for obtaining measurements of blood pH has been well validated (Harrison and Gallon, 1965; Forster et al, 1972; France et al, 1974). Finally, blood samples were collected to determine plasma renin activity and plasma aldosterone level in the resting state after the patients had been recumbent for half

an hour and another sample was taken four hours later when the patient was ambulant. The blood collected for the measurement of renin activity was separated in a cold centrifuge and the plasma was stored at -20°C . Plasma renin activity was measured using a radioimmunoassay for angiotensin 1 and was expressed as ng of angiotensin 1 generated per ml of plasma during a three hour incubation (Stockigt et al, 1971). The plasma aldosterone levels were determined by a highly specific radioimmunoassay method (Al-Dujaili and Edwards, 1978). Both of these assays were carried out in the laboratory of Dr. C.R.W. Edwards at St. Bartholomew's Hospital, London.

Urine

Each patient collected a 24-hour sample of urine and a Technicon SMA linked to a Vickers SP120 was used to measure the concentrations of urinary sodium, potassium, urea, creatinine, calcium and phosphate. The concentration of magnesium in the urine was measured by using a Perkin-Elmer Atomic Absorption Spectrophotometer. The pH of the urine was determined by using a Pye Unicam pH meter.

Ileostomy Effluent

Each ileostomist also collected a 24-hour sample of ileostomy effluent. This was weighed and the volume was measured. Aliquots of the effluent were taken to determine the dry weight of each sample using a TECAM Dri-Block DB3-H and further aliquots were drawn up into a bladder syringe and injected into 12 two-ml Eppendorf centrifuge

tubes. These tubes were spun at 12,000 rpm for 15 minutes in a microcentrifuge type-320 supplied by Burkard Scientific Sales Ltd., Rickmansworth, Hertfordshire. The centrifugation separated the solid component from the liquid part of the effluent. The fluid supernatant was then pipetted from the 12 centrifuge tubes into two plain tubes which were stored at -20°C to await analysis. Subsequently the pH of the fluid was determined immediately after defrosting using the Radiometer ABL2 Acid-Base Laboratory. In addition, the sodium and potassium levels were measured using the Technicon SMA linked to a Vickers SP120. In the present study, undiluted ileostomy fluid was used but it is suggested that a 1:1 dilution with distilled water would be preferable for analysis with the Technicon SMA because of the high viscosity of some of the samples. The concentrations of calcium and magnesium in the ileostomy fluid were estimated using the Perkin-Elmer Atomic Absorption Spectrophotometer.

Control Subjects

The 39 healthy subjects who were age- and sex-matched to the ileostomists who had had ulcerative colitis, acted as a control group for the studies of water and electrolyte balance and acid:base status. All of them had blood taken for the biochemical profile, plasma magnesium measurement and determination of blood pH. They also had blood taken for resting and ambulant aldosterone and plasma renin activity determination. In addition, every subject collected a 24-hour sample of urine for the measurement of urinary electrolytes and pH. The methods employed for the measurement of these variables were the same as those used for the samples collected from the ileostomists.

RESULTS

The results of the plasma biochemical profile have already been given in Chapter 4 but the results relevant to the present chapter are shown in Table 7.1. In summary, there was no statistically significant difference between the three groups in the value of plasma sodium, potassium, chloride, bicarbonate, urea, creatinine, calcium, magnesium or phosphate. However, the mean values of total protein and albumin were significantly raised in the ileostomists who had had ulcerative colitis compared to those in the healthy subjects ($p < 0.001$ and $p < 0.02$, respectively). There was no elevation in the mean value of the ESR in these ileostomists as compared to that in the control subjects nor any other sign of inflammation, so it is unlikely that the higher total protein value was due to an inflammatory process. In addition, any such inflammation would tend to cause a reduction in the plasma albumin as opposed to the high level which was found. It is said that, apart from an artefactual rise if blood is taken after prolonged venous stasis, a raised serum albumin is only found in patients who are dehydrated (Zilva and Pannall, 1979; Varley et al, 1980). In the present study, the blood samples were taken without prolonged venous stasis, and in any case they were collected from the patients and the control subjects in an identical manner.

The results of the measurements of resting and ambulant plasma aldosterone and plasma renin activity in the patients and control subjects are given in Table 7.2. The plasma aldosterone values and renin activity were found to follow a log-normal distribution and the results given in Table 7.2

Table 7.1 Mean plasma biochemical results $\pm$ 1 standard deviation related to water and electrolyte balance and acid:base status in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the ulcerative colitis group

Variable	Ulcerative colitis patients n = 39	Control subjects n = 39	Crohn's disease patients n = 39
Sodium mmol/l	141.9 $\pm$ 3.0	141.2 $\pm$ 2.4	141.2 $\pm$ 2.9
Potassium mmol/l	3.90 $\pm$ 0.70	4.00 $\pm$ 0.71	4.02 $\pm$ 0.52
Chloride mmol/l	102 $\pm$ 3	102 $\pm$ 2	100 $\pm$ 3
Bicarbonate mmol/l	26 $\pm$ 5	25 $\pm$ 5	28 $\pm$ 4
Urea mmol/l	5.7 $\pm$ 1.1	6.0 $\pm$ 2.0	5.3 $\pm$ 1.5
Creatinine μ mol/l	83 $\pm$ 21	84 $\pm$ 17	75 $\pm$ 18
Calcium mmol/l	2.45 $\pm$ 0.14	2.40 $\pm$ 0.09	2.40 $\pm$ 0.13
Phosphate mmol/l	0.98 $\pm$ 0.20	0.88 $\pm$ 0.16	0.99 $\pm$ 0.16
Magnesium mmol/l	0.52 $\pm$ 0.06	0.50 $\pm$ 0.06	0.50 $\pm$ 0.06
Total Protein g/l	74.8 $\pm$ 4.8**	70.1 $\pm$ 4.3	71.5 $\pm$ 4.0
Albumin g/l	44.2 $\pm$ 2.9*	42.7 $\pm$ 2.2	41.3 $\pm$ 3.0
Blood pH	7.39 $\pm$ 0.02	7.40 $\pm$ 0.02	7.40 $\pm$ 0.02

* = $p < 0.02$

** = $p < 0.001$

Table 7.2 Mean log values of plasma aldosterone and renin activity $\pm$ 1 standard deviation in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the ulcerative colitis group

	Ulcerative colitis patients n = 39	Control subjects n = 39	Crohn's disease patients n = 12
Aldosterone pg/ml log			
Resting	2.19 $\pm$ 0.25 ^{****}	1.85 $\pm$ 0.26	2.11 $\pm$ 0.26 ^{***}
Ambulant	2.30 $\pm$ 0.29 ^{****}	1.96 $\pm$ 0.28	2.29 $\pm$ 0.38 ^{***}
Renin pg/ml/hr log			
Resting	2.90 $\pm$ 0.41 ^{**}	2.65 $\pm$ 0.42	3.22 $\pm$ 0.19 ^{****}
Ambulant	3.18 $\pm$ 0.41	3.02 $\pm$ 0.43	3.34 $\pm$ 0.28 [*]

* = $p < 0.05$

** = $p < 0.02$

*** = $p < 0.01$

**** = $p < 0.001$

and Figures 7.1, 7.2, 7.3 and 7.4 are therefore expressed accordingly. Student's t test was used to test for statistically significant differences between these log values. The results given in Table 7.2 show that the mean plasma aldosterone levels were significantly higher in both groups of ileostomists as compared to those in the control group. These differences are shown diagrammatically in Figures 7.1 and 7.2. The mean resting and ambulant plasma renin activities were also raised in both groups of ileostomists compared to those in the control group but the higher ambulant level was not statistically significant in the ileostomists who had had ulcerative colitis. The log distribution of plasma renin activities in the three groups are shown in Figures 7.3 and 7.4.

The results of the urinary analysis are given in Table 7.3. The mean 24-hour volume of urine in the ileostomists was lower than that in the control group. The difference was not statistically significant in the ileostomists who had had ulcerative colitis. However, as was demonstrated in Chapter 6, these patients were drinking significantly more than the control subjects ($p < 0.001$) to compensate for the additional loss of fluid in the faeces.

The urine was more acidic in the ileostomists as compared to that in the control subjects and despite eating more salt the ileostomists had to conserve sodium in their kidneys due to the excess loss in the ileostomy effluent. The urinary loss of potassium was raised in the ileostomists who had had ulcerative colitis and the sodium to potassium ratio was low in both groups of patients with an ileostomy. All of these

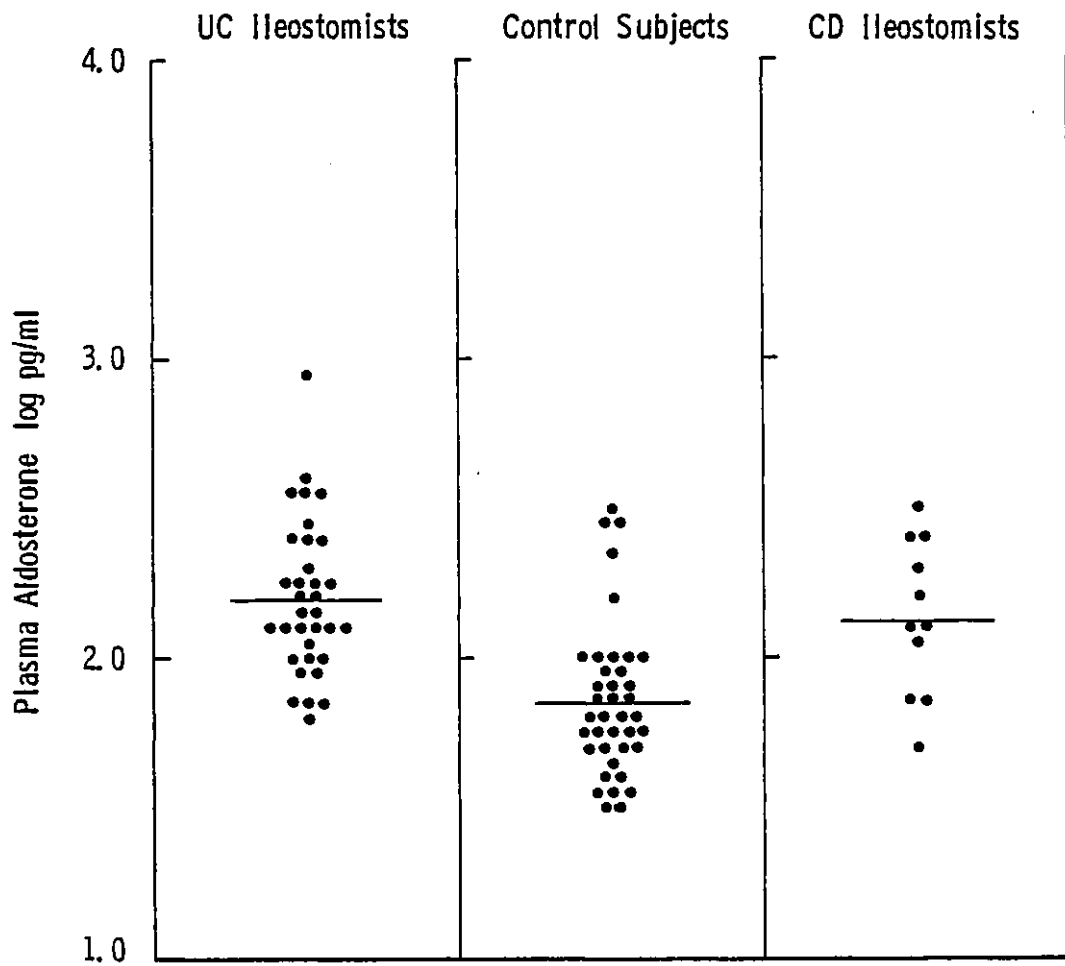


Figure 7.1. Resting plasma aldosterone in ileostomists with previous ulcerative colitis (UC) or with Crohn's disease (CD) compared with those in healthy control subjects matched for age and sex to the UC patients.

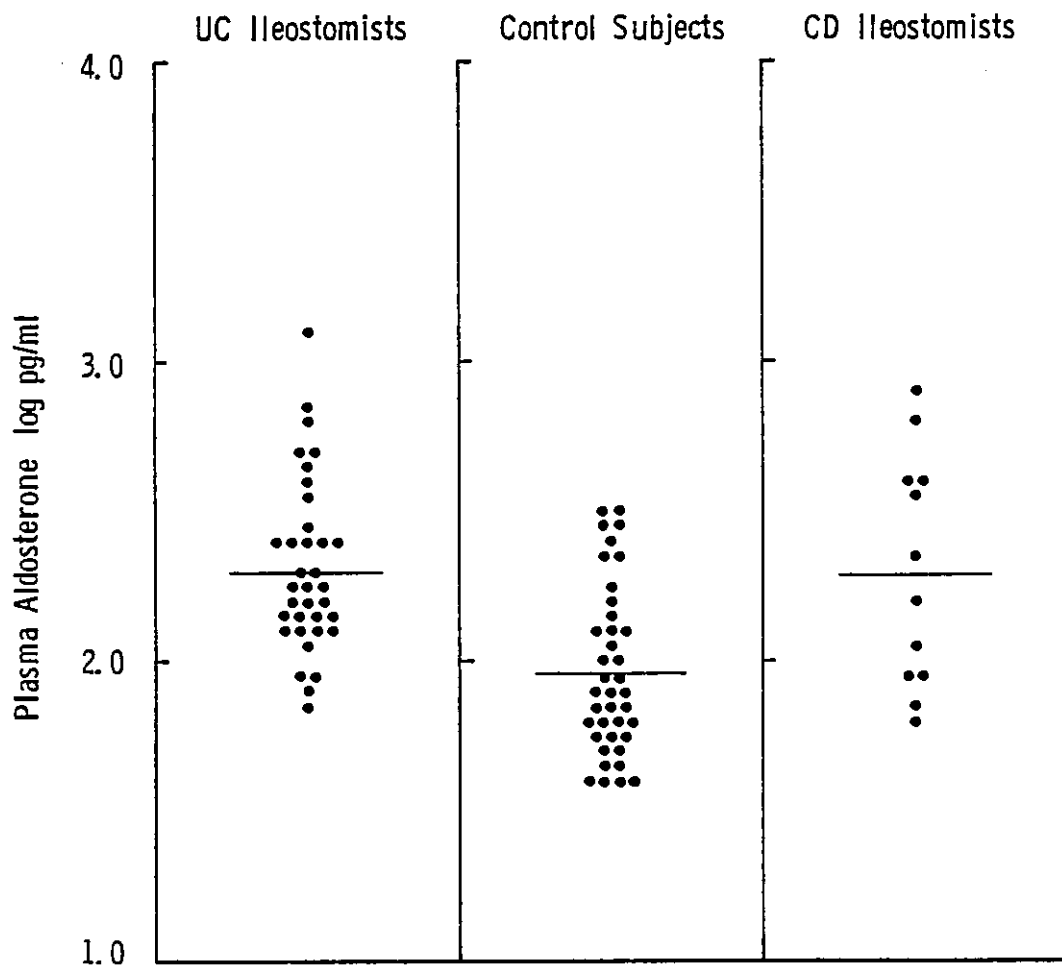


Figure 7.2. Ambulant plasma aldosterone levels in ileostomists with previous ulcerative colitis (UC) or with Crohn's disease (CD) compared with those in healthy control subjects matched for age and sex to the UC patients.

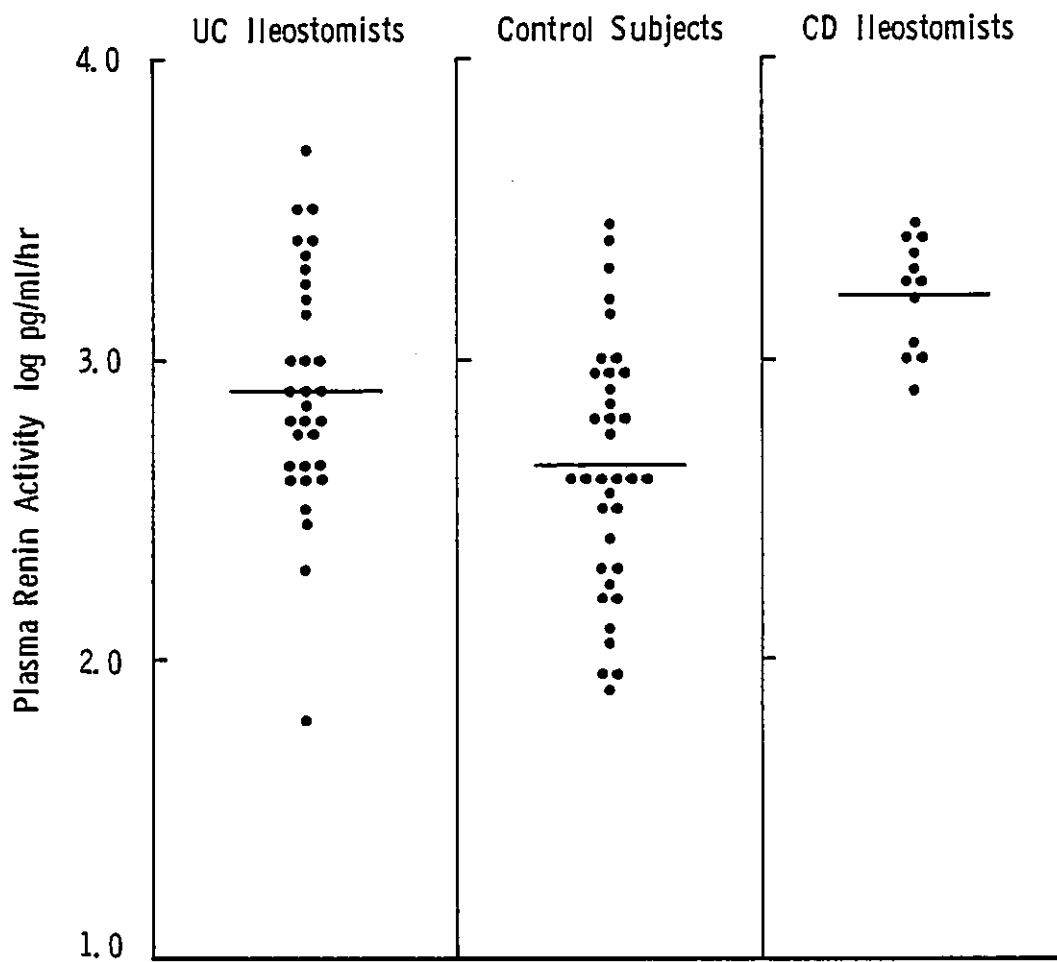


Figure 7.3. Resting plasma renin activity in the ileostomists with previous ulcerative colitis (UC) or with Crohn's disease (CD) compared with that in healthy control subjects matched for age and sex to the UC patients.

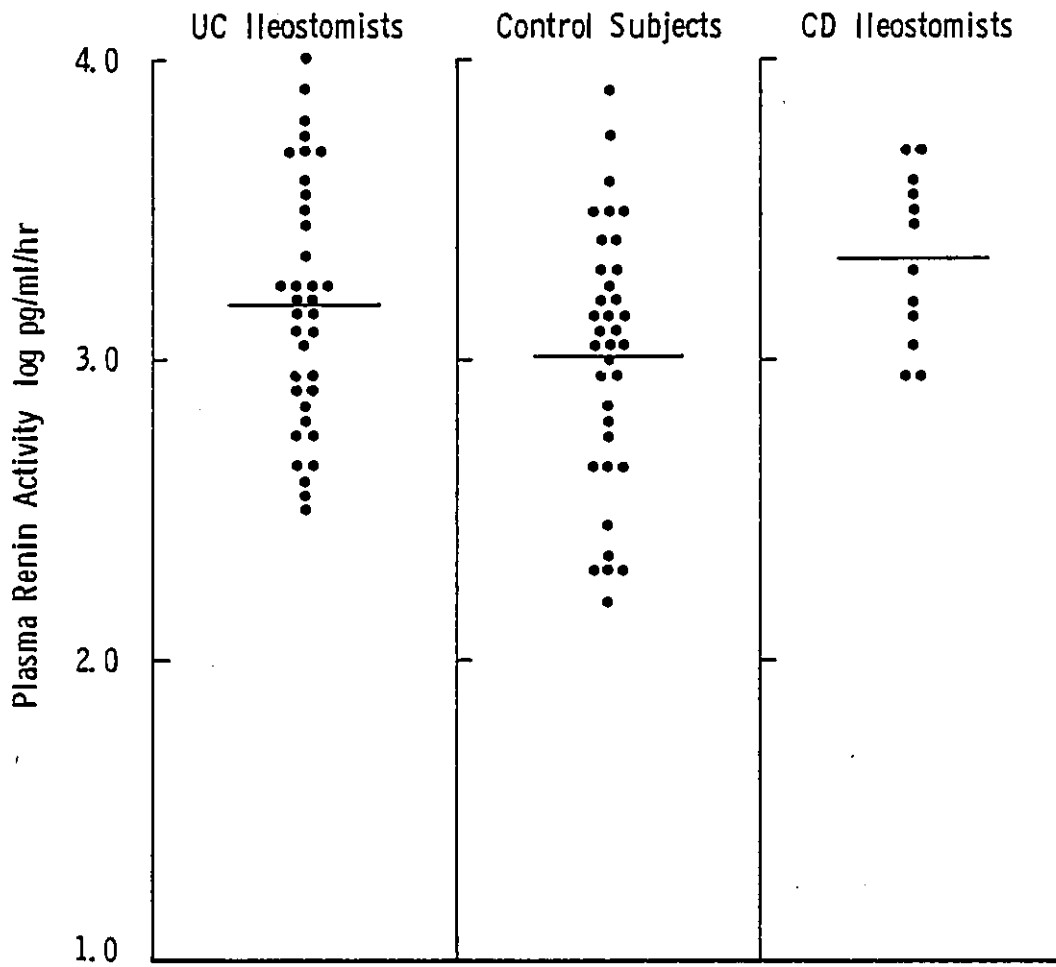


Figure 7.4. Ambulant plasma renin activity in the ileostomists with previous ulcerative colitis (UC) or with Crohn's disease (CD) compared with that in healthy control subjects matched for age and sex to the UC patients.

Table 7.3 Mean urinary biochemical values + 1 standard deviation of variables related to water and electrolyte balance and acid:base status in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the ulcerative colitis group

Variable	Ulcerative colitis patients n = 39	Control subjects n = 39	Crohn's disease patients n = 12
24 hour urine volume, l	1.34 ± 0.40	1.44 ± 0.56	0.89 ± 0.32 ^{***}
pH	5.29 ± 1.04 ^{***}	5.95 ± 1.05	5.69 ± 0.62
Sodium mmol/day	113 ± 65 [*]	142 ± 59	58 ± 47 ^{****}
Potassium mmol/day	79 ± 25 ^{***}	58 ± 20	52 ± 14
Urea mmol/day	324 ± 97	309 ± 91	209 ± 66
Creatinine mmol/day	13.3 ± 3.9	12.7 ± 4.0	10.0 ± 2.9 [*]
Creatinine clearance	116 ± 41	107 ± 35	94 ± 21
Sodium:Potassium	1.5 ± 0.8 ^{****}	2.5 ± 0.8	1.2 ± 1.0 ^{****}
Calcium mmol/day	4.33 ± 1.59	4.45 ± 2.48	2.57 ± 1.42 ^{**}
Phosphate mmol/day	25.02 ± 7.34	24.97 ± 10.59	17.02 ± 4.14 ^{**}
Magnesium mmol/day	2.57 ± 0.94 ^{**}	3.23 ± 1.37	1.57 ± 0.60 ^{****}

* = p<0.05

** = p<0.02

*** = p<0.01

**** = p<0.001

results are compatible with the finding that the ileostomists have a mild degree of secondary aldosteronism as a result of the excess loss of salt and water from the intestine.

Table 7.4 gives the results of the analysis of the ileostomy effluent. Wrong (1971) gives the approximate values calculated from faecal dialysates for normal faeces. He states that the normal loss of water in the faeces is less than 150 ml per day. Using this value, the loss of sodium in faeces can be calculated to be 3.9 mmol/day, of potassium 12 mmol/day, of calcium 1.9 mmol/day, and of magnesium 3.2 mmol/day. The mean faecal pH is 7.0 (range 6 - 8). The values given for the faecal excretion of calcium and magnesium in the faecal dialysate do not reflect the whole loss of calcium and magnesium in the faeces because significant amounts are passed as insoluble salts in the stool. By comparison with these data, it can be seen that the ileostomists investigated in the present study were losing about 500 ml more fluid in the faeces per day and about 65 mmol more sodium than would be expected in a normal subject. There was a reduced loss of potassium in the ileostomists as compared to normal but the pH of the ileostomy fluid was found to be similar to that of normal faecal dialysate. The losses of calcium and magnesium in ileostomy effluent and whole stool rather than faecal dialysate are considered in detail in Chapter 9.

DISCUSSION

The results of the analysis of fluid and electrolyte losses in the ileostomy effluent of the ileostomists in the present study were similar to those previously reported

Table 7.4 Mean ileostomy effluent values $\pm$ 1 standard deviation of variables related to water and electrolyte balance and acid:base status in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease

Variable		Ulcerative colitis patients n = 39	Crohn's disease patients n = 12
24-hr volume	l	606 $\pm$ 287	635 $\pm$ 372
24-hr weight	g	644 $\pm$ 297	659 $\pm$ 365
24-hr dry weight	g	66 $\pm$ 31	57 $\pm$ 20
Sodium	mmol/day	71 $\pm$ 36	79 $\pm$ 45
Potassium	mmol/day	5.1 $\pm$ 3.9	4.8 $\pm$ 2.7
Calcium	mmol/day	7.7 $\pm$ 3.8	6.1 $\pm$ 3.0
Magnesium	mmol/day	3.5 $\pm$ 1.8	2.7 $\pm$ 1.2
pH		7.1 $\pm$ 0.9	7.0 $\pm$ 0.8

(Crawford and Brooke, 1957; Smiddy et al, 1960; Nuguid et al, 1961; Kramer et al, 1962; Kanaghinis et al, 1963; King et al, 1978). The main differences from the fluid and electrolyte content of normal faeces are the increased losses of sodium and water. In 1962, Gallagher and his colleagues demonstrated that some patients with well established ileostomies were liable to develop salt and water depletion as a result of the increased loss from the bowel. Subsequently, other workers demonstrated that healthy ileostomists have a persistent sodium and water depletion of about seven per cent and 11 per cent respectively (Clarke et al, 1967; Hill et al, 1975a). Turnberg and his colleagues (1978) found that their patients with well established ileostomies were depleted of total exchangeable sodium and potassium, but had normal serum electrolyte concentrations and normal extracellular and total body fluid volumes. It must be pointed out that in none of these investigations was an age- and sex-matched control group studied. It is particularly important, as is demonstrated in many chapters of the present thesis, that this type of investigation should always include a matched control population whenever this is feasible. Nevertheless, all these studies suggest that ileostomists have a lower total exchangeable sodium concentration than normal. In addition, Turnberg and his colleagues found a lower total exchangeable potassium than normal. However, this group found normal serum electrolyte concentrations and did not find a reduction in total body water. Therefore, they concluded that the low exchangeable sodium and potassium levels were due to intracellular depletion. In the present study, the significantly raised

mean plasma levels of total protein and albumin suggest that there is a reduction in plasma volume. This, in turn, suggests that, despite having normal plasma sodium and potassium concentrations, the total exchangeable sodium and potassium in the plasma may be reduced.

The present study yielded evidence of renal conservation of sodium and water as has been reported previously (Clarke and McKenzie, 1969; Singer et al, 1973). In addition, the dietary analysis, undertaken as part of the present investigation, demonstrated a higher salt and water intake in the ileostomists as compared to that in the control subjects. All of these blood and urinary changes suggest that there is a depletion of salt and probably water in ileostomists and that the body is attempting to compensate for this depletion. However, Isaacs and his colleagues (1976) found normal levels of plasma aldosterone in six patients and Turnberg and his co-workers (1978) found normal levels of plasma aldosterone and renin activity in most of their patients. The present study, by using a larger group of ileostomists and age- and sex-matched control subjects has demonstrated a significantly raised mean level of plasma aldosterone in ileostomists as compared to healthy subjects matched for age and sex ($p < 0.001$). The plasma renin activity was also raised in these patients but the increase was not as marked.

A higher rise of plasma aldosterone as compared to that of plasma renin activity may be due to factors affecting aldosterone release. These factors are: sodium depletion (Oelkers et al, 1974), potassium excess (Fraser et al, 1979), ACTH output as an acute stimulus (Fraser et al, 1979),

increased serotonin (Mantero et al, 1979) and dopamine antagonists (Edwards et al, 1980). In addition, there may be other stimuli that are at present unknown. As has been discussed, ileostomists have been shown to be sodium depleted. Therefore, as sodium depletion is known to make the cells of the adrenal cortex more sensitive to smaller rises in Angiotensin II (Oelkers et al, 1974; Coghlan et al, 1979), it is likely that this is the explanation for the relatively higher level of plasma aldosterone compared to the plasma renin activity in these patients.

There has been some discussion as to whether the ileum adapts to conserve more salt and water than normal in patients who have had a proctocolectomy with formation of an ileostomy. Crawford and Brooke (1957) found that their patients passed on average two or more litres per day through their ileostomy during the first postoperative week. They found that, soon after this, the volume decreased to about 500 ml per day. However, other workers have found that the long established ileostomy puts out an effluent of higher volume and containing more sodium than the newly established ileostomy (Nuguid et al, 1961; Kanaghinis et al, 1963; Hill et al, 1974). The differences between these results may well depend on the volume of intravenous fluid and oral supplements that the patients were given in the early postoperative period. In any case, several investigators have shown that about 1,500 ml per day of fluid enters the colon from the ileum in a normal subject (Phillips and Giller, 1973; Debongnie and Phillips, 1978; MacGregor et al, 1978). Therefore, the output of a well established ileostomy appears to be about a third of that which normally passes into the colon so that

ileostomy adaptation may be presumed to have taken place. A number of theories have been proposed to explain such an adaptation. An increased output of antidiuretic hormone (ADH) has been suggested (LeVeen et al, 1962). However, the ingestion of sufficiently large quantities of water to cause a considerable increase in urinary output has not been shown to result in an increase in the volume of the ileostomy effluent (Kramer et al, 1962; Hill et al, 1976). Therefore, it is unlikely that ileostomy adaptation is caused primarily by ADH. Another possibility is a change in bowel motility which might allow more time for salt and water absorption to take place. Some evidence in support of this theory is presented later in the present thesis as there is an alteration in some of the gastrointestinal hormones controlling bowel motility (Chapter 12). Nevertheless, an increased output of aldosterone, as is demonstrated in the present study, is the most likely explanation for ileostomy adaptation. Previous investigations give indirect support to this hypothesis. For instance, Hill and his colleagues (1974) found that a three-litre intravenous infusion of normal saline given to five ileostomists not only caused an increase in urinary volume and sodium output but also caused an increase in the ileostomy effluent volume and sodium output. This effect was almost certainly due to the intravenous fluid causing a sharp reduction in aldosterone release. In addition, Isaacs and his colleagues (1976) demonstrated an increased potential difference across the terminal ileal mucosa of ileostomists compared to that normally found, suggesting that there may be increased sodium absorption.

The acid:base balance in ileostomists is also of importance.

It was shown in Table 7.3 that the pH of the urine in the ileostomists was lower than that in the control subjects. This finding corresponds well to the increased level of aldosterone which causes the renal tubular cells to retain sodium in exchange for potassium and hydrogen ions which are excreted in the urine. Despite this excessive loss of hydrogen ions, the ileostomists maintained a normal blood pH and the pH of the ileostomy effluent was similar to that of normal faeces. Previously, it has been suggested that the more acidic urine found in ileostomists might in part be due to increased loss of bicarbonate ions in the ileostomy effluent as compared to that in normal faeces (Clarke and McKenzie, 1969). However, Wrong (1970) demonstrated that the colonic mucosa normally secretes bicarbonate ions and, as has been mentioned, the ileostomy effluent was found to have a similar pH to that of normal faeces. Therefore, the cause of the more acidic urine passed by ileostomists is likely to be due to the action of aldosterone on the renal tubular cells.

In primary aldosteronism sodium is conserved in the kidney in exchange particularly for potassium ions but also for hydrogen ions. This leads to an intracellular depletion of potassium and this ion is thought to be replaced by hydrogen ions. As a result, it is suggested that the patients develop an intracellular acidosis but an extracellular alkalosis (Zilva and Pannall, 1979). In the present study, where aldosteronism has been demonstrated as a response to salt and water depletion, sodium was being conserved by the renal tubules of the patients in exchange for potassium and hydrogen ions. Although the pH of the blood in these ileostomists was found to be normal, it is possible that

there is a reduction in intracellular potassium with a resulting intracellular acidosis.

The ileostomists taking part in the present study all seemed to be in good general health and so it can be questioned if this degree of sodium and water depletion is of any clinical significance. Certainly, they are at increased risk of developing severe salt and water depletion if they develop gastroenteritis or suffer from ileostomy diarrhoea for any other reason. They are also at risk in hot climates where sodium and water losses in sweat may also be considerable. In addition, the secondary hyperaldosteronism results in an acidic urine and reduced urine volume, both of which favour the formation of renal stones. Finally, if there is a reduction of intracellular potassium and increased intracellular acidosis, these factors may influence important aspects of cellular metabolism. For example, it is known that metabolic acidosis may result in osteoporosis (Lemann et al, 1966). This may also occur with intracellular acidosis. An attempt to investigate this possibility has been made in the present study and the results are discussed in Chapter 8 where calcium and magnesium metabolism are considered in detail.

For the reasons given in the previous paragraph it would seem to be important to attempt to correct salt and water depletion in ileostomists. The simplest suggestion would be to ask all patients to increase their salt and water ingestion. However, Kanaghinis and his colleagues (1963) found that increasing either salt or potassium chloride ingestion in ileostomists resulted in an increased loss of

salt and water in the ileostomy effluent. In addition, the urinary excretion of sodium and water was reduced. They explained these findings by suggesting that the added sodium was producing an osmotic effect which paradoxically caused increased sodium and water loss in ileostomy effluent. Therefore, it seems unwise to recommend an increase in the intake of salt beyond that which the patients appear to take naturally (Chapter 6). Another suggestion that has been made is to add either sodium bicarbonate or sodium citrate to the diet. These substances would have the advantage of providing additional sodium as well as tending to correct the acidic urine. Unfortunately, it is probable that the sodium given orally as part of these compounds would result in the same osmotic effect as that found with sodium chloride.

There remains one way in which it might be possible to increase sodium and water retention by the small intestine of patients with an ileostomy. That is to use an isotonic glucose-electrolyte mixture as is recommended for the oral therapy of cholera (Sladen, 1974; Leading Article, *Lancet*, 1975). The addition of glucose and some amino acids, such as glycine, to these electrolyte solutions causes a considerable increase in sodium and water absorption by the small intestine of cholera victims. Therefore, there is reason to believe that these mixtures may be of value in stimulating sodium absorption from the intestine in patients with an ileostomy. A proper controlled trial of the addition to the diet of salt, sodium bicarbonate, sodium citrate and finally glucose-aminoacid-

electrolyte mixtures should be undertaken in patient with an ileostomy to assess the therapeutic value of these agents.

CHAPTER 8

HAEMATOLOGICAL ASPECTS

INTRODUCTION

There have been few investigations into the general haematology of patients with an ileostomy. Daly (1968) took blood from 100 ileostomists, who had had ulcerative colitis, to measure both the haemoglobin concentration and serum vitamin B₁₂ level. Eight out of these 100 ileostomists were found to have a low haemoglobin concentration. Two of these patients were men, one of them was known to have cirrhosis of the liver; the second was an otherwise healthy man, who had a typical iron deficiency picture, which rapidly improved with a course of oral iron and advice concerning his diet. The remaining six anaemic patients were women. In four of these patients the anaemia was attributed to heavy menstrual periods and in one the cause was cirrhosis of the liver. The last patient was a 74 year old widow who was living on an inadequate diet. In each of the 100 ileostomists the serum B₁₂ level was within the normal range.

Several workers have studied vitamin B₁₂ absorption in small groups of ileostomists, who had had ulcerative colitis, using the Schilling test (Jagenburg et al, 1971; Miettinen and Peltokallio, 1971; Lenz, 1976). In a few individuals the urinary excretion of vitamin B₁₂ was found to be low but in general the absorption was normal. Jagenburg and his colleagues found that both the serum vitamin B₁₂ and the

serum folate levels were normal in all their ten patients. There have been no other studies of folate metabolism in patients with a conventional ileostomy.

PATIENTS AND METHODS

All the 51 ileostomists taking part in the present study had detailed haematological investigations carried out. They each had blood taken for the measurement of a full blood count, serum vitamin B₁₂, serum and red cell folate, serum iron and iron binding capacity. The full blood count was measured using a Coulter counter. The serum vitamin B₁₂ was determined by a radio-isotopic method (Britt et al, 1969). Serum iron and iron binding capacity were determined on a Technicon auto-analyser. Finally, serum and red cell folate were assayed by using a micro-biological method with *Lactobacillus casei* (Association of Clinical Pathologists: Broadsheet, 1973). Iron and vitamin B₁₂ absorption were measured in every patient using the Oxford Shadow Shield total body counter (Warner and Oliver, 1966; Callender et al, 1966). Each patient was given a standard oral dose of five mg of ferrous iron, with 50 mg of ascorbic acid to which two to four μCi of ⁵⁹Fe was added as ferric chloride. The percentage of labelled iron retained after one week was measured on the total body counter. Subsequently, each patient was given 0.5 μg of vitamin B₁₂, labelled with 0.5 μCi of ⁵⁸Co and the retention after one week was determined by the same method.

The 39 patients who had had ulcerative colitis, subsequently underwent further investigation of iron metabolism. Each of them had another measurement of their full blood count and their serum ferritin was determined. All the serum ferritin estimations were carried out at the University Hospital of Wales in Cardiff using an immunoradiometric assay (Addison et al, 1972). Following this, these ileostomists were randomly divided into two groups, half of them received ferrous fumarate (Fersamal) 200 mg three times daily for three months while the other half, acting as controls, were not given any supplements of iron. At the end of the three month period, each patient in both groups, had the measurements of their full blood count, serum ferritin and iron absorption repeated.

Twenty-five of the ileostomists who had had ulcerative colitis and who were either male or postmenopausal females had their rate of iron loss determined by measuring the retention of ^{59}Fe after approximately six weeks and calculating the percentage loss per day using this value. Ten of these patients had their ileostomy effluent tested for occult blood using the 'Haemoccult' test. This is a guaiac resin test modified by Greigor (1971); it is made by Smith Kline Instruments Incorporated in the United States of America and marketed in England by Eaton Laboratories, (Kratochvil et al, 1971; Morris et al, 1976; Hardcastle et al, 1980). The ileostomy effluent was tested, in this manner, on at least three occasions in each patient. Finally, as has been discussed in Chapter 6, the dietary iron intake was estimated for each of the 51 patients.

The 39 age- and sex-matched healthy control subjects were also studied, with measurements being made of the full blood count, serum ferritin, serum iron and iron binding capacity, and with estimations being made of their dietary intake of iron. These subjects did not act as healthy controls for the measurements of absorption on the total body counter as it was not considered justifiable to employ radioactive isotopes in them. Instead, 35 healthy subjects who had previously been studied for the absorption of iron using the Oxford total body counter, acted as controls. The results that had been obtained with these subjects were compared with the results obtained in the ileostomists. Of these 35 control subjects, 19 were men, with a mean age of 46 and the remaining 16 were women with a mean age of 29. Therefore, the mean age of the male subjects acting as healthy controls for iron absorption was similar to that of the male patients who had had ulcerative colitis, whose mean age was 50 years. The mean age of the women acting as healthy control subjects was significantly less than the mean age of the female ileostomists, which was 48. This may be important because regular menstrual blood loss would be occurring in more of the female control subjects than in the female ileostomists. This suggests that more iron would be likely to be retained by the younger group of healthy female control subjects than by the older group of female ileostomists.

One hundred and twenty-one healthy subjects had previously had vitamin B₁₂ absorption measured on the Oxford Shadow Shield total body counter. This large number of subjects

was used as the healthy control group for vitamin B₁₂ absorption.

RESULTS

The results obtained by the measurement of the full blood count in the patients with an ileostomy and the healthy control subjects have been given in Chapter 4. In summary, if correction is made for the apparent haemo-concentration found in the ileostomy patients, as suggested by a significantly raised serum albumin and total protein ($p < 0.02$ and $p < 0.001$ respectively), then both the ulcerative colitis and Crohn's disease groups of ileostomists had a significantly lower haemoglobin than the healthy control subjects ($p < 0.05$ and $p < 0.001$ respectively). In addition, the group of patients who had had ulcerative colitis had a significantly low mean corpuscular volume, MCV ($p < 0.001$) and a significantly low mean corpuscular haemoglobin, MCH ($p < 0.01$). These results are included in Table 8.1.

Iron metabolism

The abnormalities in iron metabolism found in the present study occurred in both the male and female patients. For this reason the male and female ileostomists are considered as one group when comparing them to the healthy control subjects.

The results of the full blood count in the patients with an ileostomy suggested a degree of iron deficiency. Further investigations of iron metabolism were undertaken and are recorded in Table 8.1. This Table shows that no significant

Table 8.1 Iron metabolism in ileostomists compared to that in healthy control subjects. The values given are means $\pm$ 1 standard deviation

	Ulcerative colitis group n = 39	Healthy control group n = 39	Crohn's disease group n = 12
Haemoglobin g/dl	14.4 $\pm$ 1.5	14.1 $\pm$ 1.5	12.9 $\pm$ 1.4**
Corrected haemoglobin g/dl	13.4 $\pm$ 1.4*	14.1 $\pm$ 1.5	12.1 $\pm$ 1.3****
Mean corpuscular volume (MCV) fl	86.1 $\pm$ 4.4****	89.6 $\pm$ 3.8	89.1 $\pm$ 6.2
Mean corpuscular haemoglobin (MCH) pg	29.5 $\pm$ 2.0***	30.7 $\pm$ 1.5	30.1 $\pm$ 2.5
Mean corpuscular haemoglobin con- centration (MCHC g/dl	33.9 $\pm$ 1.1	33.8 $\pm$ 0.9	33.6 $\pm$ 1.0
Serum Iron μ mol/l	16.9 $\pm$ 6.7	18.3 $\pm$ 7.1	16.1 $\pm$ 7.9
Serum iron binding capacity μ mol/l	67.1 $\pm$ 10.0	63.7 $\pm$ 15.6	68.6 $\pm$ 13.0
Serum ferritin μ g/l	41.3 $\pm$ 33.7***	78.6 $\pm$ 68.4	-
Iron retention %	26.5 $\pm$ 17.6****	12.9 $\pm$ 7.5	25.5 $\pm$ 23.1****
Loss of iron/day %	+ 0.3 $\pm$ 0.4	0.1 $\pm$ 0.1	-

* = p 0.05
 ** = p 0.02
 *** = p 0.01
 **** = p 0.001

+ Iron loss was only recorded
 in males and post menopausal
 female patients and healthy
 controls

difference was found in either the serum iron or the iron binding capacity between the patients with an ileostomy and the healthy control subjects. However, serum ferritin, which was only measured in the patients who had had ulcerative colitis, was significantly lower in the ileostomists than in the healthy control subjects ($p < 0.01$). In addition, the retention of iron, measured on the total body counter, was significantly raised in the ileostomists who had had ulcerative colitis and also in those with Crohn's disease compared to the healthy control subjects ($p < 0.001$ and $p < 0.01$ respectively).

These more detailed investigations of iron metabolism also indicated that these patients with an ileostomy, whether they had had ulcerative colitis or had Crohn's disease, were mildly iron deficient. Could this be explained by iron deficiency resulting from the chronic blood loss occurring while the patient had colitis combined with further blood loss at the time of the operation? In an attempt to answer this question, the ileostomists who had had ulcerative colitis were divided into two groups. The first group was made up of the 25 patients who had had an ileostomy for three years or more. These patients had had sufficient time to make up for any iron deficiency occurring as a result of the previous illness or operation. The remaining 15 patients, who had had their operation less than three years previously made up the second group. These patients might be expected to have a significantly lower mean serum ferritin level and higher mean retention than the patients in the first group if the iron deficiency was caused by

the previous illness and operation. The mean serum ferritin in the two groups was $45.6 \pm 34.1 \mu\text{g/l}$ and $33.7 \pm 32.9 \mu\text{g/l}$ respectively (the difference is not statistically significant). The mean percentage iron retention in the two groups was 23.8 ± 16.8 and 31.3 ± 18.6 respectively (the difference is not statistically significant). Both the mean serum ferritin and mean iron retention are nearer to normal in the patients who have had an ileostomy for more than three years. However, as is shown above, the difference between the two groups is not statistically significant. In addition, the mean values of both the serum ferritin and iron retention remain significantly different when the results obtained in the patients who have had an ileostomy for three years or more are compared to the results obtained in the healthy control subjects ($p < 0.05$ and $p < 0.01$ respectively). Therefore, a part of the iron deficiency found in these patients may result from the previous colitis or operation but it is unlikely to be the sole cause of this deficiency.

Further investigations of iron metabolism were undertaken to determine whether oral supplements of iron would correct the apparent iron deficiency and also to determine whether there was either an increased iron loss or a deficient intake of iron in the diet in patients with a well established ileostomy. Table 8.2 gives the results of the study where the patients who had had ulcerative colitis were randomly divided into two groups. One group of patients was given iron supplements for three months while the remaining patients received no iron and made up a control group. The value of the variables, in the two groups, before and after the three month period are shown in the Table. It may be

Table 8.2 Measurements of the full blood count and iron metabolism in ileostomists who had had ulcerative colitis. The patients were randomly divided into two groups, one of which was given iron supplements for three months while the other group received no iron. The values given are means $\pm$ 1 standard deviation

	Group 1 n = 19		Group 2 n = 20	
	Baseline values	Values after iron supplements for 3 months	Baseline values	Values 3 months later after no iron supplements
Haemoglobin g/dl	14.4 $\pm$ 1.5	14.4 $\pm$ 1.4	14.4 $\pm$ 1.5	14.3 $\pm$ 1.6
Mean corpuscular volume fl	86.6 $\pm$ 3.2	87.7 $\pm$ 3.6	85.6 $\pm$ 5.3	86.5 $\pm$ 5.39
Mean corpuscular haemoglobin pg	29.6 $\pm$ 1.3	29.9 $\pm$ 1.4	29.5 $\pm$ 2.5	29.2 $\pm$ 2.5
Mean corpuscular haemoglobin g/dl concentration	33.8 $\pm$ 1.1	33.9 $\pm$ 1.0	33.9 $\pm$ 1.1	33.5 $\pm$ 1.2
Serum iron μ mol/l	16.6 $\pm$ 7.5	18.6 $\pm$ 5.9	17.3 $\pm$ 6.1	19.2 $\pm$ 7.5
Serum iron binding capacity μ mol/l	64.3 $\pm$ 8.4	62.7 $\pm$ 16.6	69.8 $\pm$ 10.9	70.1 $\pm$ 13.0
Serum ferritin μ g/l	35.9 $\pm$ 31.2	59.4 $\pm$ 42.0	46.5 $\pm$ 36.0	45.9 $\pm$ 35.7
Iron retention %	24.8 $\pm$ 14.7	14.5 $\pm$ 11.2	28.1 $\pm$ 20.3	23.6 $\pm$ 18.8

seen that both the serum ferritin and iron retention were nearer to normal after the iron supplements in group one; whereas in group two the mean serum ferritin remained low and the mean iron retention remained high. These findings are illustrated in Figures 8.1 and 8.2

Referring back to Table 8.1 it may be seen that the percentage loss of ^{59}Fe per day was greater in the ileostomists who had had ulcerative colitis than the loss occurring in the healthy control subjects. Unfortunately, the loss of ^{59}Fe has only been measured in five healthy control subjects on the Oxford total body counter. Therefore, no definite conclusion can be drawn but it appears that the patients with an ileostomy may be losing more iron from their bowel than healthy normal subjects.

Finally, the intake of iron in the diet was estimated by the method described in Chapter 6. The patients with an ileostomy who had had ulcerative colitis had a mean daily iron intake of $16.1 \pm 12.6\text{mg}$. The healthy control subjects who were age- and sex-matched to the patients had a mean daily iron intake of $17.0 \pm 13.5\text{mg}$. The difference between the intake of iron in the patients and in the healthy control subjects is not significant.

Vitamin B₁₂ metabolism

The lower limit of normal for the serum vitamin B₁₂ assay that is carried out in Oxford is 170pg/ml. The mean serum vitamin B₁₂ level in the 39 ileostomists who had had

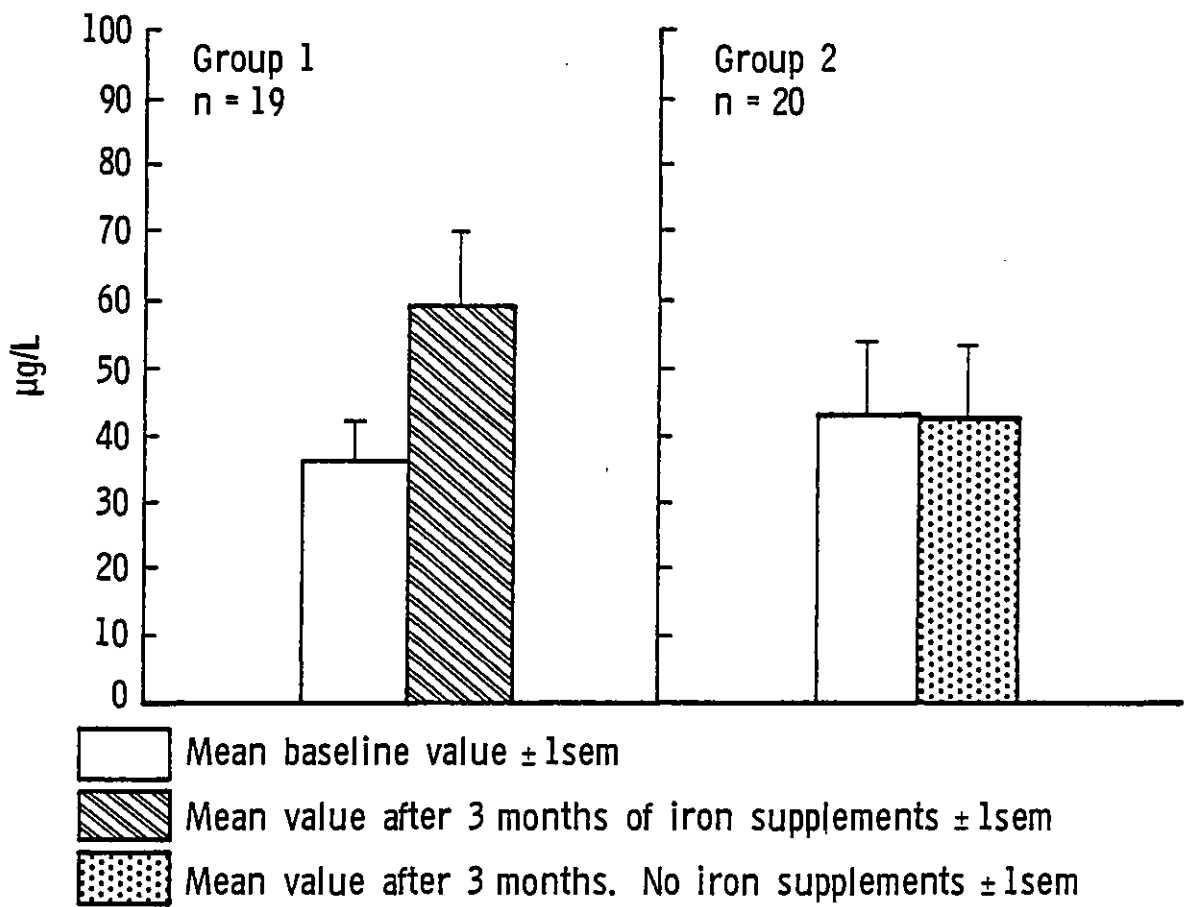


Figure 8.1. Serum ferritin values in ileostomists who had had ulcerative colitis. The patients were randomly divided into two groups, one of which was given iron supplements for three months while the other group received no iron.

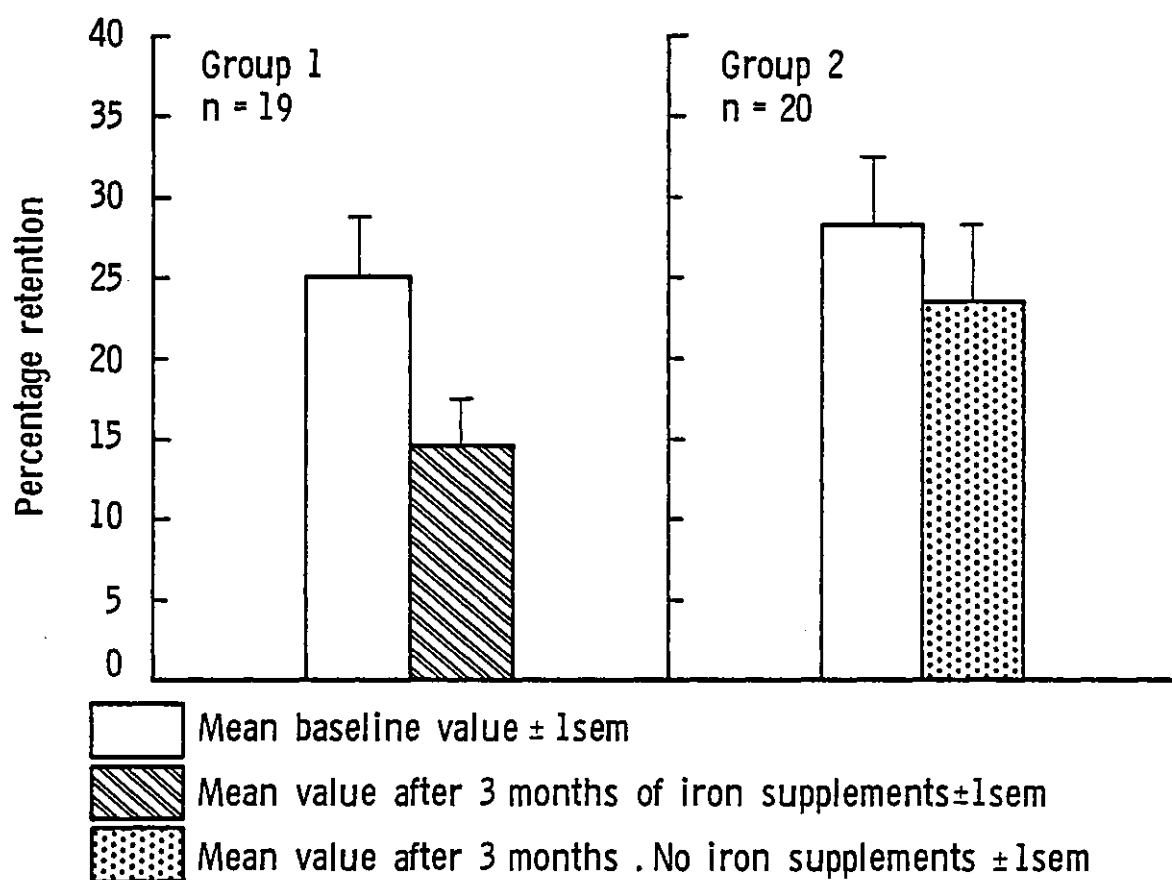


Figure 8.2. Iron retention in ileostomists who had had ulcerative colitis. The patients were randomly divided into two groups, one of which was given iron supplements for three months while the other group received no iron.

ulcerative colitis was 395 ± 121.7 pg/ml. The values ranged from 160 to 750 pg/ml. Only one of these patients had a serum vitamin B₁₂ level below the lower limit of normal. The 12 patients with an ileostomy who had Crohn's disease had a mean serum vitamin B₁₂ level of 369.2 ± 177.4 pg/ml with a range from 140 - 750 pg/ml. Only one of these patients had a value below the lower limit of normal but several of the patients were receiving regular parenteral vitamin B₁₂ because they had had an appreciable length of terminal ileum resected.

The mean retention of vitamin B₁₂ labelled with ⁵⁸Co in the 121 healthy control subjects, who had previously been studied on the Oxford total body counter, was 63.8 ± 12.9 per cent (range 34.4 - 84.6%). The mean retention of vitamin B₁₂ in the 39 ileostomists who had had ulcerative colitis was 74.4 ± 17.0 per cent (range 43.0 - 100%). The ileostomists who had had ulcerative colitis retained a significantly greater percentage of labelled vitamin B₁₂ than the healthy control subjects ($p < 0.001$).

The ileostomists who had Crohn's disease retained 51.4 ± 25.5 per cent (range 23.0 - 86%). These patients retained significantly less labelled vitamin B₁₂ than the healthy controls ($p < 0.01$). These findings are illustrated in Fig.8.3.

Serum and red cell folate

The normal range for the serum folate assay that is carried out in Oxford is 2.1 - 28.0 µg/l and the normal range for the red cell folate assay is 160 - 640 µg/l. Each of

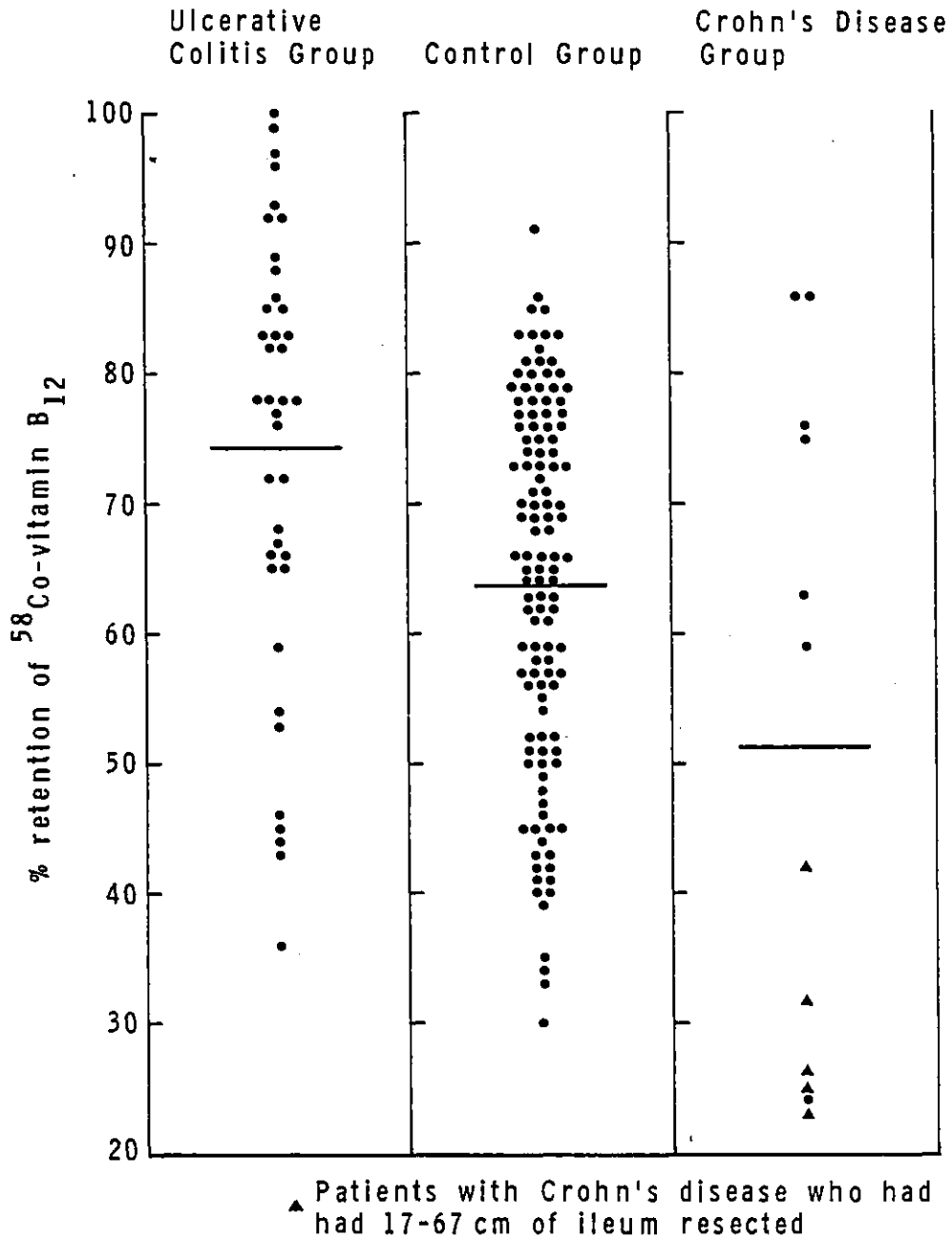


Figure 8.3. Vitamin B₁₂ absorption in ileostomists with previous ulcerative colitis (UC) or with Crohn's disease compared with that in a large group of healthy control subjects.

the 39 patients who had had ulcerative colitis had normal serum and red cell folate levels. The mean serum folate was $8.1 \pm 3.7 \mu\text{g/l}$ (range 3.2 - 18 $\mu\text{g/l}$) and the mean red cell folate was 502.2 ± 176.9 (range 255 - 895 $\mu\text{g/l}$). One of the patients who had an ileostomy for Crohn's disease had a low serum folate level but all of them had normal red cell folate levels. The mean serum folate in these patients was $7.2 \pm 3.5 \mu\text{g/l}$ (range 1.9 - 14.7 $\mu\text{g/l}$) and the mean red cell folate was $392 \pm 135.8 \mu\text{g/l}$ (range 205 - 726 $\mu\text{g/l}$).

DISCUSSION

The haematology of ileostomists who had had ulcerative colitis has been thought to be normal. Daly (1968) found that a few of his patients were anaemic but he found an adequate explanation for this anaemia in each patient so affected. Jagenburg and his colleagues (1971) found that all their ten patients with conventional ileostomies had a normal haemoglobin level, a normal serum iron and normal iron binding capacity. Serum vitamin B₁₂ levels were found to be normal in every patient by Daly (1968) and also by Jagenburg and his colleagues (1971). In addition, vitamin B₁₂ absorption has been reported as normal in the great majority of ileostomists who have had ulcerative colitis (Jagenburg et al, 1971; Miettinen and Peltokallio, 1971; Lenz, 1976). Serum folate was found to be normal by Jagenburg and his co-workers (1971) in their ten patients with a conventional ileostomy.

In the present study, abnormalities of the haematology of ileostomists have been demonstrated. Evidence of mild

iron deficiency was found even in those patients who had had a proctocolectomy for ulcerative colitis. Some of these patients were anaemic if allowance is made for the apparent haemoconcentration. All the abnormalities found supported a diagnosis of iron deficiency; these were a low MCV, a low MCH, a low serum ferritin and a high iron retention on the body counter. It is interesting that, despite these findings, both the serum iron and iron binding capacity in the patients were not significantly different from those in the healthy control subjects. This is likely to indicate that the measurements of serum iron and iron binding capacity are not a sensitive method for diagnosing iron deficiency.

An attempt was made to discover the cause of the iron deficiency. Blood loss from the previous illness and operation probably plays a part in this abnormality but it is not the only or even the main cause. This was demonstrated by finding that the ileostomists who had had ulcerative colitis were still deficient of iron even if their operation had been undertaken three or more years previously. One possible explanation was that the patients might be taking a diet deficient in iron. As has been shown this does not appear to be the answer because the ileostomists were found to be eating a similar amount of iron as the age- and sex-matched healthy control subjects. Ascorbic acid (vitamin C) is known to enhance iron absorption (Moore, 1955) and so possibly the ileostomists might have been taking a diet low in ascorbate. Once again this was not found when their diet was analysed. The ileostomists who had had ulcerative colitis ate an average of 62.8 ± 37.4 mg of ascorbate per day and the

mean intake of ascorbate by the healthy controls subjects was 62.3 ± 33.8 mg per day. There was no significant difference between the vitamin C intake in the patients and that in the healthy control subjects. Other factors, such as tea and possibly coffee have been shown to inhibit the absorption of inorganic iron (Disler et al, 1975). It was demonstrated in Chapter 6 that the fluid intake of the patients with an ileostomy for ulcerative colitis were drinking, on average, about 350 ml more fluid per day than the healthy control subjects. Some of this higher fluid intake will have been taken as tea and coffee which could inhibit iron absorption. However, some of the fluid will have been taken as drinks, such as orange juice which contain ascorbate and might enhance iron absorption. In addition, Disler and his colleagues (1975) showed that organic iron, in cooked meat, was not affected by the ingestion of tea. There was no evidence to suggest that the ileostomists taking part in the present study were eating a diet deficient in meat. Therefore, it seems unlikely that the iron deficiency found in these ileostomists was due either to a diet deficient in iron or to any factors in the diet that might inhibit the absorption of iron.

It has been shown that the ileostomists who had had ulcerative colitis and who were taking part in the present study could absorb iron from the bowel normally. Moreover, if the iron deficiency found in these patients was not due either to the illness and operation nor to an abnormal diet, then the only other possible cause must have been increased loss of iron from the body. This conclusion was supported by

finding an apparently higher percentage loss of iron in the ileostomists who had had ulcerative colitis, than in the five healthy subjects whose iron loss had previously been studied on the Oxford total body counter. This finding was not conclusive, possibly due to the small number of control subjects, as the difference in iron loss between the ileostomists and the controls was not statistically significant.

Assuming that an increased iron loss is the cause of the iron deficiency in these patients with an ileostomy, then what could be the reason for the increased loss ? No occult blood was found in the ileostomy effluent of the ten patients in whom this was studied. In addition, apart from a very small amount of blood that may be lost from minor trauma to the stoma itself, there is no known reason why ileostomists who have had ulcerative colitis should lose blood from their bowel. Possibly there is an increase in the cell turnover of the small intestinal mucosa, thus leading to an increased loss of iron-containing cells from the bowel or possibly the colon does absorb a small amount of iron in the normal subject. This study has found no definite cause for this iron deficiency. However, a course of oral ferrous fumarate corrected both the low serum ferritin and high iron retention nearly to normal. It is important to stress that the discovery of mild iron deficiency in these ileostomists was found only by detailed study and particularly by matching the group as a whole to age- and sex-matched healthy subjects. There were few individuals who were actually anaemic and few with a serum ferritin below $12 \mu\text{g/l}$, indicating marked iron deficiency. It appears that most of the patients are capable of maintaining

their iron balance, without becoming markedly deficient of iron, by increasing their iron absorption from the small intestine.

The ileostomists who had Crohn's disease had a lower mean haemoglobin concentration than the healthy control subjects and four of the 12 were anaemic, even without allowance being made for haemoconcentration. The mean MCV, MCH and MCHC were not significantly different from those of the healthy subjects. The mean iron retention was significantly raised. Due to the small number of these patients, it is less easy to draw firm conclusions. Nevertheless, they also have a high mean iron retention in both male and female patients. However, among these patients with Crohn's disease, it is quite possible that some are losing occult blood in the ileostomy effluent due to inflammation in the small intestine.

The study of vitamin B₁₂ metabolism also revealed some unexpected findings. The serum levels of vitamin B₁₂ were normal in the patients who had had ulcerative colitis. This finding agreed with the results of Daly (1968) and Jagenburg and his colleagues (1971). However, it was a surprise to find a significantly greater retention of vitamin B₁₂ in these ileostomists as compared to that in a large group of healthy control subjects. Previous studies of vitamin B₁₂ absorption in ileostomists who had had ulcerative colitis using the Schilling test have shown it to be normal in the great majority of patients and low in a few (Jagenburg et al, 1971; Miettinen and Peltokallio, 1971; Lenz, 1976). These studies were carried

out in small numbers of patients and healthy control subjects were not studied. Furthermore, the Schilling test is an indirect test of vitamin B₁₂ absorption which is subject to considerable error and is certainly much less accurate than the direct test of absorption employed in the present study.

The reason for the enhanced absorption of vitamin B₁₂ is not known. However, the results of the present study taken in conjunction with data obtained by other workers suggest some possible causes.

1. Aldosteronism has been found in the ileostomists taking part in the present study and there is a considerable amount of data to suggest that there is increased sodium and water retention by the ileum of ileostomists (Chapter 7). In association with this Isaacs and his colleagues (1976) found an increased electrical potential difference across the terminal ileal mucosa. It seems possible that this increased absorption of sodium and water or the increased potential difference across the terminal ileal mucosa might increase the absorption of vitamin B₁₂ of patients with an ileostomy.

2. The gastrointestinal hormone profile of the ileostomists taking part in the present study was found to be different from that of a group of healthy subjects (Chapter 12). It is suggested that these hormonal differences might indicate a change in small intestinal motility in the ileostomists possibly resulting in an increased transit time through the terminal ileum. If this were the case, the vitamin B₁₂-intrinsic

factor complex would be in contact with the vitamin B₁₂ receptors for a longer time than normal which might result in an increased absorption of vitamin B₁₂.

3. There is some evidence to suggest that the terminal ileum of ileostomists with an intact small intestine absorbs more bile salts than normal (Chapter 11). In addition, Percy-Robb and his co-workers (1971) found a linear relationship between the size of the bile salt pool and the absorption of vitamin B₁₂ in their patients with an ileostomy. Therefore, if the terminal ileum of ileostomists does absorb more bile salts than normal, this might be associated with an increased absorption of vitamin B₁₂.

4. Finally, Teo and his colleagues (1981) found in some in vitro studies that dihydroxy bile acids inhibited the binding of intrinsic factor to vitamin B₁₂. It has been shown that ileostomists form only a very small quantity of secondary bile salts and therefore have minimal or absent levels of deoxycholate in their bile salt pool. Therefore, the quantity of dihydroxy bile salts in the bile of ileostomists is reduced. This might allow greater binding of intrinsic factor to vitamin B₁₂ with resulting increased absorption of the vitamin.

The ileostomists who had Crohn's disease retained significantly less vitamin B₁₂ than the healthy control subjects ($p < 0.01$). Five out of these 12 ileostomists retained less than 32 per cent of the dose. In this connection, it is relevant that Callender and her colleagues (1960) showed that patients with pernicious anaemia had a

range of vitamin B₁₂ retention of 0 - 36 per cent. Four out of these five patients with low vitamin B₁₂ retention, had had a resection of terminal ileum ranging from 17 - 67 cm. The remaining patient had had only a minimal resection of terminal ileum and had no clinical evidence of recurrent disease. However, in general, it appears that the malabsorption of vitamin B₁₂ was associated with terminal ileal resection. This finding correlates well with the results of other workers (Booth, 1961; Katz et al, 1963; Fromm et al, 1973; Lenz, 1975). The findings of the present study also suggest that resection of only a short length of terminal ileum (about 20 cm) may be sufficient to cause malabsorption of vitamin B₁₂. All the ileostomists who had Crohn's disease who took part in the present study and who had had 17 or more centimetres of terminal ileum resected were receiving regular parenteral vitamin B₁₂. This explains why the ileostomists with Crohn's disease had normal serum levels of vitamin B₁₂ even though some of them were unable to absorb the vitamin normally.

Finally, all the ileostomists had normal red cell folate levels and only one of the 51 patients had a low plasma folate level. Therefore it appears that folate metabolism is normal in patients with an ileostomy who had had ulcerative colitis. It also appears to be normal in ileostomists who have Crohn's disease provided that they have not had substantial amounts of small intestine resected and also have no clinical evidence of residual or recurrent disease.

CHAPTER 9

CALCIUM METABOLISM

INTRODUCTION

Previously calcium metabolism has not been studied in detail in patients with an ileostomy who have had had ulcerative colitis and who have retained an intact small intestine. Daly (1968) measured the level of plasma calcium in 100 ileostomists who had had ulcerative colitis and found a normal level in all of the patients except for one who had a high level and another who had a low level. Both of these patients were in good health and were not investigated further. Clarke and McKenzie (1969) measured urinary calcium and phosphate in 14 ileostomists. They found a significantly low 24-hour urinary excretion of calcium in the patients with an ileostomy as compared to that in 15 control subjects. Singer and his colleagues (1973) found no statistically significant difference between the plasma and urinary calcium values in 20 ileostomists and those in 20 control subjects.

There are several reasons why calcium metabolism might be altered in ileostomists who previously suffered from ulcerative colitis. As was demonstrated in Chapter 7, there is a marked alteration in the metabolism of salt and water in the kidneys of patients with an ileostomy. The handling of calcium by the kidney is thought to be linked to that of sodium (Bijvoet, 1977). In addition, the secondary aldosteronism found in the ileostomists who took part in the

present study might alter intracellular pH and might also affect the metabolism of bone (Chapter 7). Finally, it is thought that the colonic mucosa may secrete calcium (Phillips and Giller, 1973) and therefore, if the colon is absent, this source of loss is removed.

Calcium metabolism in ileostomists with Crohn's disease has not been studied previously. However, patients with Crohn's disease of the small intestine are known to be at risk of developing osteomalacia (Compston et al, 1978). This risk also applies to ileostomists with Crohn's disease if they have had a small bowel resection or have residual disease of the small intestine.

PATIENTS AND METHODS

The calcium metabolism of all the 51 ileostomists taking part in the present study was investigated. Calcium absorption was determined using the Oxford Shadow Shield Total Body Counter (Warner and Oliver, 1966). After an overnight fast, each patient was given a standard oral dose of 200 mg of calcium gluconate labelled with 4 - 6 μ Ci of ^{47}Ca and the percentage of labelled calcium retained after one week was measured. During the course of the study, every patient had blood taken for the measurement of plasma electrolytes, calcium, phosphate, total protein, albumin and alkaline phosphate. These variables were determined as part of the biochemical profile using a Vickers M300 Discrete Analyser as described in Chapter 4. All the patients

collected a 24-hour sample of urine and the urinary electrolytes, creatinine, calcium and phosphate were measured using a Technicon linked to a Vickers SP120 (Chapter 7). The patients also collected a 24-hour sample of ileostomy effluent which was weighed and the volume measured. The percentage dry weight was determined and some of the effluent was centrifuged to separate the solid and fluid components as described in Chapter 7. The Technicon SMA was used to measure the sodium and potassium concentrations in the ileostomy fluid and a Perkin-Elmer Spectrophotometer was used to measure the calcium concentration. Magnesium concentrations in the blood, urine and ileostomy fluid were also measured by means of the Perkin-Elmer Spectrophotometer.

A further sample of venous blood was taken for the measurement of fasting plasma levels of parathormone, calcitonin and 25-hydroxy vitamin D (25 - OHD). These samples were immediately placed in ice, separated in a cold centrifuge and stored at -20°C . Plasma immunoreactive parathyroid hormone and calcitonin were measured in the radioimmunoassay laboratory at Liege University, Belgium. The assay for immunoreactive parathormone used guinea pig antiserum (Wellcome Laboratories, London) previously characterised as having predominantly N-terminal specificity (Woo and Singer, 1974; Franchimont and Heynen, 1976). The assay for immunoreactive calcitonin determined both small and big calcitonin (Heynen and Franchimont, 1974; Heynen et al, 1975). Plasma 25 - OH vitamin D concentrations were

measured at St. Thomas's Hospital, London, by a competitive protein-binding assay using normal human serum as the binding protein (Edelstein et al, 1974).

The metacarpal indices were measured from a hand X-ray taken of the non-dominant hand of each patient with the X-ray tube one metre above the hand to avoid any magnification effect. The radiographs were placed on an Exon X-ray screen laid horizontally on a desk and the length (L) of the second metacarpal was measured with a ruler. The outer diameter (D) of the bone and the diameter of the medullary space (d) were measured at the midpoint of the shaft using a Vernier caliper and a mounted magnifying glass (Dequeker, 1976). From these three measurements, several metacarpal indices were calculated. Finally, the dietary intake of calcium, phosphate and magnesium was estimated for each of the 51 ileostomists as described in Chapter 6.

The 39 healthy subjects who were age- and sex-matched to the ileostomists who had had ulcerative colitis acted as controls for the measurements of the plasma biochemical profile, 24-hour urinary determinations and dietary intake. In addition, they also had an X-ray taken of the non-dominant hand for the purpose of measuring the metacarpal indices. These measurements were made in the same way as those using the hand X-rays of the patients. These subjects did not act as healthy controls for the measurements of absorption on the total body counter as it was not considered justifiable to employ radioactive isotopes in them. Instead, 31 healthy

subjects (18 men and 13 women), who had previously been studied for the absorption of calcium using the Oxford total body counter acted as controls.

The values obtained for plasma parathormone, calcitonin and vitamin D in the ileostomists were compared to results previously obtained using blood samples from healthy subjects who had been studied at the respective laboratories.

RESULTS

The mean retention of calcium in the ileostomists and control subjects is given in Table 9.1. It may be seen that the ileostomists who had had ulcerative colitis were retaining significantly more calcium than the healthy control subjects ($p < 0.001$). This difference applied to both the male and female patients ($p < 0.01$ and $p < 0.05$, respectively). It should be mentioned that the control subjects were not age- and sex-matched to the ileostomists (the mean ages were 33 ± 12 and 48 ± 13 , respectively). However, it has been found that calcium absorption tends to decline with age (Ackermann and Toro, 1953, 1954; Bullamore et al, 1971) so it could be expected that the ileostomists, being an older group of subjects, would actually absorb less rather than more.

The mean plasma biochemical values related to calcium absorption are given in Table 9.2. The mean values of calcium, phosphate and magnesium were similar in patients and control subjects even if a correction is made for the significant difference in plasma albumin. As mentioned in

Table 9.1 Mean calcium retention + 1 standard deviation in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the ulcerative colitis group

Variable	Ulcerative colitis patients			Control subjects			Crohn's disease patients		
	M n = 23	F n = 16	Total n = 39	M n = 18	F n = 13	Total n = 31	M n = 5	F n = 7	Total n = 15
% retention	23.5**	19.4*	21.8***	18.5	14.6	16.9	24.5	13.1	17.8
	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$	$\pm$
	6.1	6.7	6.1	6.4	3.6	5.7	7.9	4.2	8.2

* = $p < 0.05$

** = $p < 0.01$

*** = $p < 0.001$

Table 9.2 Mean plasma biochemical results $\pm$ one standard deviation related to calcium metabolism in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the ulcerative colitis group

Variable	Ulcerative colitis patients n = 39	Control subjects n = 39	Crohn's disease patients n = 12
Sodium mmol/l	141.9 $\pm$ 3.0	142.2 $\pm$ 2.4	141.2 $\pm$ 2.9
Potassium mmol/l	3.90 $\pm$ 0.70	4.00 $\pm$ 0.71	4.02 $\pm$ 0.52
Bicarbonate mmol/l	26 $\pm$ 5	25 $\pm$ 5	28 $\pm$ 4
Creatinine μ mol/l	83 $\pm$ 21	84 $\pm$ 17	75 $\pm$ 18
Calcium mmol/l	2.45 $\pm$ 0.14	2.40 $\pm$ 0.09	2.40 $\pm$ 0.13
Phosphate mmol/l	0.48 $\pm$ 0.20	0.88 $\pm$ 0.16	0.99 $\pm$ 0.16
Magnesium mmol/l	0.52 $\pm$ 0.06	0.50 $\pm$ 0.06	0.50 $\pm$ 0.06
Total protein g/l	74.8 $\pm$ 4.8 ^{***}	70.1 $\pm$ 4.3	71.5 $\pm$ 4.0
Albumin g/l	44.2 $\pm$ 2.9 [*]	42.7 $\pm$ 2.2	41.3 $\pm$ 3.0
Alkaline phosphatase iu/l	211 $\pm$ 64.1 [*]	181.9 $\pm$ 40.1	232.0 $\pm$ 55.2 ^{**}

* = $p < 0.02$

** = $p < 0.01$

*** = $p < 0.001$

Chapter 4, the mean level of alkaline phosphatase was significantly raised in both groups of ileostomists when compared to that in the control group. However, it is not known whether the isoenzyme responsible for this raised level comes from bone, liver or bowel.

Table 9.3 gives the mean urinary values. It can be seen that the 24-hour urinary output of calcium and phosphate was lower in the ileostomists with Crohn's disease than in the control subjects. However, if the urinary values of calcium and phosphate are divided by the urinary output of creatinine this tends to correct for the difference in body weight. When this correction has been made the urinary output of calcium and phosphate in the patients with Crohn's disease is no longer significantly different from that in the control subjects. The 24-hour urinary excretion of magnesium in both groups of ileostomists was found to be significantly lower than that in the control group.

The 24-hour loss of calcium in the ileostomy fluid of the ileostomists who had had ulcerative colitis and those with Crohn's disease was 7.7 ± 3.8 mmol and 6.1 ± 3.0 mmol, respectively. These results were similar to those of previous studies (Nuguid et al, 1961; King et al, 1978). In addition, these 24-hour losses were of the same order as the 5.3 ± 2.9 mmol/24hr of calcium and 2.5 ± 1.0 mmol/24hr of magnesium found by Phillips and Giller (1973) to be the mean losses in the faeces of five healthy subjects. It is not possible to make detailed comparisons between these various sets of results because the faecal content of calcium and magnesium vary considerably with dietary intake, age and climate.

Table 9.3 Mean urinary biochemical values + one standard deviation of variables related to calcium metabolism in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the ulcerative colitis group

Variable	Ulcerative colitis patients n = 39	Control subjects n = 39	Crohn's disease patients n = 12
24 hr urine volume 1	1.34 ± 0.40	1.44 ± 0.56	0.89 ± 0.32 ^{***}
Sodium mmol/day	113 ± 65*	142 ± 59	58 ± 47 ^{****}
Potassium mmol/day	79 ± 25 ^{***}	58 ± 20	52 ± 14
Creatinine mmol/day	13.3 ± 3.9	12.7 ± 4.0	10.0 ± 2.9*
Calcium mmol/day	4.33 ± 1.59	4.45 ± 2.48	2.57 ± 1.42 ^{**}
Phosphate mmol/day	25.02 ± 7.34	24.97 ± 10.59	17.02 ± 4.14 ^{**}
Magnesium mmol/day	2.57 ± 0.94 ^{**}	3.23 ± 1.37	1.57 ± 0.60 ^{****}
Calcium:creatinine	0.34 ± 0.11	0.35 ± 0.15	0.27 ± 0.17
Phosphate:creatinine	2.03 ± 0.75	2.02 ± 0.78	1.81 ± 0.67

* = $p < 0.05$

** = $p < 0.02$

*** = $p < 0.01$

**** = $p < 0.001$

Parathyroid hormone and calcitonin values follow a log normal distribution. The mean log parathyroid hormone in the patients who had had ulcerative colitis was 0.17 ± 0.25 log mIU/l and that in the patients with Crohn's disease was 0.12 ± 0.22 log mIU/l. The mean value found in 50 healthy subjects whose plasma level had previously been measured was 0.13 ± 0.18 log mIU/l. There was no significant difference between these results. Similarly, there was no significant difference between the log mean plasma calcitonin levels in the two groups of patients (2.32 ± 0.27 log pg/ml and 2.35 ± 0.29 log pg/ml, respectively) and that in a control group of healthy subjects (2.26 ± 0.21 log pg/ml).

The level of plasma 25-hydroxy vitamin D (25-OHD) varies greatly between summer and winter. The mean winter level in 57 healthy subjects previously studied at St. Thomas's Hospital, London, was 27.5 ± 12.4 nmol/l. Unfortunately it was not possible to study all the ileostomists taking part in the present study, during the winter months. However, 20 of the ileostomists who had had ulcerative colitis were studied in the winter when their mean plasma 25-OHD was 21.4 ± 9.6 nmol/l. The remaining 19 patients who had had ulcerative colitis were studied during the mild summer of 1979 when their mean plasma 25-OHD was 46.4 ± 19.2 nmol/l. The ileostomists with Crohn's disease were mainly studied in the summer months when their mean 25-OHD value was 35.4 ± 18.8 nmol/l. These results indicate that the mean plasma 25-OHD level in the ileostomists who had had ulcerative colitis may be slightly low but approximates to normal and the mean value in the patients with Crohn's disease is probably low for measurements made in the summer.

The results of the measurement of the metacarpal indices in the patients compared to those of age- and sex-matched control subjects are given in Table 9.4. The indices in both groups of ileostomists were lower than those in the control group but the differences were not statistically significant. Finally, as is discussed in Chapter 6, no significant difference was found in the dietary intake of calcium, phosphate or magnesium in the ileostomists when compared to that in the control subjects.

DISCUSSION

In the introduction of the present chapter it was seen that the calcium metabolism of ileostomists has been little studied in the past. There are several reasons for this. First, calcium absorption is known to take place in the small intestine (Wensel et al, 1969) and so removal of the colon might not be expected to alter calcium metabolism. In addition, when calcium concentrations have been measured in the blood and urine of ileostomists no marked abnormalities have been detected (Daly, 1968; Clarke and McKenzie, 1969; Singer et al, 1973). Finally, no complications arising from abnormal calcium metabolism have been observed in the large surveys of the general health of ileostomists (Daly, 1968, Roy et al, 1970; Ritchie, 1971b).

When the present study was planned an investigation into the calcium metabolism of ileostomists was included because it was thought that, with the passage of time, a small change in calcium handling might have a marked effect on the body and

Table 9.4 Mean metacarpal indices $\pm$ one standard deviation in a group of ileostomists who had had ulcerative colitis and in another group with Crohn's disease compared to those in a group of healthy subjects age- and sex-matched to the ulcerative colitis group

	Ulcerative colitis patients n = 39	Control subjects n = 39	Crohn's disease patients n = 12
Length L. mm	68.51 $\pm$ 3.99	68.26 $\pm$ 4.15	66.38 $\pm$ 3.34
Outer diameter D. mm	9.07 $\pm$ 1.08	9.03 $\pm$ 1.09	8.55 $\pm$ 0.77
Inner diameter d. mm	4.34 $\pm$ 1.36	4.12 $\pm$ 0.95	4.02 $\pm$ 0.95
$D^2 - d^2$	62.78 $\pm$ 12.61	64.91 $\pm$ 14.51	56.72 $\pm$ 10.57
$\frac{D^2 - d^2}{DL}$	0.1008 $\pm$ 0.0141	0.1042 $\pm$ 0.0108	0.0993 $\pm$ 0.0103

$$D^2 - d^2 = \text{cortical area}$$

$$\frac{D^2 - d^2}{DL} = \frac{\text{cortical area}}{\text{surface area}}$$

particularly on the skeleton.

The retention of calcium as measured by the total body counter was found to be raised in the ileostomists when compared to that in healthy control subjects. This might reflect increased gastrointestinal absorption, decreased endogenous secretion of calcium into the bowel, diminished urinary losses or increased uptake by the bone. No evidence for a decreased loss of calcium in the urine was found in the ileostomists taking part in the present study as compared to that in the control subjects. However, from the data obtained in the present study, it is not possible to distinguish between the other three possible causes of the increased retention of calcium in the ileostomists.

Endogenous secretion of calcium may play a significant role because Phillips and Giller (1973) found that the colon secreted calcium in four out of five healthy subjects whom they investigated. The mean secretion of calcium by the colon in these four subjects was 2.0 ± 1.2 mmol per day. The remaining subject had a net absorption of 2.0 mmol per day. If most subjects do have a net secretion of calcium by the colon, then increased calcium retention might be expected after proctocolectomy.

Another possibility is that increased absorption of calcium by the bowel may be occurring in the ileostomists and that this might be related to increased uptake of calcium by the skeleton. It can be postulated that patients with severe colitis might be in a state of negative calcium

balance due to chronic ill health, anorexia, and possibly increased losses from the inflamed colon. In addition, almost all of the ileostomists taking part in the present study had received considerable quantities of both oral and parenteral corticosteroids given as short courses of intensive medical treatment. Corticosteroids are known to cause a reduced intestinal absorption of calcium and an increased urinary excretion (Gallagher et al, 1973). As a result of these factors it is likely that patients undergoing proctocolectomy with the formation of an ileostomy have a calcium deficit at the time of operation. It is also likely that, with the return to good health following the operation, the body attempts to replace the lost calcium. A positive balance would be reflected by an increase in the retention of calcium, such as that found in the present study. This hypothesis is supported by the finding that the ileostomists who had had ulcerative colitis and whose operation had been more than three years before the study had a lower percentage retention of calcium than those whose operation had been less than three years previously (20.9 ± 6.3 and 23.4 ± 6.0 , respectively). This may indicate that some of the calcium deficit had been overcome in those patients who had had their ileostomy for the longer period of time.

The presence of a calcium deficit in patients with an ileostomy may be clinically important for several reasons. First, if chronic colitis and repeated courses of steroid therapy do lead to a state of negative calcium balance, this could be important in the long-term management of patients with this disease and might be a factor in deciding to

undertake surgery at an earlier stage than has been normal. This would apply particularly to female patients who are at greater risk of developing osteoporosis. Secondly, it may be worth recommending a high calcium intake and adequate exercise following the operation of proctocolectomy as both these factors could contribute to the restoration of any calcium deficit.

The ileostomists with Crohn's disease were also found to have a high retention of calcium as measured on the total body counter. It is probable that the same factors causing a negative calcium balance also occur in these patients. Moreover, in patients with Crohn's disease involving the small intestine there is an added risk of osteomalacia developing, particularly after surgical resection (Compston et al, 1978). Factors contributing to the development of osteomalacia in these patients include malabsorption of vitamin D and calcium, anorexia, and an abnormally high loss of 25-OHD as a result of impairment of the enterohepatic circulation (Arnaud et al, 1975). It is apparent that bone biopsy is the only certain method of diagnosing osteomalacia although the alkaline phosphatase is raised in patients with severe mineral loss (Compston et al, 1978). Therefore, close attention should be given to calcium metabolism in all patients with Crohn's disease.

The mean plasma level of magnesium was found to be similar in both groups of ileostomists to that in the control group. In addition, the dietary intake of magnesium and the loss in the ileostomy effluent appear to be similar to those in normal

subjects. However, the 24-hour urinary excretion of magnesium was significantly lower in both groups of patients than in the control group. There is no obvious explanation for this finding. Magnesium absorption is known to take place in the small intestine in man (Aikawa et al, 1958). Certainly, it is possible to become magnesium deficient with severe ulcerative colitis, Crohn's disease and following a small bowel resection (Thoren 1962 and 1971; Nielson and Thaysen, 1971).

It would seem that magnesium malabsorption ought not to occur in the ileostomists who took part in the present study and who had had ulcerative colitis with minimal ileal resection. It is known that patients with primary hyperaldosteronism can have malabsorption of magnesium from the bowel but at the same time they have been found to have increased urinary excretion of magnesium (Mader and Iseri, 1955; Milne et al, 1957). Another possibility is that, despite the similar magnesium content of the ileostomy effluent and normal faeces, the colon may normally absorb a small amount of magnesium and that therefore slightly more magnesium might be lost in the ileostomy effluent than in normal faeces. This small additional loss might then be corrected by increased urinary retention. The results of the present study of magnesium metabolism in ileostomists are inconclusive and further investigation of this aspect of metabolism is required. Nevertheless, it is important to bear in mind the possibility of magnesium deficiency developing in patients with Crohn's disease involving the small intestine or in any patient with ileostomy diarrhoea.

CHAPTER 10

URINARY STONES

INTRODUCTION

There has been considerable interest in the incidence of urolithiasis in patients with an ileostomy. Table 10.1 gives details of the more important published studies. It should be noted that some of these studies included only those patients whose primary disease had been ulcerative colitis, whereas other studies included patients with either ulcerative colitis or Crohn's disease. This may be important when considering the incidence, aetiology and composition of urinary stones in patients with an ileostomy because there have been reports of an increased incidence of urinary stones in patients who are receiving medical treatment for ulcerative colitis (Bennet and Hughes, 1972), and also in patients who have Crohn's disease of the small intestine (Deren et al, 1962; Gelzayd et al, 1968). However, the aetiology of the urolithiasis in these two conditions is thought to be different, a factor which is discussed later in this chapter.

It can be seen in Table 10.1 that when ileostomists with ulcerative colitis have been surveyed a high incidence of urolithiasis has been reported from Australia, the United States of America and Czechoslovakia. However, in the two main surveys carried out in England, no increased incidence has been detected (Alexander, 1970; Goligher, 1980). There is probably about a one per cent incidence of urinary stones

Table 10.1 The incidence of urolithiasis in patients with an ileostomy

No: of patients	Disease	% Incidence	Country	Authors
163	UC or Crohn's	7.4	USA	Deren et al 1962
74	UC	12	Czechoslovakia	Marataka and Nedbal 1964
79	UC or Crohn's	18	USA	Gelzayd et al 1968
333	UC	8.4	Australia	Bennet and Hughes 1972
300	UC	0.7	England (Birmingham)	Alexander 1970
150	UC	1.3	England (Leeds)	Goligher 1980
311	UC or Crohn's	4.3	England (London)	Ritchie 1971b

in the general population in England (Williams, 1965).

None of the surveys carried out in the United Kingdom or elsewhere in the world has involved active investigation for asymptomatic urinary stones. As part of the present study, it was decided to undertake such an investigation in order to discover whether there was an increased incidence of urolithiasis in the patients who had had an ileostomy formed in Oxford. In addition, it was hoped to shed further light on the aetiology of any stones found and to institute treatment while these stones were still small and asymptomatic.

PATIENTS AND METHODS

Each of the 51 ileostomists who took part in the present study had a limited intravenous urogram to demonstrate any stones in the urinary tract. The examination was limited in that only two or three radiographs were taken of the abdomen of the patients in order to limit the amount of radiation to which they were exposed. This method follows the recommendation of Ardran and his colleagues (1978) who devised a technique for the diagnosis of diverticulosis for epidemiological studies involving a low X-ray dosage which conformed with the guidelines recommended by the World Health Organisation (BIR Bulletin, 1975). Two or three radiographs were thought to be sufficient for the diagnosis of urinary stones in the present study and, as the patients were already receiving a small amount of radiation from the isotopes used in the studies involving

the total body counter, it was considered important to keep the X-ray dosage to a minimum.

All of the 51 ileostomists had blood taken for the investigation of possible causes of urolithiasis. The plasma levels of sodium, potassium, chloride, bicarbonate, urea, creatinine, calcium, magnesium, phosphate, total protein, albumin and blood pH were measured by the methods described in Chapters 4 and 7.

In addition, the concentrations of urinary sodium, potassium, calcium, magnesium and phosphate were measured in a 24-hour sample of urine collected by each patient as described previously (Chapter 7). Urinary uric acid concentrations were measured by a uricase method using reagents supplied by Boehringer Mannheim. The pH of the urine was determined using a Pye Unicam pH meter and a fresh mid-stream urine specimen was examined for infection by microscopy and culture.

The absorption of calcium from the gastrointestinal tract was determined using the Oxford Shadow Shield total body counter as described in Chapter 9. Finally, the diet of the ileostomists was studied and compared to that of the control subjects as already discussed in Chapter 6.

The same plasma and urinary variables were measured in samples collected from the 39 healthy control subjects who were age- and sex-matched to the 39 ileostomists who had ulcerative colitis. The methods used for analysing these samples were the same as those used to analyse the samples obtained from the ileostomists. However, intravenous urograms

were not undertaken in the healthy control subjects as it was judged unethical to expose them to X-rays in view of the very low incidence of urinary stones that is known to occur in the general population (Williams, 1965).

RESULTS

Four out of the 39 ileostomists who had had ulcerative colitis were found to have urolithiasis. These stones were all small and were located either in the parenchyma of the kidney or in the renal pelvis. They were all calcified. Only one of these four patients had a history of urolithiasis. This patient had developed symptoms of urinary stones while suffering from ulcerative colitis some years before being treated surgically by proctocolectomy and ileostomy. The stones had been removed surgically and he had had no symptoms or urolithiasis since that time. These four patients were all male; their mean height, weight, age and duration of ileostomy are shown in Table 10.2 and compared with those of the other male ileostomists who had had ulcerative colitis. From this Table it may be seen that the patients with urolithiasis were of above average height and weight but that the duration of the ileostomy was shorter than average.

Another male patient who had had ulcerative colitis was found to have a non-functioning kidney. This patient subsequently had a retrograde ureterogram but the radio-opaque solution would only pass into the lowest few centimetres of the left ureter. Therefore five out of the 39 (13%) ileostomists who had had ulcerative colitis were found to have an abnormality in the urinary tract. As all of these were male, 22 per cent of the 23 male ileostomists who had had ulcerative colitis were found to have an abnormal urinary tract.

None of the 12 ileostomists with Crohn's disease were found to have urolithiasis.

Table 10.2 The mean values $\pm$ one standard deviation of height, weight, age and duration of ileostomy in the four male ileostomists with urolithiasis compared to those of the other male ileostomists who had had ulcerative colitis

Variable		Male ileostomists with urolithiasis n = 4	Other male ileostomists who had had ulcerative colitis n = 19
Height	cm	182 $\pm$ 12	176 $\pm$ 8
Weight	kg	79.3 $\pm$ 13.1	75.9 $\pm$ 9.8
Age	years	49 $\pm$ 5	49 $\pm$ 4
Duration of ileostomy	years	2.5 $\pm$ 1.0	5.1 $\pm$ 3.7

Table 10.3 shows the mean plasma biochemical values found in the two groups of ileostomists compared to those found in the healthy control subjects. It may be seen that, apart from the total protein and albumin values which have already been discussed in Chapters 4 and 7, none of the mean plasma levels in the ileostomists were significantly different from those of the control subjects. However, four of the male and one of the female ileostomists who had had ulcerative colitis were found to have a raised plasma level of uric acid and a further male patient was already taking Allopurinol for the treatment of gout. In addition, one of the male and one of the female ileostomists with Crohn's disease were also found to have a raised plasma level of uric acid, whereas only one subject (a female) out of the 39 healthy control subjects was found to have a raised plasma uric acid level.

Two of the four ileostomists with urolithiasis had raised plasma levels of uric acid and a third had a level towards the upper limit of normal. Moreover, the patient who had a non-functioning left kidney was the patient who was already taking Allopurinol to treat arthritis due to gout. Therefore, of the five ileostomists who had an abnormality of the urinary tract, three had a high plasma uric acid level (including the one taking Allopurinol) and a fourth had a plasma level towards the upper limit of normal. The values of the other biochemical variables in the plasma of the patients who had an abnormal renal tract were not significantly different from those of either the healthy control subjects or the ileostomists without urolithiasis.

Table 10.4 gives the results of the mean urinary biochemical values. The mean 24 hour volume of the ileostomy effluent in the patients who had had ulcerative

Table 10.3 Mean plasma biochemical values + one standard deviation of variables that may be related to urolithiasis in ileostomists compared to values in healthy control subjects age- and sex-matched to the patients who had had ulcerative colitis

Variable	Ileostomists who had had ulcerative colitis n = 39	Healthy control subjects n = 39	Ileostomists with Crohn's disease n = 12
Sodium mmol/l	141.9 ± 3.0	141.2 ± 2.4	141.2 ± 2.9
Potassium mmol/l	3.90 ± 0.70	4.00 ± 0.71	4.02 ± 0.52
Chloride mmol/l	102 ± 3	102 ± 2	100 ± 3
Bicarbonate mmol/l	26 ± 5	25 ± 5	28 ± 4
Urea mmol/l	5.7 ± 1.1	6.3 ± 1.9	5.3 ± 1.5
Creatinine μmol/l	83 ± 21	84 ± 17	75 ± 18
Calcium mmol/l	2.45 ± 0.14	2.40 ± 0.09	2.40 ± 0.13
Phosphate mmol/l	0.98 ± 0.20	0.88 ± 0.16	0.99 ± 0.16
Magnesium mmol/l			
Total Protein g/l	74.8 ± 4.8**	70.1 ± 4.3	71.5 ± 4.0
Albumin g/l	44.2 ± 2.9*	42.7 ± 2.2	41.3 ± 3.0
Uric Acid μmol/l	354 ± 100 †	332 ± 86†	328 ± 80†
Blood pH	7.39 ± 0.02	7.40 ± 0.02	7.40 ± 0.02

* p < 0.02 † Normal range for plasma Uric Acid in Laboratory was
 ** p < 0.001 210 - 480 μmol/l for males and 150 - 390 μmol/l for females

6 ileostomists who had had ulcerative colitis, 1 healthy control and 2 ileostomists with Crohn's disease had high Uric Acid vales

Table 10.4 Mean urinary biochemical values + one standard deviation of variables that may be related to urolithiasis in ileostomists compared to the values in healthy control subjects age- and sex-matched to the patients who had had ulcerative colitis

Variable	Ileostomists who had had ulcerative colitis n = 39	Healthy control subjects n = 39	Ileostomists with Crohn's disease n = 12
24 hr urine volume l	1.34 ± 0.40	1.44 ± 0.56	0.89 ± 0.32 ^{***}
pH	5.29 ± 1.04 ^{***}	5.95 ± 0.05	5.69 ± 0.62
Sodium mmol/day	113 ± 65 [*]	142 ± 59	58 ± 47 ^{****}
Potassium mmol/day	79 ± 25 ^{***}	58 ± 20	52 ± 14
Creatinine mmol/day	13.3 ± 3.9	12.7 ± 4.0	10.0 ± 2.9 [*]
Sodium:potassium	1.5 ± 0.8 ^{****}	2.5 ± 0.8	1.2 ± 1.0 ^{****}
Calcium mmol/day	4.33 ± 1.59	4.45 ± 2.48	2.57 ± 1.42 ^{**}
Phosphate mmol/day	25.02 ± 7.34	24.97 ± 10.59	17.02 ± 4.14 ^{**}
Magnesium mmol/day	2.57 ± 0.94	3.23 ± 1.37	1.57 ± 0.60
Urate mmol/day	3.0 ± 1.1	2.7 ± 1.1	-

* = p < 0.05

** = p < 0.02

*** = p < 0.01

**** = p < 0.001

colitis was 600 ± 300 ml. This indicates that several hundred ml more fluid is lost every day from the intestine of a patient with an ileostomy than is lost by a normal subject. Therefore it is interesting to find that the mean 24 hour volume of urine in the ileostomists who had had ulcerative colitis was not significantly less than that of the healthy subjects. As was mentioned in Chapters 6 and 7 this additional loss of fluid was made up by these ileostomists drinking on average 350 ml more fluid per day than the healthy control subjects. The pH of the urine in these ileostomists was found to be significantly more acidic than that in the healthy subjects ($p < 0.01$). The 24 hours loss of sodium was significantly less ($p < 0.05$) and the 24 hour loss of potassium was significantly more than that in the control subjects ($p < 0.01$). The sodium:potassium ratio was significantly low ($p < 0.001$). The excretion of calcium and phosphate was similar in these patients and the healthy subjects. Finally, the mean 24 hour urinary excretion of magnesium was significantly lower in these ileostomists than that in the control group.

There was no significant difference in the mean 24 hour excretion of uric acid in the urine between the patients and control subjects. In addition, the excretion of uric acid was apparently not raised in the patients who had hyperuricaemia. However, the results of the urinary acid determination may be inaccurate because it was not possible to measure the urate concentration in the fresh urine as the necessary facilities were not available and so all the samples had to be frozen. The urate concentration was subsequently measured at a later date. This measurement

should be undertaken using fresh urine because urate may either precipitate in stored urine or be degraded by bacteria.

The results of the urine analysis in the patients with Crohn's disease showed marked differences from those in the healthy subjects (Table 10.4). The mean 24 hour volume was significantly low ($p < 0.01$). The excretion of sodium, creatinine, calcium, phosphate and magnesium was also significantly low. These differences are discussed in Chapters 7 and 9. In addition, the sodium:potassium ratio was low ($p < 0.001$).

The microscopy and culture of the mid-stream urine samples showed that no patient had a urinary tract infection. However, as was described in Chapter 9, the absorption of calcium as measured on the total body counter was significantly raised in the ileostomists who had had ulcerative colitis when compared to that in control subjects ($p < 0.001$). The analysis of dietary intake which was discussed in detail in Chapter 6, showed no statistically significant difference in the dietary intake of simple sugars, calcium, phosphate, magnesium or vitamin D in either of the groups of ileostomists compared to the control group. However, the ileostomists with Crohn's disease had a significantly greater sodium intake than the control subjects ($p < 0.01$). The ileostomists who had had ulcerative colitis tended to consume more sodium and more simple sugars than the healthy subjects but the differences were not statistically significant.

DISCUSSION

In this study a high incidence of asymptomatic urinary stones has been demonstrated in the ileostomists who had had ulcerative colitis. Four out of these 39 ileostomists (10%) definitely had renal stones and a fifth was found to have a non-functioning left kidney which might have been the result of nephrolithiasis. If this patient is included, 13 per cent of these ileostomists were found to have evidence of urolithiasis. All of these patients were male and so either four or five out of 23 had urolithiasis (17% or 22%, respectively). This is the first study in the United Kingdom that has found a high incidence of urolithiasis in ileostomists who had had ulcerative colitis. The urinary stones found in this study were asymptomatic and would not have been discovered without the aid of an intravenous urogram because, although all the stones were calcified, they were small and could easily have been thought to be flecks of intra-abdominal calcification if the exact site had not been located. If intravenous urograms were to be performed on ileostomists in parts of the world where a high incidence of symptomatic urinary stones has been found, it is possible that an even higher incidence of stones would be discovered (Table 10.1).

It has not been possible to analyse the stones in any of these patients as a stone has been passed by only one of the patients and that stone was not recovered. However, all the stones were calcified and no radiolucent stones were detected in the patients taking part in this study. Nevertheless, the author is currently treating another male ileostomist with

hyperuricaemia who had developed radiolucent urinary calculi but who did not take part in the present study.

Several workers have suggested that the high incidence of urolithiasis in ileostomists is mainly due to an increased incidence of uric acid stones (Deren et al, 1968; Clarke and McKenzie 1969; Bennet and Hughes, 1972). An increased incidence of calcium containing stones has also been suggested by Deren and his colleagues (1962) and by Grossman and Nugent (1967). There was no apparent increase in uric acid calculi in the patients who took part in the present study. However, it is possible that uric acid crystals may have acted as the nuclei for some of these stones. Indeed, a high incidence of calcium-containing urinary stones has been reported in patients with hyperuricaemia (Smith et al, 1969).

A decreased urine volume and a persistently acid urine have been thought to be the main causes of the increased incidence of nephrolithiasis in ileostomists who have had ulcerative colitis (Deren et al, 1962; Gelzayd et al, 1968; Clarke and McKenzie, 1969; Bennet and Hughes, 1972). A decreased urine volume as a result of the increased loss of fluid from the gastrointestinal tract increases the concentration of substances that easily precipitate out in the urine, such as uric acid and calcium. In the present study, the ileostomists who had had ulcerative colitis were found to have a smaller mean 24 hour urine volume than the healthy subjects but the difference was not statistically significant (Table 10.2). Nevertheless, there are almost certainly periods

of time when the urine volume of every ileostomist becomes significantly reduced. This may be all that is required to allow for the precipitation of crystals. The urine collections in the present study were carried out over a period of one year in both the patients and control subjects but the summer during which these calculations were made was mild.

The passage of a persistently acid urine favours the precipitation of uric acid which has a pK value of 5.75. The suggested reasons for the passage of an acid urine by ileostomists have been the conservation of sodium in the kidney in exchange for hydrogen ions and loss of excess bicarbonate from the intestine (Deren et al, 1962; Clarke and McKenzie, 1969). It is known that patients with aldosteronism exchange sodium for potassium and hydrogen ions in the kidney. Therefore, as the ileostomists taking part in the present study had significantly raised mean levels of aldosterone ($p < 0.001$) and significantly low levels of urinary sodium ($p < 0.05$) compared to those in the healthy control subjects, then a urine containing increased quantities of hydrogen and potassium ions would be expected. In fact, excretion of these cations was significantly raised compared to that of the control subjects ($p < 0.01$, $p < 0.001$ respectively).

For the reasons given in the discussion in Chapter 7 it is unlikely that there is an excessive loss of bicarbonate through a well established ileostomy. Therefore, bicarbonate loss from the intestine is probably not a significant factor in causing the more acidic urine found in ileostomists.

In addition to having a smaller 24 hour urine volume

and passing a more acidic urine, two out of the four ileostomists who had urolithiasis (or three out of the five, if the patient with a non-functioning kidney is included) had high plasma levels of uric acid; and one of the remaining two patients had a level towards the upper limit of normal ($440 \mu\text{mol/l}$, normal range $210\text{--}480 \mu\text{mol/l}$). Therefore, there appears to be a high tendency for these patients with hyperuricaemia to form urinary stones. For this reason it seems probable that the patient who was found to have a non-functioning kidney may have had the kidney damaged as a result of urolithiasis. It is known that this patient's kidneys appeared normal at laparotomy when he had a proctocolectomy and formation of an ileostomy. Therefore, it must be concluded that the left upper urinary tract was damaged either at the time of operation or subsequently by urolithiasis.

In total, six out of the 23 male ileostomists who had had ulcerative colitis had a plasma uric acid level above the upper limit of normal. This is a high incidence which is unlikely to have occurred by chance. There are three possible explanations for this finding. Perhaps there is a genetic factor which links ulcerative colitis to gout, but such an association has not been found in large surveys of patients with ulcerative colitis (Edwards and Truelove, 1964; Goligher, 1980). However, a high incidence of gout has not been found in large surveys of ileostomists (Daly, 1968; Ritchie, 1971b). Even if it does occur, it is not surprising that the association has not previously been recorded, because at the start of the present study only two of the patients with hyperuricaemia were known to have gout. Two out of the 12 ileostomists with

Crohn's disease, one male and one female, were also found to be hyperuricaemic. This finding makes a genetic cause less likely unless Crohn's disease is genetically linked to ulcerative colitis, which is possible.

Another possible cause for this high incidence of uricaemia in ileostomists is that there might be an alteration in the handling of uric acid in the kidney of these patients. This possibility seems the more likely at first sight. However, if this were the case, a high mean plasma urate and an altered mean urinary urate might be expected but these have not been found in either the present or previous studies (Clarke and McKenzie, 1969; Singer et al, 1973). Therefore, a third possibility arises. All the ileostomists who had had ulcerative colitis and who had hyperuricaemia were male. Men are known to have a much higher incidence of gout than women. Perhaps the metabolic changes that follow an ileostomy tend to cause frank hyperuricaemia in those patients who previously had plasma uric acid levels towards the upper limit of normal.

Several workers have suggested that solutes such as sodium, potassium, magnesium and urea help to maintain calcium and urate in solution in the urine (Hammarsten, 1929; Medes, 1932 Mukai and Howard, 1963; Modlin, 1967). The mean 24 hour urinary sodium and magnesium excretion were found to be low in the urine of ileostomists taking part in the present study. Therefore, this low level of solutes may be another factor tending to increase the incidence of nephrolithiasis in ileostomists. In addition, Blacklock (1976) suggested that a higher incidence of upper urinary tract stones found in the general population might be linked to a higher dietary intake

of refined carbohydrate. The analysis of the diet of ileostomists taking part in the present study who had had ulcerative colitis compared to that of the control subjects, showed that the ileostomists were eating more simple sugars than the healthy subjects but the difference was not statistically significant.

Several surveys have demonstrated an increased incidence of urolithiasis in patients with Crohn's disease as well as in patients receiving medical treatment for ulcerative colitis (Deren et al, 1962; Gelzayd et al, 1968). However, the possible role of ileal dysfunction was not appreciated until two groups of workers demonstrated a high urinary excretion of oxalate in patients who had had an ileal resection (Hofmann et al, 1970; Dowling et al, 1971). Chadwick and his colleagues (1973) demonstrated that the hyperoxaluria in these patients was due to increased intestinal absorption of oxalate. This increased absorption of oxalate takes place mainly in the colon and hyperoxaluria was not found in patients with an ileostomy (Modigliani et al, 1978). The high oxalate absorption is thought to occur because oxalate is normally precipitated with calcium in the small intestine, whereas, when steatorrhoea is present, the calcium is precipitated with unabsorbed fatty acids leaving the oxalate in solution and thus available for absorption. In addition, the absorption of oxalate may be increased in the colon by the presence of long chain fatty acids (Dobbins and Binder, 1976). Therefore, although there is an increased incidence of urolithiasis due to hyperoxaluria in patients with Crohn's disease this abnormality does not occur in ileostomists with Crohn's disease.

No urinary stones were found in the ileostomists with Crohn's disease who took part in the present study. Indeed, the 24 hour urinary excretion of calcium and phosphate was reduced, thus making the formation of calcium-containing stones less likely. However, other factors favouring urolithiasis such as a significantly low mean 24-hour urine volume and also significantly low mean 24-hour urinary excretions of sodium and magnesium were found in these ileostomists. In addition, two of these patients had hyperuricaemia. Therefore, ileostomists with Crohn's disease have similar features increasing the chance of urolithiasis.

The present study has demonstrated that there is a high incidence of urolithiasis in ileostomists even in the United Kingdom. It has also shown that male ileostomists with hyperuricaemia seem particularly likely to develop urolithiasis. Therefore, it is suggested that doctors should be alert to the possibility of urolithiasis occurring in ileostomists. Regular estimations of the plasma uric acid level should be made and treatment with Allopurinol should be begun early in ileostomists with hyperuricaemia. Ileostomists should be encouraged to drink more than they feel that they require. Finally, as is discussed in Chapter 7, a controlled trial of agents that might correct the hyperaldosteronism in order to render the urine less acidic in these patients would be worthwhile.

CHAPTER 11

GALLSTONES

INTRODUCTION

In a lecture concerning the formation of gallstones, delivered at the West London Hospital in 1961 and later reported in the British Medical Journal (1962), A.J.Harding Rains began by stating:

"One is careful in laying claims to originality in the reporting and measurement of natural phenomena. Research into the literature of the subject will reveal that others have followed similar pathways and you will be reminded of the saying that "there is nothing new under the sun", and that you have merely completed a circle and brought understanding back to where it was some fifty or even one hundred years ago. Research is not like that, however; it is a spiral. At each full circle we have achieved an advance in our understanding. We are not back to where we were but rather projected forwards. Though gallstones is an age old disease of mankind, let us join the spiral and turn it through the last two hundred years".

Despite many twists of the spiral the causation of gallstones remains a subject of controversy. In the last few years different authors have emphasised several possible aetiological factors: the role of bile supersaturated with cholesterol, the importance of disordered bile pigment metabolism even in the formation of 'cholesterol' stones, and the contribution of disordered motility of the bile ducts and gallbladder

(Carey and Small, 1978; Duvaldestin et al, 1980; La Morte et al, 1979 respectively).

The situation as regards the relationship between gallstones and ileostomy is no less controversial. Hill and his colleagues (1975b) found a 24.5 per cent incidence of gallstones in a study of 108 patients with an ileostomy. They estimated that this incidence was about three times that expected in a sample of the general population of similar age and sex. On analysis of their data, they found that the incidence of gallstones was high in those patients whose primary disease was Crohn's disease or who had had more than 10 cm of terminal ileum removed. They found no increased incidence in those patients who had had less than 10 cm of terminal ileum removed and whose primary disease was ulcerative colitis. However, a study from Cardiff reports a 20 per cent incidence of gallbladder disease in a group of 55 patients all of whom had had ulcerative colitis while no patient with gallstones appeared to have had more than 10 cm of ileum resected (Jones et al, 1976). Loss of functioning terminal ileum due to either resection or disease is known to cause loss of bile salts due to impairment of the entero-hepatic circulation and this results in an increased incidence of cholelithiasis (Heaton and Read, 1969; Cohen et al, 1971; Dowling et al, 1972). Therefore, it is well documented that ileostomists with Crohn's disease have an increased chance of developing gallstones but it is less clear whether this is also the case in ileostomists who had had ulcerative colitis and who had only a minimal resection of the terminal ileum.

The metabolism of bile salts in patients with an ileostomy is also uncertain and subject to debate. The main aim of the work reported in this chapter was to determine whether there was a high incidence of gallstones in those ileostomists taking part in the present study who had had ulcerative colitis and who had had less than 10 cm of terminal ileum resected.

PATIENTS AND METHODS

All of the 51 ileostomists taking part in the present study were examined for gallstones after an overnight fast by the use of ultrasound. Two pieces of equipment were used for this purpose, a grey scale B-scan ultrasound was carried out using a Nuclear Enterprises Ltd, Diasonograph, NE4200 and a real time scan was undertaken using a Toshiba Sonolayer, model SAL-20A. It was judged that accurate results were obtained with the skilled use of these machines. Nevertheless, it was decided to perform an oral cholecystogram on any patient who was suspected of having cholelithiasis on the basis of the ultrasound findings. The oral cholecystograms were carried out using 3 gm of sodium iopodate as the radio-opaque material.

All of the 39 healthy subjects who were age- and sex-matched to the ileostomists who had had ulcerative colitis were examined for gallstones using the same ultrasonic equipment. However, those of the control subjects who were diagnosed as having cholelithiasis by ultrasound were not subjected to cholecystography as it was thought that it would be unethical

to expose them to the necessary X-radiation.

The excretion of bile salts in the ileostomy effluent of the ten ileostomists who had had ulcerative colitis is being measured at the Bacterial Metabolism Research Laboratory in Colindale and being compared to the excretion in normal subjects. However, the results of these measurements are not available at the time of writing.

RESULTS

On ultrasound examination ten of the 39 ileostomists who had had ulcerative colitis and one of the 12 with Crohn's disease were suspected of having gallstones. Subsequent cholecystography confirmed the presence of gallstones in all these patients except in one of those who had suffered from ulcerative colitis. Most of these patients had multiple gallstones and all of them were asymptomatic. Four of the ten ileostomists had calcified stones. All of the patients with gallstones who had previously suffered from ulcerative colitis had had less than 10 cm of terminal ileum resected. The details of the patients and of the healthy subjects who were found to have cholelithiasis are given in Table 11.1

The results shown in Table 11.1 demonstrate that 23.1 per cent of the ileostomists who had had ulcerative colitis were found to have gallstones compared to only 5.1 per cent of the age- and sex-matched healthy control subjects. Only one of the patients with Crohn's disease was found to have cholelithiasis but the number of patients in this group was too small to draw any conclusions. The ileostomists with

Table 11.1 Details of the ileostomists and healthy subjects who were found to have gallstones. The healthy subjects were matched for age and sex to the patients who had had ulcerative colitis

Variable	Ileostomists who had had ulcerative colitis n = 39		Healthy control subjects n = 39		Ileostomists with Crohn's disease n = 12	
No. of subjects with gallstones	9		2		1	
Incidence of gall- stones per cent	23.1		5.1		8.3	
Sex of subjects with gallstones	M 5	F 4	M 1	F 1	M -	F 1
Mean age years $\pm$ 1 SD	57 $\pm$ 9 (46 $\pm$ 14)	53 $\pm$ 10 (43 $\pm$ 11)	53 (50 $\pm$ 14)	51 (48 $\pm$ 11)	-	34 (47.2 $\pm$ 14.5)
Mean weight kg $\pm$ 1 SD	75.8 $\pm$ 5.7 (76.0 $\pm$ 10.8)	57.7 $\pm$ 7.5 (62.8 $\pm$ 9.9)	86.4 (78.6 $\pm$ 10.5)	101.7 (57.6 $\pm$ 6.1)	-	71.2 (54.9 $\pm$ 8.2)
Mean duration of ileostomy years $\pm$ 1 SD	6.2 $\pm$ 4.1 (5.1 $\pm$ 3.7)	7.8 $\pm$ 4.5 (6.2 $\pm$ 3.7)	-	-	-	4.0 (5.7 $\pm$ 3.7)

M = Male F = Female

The figures in brackets are the mean values $\pm$ 1 standard deviation (SD) for the other subjects in each sex matched group

gallstones who had had ulcerative colitis were older and had had their ileostomy for longer than the patients who did not have cholelithiasis but the differences were not statistically significant. The two control subjects with gallstones were considerably heavier than their colleagues, whereas this was not the case with the ileostomists.

DISCUSSION

The present study is the first to demonstrate a high incidence of gallstones in a group of well documented ileostomists who had had ulcerative colitis and who had had less than 10 cm of terminal ileum removed when compared to the incidence in a group of healthy control subjects matched for age and sex. These results are similar to those of Jones and his colleagues (1976) but they are not in agreement with those of Hill and his colleagues (1975b). As mentioned in the introduction of the present chapter, Hill and his colleagues found a 24.5 per cent overall incidence of gallstones in their patients, but the incidence was not found to be increased in those ileostomists whose primary disease had been ulcerative colitis and who had had less than 10 cm of terminal ileum resected.

It is difficult to explain why the results obtained in the present study are so different from those of Hill and his colleagues. As described already, each of the ileostomists taking part in the present study had a well documented case history and detailed operation notes. In addition, both ultrasound examination and cholecystography were used to

confirm the presence of gallstones. Therefore, there is no doubt about the increased incidence of cholelithiasis in the ileostomists, who took part in the present study, who had suffered from ulcerative colitis and who had had a minimal resection of terminal ileum. In several of the patients the cholecystogram was initially thought to be normal but with careful examination and compression films, the gallstones found by ultrasound were confirmed by cholecystography. Therefore, it is possible that the use of ultrasound as well as cholecystography is more accurate than cholecystography alone and this might explain the discrepancy in the results obtained in the present study when compared to those obtained by Hill and his colleagues.

Why should ileostomists with an intact small intestine develop gallstones? It has been found that the excretion of bile salts in these patients is normal (Percy-Robb et al, 1971; Miettinen and Peltokallio, 1971; Huibregtse et al, 1977). Moreover, Morris and his colleagues (1973) reported that the rate of loss of radiolabelled bile salts from the bile was normal. However, they only studied six ileostomists and five control subjects and although there was no significant difference in the loss of radiolable from the bile between the patients and control subjects, the ileostomists appear to have had a lower mean half-life of whole bile radioactivity than that of the control group. Therefore, it is possible that the mean loss of bile salts in ileostomists with an intact small intestine is higher than that in normal subjects but that this loss might still be within the normal range. Further information regarding bile salt loss in ileostomists will be

available in the near future from the study of the excretion of bile salts in the patients who took part in the present study.

In addition to the apparently normal loss of bile salts, Morris and his colleagues (1973) have found a normal bile salt pool size in their ileostomists. Both these findings were surprising when it is considered that secondary bile salts make up 24 per cent of the bile salt pool in normal subjects (Heaton, 1972) and that secondary bile salts are only formed in the colon (Morris et al, 1973). Moreover, only very low levels of secondary bile salts are found in ileostomists. To explain these findings an increased absorption of bile salts by the terminal ileum of ileostomists must be proposed and this would also explain why the faecal excretion of bile salts in ileostomists is near to normal.

Percy-Robb and his colleagues (1971) reported a linear relationship between the biological half-life of the cholic acid pool and the urinary recovery of vitamin B₁₂, after an oral dose of 0.5 µg of vitamin B₁₂. The half-life of the cholic acid pool became more prolonged as the urinary recovery of vitamin B₁₂ increased. Therefore, if there is an increased absorption of bile salts in the terminal ileum of an ileostomist compared to that in a normal subject then the absorption of vitamin B₁₂ might also be increased above normal in the ileostomists. This is precisely what was found to occur in the present study (Chapter 8).

Other changes in the metabolism of bile salts are known

to take place in ileostomists. As mentioned previously, very low or absent levels of deoxycholate are found in the bile of ileostomists (Miettinen and Peltokallio, 1971; Percy-Robb et al, 1971; Morris et al, 1973). In addition, there is minimal transfer of radioactivity from labelled taurocholate to the dihydroxy fraction of the bile salt pool (Morris et al, 1973). The terminal ileum of ileostomists is known to contain considerable numbers of bacteria capable of dehydroxylating bile salts (Gorbach et al, 1967; Finegold et al, 1970). Therefore, an ileostomist's failure to produce secondary bile salts cannot be due to a total absence of suitable bacteria. However, this bacterial flora is different from that of the normal colon. Finegold and his colleagues (1970) found that one gram of ileostomy effluent contained ten times fewer bacteria and 400 times fewer anaerobes than a gram of faeces. Moreover, the relative proportions of the various aerobic organisms in the ileostomy effluent may be different from that in normal faeces (Gorbach et al, 1967). Therefore, the reduction in the number of organisms and the different proportions of these organisms in the ileostomy effluent as compared to that in faeces may explain the failure of dehydroxylation of bile salts in ileostomists. In addition, the period of contact between the bile salts and the organisms in vivo is much reduced in patients with an ileostomy, thus considerably shortening the time during which dehydroxylation can take place.

There is controversy over the degree of in vivo deconjugation of bile salts in ileostomists. Several groups have reported

significant deconjugation (Miettinen and Peltokallio, 1971; Percy-Robb et al, 1971; Morris et al, 1973). However, Huibregtse and his colleagues (1977) found only minor deconjugation of bile salts in vivo, but that deconjugation occurred fairly rapidly in the ileostomy bags.

Diet is another factor known to affect bile acid metabolism. Heaton (1972) reviewed the probable importance of diet in the causation of gallstones. Two of the most important dietary factors in stimulating the formation of lithogenic bile were thought to be a high intake of refined carbohydrate and also a low intake of dietary fibre. It was shown in Chapter 6 of the present study that the ileostomists ate more refined carbohydrate and less dietary fibre than the healthy control subjects matched for age and sex but the differences were not statistically significant.

In summary, the present study has demonstrated a high incidence of gallstones in ileostomists with an intact small intestine who had had ulcerative colitis when compared to that in healthy control subjects matched for age and sex. It is suggested that this high incidence of gallstones may be due to a slightly higher loss of bile salts from the bowel of these ileostomists than that in normal subjects despite a probable increase in the absorption of bile salts by the terminal ileum of these patients. Other differences in bile acid metabolism in ileostomists as compared to normal have been demonstrated by several groups of workers. The importance of these alterations in bile acid metabolism in the causation

of the increased incidence of cholelithiasis in patients with an ileostomy is not established.

CHAPTER 12

GASTROINTESTINAL HORMONES

INTRODUCTION

The human colon is known to contain endocrine cell types which are morphologically distinctive (Cristina et al, 1978). The role of the substances found in these colonic endocrine cells remains uncertain. Their discovery gives rise to several interesting questions. Are they true hormones acting on distant tissues ?. Is their action limited to the colon or do they affect the function of other parts of the gastrointestinal tract ?. What is the mechanism for their release ?. One way of beginning to answer some of these questions is to investigate the gastrointestinal hormone response to a test breakfast in patients who have had a proctocolectomy for ulcerative colitis. As has been mentioned previously, these subjects are cured of their disease and have had only a minimal resection of terminal ileum.

If patients with a well-established ileostomy, after surgery for ulcerative colitis, have a different gastrointestinal hormone response to a test breakfast from the response found in healthy subjects, then it might occur for several reasons. Firstly, it could be due to the loss of endocrine cells located in the colonic mucosa. Secondly, it might be part of an adaptive process which takes place in the small intestine following proctocolectomy. Finally, it might be a residual

effect of the ulcerative colitis although this seems unlikely. This study was designed to investigate some of these possibilities.

PATIENTS AND METHODS

Ten patients who had had a proctocolectomy and formation of an ileostomy for ulcerative colitis at least 18 months previously took part in this investigation. All of these patients were in good general health and leading normal lives. Each of them had had less than ten cm of ileum removed at the operation. Five of the patients were male and five female. Their mean age was 42 years (range 32 - 53 years), their mean weight was 67.71 ± 6.90 kg and their mean height was 168.48 ± 4.08 cm.

Ten age- and sex-matched healthy control subjects were also studied. None of them had any medical history of gastrointestinal disease. They had all taken part in the other metabolic studies and hence they had had a medical history taken, had been examined and had had blood samples taken for routine haematological and biochemical tests. Five of these subjects were male and the other five female. Their mean age was 44.8 (range 37 - 54 years), their mean weight was 71.76 ± 12.58 kg and their mean height was 165.86 ± 10.17 cm.

After an overnight fast, each subject ate a standard test breakfast consisting of two medium sized boiled eggs, 150ml of orange juice, 60g of toast, 10g of butter and

35g of marmalade; this meal contain 18g of protein, 22g of fat and 66g of carbohydrate, representing 530 calories. An indwelling intravenous catheter was placed in a suitable antecubital vein. Blood samples for blood sugar and gastrointestinal hormone assays were taken into heparinised tubes containing 400 kallidinogenase-inactivating units of aprotinin (Trasylol) per ml. The blood samples were taken 15 and 30 minutes before and at time zero, when the subjects were given breakfast. Further samples were taken 15, 30, 60, 120 and 180 minutes after the start of the meal. The plasma was separated within 15 minutes of sampling and stored at -20°C until assay.

Hormone radioimmunoassays

Radioimmunoassays were carried out at the Royal Postgraduate Medical School by conventional methods using antisera raised to synthetic gastrin 1 (Russell et al, 1976), natural human pancreatic polypeptide (Adrian et al, 1976), natural porcine motilin (Bloom et al, 1976), natural porcine gastric inhibitory polypeptide (Sarson et al, 1980), natural porcine glucagon (Alford et al, 1977), and natural bovine neurotensin (Blackburn et al, 1979). Insulin was measured using commercially obtained antisera (Wellcome, UK) and label (Radiochemical Centre, Amersham, IM38). The assays could detect the following plasma changes with 95 per cent confidence gastrin, 2 pmol/l; pancreatic polypeptide, 4 pmol/l; motilin 3 pmol/l; gastric inhibiting polypeptide, 3 pmol/l; pancreatic glucagon, 1.5 pmol/l; enteroglucagon 8 pmol/l; neurotensin, 5 pmol/l and insulin 6 pmol/l.

Cross-reaction of the antisera raised to the various peptides assayed was less than 0.5 per cent. Antiserum R59, which showed a high degree of cross-reactivity with ileal extracts and fully detected gravimetrically determined glicentin, was used to measure total plasma glucagon. Enteroglucagon concentration was derived by subtraction of the pancreatic glucagon measured by the specific antiserum R85 from total plasma glucagon. Blood glucose was measured in Oxford by the GOD-PAP [Glucose oxhide dehydrogenase-4-(p-benzoquinonine-mono-imino)phenazone] method using a Boehringer Mannheim auto-analyser.

Statistical significance was assessed by the use of Student's t test. The integrated response (IR) was calculated by adding the plasma hormone concentration at the beginning and end of each time period after the meal, dividing this by two and multiplying by the number of minutes in that time period. These results were summed and then the mean basal concentration multiplied by the number of minutes in the whole time period were subtracted.

For example:

Hormone Z	Mean	+15	+30	+60	+120	+180
	Basal	min	min	min	min	min
	a	b	c	d	e	f

$$\text{IR for hormone Z in patient 1} = \left[\frac{a+b}{2} \times 15 + \frac{b+c}{2} \times 15 + \frac{c+d}{2} \times 30 + \frac{d+e}{2} \times 60 + \frac{e+f}{2} \times 60 \right] - a \times 180$$

In Table 12.1 IR results are expressed in nmol/l over 180 minutes. The mean IR for each hormone was calculated to give the results shown in Table 12.1.

Table 12.1 Blood glucose and gastrointestinal hormone response to a test meal in patients who have a well established ileostomy after surgery for ulcerative colitis compared to the response in healthy control subjects

		Normal Subjects n = 10	Ileostomy Patients n = 10
Glucose	B	4.6 ± 0.2	4.6 ± 0.2
	P	6.0 ± 0.6	5.6 ± 0.4
	IR	41.0 ± 40.0	47.0 ± 33.0
Insulin	B	44.0 ± 6.0	52.0 ± 10.0
	P	249.0 ± 26.0	341.0 ± 87.0
	IR	21.0 ± 3.0	26.0 ± 6.0
GIP	B	13.0 ± 2.0	13.0 ± 2.0
	P	37.0 ± 3.0	35.0 ± 3.0
	IR	3.0 ± 0.3	2.9 ± 0.3
Gastrin	B	9.0 ± 2.0	6.0 ± 1.0
	P	5.0 ± 14.0	25.0 ± 10.0
	IR	4.0 ± 1.0	2.0 ± 0.8
Motilin	B	49.0 ± 9.0	79.0 ± 11.0*
	P	72.0 ± 9.0	91.0 ± 12.0
	IR	0.7 ± 1.2	-0.5 ± 1.3
HPP	B	49.0 ± 4.0	51.0 ± 9.0
	P	213.0 ± 30.0	279.0 ± 69.0
	IR	26.0 ± 4.0	34.0 ± 8.0
Entero-glucagon	B	33.0 ± 3.0	25.0 ± 2.0*
	P	37.0 ± 6.0	33.0 ± 4.0
	IR	-0.1 ± 0.6	0.8 ± 0.3
Neuro-tensin	B	44.0 ± 4.0	41.0 ± 4.0
	P	46.0 ± 3.0	49.0 ± 4.0**
	IR	-0.1 ± 0.3	1.1 ± 0.3

All hormone levels (B = basal, P = peak) given as pmol/l $\pm$ 1 SEM
blood glucose levels given as mmol/l $\pm$ 1 SEM

IR = integrated response of hormone after the test breakfast expressed as nmol/l over 180 minutes + 1 SEM

blood glucose response given in mmol/l over 180 minutes $\pm$ 1 SEM

[illegible]

RESULTS

Mean basal levels, mean peak postprandial levels and the mean postprandial integrated response for blood glucose and each hormone are shown in Table 12.1. The results are given for both the ileostomists and the healthy control subjects.

It may be seen from the Table that the basal motilin level was significantly raised in the ileostomists ($p < 0.05$), whereas the basal enteroglucagon level was significantly low in these patients as compared to the healthy control subjects ($p < 0.05$). In addition the integrated response of neurotensin was significantly greater in the patients as compared to that in the healthy controls ($p < 0.02$). There were no significant differences in the values of glucose, insulin, gastric inhibitory peptide (GIP), gastrin and human pancreatic polypeptide (HPP) when comparing the results obtained in the patients with those obtained in the healthy control subjects.

DISCUSSION

It can be seen from the results given in Table 12.1 that, patients who have had a proctocolectomy with formation of an ileostomy for ulcerative colitis have a nearly normal gastrointestinal hormone profile. However, there are some statistically significant differences between the hormone values in these patients and those in the healthy control subjects. The significantly low level of enteroglucagon found in the ileostomists is interesting because this hormone is found in highest concentration in the terminal ileum and

significant amounts are also found in the colon (Polak and Bloom, 1979). The low basal level of enteroglucagon found in these ileostomists may well be due to the loss of colonic cells that contain enteroglucagon. Alternatively, the low level might be due to a functional adaptation of the remaining gastrointestinal tract. Perhaps the small intestine is better adapted to fulfil its new role, without the colon, when there are lower levels of circulating enteroglucagon. As is shown in Table 12.1, two gastrointestinal hormone values were significantly greater in the ileostomists than in the healthy control subjects. There was a high basal level of motilin and an increased integrated response of neurotensin. These hormones have many physiological actions and their precise roles are not fully understood. However, they are both thought to have possible physiological actions on the control of gastrointestinal motility. It is possible that the raised levels of these two hormones in conjunction with the low basal level of enteroglucagon, which is also thought to affect bowel motility, might be an expression of an altered physiological response in these ileostomists. Further study of gastrointestinal hormones in ileostomists would be interesting. It is usual for about 1,500 ml of fluid to enter the colon in a healthy subject every day (Phillips and Giller, 1973). In a patient with a well established ileostomy the volume of the ileostomy effluent is about 600 ml per day. Therefore, ileostomy adaptation may be said to have occurred and a serial study of gastrointestinal hormones in ileostomists during the first few months after their operation might throw further light on the physiological role of these hormones.

CHAPTER 13

GENERAL DISCUSSION AND CONCLUSIONS

As was pointed out in the introduction to this thesis, ulcerative colitis continues to be a major disease for which current medical therapy is far from perfect. The result is that many of the patients require to be treated by major surgery at some stage in their illness. The most widely used surgical procedure is proctocolectomy with a permanent ileostomy formed by a full-thickness eversion of the terminal ileum (Brooke-type stoma). In addition, Crohn's disease has become much more common than previously and, when the large bowel is severely involved, proctocolectomy is sometimes indicated. Both diseases frequently affect young people so that there are appreciable numbers of patients who are given a permanent ileostomy at any age when the normal expectation of life may be up to 50 years or even more. For the most part, the previous surveys have concentrated on the general health of these subjects, as judged superficially and without detailed study of them as individuals. Previous metabolic studies have been on a small scale and have usually been confined to the investigation of a single metabolic aspect. The present study represents an attempt to overcome some of these deficiencies by investigating a good-sized sample of ileostomists in considerable detail, not only from the viewpoint of their general health and social adaptation, but also as regards a variety of metabolic functions. From the metabolic angle, the inclusion of a control group of healthy subjects, matched for age and sex, has enabled subtle abnormalities of function to be detected. Although none of

abnormalities are dramatic, they are persistent and there is therefore the possibility of serious consequences in the long term.

Proctocolectomy with a permanent Brooke-type ileostomy is not the only radical surgical treatment available for patients with ulcerative colitis or Crohn's colitis. In some patients, colectomy with an ileo-rectal anastomosis is a possible alternative. In those in whom this procedure works well, psychological and social adaptation is easier and any metabolic derangement is likely to be less pronounced than with a permanent ileostomy. Unfortunately, especially in ulcerative colitis, the rectum may continue to show active disease, so that diarrhoea may be troublesome and there is a definite risk of cancer developing.

An alternative to the Brooke-type spout ileostomy is the continent ileostomy devised by Kock (1969). In this procedure, the terminal ileum is converted into an internal reservoir with a nipple valve which prevents the contents from leaking. The stoma is a small opening flush with the skin and it requires only a small pad of gauze to cover it. The reservoir is emptied three or four times a day by passing a soft catheter into it and draining the contents into a suitable receptacle for disposal. It has considerable advantages from a cosmetic point of view and enthusiasts for the procedure claim that the quality of life is much improved compared with that experienced with a conventional ileostomy.

On the other hand, about 50 cm of the terminal ileum is employed in making the reservoir so that any metabolic disturbances occurring with a continent ileostomy are likely to be more pronounced than with a conventional ileostomy. Furthermore, the contents are stagnant for a number of hours between emptying and the possibility of metabolic derangements already known to be associated with a "stagnant loop" must be recognised. At present only limited studies have been made of the metabolic functions of patients with a Kock's ileostomy. It has been found that the absorption of fat, bile salts and vitamin B₁₂ is depressed in a proportion of these patients when compared with subjects with a Brooke-type ileostomy (Jagenburg et al, 1971; Philipson et al, 1975; Nilsson et al, 1979). In addition, there is an appreciable risk of incontinence with the reservoir ileostomy and also a considerable degree of surgical morbidity (Goligher, 1980).

Another surgical procedure, which is still in an experimental stage, is to perform a proctocolectomy and to anastomose the terminal ileum to the anus (ileo-anal anastomosis), coupled with the construction of an ileal reservoir without a nipple valve (Parks and Nicholls, 1978; Parks et al, 1980). This is a difficult surgical procedure and it is likely to result in metabolic disturbances similar to those associated with a Kock's continent ileostomy.

It seems likely that proctocolectomy with a permanent

Brooke-type ileostomy will continue to be employed in many patients during the foreseeable future and this procedure will be the yardstick by which the success or failure of the other operations will be judged. It is therefore evident that patients with a conventional permanent ileostomy should be studied from all angles. In particular, further detailed studies of metabolic functions will be required and a search should be made for simple methods of overcoming any abnormalities that commonly occur.

For example, the present study has shown that aldosteronism is a feature of patients living with a permanent ileostomy. It appears to be a response to the abnormal losses of sodium and water through the ileostomy. As a result the urine is unduly acidic and tends to be of low volume, both of which increase the risk of urinary stones. There may be other consequences of prolonged aldosteronism which are not yet apparent. It seems to be highly desirable that a simple method of preventing aldosteronism in these patients should be developed but this will demand further research. Likewise, the probable abnormal loss of bile salts through the stoma may be responsible for the high risk of developing gallstones which was found in the present study. Detailed studies of the bile salt pool are required before any corrective measures can be suggested. Ileostomists are commonly iron-deficient and it is probable that they should be given supplements of oral iron for some months after the ileostomy has become well established and their iron status should be checked occasionally during the course of prolonged supervision. Similarly, they

appear to be calcium-deficient as a result of their illness and its medical treatment with corticosteroids and it is possible that they should be given supplements of vitamin D and calcium for several months once the ileostomy is functioning well.

Although several of these possibilities will have to await the outcome of future research, there are various practical recommendations that can be made immediately for the care of ileostomists.

1. Great attention should be paid to the psychological preparation of any patient who is recommended to have an ileostomy performed as an elective procedure. This should be supplemented by continued reassurance and explanation post-operatively, an aspect of supreme importance when the ileostomy has been performed as an emergency procedure so that pre-operative preparation is necessarily scanty or even absent. If possible, close members of the family should be involved in this process of explanation and reassurance. (See also Appendix).
2. Preoperative reassurance with regard to sexual activity should be given to both the patient and their spouse. Postoperatively, enquiry should be made as regards sexual activity and skilled counselling should be given when necessary.
3. The patient should be encouraged to eat a normal diet but should be warned of the necessity to chew thoroughly any items of diet that are hard or fibrous.

4. The patient should be instructed to consume ample quantities of fluid in order to ensure a good urinary volume.
5. Ample salt should be consumed.
6. Any patient visiting a country with a hot climate should be advised to drink more fluid and take more salt than usual. In addition, any patient who develops diarrhoea and/or vomiting should be encouraged to seek medical advice early due to the risk of becoming rapidly dehydrated and salt depleted.
7. Once the ileostomy is working well, a course of a suitable iron preparation, such as ferrous fumarate, should be given for a few months and thereafter their iron status should be checked occasionally.
8. The plasma uric acid should be checked from time to time as a high level is apparently associated with urinary stones.
9. Doctors should recognise that patients with an ileostomy have an increased risk of developing both urinary stones and gallstones.
10. Long term follow up should be arranged for all patients who have a permanent ileostomy. This ensures that any psychological or sexual problems can be discussed and that all the metabolic abnormalities found in the present study

can be detected early and corrected. In addition, it enables the stoma care nurse to check the stoma and provides her with an opportunity to inform the patient about any new appliances or equipment.

21 December, 1981.

Dear John,

Re: MD Thesis: The Health of Ileostomists - H. J. Kennedy

Thank you so much for your comments about this man. I have just heard from Brian Brooke, who agrees that the thesis should be awarded. I should be grateful if you would sign the enclosed form and return it to me.

With kind regards,

Yours ever,

Professor J. E. Lennard-Jones,
The London Hospital Medical College,
Academic Unit of Gastroenterology,
Whitechapel,
E1 1BB.

CHAPTER 14

SUMMARY

When radical surgery is required for the treatment of ulcerative colitis, the standard operation is proctocolectomy with the formation of a permanent ileostomy. When Crohn's disease affects the large bowel, the same procedure is sometimes necessary, although in this case the disease is not cured and resection of part of the small intestine may also be indicated, either before, during or after the proctocolectomy. The result is that there are many patients living with a permanent ileostomy. Previous surveys of such patients have suggested that their general health is good and that their expectation of life probably approximates to the normal. Previous metabolic studies have been confined to small groups of ileostomists and have usually been concerned with a single aspect of metabolism; furthermore virtually none of these studies have employed a proper control group (Chapter 1).

The aims of the present study were to survey the general state of health of a group of ileostomists, including social psychological and sexual aspects, and to investigate a range of metabolic functions in the same patients (Chapter 2).

The ileostomists studied were taken at random from patients who had been treated by proctocolectomy and ileostomy in Oxford, the sole considerations being that the ileostomy had been established for at least one year and that they lived close enough to Oxford to attend for repeated

investigations. Such patients were invited to volunteer to take part in the study after the details had been explained to them. There were 39 ileostomists who had previously suffered from ulcerative colitis and who had had only a minimal resection of the terminal ileum. In addition, there were 12 patients with Crohn's disease who had no clinically active disease involving the remaining intestine at the start of the study. There was a control group of 39 healthy volunteers who were matched for age and sex with the 31 ileostomists who had had ulcerative colitis (Chapter 3).

The assessment of the general health of the ileostomists was based on the clinical history and a standard physical examination, supplemented by a range of haematological and biochemical tests. As judged by these criteria, virtually all the patients were found to be in good general health (Chapter 4).

On the social side, virtually all the patients had adapted well to life with an ileostomy. All but one had returned to their previous full time occupations. Their hobbies and recreations were unimpaired, with the exception that some of them avoided swimming because they were embarrassed by having an ileostomy. Most of the patients accepted their stoma but a minority continued to resent the fact that they were burdened with this abnormality. It has been the practice in Oxford for many years to explain the consequences of an ileostomy to any patient for whom this procedure is recommended, to arrange one or more meetings with a suitable patient already

living with an ileostomy and to give reassurance and detailed instructions during the post-operative period. Nevertheless, it became apparent that there was a substantial number of the patients who considered that explanation and guidance had been inadequate; practical recommendations to overcome this deficiency are made. Two intelligence quotients of the patients showed them to be of average or good intelligence. Based on the results of personality inventories, the female patients were found to have normal feminine characteristics and at interview were willing to discuss all aspects of life with an ileostomy with apparent freedom. By contrast, the men were inclined to be introverted, to conform rigidly to accepted standards of behaviour and appeared to be less able to discuss intimate problems. There was no evidence of a neurological disturbance of sexual function in either sex. However, some of the men experienced psychological difficulties with sexual activities and this applied especially to young unmarried men. All the sexually active women had normal sexual feelings but three of them suffered from dyspareunia and several felt themselves to be less attractive because of the ileostomy (Chapter 5).

A dietary survey of the ileostomists has been made by having them keep a detailed record of all food and drink consumed over the course of one week, supplemented by an interview. The 39 control subjects recorded their dietary intake in an identical manner. The details were analysed by computer. The interview showed that nearly half the ileostomists ate an entirely unrestricted diet, but the others avoided one or more of certain items, such as nuts, skins and pips. The

computer analysis showed that the dietary intake of the patients closely resembled that of the control subjects, the exceptions being that they drank more fluid and consumed more salt. It is recommended that ileostomists should eat a normal diet but that they should be careful to chew indigestible food thoroughly and that they should drink ample fluid (Chapter 6).

Investigation of the water and electrolyte balance yielded evidence of haemoconcentration which was presumed to be due to excessive loss of fluid and sodium from the intestine. There was evidence of aldosteronism and of increased plasma renin activity. The urine indicated renal conservation of sodium and excessive loss of potassium and hydrogen ions. It is concluded that a controlled trial of supplementing the diet with sodium chloride, sodium bicarbonate or a glucose; electrolyte mixture is called for in order to determine the best method of overcoming the aldosteronism (Chapter 7).

There was evidence of a mild degree of iron deficiency in the ileostomists. This was probably due to a pre-existing iron deficiency as a result of their preceding illness and operation, as the abnormality was less pronounced in the patients in whom the ileostomy had been established for more than three years. However, there was also evidence of excessive iron loss. A controlled trial of ferrous fumarate showed that the iron deficiency was largely corrected by this means. Circulating levels of vitamin B₁₂ were normal in the ileostomists, but it is relevant that some of the Crohn's disease group were receiving parenteral supplements. The absorption of vitamin B₁₂ was low in some of the ileostomists

who had had an ileal resection. Surprisingly, the absorption of vitamin B₁₂ in the ileostomists who had had ulcerative colitis was enhanced. The explanation for this enhancement is uncertain, but it is possible that it is related to the aldosteronism, changes in the gut hormone profile, or to enhanced absorption of bile salts from the terminal ileum; further research is required to elucidate the issue. All the ileostomists had normal levels of plasma folate and red blood cell folate, which can be taken as an indication of a good dietary intake and adequate absorption (Chapter 8).

The ileostomists who had had ulcerative colitis showed an increased retention of calcium. Otherwise, their calcium metabolism was normal and it is postulated that the increased retention represents a correction of a previous state of calcium depletion as a result of the disease and of its treatment with corticosteroids. The patients with Crohn's disease had normal retention, but it is possible that this was due to the disease impeding the absorption and thus rendering difficult the correction of any calcium deficit (Chapter 9).

There was a definite incidence of urinary stones, which occurred only in the male ileostomists. Several of the patients with urolithiasis had high plasma uric acid levels. Other factors that may be relevant were the low pH of the urine, the tendency to have a low urine volume, and the low concentration of sodium and magnesium in the urine. It is suggested that ileostomists should be encouraged to have an ample fluid intake and that regular estimation of the plasma

uric acid should be part of their follow-up supervision. The possibility of avoiding aldosteronism by appropriate supplements, as already mentioned, might be more helpful but this requires formal study (Chapter 10).

The ileostomists who had had a proctocolectomy performed for ulcerative colitis with only minimal resection of the terminal ileum nevertheless frequently had gallstones, possibly because of loss of bile salts through the stoma or possibly because they are deficient in secondary bile salts which are normally found in the colon and then partly absorbed. Although the patients with Crohn's disease are theoretically at a greater risk of developing gallstones, only one of the 12 ileostomists with this disease had gallstones; but this may represent a sampling error in view of the small number of patients in the group (Chapter 11).

The gut hormone profile was largely normal in the ileostomists but there were three abnormalities. The basal enteroglucagon was significantly low, the basal motilin was significantly elevated, and the integrated response of neurotensin was also significantly raised. These findings may result from the loss of endocrine cells normally present in the colon and secondary adaptation of the small intestine (Chapter 12).

Some of these findings are discussed with special reference to future research and some practical recommendations for immediate implementation are made (Chapter 13).

APPENDIX

A check list to ensure that patients requiring the formation of an ileostomy are given a full and adequate explanation of the operation and subsequent life with a stoma.

ILEOSTOMY CHECK LIST

		Please tick
Explanation by physician and surgeon	: the patient	()
(preferably together) to	: the close family	()
Introduction of patient and his/her family to	: the stoma care nurse	()
(well in advance of operation when possible)	: the ward sister	()
	: a suitable ileostomist	()

PREOPERATIVE EXPLANATIONS: Given in conjunction with booklets containing illustrations.

	Doctor	Stoma care nurse
1. Reasons for operation	()	()
2. The operation and early post-operative period. (iv infusion, nasogastric tube, urinary catheter, how long in bed, how long before eating, how long in hospital, and how long off work)	()	()
3. Nature, appearance and function of the stoma and ileostomy effluent (including odour)	()	()
4. General discussion about appliances (types, availability, disposal and frequency of changing)	()	()
5. Effect of ileostomy on:		
work	()	()
diet and fluid intake	()	()
social activities	()	()

	Doctor	Stoma care nurse
clothing	()	()
sports and hobbies	()	()
swimming	()	()
sex	()	()
bathing or showering	()	()
6. Mark suitable site on abdomen	()	()
7. Ileostomy Association	()	()

POSTOPERATIVE EXPLANATION In Hospital

1. Repeat preoperative explanations to patient and family	()	()
2. Select appliance with the patient : from a limited choice of the best makes		()
3. Show patient and family how to change and empty the appliance		()
4. Teach the patient how to care for the stoma and the appliance until confident to manage alone		()
5. Give details of how to obtain appliances and equipment and give adequate supplies to take home		()
6. Ask patient and family if there are any questions		()
7. Inform general practitioner and district nurse of discharge and arrange outpatient appointments - surgical and stoma care	()	()

At Home

1. Home visit a few days after leaving hospital	()
2. If home visit not possible - arrange for district nurse to visit, and telephone the patient to check on progress	()

3. Surgical and stoma care clinics (must have time to listen to the problems of the patients and his family. Go through check list again, in particular mention work, social activities, sports, sex and stoma/appliance problems)

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