"MAKING COLONOSCOPY EASIER : ADVANCES IN PROCEDURE AND PRACTICE"

Thesis submitted to the University of London for the degree of
Doctor of Medicine (MD)

by
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Abstract

Colonoscopy is widely accepted as the procedure of choice for investigation of the large bowel. It is unique in providing detailed views of the colonic mucosa and in allowing direct access for biopsy or therapeutic intervention. However, colonoscopy remains a technically difficult, invasive and poorly understood procedure. This thesis examines colonoscopy in detail and explores methods of making the procedure easier for the endoscopist and more acceptable to the patient. Colonic anatomy is assessed both in vivo (at laparotomy) and from barium enema series in order to define the anatomical challenge faced by the endoscopist and to appreciate the anatomical basis of difficulty during colonoscope insertion. In a series of consecutive colonoscopies, fluoroscopy is used to visualise the configuration of the colonoscope and define the causes of difficulty during colonoscope insertion. Causes of failed bowel preparation are assessed and a new mannitol/Picolax mixture is compared to two-dose polyethylene glycol-electrolyte lavage solution as bowel preparation for colonoscopy. Different methods of sedation/analgesia for colonoscopy are evaluated; the efficacy, safety and acceptability of patient-controlled inhalation with nitrous oxide/oxygen mixture is compared to conventional intravenous benzodiazepine/opiate medication and to placebo. The possible benefits to colonoscopy of premedication with intravenous anti-spasmodic are investigated in a double-blind, placebo-controlled study. Use of both nitrous oxide inhalation and intravenous anti-spasmodic medication for screening flexible sigmoidoscopy are also assessed. The development of a new, non-x-ray, magnetic method of imaging the colonoscope within the abdomen during endoscopy is described. Clinical evaluation of this imaging system is undertaken in a consecutive series of colonoscopies to assess its effect on performance and insertion technique.
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Statement

While having prime responsibility for the implementation, co-ordination and analysis of the studies comprising this thesis, I wish to acknowledge the immense support provided by my colleagues at St. Mark's Hospital, particularly Dr. Christopher Williams my supervisor and mentor who was closely involved with the design of all the work described.

By the nature of clinical research much of the work presented has been a team effort, involving collaboration with many clinicians and clinical staff. Advice was sought from my surgical colleagues Mr. Robin Phillips (St. Mark's Hospital) and Mr. Roger Leicester (St. George's Hospital) regarding the methodology of the anatomy studies described in Chapter 2 and I am indebted to the surgeons of the St. Mark's Association who carried out the colonic measurements, particularly Dr. Testsu Muto and Dr. Tadahiko Masaki (1st Department of Surgery, Tokyo University Hospital, Japan). Dr. Clive Bartram, Dr. Steve Halligan and Dr. Craig Jobling of the Department of Radiology St. Mark's Hospital contributed to the design of the studies recorded in Chapters 4 and 5 and Drs. Halligan and Jobling performed measurements of the barium enemas. Assistance in the running of the studies described in Chapter 4, 5, 6 and 7 was given by Dr. Manabu Fukumoto during a 1 year research attachment to St. Mark's Hospital from Toho University Hospital, Japan.

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Dedication

... to my parents Fred and Iris who have provided encouragement, support and understanding throughout my medical education.
Chapter 1 : Introduction

1.1 : The Challenge

The development of endoscopy services over the last 25 years has brought about a diagnostic and therapeutic revolution in Gastroenterology. Endoscopy allows direct visualisation of the mucosal surface, provides the opportunity for immediate therapeutic intervention and in many cases replaces the need for operation. This is particularly true for investigation of the large bowel, where flexible sigmoidoscopy and total colonoscopy not only afford comprehensive assessment and identification of colorectal disease (with photography and tissue biopsy) but also therapeutic intervention with polypectomy, electrocoagulation, photocoagulation and stricture dilatation. However despite major advances, colonoscopy remains one of the most demanding of endoscopic procedures. For the patient, bowel preparation is a necessity prior to colonoscopy, and the examination itself is potentially embarrassing, definitely invasive and sometimes painful. For the endoscopist, colonoscopy may prove difficult because of poor preparation, colonic spasm, looping of the colonoscope or acute bends within the colon caused by unusual fixation of the bowel. Because of the variety of different colons encountered and the precise hand-eye co-ordination required to perform safe and accurate colonoscopy the procedure is difficult to learn and remains, to some extent, still within the realms of the specialist. This thesis will attempt to increase our understanding of large bowel endoscopy, highlight areas of clinical difficulty and investigate possible improvements in clinical practice in an attempt to make colonoscopy easier for patient and endoscopist.
1.2: Historical perspective

Throughout the history of medicine, physicians have attempted to visualise the inside of the alimentary tract. The earliest report of successful proctoscopy was by Hippocrates in 440 BC who used a bi-valved vaginal speculum to examine the anus and distal rectum (Milne, 1907). Little further progress was made in endoscopy of the large bowel until the turn of the century. In an address to the American Surgical Association in 1901 regarding "the necessity of employing new methods of diagnosis in rectal and urinary disease", Howard Kelly described the use of a tubular speculum to examine the rectum and sigmoid flexure (Ravitch, 1981). He graphically reports the benefits of direct examination of the rectum as follows, "a distinguished colleague had suffered excessively from previous examinations without a diagnosis being reached; by means of this tubular inspection in the knee-chest posture, without producing the slightest discomfort, I was able to expose to view an extensive adenocarcinoma high-up in the rectum and with these alligator forceps to remove a piece of tissue without his knowledge, sufficient to show the nature of the disease". The device described by Kelly relied on external illumination and it was not until 20 years later that the rigid sigmoidoscope connected to a tungsten light-source was developed (Norbury, 1923). During much of this century examination of the rectum and distal sigmoid has been practised using the rigid sigmoidoscope whilst barium radiology has provided an indirect view of the remaining colon (Haenisch, 1911). The first real attempt to visualise the proximal sigmoid colon directly was by Matsunaga and Niwa in the late 1950's using a modified gastrocamera (Matsunaga et al, 1959; Niwa, 1960). This was a flexible endoscope shaft with a tiny camera at the tip, originally designed for taking multiple photographs of the stomach lining. Mechanically its use was severely limited by its inflexibility and
limited tip angulation; guidance required fluoroscopy, as there was no means of viewing down the instrument. During the 1960's several attempts were described to develop the first forward viewing flexible sigmoidoscope, mostly with little or no success (Kanazawa & Tanaka, 1965; Niwa et al, 1969; Oshiba & Watanabe, 1965; Turell, 1963; Fox, 1969). Frustrated by the lack of progress in intubating from below, an Italian group attempted retrograde intubation of the colon (Provenzale & Revignas, 1969). Their patients were required to swallow a long, soft, polyvinyl tube with a mercury bag at its tip which was allowed to traverse the entire intestinal tract and emerge from the anus. This then served as a pulley to draw back a flexible sigmoidoscope tied to its tip. Though success in intubating the sigmoid colon was reported, the procedure was clearly impractical, taking several days to complete and involving large doses of screening radiation for the patient. It was not until the late 1960's that true fibreoptic sigmoidoscopy came into its own with several reports of success in intubating the sigmoid colon (Overholt & Pollard, 1967; Overholt, 1969). Fibreoptic technology was first invented by Hopkins (Hopkins & Kapanay, 1954) in 1952 and was further developed by Hirschowitz, whose team were the first to construct a flexible optical bundle for image transmission (Hirschowitz et al, 1957). Their work culminated in the development and clinical evaluation of the first fibreoptic gastroscope (Hirschowitz, 1961).

Modern fibreoptic endoscopes for medical use contain 20-40,000 fine glass fibres making up a fibre bundle. Each fibre transmits light by repeated internal reflections from one end of the fibre to the other. No matter what the overall configuration of the fibre bundle, provided the orientation and position of each of the fibres is the same at both ends of the endoscope, the image seen at the tip is accurately relayed to the endoscopist. Thus direct vision during intubation is achieved despite a truly flexible shaft and, when necessary, an acutely-angled tip.
Following the introduction of the 108cm flexible colonoscope, Shinya and Wolf were the first to report routine intubation of the entire colon (Wolff & Shinya, 1971). Soon afterwards they showed that colonoscopic polypectomy could also be achieved, and so began the modern age of colonoscopy (Wolff & Shinya, 1973). During the 1970's fibreoptic colonoscopy became an established procedure at many centres throughout the world and began to rival barium enema as the investigation of choice for the diseased colon (Wolff et al, 1975; Loose & Williams, 1974). The next major advance came in the mid 1980's with the introduction of video technology. The charge coupled device or CCD chip, positioned at the tip of the colonoscope and containing between 30-100,000 individual photo cells or pixels (picture elements), relays images direct to a TV monitor, so removing the need for the endoscopist to hold the colonoscope close to the face (Sivak & Fleischer, 1984). This made colonoscopy not only more hygienic, avoiding splash contamination, but also more comfortable to perform.

1.3 : Colonoscopy vs barium enema

In recent years colonoscopy has become established as the "gold standard" investigation for most colorectal disease. When compared to barium enema it is a more sensitive test in diagnosing colorectal neoplasia (Williams et al, 1982; Aldridge & Sim, 1986), and the causes of rectal bleeding (Irvine et al, 1988) and diarrhoea (Durdley et al, 1987). Although colonoscopy costs more than barium enema, its therapeutic advantages make it a more cost-effective investigation when colonic disease is suspected (Walker et al, 1991). Despite its clear advantages, (direct mucosal inspection, ability to biopsy or remove lesions), colonoscopy has not eliminated the need for barium enema. Total colonoscopy may not be achieved in all patients (Lindsay et al, 1988; Waye & Bashoff, 1991)
and then, if examination of the entire colon is mandatory to detect synchronous cancers or other coexistent lesions (Ekelund & Pihl, 1974; Peabody & Smithwick, 1961; Gelfand et al, 1979), supplementary barium enema is indicated. When colonoscopy is technically difficult for anatomical reasons, barium enema in combination with flexible sigmoidoscopy may be a more acceptable method of cancer surveillance (Williams et al, 1982). Barium enema is superior to colonoscopy in demonstrating gross colonic anatomy, diverticular disease, colonic fistulae and in localising a lesion prior to surgery (Frager et al, 1987). It also has the advantage that it provides a permanent record of the colon, which can be subsequently reviewed. Patient preference for colonoscopy or barium enema is unclear. Van Ness et al. questioned 107 patients who had recently undergone both colonoscopy (with light sedation) and barium enema (Van Ness et al, 1987). They found that patients reported less procedure discomfort during colonoscopy and required less time off work afterwards. However a recent report in the radiological literature suggests that despite sedation, patients find colonoscopy more painful than double contrast barium enema (Steine, 1994).

1.4: Large bowel endoscopy today: indications and present facilities

Flexible sigmoidoscopy is established as a useful initial examination for patients with lower gastrointestinal symptoms and can be quickly performed following a phosphate enema in an out-patient setting (Leicester et al, 1982). The diagnostic rate is higher than that of rigid sigmoidoscopy and patient comfort and acceptance of the procedure is also better (Marks et al, 1979; Winawer et al, 1987). As a procedure it is less technically demanding than total colonoscopy and can be successfully performed by general practitioners, nurse technician

Colonoscopy in the UK is performed at teaching centres and most district general hospitals and is the investigation of choice for rectal bleeding (Irvine et al, 1988), diarrhoea (Durdey et al, 1987), detection of colorectal neoplasia (Aldridge & Sim, 1986) and assessment of inflammatory bowel disease (Lindsay et al, 1988). It is also considered to be the procedure of choice in the surveillance of patients at increased risk of colorectal cancer i.e. those with previous colonic neoplasia (Waye & Braunfeld, 1982), a strong family history of cancer (Hodgson et al, 1993) or long-standing ulcerative colitis (Yardley et al, 1979).

Demand for flexible sigmoidoscopy and colonoscopy is increasing and a recent report by the Endoscopy Section Committee of the British Society of Gastroenterology suggests that present availability in the UK both of equipment and skilled endoscopists falls well below the desired level (Report by the Endoscopy Section Committee British Society of Gastroenterology, 1987). There is therefore a perceived need to increase the numbers of patients who can be examined without compromising accuracy, patient safety or satisfaction and to improve, and if possible accelerate, the training of skilled endoscopists.

1.5. : Colonic anatomy

An appreciation of colonic anatomy is fundamental to colonoscopy as the length, position and the degree of mobility of the colon will to a large extent determine the potential for colonoscope looping during intubation. Knowledge of variations in colonic anatomy therefore forms the basis for understanding
many of the causes of difficulty during colonoscopy and will be addressed in detail in this thesis.

1.5.1: Embryology of the colon

The mesenteric attachments and final position of the colon are determined during foetal life. During the second month of gestation the primitive gut undergoes a phase of rapid growth, resulting in the formation of the primary intestinal loop. The primary intestinal loop rotates counter clockwise around an axis formed by the superior mesenteric artery, (figure 1.1) (Sadler, 1985). As a result of rapid growth, coiling and gut elongation the abdominal cavity temporarily becomes too small to contain all the intestinal loops and they enter the extra-embryonic coelom in the umbilical cord (physiological umbilical hernia). By the third month of intrauterine development the herniated intestinal loops begin to return to the abdominal cavity. The primitive caecum is the last part of the gut to re-enter the abdominal cavity. It is temporarily located in the right upper quadrant directly below the right lobe of the liver but subsequently descends into the right iliac fossa, assuming its usual adult location, (figure 1.2). During this process the distal end of the caecum forms a narrow diverticulum, the primitive appendix. As the gut returns to the abdominal cavity its mesenteries are pressed against the posterior abdominal wall. Normally, the mesenteries of the ascending colon, descending colon and lower rectum fuse with the parietal peritoneum of the posterior abdominal wall, thus rendering these parts of the bowel retroperitoneal and fixed. Additionally a remnant of mesentery attaches the splenic flexure of the colon to the left diaphragm (phrenico-colic ligament), fixing its position in the left upper quadrant. The mesenteries of the transverse and sigmoid colon however do not fuse completely and these parts of the bowel
FIGURE 1.1
Development of the primary intestinal loop by counter-clockwise rotation around an axis formed by the superior mesenteric artery.
FIGURE 1.2

Counter-clockwise rotation of the primitive caecum towards the right iliac fossa.

Final position and mesenteric attachments of the colon; the mesenteries of the descending and ascending colon have fused completely with the posterior abdominal wall.
remain suspended in the abdominal cavity on their respective mesocolons. The sigmoid mesocolon is V-shaped and attached to the pelvic wall between the point where the external iliac artery bifurcates and the third sacral vertebrae in the midline (Williams & Warwick, 1980). The transverse mesocolon is a broad V shape and is attached across the posterior wall of the upper abdomen crossing the duodenum and the head of the pancreas.

### 1.5.2: Anatomical variations

Variations in adult colonic anatomy may arise during development, depending upon both the degree of final rotation and migration of the gut, and the extent to which the colonic mesenteries fuse with the posterior abdominal wall. Due to failure of the caecum to migrate during intrauterine development its final position has been described in adults in the right upper quadrant and even the centre of the abdomen (Auh et al, 1985; Smith, 1911). Of particular importance to colonoscopy however is the degree of potential mobility of the colon on its mesenteric attachments. As described earlier, the ascending and descending colon usually fuse with the posterior abdominal wall to become fixed and retroperitoneal. However the frequency with which incomplete fusion occurs is unclear. The last English language study to assess colonic attachments was by Sir Frederick Treves in 1885 (Treves, 1885). He described the anatomy of 100 cadavers at post mortem and found that 52 had neither a descending nor ascending mesocolon, 14 had both, 12 an ascending mesocolon and 22 a descending mesocolon alone; thus 26% possessed ascending mesocolons and 36% some degree of persisting descending mesocolon. Exact measurements of the mesocolons were not described by Treves but he comments that in his experience the ascending mesocolon, when present, varied between 1 and 2
27

inches (2.5-5cm) in length, and the descending mesocolon 1-3 inches (2.5-7.5cm). The presence of a large persisting descending mesocolon has also been described by Morgenstern who comments that this variation may be more common than was previously thought (Morgenstern, 1960). Mobility of the right colon due to a persisting ascending mesocolon, associated with caecal volvulus, has been described by Wolfer et al. (Wolfer et al, 1942). Variations in the degree of mobility of the transverse colon have also been noted: in a barium enema study, Moody assessed the variation in the position of the transverse colon in the supine and erect positions, finding that the transverse colon dipped as low as the true pelvis in 17% of individuals (Moody, 1927).

1.5.3 : Relevance for colonoscopy

A redundant sigmoid colon may predispose to the formation of so-called "N" and alpha loops during intubation whilst increased mobility of the descending colon because of a persisting descending mesocolon may allow medial deviation of the left colon by the colonoscope during intubation and a tendency for complex loops such as the reversed splenic flexure and reversed alpha loop to form (Williams, 1990; Hunt, 1981). Moreover if the first point of retroperitoneal fixation of the descending colon is low in the pelvis a long and narrow sigmoid "N" loop may occur, making the junction from the sigmoid to the descending colon an acute bend that is difficult to pass (Sakai, 1972). Mobility of the splenic flexure due to a lax phrenico-colic ligament can also cause problems during intubation, reducing the effectiveness of "straightening" manoeuvres in the transverse colon by removing the "fulcrum" which allows the endoscopist to lever up any transverse loop when pulling back on the shaft (Sakai, 1987). In addition mobility and subsequent looping of the transverse colon may produce
increased frictional resistance to insertion of the instrument tip, and so result in secondary looping in the sigmoid colon as well, frustrating attempts at inward passage of the colonoscope.

1.5.4 : Racial variations in colonic anatomy

Racial variation in the size of the sigmoid colon has been noted by Lisowski who found a high incidence of long suprapelvic sigmoid loops (in association with a high incidence of sigmoid volvulus) in Ethiopians (Lisowski, 1955). No study has compared colonic anatomy between Caucasian and Oriental patients but anecdotal reports from visiting endoscopists (CB Williams, 1994 personal communication) have suggested that colonoscopy is easier in Orientals (see Chapter 2), possibly due to differences in colonic anatomy.

1.6 : Defining the procedure of colonoscopy

Colonic anatomy defines the anatomical challenge faced by the colonoscopist but many other factors both before and during the procedure contribute towards the relative success or failure of the procedure. In attempting to improve colonoscopy all aspects of the procedure need to be examined (figure 1.3).

1.6.1 : Patient selection

The main indications for the procedure have been described above. There are few absolute contraindications to colonoscopy. The patient however must be fit enough to tolerate bowel preparation and the procedure itself. Colonoscopy may be dangerous early after myocardial infarction, when cardiac rhythm is likely to
FIGURE 1.3
Schematic representation of day-case colonoscopy

IN THE CLINIC

Patient selection

Psydological preparation

AT HOME

Bowel preparation

IN THE UNIT

Conscious sedation

±Anti-spasmodic

Colonoscope insertion

±Paediatric colonoscope

±Fluoroscopy

hand pressure

position changes

endoscopist

Colonoscope withdrawal

±Stiffening devices
be unstable, or when severe inflammatory disease weakens the bowel wall (Williams, 1990).

1.6.2: Psychological preparation

Colonoscopy is an invasive and potentially embarrassing procedure but one where patient feedback and co-operation are important. Patients may be understandably anxious prior to colonoscopy, not only because of possible findings, but also of the procedure itself, particularly if a previous examination has been unpleasant (Gebbensleben & Rohne, 1990). It has been proposed by some authors that psychological and other relaxation techniques prior to endoscopy improve patient acceptance and minimise the need for pharmacological sedation (Berry, 1969; Dunk et al, 1990). Various psychological approaches have been evaluated such as a detailed explanation of the aim and nature of the examination, creation of a calm and relaxed atmosphere, the presence of a friend or relative during the examination or the presence of background music (Probert et al, 1991; Martin et al, 1990; Lanius et al, 1990; Levy et al, 1993). None of these approaches however, has been found to influence significantly the patients' overall impression of the procedure. Despite the fact that no specific psychological approach has been shown to influence patients' perception, clear explanation prior to the procedure (with opportunity for the patient to ask questions) and a relaxed and sympathetic atmosphere within the Endoscopy Unit is clearly desirable and appreciated by the patient (Salmon et al, 1994).
Bowel preparation is a fundamental preliminary for safe and accurate colonoscopy. An "ideal" preparation would be easy to administer, have a rapid onset of action, produce satisfactory cleansing in approaching 100% of all patients, be cheap, easily packaged for postal delivery and above all be safe and acceptable to the patient. At present no such ideal exists. Available preparations may be effective in cleansing the bowel but cause distress to some patients, or can be well tolerated but ineffective in cleansing. Recently the importance of good bowel preparation has been further stressed by a report suggesting that patients' tolerance of colonoscopy may be directly influenced by the success or failure of the preparation (Probert et al, 1993).

1.6.3.1 : Purge + enema regimes

Historically the earliest preparations for colonoscopy involved purge (castor oil, senna or bisacodyl) and enema regimes accompanied by dietary restrictions for several days (Teague & Manning, 1977). Though adequate preparation was usually achieved, such involved and time-consuming regimens were often unacceptable to patient and endoscopy staff alike. This has led to an on-going search for a rapidly cleansing, oral means of bowel preparation for colonoscopy.

1.6.3.2 : Mannitol

A 10% solution of mannitol, a non-absorbed disaccharide, provides a hypertonic purge that produces rapid and effective preparation of the bowel (Noya et al, 1982). Its sweet taste however makes it difficult for some patients to
tolerate (Gilmore et al, 1981). The use of mannitol declined after a case report of
an explosion during electrosurgery (Bigard et al, 1979) related to an increase in
explosive gas formation with mannitol preparation; mannitol can be fermented
by colonic bacteria under anaerobic conditions into hydrogen. However ignition
of colonic gas is only possible in the presence of oxygen-rich air. Use of carbon
dioxide as the insufflating agent during colonoscopy effectively eliminates the

1.6.3.3 : Normal Saline

Oral lavage with 3-4 litres of physiological saline produces rapid and effective
cleansing of the bowel (Levy et al, 1976). However the salty taste of the solution
makes it difficult for patients to tolerate. Increased absorption of salt and water
during preparation with normal saline may occur and be dangerous for elderly
patients or those with cardiac or renal problems.

1.6.3.4 : Picolax

Picolax is a combination of the osmotic laxative magnesium citrate and the
stimulant laxative sodium picosulphate. It is cheap, easily packaged and has a
lemon taste that is generally well tolerated by patients. It has been shown to be
effective preparation for barium enema (Bartram, 1984) but few studies have
assessed its use for bowel cleansing at colonoscopy. When compared to a
standard 4 litre preparation of polyethylene glycol-balanced electrolyte solution
(PEG-BES) as preparation for colonoscopy, 2 sachets of Picolax was shown to

\(^{1}\)Ferring Pharmaceuticals Ltd, Feltham UK.
be better tolerated but a worse cleansing agent than PEG-BES (Dakkak et al, 1992). In this study an unacceptable 41% of patients receiving Picolax were found to have a poor preparation.

1.6.3.5: Polyethylene glycol-balanced electrolyte solution (PEG-BES)

In 1980 Davis et al. developed an oral lavage solution, punningly named by them "Golytely", which contained the non-absorbed solute polyethylene glycol combined with a mixture of essential electrolytes (Davis et al, 1980). PEG-BES has the advantage that it causes little or no shift in fluid or electrolytes and so is safe to use as bowel preparation for the elderly and for patients with cardiac, renal or hepatic disease. When used as bowel preparation for colonoscopy the current manufacturers recommendation is that 4 litres of the solution should be drunk over a 3-4 hour period, starting at 6:00pm the evening before colonoscopy. Cleansing occurs within a few hours and does not require the patient to undergo strict dietary restriction. Trials comparing PEG-BES to traditional purge and enema regimes as bowel preparation for colonoscopy have shown that PEG-BES not only produces a better preparation but is also better tolerated and preferred by patients (DiPalma & Marshall, 1984; Ernstoff et al, 1983; Thomas et al, 1982). However many patients still find the 4 litres of solution required for cleansing difficult to consume and the solution itself salty and unpalatable (Hangartner et al, 1989; Dakkak et al, 1992; Froehlich et al, 1991). Various modifications to the standard 4 litre preparation have been evaluated. Several groups have suggested that the addition of bisacodyl or senna 1 - 2 days before colonoscopy improves PEG-BES preparation and may allow a reduction in the volume of PEG-BES required for cleansing (Rings et al, 1989; Ziegenham et al, 1991; Vilien & Rytkonen 1990). However such regimes, though suitable for in-patients, are time
consuming and involved for out-patients. In order to reduce fullness and vomiting, addition of prokinetic agents such as metoclopramide or cisapride to the 4 litre PEG-BES preparation has been suggested, but no convincing evidence of an advantage over a standard administration technique has been demonstrated (Brady et al, 1985; Haringsma et al, 1986). One of the more successful approaches is to reduce the volume of PEG-BES drunk by the patient at any one time. It has been shown that fractionating the administration of PEG-BES improves patient acceptability without compromising bowel preparation (Rosch & Classen 1987).

In an attempt to improve the taste of PEG-BES, a new low sodium solution "Nulytely" was introduced in 1986. A comparative trial with "Golytely" appeared to show an improvement in palatability with the new solution (DiPalma & Marshall, 1990). However a subsequent trial assessing the taste of both solutions in healthy volunteers has not confirmed any advantage in palatability with "Nulytely" (Froelich et al, 1991). A recent paper has assessed the palatability of flavouring PEG-BES and concludes that the addition of lemon flavouring improves the taste and acceptability compared to other flavours or no flavouring (Matter et al. 1993). Despite problems with the taste and volume of PEG-BES preparation, and its high cost\textsuperscript{2}, it has become the most widely used bowel cleansing agent and the gold standard with which to compare new products.

\textsuperscript{2}4 sachets (to make 4 litres) of Klean-prep (PEG-BES), Norgine Ltd, Oxford approx. cost £8-00.
1.6.3.6 : Sodium phosphate

Recently much interest has been generated by the use of the highly osmotic cathartic, sodium phosphate as bowel preparation for colonoscopy. Sodium phosphate preparation has been compared to a standard 4 litre PEG-BES regime and was found to have similar cleansing ability but better patient acceptability (Vanner et al, 1990). It has the advantage that it is a small volume preparation; two 45ml quantities being drunk at 6-00pm the evening before and 6-00 am the morning of colonoscopy. However a question mark remains regarding safety, due to the transient hyperphosphataemia that may occur following administration (Physicians Desk Reference, 1987). This can potentially lead to concomitant hypocalcaemia and cardiac arrhythmias (McConnell, 1971). Sodium phosphate is not currently licensed for use as bowel preparation in the UK.

1.6.4 : Sedation/analgesia for colonoscopy

Ideally during colonoscopy all patients would be relaxed and comfortable yet still able to respond appropriately to commands. In an attempt to achieve this aim, sedative and analgesic drugs are often administered to the patient before or during the examination.

Given the choice, most patients attending for gastroscopy prefer sedation (Martin et al, 1990; Thompson et al, 1980). A single study has looked at patients' preferences prior to colonoscopy: when told the advantages and disadvantages of sedation, 63% preferred a "tranquillising injection" (Gebbensleben & Rohde, 1990). However the remaining 37% were prepared to start the procedure without sedation. How often patients' wishes for sedation are taken into account is unknown. World-wide, use of sedation varies greatly. Most colonoscopists in the
UK and America routinely use conscious sedation with benzodiazepine and opiate drugs (Keeffe & O'Connor, 1990) but in Japan many endoscopists use no sedation at all (Ueno et al, 1991), whilst in France examinations are frequently performed with the patient under a general anaesthetic (Guem et al, 1993). Present methods tend to be endoscopist-controlled, relying on the endoscopist to assess the sedation needs of the patients. Endoscopy staff however may be poor judges of patient discomfort during endoscopy (Schultz et al, 1994).

1.6.4.1 : Colonoscopy without sedation: selective sedation

With improvements in colonoscopic equipment and intubation techniques it has been argued that sedation is unnecessary for many patients undergoing colonoscopy (Herman, 1990). Withholding sedation not only avoids the risk of drug related side effects and over sedation but also allows the patient to cooperate fully during the procedure and respond if over-insufflation or excessive loop formation occurs. Post-examination recovery times are short and the patient is able to return to work or drive without the need for an escort. Three series describe avoidance of sedation for colonoscopy. In an uncontrolled prospective Japanese series of 7,366 patients undergoing approximately 12,000 colonoscopies, total colonoscopy was achieved in 98% of patients without sedation (Ueno et al, 1991). In an American series of 212 patients, 83% of patients required no sedation for cecal intubation (Herman, 1990). However 17% of patients in this study did receive sedation on criteria by the endoscopist. This "selective" method of sedation has also been evaluated in Singapore (Seow-Choen et al, 1994); 40 patients commenced colonoscopy without sedation of which 23% were subsequently given sedation during the examinations and 77% were judged not to require sedation at all. In this small study only 3% of patients
reported severe pain. No attempt was made in the two larger studies described earlier to ascertain patients' preferences with regard to sedation or to assess pain levels during the examinations.

1.6.4.2: "Conscious sedation"

The term "conscious sedation" has been defined as "the administration of medications that allow the introduction and manipulation of endoscopes, yet provide a relaxed patient able to respond and maintain vital functions" (Benjamin & Lightdale, 1990). Conscious sedation for colonoscopy is usually achieved by the intravenous administration of a benzodiazepine drug such as diazepam or midazolam, in combination with an opiate drug such as pethidine (Keeffe & O'Connor, 1990). Many questions regarding the type of drugs used, the method of administration and optimal methods of maintaining patient safety have been posed over the last 15 years.

1.6.4.3: Benzodiazepines

The benzodiazepine drugs or minor tranquillisers exert their effect by potentiating the inhibitory neurotransmitter gamma-aminobutyric acid at receptor sites in the spinal cord, cerebral cortex, hippocampus and cerebellum (Haefely & Hunkeler, 1975). They produce dose-dependent cerebral depression; an increasing dose causing first mild sedation, then sleep and finally anaesthesia (Reeves et al, 1985). The first injectable benzodiazepine to be introduced was diazepam and two preparations are available. The original injectable form
"Valium"\textsuperscript{3}, (diazepam 5mg/ml in an aqueous vehicle) is a relatively viscous solution and causes pain at the injection site and a high incidence of thrombophlebitis (Kawar & Dundee, 1982). This led to the development of an emulsion preparation ("Diazemuls"\textsuperscript{4}) which has been shown to be associated with fewer local complications (Jensen et al, 1981). When given intravenously diazepam has a rapid onset of action (1-2 minutes) but a relatively long elimination half life that varies from 24-52 hours (McCloy & Pearson, 1990). Diazepam is eliminated in the liver but produces active metabolites with some pharmacological activity. In addition it is excreted in the bile and undergoes enterohepatic circulation which may result in a second peak effect 4-6 hrs after the initial dosing (Bell, 1990).

1.6.4.4 : Diazepam vs midazolam

During the 1970's and early 1980's, intravenous diazepam became established as the standard method of inducing anxiolysis, sedation and amnesia during colonoscopy. In 1986 the synthetic benzodiazepine midazolam was introduced which offers potential advantages over diazepam. Compared to diazepam, midazolam is water soluble, more potent, has a quicker onset of action, shorter elimination half-life (1.5-5hrs) and causes greater amnesia (Carrougher et al, 1993; Al-Khudhari et al, 1982; Reves et al, 1985; Gilvarry et al, 1990). Because of these factors midazolam was adopted enthusiastically and early clinical experience showed it to be superior to diazepam for upper gastrointestinal endoscopy (Cole et al, 1983). However soon after the introduction of midazolam a series of major cardiorespiratory events, including some deaths, were reported

\textsuperscript{3}Roche Products Ltd, Welwyn Garden City, UK.
\textsuperscript{4}Dumex Ltd, Tring, UK.
to the US Food and Drug Administration. These reports raised concerns that the use of midazolam for endoscopic conscious sedation might constitute a serious risk (FDA's regulation on the new drug Versed®, 1988). In 1989, in a double blind study, bolus administration of midazolam (0.07mg/kg) was compared to diazepam (0.15mg/kg) (Lewis et al, 1989). This study showed a significant increase in over-sedation with midazolam and raised further concerns regarding its use for colonoscopy. However midazolam is 2-5 times as potent as diazepam and in many cases was being administered in too large a dose, particularly in elderly patients (Whitwam et al, 1983). In addition although midazolam has a more rapid onset of action, peak drug effect occurs later for midazolam than diazepam (Buhrer et al, 1990). This may have resulted in inadequate intervals of observation between repeat dosing of midazolam, thereby contributing to over-sedation. These factors led to a reduction in the recommended initial dose of midazolam to 0.03mg/kg and the recommendation that further doses be titrated with suitable periods (minimum of 2 minutes) of observation in between (Lewis & Benjamin, 1990). Following these changes there was a significant reduction in the frequency of reported adverse cardiopulmonary events (Arrowsmith et al, 1991). Ginsberg et al. in 1992 compared the new lower dose of midazolam to the current recommended dose of diazepam (0.10mg/kg) as sedation for colonoscopy and found that midazolam was comparable to diazepam in efficacy but produced more amnesia (Ginsberg et al, 1992). Surprisingly 21% of their patients receiving diazepam were found to be over-sedated, which raises the possibility that diazepam doses may be unnecessarily high in a number of patients, particularly those over 65 years. Midazolam is now more commonly used as sedation for endoscopic procedures than diazepam; in the 1989 survey of sedation and

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5Roche Laboratories, USA.
monitoring practices by the American Society of Gastrointestinal Endoscopy, midazolam rather than diazepam was used routinely by 73% of respondents. Despite early worries regarding the use of midazolam, the new lower doses recommended appear safe as sedation for colonoscopy, provided that individual factors which may reduce dosage requirements, such as age and medical history, are taken into consideration.

1.6.4.5: Benzodiazepine antagonists

The effects of benzodiazepines can be rapidly reversed in 1-5 minutes by the competitive benzodiazepine antagonist, flumazenil (Haefely et al, 1988). Flumazenil has a shorter elimination half-life than midazolam (53mins vs 120mins) and therefore rebound sedation is a theoretical possibility (Lauven et al, 1985). However, when flumazenil has been used to reverse conscious sedation, rebound sedation has not been found (Bartelsman et al, 1990, Jensen et al, 1989, Zuurmond et al, 1989). In a recent study the effects of flumazenil reversal after midazolam premedication for colonoscopy has been evaluated (Saletin et al, 1991). Compared to placebo, patients receiving reversal with flumazenil recovered quicker and could be discharged earlier. This allowed information regarding the examination to be discussed soon after the procedure and, in many cases, effectively saved a further out-patient appointment. It remains to be seen however whether the savings in bed-space and nursing time afforded by the routine administration of flumazenil will out weigh its present high cost (£16.32, per 5ml, 500 microgram ampoule\textsuperscript{6})

\textsuperscript{6} British National Formulary 1994
1.6.4.6 : Analgesia for colonoscopy

Patients may experience pain during colonoscope insertion due to excessive gas insufflation or more commonly, stretching of the bowel mesentery (Williams, 1990). For this reason most colonoscopists choose to administer an analgesic as well as an anxiolytic for the examination. The opiate analgesic pethidine (meperidine) is the most commonly used drug for colonoscopy (Keeffe & O'Connor, 1990) but because of the risk of hypotension and respiratory depression associated with its use (Shafer & Varvel, 1991), other opiate analgesic drugs (sufentanil, alfentanil and fentanyl), with shorter half lives than pethidine, have been introduced. Compared to pethidine however, these drugs are less effective when used for analgesia during colonoscopy (Chokhavatia et al, 1993). Ketorolac triomethamine, a new parenteral non-steroidal anti-inflammatory drug (NSAID) has been shown to be as effect as pethidine for the control of post-operative (Yee et al, 1986) and dental pain (Fricke & Angelloci, 1987). However when used for colonoscopy discomfort it was found to be no more effective than placebo (Deal et al, 1993), probably because NSAIDs have little central analgesic activity and are less effective than opiate drugs against visceral pain, perceived via sympathetic neurones (Snyder et al, 1974).

1.6.4.7 : Safety with benzodiazepine/opiate sedation

Benzodiazepine drugs are carried in the blood stream highly protein-bound (Reeves et al, 1985). Factors which affect protein binding will produce predictably large changes in the free fraction of the drug. A reduction in usual drug dosage is therefore indicated for patients with hypoproteinaemia, jaundice, renal failure or those who are taking other drugs that are highly protein-bound
(Branch et al, 1976; Vinik et al, 1982; Fee et al, 1984). Benzodiazepines and opiates given independently may cause cardiopulmonary depression (Reeves et al, 1985; Laurence & Bennett 1987); given together, clinically-significant synergism may occur (Loebel & Danzig 1970). Caution is therefore advised when both a benzodiazepine and an opiate are given in combination. It has been recommended that, if an opioid-benzodiazepine combination is used, the opioid should be given first, before titrating in the benzodiazepine, which should be administered in a reduced dosage (McCloy & Pearson, 1990). Electronic monitoring should be available, as well as access to opiate and benzodiazepine antagonists (Bell et al, 1991). In addition, at-risk patients such as the elderly and those with significant cardiovascular or pulmonary disease should receive supplemental oxygen (2-4 litre/min). This has been shown to reduce oxygen desaturation during colonoscopy (Gross & Long, 1990; Simon et al, 1991).

1.6.4.8 : Other drugs for sedation

Major tranquillisers such as the phenothiazines or butyrophenones, the hypnotic propofol and the hypnoanalgesic ketamine have all been suggested as alternative methods of producing sedation/analgesia for colonoscopy.

In a small study, published only in abstract form, a phenothiazine plus meperidine combination produced equivalent sedation/analgesia but less cardiovascular suppression than a midazolam/meperidine combination (Valenzuela et al, 1991). However phenothiazines are known to have unpleasant psychological side effects which effectively limit their use. When used for premedication, many patients report that they feel imprisoned and unable to move (Lauven, 1990).
The short-acting hypnotic and mild analgesic drug propofol has also been used to induce sedation in patients during colonoscopy (Gepts et al, 1985). Because of the risk of complete loss of consciousness this approach, despite computerisation of the delivery system (Church et al, 1991), necessitates electronic monitoring, supplemental oxygen and the presence of a trained anaesthetist. The use of propofol for colonoscopy has been reported in a series of 500 French patients (Guern et al, 1993). Recently a single blinded study comparing propofol to midazolam as sedation for colonoscopy has suggested that recovery is faster but amnesia less with propofol (Munoz-Navas et al, 1994).

The hypno-analgesic agent ketamine produces minimal respiratory depression. Its use has been proposed as an adjunct to midazolam as sedation/analgesia for colonoscopy (Rosing et al, 1991). However the use of ketamine is limited because of its association with a marked dose-dependent increase in blood pressure so that it is contraindicated in patients with borderline hypertension, or ischaemic heart disease. It can also produce myoclonic twitching and nystagmus as well as unpleasant post-sedation emergence reactions, such as bad dreams (Lauven, 1990).

1.6.4.9 : Epidural analgesia

It has been suggested that epidural analgesia may be of use when attempting to colonoscope patients who are extremely anxious or technically difficult to intubate (Bleiberg et al, 1982). Epidural analgesia renders the procedure painless, but this advantage has to be weighed against the risk to the patient of hypotension (related to epidural analgesia) or colonic perforation: a painless procedure means the endoscopist has little feedback about traumatic loop formation and stretching of mesenteries and so may lead to "painless" perforation. Bleiberg et al. used
epidural analgesia to re-examine 29 patients who had previously proved difficult to intubate (Bleiberg et al, 1982). Although total colonoscopy was achieved in 27 of the 29 patients, 2 developed significant hypotension and one sustained a colonic perforation, an unacceptably high complication rate.

1.6.4.10 : Patient controlled analgesia/sedation : parenteral administration

In the last 4 years patient-controlled analgesia (PCA) has become an acceptable and desirable method of pain relief in a number of clinical settings (Rowbotham, 1992). Electronic syringe pumps which deliver a preset dose of opiate analgesic following the press of a button, have been successfully used for the control of pain postoperatively (Sechzer, 1990), during childbirth (Scott, 1970), and for sickle cell crises (Evans et al, 1976). In such systems patients can repeatedly self-administer doses of opiate analgesia, provided that a suitable "lock-out period" has elapsed between doses. The use of intravenous and intramuscular PCA with opiate drugs requires careful monitoring of the patient to ensure that oversedation and hypoventilation leading to oxygen desaturation does not occur (Wheatley et al, 1990). A recent abstract compares the use of PCA to endoscopist-controlled analgesia (ECA) for colonoscopy (Nguyen et al, 1992). In this small pilot study 10 patients were randomised in each group. Despite a safe lock-out period, those patients who self-administered analgesia received nearly twice as much fentanyl analgesia as those in the endoscopist-controlled analgesia group, without an increase in recovery times. In another pilot study, PCA for maintaining analgesia during ERCP has also been evaluated, but no benefit was found over standard intravenous administration (Jowell et al, 1994).
1.6.4.11 : Patient-controlled nitrous oxide/oxygen inhalation

Nitrous oxide/oxygen 50/50 gaseous mixture has analgesic, sedative, and amnesic qualities (Pinell & Linscott, 1987). It has been widely used for patient-controlled analgesia during childbirth, as well as for painful procedures in traumatology, dentistry and for the relief of the pain of myocardial infarction (Minnitt, 1934; Thal et al, 1979; Allen, 1976; Kerr et al, 1975). It is safe, fast-acting (analgesia noted approximately 60 seconds after inhalation) and has a short duration of action; most of the gas is eliminated unchanged via the lungs in 1-5 mins (Brandt & Bugg, 1984).

The pharmacological profile of nitrous oxide/oxygen mixture and the patient-controlled method of administration suggested that it could be a useful alternative as conscious sedation/analgesia for colonoscopy. Encouraging results have been obtained in a previous uncontrolled study (Bennet et al, 1971), and recently Lindblom et al. compared the use of patient-controlled nitrous oxide/oxygen mixture to a midazolam/ketobemidone combination as analgesia for colonoscopy (Lindblom et al, 1994). They found that analgesia was comparable in both patient groups but that recovery times were less for patients receiving nitrous oxide/oxygen mixture.

1.6.5 : Anti-spasmodic premedication

Some endoscopists routinely use premedication with anti-spasmodic drugs, to improve visualisation of the colonic mucosa during insertion and withdrawal (Macrae et al, 1983). However, no consensus has been established regarding the use of such drugs, and particularly whether or not they influence the ease of the procedure. Previous studies have found no benefit with intramuscular glucagon,
intramuscular dicyclomine hydrochloride or intravenous atropine (Norfleet, 1974, Bond et al, 1974, Waxman et al, 1991). However a recent abstract suggests that intravenous glucagon given prior to colonoscopy reduces colonoscope insertion times compared to placebo (Jamal et al, 1992).

1.6.6 : Colonoscope insertion

Once the patient has undergone satisfactory bowel preparation and a policy for sedation has been decided upon the next stage in the procedure is insertion of the colonoscope to the caecum (or terminal ileum). Intubation is technically demanding and difficulty in passing the colonoscope may occur. Even expert colonoscopists report difficulty in up to 30% of cases (Williams et al, 1982) and the published figures for the rate of total colonoscopy in the West vary considerably (55-98%) (Lindsay et al, 1988; Aldridge & Sim 1986, 1986; Waye & Bashoff, 1991; Ravi et al, 1988, Durdey et al, 1987; Irvine et al, 1988; Bat & Williams, 1989; Church, 1994). The reasons for failure, when reported, are also varied and vague. This is probably because in many difficult cases fluoroscopy is not available (Rauh et al, 1989), so that the configuration of the colonoscope shaft inside the patient cannot be assessed. The cause of failure during colonoscope insertion has been described as either due to patient discomfort (Church, 1994; Freeman et al, 1993), colonic fixation (Waye & Bashoff, 1991), tortuosity (Church, 1994), redundancy (Freeman et al, 1993) or unknown anatomical reasons (Waye & Bashoff, 1991).
1.6.6.1 : Recurrent looping of the colonoscope

As the flexible colonoscope is inserted there is a tendency for loops to form, particularly in the sigmoid and transverse colon where the colon hangs freely on the sigmoid and transverse mesocolons, (although occasionally other parts of the colon may be mobile, as described earlier, see Chapter 2). Once a loop has formed, pushing the colonoscope inwards tends only to make the loop larger, imparting force through the apex of the loop and stretching the colonic mesenteries, which risks perforation (Wu, 1978). In most cases the loop must be straightened before further progress can be made (Webb, 1991). However when the colon is mobile or redundant, a similar or different loop may occur once further inward force is used (Hunt, 1981).

1.6.6.2 : Bowel adhesions

A sigmoid colon with congenital, diverticular or previous surgical adhesions may produce fixed bends that impede the inward progress of the colonoscope, sometimes preventing successful colonoscopy (Sankaran, 1994). Sigmoid colon diverticular disease causing pelvic adhesions has been described as the major reason for failure at colonoscopy (Webb, 1991). An abstract mentions an increased difficulty in reaching the caecum in patients who have had previous surgery (Ravi et al, 1988): a 58% total colonoscopy rate was achieved when patients had undergone previous abdominal or pelvic surgery compared with an 82% success rate in patients who had not had surgery.
1.6.7 : Insertion technique and aids to colonoscope insertion

A detailed explanation of basic insertion technique is beyond the scope of this thesis and already covered in standard texts on the subject (Williams, 1990; Sakai, 1987). Fundamental principles include minimising air insufflation, frequent withdrawal manoeuvres to straighten the instrument and shorten the colon and awareness of patient discomfort during the procedure. Ancillary and technical aids to colonoscope insertion are discussed below.

1.6.7.1 : Hand pressure

Abdominal hand pressure can be helpful in the performance of colonoscopy by externally splinting the endoscope to prevent loop formation (Sakai, 1972; Gaisford, 1974; Gaisford, 1976). Waye et al. have suggested a step-wise approach to abdominal pressure with first application of "non-specific" pressure (palm of the hand applied by the endoscopy assistant over either the left lower quadrant, mid abdomen or splenic flexure, depending on the presumed area of looping) followed if necessary by "specific" hand pressure (an attempt by the endoscopist to push the colon towards the colonoscope tip) (Waye et al, 1991 b). They found hand pressure to be useful in 80% of colonoscopies, particularly in preventing loop formation in the left colon. Although hand pressure is undoubtedly a useful technique, without colonoscope imaging its application remains mainly on a trial and error basis as the exact site and nature of the loop and the position of the colonoscope tip are difficult to assess.
1.6.7.2: Changes in patient position

For convenience, colonoscope insertion is usually commenced in the left lateral position (Williams, 1990). Several reports have suggested that changes in patient position from the left lateral position may be helpful in facilitating passage of the endoscope (Waye et al, 1991b; Herrera, 1991; Church, 1993; Williams, 1990). Williams points out that in the left lateral position the sigmoid/descending colon junction, descending colon and splenic flexure are dependent and therefore often fluid filled (Williams, 1990). A change to the right lateral position causes air to replace fluid in these areas, improving visualisation and hence facilitating the steering of the colonoscope tip around acute bends. Waye et al. found that a change to the supine position was successful in advancing the colonoscope 66% of the time, particularly when passing the transverse colon and that this also facilitated hand pressure application (Waye et al, 1991b). It has also been suggested that placing the patient prone aids passage of the colonoscope across the transverse colon, possibly by the patients own weight pressed against the endoscopy couch splinting the abdomen and acting in the same way as non-specific abdominal pressure (Herrera, 1991). Church found that turning the patient to the right lateral position was successful in passing the colonoscope from the ascending colon into the caecum 77% of the time (Church, 1993).

1.6.7.3: Different types of endoscope

Occasionally during intubation with a standard adult (1.3cm) colonoscope (eg. Olympus CFLB3, CFLB3R, CF1TL, CF1T10L, CFV10) an acute, impassable bend is encountered secondary to colonic adhesions. When this occurs total colonoscopy may still be possible but a change of colonoscopic instrument is
required. Kozarek et al. have recommended the use of a 9.8mm gastroscope (Olympus XQ-10), which also has acutely angling tip characteristics and proved successful in passing 77% of fixed/strictured sigmoid colons when the adult 1.3cm colonoscope had failed (Kozarek et al, 1989). Bat and Williams suggest that the shaft characteristics of the floppy 10mm paediatric colonoscope (Olympus PCF floppy, PCF 10-floppy) are more suited to the negotiation of fixed sigmoid bends: in (92%) of cases where the sigmoid colon could not be passed with an adult colonoscope, a change to the more floppy paediatric colonoscope allowed successful intubation (Bat & Williams, 1989).

1.6.7.4 : Stiffening devices

Many of the technical problems of colonoscopy are due to looping of the colonoscope in the sigmoid colon. In the early 1970's rigid overtubes were developed to stiffen the colonoscope and prevent sigmoid looping (Dehyle, 1972). However initial devices were awkward to use as they had to be in place on the colonoscope before intubation and required fluoroscopy for safe insertion. Williams has described a split over-tube stiffening device which can be inserted at any time during the examination and does not require fluoroscopy (Williams, 1983). An internal stiffening device has also been developed which is passed down the biopsy channel of the colonoscope and can be set to produce varying degrees of stiffness (Sullivan, 1990).

1.6.8 : Imaging colonoscopy

Fundamental to understanding colonoscopic technique and the difficulties that may occur during colonoscope insertion is the ability to visualise the
colonoscope within the abdomen. Detailed images of the mucosal surface are
given from the tip of the colonoscope but the endoscopist can only guess at the
configuration of the colonoscope or the exact anatomical location of the
colonoscope tip within the abdomen. An inability to visualise the colonoscope
has many consequences for the procedure. Firstly, lesions encountered may be
incorrectly located anatomically, with resultant confusion at surgery (Frager et
al, 1987). Secondly, caecal intubation may be wrongly assessed (Cirocco &
Rusin, 1991) resulting in failure to identify right sided lesions, though this is rare
if clear visualisation of the ileocaecal valve and appendix orifice are insisted
upon. Thirdly, loop formation during intubation may be incorrectly assessed and
the manoeuvres to straighten the loop and complete the examination may be
prolonged or missed altogether. Finally, learning to perform colonoscopy may be
prolonged because the withdrawal and torqueing manoeuvres essential to good
technique are difficult to appreciate when the shaft of the colonoscope cannot be
visualised.

1.6.8.1: Accuracy of tip location

It is widely recognised that the internal markings of the colon are variable
(Williams, 1990), and until the ileo-caecal valve or appendix are clearly
identified (Cirocco & Rusin, 1993) the endoscopist is effectively unsure of the
anatomical position of the colonoscope tip. Taibibian et al. have demonstrated
the difficulties encountered by the endoscopist in locating the colonoscope tip
(Taibibian et al, 1988). When doubt existed regarding the anatomic position of
the most proximal point reached during intubation or of the location of a small
lesion that would be difficult to palpate at operation, they placed a metal clip on
the colonic wall to confirm the position radiologically. The endoscopist
incorrectly identified the location of the colonoscope tip in 34% of cases. The caecum had not been reached in 20% of cases when the endoscopist thought it had. In 33% the endoscopist incorrectly identified the farthest area reached and in 63.6% the clinical impression of the anatomical site of a small lesion was inaccurate. Inaccuracy in the location of the colonoscope tip has also been described (Cirocco & Rusin, 1991); 15% of fluoroscopic checks showed the colonoscope to be in a different position from that estimated by the endoscopist. Frager et al. have also highlighted the difficulty encountered by the endoscopist in accurately identifying the position of colonic neoplasia (Frager et al, 1987).

1.6.8.2 : Fluoroscopy

Fluoroscopy has been used as an aid to intubation since the inception of colonoscopy in 1969. Many early colonoscopic series relied on fluoroscopy to ensure safe passage of the colonoscope (Classen, 1971; Williams & Teague, 1973; Wolff & Shinya, 1971). However as endoscopists have gained more experience and improvements have occurred in colonoscope design, the use of fluoroscopy has become less frequent (Teague et al, 1973). In a recent survey in America, 75% of endoscopists routinely perform colonoscopy without fluoroscopy, despite the belief of the majority of non-users that access to fluoroscopy would improve colonoscopic practice (Rauh et al, 1989).

1.6.8.2.1 : Advantages of fluoroscopy

Use of fluoroscopy has a number of advantages. Firstly it allows accurate location of lesions encountered during colonoscopy and helps correlate any findings from a prior barium enema (Rauh et al, 1989; Hunt, 1981; Gaisford,
1972; Gaisford, 1973). Secondly it allows the endoscopist to check the proximal depth of insertion and confirm that caecal intubation has been achieved (Wolff, 1979; Hunt, 1981; Waye, 1989). Thirdly it allows accurate diagnosis of looping configurations and acts as an aid to their straightening (Geenan et al, 1974; Webb, 1991); fluoroscopy is considered mandatory for the placement of rigid sigmoid over-tubes (Hunt, 1981; Talbott & MacKeigan, 1978; Berci et al, 1973). Finally, fluoroscopy can be used as a teaching aid, particularly when the trainee is learning the manoeuvres necessary to straighten sigmoid loops (Hunt, 1981; Geenan et al, 1974; Webb, 1991).

1.6.8.2.2: Disadvantages of fluoroscopy

Despite its apparent advantages, fluoroscopy has not gained widespread acceptance (Rauh et al, 1989). Fluoroscopy equipment is bulky, heavy and expensive to buy and maintain. By definition it presents a potential radiation hazard to patients and endoscopy staff alike and may cause damage to the fibreoptic bundles of some colonoscopes (Sakai, 1981). During screening endoscopy staff are required to wear heavy lead aprons for their own protection which may be restrictive and uncomfortable. The image produced with fluoroscopy is also far from ideal. It produces a flat, 2-dimensional image in one view only so that depth and the true degree of colonoscope looping is not easy to interpret. The 9 inch fluoroscopy screen provides only a localised image of the colonoscope shaft, so that looping configurations are difficult to appreciate at a glance without moving the patient or fluoroscopy table. Difficulty is further compounded by the necessity to keep the time of screening to a minimum, thereby providing only momentary glimpses of the colonoscope.
1.6.8.5: Alternative methods of locating the colonoscope

Transillumination of the abdominal wall has been used as an adjunctive method of detecting the position of the colonoscope tip. With the colonoscope tip in the caecum, transillumination was possible in 90% of cases with a fibreoptic colonoscope but in just 54% with the less brilliant illumination afforded by a video colonoscope (Waye et al, 1988). Taking into account the variable anatomy of the colon, transillumination, even when possible, remains an unreliable marker of anatomical location.

Leicester and Williams have described the use of a metal detector to assess the position of an endoscope during flexible sigmoidoscopy or limited colonoscopy (Leicester & Williams, 1981). Although effective in locating the tip of the endoscope at the splenic flexure, when the endoscope is straight, this device lacks accuracy at other locations, particularly when different parts of the metallic colonoscope are in close proximity.

When fluoroscopy is not available, it has been suggested that the endoscopic placement of a mucosal clip, followed by a plain abdominal x-ray is a useful way of checking the position of the colonoscope tip (Lehman et al, 1985). This method is undoubtedly accurate but time-consuming and retrospective. It has therefore not been widely adopted.
1.7: Aims of the thesis

The studies presented in this thesis will attempt to contribute to understanding of large bowel endoscopy, highlight areas of clinical difficulty and investigate possible improvements in clinical practice.

**AIM 1**: to define, *in vivo*, variations in colonic anatomy and mesenteric attachments and gain further understanding of the anatomical basis for difficulty during colonoscopy (Chapter 1).

**AIM 2**: to assess the incidence and causes of difficulty at colonoscopy (Chapter 2).

**AIM 3**: to attempt to define who is "at risk" of a technically difficult colonoscopy (Chapter 3 and 4).

**AIM 4**: to investigate whether assessment of a previous barium enema can predict difficulty at colonoscopy (Chapter 5).

**AIM 5**: to study a potentially more pleasant and effective bowel preparation for colonoscopy (Chapter 6).

**AIM 6**: to evaluate alternative strategies for sedation/analgesia during colonoscopy (Chapter 7).

**AIM 7**: to assess the role of anti-spasmodic premedication for colonoscopy (Chapter 8).
AIM 8: to evaluate the possible advantages of patient-controlled analgesia and anti-spasmodic premedication for screening flexible sigmoidoscopy in a primary health care setting (Chapter 9).

AIM 9: to develop and evaluate a real-time, non-x-ray, method of imaging the colonoscope within the abdomen (Chapter 10).
Chapter 2: Peroperative comparison of Western and Oriental colonic anatomy and mesenteric attachments

2.1: Introduction

During colonoscope insertion the endoscopist attempts to pass the colonoscope to the caecum. The ease with which this is possible will depend to a certain extent upon the colonic anatomy encountered. If the colon is long or mobile there is a tendency for the colonoscope to loop during insertion, which impedes forward progress and may prevent total colonoscopy. The degree of variation in colonic length and fixation of relevance to colonoscopy has not been clearly defined and no attempt has been made to compare anatomy in different racial groups. Anecdotal reports from visiting endoscopists have suggested that colonoscopy is easier in Oriental than in Western patients (Williams, 1994 personal communication). Compared to their Western counterparts Oriental physicians routinely achieve total colonoscopy, with short intubation times and without patient sedation (Parry & Goh, 1993; Ueno et al, 1991). If colonoscopy is easier in Oriental patients there are likely to be underlying anatomical reasons for this. In this Chapter an attempt is made to define and compare the variations in colonic anatomy and mesenteric attachments (with relevance to colonoscopy) in Western and Oriental patients at laparotomy.

2.2: Methodology

Colorectal surgeons in the UK and Far East were contacted by post and asked to take part in the study. All adult patients attending for laparotomy were considered suitable for the study, excluding only those who had undergone a
previous colonic resection or who were found to have malignant or inflammatory
disease that distorted the appearance of their colonic anatomy. Details of patients'
age, sex, past surgical history, previous colonoscopy and indication for
laparotomy were recorded (table 1).

Once adequate exposure of the colon was achieved at laparotomy, but before
mobilisation of the bowel, a series of observations and measurements were taken
according to a set protocol, the bowel being pulled by the surgeon to mimic the
possible displacements produced by the colonoscope during intubation. Distances between left and right anterior/superior iliac spines were measured in
order to record the abdominal dimensions of the patient. Measurements of the
"sigmoid loop" were taken with the bowel pulled maximally towards the
xiphisternum and with the pubic symphysis as a point of reference (figure 2.1). If
the sigmoid colon was not free on a sigmoid mesocolon and could not be
distended into a loop, a sketch was made showing the position of adhesions.
Mobility of the descending colon was measured by pulling the mid-descending
colon medially and measuring the distance from the mid-descending to the point
of mesenteric attachment on the left abdominal wall (figure 2.1). The appearance
of the splenic flexure was recorded as being either fixed, mobile, or covered
(figure 2.2) and the distance was measured between the symphysis pubis and the
point of maximal displacement of the splenic flexure towards the pelvis. The
extent of downward mobility of the transverse colon was assessed by pulling the
mid transverse colon maximally towards the pubic symphysis and measuring the
distance from the mid point of the transverse colon to the pubic symphysis
(figure 2.3). The length of the transverse mesocolon was measured by pulling the
mid transverse colon towards the xiphisternum and measuring the distance from
the mid transverse colon to the lowest point of fixation of the mesocolon. Medial
TABLE 1

Details of Western and Oriental patients undergoing laparotomy.

<table>
<thead>
<tr>
<th></th>
<th>Western Patients (n=115)</th>
<th>Oriental Patients (n=114)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (yrs)</td>
<td>63.01</td>
<td>61.36</td>
</tr>
<tr>
<td>range (yrs)</td>
<td>19-85</td>
<td>25-85</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>66</td>
<td>65</td>
</tr>
<tr>
<td>female</td>
<td>49</td>
<td>43</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>colon cancer</td>
<td>111</td>
<td>112</td>
</tr>
<tr>
<td>constipation</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>IBD</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>gastrectomy</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>cholecystectomy</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Past Surgical History</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hysterectomy</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>cholecystectomy</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>appendicectomy</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>hernia repair</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>other</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td><strong>Colonoscopy prior to laparotomy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>18</td>
<td>76</td>
</tr>
<tr>
<td>no</td>
<td>97</td>
<td>38</td>
</tr>
</tbody>
</table>
FIGURE 2.1

Sketches demonstrating the method of measurement of the sigmoid loop and descending colon; a = maximum height of sigmoid loop, b = symphysis pubis-sigmoid/descending junction, c = maximum height of sigmoid mesocolon, a + d = maximum length of rectum + sigmoid colon, e = maximum length of descending mesocolon, f = maximum length of descending colon.
FIGURE 2.2

Sketches of the different appearances of the splenic flexure; \( g \) = splenic flexure - symphysis pubis distance.

**FIXED**
("normal" variant - phrenico-colic ligament anchors flexure in the left upper quadrant)

**MOBILE**
(lax, long or absent phrenico-colic ligament)

**COVERED**
(flexure fixed in LUQ by phrenico-colic ligament plus encased in peritoneum causing an acute bend at the splenic flexure)
FIGURE 2.3

Sketches demonstrating the method of measurement of the transverse colon, ascending colon and caecum;

- \( h \) = mid-transverse colon - pubic symphysis,
- \( i + j \) = maximum length of the transverse colon,
- \( k \) = maximum length of transverse mesocolon,
- \( l \) = maximum length of ascending mesocolon,
- \( m \) = maximum length of ascending colon + caecum.
mobility of the ascending colon was measured using a similar technique to that for the descending colon (figure 2.3).

2.3 : Statistical Analysis

Length measurements were compared using the Mann-Whitney test and categorical data by Fisher's exact test. A \( P \) value of \(< 0.05\) was considered significant.

2.4 : Results

Twenty three UK-based and 13 South East Asian based surgeons (Japan, Hong Kong and Singapore) contributed measurements to the study. Full sets of data were obtained from 115 Western (Caucasian) and 114 Oriental patients. The two study populations were similar with regard to age, sex, indication for laparotomy and past surgical history, (table 1). More Oriental (87%) than Western (16%) patients had been examined by colonoscopy prior to laparotomy.

There was no overall difference in abdominal dimension between the two study groups as assessed by pubic symphysis to xiphisternal or superior anterior iliac spine to superior anterior iliac spine lengths, (table 2).

In 20 (17%) Western patients a sigmoid loop could not be formed, (diverticular adhesions in 9, post-surgical adhesions in 2 and congenital adhesions in 9 patients) compared to 9 (8%) Oriental patients (diverticular adhesions in 1, post-surgical adhesions in 4 and congenital adhesions in 3), \( P=0.047\). When a sigmoid loop could be formed there was no significant difference between Oriental and Western patients with regard to either rectosigmoid length, length of the sigmoid
## TABLE 2

Measurements of abdominal dimensions and the sigmoid loop in Western and Oriental patients undergoing laparotomy.

<table>
<thead>
<tr>
<th></th>
<th>Western Patients (n=115)</th>
<th>Oriental Patients (n=114)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.S. Iliac spine - A.S. Iliac spine</td>
<td></td>
<td></td>
<td>NS*</td>
</tr>
<tr>
<td>median (cm)</td>
<td>26</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>range (cm)</td>
<td>19-42</td>
<td>21-45</td>
<td></td>
</tr>
<tr>
<td>Pubic symphysis - xiphisternum</td>
<td></td>
<td></td>
<td>NS*</td>
</tr>
<tr>
<td>median (cm)</td>
<td>31</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>range (cm)</td>
<td>24-49</td>
<td>24-50</td>
<td></td>
</tr>
<tr>
<td>Length of rectum + sigmoid colon</td>
<td></td>
<td></td>
<td>NS*</td>
</tr>
<tr>
<td>median (cm)</td>
<td>34</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>range (cm)</td>
<td>17-78</td>
<td>15-55</td>
<td></td>
</tr>
<tr>
<td>Length of sigmoid mesocolon</td>
<td></td>
<td></td>
<td>NS*</td>
</tr>
<tr>
<td>median (cm)</td>
<td>11</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>range (cm)</td>
<td>2-26</td>
<td>4-20</td>
<td></td>
</tr>
<tr>
<td>Pubic symphysis - sigmoid/descending junction</td>
<td></td>
<td></td>
<td>NS*</td>
</tr>
<tr>
<td>median (cm)</td>
<td>13</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>range (cm)</td>
<td>3-30</td>
<td>5-19</td>
<td>*Mann-Whitney</td>
</tr>
</tbody>
</table>
mesocolon or distance from the pubic symphysis to the first retroperitoneal point of attachment of the descending colon (sigmoid/descending junction), (table 2). Medial mobility of the descending colon was similar in the Western (median = 5cm, range 0-17cm) compared to the Oriental patients (median = 4cm, range 0-10cm), however a colonoscopically "significant" descending mesocolon of ≥ 10cm was seen in 10 (8%) Western patients but only 1 (0.9%) Oriental patient, \( P=0.01 \). The descending colon was slightly shorter in the Western (median = 18cm, range 9-42cm) than the Oriental patients (median = 20 cm, range 6-38cm), \( P=0.04 \).

A mobile splenic flexure was seen more often in Western (20%) compared to Oriental (9%) patients, \( P=0.016 \). When pulled towards the symphysis pubis the distance from the splenic flexure to the symphysis pubis was less in the Western (median = 24 cm, range 7-40 cm) than in the Oriental patients (median = 27cm, range 4-40cm), \( P=0.003 \).

Mobility of the transverse colon was greater in the Western patients: when the transverse colon was pulled maximally downwards, the distance from the symphysis pubis to the mid transverse colon was less in the Western compared to Oriental patients, (table 3). In 34 (30 %) of the Western patients the mid-transverse colon reached the symphysis pubis or lower when pulled downwards in contrast to 12 (11%) of the Oriental patients, \( P<0.001 \). However there was no significant difference in either the length of the transverse mesocolon or the maximum length of the transverse colon, (table 3).

Medial mobility of the ascending colon was greater in the Western (median = 4.5cm, range 0-15 cm) compared to Oriental patients (median = 3cm, range 0 - 10cm), \( P=0.003 \). An ascending mesocolon of ≥ 10cm was present in 11 (9%) Western patients compared to 2 (2%) Oriental patients, \( P = 0.02 \). However there
<table>
<thead>
<tr>
<th></th>
<th>Western Patients (n=115)</th>
<th>Oriental Patients (n=114)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appearence of splenic flexure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>fixed</td>
<td>64</td>
<td>87</td>
<td>NS*</td>
</tr>
<tr>
<td>covered</td>
<td>27</td>
<td>17</td>
<td>NS*</td>
</tr>
<tr>
<td>mobile</td>
<td>24</td>
<td>10</td>
<td>P=0.016*</td>
</tr>
<tr>
<td><strong>Mid-transverse colon-pubic symphysis</strong></td>
<td>5.5</td>
<td>8</td>
<td>P=0.0045‡</td>
</tr>
<tr>
<td>median (cm)</td>
<td>(-7) - (+ 30)</td>
<td>0-25</td>
<td></td>
</tr>
<tr>
<td>range (cm)</td>
<td>25-81</td>
<td>23-87</td>
<td></td>
</tr>
<tr>
<td><strong>Length of Transverse</strong></td>
<td>45</td>
<td>42</td>
<td>NS‡</td>
</tr>
<tr>
<td>median (cm)</td>
<td>25-81</td>
<td>23-87</td>
<td></td>
</tr>
<tr>
<td><strong>Transverse mesocolon</strong></td>
<td>14</td>
<td>14</td>
<td>NS‡</td>
</tr>
<tr>
<td>median (cm)</td>
<td>6-35</td>
<td>4-71</td>
<td></td>
</tr>
<tr>
<td>range (cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s exact test
‡ Mann-Whitney
was no difference between the two groups with regard to length of the ascending colon + caecum, (Western median length = 17cm, range 7-31cm; Oriental median length = 16.5 cm, range 9-26 cm. An ascending and descending mesocolon of ≥ 10cm was present in 6 (5%) Western patients but was not found in Orientals.

After adding the segmental lengths of the colon together (excluding those patients with sigmoid adhesions), there was no significant difference in total colonic length between the Western (median 114 = cm, range 68-159 cm) and Oriental patients (median = 111cm, range 78-161cm).

2.5: Discussion

This study represents the first in vivo attempt to define variations in colonic anatomy and mesenteric attachments. Compared to the findings of Treves (Treves, 1885) this study has shown a much larger variation in colonic mobility in Western patients. In 86% some degree of medial deviation of the descending colon was possible and 8 % possessed a colonoscopically "significant" (≥ 10cm) persisting descending mesocolon (likely to cause unusual looping such as the reversed splenic flexure loop during colonoscope insertion). In 81% of Western patients some degree of medial deviation of the ascending colon was also possible, and 9% of patients possessed an ascending mesocolon of ≥ 10cm. There was a tendency for patients with a mobile descending colon to possess also a mobile ascending colon, a finding in keeping with the observations of Treves (Treves, 1885).

Western compared to Oriental patients were found to have increased mobility of the splenic flexure, transverse colon and ascending colon. There was also a higher incidence of a long (≥ 10cm) persisting descending mesocolon (8% vs 1%) in Western patients. These anatomic differences may go some way to
explaining the apparent difficulty of colonoscopy in Western patients. Ease of intubation is also related to other factors apart from colonic anatomy, such as the skill of the colonoscopist, the endoscopic equipment available and the patients' tolerance of the procedure. However the increased mobility of the Western colon would suggest that atypical colonoscope looping would be more likely in Western patients. This study has also shown a greater incidence of sigmoid adhesions in Western compared to Oriental patients. This suggests that difficulty during intubation, due to acute angulation of the colonoscope in the sigmoid colon, could occur more frequently in Western patients. The increased incidence of sigmoid adhesions in Western patients may be a reflection of the known differences in distribution and incidence of diverticular disease between East and West (Guo-zung et al, 1984).

Contrary to expectation, the study has found no difference in total colonic length between Western and Oriental patients in spite of the general perception in the West that Oriental patients have longer colons. The values for total colonic length in Western laparotomy patients (median = 113 cm in males and mean = 115 cm in females) are less than those previously reported by Treves, or Underhill at post mortem (Treves, 1885; Underhill, 1955). Treves found that the average length of the entire colon was 4 feet 8 inches (142.2cm) in males and 4 feet 6 inches (137.2 cm) in females whilst Underhill, also in a study of 100 cadavers, reported the length of the colon as 5 feet 11 inches in males (180.34 cm) and 5 feet 2 inches (157.48 cm) in females. The study findings are more in keeping with those of Hirsch et al. who measured the length of the colon "in vivo" by passing a polyvinyl tube from mouth to anus; they found a range of values for total colonic length from 91-125 cm (Hirsch et al, 1956). Complete loss of muscle tone after death may explain the greater length measurements recorded in postmortem studies.
The figures for total colonic length in Oriental patients (median = 112 cm) are slightly less than those described by Sadahiro et al, who measured colonic length from double contrast barium enema examinations and found that after correction for magnification the total length of the colon was on average 129.54cm ± 15.95 cm (Sadahiro et al, 1992). This discrepancy may be explained by the fact that Sadahiro et al. took measurements from patients whose barium enema series had been facilitated by the use of anti-spasmodic medication, which may have reduced muscle tone and hence increased the length of the colon.

2.6 : Conclusions

In this study, provided a sigmoid loop was present, the length of the Western colon measured at laparotomy varies between 68-159cm. Eight percent of Western patients possess a persisting descending mesocolon of ≥ 10cm, 20% have a mobile splenic flexure and 17% sigmoid adhesions, all factors that may predispose to difficulty during colonoscopy insertion. The Western colon is on average more mobile and has a higher incidence of sigmoid adhesions than its Oriental counterpart. These findings may explain the apparent difficulty of colonoscopy in Western compared to Oriental patients.
Chapter 3: What makes colonoscopy difficult?

3.1: Introduction

Several previous series have reported total colonoscopy rates and assessed factors related to incomplete examinations (Church, 1994; Nivatvongs et al, 1982; Waye & Bashoff, 1991a; Pham et al, 1994). However the exact causes for difficulty during colonoscopy have not been clearly defined. Excluding patients with failed preparation or colonic stricture, lower total colonoscopy rates have been described in patients < 20 yrs of age (Church, 1994), patients > 80 yrs (Church, 1994), patients with previous abdominal or pelvic surgery (Church, 1994; Nivatvongs et al, 1982) and in women compared to men (Church, 1994; Waye & Bashoff, 1991a; Pham et al, 1994). In a study where difficulty and patient pain were assessed by the endoscopy nurse, a significant correlation was found between hysterectomy and increased pain and increased difficulty of the procedure and female gender (Hull et al, 1994). Interestingly, no clear association between diverticular disease and incomplete colonoscopy has been described except when diverticular inflammation has caused a colonic stricture (Forde & Treat, 1985). The studies described above are all retrospective reviews which rely on the subjective opinion of the endoscopist as to the incidence and cause of difficulty. Moreover fluoroscopy has not been employed to assess the configuration of the colonoscope during difficult cases. In this Chapter a series of colonoscopies are assessed prospectively (using fluoroscopy) to define the incidence of technical difficulty during colonoscope insertion, the factors associated with difficulty, the configuration of the colonoscope when difficulty occurs and the strategies which result in successful intubation.
3.2 : Method

Consecutive patients attending for colonoscopy were prospectively studied. All examinations were performed by one experienced endoscopist (CBW). Patients with failed bowel preparation and those found to have a colonic stricture were excluded from the study. All patients were premedicated with hyoscine n-butyl bromide (20mg iv.) and then sedated with titrated doses of pethidine and diazepam. Though available, pulse oximetry was not routinely used. An independent observer timed the procedures and difficulty was said to occur during insertion when the tip of the colonoscope had not advanced for a 5 minute period. When difficulty occurred, fluoroscopy was used to assess the configuration of the colonoscope, to aid in the straightening of loops and to determine further intubation strategy. Patient details including age, sex, past surgical history, indication for colonoscopy, endoscopic findings, patient sedation, time taken to complete colonoscope insertion and depth of insertion were recorded.

3.3 : Statistical analysis

Continuous data were compared using un-paired t-tests and categorical data Fisher's exact or the chi-squared test.

3.4 : Results

Of 500 patients entered into the study, 80 (16%) were found to be technically difficult to intubate. Patient details and findings at colonoscopy are recorded in table 4. Comparing age, previous surgical history, indication for colonoscopy and
the finding of diverticular disease there were no significant differences between the difficult and not difficult groups. However, significantly more female (23%) than male (11%) patients were found to be difficult to colonoscope (table 4). There was no difference in the incidence of previous pelvic surgery comparing those female patients who were difficult to colonoscope (32%) and those who were not (25%).

Total colonoscopy was eventually achieved in 99% of patients. In all difficult cases the median time taken to complete intubation was 24 minutes (max. 1hr) and the median sedation used was pethidine 40mg iv., "Diazemuls" 4mg iv. (maximum sedation = pethidine 100mg iv., "Diazemuls" 10mg iv.). There were no complications related to colonoscope insertion recorded in this study.

In 65 (80%) of the 80 difficult examinations recurrent looping of the colonoscope was found to be the cause of difficulty. Fluoroscopy showed that in 13 of these patients a reversed splenic flexure loop had occurred, in 12 an "alpha loop", in 10 "N"-shaped sigmoid loops, in 1 a transverse "gamma" loop, and in 16 there were multiple loops. In a further 13 patients recurrent looping was considered by the endoscopist to be the cause of difficulty though this could not be confirmed by fluoroscopy because of equipment failure. The split over-tube stiffening device (Gortex PTFE, Olympus Ltd) was used successfully to prevent recurrent sigmoid colon looping in 9 patients. Total colonoscopy was eventually achieved in all patients where recurrent looping of the colonoscope occurred.

The cause of difficulty in the remaining 15 examinations was a fixed sigmoid colon, thought to be secondary to diverticular adhesions in 5 patients, previous surgery in 8, and congenital adhesions in 2. Seven of the patients with a fixed sigmoid colon secondary to surgical adhesions were female; 5 had previously undergone hysterectomy and 2 other forms of pelvic surgery. No patient had undergone pelvic irradiation. The Olympus PCF paediatric colonoscope was -
## TABLE 4

Comparison of patient details in *difficult* and *not difficult* colonoscopy groups

<table>
<thead>
<tr>
<th></th>
<th>Difficult (n=80)</th>
<th>Not Difficult (n=418)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (years)</td>
<td>60.3</td>
<td>61.3</td>
<td>NS*</td>
</tr>
<tr>
<td>range (years)</td>
<td>23-87</td>
<td>17-88</td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>34 (42.5%)</td>
<td>272 (65%)</td>
<td>NS*</td>
</tr>
<tr>
<td>female</td>
<td>46 (57.5%)</td>
<td>146 (35%)</td>
<td>P&lt;0.0006#</td>
</tr>
<tr>
<td><strong>Previous surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>abdominal</td>
<td>7 (8.7%)</td>
<td>42 (10%)</td>
<td>NS†</td>
</tr>
<tr>
<td>pelvic</td>
<td>15 (18%)</td>
<td>37 (8.8%)</td>
<td>NS†</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyp follow-up</td>
<td>26 (32%)</td>
<td>166 (39.7%)</td>
<td>NS#</td>
</tr>
<tr>
<td>Family history Ca.</td>
<td>19 (23.7%)</td>
<td>137 (32.7%)</td>
<td>NS#</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>7 (8.7%)</td>
<td>32 (7.6%)</td>
<td>NS‡</td>
</tr>
<tr>
<td>Bleeding</td>
<td>8 (10%)</td>
<td>24 (5.7%)</td>
<td>NS†</td>
</tr>
<tr>
<td>UC/Crohn's</td>
<td>14 (17.5%)</td>
<td>45 (10.7%)</td>
<td>NS‡</td>
</tr>
<tr>
<td>Other</td>
<td>6 (7.5%)</td>
<td>14 (3.3%)</td>
<td>NS‡</td>
</tr>
<tr>
<td><strong>Findings</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diverticular disease</td>
<td>14 (17.5%)</td>
<td>72 (17.2%)</td>
<td>NS‡</td>
</tr>
</tbody>
</table>

*unpaired t-test  
†Fisher's exact test  
#chi-squared test
- used on 5 occasions to pass the sigmoid colon successfully when the adult colonoscope had failed. In 4 patients (3 with surgical adhesions, 1 with severe diverticular disease) fixation of the sigmoid colon prevented total colonoscopy.

3.5: Discussion

The results from this study show that even an expert colonoscopist experiences difficulty during intubation in 16% of patients. Age of the patient, and indication for colonoscopy were not related to a difficult intubation. Overall the incidence of diverticular disease was similar in patients regardless of difficulty at colonoscopy. However, the grade of diverticular disease was not recorded and therefore severe diverticular disease may have been more frequent in the difficult colonoscopy group. More women than men were considered to be difficult to intubate. Women are more likely to have had pelvic surgery prior to colonoscopy than men, however the incidence of previous pelvic surgery was similar in female patients whether judged difficult or not difficult to colonoscope, a finding that has been reported once before (Waye & Bashoff, 1991). This suggests that other gender-related factors may be important in determining difficulty at colonoscopy (see Chapter 4).

Although the 4 patients with failed colonoscopies had fixed sigmoid colons, overall most difficulty was caused by unpredictable, recurrent looping of the colonoscope, particularly in the left colon. Fluoroscopic screening was helpful in visualising the manoeuvres necessary to remove loops, even though its use involved temporary cessation of the examination in preparation for screening and the wearing of cumbersome lead aprons. Screening time was not formally recorded but was kept to a minimum, with fleeting glimpses of the colonoscope only. This sometimes made interpretation of the images difficult. In all cases of
recurrent looping a successful manoeuvre was eventually found to reduce the loop and achieve total colonoscopy. Though not essential for insertion, screening was also of use in ensuring the appropriate use of the split over-tube stiffening device, which prevented sigmoid looping in 9 patients. The most common loop to cause difficulty during insertion was the reversed splenic flexure loop, which occurs when the descending colon can move medially due to a large persisting descending mesocolon. In Chapter 1 a large $\geq 10$cm mesocolon was noted in 8% of individuals at laparotomy. In this study a reversed splenic flexure loop caused difficulty in 13 (2.6%) of those patients examined.

Sigmoid colon adhesions causing acute sigmoid bends were found to be a less frequent cause of difficulty during intubation than recurrent looping of the colonoscope. When they occurred, the more floppy 10mm paediatric colonoscope frequently proved successful in negotiating a fixed sigmoid colon after the adult 1.3cm colonoscope had failed.

Difficult cases at colonoscopy did not usually require "heavy sedation" or a prolonged examination and, with the advantage of fluoroscopy and other aids to colonoscopy such as the paediatric colonoscope and split overtube, the whole colon was successfully examined without complications in all but 4 (1%) patients.

3.6 : Conclusions

An experienced colonoscopist encounters difficulty during colonoscope insertion in 10-20% of patients. Age and indication for colonoscopy do not appear to be related to technical difficulty, however female patients are more likely to prove difficult to intubate than men. Unpredictable, recurrent looping of the colonoscope in a mobile or long colon is the most common cause of difficulty
at colonoscopy, although failed total colonoscopy is more likely to occur when the sigmoid colon is fixed secondary to adhesions. Total colonoscopy can be achieved in almost all patients without heavy sedation or prolonged intubation times, provided aids to colonoscopy such as fluoroscopy, the split over-tube stiffening device and the paediatric colonoscope are available.
Chapter 4: Why are women more difficult to colonoscope than men?

4.1: Introduction

In Chapter 3 it was found that female gender was associated with technical difficulty at colonoscopy. To confirm this finding, the endoscopy database at St. Mark's Hospital was analysed. Of 2194 colonoscopies performed by one experienced colonoscopist (CBW) between January 1988 and May 1993, 327 of 1067 procedures in women (31%) were recorded as technically difficult, (taking into account the duration of the procedure, the final depth of insertion and the degree of observed patient discomfort) in contrast to only 177 of the 1127 procedures (16%) in men, $P<0.0001$ ($\chi^2$ test). Others have also reported differences between the sexes in the tolerance and technical difficulty of colonoscopy (Waye & Bashoff, 1991; Hull et al, 1994; Nivatvongs et al, 1982; Ravi et al, 1988; Church, 1994). In this Chapter possible gender-related differences in colonic anatomy will be explored that may explain why women are more difficult to colonoscope than men.

4.2: Method

Normal barium enemas (without significant diverticular disease, colitis, megacolon, stricture or resection) of 183 Caucasian female and 162 Caucasian male patients were randomly identified from "in file", double-contrast, barium enema x-ray films at St. Mark's Hospital. All enema series had been performed by a standardised technique (using large overhead films, taken with a fixed film-tube distance in set radiographic positions). From the prone film of each enema series the total length of the colon was measured using an opisometer (mapping wheel).
passed along the long axis of the bowel. Of the 345 normal enema films identified, 204 were randomly selected for more detailed measurements of colonic anatomy and mobility (104 female patients, 100 male patients). For this subset, segmental colonic lengths (rectum + sigmoid colon, descending colon, transverse colon, ascending colon + caecum) were measured from the prone film (figure 4.1). The junction between the sigmoid and descending colon was arbitrarily designated as being at the upper border of the iliac crest. The distance from the upper border of the 12th thoracic vertebra (T12) to the lower border of the 4th lumbar vertebra (L4) was also measured from the prone film as an indicator of the stature of each patient. Because of a known magnification factor of +17% on each enema film, all measurements taken were appropriately corrected.

Mobility of the descending colon was assessed by measuring the distance from the mid-point of the third lumbar vertebra to the mid-point of the descending colon in the right and left lateral decubitus views and then subtracting for the difference. Mobility of the transverse colon was assessed on prone and erect films by measuring the maximum perpendicular distance between the transverse colon and a line passing through both hepatic and splenic flexures (figure 4.2), and then subtracting for the difference. The transverse colon was considered to be "redundant" when it sagged into the true pelvis on the erect film (figure 4.3). All measurements and observations were performed independently by two observers, blinded as to the sex of the patient.
FIGURE 4.1

Barium enema (prone film) demonstrating the method of measurement of colonic segmental lengths; the sigmoid/descending junction is designated as being at the upper border of the iliac crest.
FIGURE 4.2
Prone enema film demonstrating the method for measuring transverse mobility; maximum perpendicular distance from a line joining both flexures in the prone film minus the maximum perpendicular distance from a line joining both flexures in the erect film.
FIGURE 4.3

Erect barium enema film demonstrating “redundancy of the transverse colon” i.e. the transverse colon sags to the true pelvis
4.3 : Statistical analysis

The Mann-Whitney test was used to compare measurements of colonic length and mobility between male and female patients. Fisher's exact test was used to compare the incidence a redundant transverse colon between the sexes. A P value of < 0.05 was considered significant.

4.4 : Results

Male and female patients were similar with regard to age at the time of the enema (females mean age = 50.2 yrs, range = 19-85, males mean age = 51.5 yrs, range = 15-86 yrs). The two observers' measurements were averaged for continuous data and there was complete agreement over non-continuous data (presence of a "redundant" transverse colon). Total colonic length was greater in females (median = 125cm, range = 89-173cm) compared to males (median = 120cm, range = 81-169cm), P < 0.05, despite women being of smaller stature than men (female T12-L4 median distance = 15cm, male T12-L4 median distance = 19cm), P<0.0001.

Assessment of colonic segmental lengths (table 5) showed that there was no significant difference in rectum + sigmoid colon, descending colon or ascending colon + caecum lengths between the sexes. Transverse colon length was however greater in females (median length = 40 cm, range 16-70 cm) than males (median = 33cm, range 17-52cm), P < 0.0001.

There was no significant difference between the sexes with regard to the degree of measured mobility of the descending colon or transverse colon, table 5. However "redundancy" of the transverse colon was a more frequent finding in female (62%) compared to male (26%) patients, P<0.0001.
<table>
<thead>
<tr>
<th>Segment</th>
<th>Female (n=104)</th>
<th>Male (n=100)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rectum + sigmoid colon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median length (cm)</td>
<td>56</td>
<td>59</td>
<td>NS*</td>
</tr>
<tr>
<td>range (cm)</td>
<td>22 - 100</td>
<td>31 - 103</td>
<td></td>
</tr>
<tr>
<td><strong>Descending colon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median length (cm)</td>
<td>23</td>
<td>25</td>
<td>NS*</td>
</tr>
<tr>
<td>range (cm)</td>
<td>11 - 43</td>
<td>8 - 36</td>
<td></td>
</tr>
<tr>
<td><strong>Transverse colon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median length (cm)</td>
<td>48</td>
<td>40</td>
<td>p&lt;0.0001*</td>
</tr>
<tr>
<td>range (cm)</td>
<td>19 - 83</td>
<td>20 - 67</td>
<td></td>
</tr>
<tr>
<td><strong>Ascending colon + caecum</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median length (cm)</td>
<td>23</td>
<td>23</td>
<td>NS*</td>
</tr>
<tr>
<td>range (cm)</td>
<td>11 - 41</td>
<td>15 - 38</td>
<td></td>
</tr>
<tr>
<td><strong>Descending medial mobility</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>median length (cm)</td>
<td>4</td>
<td>3.5</td>
<td>NS*</td>
</tr>
<tr>
<td>range (cm)</td>
<td>0 - 12.5</td>
<td>0 - 10.7</td>
<td></td>
</tr>
<tr>
<td><strong>Transverse mobility</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median length (cm)</td>
<td>6</td>
<td>6</td>
<td>NS*</td>
</tr>
<tr>
<td>range (cm)</td>
<td>(-4) - (+15)</td>
<td>0.5 - 11</td>
<td></td>
</tr>
</tbody>
</table>

*Mann-Whitney
4.5 : Discussion

Two recent abstracts have highlighted the difficulties encountered by female patients undergoing colonoscopy. Women compared to men were more likely to experience discomfort during the procedure (Schmitt et al, 1994) and miss work the following day (Newcomer et al, 1994). It has been suggested that women may be more difficult to colonoscope because of previous pelvic surgery, particularly hysterectomy (Hull et al, 1994; Ravi et al, 1988; Church, 1994). However, Waye et al. found that there was no higher incidence of previous hysterectomy in female patients with failed colonoscopies, than in those who had undergone total colonoscopy (Waye & Bashoff, 1991). This is in agreement with the findings of Chapter 3, that the incidence of previous pelvic surgery was similar in "difficult" and "not difficult" groups and that looping of the colonoscope in a long or mobile colon was the most common cause of difficulty at colonoscopy. This study has found that total colonic length is greater in women, despite their smaller stature, and that this difference is most prominent in the transverse colon. These findings are in keeping with those of Sadahiro et al. who studied the barium enemas of Japanese patients and also found a difference in total colonic length between men and women (mean males = 125.87cm, mean females = 132.83cm) (Sadahiro et al, 1992). However, measurements of Western colonic anatomy at laparotomy in Chapter 2, failed to show a significant difference in total colonic length between the sexes (median = 113 cm in males and median = 115 cm in females), possibly because of the smaller number of patients in whom total colonic length was measured (50 male vs 45 female). Increased colonic length will tend to predispose to loop formation, difficulty in passing the colonoscope and patient discomfort during intubation. Without continuous imaging of the colonoscope configuration, the exact frequency with
which different loops occur remains uncertain and formation of transverse loops may be a more common cause of difficulty, particularly in female patients, than was previously thought. In addition the greater length and looping tendency in a long transverse colon, with consequent frictional resistance, may also result in more frequent secondary looping of the colonoscope in the sigmoid colon.

It is possible that other sex-related anatomical factors have an influence over the relative difficulty of colonoscopy. The female pelvis is deeper and more convex than its male counterpart, which may predispose to loop formation in the sigmoid colon. Also, women are less muscular than men, whose abdominal walls may provide more resistance to prevent the colonoscope from looping, acting in the same way as non-specific abdominal hand pressure during intubation. Physiological factors such as differences in pain thresholds may also be important and finally psychological factors such as expectations of procedural pain and pain relief and the subsequent reporting of pain may all influence tolerance and difficulty of colonoscopy.

4.6 : Conclusions

Women are more frequently difficult to colonoscope than men. This may be related to several factors including the shape of the pelvis and the condition of the abdominal wall musculature. Despite being on average smaller than men, women possess longer colons. This may result in a greater tendency for colonoscope looping during intubation.
Chapter 5: Can difficulty at colonoscopy be predicted from a previous barium enema?

5.1: Introduction

In Chapters 2, 3 and 4 the anatomical basis of difficulty at colonoscopy has been investigated: patients with long, mobile or unusually fixed colons are more likely to be technically difficult to colonoscope. Prior to colonoscopy, little information is available regarding each individual’s colonic anatomy and therefore it is difficult to predict which patients will have difficult endoscopic examinations. Some patients however have already been examined by barium enema and therefore a radiological record of their colonic anatomy is available for assessment. In this Chapter anatomical factors are sought, from review of previous barium enema appearances, which may be predictive of difficulty at colonoscopy.

5.2: Method

The endoscopy records of all patients colonoscoped by one experienced endoscopist (CBW) at St. Mark's Hospital between January 1991 and May 1993 were retrospectively reviewed. Forty eight patients were identified who had both a difficult colonoscopy and a barium enema performed within three years of the colonoscopy. Difficulty at colonoscopy was a subjective assessment by the endoscopist, at the time of endoscopy reflecting the duration of the procedure and patient discomfort during it.

Barium enemas of patients who were difficult to colonoscope were compared to those of 46 control subjects (randomly selected patients colonoscoped by the
same endoscopist during the same time period in whom no difficulty had been encountered). Each enema was assessed independently by 2 radiologists who were unaware of the colonoscopist's evaluation of difficulty. From the prone film the rectum + sigmoid colon and total colonic lengths were measured in centimetres using an opisometer (mapping wheel) and an assessment of the degree of diverticular disease was made (figure 5.1). Length measurements were taken in the long axis of the bowel and the upper border of the iliac crest was designated as defining the border between the sigmoid and descending colon.

The mobility of the descending colon was assessed by measuring the distance from the mid-point of the third lumbar vertebra to the mid-point of the descending colon in the right and left lateral decubitus views and then subtracting for the difference. Mobility of the transverse colon was defined as the difference in vertical height from the third lumbar vertebra to the most dependent part of the transverse colon in prone and erect films (at St.Mark's Hospital an erect, 35cm by 43cm film is taken as part of a standard barium enema series). The transverse colon was considered to be redundant when it sagged into the true pelvis on the erect film.

5.3 : Statistical analysis

Rectum + sigmoid colon and total colonic lengths as well as mobility of the descending and transverse colon were compared between the two study groups using un-paired t-tests. Diverticular disease score and redundancy of the transverse colon were compared using Fisher's exact test. Statistical significance was assigned to any probability value of less than 0.05.
FIGURE 5.1
Radiological classification of diverticular disease severity

<table>
<thead>
<tr>
<th>SCORE</th>
<th>DEFINITION (barium enema appearance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No diverticula or muscle thickening</td>
</tr>
<tr>
<td>1</td>
<td>Scattered diverticula only / no muscle thickening</td>
</tr>
<tr>
<td>2</td>
<td>Continuous diverticula / minor muscle thickening</td>
</tr>
<tr>
<td>3</td>
<td>Distorted diverticular segment / marked muscle thickening</td>
</tr>
</tbody>
</table>
5.4 : Result

The two study groups were similar with regard to age, sex (male difficult vs female difficult, P=0.06) and racial origin (table 6). The two radiologist's measurements were averaged for continuous data and there was complete agreement over non-continuous data (diverticular disease score and the presence of a redundant transverse colon). Rectosigmoid length, total colonic length and mobility of the transverse colon were greater in the difficult colonoscopy group compared to the control group, but there was no difference between the two groups in mobility of the descending colon (table 7). Redundancy of the transverse colon was recorded in 31 (65%) of the difficult colonoscopy group compared to 8 (17%) of the control group, P<0.0001. The presence of grades 2/3 diverticular disease was also greater in the difficult (23%) compared to control group (4%), P=0.02. Examples of barium enemas of patients who were difficult to colonoscope are given in figures 5.3, 5.4, 5.5.
<table>
<thead>
<tr>
<th></th>
<th>Difficult examination (n=48)</th>
<th>Not Difficult examination (n=46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at time of colonoscopy</td>
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<td></td>
</tr>
<tr>
<td>mean (years)</td>
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<td>62</td>
</tr>
<tr>
<td>range (years)</td>
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<td>23-81</td>
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<tr>
<td>Sex</td>
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</tr>
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</tr>
<tr>
<td>African</td>
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<td>1</td>
</tr>
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</table>
### TABLE 7

Measurements of colonic segmental length and mobility in *difficult* and *not difficult* groups.

<table>
<thead>
<tr>
<th></th>
<th>Difficult (n=48)</th>
<th>Control (not difficult, n=46)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rectosigmoid length</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (cm)</td>
<td>61</td>
<td>53</td>
<td>P=0.01*</td>
</tr>
<tr>
<td>upper 95% C.I. (cm)</td>
<td>64.1</td>
<td>57.9</td>
<td></td>
</tr>
<tr>
<td>lower 95% C.I. (cm)</td>
<td>57.3</td>
<td>50.3</td>
<td></td>
</tr>
<tr>
<td><strong>Total colonic length</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (cm)</td>
<td>157</td>
<td>140</td>
<td>P&lt;0.0001*</td>
</tr>
<tr>
<td>upper 95% C.I. (cm)</td>
<td>162</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>lower 95% C.I. (cm)</td>
<td>152.3</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td><strong>Mobility of the transverse colon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (cm)</td>
<td>10</td>
<td>7</td>
<td>P=0.003*</td>
</tr>
<tr>
<td>upper 95% C.I. (cm)</td>
<td>11.7</td>
<td>8.4</td>
<td></td>
</tr>
<tr>
<td>lower 95% C.I. (cm)</td>
<td>8.7</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td><strong>Mobility of descending colon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (cm)</td>
<td>4.1</td>
<td>4.3</td>
<td>P=0.92*(NS)</td>
</tr>
<tr>
<td>upper 95% C.I. (cm)</td>
<td>5.6</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>lower 95% C.I. (cm)</td>
<td>2.9</td>
<td>3.0</td>
<td></td>
</tr>
</tbody>
</table>

* = Un-paired t-test
C.I. = confidence interval
FIGURE 5.2

Prone barium enema film of a patient who was technically difficult to intubate demonstrating severe sigmoid colon diverticular disease.
FIGURE 5.3

Prone barium enema film of a patient who was technically difficult to intubate demonstrating a long (95cm) sigmoid colon.
FIGURE 5.4

Prone barium enema film of a patient who was technically difficult to intubate demonstrating a long overall colon (190cm).
5.5 : Discussion

This retrospective study has shown that a barium enema may be used to predict which colonoscopies will be technically difficult. The measurements and observations taken were easy to perform and could easily become adopted by the radiologist as part of the routine reporting of barium enemas, particularly when a need for subsequent colonoscopy has been identified from the enema. Increased rectosigmoid length, total colonic length, transverse colon mobility and increasing severity of diverticular disease were all associated with technically difficult colonoscopies. In Chapter 3 it was demonstrated that the most common cause of difficulty at colonoscopy was recurrent looping of the colonoscope. It is not surprising therefore that an increase in both rectum + sigmoid and total colonic lengths was found in the difficult colonoscopy group compared to the controls, as increased colonic length predisposes to looping during intubation. In this study, grades 2 or 3 diverticular disease was a more frequent finding in the difficult colonoscopy group. In Chapter 3 no increase in the incidence of diverticular disease was found, however severity of disease was not assessed in this earlier study. Diverticular disease as a cause of difficulty during colonoscopy has been suggested previously (Webb, 1991) and is likely to be due to fixed angulation of the sigmoid colon secondary to recurrent inflammation and adhesions. In addition the colonoscopist may encounter difficulty in locating and steering down the colonic lumen when confronted by multiple diverticular openings. Redundancy of the transverse colon was strongly associated with difficulty at colonoscopy. Without the use of continuous imaging of the colonoscope during intubation (Chapter 9) the exact frequency with which different loops occur is uncertain and formation of transverse loops may be a
more common cause of difficulty than previously thought, possibly also contributing to looping of the sigmoid colon as well.

It is well recognised that colonoscopic complications are more likely to occur when the procedure is technically difficult, or the endoscopist inexperienced (Hall et al, 1991; Silvis et al, 1976). Prior prediction of potential difficulty at colonoscopy would therefore be desirable, to allocate difficult cases to specialist endoscopy lists and to ensure that aids to colonoscopy such as the paediatric colonoscope (Bat & Williams, 1991), over-tube stiffening device (Williams, 1983) and fluoroscopic imaging (Rogers, 1990) were available. Moreover, patients who are difficult to intubate are more likely to require extra medication and so could be warned to make appropriate post-procedural arrangements.

5.6 : Conclusions

If a patient has been investigated previously by barium enema this can provide a useful guide to probable technical difficulty of colonoscopy. Increased total colonic length, rectosigmoid length, redundancy of the transverse colon and severe diverticular disease are all associated with difficulty at colonoscopy. Assessment of colonic anatomy from a previous barium enema is quick and easy to perform and may allow appropriate allocation of potentially difficult cases to specialist endoscopy lists.
Chapter 6: Bowel preparation for colonoscopy

6.1: Introduction

As outlined in Chapter 1, effective bowel cleansing is an essential prerequisite for accurate and safe colonoscopy. In this chapter, factors associated with poor preparation are investigated and an attempt is made to identify a preparation that is well tolerated, easy to comply with and effective.


Analysis of the endoscopy database at St. Mark's Hospital showed that of the 8259 patients who had undergone colonoscopy with a senna (30g) + Picolax (1½ sachets) + dietary restriction (4 days) preparation between March 1983-March 1992, only 441 (5.3%) were recorded as having a poor preparation. Univariate analysis demonstrated that an indication for colonoscopy of inflammatory bowel disease (table 8), age over 70 years (table 9) and the finding of diverticular disease (25% poor preparation group vs 16% good preparation group, P=0.001 chi-squared test) were all associated with a higher incidence of poor preparation.

Despite the relatively low incidence of failure with the preparation described above, day-case patients may prefer a more rapid method of bowel cleansing without the need for elaborate dietary restriction.

6.3: Experience at St. Mark's Hospital

At St. Mark's Hospital (over several years) a mixture of mannitol (100mg), magnesium citrate (3g) and sodium picosulphate (10mg), (mannitol/Picolax), has
### TABLE 8

Association between indication for colonoscopy and poor preparation

<table>
<thead>
<tr>
<th>Main indication for colonoscopy</th>
<th>Total exams (n=8259)</th>
<th>Poor prep. (n = 441)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyps / polyp follow -up</td>
<td>3142</td>
<td>168 (5.3%)</td>
<td>NS*</td>
</tr>
<tr>
<td>Inflamm. bowel disease</td>
<td>1803</td>
<td>170 (9.4%)</td>
<td>p&lt;0.001*</td>
</tr>
<tr>
<td>Bleeding</td>
<td>798</td>
<td>53 (6.6%)</td>
<td>NS*</td>
</tr>
<tr>
<td>Family History of Ca.</td>
<td>436</td>
<td>8 (1.8%)</td>
<td>NS*</td>
</tr>
<tr>
<td>Cancer Follow Up</td>
<td>360</td>
<td>15 (4.1%)</td>
<td>NS*</td>
</tr>
<tr>
<td>Pain</td>
<td>306</td>
<td>10 (2.7%)</td>
<td>NS*</td>
</tr>
<tr>
<td>Polyposis Follow -uo</td>
<td>288</td>
<td>7 (2.4%)</td>
<td>NS*</td>
</tr>
<tr>
<td>Other</td>
<td>268</td>
<td>10 (3.7%)</td>
<td>NS*</td>
</tr>
</tbody>
</table>

*chi-squared test
**TABLE 9**

Association between age and poor preparation

<table>
<thead>
<tr>
<th>Age</th>
<th>Total exams (n = 8259)</th>
<th>Poor prep. (n = 441)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-30</td>
<td>432</td>
<td>27 (6.3%)</td>
<td>NS*</td>
</tr>
<tr>
<td>31-40</td>
<td>845</td>
<td>30 (3.6%)</td>
<td>NS*</td>
</tr>
<tr>
<td>41-50</td>
<td>1280</td>
<td>43 (3.4%)</td>
<td>NS*</td>
</tr>
<tr>
<td>51-60</td>
<td>2765</td>
<td>114 (4.1%)</td>
<td>NS*</td>
</tr>
<tr>
<td>61-70</td>
<td>2458</td>
<td>131 (5.3%)</td>
<td>NS*</td>
</tr>
<tr>
<td>&gt;70</td>
<td>480</td>
<td>96 (20%)</td>
<td>P&lt;0.001*</td>
</tr>
</tbody>
</table>

* chi-squared test
been used as a rapid bowel preparation for day-case colonoscopy patients. Administered as two 500ml fractions the evening before and the morning of colonoscopy this sweet, lemon-tasting mixture appears to be both effective and well tolerated. At St. Mark's, carbon dioxide insufflation is used routinely for colonoscopy, therefore the use of a mannitol based preparation is safe (Taylor et al, 1982) To assess the efficacy of mannitol/Picolax preparation, two initial pilot studies were carried out.

6.4: Taste trial with mannitol/Picolax solution

Twenty healthy volunteers were asked to taste four different bowel preparations, PEG-BES (Klean-prep7), Picolax alone, 10% mannitol solution and the mannitol/Picolax mixture. All solutions were chilled overnight prior to tasting and the volunteers were blinded as to the identity of each solution. After tasting 20-50mls of each solution, they were asked to rank each in order of preference (table 10). All 20 volunteers considered the PEG-BES solution to be the least pleasant tasting solution and 15 ranked the mannitol/Picolax solution as the best.

7Klean-prep, Norgine Ltd, Oxford, UK.
## TABLE 10

Volunteers' (n=20) taste preferences for 4 different bowel preparations

<table>
<thead>
<tr>
<th></th>
<th>1st choice</th>
<th>2nd choice</th>
<th>3rd choice</th>
<th>4th choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mannitol/Picolax</td>
<td>15</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Mannitol</td>
<td>2</td>
<td>8</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>PEG-BES</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Picolax</td>
<td>3</td>
<td>7</td>
<td>10</td>
<td>0</td>
</tr>
</tbody>
</table>
6.5 : Pilot study assessing the use of a mannitol/Picolax mixture as bowel preparation for colonoscopy.

6.5.1 : Method

Twenty consecutive patients attending for day case colonoscopy were given mannitol/Picolax mixture as bowel preparation for colonoscopy. They received the mixture in two equal sachets with instructions to mix each with 500ml of water and to chill the solution. They then drank the first fraction at 6-00 pm the day before colonoscopy over a 1 hour period followed by the second fraction at 6-00 am on the day of colonoscopy. Patients were encouraged to drink at least one further litre of water. A light lunch was allowed the day before colonoscopy but thereafter clear fluids only. Prior to the examination patients filled in a questionnaire regarding their experience of the preparation. They were asked to rate (none, a little, a lot) whether they had experienced nausea, vomiting, headache, dizziness, abdominal cramps and perianal soreness. In addition patients rated the taste of the preparation (pleasant, tolerable, unpleasant). After the examination the endoscopist assessed the degree of bowel cleansing as excellent, good, fair or poor according to the descriptions given in table 12).

6.5.2 : Results

12 patients rated the taste of the mannitol/Picolax as pleasant, 6 as tolerable and none as unpleasant. Eighteen of the 20 patients were able to complete their preparations in full and the remaining 2 ingested more than half of the solution. Overall, the preparation was judged to be no problem by 16 patients, mildly bothersome by 3 and 1 patient found it distressing. Nineteen of the 20 patients
had excellent (n=4) or good (n=15) preparation as judged by the endoscopist and 1 patient was poorly prepared. Of the 12 patients who had previously had a colonoscopy at St. Mark's (all given a senna + Picolax + 2 day dietary restriction preparation), 9 preferred the mannitol/Picolax preparation and 3 felt there was no difference. Nineteen of the 20 patients said they would be prepared to receive the mannitol/Picolax preparation again in the future.

6.5.3 : Discussion

These initial pilot studies appeared to confirm clinical experience over several years that mannitol/Picolax mixture is effective and well tolerated as bowel preparation for colonoscopy. However this assumption required testing in a formal clinical trial. PEG-BES is recognised as the "gold standard" for bowel preparation (DiPalma & Brady, 1989), and fractionating its administration is known to improve tolerance (Rosch et al, 1992). It was therefore decided to compare in a randomised, single-blind trial, the cleansing ability, safety and patient acceptability of mannitol/Picolax mixture against a fractionated administration of PEG-BES.

6.6 : Two dose PEG-BES vs a mannitol/Picolax mixture as bowel preparation for day-case colonoscopy.

6.6.1 : Patients and Methods

Eighty nine consecutive patients attending for day case colonoscopy were randomised to receive either, 4 litres of PEG/electrolyte (Klean-prep) oral lavage (polyethylene glycol 236g, sodium sulphate 22.74g, sodium chloride 5.86g,
potassium chloride 2.97g, aspartamine 0.2g, vanilla flavouring) or one litre of mannitol/Picolax mixture (mannitol 100mg, sodium picosulphate 10mg, magnesium oxide 3g, citric acid 12g). Patients with an increased risk for poor preparation (i.e. those with known inflammatory bowel disease, age > 70yrs or who were known to have diverticular disease from a previous examination) were randomised separately in order to balance the two study groups. All patients were allowed a normal diet until the midday meal on the afternoon before the day of colonoscopy and thereafter clear fluids only. Patients receiving PEG were given the option of chilling the solution which was then drunk according to the following protocol. Those patients with a morning appointment (n=4) drank 3 litres of the solution at a rate of 250ml/15 minutes, starting at 6.00pm the day before colonoscopy followed by a further 1 litre at 6.00 am the following morning. Patients with an afternoon appointment for colonoscopy (n=41) were asked to drink 2 litres the evening before and 2 litres on the morning of the procedure. In the mannitol/Picolax group, patients were instructed to drink 500ml of the chilled solution at 6.00pm the day before and a further 500ml at 6.00 am on the morning of colonoscopy. They were also asked to drink at least 1 litre of water in addition to their preparation.

On arrival at the Endoscopy Unit all patients were given a questionnaire asking about their experience of the preparation, including taste, ability to complete the preparation, side-effects encountered and whether or not they would be prepared to repeat the preparation if a future colonoscopy were necessary (table 11). In the first 42 patients lying and standing blood pressures were recorded and a venous blood sample taken for haemoglobin, packed cell volume, urea and electrolytes and serum osmolarity.

All examinations were performed by one of two experienced colonoscopists (CBW, BPS), unaware of the type of preparation given who scored the degree of
bowel cleansing according to the descriptions in table 12. Carbon dioxide was used as the insufflating agent during all examinations.

6.6.2 : Statistical analysis

Bowel preparation was allocated to patients according to a randomisation arranged in block sizes of 3. Data for cleansing of the colon, taste, ability to complete the preparation and patient side-effects were assessed using Fisher's exact test after combining the data into 2 by 2 contingency tables. Because of multiple testing, demonstration of significance was taken to require a calculated P value of less than 0.01.
<table>
<thead>
<tr>
<th>Table 11: Patients experience of bowel preparation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Ability to complete preparation -</td>
</tr>
<tr>
<td>full</td>
</tr>
<tr>
<td>&gt; half</td>
</tr>
<tr>
<td>&lt; half</td>
</tr>
<tr>
<td>Overall impression -</td>
</tr>
<tr>
<td>no problem</td>
</tr>
<tr>
<td>bothersome</td>
</tr>
<tr>
<td>distressing</td>
</tr>
<tr>
<td>Taste -</td>
</tr>
<tr>
<td>pleasant</td>
</tr>
<tr>
<td>tolerable</td>
</tr>
<tr>
<td>unpleasant</td>
</tr>
<tr>
<td>Vomiting -</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild</td>
</tr>
<tr>
<td>severe</td>
</tr>
<tr>
<td>Nausea -</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild</td>
</tr>
<tr>
<td>severe</td>
</tr>
<tr>
<td>Fullness -</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild</td>
</tr>
<tr>
<td>severe</td>
</tr>
<tr>
<td>Dizziness -</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild</td>
</tr>
<tr>
<td>severe</td>
</tr>
<tr>
<td>Perianal soreness -</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild</td>
</tr>
<tr>
<td>severe</td>
</tr>
<tr>
<td>Sleep disturbance -</td>
</tr>
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<td>none</td>
</tr>
<tr>
<td>mild</td>
</tr>
<tr>
<td>severe</td>
</tr>
<tr>
<td>Abdominal cramps -</td>
</tr>
<tr>
<td>none</td>
</tr>
<tr>
<td>mild</td>
</tr>
<tr>
<td>severe</td>
</tr>
</tbody>
</table>
TABLE 12

Description of bowel preparation grading and comparison between PEG and mannitol / Picolax mixture.

<table>
<thead>
<tr>
<th>Description</th>
<th>PEG (n=45)</th>
<th>Mannitol / picolax (n=44)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXCELLENT</td>
<td>43</td>
<td>34</td>
<td>p=0.01*</td>
</tr>
<tr>
<td>GOOD</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>FAIR</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>POOR</td>
<td>2</td>
<td>10</td>
<td></td>
</tr>
</tbody>
</table>

EXCELLENT: no more than small quantities of clear fluid present.

GOOD: small amounts of fluid residue, easily suctioned allowing a completely reliable examination.

FAIR: Enough residue, fluid or solid to prevent a completely reliable examination. (ie. small polyps < 5mm could not be excluded).

POOR: Large amounts of residue present making endoscopic view uninterpretable; additional cleansing required.

* Fisher's exact test
6.6.3 : Results

Forty five patients were randomised to receive PEG-BES and 44 mannitol/Picolax. In the PEG group there were 28 females, and 17 males with an age range of 27-87 years, median 52 years. In the mannitol/Picolax group there were 22 females and 22 males with an age range of 18-73 years, median 49 years. The two patient groups were similar with regard to age, sex, indication for colonoscopy, findings at colonoscopy, history of constipation, laxative administration, and drug history (table 13).

Thirty eight patients (86%) receiving mannitol/Picolax were able to complete their preparation in full, compared to 27 (60%) given PEG/electrolyte, P=0.01. More patients found the taste of mannitol/Picolax acceptable compared to PEG (88% vs 75%).

There were no significant differences between the two preparations in the incidence of nausea, vomiting, fullness, dizziness, abdominal cramps or perianal soreness. When asked if they would be prepared to repeat the preparation 39 patients (86%) in the PEG group said they would compared to 41 (93%) in the mannitol/Picolax group, (NS).

Good or excellent bowel cleansing occurred in significantly more patients receiving PEG/electrolyte (96%) than those allocated mannitol/Picolax (77%), P=0.01. Rescheduling of the procedure and additional cleansing was necessary in 1 patient in the PEG group but 5 receiving mannitol/Picolax. Of the 42 patients who underwent assessment of blood pressure and blood parameters, 20 received PEG and 22 mannitol/Picolax. There was a postural drop in blood pressure (systolic drop of 20mm Hg on standing), raised packed cell volume and raised serum osmolarity in 3 patients receiving mannitol/Picolax preparation. One patient receiving PEG had a postural drop in blood pressure but this was not -
### TABLE 13

Patient details in the PEG and mannitol/Picolax groups.

<table>
<thead>
<tr>
<th></th>
<th>Klean-prep (n=45)</th>
<th>Mannitol/Picolax (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (yrs)</td>
<td>50.9</td>
<td>49.9</td>
</tr>
<tr>
<td>range (yrs)</td>
<td>27-87</td>
<td>18-73</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>female</td>
<td>28</td>
<td>23</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>family history of cancer</td>
<td>27</td>
<td>23</td>
</tr>
<tr>
<td>polyp follow up</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>ulcerative colitis follow up</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>Findings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>polyp</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>cancer</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Regular Laxatives</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>no</td>
<td>42</td>
<td>43</td>
</tr>
<tr>
<td><strong>Stool frequency</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 motions/day</td>
<td>37</td>
<td>36</td>
</tr>
<tr>
<td>&gt;3 motions/day</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>&lt;1 motion/day</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td><strong>Drug history</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ca antagonist</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Codeine</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
- accompanied by any biochemical or haematological abnormalities.

6.6.4 : Discussion

Prior to this study, mannitol/Picolax mixture appeared to be close to the ideal preparation (see Chapter 1), being cheap (approximate cost per patient = £0.60p), easily packaged (2 sachets), well tolerated and effective. This study has confirmed the acceptability of mannitol/Picolax; 91% recorded its taste as pleasant or tolerable and 86% were able to complete it in full; probably a consequence of the relatively small volume and split-administration. However, mannitol/Picolax is clearly inferior as a cleansing agent to two-dose PEG even though the 77% good/excellent cleansing rate compares favourably with preparation by two sachets of Picolax alone (Dakkak et al, 1992). Recently mannitol has been disregarded as bowel preparation because of reports that its use may be associated with a build-up of potentially explosive gases (Bigard et al, 1979). However the risk of combustion is only present if oxygen is used as the insufflating agent (Taylor et al, 1981); at St.Mark's Hospital carbon dioxide insufflation is used routinely during colonoscopy to reduce post-procedure bloating. Of more concern than a risk of combustion was the finding of clinical and biochemical dehydration in 3 patients receiving mannitol/Picolax. All were over 60 years and therefore caution is clearly required when prescribing mannitol/Picolax to elderly patients and those with known cardiac or renal problems.

It was surprising to find that such a high percentage (96%) of patients receiving PEG/electrolyte had excellent or good cleansing as rated by the endoscopist. This was despite the fact that the administration had been split into two doses and that 36% of patients did not complete their preparation in full.
PEG/electrolyte was also well tolerated by the majority of patients, possibly a reflection of the split-administration regime. Rosch et al. have demonstrated that a fractionated administration of PEG/electrolyte mixture is preferred by "in-patients" asked to drink up to 6 litres of solution (Rosch et al, 1987). Using a 4 litre split administration regime in "out-patients", this study has demonstrated only a 6% incidence of vomiting. This compares favourably with studies in which the full 4 litres is drunk continuously (the currently recommended method of administration), where a 10-20% incidence of vomiting has been recorded (Hangartner et al, 1989; DiFebo et al, 1990; Dakkak et al, 1992). Of the 20 patients who both received PEG/electrolyte and were tested for postural changes in blood pressure and changes in blood parameters, only one patient showed an abnormality: a postural drop in blood pressure in a 56 year old man who was also taking anti-hypertensive medication. This low incidence of biochemical or haemodynamic abnormality further emphasises the beneficial safety profile of PEG/electrolyte (Davis et al, 1980).

2.5: Conclusions

Patients with a history of inflammatory bowel disease, diverticular disease and those over 70 years of age have an increased risk of poor preparation. Two-dose PEG-BES oral lavage is superior overall as a cleansing agent to a mannitol/Picolax combination. The split administration regime is likely to explain the high level of patient acceptability to PEG-BES found in this study. For patients intolerant of PEG-BES, mannitol/Picolax is an acceptable alternative as bowel preparation for colonoscopy, provided that carbon dioxide is used as the insufflating agent during the procedure. However, mannitol/Picolax preparation is unsuitable for elderly patients and those with cardiovascular or renal disease.
In considering which preparation to administer for an individual, it is important to consider factors such as age, medical history and previous experience of colonoscopy preparation. The quest for a single ideal bowel preparation may be unrealistic because of the large variation in patient preferences and intestinal physiology.
Chapter 7: Sedation/analgesia for colonoscopy

7.1: Introduction

Ideally sedative and analgesic drugs would be unnecessary for colonoscopy, and patients would be spared the risk of drug side effects and prolonged recovery times. However colonoscopy is an invasive and occasionally painful procedure. Each individual will tolerate the examination differently, and the necessity for sedation/analgesia depends upon a variety of factors such as the patients' colonic anatomy, their pain thresholds and the skill of the endoscopist. Prior to the examination (unless a previous barium enema is available for analysis, see Chapter 5) it is difficult to predict how each patient will tolerate the examination. Some appear calm prior to the procedure but in fact prove technically difficult to intubate and need sedation; others, despite appearing anxious prior to the procedure, require little or no sedation as the examination is completed successfully in a few minutes without discomfort. Most methods of sedation/analgesia for colonoscopy are endoscopist-dependent, involving either the administration of sedative drugs to all patients prior to the examination or selective sedation where drugs are given if considered necessary by the endoscopist. In this Chapter the possible benefits are investigated of patient-controlled analgesia/sedation with nitrous oxide/oxygen mixture comparing its use with that of conventional intravenous opiate/benzodiazepine medication and placebo.
7.4.2: Method

Consecutive patients attending for day-case colonoscopy were invited to take part in the study. Patients were excluded if they had a history of chronic obstructive airways disease, pneumothorax, bowel obstruction or malignant hyperpyrexia. Eight patients who were eligible declined the study: four had previously had a colonoscopy and requested conventional intravenous sedation as before, two were unhappy at having to control their own analgesia during the procedure and two female patients had experienced nausea with nitrous oxide/oxygen analgesia during childbirth.

All patients who entered the study marked their degree of anxiety prior to the procedure on a 100 mm visual analogue scale (0 = totally calm, 100 = extremely anxious). Baseline recordings of pulse, blood pressure and oxygen saturation were made in the left lateral position. Patients were randomised to receive one of three treatment regimes prior to colonoscopy: conventional intravenous sedation (midazolam 2.5 mg i.v., pethidine 50 mg i.v., hyoscine butylbromide 20 mg i.v. plus inhaled air) or nitrous oxide/oxygen inhalation (hyoscine butylbromide 20 mg i.v. plus inhaled Entonox®) or placebo (hyoscine butylbromide 20 mg i.v. plus inhaled air). The examinations were performed by one of two experienced endoscopists (CBW, BPS) with the assistance of specialist endoscopy nurses. All endoscopy personnel including the colonoscopists were unaware of the nature of either the intravenous medication or the gas mixture given. Air and nitrous oxide/oxygen cylinders were covered from view and the inhaled gas was administered via a mouth-piece attachment and demand valve.

®British Oxygen Company, UK.
For the first minute of the procedure patients were instructed to breathe the allocated gas continuously. Additional breaths of gas were taken if discomfort occurred thereafter during intubation. If, in spite of the inhaled gas and medication given, the patient was considered to be in undue discomfort by the colonoscopist, additional boluses of intravenous sedation were given (pethidine 25-50 mg, midazolam 1-2.5 mg) and repeated as required. An independent nurse observer recorded episodes of patient discomfort (subjectively from the patient's appearance and reactions), blood pressure at 5 minute intervals and oxygen saturation as well as the time and extent of the intubation. After the procedure the colonoscopist recorded the technical difficulty of the examination (easy, average, difficult) and the nurse observer scored her impression of the patient's degree of pain during the examination on a 100mm visual analogue scale (0 = no pain, 100 = agony). Patients were kept recumbent in the recovery area, given refreshments and assessed for fitness to leave the unit by the recovery nurse, who was also unaware of the sedation regime used. In declaring fitness to leave the department a return to baseline pulse and blood pressure was mandatory. In addition the verbal and motor responses of patients were assessed and the patient's own perception of return to normality was taken into consideration. The time from the start of the procedure to the point at which the patient was declared fit to leave the department was recorded. Patients then completed a questionnaire regarding their experience of the colonoscopy, asking specifically about nausea, vomiting, paraesthesia, dizziness, drowsiness and headache. One hundred millimetre visual analogue scales were used for patients to estimate their levels of pain (0 = no pain, 100 = agony) and sedation (0 = wide awake, 100 = asleep) during the procedure. The distance in millimetres from the left end-point was taken to indicate the amount of pain or sedation. This technique has been validated for pain (Maxwell, 1978) and previously used in endoscopy studies.
(Quiding & Hagquist, 1983; Hedenbro et al, 1991). Patients were also asked if the degree of pain-relief they received was sufficient and whether they would be prepared to have a future colonoscopy with the same medication regime.

7.4.3: Statistical method and analysis

Patient randomisation was stratified by colonoscopist and a block size of 6 was used to aid concealment of the randomised treatment. Differences in proportions were tested using the chi-squared test, with the Fisher's exact test used for smaller samples. The visual analogue scales and the post procedure recovery time were analysed using the Mann-Whitney test. A P value of ≤ 0.05 was considered significant.

7.4.4: Results

Eighty nine patients were entered into the study. Total colonoscopy was achieved in all patients. The three treatment groups were similar with regard to age, sex, medical and drug history, time taken to complete intubation, findings at endoscopy, patient anxiety before colonoscopy and degree of technical difficulty of the procedure (table 14).

There were fewer episodes of pain and need for extra medication in both the nitrous oxide/oxygen and conventional intravenous sedation groups as compared to the placebo group (figure 7.1) but no difference in these parameters between those receiving nitrous oxide/oxygen inhalation and conventional intravenous sedation. Patients' assessment of experienced pain showed no difference between the conventional intravenous sedation group (median = 10mm) and the nitrous oxide/oxygen group (median =15 mm); P=0.85, Mann-Whitney test. Patients in
TABLE 14
Patient details and endoscopic findings in intravenous sedation, nitrous oxide and placebo groups.

<table>
<thead>
<tr>
<th></th>
<th>Conventional intravenous sedation (n=29)</th>
<th>Nitrous oxide / oxygen inhalation (n=30)</th>
<th>Placebo (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>11</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>female</td>
<td>18</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median + range (years)</td>
<td>42 (17-71)</td>
<td>46 (25-74)</td>
<td>46 (25-71)</td>
</tr>
<tr>
<td><strong>Medical History</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
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<td>4</td>
<td>3</td>
</tr>
<tr>
<td>respiratory</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>other major</td>
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<td>0</td>
<td>0</td>
</tr>
<tr>
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<td>24</td>
<td>26</td>
</tr>
<tr>
<td><strong>Drug History</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
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<td>3</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>respiratory</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>other</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>none</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td><strong>Time to complete intubation</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>median (mins.)</td>
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<td>13</td>
<td>12</td>
</tr>
<tr>
<td><strong>Findings at colonoscopy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>24</td>
<td>27</td>
<td>21</td>
</tr>
<tr>
<td>polyp</td>
<td>2</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>colitis</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Patient anxiety</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median + range (mm)</td>
<td>45 (14-98)</td>
<td>42 (18-83)</td>
<td>40 (10-100)</td>
</tr>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
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<td>4</td>
</tr>
<tr>
<td>average</td>
<td>22</td>
<td>21</td>
<td>21</td>
</tr>
<tr>
<td>difficult</td>
<td>6</td>
<td>7</td>
<td>5</td>
</tr>
</tbody>
</table>
FIGURE 7.1

Column charts demonstrating observed pain episodes and need for additional intravenous sedation in the three study groups

≥ 2 pain episodes

extra iv. medication given

* Fisher's exact test
FIGURE 7.2
Box-whisker plot of patients’ perception of pain during colonoscopy

10 cm Visual analogue scale

Intravenous sedation
Nitrous oxide / oxygen inhalation
Placebo

NS (Mann-Whitney)  p = 0.05 (Mann-Whitney)
both of these groups fared better than patients receiving placebo (median = 30mm); each gave $P=0.05$, Mann-Whitney (figure 7.2). There was poor correlation between the nurse observer's assessment of patient pain and patient's own perception of pain (figure 7.3). In a substantial minority of cases there was a large discrepancy (> 40mm) between observed and perceived pain (figure 7.4).

There was no correlation between patient anxiety prior to the examination and patients' own perception of pain during the procedure, as shown by the random scatter in figure 7.5 (Spearman's rank correlation coefficient = 0.08).

Patients in the conventional intravenous sedation group (median = 56mm) experienced more sedation than those in either the nitrous oxide/oxygen (median = 20mm, $P=0.0009$, Mann-Whitney) or placebo groups (median=5mm, $P<0.0001$) (figure 7.6). There was a trend towards a higher degree of experienced sedation in the nitrous oxide/oxygen group as compared to placebo, though this did not reach statistical significance, ($P=0.06$, Mann-Whitney)

Six patients given conventional intravenous sedation developed oxygen desaturation (saturation < 90% for > 1 minute) requiring supplemental oxygen compared to no patients in the nitrous oxide/oxygen group ($P=0.01$, Fisher's exact test). Four patients receiving conventional intravenous sedation had significant hypotensive episodes (systolic drop in blood pressure of > 20mm Hg to < 100mm Hg, associated with sweating and pallor) as did 2 with nitrous oxide/oxygen inhalation and 4 with placebo (NS).

Overall a similar side-effect profile for nausea, vomiting, paraesthesia, drowsiness dizziness and headache was reported by patients in all 3 study groups (table 15). Five patients (3 in the placebo group, 1 in the nitrous oxide group and 1 in the conventional sedation group) felt the level of pain relief they had received was insufficient and were not prepared to have a future examination with the same medication regime.
Scatter plot comparing the nurse observer's estimation of patient pain to the patients' own perception of pain during colonoscopy.
FIGURE 7.4

Histogram of difference between nurse and patient pain score; note the substantial minority of cases where the difference is > 40mm.

Percentage of the total number of patients.

Difference between nurse and patient pain score.
Scatter plot of patient anxiety scores prior to colonoscopy compared to patients' perception of pain during the examination; $r = 0.08$. 

Patient anxiety scores (1-100mm visual analogue scale).
FIGURE 7.6

Box-whisker plots showing patients’ perception of sedation during colonoscopy in the three patient groups.

10 cm
Visual Analogue Scale

Intravenous sedation
Nitrous oxide / oxygen inhalation
Placebo

p = 0.0009
(Mann-Whitney)
TABLE 15

Side effects reported in the 3 study groups

<table>
<thead>
<tr>
<th></th>
<th>Conventional intravenous premedication (n=29) *</th>
<th>Nitrous oxide / oxygen inhalation (n=30)</th>
<th>Placebo (n=30) †</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nausea</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>20</td>
<td>27</td>
<td>25</td>
</tr>
<tr>
<td>mild</td>
<td>5</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>marked</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Vomiting</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>25</td>
<td>30</td>
<td>28</td>
</tr>
<tr>
<td>mild</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>marked</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Headache</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>21</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>mild</td>
<td>4</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>marked</td>
<td>1</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td><strong>Numbness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>21</td>
<td>24</td>
<td>25</td>
</tr>
<tr>
<td>mild</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>marked</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Dizziness</strong></td>
<td></td>
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</tr>
<tr>
<td>none</td>
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<td>19</td>
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<tr>
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</tr>
<tr>
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<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>Drowsiness</strong></td>
<td></td>
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<td>5</td>
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<td>20</td>
</tr>
<tr>
<td>mild</td>
<td>12</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>marked</td>
<td>9</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

* 3 patient records incomplete
† 1 patient record incomplete
FIGURE 7.7

Box-whisker plot showing the duration of stay within the recovery area for patients in the three study groups

Time (mins.)

Intravenous sedation

Nitrous oxide / oxygen inhalation

Placebo

p<0.001 (Mann-Whitney)
Duration of stay within the recovery area (figure 7.7) was significantly greater in the group receiving conventional intravenous sedation, (median = 60mins) as compared to the nitrous oxide/oxygen group (median = 32 minutes, \( P<0.001 \) Mann-Whitney) and placebo group (median = 36 minutes, \( P=0.002 \) Mann- Whitney).

**7.4.5 : Discussion**

This study has assessed three approaches to sedation/analgesia for colonoscopy. The placebo group in this study effectively received selective sedation i.e. the examination was commenced without medication and sedative drugs were given if considered necessary by the endoscopist. This strategy resulted overall, in higher patient pain scores than either nitrous oxide inhalation or conventional intravenous premedication, despite the fact that 57% of patients in this group were judged to require no sedation/analgesia at all by the endoscopist. Whilst a minor degree of discomfort for the patient may be acceptable and act as a useful warning of loop formation or overdistension, inadequate analgesia risks patient dissatisfaction and non-compliance with future examinations. Selective sedation/analgesia depends upon the endoscopist being able to recognise patient discomfort. However, this study further emphasises that endoscopy staff appear to be unable to assess patient discomfort. Furthermore anxiety prior to the procedure does not correlate with the degree of pain the patient subsequently experiences and therefore is not a useful guide in deciding upon a sedation strategy for the individual.

The results of this study, in keeping with the findings of Lindblom et al., have shown that nitrous oxide/oxygen inhalation provides equivalent analgesia to conventional intravenous sedation whilst producing less sedation and shorter
recovery times (Lindblom et al, 1994). Patient pain scores were lower in the nitrous oxide and conventional sedation groups compared to placebo however comparisons of observed pain episodes and need for additional analgesia must be interpreted with caution particularly in light of the finding that the correlation between observed pain and experienced pain is poor.

Nitrous oxide/oxygen "on demand" allows patients to self-administer analgesia immediately on experiencing discomfort, therefore not only targeting pain relief appropriately but also reassuring patients that they can actively reduce discomfort if necessary. In addition the endoscopist can pre-empt discomfort by asking the patient to take extra breaths of gas prior to the negotiation of difficult bends. Over-sedation is not possible with nitrous oxide patient-controlled analgesia as, if the patient becomes drowsy, the mouth piece falls away from the face, allowing excretion of the gas and recovery within a few minutes. The reduced sedation after nitrous oxide/oxygen inhalation was demonstrated from the patients' responses and by the greatly reduced post-procedure recovery time compared to conventional intravenous sedation. Reducing the recovery time lessens the burden on nursing time and has clear benefits to the logistics of running a busy unit. In addition patients can be told the results of the examination soon after the procedure, in many cases effectively saving the need for a further out-patient appointment. The question of whether or not patients can drive soon after nitrous oxide/oxygen inhalation requires clarification. The current recommendation in the United Kingdom is that patients should not drive for 12 hours after administration. This seems excessively cautious given the pharmacokinetics of nitrous oxide and the rapid recovery observed after inhalation has ceased.

No patient in this study experienced serious cardiopulmonary side effects. However 6 patients receiving conventional intravenous sedation developed
oxygen desaturation requiring supplemental oxygen, compared to none in the nitrous oxide/oxygen group. These findings further suggest that nitrous oxide/oxygen inhalation has no appreciable effects on the cardiopulmonary system so that vital signs are unaffected by its use and monitoring is unnecessary (Stewart et al, 1986); indeed patients are effectively receiving supplemental 50% oxygen. This is in contrast to the use of conventional benzodiazepine/opiate sedation where electronic monitoring and supplemental oxygen are often desirable (Bell et al, 1989) and oxygen desaturation leading to cardiac arrhythmias and even cardiac arrest is a recognised complication (Simon et al, 1991). Hypotension was seen in all groups studied and may occur as a result of drug administration, or as a vagally mediated response to endoscope insertion (Herman, 1993).

The side effect profile of both nitrous oxide/oxygen inhalation and conventional intravenous sedation was similar. Overall, 94% of patients were satisfied with the sedation/analgesia they received and would be prepared to have a future examination with the same medication. This high level of acceptability may be a reflection of patient satisfaction with the procedure as a whole, rather than an informed choice regarding methods of sedation/analgesia; most patients had not undergone colonoscopy before and therefore could not compare a previous experience of sedation/analgesia.

Although nitrous oxide/oxygen analgesia is established as safe for patients, fears have been raised about the long-term risks of nitrous oxide exposure for medical and dental personnel. The safety of nitrous oxide during the first trimester of pregnancy has not been clearly determined. Foetal toxicity (gestational defects and spontaneous abortion) has been demonstrated with long-term, high-concentration exposure (Cohen et al, 1980). Low concentration or trace exposure however has not revealed any teratogenic effects (Holocomb et al,
1976; Rosenberg & Vanittinen, 1978; Vieira et al, 1980). Chronic exposure to nitrous oxide can cause impairment of the vitamin B12-dependent enzyme methionine synthetase, which may result in bone marrow depression, megaloblastic changes and neurologic dysfunction (Nunn, 1987; Koblin et al, 1982). These problems have only been documented in abusers of nitrous oxide or in medical personnel chronically exposed to high concentrations of nitrous oxide, as used for anaesthesia. There should be no hazard in a well-ventilated endoscopy unit with intermittent use of 50% nitrous oxide, but regular monitoring of atmospheric gas concentrations and installation of a scavenging device (Dula et al, 1983) would nonetheless be wise precautions if routine adoption was considered.

7.5: Conclusions

Patient anxiety prior to colonoscopy appears to be a poor predictor of the amount of pain subsequently experienced during the examination. Endoscopy personnel are poor judges of patient pain during colonoscopy. Offering selective sedation/analgesia (placebo group) for colonoscopy results in greater discomfort as judged by the patient compared to conventional intravenous premedication or nitrous oxide inhalation. Nitrous oxide/oxygen inhalation provides equivalent analgesia but less sedation than conventional intravenous sedation (pethidine 50 mg, midazolam 2.5 mg) and results in significantly shorter recovery times. Use of nitrous oxide inhalation for colonoscopy is safe, and the added precautions of routine electronic monitoring and supplemental oxygen do not appear to be necessary.
Chapter 8: Is intravenous premedication with anti-spasmodic advantageous to colonoscopy?

8.1: Introduction

Some endoscopists administer anti-spasmodic premedication to improve visualisation of the mucosal surface during colonoscopy and perhaps to ease colonoscope insertion (Macrae et al, 1983). This has been standard practice at St.Mark's Hospital since 1970 using hyoscine n-butyl bromide (Buscopan) given as a bolus after initial, titrated sedative/analgesic injections. However, routine administration of anti-spasmodic is controversial as previous studies have failed to show a benefit with the use of such drugs (Bond et al, 1974; Waxman et al, 1991). Moreover many endoscopists consider that reduced colonic muscle tone makes insertion more difficult, a view supported by a study of intramuscular glucagon (Norfleet, 1974). In this Chapter a prospective study is described which investigates the effects of anti-spasmodic premedication on the performance of colonoscopy.

8.2: Method

Consecutive patients attending for day-case colonoscopy were entered into the study excluding those with a previous history of glaucoma, obstructive uropathy, autonomic dysfunction, unstable angina or tachyarrhythmias. Patients already taking anti-cholinergic medications or who gave a history of allergy to such drugs were also excluded. Informed consent was obtained and no patient refused to

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9Boehringer Ingelheim Ltd, Bracknell, Berks. England
take part in the study. At the beginning of the procedure patients were placed in the left lateral position and intravenous access secured. Patients were then sedated with titrated doses of pethidine (0.7mg/kg) and midazolam (0.03mg/kg). They also received either hyoscine (1ml = 20mg hyoscine-n-butyl bromide) or placebo (1ml of water for injection) by slow intravenous injection from pre-filled syringes. Olympus CF10 colonoscopes were used for all procedures which were performed by a single experienced endoscopist (BPS) blinded to the premedication given. Patients were observed by a trained nurse and monitored using pulse oximetry. When the colonoscope tip had been inserted into the rectum an endoscopy nurse began timing the procedure. A record of the intubation time to the caecum (clear identification of the ileocaecal valve) and withdrawal time were recorded. After the procedure the endoscopist rated the degree of observed colonic spasm (very relaxed-very spastic) and the difficulty of the procedure (very easy-very difficult) using 100mm visual analogue scales. Patients were given refreshments in the recovery area and when clinically considered fit to be discharged were asked to rate their degree of experienced pain during the examination using a 100 mm visual analogue scale (no pain-agony). All visual analogue scales were scored by measuring the distance in millimetres from the left end point to the mark on the scale line. Basic patient details, findings at colonoscopy and quality of bowel preparation (good, adequate, poor) were also recorded.

8.3 : Statistical analysis

Patients were randomised in block sizes of 3. The Mann-Whitney test was used to compare intubation time, total procedure time, degree of colonic spasm
and difficulty of the procedure between the two study groups. A P value of < 0.05 was considered significant.

**8.4 Results**

Twenty nine patients were randomised to receive hyoscine and 27 placebo. Both study groups were similar with regard to age, sex, indication for colonoscopy, findings at colonoscopy, total sedation requirements and quality of preparation, table 16. Total colonoscopy was achieved in all study patients.

The time taken to complete intubation was less in those patients premedicated with hyoscine (median time = 13mins., range 5-22) compared to those receiving placebo (median = 17.5mins., range 6-32mins), P=0.045. The time taken to examine the colon on withdrawal however was similar in the two study groups; median withdrawal time was 11.5mins, range 6-32mins and 12mins range 6-20mins., in the hyoscine and placebo groups respectively. Scores, by the endoscopist, for the degree of colonic spasm (median hyoscine group = 19mm, range 3-80mm; median placebo group = 53.5, range 6-93, P=0.01) and difficulty of the procedure (median hyoscine group = 23.5mm, range 6-78mm; median placebo group = 50, range 12-89mm, P<0.05) were lower in those patients receiving hyoscine compared to those given placebo. There was no significant difference in patient pain scores between the two study groups (median hyoscine group = 14.5mm, range 0-50, median placebo group = 22.5, range 0-76mm). Apart from 4 episodes of transient oxygen desaturation, 2 in the hyoscine group and 2 in the placebo group there were no complications in the study. No side effects to the medication were reported.
### TABLE 16
Patient details and endoscopic findings in the hyoscine and placebo groups.

<table>
<thead>
<tr>
<th></th>
<th>Hyoscine (n=29)</th>
<th>Placebo (n=27)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (yrs.)</td>
<td>44</td>
<td>44.9</td>
</tr>
<tr>
<td>range (yrs)</td>
<td>25-69</td>
<td>29-73</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>female</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td><strong>Indication</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>family history cancer</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>polyp follow - up</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>change bowel habit</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>rectal bleeding</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Sedation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>midazolam (median mg)</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>pethidine (median mg)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td><strong>Findings at colonoscopy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>17</td>
<td>20</td>
</tr>
<tr>
<td>Polyp(s)</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Diverticular disease</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td><strong>Preparation quality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>good</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>adequate</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>poor (not preventing total colonoscopy)</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
8.5 : Discussion

This study has demonstrated that premedication with intravenous hyoscine n-butyl bromide reduces colonic spasm, colonoscope insertion times and the endoscopist's subjective impression of the difficulty of the procedure. Hyoscine n-butyl bromide was chosen as the study drug because of its rapid onset of action when given intravenously (Guignard et al, 1968), its low cost\(^{10}\), and its proven value in preventing bowel spasm during barium enema (Bartram, 1986), small bowel enema (Halligan et al, 1994) and sphincter of Oddi cannulation (Hannigan et al, 1982). Moreover, the duration of action of hyoscine, 15-30 minutes (Guignard et al, 1968) usually means adequate colonic relaxation is provided during insertion and withdrawal of the colonoscope. This study represents the first clinical trial of hyoscine as a premedication for colonoscopy. Previous similar studies from the USA (where "Buscopan" is not licensed) have utilised other drugs. Norfleet compared the use of intramuscular glucagon to placebo and found that there was no difference in either the endoscopist's estimation of the degree of colonic spasm or procedure difficulty between those with and without glucagon (Norfleet, 1978). He also found that total procedure time was prolonged in those patients receiving glucagon and concluded that an interaction between sedative drugs and glucagon might be responsible in making the procedure more difficult, possibly by reducing the effectiveness of the study drug. Bond et al. assessed the use of the anticholinergic agent dicyclomine hydrochloride administered as premedication for colonoscopy by intramuscular injection (Bond et al, 1974). Motility scores, difficulty of the procedure and total procedure times were also no different from placebo. However in both these studies the

\(^{10}\)Hyoscine n-butyl bromide 1ml (20mg) for injection, approx. cost 20p, British National Formulary 1994.
intramuscular method of administration was used which may have slowed any anti-spasmodic effect, particularly during colonoscope insertion. Most recently, the use of intravenous atropine as premedication for colonoscopy has been assessed in a double-blind, placebo-controlled trial (Waxman et al, 1991). Ease of the procedure, and total procedure time were found to be similar between atropine and placebo groups, but colonoscope insertion times were not reported.

In this study patient pain scores during colonoscopy were similar in both hyoscine and placebo groups. However, patients were not questioned about post-colonoscopy pain. It is possible that without anti-spasmodic more air may be insufflated during intubation in order to counter spasm, contributing to the distension and discomfort reported by many patients after colonoscopy (Hussein et al, 1984).

A potential advantage of premedication with hyoscine is that its peripheral anti-cholinergic effects may help to prevent vasovagal episodes during endoscopy (Macrae et al, 1983); none were seen in either group in this study. Hyoscine n-butyl bromide is also a quaternary ammonium derivative of hyoscine and does not cross the blood brain barrier readily. Therefore central sedative effects are minimal and driving is not contraindicated after its use, unless the patient experiences drowsiness (Reynolds, 1989).

8.6: Conclusions

Intravenous premedication with the anti-spasmodic hyoscine n-butyl bromide (Buscopan) significantly reduces colonic spasm, colonoscopy insertion times and the endoscopist's impression of procedure difficulty compared to placebo. The benefits of premedication with hyoscine and its excellent safety profile suggest that it can be used routinely for colonoscopy.
Chapter 9: Evaluation of intravenous anti-spasmodic and patient-controlled analgesia for screening flexible sigmoidoscopy.

9.1: Introduction

Flexible sigmoidoscopy is a safe procedure (Marks et al, 1987) and current opinion suggests that it is the most practical method of screening for colorectal cancer (Atkin et al, 1993); approximately 55% of neoplastic lesions occur in the rectum and sigmoid colon (American Cancer Society, 1980) and are therefore within the reach of the flexible sigmoidoscope. The American Cancer Society currently recommends screening by flexible sigmoidoscopy every 3-5 years from age 50 (Levin & Murphy, 1992). However, the procedure is not without its limitations; difficulty may be experienced in passing the endoscope if diverticular disease, pelvic adhesions or colonic spasm are encountered and patients may experience discomfort due to stretching of the sigmoid mesocolon or sigmoid adhesions. To maintain compliance with repeated screening it is essential that the procedure be acceptable to the patient, involve a minimum of discomfort, and be quick and accurate.

9.1.1: Sedation/analgesia for screening flexible sigmoidoscopy

Flexible sigmoidoscopy, by definition, is a less invasive procedure than colonoscopy, can be performed quicker and involves less discomfort for the patient. "Heavy" intravenous sedation/analgesia with the risk of drug side effects, oversedation and prolonged recovery times is clearly inappropriate in all but a few very anxious patients. However, Fox et al. have shown that flexible sigmoidoscopy is a stressful procedure and one where endoscopy staff tend to
underestimate the distress and pain experienced by patients (Fox et al, 1987). Pain experienced during sigmoidoscopy was found to be the major factor in determining patients' perceptions of the procedure and more than half of the patients in Fox's study would have preferred some form of analgesia. In Chapter 7, patient-controlled analgesia with inhaled nitrous oxide/oxygen mixture was shown to provide effective, short-acting analgesia for colonoscopy, without the risk of inducing prolonged or deep sedation. A similar approach might be beneficial for flexible sigmoidoscopy.

9.1.2 : Anti-spasmodic premedication for flexible sigmoidoscopy

In Chapter 8, premedication with the anti-spasmodic hyoscine n-butyl bromide (Buscopan) was shown to be of benefit during colonoscopy. Reducing muscle activity (that may be increased following preparation with a phosphate enema (Finlay et al, 1988) with anti-spasmodic premedication may also be of benefit for flexible sigmoidoscopy by facilitating intubation, reducing patient discomfort and allowing a more accurate examination. One previous study has assessed the possible benefits of glucagon premedication for flexible sigmoidoscopy (Foster et al, 1981). In that study all procedures were performed by hospital gastroenterologists in an out-patient setting. No benefit in the ease of the procedure, total duration of the procedure or patient discomfort, was found with intravenous glucagon compared to placebo.

9.2.2 : Aim

The purpose of this study was to ascertain whether the ease and acceptability of screening flexible sigmoidoscopy in a primary health care setting could be
improved by premedication with the smooth-muscle relaxant hyoscine n-butyl-bromide and by offering patient-controlled analgesia with inhaled nitrous oxide/oxygen mixture.

9.2.2 : Method

In a double blind placebo-controlled study, asymptomatic average risk men and women aged between 55-75yrs attending for cancer screening flexible sigmoidoscopy were randomly allocated to one of three treatment arms; hyoscine (hyoscine n-butyl-bromide 20 mg i.v. + "on-demand" inhaled oxygen), nitrous oxide (sterile water injection + "on demand", inhaled 50/50, nitrous oxide/oxygen mixture) or placebo (sterile water injection + "on-demand", inhaled oxygen). Individuals were excluded if they had a previous history of chronic obstructive airways disease, pneumothorax, bowel obstruction, malignant hyperpyrexia, glaucoma, obstructive uropathy, autonomic dysfunction, unstable angina or tachyarrhythmias. In addition any person already taking anti-cholinergic medications or who gave a history of allergy to such drugs or nitrous oxide was excluded from the study. Written consent was obtained after an explanation of the procedure and no subject refused to take part in the study. Screenees were prepared with a single Fletcher's phosphate enema\textsuperscript{11}. If this proved to be unsuccessful, either at the time of administration or subsequently at sigmoidoscopy, a further enema was given. Just prior to the procedure subjects were briefly instructed in the use of the gas which was administered via a mouth-piece attachment and demand valve. They were told that slight discomfort might occur during sigmoidoscopy but to use the gas on-demand if they felt it was

\textsuperscript{11}Pharmax Ltd, Bexley, Kent, UK.
necessary. Oxygen and nitrous oxide cylinders were covered from the view of screenees and endoscopy staff. After placing the subject in the left lateral position the intravenous injection was administered as a slow bolus injection from pre-filled syringes. Electronic monitoring, though available, was not used routinely; however an endoscopy assistant observed the screenees throughout the procedure (and immediate post-procedure recovery period) for evidence of pallor, sweating or distress. All procedures were performed by one general practitioner (previous experience of 50 examinations) using an Olympus CF10 colonoscope. The maximum depth of insertion, endoscopic findings and total duration of the procedure were recorded. If the bowel preparation was adequate and the individual appeared to be tolerating the procedure well, the examination was continued beyond the usual 60cm limit of insertion for flexible sigmoidoscopy. Polyps were removed at the time of sigmoidoscopy. After the procedure screenees received refreshments and were then asked to complete a questionnaire regarding their experience of the sigmoidoscopy. Subjects scored their degree of pain during sigmoidoscopy on a 100mm visual analogue scale (0 = no pain, 100 = agony). The distance in millimetres from the left end point was taken to indicate the amount of pain experienced. Subjects were also asked if they felt their pain relief had been sufficient and to rate (none, a little, a lot) the following side effects :- headache, nausea, vomiting, dizziness, drowsiness, blurred vision, dry mouth and palpitations. Finally individuals were asked whether or not they would be prepared to repeat the procedure if it were necessary again in the future.
9.2.3 : Statistical analysis

Screenees were randomised using block sizes of 3. Depth of insertion, duration of the procedure and individuals' pain scores were compared between the groups using the Mann-Whitney test. A P value of < 0.05 was considered significant.

9.2.4 : Results

A total of 131 screenees who met the entry criteria were entered consecutively into the trial. Forty received hyoscine, 48 nitrous oxide and 43 placebo. There were no significant differences between the profiles of the screenees in the 3 study groups. Subject details and endoscopic findings are displayed in table 17.

There was no difference between the study groups with regard to the maximum depth of insertion; hyoscine median depth = 60cm, range 25-100cm, nitrous oxide median = 60cm, range 35-100cm, placebo median = 60cm, range 30-90cm. Excluding all examinations involving polypectomy, the time taken to complete the procedure was significantly less in the hyoscine group (median duration = 12.5 min, range 5-23 min) than the placebo group (median duration = 18 min, range 10-26 min.), P=0.0008, Mann-Whitney, (figure 9.1). There was no significant difference in procedure time comparing the nitrous oxide group (median duration = 15 min., range 6-31 min.) to placebo.

During intubation 2 subjects (1 receiving nitrous oxide, 1 placebo) were noted to become pale and sweaty. Electronic monitoring was implemented and vasovagal reactions confirmed (systolic blood pressure < 100mmHg + bradycardia < 60 beats per minute). In both individuals temporary cessation of the examination resulted in a normalisation of cardiovascular parameters and allowed the procedure to be completed.
<table>
<thead>
<tr>
<th></th>
<th>hyoscine (n=40)</th>
<th>nitrous oxide (n=48)</th>
<th>placebo (n=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean (years)</td>
<td>63</td>
<td>63.5</td>
<td>64.3</td>
</tr>
<tr>
<td>range (years)</td>
<td>46-74</td>
<td>53-75</td>
<td>55-75</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>22 (55%)</td>
<td>30 (62%)</td>
<td>27 (63%)</td>
</tr>
<tr>
<td>female</td>
<td>18 (45%)</td>
<td>18 (38%)</td>
<td>16 (37%)</td>
</tr>
<tr>
<td>No. patients undergoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>polypectomy</td>
<td>8 (20%)</td>
<td>19 (39%)</td>
<td>15 (34%)</td>
</tr>
<tr>
<td>Total no. polyps resected</td>
<td>8</td>
<td>29</td>
<td>27</td>
</tr>
<tr>
<td>No. patients with moderate/severe diverticular disease</td>
<td>5 (13%)</td>
<td>6 (13%)</td>
<td>5 (12%)</td>
</tr>
</tbody>
</table>
FIGURE 9.1

Data plot showing duration of procedure in the three study groups, bar is median value

$p=0.0008^*$

NS* NS*

duration of procedure (minutes)

hyoscine nitrous oxide placebo

* Mann-Whitney test
FIGURE 9.2
Data plot of patients' pain scores during flexible sigmoidoscopy; bar is median value

100mm visual analogue pain scale

* Mann-Whitney test
Overall 53% of screenees used the on-demand gas (hyoscine group 23, nitrous oxide group 23, placebo group 24). Comparing pain scores in those individuals who used the gas, significantly lower scores were obtained in the nitrous oxide group (median = 10 mm, range 0-83) compared to placebo group (median = 30 mm, range 4-77mm), P=0.045 by Mann-Whitney, (figure 9.2). There was no significant difference in pain scores between the hyoscine (median = 24.5 mm, range 0-100mm) and placebo groups. Eleven (8%) screenees reported that pain relief had not been sufficient, 3 receiving hyoscine, 3 nitrous oxide and 5 placebo. Only 2 people who used inhalation considered it difficult to use. Seven (5%) screenees, 3 receiving hyoscine, 1 nitrous oxide and 3 placebo were not prepared to repeat the examination in the future, without additional sedation/analgesia.

No individuals in the study reported significant side effects and all were discharged shortly after the procedure.

9.2.5 : Discussion

In this study the possible benefits for the screenee and endoscopist of premedication with the smooth muscle relaxant hyoscine n-butyl-bromide and of patient-controlled analgesia with inhaled nitrous oxide/oxygen mixture have been assessed. The study was deliberately conducted in a primary health care setting (where most benefit from anti-spasmodic and patient-controlled analgesia might be expected), with an endoscopist of intermediate experience, rather than in a specialist centre with an expert endoscopist (Foster et al, 1981). Due to availability, a colonoscope was used for all examinations and therefore it was decided to examine as much of the distal colon as possible, often inserting the colonoscope beyond the usual 60cm limit of a standard screening flexible
sigmoidoscope. The colonoscope was inserted on average 60cm in all patient groups and care was taken on withdrawal to examine behind every haustral fold. This explains the relatively long total procedure times, even after excluding those patients who underwent polypectomy. Total procedure time was significantly less in those patients premedicated with hyoscine n-butyl-bromide and this may be explained by the reduction in colonic tone and spasm afforded by hyoscine, allowing more accurate and rapid steering during intubation and easier visualisation of the colonic wall during withdrawal. There were no significant local or systemic side effects associated with the use of hyoscine. Two patients were observed to develop vasovagal reactions but neither of these received hyoscine; it has been suggested that anti-cholinergic drugs such as hyoscine may be protective against vasovagal episodes at endoscopy (Macrae et al, 1983).

Over half of the patients in this study experienced sufficient discomfort to use the "on-demand" gas. Several previous studies have also reported a high incidence of discomfort during flexible sigmoidoscopy (Fox et al, 1987; Rex et al, 1990; Schuman et al, 1988). Inhalation of nitrous oxide/oxygen mixture provided analgesia without heavy sedation and resulted in significantly lower pain scores in those patients who used it compared to placebo. Most subjects who used the gas took breaths during passage of the colonoscope through the mid-sigmoid region. Once the mid-sigmoid was negotiated however they rarely took further breaths and all patients in this study were able to leave the endoscopy unit shortly after completion of the procedure. Only 2 individuals found the patient-controlled "on-demand" system difficult to use. Use of a mouth-piece attachment to deliver the gas rather than a mask makes the system (in our experience) easier to use, less "claustrophobic" and generally preferred by patients. The use of nitrous oxide inhalation was not associated with any increase in side effects compared to placebo. One screenee randomised to the nitrous
oxide group developed a vasovagal reaction during intubation but this occurred prior to breathing the gas.

4.3 : Conclusions

Patient-controlled analgesia with inhaled nitrous oxide/oxygen mixture is safe, easy to use and appears to reduce patient discomfort compared to placebo at screening flexible sigmoidoscopy, when performed by an endoscopist of intermediate experience. In this study premedication with hyoscine n-butyl bromide reduced procedure time for screening flexible sigmoidoscopy compared to placebo but did not reduce patient discomfort.
Chapter 10: Magnetic imaging of colonoscopy

10.1: Introduction

Frustrated by the restrictions imposed by the use of fluoroscopy, an alternative method of imaging the colonoscope was sought, utilising low power magnetic fields. Two similar systems have been independently developed, one by the Departments of Engineering and Computing at Imperial College in collaboration with St.Mark's Hospital (Williams et al, 1993), the other by the Department of Engineering at Sheffield University in collaboration with The Ipswich Hospital (Bladen et al, 1993a).

10.2: The principle of the method.

The system operates by determining the position and orientation of discrete points along the colonoscope and uses this information to produce an image of the colonoscope configuration on a display unit (Bladen et al, 1993b). Three sets of "generator coils" situated beneath the endoscopy table, sequentially produce pulsed, low-strength (10KHz) magnetic fields external to the patient (figure 10.1). These fields are detected by a series of 15 sensor coils, positioned at 12cm intervals along the length of a catheter that is inserted down the biopsy channel of the colonoscope. In response to each magnetic pulse the sensor coils produce an electrical current that is proportional in strength to the distance from the generator coil. Thus for each point along the length of the colonoscope, three distances, (from each of the generator assemblies to the sensor coil) can be calculated. These distances can be considered as the radii of three spheres, the intersection of which gives the 3-dimensional (x,y,z) location of the sensor coil.
FIGURE 10.1
Schematic representation of magnetic imaging system

sensor coils in catheter

magnetic field generators

patient couch

Display unit

Graphics unit

Point location algorithm

Signal processor

Field generation driver
The exact mathematics involved in the point-location algorithm of this system are beyond the scope of this thesis but the basic principle of point location (triangulation) is shown in figure 10.2. Once the position of the sensor coils has been calculated a smooth curve can be fitted through each of the calculated points. A computer graphics image of the colonoscope shaft is thus built-up and displayed on a computer monitor. A three-dimensional effect is created by differential grey shading i.e. the further away the colonoscope from the viewer, the darker the shading (figure 10.3). The image is updated, with recalculation of the position of each of the sensor coils every 0.2 seconds, so that the system is effectively real-time on the viewing monitor. The entire procedure can be recorded on computer disk (approximately 6 entire patient records can be stored on one standard floppy disk) and replayed for teaching or research purposes in a "Windows" based viewing program. The viewing program allows measurements to be taken between points of interest and snap-shot images to be imported into other "Windows" based graphics programmes.

10.3 : Accuracy of the system

Initial testing involved analysis of a single sensor coil in a 40cm by 40cm plastic grid placed above the generator coil assembly. The three-dimensional (x,y,z) position of the coil was calculated by the imaging system and compared to the actual position on the grid. In each grid location the sensor coil was positioned in 6 different orientations and calculations taken. Throughout the field range of the grid and regardless of the orientation of the coil, the imager was accurate in single point location to within ± 0.5cm. Having achieved satisfactory

12Microsoft Corporation, USA.
Location of an individual point using triangulation: the point $P$ lies at the intersection of the radii of the three theoretical spheres generated around coils $(0,1,2)$. 
FIGURE 10.3

AP view of the colonoscope using magnetic imaging system. The colonoscope shaft is shaded differentially to give depth; white nearest the viewer, black farthest away. Red crosses correspond to the positions of the sensor coils.
accuracy with single point location, the ability of the system to locate accurately a series of points and connect them with a smooth curve was evaluated. To do this a plastic catheter containing sensor coils at 12 cm intervals was fixed (in a shape) within the plastic grid. Direct measurements were taken to the nearest millimetre between fixed points (sensor coils) on the catheter, using a pair of dividers. These "actual" measurements were compared to similar measurements taken from an image generated by the imaging system (using a software measurement programme). Examples of simple, 2-dimensional measurements (with the entire catheter flat) are shown in figures 10.4 and 10.5. Measurements from a more complex 3-dimensional image are shown in figure 10.6. In total 4 flat shapes (16 measurements) and 10, 3-dimensional shapes (48 measurements) were evaluated. All imager measurements were within ± 0.6cm of the actual values.

Having assessed the imaging system in laboratory conditions, similar tests were carried out in the Endoscopy Unit. It was expected that there might be a reduction in accuracy in the Endoscopy room because of interference to the magnetic fields from the Endoscopy equipment. The imaging system will not work if the generator coils are in close proximity to large amounts of metal because of interference to magnetic field generation, therefore a wooden bed with a sliding tray to accommodate the generator coil assembly was constructed. The plastic grid was again utilised to hold the catheter containing the sensor coils in a variety of 2 and 3 dimensional shapes on the table in the Unit. The degree of accuracy of the system was found to be unchanged from that found in the laboratory.

Next the catheter was passed down the biopsy channel of a Pentax EC 3801L video colonoscope. The colonoscope was positioned in a variety of common looping states; "N", alpha, reverse alpha, gamma; (Williams & Cotton, 1990).
FIGURE 10.4

Magnetic imaging system view of catheter in a 2-D shape: actual vs imager measurements

<table>
<thead>
<tr>
<th>measurement (from sensors)</th>
<th>imager (cm)</th>
<th>actual (cm)</th>
<th>difference (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>24</td>
<td>23.5</td>
<td>0.5</td>
</tr>
<tr>
<td>1-4</td>
<td>23</td>
<td>23.4</td>
<td>0.4</td>
</tr>
<tr>
<td>3-6</td>
<td>24</td>
<td>23.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>
FIGURE 10.5

Magnetic imaging system view of catheter in a 2-D shape: actual vs imager measurements

<table>
<thead>
<tr>
<th>measurement (sensor-sensor)</th>
<th>actual (cm)</th>
<th>imager (cm)</th>
<th>difference (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>11.5</td>
<td>11.3</td>
<td>0.2</td>
</tr>
<tr>
<td>0-2</td>
<td>14</td>
<td>13.5</td>
<td>0.5</td>
</tr>
<tr>
<td>0-3</td>
<td>20</td>
<td>19.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2-4</td>
<td>16</td>
<td>16</td>
<td>0.0</td>
</tr>
<tr>
<td>2-5</td>
<td>16</td>
<td>15.5</td>
<td>0.5</td>
</tr>
<tr>
<td>2-6</td>
<td>23</td>
<td>22.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>
FIGURE 10.6

Magnetic imaging system view of catheter in a 3-D shape: actual vs imager measurements

<table>
<thead>
<tr>
<th>measurement</th>
<th>actual (cm)</th>
<th>imager (cm)</th>
<th>difference (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 4</td>
<td>18.3</td>
<td>18.3</td>
<td>0.0</td>
</tr>
<tr>
<td>2 - 4</td>
<td>17.3</td>
<td>17.0</td>
<td>0.3</td>
</tr>
<tr>
<td>3 - 5</td>
<td>18.5</td>
<td>17.9</td>
<td>0.6</td>
</tr>
<tr>
<td>1 - 6</td>
<td>7.4</td>
<td>6.8</td>
<td>0.6</td>
</tr>
</tbody>
</table>
Although exact measurements could not be made because the catheter was inside the colonoscope, the images produced by the imaging system appeared similar to the actual appearance of the colonoscope and simultaneous x-ray pictures. The metal casing of the colonoscope did not appear to interfere significantly with the accuracy or quality of the image produced.

10.4 : Preliminary clinical evaluation

Independent advice was sought to confirm the electrical safety of the imaging system and ethical committee approval was obtained for its use with patients. During the initial evaluation period of 6 weeks the system was used as an aid to colonoscopy and flexible sigmoidoscopy in over 100 procedures. The experience described below represents the World's first clinical use of magnetic imaging during endoscopy.

After gaining familiarity with the use of the imaging system, a series of colonoscopies were performed by one experienced endoscopist (BPS) to evaluate its usefulness in colonoscopic practice.

10.4.1 : Method

In 61 consecutive colonoscopies the endoscopist and endoscopy personnel were randomised to perform the procedure either with, or blindly without, the imager view. Relevant patient details were recorded (table 18). Pentax EC 3801L video and FC 382FH fibreoptic colonoscopes were used for the examinations. Patients were placed in the left lateral position, intravenous access secured and continuous nasal oxygen (2l/min) administered via nasal cannulae.
<table>
<thead>
<tr>
<th></th>
<th>With imager view (n=29)</th>
<th>Without imager view (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>female</td>
<td>15</td>
<td>13</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median (yrs)</td>
<td>61</td>
<td>59</td>
</tr>
<tr>
<td>range (yrs)</td>
<td>37-89</td>
<td>34-83</td>
</tr>
<tr>
<td><strong>Past Surgical History</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hysterectomy</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>right hemicolecotomy</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>anterior resection</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>other abdominal surgery</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Sedation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pethidine - mean (mg)</td>
<td>47</td>
<td>48</td>
</tr>
<tr>
<td>midazolam - mean (mg)</td>
<td>2.9</td>
<td>3.1</td>
</tr>
<tr>
<td><strong>Preparation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>acceptable</td>
<td>20</td>
<td>16</td>
</tr>
<tr>
<td>poor</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td><strong>Diagnosis</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>polyp</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>cancer</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>colitis</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>angiodysplasia</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
All patients received intravenous sedation by slow bolus injection and were monitored throughout the procedure with pulse oximetry. In order to provide more anatomical information on the imager display, at the beginning of each procedure a single sensor coil was used to register anatomic landmarks (marker 1 - 10th rib in the right mid axillary line, marker 2 - 10th rib in the left mid axillary line, marker 3 - anus, marker 4 - fourth lumbar vertebra and marker 5 - umbilicus), (figure 10.7). If the position of the patient changed during the procedure the same anatomic points were re-registered in the new patient position. The imager view was recorded continuously throughout intubation in both study groups, except when the catheter was withdrawn from the biopsy channel to facilitate suction, biopsy or polypectomy. For examinations in which the endoscopist was randomised to perform the procedure blindly (without the imager view) he was asked at regular intervals by an independent observer, aware of the imager view, to give an estimation of the anatomical location of the colonoscope tip, whether the endoscopist considered a loop had formed and if so which type of loop he believed it to be. Changes in patient position were recorded. When abdominal pressure was requested, the endoscopy assistant placed a single sensor coil on the palm of the hand, (represented by a blue sphere on the imager display) so that the position of the hand could be seen in relation to the colonoscope (figure 10.8). When the endoscopy staff were without the imager view, non-specific hand pressure (Waye et al, 1991) was applied over the area where the endoscopist considered the colonoscope to be looping. After the examination the quality of bowel preparation, clinical findings, total time and extent of the intubation were recorded. All images obtained were saved on computer disk and retrospectively analysed. For each procedure the type of loops that formed during intubation and their duration were recorded, as well as the number of attempts taken to straighten the colonoscope successfully and
FIGURE 10.7
View of caecal intubation in AP and lateral views demonstrating the position of surface body markers; 1 = 10th rib in the right mid-axillary line, 2 = 10th rib in the left mid-axillary line, 3 = anus, 4 = 4th lumbar vertebra, 5 = umbilicus.
FIGURE 10.8

Lateral view of the colonoscope using magnetic imaging demonstrating accurate sigmoid abdominal pressure; the blue sphere represents an additional sensor coil attached to the endoscopy assistant’s hand.
advance the colonoscope tip. In addition the accuracy of abdominal pressure and whether or not it was of benefit in advancing the colonoscope was recorded.

10.4.2 : Statistical analysis

Un-paired t-tests were used to compare intubation time and duration of loop formation per patient between the two study groups. Categorical data were compared by Fisher's exact test after combining the data into 2 by 2 contingency tables. A P value was considered significant when <0.05.

10.4.3 : Results

Three patients were excluded from the study because of failed preparation, two because of fixed impassable sigmoid colons secondary to diverticular adhesions and one because she subsequently refused the procedure. In 29 procedures the endoscopist and endoscopy assistant performed the colonoscopy blindly, without the assistance of the imager view. In 26 procedures both were allowed to see the imager view. Findings at colonoscopy are shown in table 18. Total colonoscopy (i.e. insertion of the instrument to the caecum or surgical anastomosis) was achieved in all patients except one; in this case the endoscopist was without the imager view and the procedure was abandoned due to recurrent looping of the colonoscope in a long and mobile sigmoid colon. There was no significant difference in the time taken to complete intubation between the two study groups (mean intubation time without the imager = 12 minutes, range 2-30 minutes, mean time with the imager view = 13 minutes, range 4-30 minutes.
10.4.3.1 : Looping during intubation

The type and frequency of loops formed in the two study groups during intubation is shown in table 19 and examples are shown in figures 10.9 and 10.10. An "N" loop occurred in the sigmoid colon in 65% of all patients and was the most common loop to occur at any time during intubation in both study groups. More patients examined without the imager view developed an alpha loop (35%) compared to those examined with the imager (7%), though this did not quite reach statistical significance (P=0.08 by Fisher's exact test). Comparing looping between male and female patients there were no differences between the sexes apart from a higher incidence of deep transverse looping in females (36%) versus (7%) in males, P<0.05). In 3 of the 4 procedures where no loops formed at any stage during intubation, the endoscopist had the benefit of the imager view. There was no difference between the two study groups with regard to the duration of time that the colonoscope was looping (mean time per patient without the imager view = 7.3 minutes, range 0.3-28 minutes, mean time per patient with the imager view = 6.2 minutes, range 0.8-21 minutes). However there were significantly fewer attempts at straightening the colonoscope once a loop had formed when the imager view was available to the endoscopy personnel (P=0.03 by Fisher's exact test), table 20. On 2 occasions caecal intubation was possible despite the presence of a sigmoid loop throughout colonoscope insertion (figure 10.11).

10.4.3.2 : Effect of hand pressure

Abdominal pressure was used on 10 occasions in both study groups. Advancement of the colonoscope tip and straightening of a loop associated with
<table>
<thead>
<tr>
<th>Loop Description</th>
<th>Imager (n=29)</th>
<th>No Imager (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;N&quot; or sigmoid spiral</td>
<td>22</td>
<td>28</td>
</tr>
<tr>
<td>Alpha</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Deep transverse</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Reverse sigmoid spiral</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Gamma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Reverse splenic flexure</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Reverse alpha</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Reverse transverse</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Transverse spiral</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Total: 38  46
FIGURE 10.9

AP views of the colonoscope using magnetic imaging demonstrating common loop configuration: from left to right, N or spiral loop, alpha loop, deep transverse loop and gamma loop.
FIGURE 10.10

AP views of the colonoscope using magnetic imaging demonstrating unusual looping configurations: from left to right, reverse alpha loop, reversed splenic flexure loop, transverse corkscrew loop, reverse sigmoid spiral loop.
### TABLE 20

Number of straightening attempts per procedure.

<table>
<thead>
<tr>
<th>Attempts</th>
<th>Imager (n=29)</th>
<th>No imager (n=26)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>25</td>
<td>15</td>
<td>p=0.03</td>
</tr>
<tr>
<td>6-10</td>
<td>4</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>11-15</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
FIGURE 10.11

AP and lateral views of the colonoscope using magnetic imager showing caecal intubation with an alpha loop.
hand pressure occurred more frequently when the endoscopy personnel could see
the imager view (table 21).

10.4.3.3 ; Change of patient position

A change from the left lateral to the right lateral position was used on 15
occasions without the imager view (11 when negotiating the sigmoid/descending
junction, 4 the splenic flexure), and on 10 occasions with the imager view (6
when negotiating the sigmoid / descending, 4 the splenic flexure). The change
was considered to be beneficial on 7 (47%) occasions without the imager view
and 4 (40%) with the imager view, not significant by Fisher's exact test.

10.4.3.4 ; Accuracy without the imager view

Although the endoscopist was always correct in identifying the presence of a
loop, he was inaccurate in his assessment of the type of loop 42% of the time. A
sigmoid spiral loop was correctly diagnosed on 24 out of 28 occasions and a deep
transverse loop 3 times out of 5. However alpha looping occurred 9 times but
was only correctly recognised once whilst all 3 reverse sigmoid spiral loops and
1 gamma loop were incorrectly diagnosed. The endoscopist was incorrect in his
estimation of the anatomical location of the colonoscope tip 13% of the time. In
one patient a carcinoma at the sigmoid/descending junction was incorrectly
located to the hepatic flexure.
TABLE 21

Effect of hand pressure during colonoscopy

<table>
<thead>
<tr>
<th>Loop</th>
<th>Imager (n=29)</th>
<th>No imager (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HP used</td>
<td>benefit</td>
</tr>
<tr>
<td>Spiral</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Alpha</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Deep transverse</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>7 (70%)</td>
</tr>
</tbody>
</table>
10.4.4 : Discussion

Until now there has been no practical method of imaging the colonoscope in real-time once it has been inserted into the patient. Intubation therefore (apart from the brief glimpses offered by fluoroscopy) has been undertaken blindly on a trial and error basis, expert colonoscopists being quicker and causing less pain than inexpert endoscopists or trainees by recognising loop formation earlier and finding the correct combination of straightening manoeuvres more rapidly. Magnetic imaging gives the endoscopist for the first time the ability to see the 3-dimensional configuration of the whole instrument and the exact location of its tip within the abdomen.

10.4.4.1 : The imaging system

The colonoscope configuration can be viewed on screen from any position, but it was found that, for ease of recognition, antero-posterior and lateral views are preferred. The lateral presentation in particular tends to give increased information about the depth and angulation of the colonoscope, particularly in the sigmoid colon.

In order to obtain more information about the anatomical position of the colonoscope a series of body landmarks were set which delineate the contours of the abdomen and pelvis. Initially coils were attached to the patient but these proved to be restrictive, particularly when moving the patient. It was found that a more convenient solution was to set the landmarks on screen at the beginning of the examination with a single sensor coil and then reset them if the patients position subsequently changed - a process that took only a few seconds.
10.4.4.2 : Comparison with/without the imager view

Analysis of the two patient groups in this small pilot study, with an expert colonoscopist performing the procedures, has not shown that the imaging device significantly decreases the time taken to achieve total colonoscopy or that it reduces the duration of looping per patient. However, with the benefit of the electronic imager, the number of attempts required to straighten the shaft is less and assistant hand-pressure is more accurate and effective in controlling loops. In order to reduce a loop that has formed during intubation, the colonoscope must be withdrawn often with variable degrees of clockwise or anti-clockwise twist. The imager allows comprehensive assessment of each loop, and so makes the manoeuvres to straighten the colonoscope logical and intuitive, rather than empirical (Appendix 1 and 2). Use of the imaging system also removes the uncertainty from the technique of abdominal pressure. Not only can the endoscopy staff accurately see where the colonoscope is looping but, by attaching an additional sensor to the assistants hand, he/she can view the hand over the abdomen in relation to the colonoscope (this was previously impossible with fluoroscopy, because of the danger of radiation to the assistants hand unless wearing a cumbersome glove). Therefore it can be ascertained quickly from the imager view whether or not abdominal pressure will be of benefit. Often the main area of loop formation was seen to be posterior in the pelvis (as the colonoscope passes over the sacral promontory) and therefore not accessible to hand pressure. However sigmoid looping can be reduced by pressing over the supra-pubic/left lower quadrant region as the colonoscope passes anteriorly from the pelvis into the abdominal cavity, (figure 10.12). Secondary looping in the sigmoid can also be reduced by abdominal pressure in the same place.
FIGURE 10.12

Lateral view of the colonoscope within the sigmoid colon using the magnetic imaging system; the tip lies posteriorly in the abdomen at the sigmoid/descending junction.
Abdominal pressure proved to be most effective in reducing deep transverse loops. The transverse colon runs anteriorly between the splenic and hepatic flexures and is therefore amenable to hand pressure by pressing upwards over the mid/lower central abdomen (figure 10.13). Occasionally, if used without imaging, abdominal pressure may actually hinder the straightening of loops. For instance once an alpha loop has formed, clockwise twist and withdrawal forces are required to straighten the colonoscope. If supra-pubic abdominal pressure is used blindly during this straightening manoeuvre the downward pressure over the loop can be seen on the imager to obstruct loop reduction, reducing the effectiveness of clockwise twist and resulting in the colonoscope tip falling back into the sigmoid (figure 10.14).

10.4.4.3 : Accuracy of tip location with the imager

In this study the endoscopist was able to locate the tip of the colonoscope accurately 87% of the time without the benefit of the imager. However he was incorrect about the anatomical location of one carcinoma, which would have resulted in confusion at surgery without subsequent analysis of the imager record. The imaging system showed that the endoscopist was always correct in assessing caecal intubation but less experienced endoscopists can mistake the mid-transverse colon or hepatic flexure as the caecum, so resulting in the right colon not being examined and lesions being missed. The ability to assess the anatomical depth of insertion is also important for flexible sigmoidoscopy or limited colonoscopy when the caecum is not reached. In addition the imaging system allows biopsies to be taken accurately from different anatomic segments of the colon for surveillance and research purposes.
FIGURE 10.13

AP view of the colonoscope using magnetic imaging demonstrating accurate placement of abdominal hand pressure to counter a deep transverse loop; blue sphere represents the endoscopy assistant's hand.
FIGURE 10.14

Lateral views of the colonoscope demonstrating 1: incorrect use of abdominal pressure for an alpha loop, 2: removal of abdominal pressure allows anterior movement of colonoscope shaft during straightening manoeuvres.
10.4.4.4 : Limitations of the imaging system

There are some limitations of the system. In its present form use of the electronic imager necessitates obstruction of the instrumentation channel by the sensor catheter, so impeding or sometimes preventing aspiration of air or fluid, unless a 2-channel instrument is available. It is anticipated that the chain of sensors will eventually be built into the shaft or inserted during repair or maintenance. This will have the added benefit that the sensor connecting leads can emerge from the endoscope umbilicus rather than adding to the complexity of the control section. An inherent limitation of the system is that, unlike fluoroscopy, neither the gas shadow of the intestine nor the bony structures can be seen; the benefits of the real-time and overall view obtained however easily compensate for this.

10.4.4.5 : Safety

The electronic imaging system has been used so far in over 100 procedures with no complications related to its use. It appears to be robust, with no system failures. The magnetic fields generated by the system are extremely small (approximately \(1 \times 10^{-6}\) that of a standard magnetic resonance scan) and should not interfere with metal within the body. Caution is necessary when examining patients with programmable pacemakers as the magnetic fields used in the imaging system could theoretically affect the pacemaker setting. Another potential problem could be the simultaneous use of diathermy. It is possible that during the use of diathermy, current could pass into the sensor catheter causing local heating of the coils within the colonoscope and damage to the main
electronics of the system. At present, it is recommended that the catheter be removed before diathermy is commenced.

10.4.4.6 : Use of electronic imaging and colonoscopic technique

Use of the electronic imaging device has allowed the entire procedure of colonoscopy to be visualised. The real-time, three-dimensional images and ability to view the colonoscope in both lateral and AP views has provided a new perspective on what actually happens during intubation. Prior to the use of electronic imaging the three-dimensionality of the pelvis and abdomen were difficult for the endoscopist to appreciate. For instance, in most patients, a loop occurs as the colonoscope is passed through the sigmoid colon. This common loop has been called an "N" loop, because this is the 2-dimensional appearance seen using fluoroscopy (Hunt, 1981). In fact this description proves to be a simplification of the actual 3-dimensional appearance and is better described as a sigmoid spiral loop. As the colonoscope is inserted through the first third of the sigmoid colon it tends to push the sigmoid colon posteriorly towards the sacral promontory before passing anteriorly out of the pelvic cavity and into the abdomen (figure 10.12). After passing anteriorly in the second third of the sigmoid colon, the colonoscope then passes posteriorly and to the left where it joins with the retroperitoneal descending colon. Thus a posterior-anterior-posterior, right to left, clockwise spiral is formed.

Awareness of normal colonic anatomy, combined with the ability to view the colonoscope tip in 3-dimensions, has the potential to allow more accurate steering around acute bends (where the endoscopic view is limited) by directing the colonoscope tip towards the likely anatomic direction of the colonic lumen. It has been found that this is of particular use when passing the sigmoid/
FIGURE 10.15
AP and lateral views of unsuccessful descending colon intubation: the colonoscope tip is pointing anteriorly.
FIGURE 10.16

AP and lateral view of successful descending colon intubation: the colonoscope tip is pointing posteriorly.
descending junction. Figure 10.15 shows the tip of the colonoscope pointing anteriorly at the sigmoid/descending junction. Using the imager view the direction of the colonoscope tip is redirected posteriorly resulting in successful intubation of the retroperitoneal descending colon (figure 10.16). A similar technique can be used at the splenic flexure.

10.5 : Conclusions

Magnetic imaging of colonoscopy appears on preliminary clinical experience to be both safe and practical. The imager allows anatomical localisation of the colonoscope tip and a comprehensive assessment of colonoscope looping. Use of the imaging system increases the accuracy of loop removal and the logical application of abdominal hand pressure. Trainee or intermediate grade endoscopists may derive even greater benefit from the imaging system. Electronic imaging, when commercially available, appears likely to have a major impact on training and performance of colonoscopy.
Chapter 11 : Conclusions from the thesis

In attempting to make colonoscopy easier various aspects of the procedure have been examined. This thesis has assessed colonic anatomy, bowel preparation, sedation, endoscopic equipment and endoscopic technique. Chapter 2 defined (for the first time in vivo) the variations in colonic anatomy and mesenteric attachments in Western and Oriental populations. A large variation was seen in the degree of colonic mobility of the Western colon, giving substance to the reasons for unusual loop formation during colonoscope insertion. The Western descending colon, splenic flexure, transverse colon and ascending colon proved to be more mobile than their Oriental counterparts, whilst the sigmoid colon in the West was more frequently fixed by adhesions. Taken together these anatomical factors strongly suggest that colonoscopy may be more difficult in Western patients and suggest the need for further aids to colonoscopy (such as magnetic imaging), particularly in the West. In Chapter 3 a series of colonoscopies at a specialist Western centre were prospectively assessed looking specifically at the incidence and causes of difficulty during colonoscope insertion. Although 99% total colonoscopy was eventually achieved, 16% of procedures were considered technically difficult, mainly due to recurrent, unpredictable looping of the colonoscope. Most looping to cause difficulty occurred in the sigmoid colon due to reverse splenic flexure, "N" or alpha loops. Technical aids, such as fluoroscopy, the split over- tube stiffening device and the paediatric colonoscope proved invaluable in difficult cases. Any endoscopy unit performing regular colonoscopy would undoubtedly benefit from access to such equipment. Retrospective analysis, showed that female gender was strongly associated with difficulty at colonoscopy but that this did not appear to be related to a higher incidence of pelvic surgery.
Chapter 4 demonstrated that women tend to have longer colons than men. This may contribute to a greater looping tendency and hence increased difficulty during colonoscope insertion. The difference in length was seen particularly in the transverse colon and interestingly deep transverse looping was seen more frequently in women than men in the small number of patients studied with the magnetic imaging system.

Prior prediction of difficult cases is clearly desirable and in Chapter 5, assessment of a previous barium enema showed factors (rectosigmoid length, total colonic length, severe diverticular disease and redundancy of the transverse colon) that were associated with technical difficulty at colonoscopy. Whilst many patients continue to be examined by barium radiology, assessment of a previous barium enema may be valuable in channelling potentially difficult cases requiring colonoscopy, towards specialist centres.

Bowel preparation for colonoscopy remains a significant problem due to the large variability in patient needs and their colonic physiology. In Chapter 6 a new method of bowel preparation for colonoscopy, mannitol/Picolax mixture was compared to PEG oral lavage. Mannitol/Picolax proved to be well tolerated but less effective at cleansing the bowel than PEG. The split administration of PEG used in this study was well tolerated and may be the preferred method of administration of this preparation for out patients.

In Chapter 7 the necessity to offer analgesia/sedation for colonoscopy was confirmed; patients given no analgesia/sedation experienced more discomfort and were considered to require more additional medication than those receiving either inhaled nitrous oxide/oxygen mixture or conventional intravenous benzodiazepine/opiate sedation. Patient-controlled inhaled nitrous oxide/oxygen mixture appears to be a valuable alternative as sedation/analgesia for colonoscopy. Patients receiving nitrous oxide reported similar pain scores and
were considered to require no more additional medication than those receiving conventional intravenous sedation, with the added benefit of a reduced incidence of oxygen desaturation and shorter post-procedure recovery times. If widely employed nitrous oxide inhalation might prove a significant advance for routine colonoscopic practice reducing the overall cost and time of each procedure. Until further experience is obtained with nitrous oxide inhalation, intravenous access, patient monitoring and exclusion from driving after the examination are mandatory. However the possibility of a rapid turn-over system where patients can enjoy the benefits of safe, effective analgesia during colonoscopy and still leave the unit soon after the procedure without the need for patient escort and restriction from driving is now a definite possibility.

In Chapter 8 premedication with the anti-spasmodic agent hyoscine n-butyl bromide was found to reduce the time taken to complete colonoscope insertion to the caecum compared to placebo. Other studies comparing intubation with or without anti-spasmodic agents have not shown a benefit and therefore a larger study assessing the use of hyoscine is required before advocating its routine use. Potential benefits of hyoscine premedication include increased lesion recognition and safer insertion due to improved visualisation whilst disadvantages include tachycardia and hypotension, particularly in the elderly (Rameh et al, 1994). These factors all require more detailed evaluation.

Whenever sigmoidoscopy is undertaken (particularly in a screening situation) adequate visualisation of the colonic mucosa and attention to patient comfort are an important part of ensuring both accuracy and compliance with future examinations. In Chapter 9 intravenous premedication with hyoscine and analgesia with inhaled nitrous oxide/oxygen inhalation proved to be of benefit for screening flexible sigmoidoscopy. In a general practice setting, nitrous oxide
inhalation reduced patient pain scores whilst hyoscine premedication reduced total procedure time compared to placebo.

In Chapter 10 the development of a new technique to image the procedure of colonoscopy has been described. Utilising low power magnetic fields and computer technology accurate, three-dimensional, real-time images of the colonoscope shaft were generated during colonoscopy. Colonoscope looping was visualised in anterioposterior and lateral views confirming the appearances previously seen using fluoroscopy and providing a new insight into the "true" three-dimensional appearances of sigmoid loops. By incorporating anatomical body markers the system provides accurate localisation of the colonoscope tip thus allowing colonic lesions to be correctly located and caecal intubation to be clearly identified. In an initial pilot study assessing the effect of magnetic imaging on the performance of colonoscopy the imaging system was found to allow more accurate straightening of loops and appropriate use of abdominal hand pressure. However intubation time, sedation requirements and the duration of colonoscope looping were not improved significantly; possibly a reflection of the small numbers of patients in this initial study and the fact that all examinations were performed by an experienced endoscopist. Initial clinical use of magnetic imaging has highlighted current limitations, particularly the need to incorporate it with existing endoscopic equipment. Further studies of the magnetic imaging system are now required to assess its effects on the performance of endoscopy by trainees (it is anticipated that visualisation of colonoscope looping may greatly accelerate the learning of colonoscopy technique), and to evaluate its potential for reducing sedation requirements, complication rates and inaccuracies of tip location. The use of magnetic imaging for other endoscopic and non-endoscopic procedures also requires evaluation. Once widely available magnetic imaging is likely to prove to be an invaluable aid
to colonoscopy and an essential tool in the development of new endoscopic equipment.
Chapter 12: The future of large bowel endoscopy

12.1: Diagnostic + therapeutic colonoscopy/ flexible sigmoidoscopy

The immediate future of colonoscopy as a diagnostic investigation seems assured. No other imaging modality of the large bowel allows both direct visualisation of the mucosal surface and the possibility of biopsy or therapeutic intervention. Present practice in the UK is still in transition from the use of barium radiology to that of endoscopy for the initial investigation of large bowel disease. Many physicians however recognise the potential advantages of endoscopy, and in order to meet demand are in the process of developing endoscopic facilities and increasing the number of skilled personnel available to perform the examinations (Baillie, 1988; Axon et al, 1987). Already some centres offer open-access flexible sigmoidoscopy, where general practitioners can refer patients directly for flexible sigmoidoscopy, often avoiding lengthy clinic waiting times (Kalra et al, 1988; Niv & Asaf, 1992). Such services are likely to become more widely available in the future and may be staffed by primary care, staff grade or nurse/technician endoscopists, rather than specialist hospital gastroenterologists (MacMillan, 1991; Schertz et al, 1989; Maule 1994).

Indications for therapeutic colonoscopy continue to grow. Colonoscopy has already become established for the removal of small and large colonic polyps (Walsh et al, 1992), early carcinomas (Karita et al, 1991), for palliation of malignant strictures (Mathus-Viliegen & Tytgat, 1986) or dilatation of benign strictures (Oz & Forde, 1990), for ablation of angiodysplasia (Rogers, 1985) and decompression of the large bowel in sigmoid volvulus (Brothers et al, 1987) and Ogilvie's syndrome (Strodel & Brothers, 1989). It seems likely that in the future further endoscopic intervention will be possible, perhaps by developing laser
technology and combining endoscopic and laparoscopic surgical approaches (Beck & Karulf, 1993).

**12.2 : Screening colonoscopy / flexible sigmoidoscopy**

Colorectal cancer is the second most common cancer in the UK and over 19,000 people a year die from the disease (Atkin et al, 1993). Most cancers develop from pre-existing benign polyps which may be present for several years before the cancer develops (Morson, 1974). Therefore a therapeutic window exists when polyps can be removed to prevent cancer. Ideally a simple, cheap and safe screening test, (from a blood or faecal sample and involving new molecular biological or genetic techniques) would reliably show which patients have developed, or are at high risk of developing adenomas, so that colonoscopy could be appropriately scheduled. Unfortunately no such test is available at present.

Helical CT scanning with 3-dimensional virtual reality reconstruction is a new, non-invasive method of detecting colorectal neoplasia (Vining et al, 1994). After inflating the colon with air, several thousand cross sectional images are taken and then reconstructed by a computer to produce a 3-dimensional image of the entire colon. The reconstructed mucosal surface can then be visualised from any position, and it is claimed that polyps as small as 3mm can be detected anywhere in the colon. This new technology offers the possibility of safe, non-invasive colonoscopy, but at present, it remains untested in a clinical setting. The high cost and high radiation exposure of helical CT would appear to make day to day use for screening prohibitive. Presently available methods of screening for colorectal neoplasia include faecal occult blood testing, barium enema, flexible sigmoidoscopy and colonoscopy. Faecal occult blood testing is, simple, cheap
and safe. However it lacks sensitivity and specificity (Alquist et al, 1993) and still relies upon colonoscopy to be performed if a test is positive. Barium enema is readily available but unable to detect small polyps reliably (Williams et al, 1982) compared to endoscopy which has become the gold standard method of screening for colorectal neoplasia (Williams et al, 1982; Aldridge & Sim, 1986; Hodgson et al, 1993). Recent attention has been focused on flexible-sigmoidoscopy rather than colonoscopy because of its lower cost (Walker et al, 1991), and morbidity (Marks & Borenstein, 1987) and because most colorectal neoplasia is found in the left colon (American Cancer Society, 1980). A single screening flexible sigmoidoscopy offered to the population at around 55-60 years of age would seem on present evidence to be the most cost-effective method of screening the population as a whole (Atkin et al, 1993). If a national screening programme were to be implemented there would be a need for many more trained endoscopists. This need could be met by nurse endoscopists: several recent papers have described successful training programmes for nurse-specialists in flexible sigmoidoscopy (DiSaro & Sanowski, 1993; Schroy et al, 1988; Maule, 1994). As well as the development of new speciality grades within the screening service, new centres of excellence to perform screening and to train individuals in endoscopic technique will probably be required.

12.3: Teaching colonoscopy

At present, colonoscopy is taught on an apprenticeship basis with an experienced endoscopist supervising the training of one or more juniors. This process is time-consuming and frustrating for teacher and trainee alike. Correct colonoscopic technique requires a high level of manual dexterity and hand eye co-ordination and frequent repetition and experience are required before
competence can be achieved. To achieve a total colonoscopy rate of > 90%, trainees require supervised experience of between 100-200 examinations (Parry & Goh, 1992). In the future it is likely that the learning process will be greatly accelerated by new technologies. Endoscopic simulation with a dummy endoscope and graphics reconstruction of the colon offers the possibilities of repeated and realistic procedure training (without risk to patients), the ability to monitor the learning process, certify performance and even learn therapeutic procedures (Williams et al, 1990; Baillie et al, 1991; Noar, 1991). Early training on simulators would develop hand-eye co-ordination and familiarity with the handling of the colonoscope and its controls. The computer simulation can also include a 3-dimensional image of the colon as it loops and straightens according to shaft manipulation, mimicking that of the magnetic imager. Initial simulator experience could then be supplemented with supervised training on patients using real-time magnetic imaging of the colonoscope. With the benefit both of magnetic imaging and simulation, trainees will intuitively be able to appreciate why withdrawal and torqueing manoeuvres are fundamental to good colonoscopy technique. Combining intensive, early simulator training and subsequent hands-on experience using magnetic imaging, it is feasible that a training programme as short as 2 weeks could instruct endoscopists to perform safe, total colonoscopy.

Training and education in endoscopy in general are also likely to benefit from new communications technologies. Tele-endoscopy using digitised and compressed images allows a physician in a remote location to communicate aurally and visually with an endoscopist actually performing a procedure, all via a single digital telephone connection. Early experience with such technology suggests that clear, real-time views of the endoscopy suite and close-up endoscopic views can be transmitted (Bell, 1994, personal communication). If digital telephone net-works became established, the general physician
experiencing difficulty during endoscopy would be able to telephone an expert at a distant location during the procedure, who could then advise with the full benefit of an aural and visual link. Trainees would also be able to observe informally and in detail experienced endoscopists at work, without needing to be physically within the Endoscopy Unit. Conference links could be easily and cheaply established so that recognised experts could perform complex procedures at a distant location and interact directly with a larger audience.

12.4 : Colonoscope design

The design of the head of the colonoscope has changed very little in the last 25 years and the ergonomics are far from ideal. The up/down and lateral wheels were originally designed to be controlled with two hands. However push/pull and torque manipulations of the colonoscope shaft form the basis for good colonoscopic technique, (especially in the complex Western colon) and therefore if a single operator performs colonoscopy the left hand alone must stretch to control both wheels or the right hand move repeatedly from the shaft to the lateral wheel; neither variation being ideal. In the future it is conceivable that tip angulation could be controlled by a joy-stick device, operated by the left thumb which would effectively free the right hand to remain on the shaft of the colonoscope. Another theoretical advance in colonoscope technology would be to develop an "intelligent endoscope". It is conceivable that such an instrument would be able to detect the bowel lumen and steer towards it (using servomotors), automatically straightening the shaft if looping occurs and then stiffen the part of the shaft that had looped, before further insertion.

Other fundamental changes in colonoscope design have been recently proposed which attempt to miniaturise the colonoscope into a self-propelled endorobot
(Gong et al, 1994), able to navigate through the colon by remote control whilst relaying images to a TV monitor. Such devices could provide painless colonoscopy. However major problems exist in miniaturising and obtaining power for all the components necessary for a functional endoscope. Whatever miracles of technology become available in the future, it is likely that an appreciation of colonic 3-dimensional anatomy and its successful manipulation will also involve learned handskills and remain a challenge to the endoscoping gastroenterologist.
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Appendix 1

Magnetic imaging of colonoscopy: a selection of teaching material demonstrating the accurate straightening of loops encountered during colonoscope insertion.
Straightening an alpha loop

1. Colonoscope tip at splenic flexure
2. Pull back + clockwise twist
3. Colonoscope straight at splenic flexure
Straightening a complex sigmoid spiral loop

sigmoid "knot"

anti-clockwise twist exagerates looping

clockwise twist reduces loop

withdrawal + clockwise twist straightens loop
Straightening a sigmoid N or spiral spiral loop (AP view)

withdraw + clockwise twist
pull back + clockwise twist

(lateral view)

straightening a sigmoid N or spiral loop
Formation of a gamma loop
Pull back + clockwise twist + suction

Straightening a Gamma Loop
Removing a reverse splenic flexure loop.

1. Medial deviation of the descending colon allowed by a persisting descending mesocolon.
2. Tip stuck in mid-transverse.
3. Descending colon reduced to normal anatomic position.
4. Anti-clockwise twist + withdraw.
Straightening transverse and sigmoid loops (AP views)

colonoscope tip stuck in proximal transverse colon

1. recurrent sigmoid + transverse colon looping
2. pull back to straighten
3. transverse and sigmoid colon hand pressure

push to ascending with hand pressure, then suction

caecal intubation
Straightening transverse and sigmoid loops (lateral views)

1.Colonoscope tip stuck in proximal transverse colon
2.Recurrent sigmoid + transverse colon looping
3.Pull back to straighten
4.Transverse and sigmoid colon hand pressure
5.Push to ascending with hand pressure, then suction
6.Caecal intubation
Appendix 2 (see attached video).

Video footage of magnetic imaging during colonoscope insertion demonstrating
1; straightening a spiral, sigmoid loop, 2; accurate application of abdominal hand
pressure, 3; straightening a complex sigmoid loop.
Publications arising from the thesis


**Saunders BP**, Elsby B, Boswell AM, Atkin W, Williams CB. Intravenous anti-spasmodic and patient-controlled analgesia are of benefit for screening flexible sigmoidoscopy.- in press Gastrointestinal Endoscopy.

**Saunders BP**, Phillips RKS, Williams CB. Intraoperative measurement of colonic anatomy and attachments with relevance to colonoscopy.- in press British Journal of Surgery.


Saunders BP, Williams CB. Intravenous anti-spasmodic speeds colonoscope insertion. - in press Gastrointestinal Endoscopy.


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