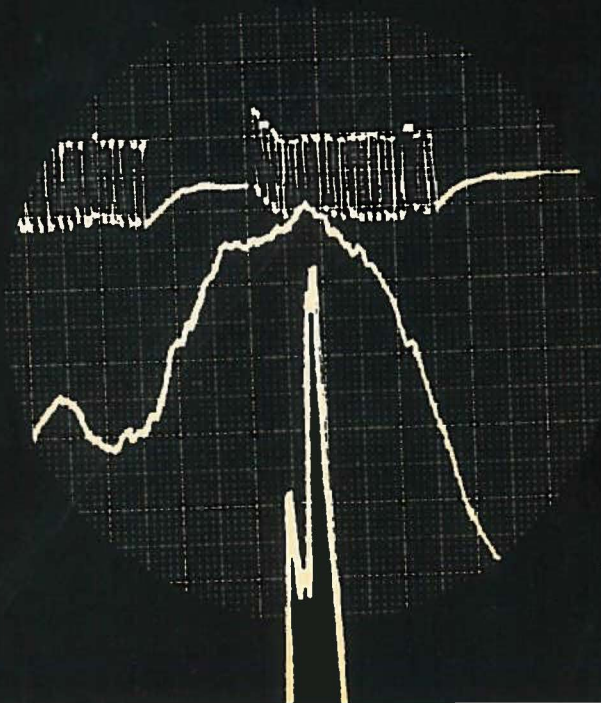
PAINFUL IRRITABLE BOWEL SYNDROME and DIVERTICULOSIS



Ger H. Ritsema

PAINFUL IRRITABLE BOWEL SYNDROME and DIVERTICULOSIS
One hypermotile state? Correlation of pain and hypermotility

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STELLINGEN bij het proefschrift "Painful irritable bowel syndrome and diverticuloisis" van Ger H Ritsema.

1 Een segmenterende sigmoid contractie, waargenomen tijdens het radiologisch onderzoek van het colon, gecorreleerd aan de karakteristieke pijn ervaring van de patient, is een positief diagnostisch criterium bij een pijnlijk irritable bowel syndrome.

2 Bij drukmeting in het sigmoid wordt de weerstand tegen de voortgang van de darminhoud gemeten.

3 De pijn bij het irritable bowel syndrome wordt veroorzaakt door drukgolven met een amplitude die boven de normale fysiologische variatie uitstijgt.

4 Segmenterende sigmoid contracties gaan gepaard met drukgolven met hoge amplitudes en pijn: colon koliek.

5 Het pijnlijk irritable bowel syndrome en de diverticulosis zijn deel van één hypermotiliteitstoestand.

6 Bij de beoordeling van de resultaten van een drukmetingsonderzoek is het voldoende de motiliteitsindex te berekenen, de oppervlakte onder de curve behoeft niet bepaald te worden.

7 Patienten met onbegrepen, discontinue buikpijnklachten behoren een fysiologisch gericht radiologisch colon onderzoek te ondergaan.

8 Een curatieve behandeling van recidiverende aften is niet bekend (Rennie JS, Reade PC, Scully C. Recurrent aphtous stomatitis. Br Dent J 1985; 159:361-7).

9 Een verbreding van de enkelvork, waarneembaar op de ongevalsfoto, wijst niet alleen op een laesie van het ligamentum deltoideum maar ook op een verscheuring van het ligamentum tibio-fibulare anterius.

10 Dubbel-blind onderzoek komt de geneeskunde wel maar de geneeskunst niet ten goede.

11 De fysiotherapeut kan psychotherapeutisch veel betekenen (Sonnen AEH. Een goede fysiotherapeut heeft veel voordelen boven de psychiater. Medisch Contact 1986; 41: 509-10).

12 De steunzool vindt geen steun in de wetenschappelijke literatuur.

13 Een radiodiagnost moet klinisch denken en meedenken.

14 Een röntgen foto geeft geen gekleurd beeld.

RIJKSUNIVERSITEIT TE GRONINGEN

PAINFUL
IRRITABLE BOWEL SYNDROME and DIVERTICULOSIS

One hypermotile state? Correlation of pain and hypermotility

PROEFSCHRIFT

TER VERKRIJGING VAN HET DOCTORAAT IN DE
GENEESKUNDE
AAN DE RIJKSUNIVERSITEIT TE GRONINGEN
OP GEZAG VAN DE
RECTOR MAGNIFICUS DR. E. BLEUMINK
IN HET OPENBAAR TE VERDEDIGEN OP
WOENSDAG 15 APRIL 1987
DES NAMIDDAGS TE 4.00 UUR

DOOR
GERRIT HOMME RITSEMA
geboren te Bierum (Gron.)

EERSTE PROMOTOR: PROF. DR. C.J.P. THIJN
TWEEDE PROMOTOR: PROF. DR. W. VEEGER
DERDE PROMOTOR: PROF. DR. O.J. TEN THIJE

Een kunstenaar schept niet,
hij rangschikt.
(Multatuli)

aan Froukje, Tita en Hendriena

VOORWOORD

Hooggeleerde Thijn, amice Kees. De suggestie om het radiologisch onderzoek van het colon te combineren met het drukmetingsonderzoek kwam van jou. De studie over de viscerale pijnproblematiek werd door jouw vraag nodig. Jouw wetenschappelijke nieuwsgierigheid heb je goed op mij weten over te brengen. Ik ben je daar zeer erkentelijk voor. Ook als mens heb ik je zeer leren waarderen. Ik dank je daarvoor.

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Zonder de patienten was het niet gegaan. Dankzij hun medewerking weten zijzelf en hun medepatienten weer iets meer over: "Waar komt die pijn toch vandaan ?"

Froukje, Tita en Hendriena, last best, dank ik bijzonder voor hun steun en begrip. Zij overwogen een bord op de studeerkamer te spijkeren: "Werk in uitvoering".

CONTENTS page

List of abbreviations used.

C	control
D	diverticulosis
HFD	High Fiber Diet
I	painful IBS
IBS	Irritable Bowel Syndrome
ID	painful IBS with diverticulosis
MI	motility index
NS	not significant
Pa	Pascal
SEM	Standard Error of the Mean
STT	spinothalamic tract
VPL nucleus	ventroposterior lateral nucleus
*	significant: $p<0.05$
**	significant: $p<0.01$
***	significant: $p<0.001$

LIST OF TABLES

1 REVIEW OF THE LITERATURE

1.1 Introduction

Around each piece of knowledge often there is a halo of uncertainty.

1.1.1 IBS: a hotch-potch

An editorial (1) stated that in the irritable bowel syndrome (IBS) doctors subscribe to an astonishing range of opinions: at one end that the disorder is psychiatric, at the other end that it is functional. In another editorial (2) it was said that this syndrome is one of the most difficult conditions to diagnose. There is a need to develop a standardised diagnostic test (2;3). The disorder can, up until now, only be identified by the exclusion of organic disease (4-6).

Patients who consult their physicians for bowel symptoms do this especially if abdominal pain is concerned (7). The presence of pain can suggest a functional abnormality (8).

An international conference about IBS (9) suggested to define IBS by its symptoms. Five subgroups were mentioned: spastic colon, painless diarrhea, atonic constipation, gas and chronic abdominal pain. These conditions are diverse in symptomatology. Different pathophysiologic defects may be found. Other authors mentioned some other symtoms, not included in the five subgroups: pellety stools; mucus in stool; nausea; a change in bowel habit; relief of pain with bowel movement and a sensation of incomplete evacuation (9-26)

Conclusion: patients thought to have IBS can have diarrhea and/or constipation with or without pain; or pain with or without alternating bowel habits. There is a hotch-potch of different conditions.

1.1.2 Incidence

1.1.2.1 IBS

The IBS is the most common disorder seen in gastroenterologic practice (21;27-29). In a leading article it is even stated that every doctor knows, or should know, that the most common cause of recurrent abdominal pain is the spastic colon or painful IBS (30).

About 70% of the patients is female (31;32). The age of onset often is between 20 and 40 years (31;33). It seldom arises de novo after 50 years of age (33). Pain, mostly described as aching or colicky, is very common and often located in the left lower abdomen (9;33;34).

Confusingly, it appeared that the symptom pattern of the spastic colon occurred in 13.6% of apparently healthy people (35). Patients reaching hospital, therefore, may be the tip of a painful iceberg (30;36). When exactly do deviations from average gut function and their perception become a functional disorder? There is a continuum between normality and disease (37).

When do scrawls on a canvas become art ?

1.1.2.2 Diverticulosis

Diverticulosis of the colon is seldom seen in patients less than 40 years of age (38;39). In postmortem studies 30 % of the colons was affected at the age of more than 50 years (40). This high incidence is contrasted with the rarity with which it is observed in tropical countries(41).

Radiologically, the disease is seen in about 40% of the colons in patients above 70 years of age in Western society (38). The diverticula are most numerous in the sigmoid colon (40;42-45). Only in 4% of the cases with diverticulosis the disease was not located in the sigmoid (39).

About 50% of the patients is female (40;43); so in contrast to the IBS there is no higher incidence in women.

Abdominal pain, usually located in the left lower abdomen and sometimes colicky, is often present (42;46;47). However, other authors stated that uncomplicated diverticulosis does not produce characteristic symptoms (48).

1.1.3 Pain

The IBS is a chronic condition characterized by abdominal pain and/or an alteration in bowel habits in the absence of any identifiable anatomic abnormality (9;15;27;49-58). No test however is infallible (59-63).

It is time to shift the emphasis to the patient and her/his pain (64-66). It is advised to put abdominal pain without bowel disturbance into a separate category when trials are done (9). Methods must be found that will enable physicians to identify this painful syndrome positively (6). Over-investigation to exclude organic disease must be prevented (67).

Pain is a subjective phenomenon. Sensations of patients, however, must be correlated to observations of doctors (68;69). If no anatomical disorder is found it may mean that the pain is caused by a functional disorder.

There is much abdominal pain (5;9;32;65;70) and the patient's request to know the cause of the pain (69). However, there is meager knowledge as to its cause (1-3;9;71-78).

The present investigation is, therefore, restricted to the painful IBS. Constipation and diarrhea without pain is not studied.

1.1.4 What causes the pain ?

Experimental physiology conjoined with clinical observation may determine the true nature of many morbid states (79). This statement also concerns the painful IBS. Many authors assumed a relation between intestinal contractions and pain of patients (80-89). Is hypersegmentation (increased contractions of the circular muscles of the colon seen during the barium enema) the source of the pain (32;33) ? Is the pain due to an abnormal response to gut distension (90) or to an abnormal gut distension (91-94) ? One author concludes that these patients have a colonic hyperalgesia (33;94).

The reproduction of the patients'pain during sigmoidoscopy, however, gives no proof for IBS, according to some authors (78; 95). The experimental data achieved by pressure recording in the sigmoid are said to be inconclusive or conflicting (96-100).

In the opinion of the present author, it is necessary to reproduce the patients' own characteristic pain and to see whether there is a relationship between pain, colonic contraction and pressure recordings. In this way it is possible to see whether the pain is caused by an abnormal function. A repeatable reproduction of the pain is necessary : first during the barium enema and secondly during the pressure recording.

According to Webster's Dictionary a functional disease is any derangement of an organ in which there is no apparent damage or structural change. According to many doctors, however, a functional disease means that the cause must be psychologic. To them the word functional is more or less identical with "of psychologic origin". But a functional disorder (in the meaning of a disturbed function of an organ) is different from a psychologic disorder, although the psyche can express itself by changes in the function.

The functional disorder must be objectified by means of experimental physiology.

1.1.5 The pathways of the visceral pain sensation

1.1.5.1 Introduction

There are two components of pain: discriminative and affective. The former includes the ability to identify the stimulus as originating from somatic or visceral tissue, the latter the experience of aversiveness which motivates protective behavior (101). Both these components have connecting pathways with the limbic lobe of the forebrain producing the emotional dimensions of the pain experience (78;101). Another discrimination is in normal and pathologic pain (102). Normal pain arises from acute or chronic stimulation of normal nociceptor endings by intense stimuli. Pathologic pain occurs spontaneously or in response to weak stimuli due to pathologic alterations of nerve excitability. Another discrimination is: physical or organic pain versus psychogenic or non-organic pain (103). A difficulty is the unreliability of the patient; pain leaves in the mind but a very imperfect recollection of its exact site (104).

Pain mechanisms should be studied in human subjects because of the availability of a sensory report. However, for ethical reasons, most experimental work on pain will have to come from animals. This may lead to controversies. Discrepancies between cats and primates (humans and monkeys) have been estimated. The animal model that is in most aspects comparable to man is the monkey. Other discrepancies may derive from differences in levels or types of anesthesia employed by different groups of investigators and in different animals.

Another problem in the pain-puzzle is the plasticity of the nociceptive system (the nervous system which receives and conveys painful stimuli to the brain; nocere = to injure, capere = to receive) in humans. It can change its character with experience of long-enduring pain. In these patients drugs appear to be more of a hindrance than a help (105).

There are two afferent components of the nervous system: sensory and non-sensory pathways. The impulses which pass upwards in the sensory paths into the brain enter consciousness and form the basis of sensation. Nociceptors receiving and

transmitting noxious stimuli are part of this sensory system.

The impulses which traverse the non-sensory pathways do not enter consciousness but subserve reflex functions; mechanoreceptor reflexes and peristaltic reflexes are part of this system (106). A simple reflexarc consists of an impulse travelling centripetally in a neuron through the dorsal root ganglion, (and sometimes the ventral root ganglion (107;108)) to the cell-body of a connecting neuron, synapsing in the spinal cord, where an excitation impulse is sent through a motor neuron to a muscle. The visceral reflex pathway involves a four neuron chain (109). The afferents of the mechanoreceptors of the pelvic colon , included in the visceral reflex path are excited by stretch or contraction and travel via the parasympathetic nerves (110).

Neurons are said to be multipolar because they have three or more processes. One axon carries impulses away from the cell-body to the peripheral tissues (efferent fiber) and two or more dendrites carry the stimulus centripetally (afferent fiber) to the cell-body. There exist complex connections in the nervous tissue. A nerve contains both afferent and efferent fibers.

A noxious stimulus in the visceral organs excites a nociceptor which sends a stimulus along visceral afferent pathways to the ascending paths of the spinal cord and the brain. We will discuss these steps in the next paragraphs.

1.1.5.2 The painful stimulus

Stimuli can be divided into innoxious (causing no injury) and noxious (causing injury) ones. A noxious stimulus triggers nociceptive reactions, including the feeling of pain in humans. Noxious stimuli are commonly associated with injury. Viscera, however, can be cut without evoking a pain sensation (104;108). In contrast, distension or an isometric or powerful contraction of the colon is painful (94;104;106;108;111;112). If there is an impaction (an obstruction), a colon contraction alters from relatively isotonic (no change in tension but a reduction in volume) to relatively isometric (no change in volume but a rise in tension) so that high pressures are caused. The afferent discharges from the mechanoreceptors are enhanced. These may cause conscious pain sensations (106). The thresholds with which these afferents respond appear to vary considerably in cats, in the lower end of the colon (113).

Gallbladder distension causes discharges in splanchnic nerve fibers (113). Pressure, applied to the biliary system above the physiological range in the ferret, evokes afferent activity in the splanchnic nerve (114). It was shown that this stimulus was painful as there was a nociceptive reflex. In animals pseudo-affective reactions , such as transient increases in blood pressures and heart rate, ascertain the presence of pain (108).

Besides powerful contractions and passive distension of a viscus, other visceral conditions causing pain are inflammation of the mucosa or of the serosa and torsion or traction on the mesentery (106). Some features of visceral pain are poor localization and reference to a somatic region (104;105;115).

1.1.5.3 Nociceptors

Specific nociceptors have functional characteristics which make them responsive only to noxious stimuli (116). Specific visceral nociceptors have been found in the heart, the lung and the testis of dogs.

Some evidence of the existence of specific nociceptors in visceral organs has been obtained (114). In the biliary system of the ferret specific nociceptors were described acting on high pressures. These nociceptors could be responsible for the sensation of pain that accompanies increases in biliary pressures produced by obstructions (108;114).

It may be that some mesenteric receptors also are nociceptors. Free nerve endings in muscles are also considered to be nociceptors; they may be present in the gut (108). Mechanoreceptors themselves may act as conductors for a pain evoking high pressure stimulus (106).

1.1.5.4 Intramural plexuses of the colon

The intrinsic nerve plexuses in the colonic wall are netlike structures, which contain afferent and efferent nerves and nerves entirely within the colon (117). The sensory fibers are long dendrites originating from the cell-bodies in the dorsal root ganglia (109). The sympathetic and parasympathetic extrinsic innervation intermingle with these meshworks.

Three plexuses can be distinguished (117):

The subserous plexus is situated on the outside of the muscles. Mechanoreceptors and possibly nociceptors are situated here, in cats (105;113).

The myenteric plexus is localized between the circular and the longitudinal muscle layers. When the wall of the colon is stretched this plexus becomes two dimensional, together with the submucous plexus. The neurons are lying in a single layer (117). There is a functional heterogeneity in the neurons (118).

The submucous plexus lies in the connective tissue of the submucosa. It was found that the colon is innervated by mechanosensitive fibers in mammals (113;119-122) and by nociceptive fibers in the domestic fowl (123). These fibers were found in the submucous plexus (119). These mechanoreceptors respond to distension of the colon in the cat (107;124;125) and in the dog (126). They probably subserve reflexes (127-129).

1.1.5.5 Visceral afferent peripheral pathways

Nociceptive fibers are generally either finely myelinated or unmyelinated (105; 110). The smaller the fibers the lesser myelinated, the slower the conducting velocity.

The sympathetic splanchnic nerve may be involved in visceral pain conduction as noxious stimuli to the biliary system gave reactions in this nerve (108;114). Mechanoreceptors that have their afferents in the splanchnic nerve responded to noxious stimuli. They, however, may also fire to apparently innoxious events such as contractions of the viscus (110). A dual role for splanchnic afferents in signalling about innoxious and noxious stimuli cannot be excluded (110).

Most sensory fibers have their endings in the serosa (130). Afferent fibers of extrinsic origin reach the gut wall through the vagus nerve for the proximal part and the splanchnic nerves for the distal part. They have their cell-bodies in the spinal ganglia (120). These fibers play a major role in reflex activity and normally a minor role in sensation (105). Most afferent fibers enter the spinal cord via the dorsal horn along the dorsal roots (105). Some fibers in animals and humans may enter via the ventral roots (107;131). The central endings of these fibers enter the superficial tract of Lissauer (132) which have now been shown to exist, in the monkey, of 80% of primary afferent fibers (105).

1.1.5.6 Ascending nociceptive pathways in the spinal cord

The most important pathways in the human spinal cord transmitting nociceptive information to the brain ascend in the anterolateral white matter on the side contralateral to the source of the noxious input (105). Clinical evidence is divided on the level at which spinothalamic tract (STT) cells cross over. Some cells decussate immediately in the monkey (105). Visceral afferents can also be shown to excite STT cells. One author divides the STT into a paleospinothalamic part and a neospinothalamic part (133). The paleospinothalamic tract has neurons which reach the limbic system of the fore-brain. The neospinothalamic tract transmits nociception along long fibers directly to the thalamus.

Visceral pain is referred to a somatic region (104;115). What is the cause of the pain referral ? It appeared in cats that 75% of the neurons responding to electrical stimulation of the splanchnic nerve also had a cutaneous receptive field (viscero-somatic neurons); 23% had only a cutaneous receptive field and no visceral input (somatic neurons) whereas 2% only had a visceral input (visceral neurons) (134). Other authors also found some spinal cord neurons which selectively responded to visceral stimuli (135). It was suggested that there might be, in humans, a convergence of cutaneous and visceral afferent input onto the same STT-cells in the spinal cord; the pattern of input following the dermatomal organization (104;105;108;115; 136). Input from visceral nociceptors would activate the shared STT cells. The brain would misinterpret the source of the pain, based on learned experience from the more common episodes in early childhood when cutaneous nociceptors activated the same pathway. This theory is called the convergence-projection theory (105). Many second order neurons responded to electrical stimulation of skin nerves as well as splanchnic nerves in cats (134;137;138). There was some inhibitory interaction between the two sets of inputs (137). Visceral noxious inputs converge mainly onto those neurons which have a noxious cutaneous input (134; 139). Other authors described viscerosomatic convergence on STT neurons in monkeys (140). Noxious intensities of visceral stimulation appeared to be necessary to activate spinal cord neurons having viscerosomatic convergence (141)

The reference of colonic pain has also been studied. It appeared that the afferents from the skin in the flank were convergent with the afferents from the colon, in cats (113).

An alternative explanation of referred pain may be that some afferents might branch to supply both visceral and somatic

structures (105;142).

Two types of nociceptive neurons are encountered in the dorsal horn: nociceptive specific neurons and multireceptive neurons (105). The nociceptive specific neurons are only activated if a damaging stimulus is given: they can provide unambiguous signals that noxious stimuli have occurred. The multireceptive neurons respond to innoxious mechanical stimuli and to noxious ones. It may be that these neurons act as detectors of noxious stimuli depending on the commands they receive from higher centers. There may be a descending control, especially in behaving animals (105). This control may be inhibitory to ascending activation (105;106). These multireceptive cells may be inhibited by the system of Diffuse Noxious Inhibitory Controls (DNIC). The describing of this system is beyond the scope of this study.

As determined from the results of chordotomies the nociceptive fibers in the STT in humans show a somatotopic organization (105). The abdominal part lies in between the leg and the thorax.

1.1.5.7 Pathways in the brain

The stimuli conducted through the STT arrive in the Ventral Posterior Lateral (VPL) nucleus of the thalamus in primates. The occurrence of neurons in the VPL nucleus that respond to nociceptive stimuli from the abdominal viscera has been demonstrated in cats and monkeys (105;143;144). The projection to the VPL nucleus is somatotopically organized (105).

Since pain produces arousal in the brain, the activity of much of the cerebral hemisphere is altered by a painful event. This makes it difficult to sort out cause and effect in the pain-processing circuitry (105). In monkeys neurons have been found in the somatosensory cortex (the postcentral gyrus), apparently receiving a projection from nociceptive neurons of the VPL nucleus of the thalamus.

Cortical neurons, in the cat, appeared to have input from small myelinated afferent fibers of the splanchnic nerve (108). Pontine reticular units, playing a role in the defecation reflex, respond to afferent impulses from the distal colon in dogs (145).

The cortical neurons are able to encode noxious stimuli (105). The final element in the interpretation of referred pain in terms of viscerosomatic convergence, is the projection to the cortex of the mixed viscerosomatic message (108).

Impulses arriving via the paleo-STT synapse with neurons which reach the limbic system and profusely project to many other parts of the brain. In this way motivational and emotional dimensions may be added to the pain experience (78;101;133).

The somatosensory cortex shows a somatotopical organization.

1.1.5.8 Conclusions

Isometric or powerful contractions of smooth muscle of the colon can be painful. An impaction of the forward going of the contents of the colon can provoke such a contraction causing high pressures. These high pressures can evoke afferent

discharges from mechanoreceptors in the colonic wall. These discharges carry stimuli in the afferent fibers. The responding thresholds of the mechanoreceptors vary widely. Mechanoreceptors may act as nociceptors if a very high pressure is present. Specific nociceptors were recently found in the biliary system of the ferret. They react to pressures above physiologic range. Specific nociceptors are possibly also present in the mesentery of the gut.

The sensory pathways consist of a relay of three neurons.

1/ The primary neuron with its afferent fibers in the sympathetic splanchnic nerve and its ascending fibers in the spinal cord.

2/ The secondary neuron ascending as the spinothalamic tract (STT) in the contralateral part of the spinal cord. There is evidence that this neuron has connections with the limbic system. This neuron reaches the ventroposterior lateral (VPL) nucleus of the thalamus.

3/ The tertiary neuron lies in between the VPL nucleus of the thalamus and the somatosensory cortex of the postcentral gyrus where the stimulus reaches consciousness.

A somatotopical organization is found in the STT, in the VPL nucleus of the thalamus and in the postcentral gyrus of the cortex.

The problem of referral of visceral pain to the superficial skin can be explained by the convergence projection theory and the misinterpreting of the brain. The nociceptive system as a whole is plastic: it can change its character with experience of long enduring pain.

1.2 Colonic anatomy; pathologic and radiologic anatomy of IBS , prediverticular disease and diverticulosis

1.2.1 Colonic anatomy

The colon is about 150 cm in adults, but variations occur. The rectum is about 15 cm long (117). The muscular coat is composed of inner circular and outer longitudinal layers of smooth muscle. The longitudinal muscle layer forms a continuous coat with three concentrations of muscle fibers into flat long bands , called taenia coli, separated by a very much thinner intertaenial zone. One taenia is located at the mesocolic border at the posterior side of the colon, the other two taenia, the anti-mesocolic ones, are situated one-third of the circumference around on the anterior and medial side. Because these taeniae are shorter than the other coats of the colon, haustra or sacculations are formed (146;147).

In the sigmoid colon the three taenia are arranged in the form of an isosceles triangle (having two equal sides), one under the mesentery and two close together , enclosing the short antimesenteric zone to form the base (146;148).

The other layers of the colon are: mucosa with the muscularis mucosae (a continuous sheet of smooth muscle lying directly beneath the mucosa); submucosa (a layer of connective tissue, providing a loose framework for the passage of vessels and nerves) and serosa (the outermost coat consisting of areolar tissue covered by a single layer of squamous mesothelial cells). The muscular coat lies in between the submucosa and the serosa. The segmental arteries which supply the colonic wall arise from

the mesenteric arcade as short and long vessels; the former penetrate the lateral muscle wall nearby the mesenteric taenia. The long vessels penetrate the muscle wall just on the mesenteric side of the antimesenteric taeniae (148). They weaken the layer of circular muscle by forming tunnels (147).

1.2.1.1 Light and electron microscopic anatomy

In light microscopic investigation the circular muscle layer is not homogeneous but is made up of discrete crescentic arcs composed of fasciculi 50-200 microns wide, incompletely separated from each other by connective tissue septa. Muscle cells, running obliquely, link these fasciculi together. These fasciculi are embedded in a proteoglycan matrix that also contains collagen and elastin fibers. Elastin is sparsely distibuted around the myenteric plexus and between the fasciculi forming a widely spaced meshwork running diagonally through the substance of the muscle layer. Larger spaces in the interfibrillary matrix contain capillaries and nerve fibers. The taeniae of the longitudinal muscle layer are also composed of fasciculi but they contain a greater amount of collagen and elastin. The circular and the longitudinal layers are bound together by muscle cells running from the taeniae into the circular layer, accompanied by collagen and, particularly, by elastin(149).

In electron microscopic study the muscle cells are of uniform size and spindle shape. The cell surface is modified by special structures: rows of caveolae (spheroidal invaginations of the cell membrane with a narrow opening to the extracellular space) alternate with dense bands (the site of insertion of actin filaments). The dense bands of adjacent cells often lie opposite to one another forming intermediate junctions, which often link the tip of one cell to the central part of a neighbouring cell. In contraction these bands remain in apposition, it is the caveolae bearing part of the cell that is distorted (149).

Elastin fibers have 2 components: a central amorphous core of the protein elastin (the major part of each mature fiber of elastin) and a surrounding layer of fine beaded filaments. Newly laid down elastin is electron dense, becoming lucent as it matures (149).

1.2.2 Pathologic anatomy of IBS, prediverticular disease and diverticulosis

The sigmoid colon in patients with the painful IBS is not removed. Sometimes, however, no diverticula could be found in a resected specimen of the sigmoid in a patient with pain in the left lower abdomen thought to be suffering from diverticulosis (146;150). The pain of these patients had disappeared after the operation(150). Probably, they suffered from painful IBS. The muscles of these specimens appeared to show thickening. This thickening is called by some authors a hypertrophy of the muscles (38;150). It was shown histologically, however, that this thickening is not the result of hypertrophy or hyperplasia (146-149;151;152). The thickening is caused by a contracted state or contracture (147;149;152-154) of the longitudinal muscle layers.

The most constant feature of diverticulosis is this thickening of the muscle layers. It precedes the appearance of the diverticula (147). The circular muscle consists of bundles of muscle fibers bunched together, between these bundles are gaps where the circular muscle may be absent so that a site of least resistance (a locus minoris resistentiae) is at hand (147). There is a shortening of the colon caused by the contracture of the longitudinal muscle leading to a corrugated appearance of the circular muscle resembling a concertina (154). The mucosa is redundant and gathered in folds. Sometimes it is herniated in tiny pouches through the irregularly thickened circular layer (153).

Early in their development diverticula, like herniae, are reducible. At first their covering may contain a few muscle fibers but soon these atrophy (147). We may call diverticula herniations of the mucosa and the muscularis mucosae through the muscular coat (146-148). The diverticula are thought to be caused by pulsion of the mucosa. They are called false diverticula. True diverticula are covered by all layers of the wall of the intestine (152;155).

These outpouches arise from the wall of the colon in four rows mostly, one at each side of the mesenteric taenia and one at the mesenteric side of each antimesenteric taenia. They never penetrate the taeniae themselves (148). The colonic wall is obviously weaker between the taeniae as it consists mainly of circular muscle. This muscle is further weakened by the gaps between the bunched bundles and by the sites at which the segmental arteries and veins pierce it. The diverticula are located at these weakened spots (42;147;148;156-161). As the false diverticula have no muscle cover they have not the power to expel feces. This can be visualised radiologically (fig 1a,b). Often the neck of these pouches are narrowed by the circular muscle so that their contained feces become inspissated. Inflammation may be caused.

1.2.2.1 Microscopic pathologic anatomy

Light microscopy reveals an exaggeration of the crescentic arcs in the circular muscle, the fasciculi are attenuated and their width reduced to 10-50 microns. The taeniae show none of the variations seen in the circular layer. In neither muscle layer is there evidence of active contraction. An obvious increase in the content of elastin fibers in the taeniae coli is seen. The amount of elastin in the circular muscle is not increased. The appearance and amount of collagen is normal in both muscle layers (149).

In electron microscopic investigation the increase in the elastin content of the taeniae is confirmed. A greater variety in the staining of elastin was noted, with some fibers staining darkly, suggesting recent deposition. Isolated groups of fine filaments of elastin were seen lying alone in the matrix suggesting active elastogenesis (149).

It is concluded that the taeniae are thickened as a result of the contracture secondary to elastin deposition (149). There was no electron microscopic evidence of active, sustained contraction in either muscle layer (no distortion of the caveolae bearing parts of the muscle cells). The contracture of the taeniae, with the increased amount of elastin fibers,

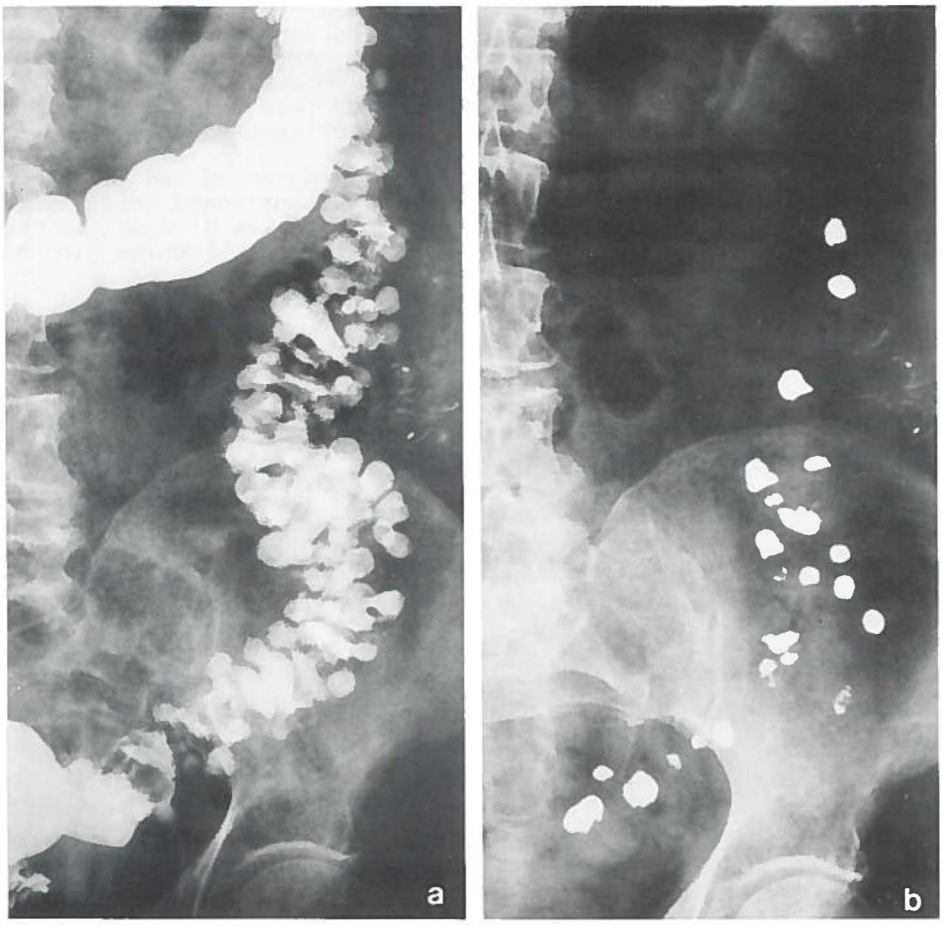
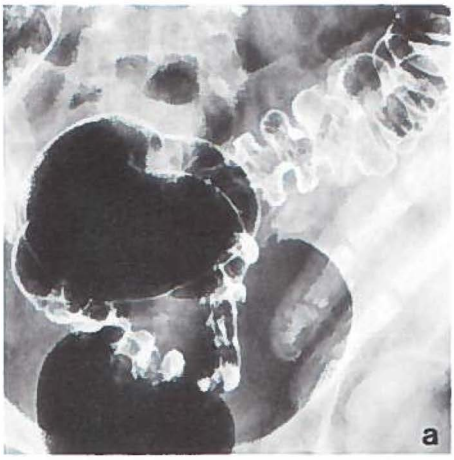


Fig. 1a The single contrast phase of the barium enema examination: diverticulosis of the sigmoid and colon descendens.

Fig. 1b The same patient, two months later. Several diverticula are still filled with bariumsulphate. The tiny white streaks on both sides above the iliac wings are probably caused by previous intramuscular injections.

shortened the sigmoid colon by about one-sixth normally. The crescentic folds of the circular muscle are more prominent, so it is understandable that, when the circular muscle contracts, isolated segments of high pressure can be formed. It is said that increased intraluminal pressure stimulates further elastin production (149). Repeated elongation and relaxation of smooth muscle triggers an increased uptake of collagen and hyaluronate in rabbit aorta (162).

So it seems that intermittent distension as caused by the movements of small stools, may trigger an increased deposition of matrix components. Elastin molecules are laid down in a contracted state (163) thus maintaining the taeniae in a shortened position.



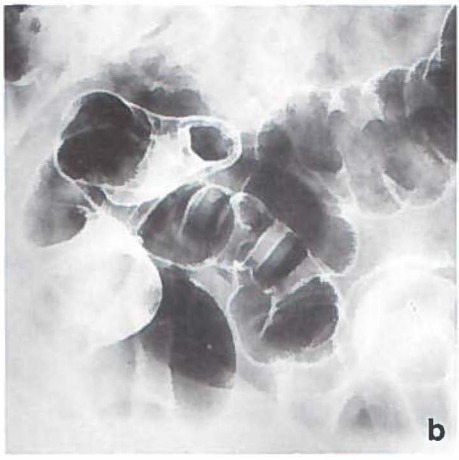


Fig. 2a A segmenting contraction of the sigmoid during the double contrast phase of the barium enema examination. The hand indicates the site of the characteristic pain.

Fig. 2b After glucagon this contraction has disappeared together with the pain.

1.2.3 Radiologic anatomy

1.2.3.1 Radiologic anatomy of IBS

X-ray signs of IBS are: a segmentation (fig 2a,b) (also called segmental contraction; segmental areas of spasm; spastic colon; increased segmentation; hypersegmentation; irregular haustration; increased haustral markings or deep cutting; contraction rings or rosary beads) and/or a contraction of lengthy segments (fig 3a,b) (also called string sign) (26;87-89;164-171). It is better not to use the term "string sign" in describing the radiologic signs of IBS as this sign is particularly restricted to Crohn's disease.

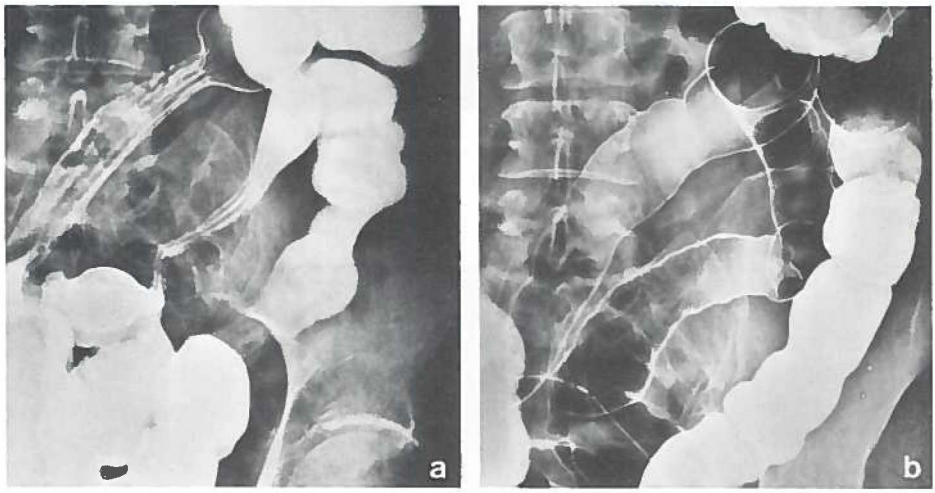


Fig. 3a A contraction of two lengthy segments of the sigmoid. The patient felt the characteristic pain in the left lower abdomen.

Fig. 3b After reassurance there is a relaxation of the sigmoid and a decrease of the pain.

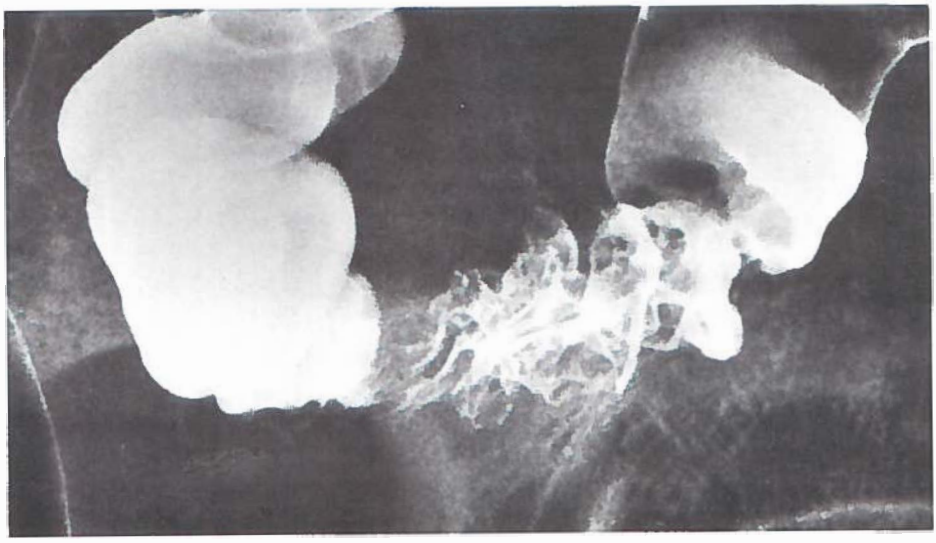


Fig. 4a Lengthy contraction of the sigmoid during a reproduction of the characteristic pain.

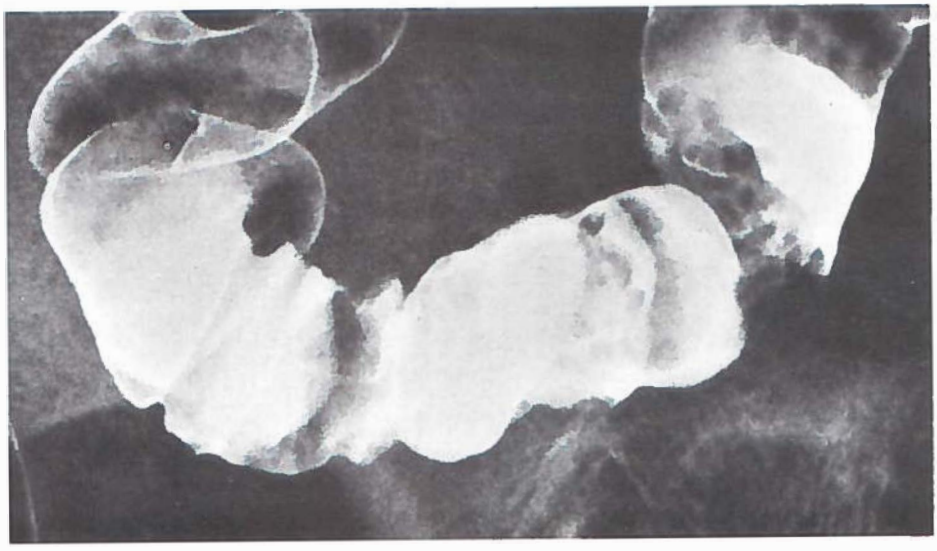


Fig. 4b The pain is decreasing, so is the contractile state of the sigmoid.

The patient may feel an urge to defecate during the beginning of the barium investigation, this can often be controlled by having her or him breathe deeply (26). In cases of a painful IBS the patient's characteristic pain may be reproduced (and recognized) during the barium enema (88;89). Active contractions in the sigmoid colon may be seen during this acute pain (fig 4a,b). Reassuring remarks from the radiologist or a muscle relaxant often relax the colon and the patient.

1.2.3.2 Radiologic anatomy of the prediverticular state

The normal segmentation of the sigmoid is replaced by a ragged outline of little convex irregularities, called saw toothed, serrated edge, pallisade or ripple border appearance (147;153). In this prediverticular state the haustra are very close together. Tiny herniations of the mucosa in the uneven thickened circular muscle may be seen (fig 5) (26;38;153).

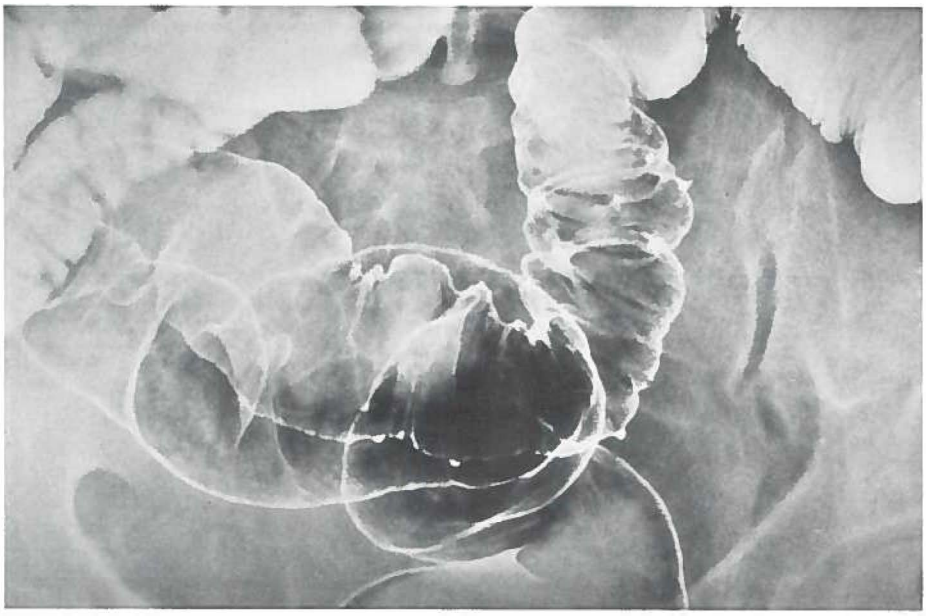


Fig. 5 Prediverticular state of the sigmoid colon in double contrast examination. Tiny herniations of the mucosa are visible.

1.2.3.3 Radiologic anatomy of diverticulosis

"Some men there are, who...love diverticulaes and turne aside into crooked waies..."(William Strong, 1647, (161)).

The word diverticulum comes from the Latin diverto (I turn aside) and, literally, means a small turning aside. The word was used to denote a by-pass, a lodging, or a wayside shelter. In Elizabethan times it was applied to a house of ill-repute (161).

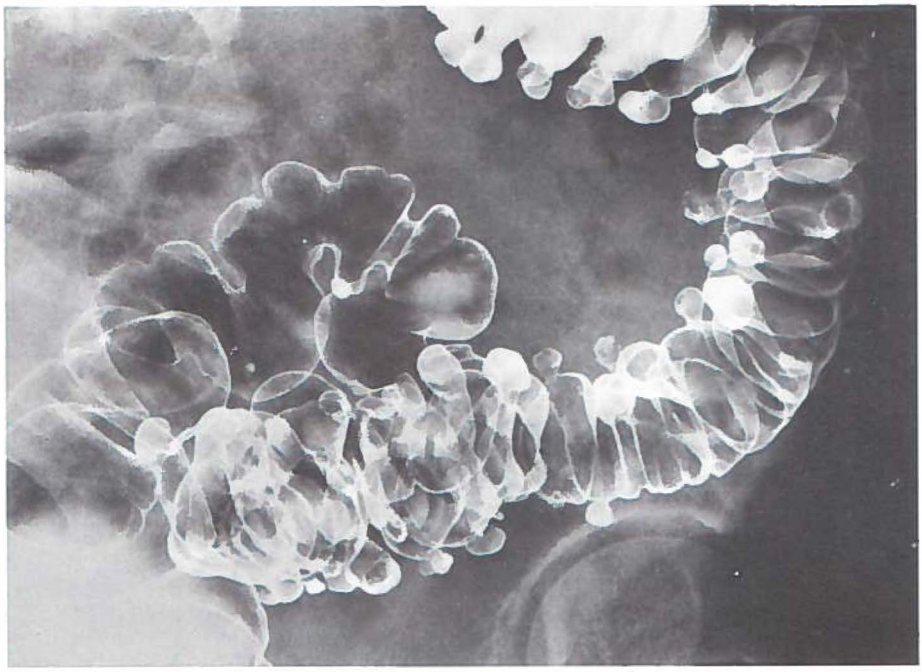


Fig. 6 Diverticulosis of the sigmoid.

Diverticula are visible as small sacs filled with barium (fig 6). If there is much fecal material in the sac, only a flask shadow may be seen (fig 7). On single contrast radiographs the pouch may be hidden behind the barium-sulphate (148). During double contrast investigation it is possible to improve the detection of the diverticula (172) (fig 8).

With double contrast the distinction of diverticula from polyps may cause difficulties. Both may cast a circular linear shadow in the face-on view. The circular line in a diverticulum has a sharp outer edge and a blurred, fuzzy inner edge; in a small sessile polyp it is the reverse (148;173).

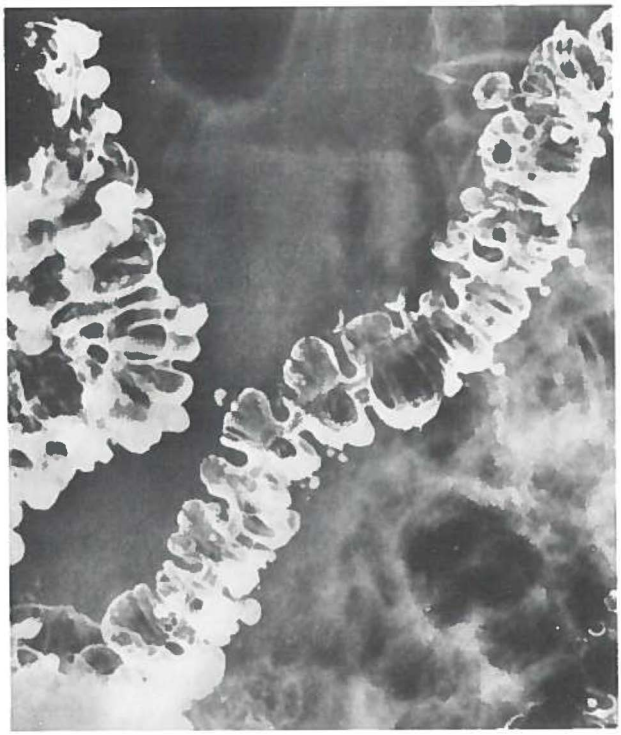


Fig. 7 Diverticulosis with two flask shadows, demonstrating fecal material in the diverticular sacs in double contrast examination of the colon.

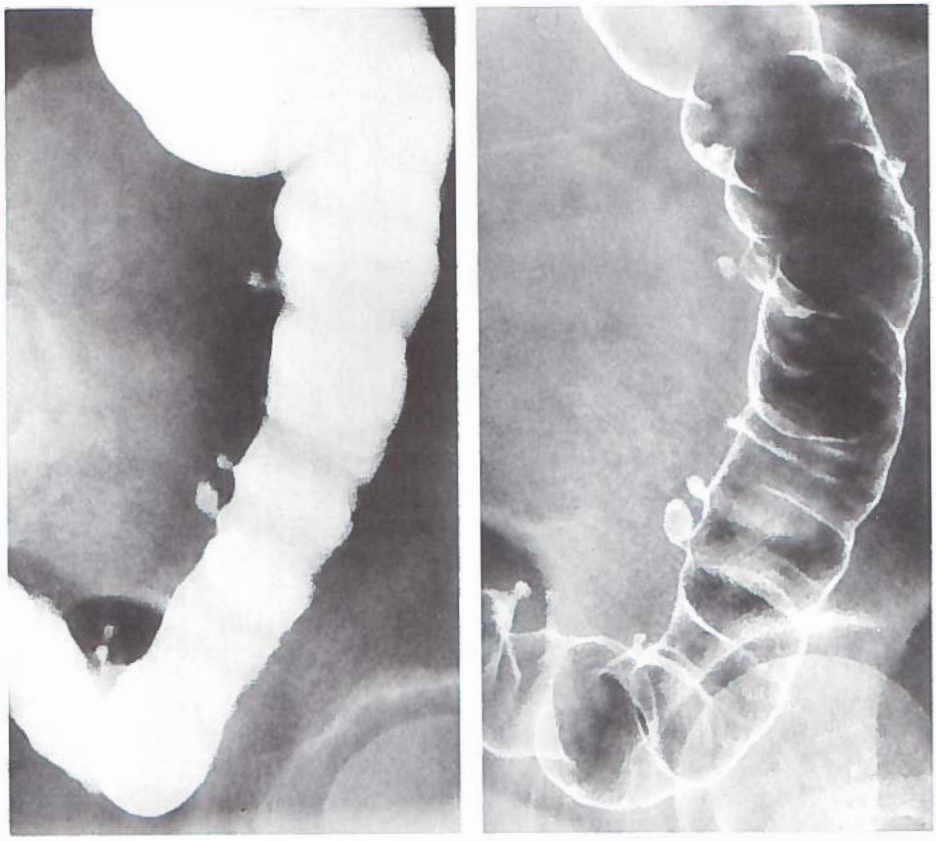
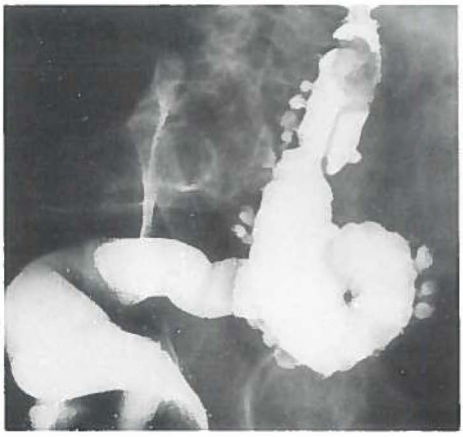


Fig. 8a Single contrast: tiny diverticula.

Fig. 8b Double contrast: more tiny diverticula.

It is best to identify a polyp as a dark stain in a white barium filled colon or as a tissue mass protruding into the gas-filled intestine, as seen in profile by good positioning. It is important to make the right diagnosis since polyps and even cancers of the sigmoid may occur in the presence of diverticula (fig 9a,b; fig 10).

Other diagnostic features of diverticulosis are: the interhaustral folds are deeper and the colon fails to elongate. The circular muscle can still be seen to contract and relax.



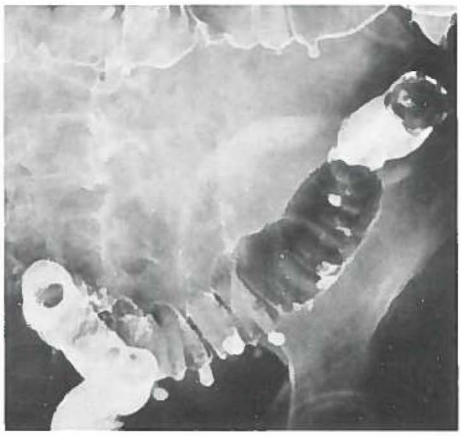


Fig. 9a Single contrast examination: diverticulosis and polyp. The polyp, with a long stem, is visible as a black stain in a white sigmoid.

Fig. 9b Double contrast examination of the same patient.

In the present study a routine single-contrast and double-contrast colon examination was carried out, in order to make as few false-negative or false-positive diagnoses of diverticula and/or of polyps or carcinomas as possible (174-177).

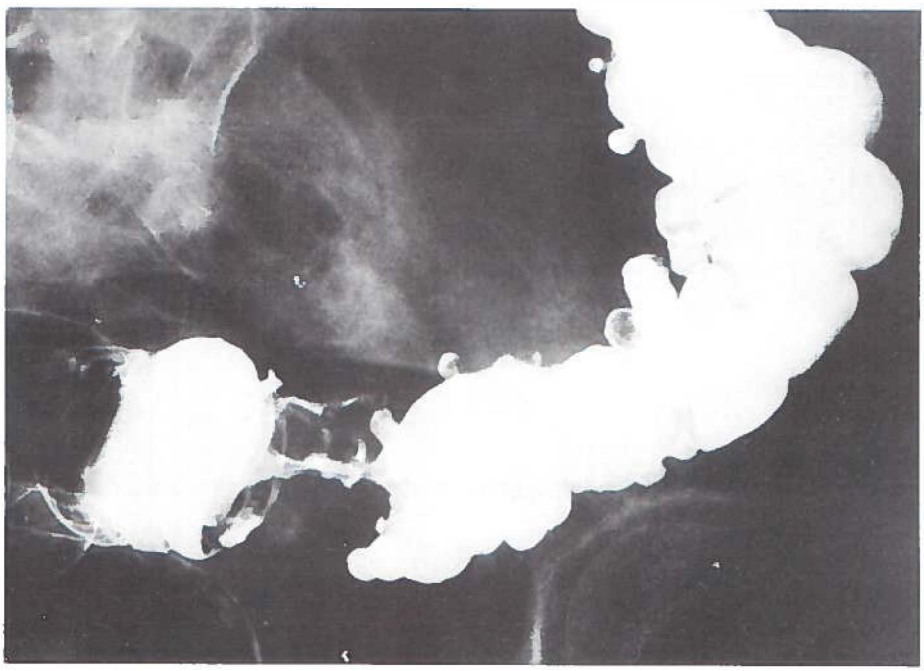


Fig. 10 Diverticulosis and cancer. Characteristic features of a malignant sigmoid tumor.

1.2.4 Complications in diverticulosis

A thorough discussion of the complications in diverticulosis is beyond the scope of this study. A short mention is necessary to make clear that this disease may become life threatening. The complications are diverticulitis and its sequences: narrowing and perforation with abscess or fistula formation (178-181). Sometimes hemorrhage is encountered (181). The barium enema is the investigation of choice (178) (fig 11). In case of a perforation (fig 12) we may be in trouble with a highly lethal condition (179). Formerly diverticulosis was known as diverticulitis (45) but this term should be used when there is evidence of inflammation (180). If the inflammation is localized in the wall of the sac the term diverticulitis is applicable. If the inflammation, through micro- or macroperforation, is localized mainly in the peridiverticular tissues and the pericolic fat, the name peridiverticulitis is more suitable (181).

More terms, however, lead to more confusion. The difference between diverticulitis and peridiverticulitis is of limited clinical value. It is more important to know if there is a perforation with a peritonitis or a sealed off perforation without a peritonitis.

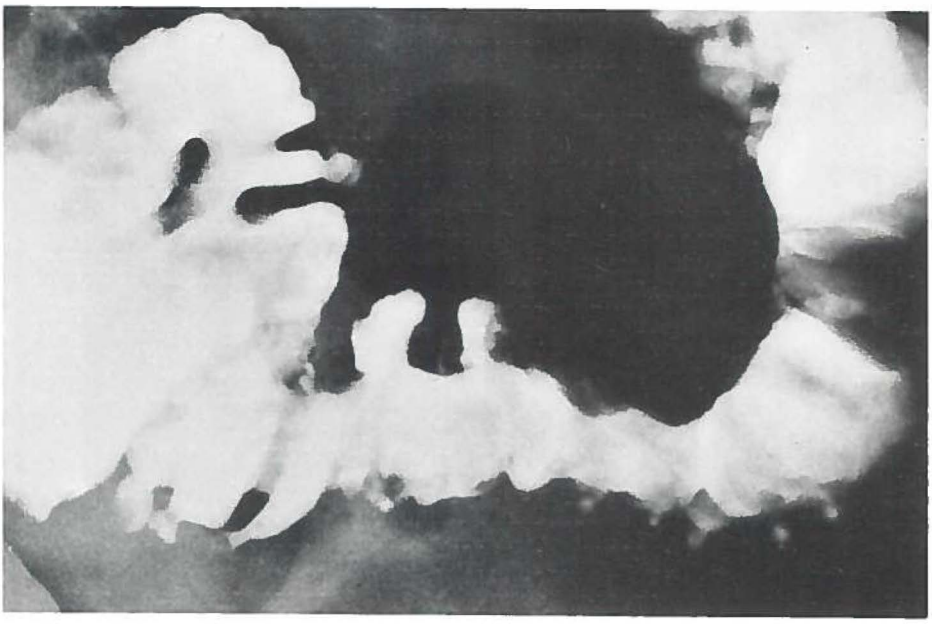


Fig. 11 Diverticulosis with diverticulitis. Narrowing of the sigmoid lumen, short blunt protrusions from the lumen, the diverticula are occluded by the inflammation.

1.3 Colonic physiology

1.3.1 Functions

1.3.1.1 Mucus secretion

The colonic mucus is a viscous substance formed by the secretion of the goblet cells (also called mucus cells) of the epithelium, combined with substances from the lamina propria (lying immediately under the epithelium): immunoglobulines and lymphoid cells and substances from the bloodstream; among others albumin and transferrin (117). Colonic mucus expressed in dry weight contains 72% proteins, 12% nucleic acid from shedding and bacterial cells and 6% glycoprotein. Colonic mucus also contains up to 100 mM potassium per liter, so in cases of diarrhea or colonic cleansing, as in preparation for a barium enema, much K may be lost. Physical properties of mucus are its gel forming ability, due to its high hydrophilia, and its forming of a protective barrier.

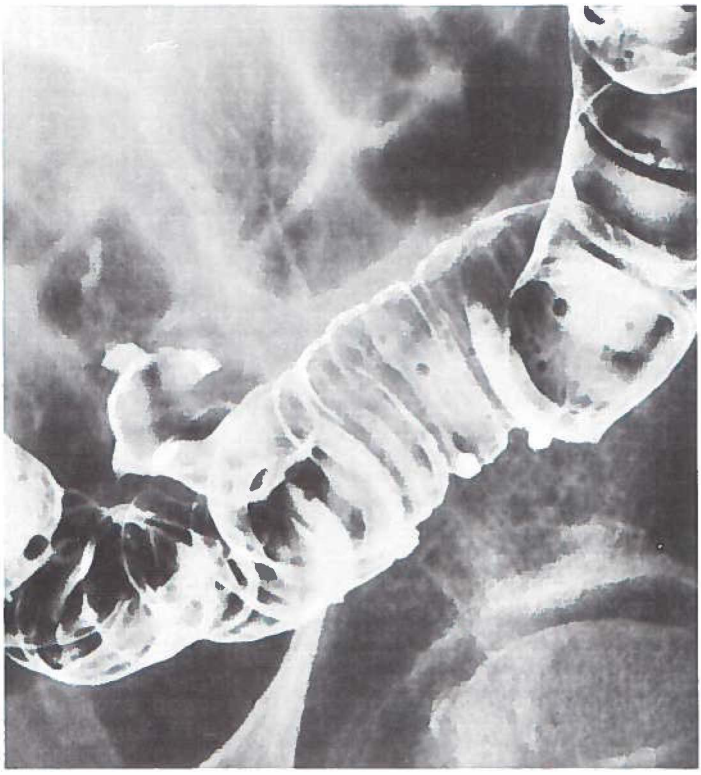


Fig. 12 Perforation with abscess in (peri)diverticulitis.

1.3.1.2 Absorption and secretion of water; interactions with fiber

Lack of a colon leads to excessive enteric loss of water (182). The cecum and proximal colon of humans absorb water more efficiently than do the descending colon and sigmoid (32; 182). About 350 ml of water is absorbed per day.

With interest growing in dietary fiber and its possible role in colonic function in health and disease, the possible interactions between fiber and the colon are to be considered. The structural or fibrous components of dietary fiber include cellulose, hemicellulose, and lignin. The nonstructural, more soluble substances are mainly found in the cell wall and include pectin, gums and mucilages and algal polysaccharides. Nonstructural polysaccharides have water holding and gelling effects (25). Water initially absorbs to the surface of the fiber; more water fills in the interstices. The ability of fiber to hold water ranges from 4.5 grams of water per gram of bran to 0.4 gram of water per gram of potato. For a long time bran has been known to expand and soften the stool. Part of the fiber material is metabolized by colonic bacteria (117). Pectin, although hydrophilic, is digested in the colon and therefore has little effect on fecal bulk (65); 50-75% of dietary fiber may be broken down in the colon (117). The increase in stool bulk induced by fiber is greater than that of stool weight, and the proportion of water to solid in the stool changes little. The trapping of gas may account for the softer, bulkier stool.

Bran will hurry gastrointestinal transit in those in whom it is slow, and may slow it in those in whom it is fast. It appears that at least 20 grams of unprocessed bran per day are necessary to have an effect on transit. Fine bran, however, has much less bulking effect, perhaps because of its weaker water holding capacity.

The colon can also secrete fluid. Fluid secretion by the colon was largely ignored by physiologists until clinical observations demonstrated that this phenomenon contributed to certain diarrheal illnesses. Colonic secretagogues are among others bile acids. The fluid secreted is an isotonic ultrafiltrate of plasma. The mechanism by which water is secreted is uncertain. In vitro, secretion is associated with increases of mucosal adenylate cyclase and cyclic AMP (adenosine 5'-phophate) (182).

Bile acids and fatty acids reduce colonic absorption and even evoke a net secretion of fluid. This phenomenon is, in vivo, dose related and rapidly reversible. The mechanism for bile acids and fatty acid secretion is uncertain and probably multifactorial, the role of altered permeability is doubtful (117). Bile acids and fatty acids are potent cytotoxins, causing mucosal damage in the colon. When bile acid reabsorption in the small gut is reduced (e.g. following resection of the ileum) cathartic bile acids flood the colon , causing diarrhea (117). Fatty acids are said to stimulate the mucus secretion and the motor activity of the colon (25). Dietary fiber alters bile acid metabolism. Lignin, a fiber component, and psyllium , like cholestyramine, will bind bile salts.

1.3.1.3 Storage of fecal matter

The distal half of the colon is responsible for storage of feces until it can be expelled voluntarily (32). The rectum is normally empty. The urge to defecate is elicited when a threshold volume is reached in the rectum (117). Stretching induces a sensation of urgency.

1.3.1.4 Motility of the colon

1.3.1.4.1 Introduction

In order to move the colonic contents from cecum to rectum motility (also called motor or contractile activity or movements of the colonic wall) is necessary. The types of movements that occur and the way they are coordinated are imperfectly understood. A colonic contraction is not always equal to a forward movement (propulsion) of the contents. Contraction of the circular muscle results in segmentation; contraction of the longitudinal muscle in shortening and straightening of the colon (32). The circular and the longitudinal muscles are capable of independent activity (183).

Movements of the gut wall are said to arise through intrinsic reflexes involving neural pathways running between mechanoreceptors and muscle layers (106). The movements may be induced by locally applied distension. There are mechanoreceptors (also called distension-sensitive receptors) in the mucosa. These receptors appear to be, in the small intestine, of two kinds: low and high threshold ones. It is postulated that low levels of distension excite the low threshold mechanoreceptors and lead to the preparatory phase of motility: contraction of the longitudinal muscle together with reciprocal inhibition of the circular muscle. This results in a zone of increased circumference of the intestine which stimulates the high threshold receptors. Through this the emptying phase is initiated: an aborally moving wave of contraction of the circular muscle coupled with reciprocal relaxation of the longitudinal muscle (106). Some authors also found this phenomenon of distension causing movements in the colon (19;94); others could not find it (184).

1.3.1.4.2 Patterns of motility

Several distinctive patterns of motility have been observed in normal human subjects.

A/ Basic tone. This is supposed to be a contractile state upon which the other contractions are superimposed (65).

B/ Segmentation (or nonpropulsive or nonpropagative segmental contractions): a to and fro movement of the contents (185). These contractions are caused by isolated units of circular smooth muscle and promote the absorption of water in the proximal part of the colon.

C/ Propulsion: the contents of the colon are displaced into a more distal part. Neither electromyography nor pressure recording have yet described the propulsive mechanism, probably due to the slowness of colonic events (117). Probably prematurely, these movements are divided into four types (32):

a/ haustral propulsion: the contents of a single segment or

haustrum are moved into the next one without being returned;

b/ multihaustral propulsion: a number of haustra are involved as a coordinated unit;

c/ mass propulsion or mass movement: the colonic lumen becomes wide ahead of multihaustral contractions and the fecal mass travels distally over a long distance. This happens only in the distal half of the colon and may be associated with synchronous contraction of circular and longitudinal muscles;

d/ peristalsis: a bolus is displaced aborally by an advancing circumferential ring of contractions preceded by a wave of relaxation in coordination with a contraction of the longitudinal muscle (27;78;106;117).

D/ Retropulsion (or retrograde propulsion): the contents of the colon flow orally. It occurs most often in the proximal part of the colon allowing prolonged contact of the liquid stool with the absorptive surface (130;186). This retrograde movement may also occur in the distal colon (183).

1.3.2 Control systems

A detailed description of the controlling mechanisms of colonic movements is beyond the aim of this study. A short summary is given for the sake of completeness. The coordination of colonic movements depends on three control systems (32).

A/ The neurogenic system is divided into a parasympathetic or cholinergic part (the predominant effects are increased activity of the colonic muscles) and a sympathetic or adrenergic part (which is predominantly inhibitory). The colocolic reflex plays another important role.

B/ The myogenic system: the smooth muscle of the colon generates spontaneous electrical impulses resembling, more or less, the pacemaker activity of the heart. These impulses can be recorded with the aid of electromyographic investigations (32) (see section 1.7).

C/ The hormonal system. Exogenous Cholecystokinine (CCK) and endogenous CCK, which may be released in response to meals, may lead to excessive colon motility. Fasting and postprandial concentrations of insulin, gastrin, polypeptide or substance P, enteroglucagon, neurotensin , motilin and gastric inhibitory polypeptide (GIP) were reported to be normal in patients with IBS (78;187). Glucagon has been reported to abolish activity and decrease the tone of the colon (32;117).

1.3.3 Methods of recording colonic motility

1.3.3.1 Introduction

The methods with which the colon motility is recorded have to lead to reproducible and quantitative results (78).

It is possible to get information about the electrical activity of the colonic muscles with electromyography or with the aid of strain gauge force transducers. The latter are fragile and their electrical characteristics may change within the bowel (130). They must be fixed to the external surface of the colon and , therefore, are not applicable in humans. Electromyography is discussed in section 1.7.

The colonic transit time is a rough way of recording the motility. It can be studied with radiopaque markers or labelled

meals.

The intraluminal pressure can be recorded with a pressure sensing device localized in the sigmoid. This method is also called manometry. The terms pressure recording and manometry are used interchangeably in the literature. Manometry is the science of pressure measurement of liquids and gases. Pressure is the force exerted by one body on another, or by a liquid or gas on its surroundings (188). So it is better to speak of pressure recording. This subject will be discussed in the following section.

The radiologist has the opportunity to study the motility of the colon wall with the aid of cinefluorography (189;190), or barium investigation and fluoroscopy (87-89). It is possible to study the impact of the wall movements on the movements of the contents.

The combination of intraluminal pressure recordings and radiologic investigation of the movements of the sigmoidal wall seemed to the present author the best method in studying the phenomena related to the motility of the colon (183;186;189-193). This subject will be discussed in section 1.3.4.2.

1.3.3.2 Intraluminal pressure recording

An increase of the intraluminal pressure in a segment of the colon mostly results from a contraction of the muscles which reduces the volume of that segment. The pressure is related to the magnitude and rate of the volume change. Such a reduction of volume may expel some of the contents of that segment. This expulsion, however, may be opposed by a resistance from adjacent segments which also, simultaneously, contract or do not relax (194). The result is an increase in pressure in that particular segment. Only a resistance to flow causes, technically speaking, a rise in pressure (27;106;195).

The absence of change of intraluminal pressure may mean a lack of contraction or may mean local contraction of a segment with no resistance to flow, actually producing propulsion. Pressure, motility and transport of contents seem in no way synonymous.

Pressure recording may estimate the resistance to the flow of the contents of the colon. The heights of pressure to which the wall of the colon is exposed are measured.

From the literature the data to which a correct pressure recording investigation must meet were gathered and tabulated (27;32;96-100;130;147;183;184;186;187;189-212) (table 1)

1/ Bowel preparation is necessary to avoid plugging the intrasigmoidal pressure sensing device and to ensure identical colonic contents in all subjects (i.e. an empty sigmoid) (199).

2/ The number of investigated persons must be given. The definition of the group must be as clear as possible. This is difficult in the IBS group because of the lack of a positive diagnostic criterion.

3/ The distance from the anus must exceed 15 cm as the rectum is about that length (117). The devices are often placed at about 30 cm from the anus (100;196-199). The real distance must be, if a rigid sigmoidoscope is used, less than the value

1/Preparation	colonic cleansing regime fasting period before study
2/N = number	control cases; patients with an IBS and/or diverticulosis
3/Site of recording	distance from anal verge in cm
4/Pressure sensing devices	balloon: length, diameter, air/fluid filled open ended tubes: diameter of lumen, constant flushing, air/fluid transmission electronical: microtransducers or strain gauges radiotelemetering capsules
5/Way of introduction	rigid or flexible sigmoidoscope
6/Calibration	no basal pressure recording
7/Recording equipment	paper speed aid of radiologic equipment and video
8/The procedure and the duration of recording in minutes per period	resting period fasting period postprandial period: standard meal post-gut-relaxant period: kind of drug
9/Pain-pressure correlation	

Table 1 Necessary data of motility recording

read off the barrel, because of the inevitable stretching of the sigmoid. This problem is overcome with the aid of a flexible sigmoidoscope (187). The position of the device in the sigmoid has to be checked. This can be done through fluoroscopy if the sigmoid is coated with bariumsulphate.

4/ The applied pressure sensing device may be a balloon, an open ended tube or, more recently, an electronic micro-transducer. The particular form of the wave-patterns depend on it.

Balloons may constitute a foreign body which may modify motility. They may be moved to another site by a powerful contraction (130;186;194). This technic may be not capable of recording changes with a frequency of more than five to nine per minute (186). The length and diameter of the balloons must be mentioned. Errors arise out of the use of balloons of various shapes and volumes. The balloons may be filled to different pressures with air or fluid. It is a complex problem with many items which have to be considered so that mistakes are easily made.

That may be the reason why later open ended tubes were applied. The studies applying these tubes have yielded results which differ from earlier work (186;191). Mostly, however, a control group and a group with patients is studied so that a comparison between different investigations is possible.

To prevent plugging, flushing of the tubes is necessary. With flushing, however, it is impossible to use barium contrast to visualize the colonic wall in order to see its motility during the pressure waves. So when the combination of pressure recording and radiological study is employed, no flushing can be realized. Electronic microtransducers offer a good solution to

this problem, they need no flushing. These electronic pressure catheters have been used, but not in combination with radiography (200).

5/ The pressure catheter is mostly introduced into the sigmoid through the biopsy-channel of a flexible sigmoidoscope.

6/ The equipment must be calibrated so that it is known what the pressure equivalent is of a measured wave on the recording paper (183;211). The basal pressure is not included, only the waves over this base line. This basal pressure probably is mainly a manifestation of the hydrostatic pressure of the tissue mass above the point of reference (211), or of the basic tone of the sigmoid colon (65).

7/ The kind of recording apparatus, transducers and amplifiers must be mentioned.

When the paper speed is low, e.g. 2.0-0.5 cm/min, it is impossible to measure accurately the height and duration of each separate wave (27;99;198;200). A speed of about 15 cm/min (2.5 mm/sec) or higher is more suitable to that aim (183).

8/ The patients are lying at ease on a couch in a quiet room. A fasting period, a stimulated state after a standard meal and a period after a parasympathomimetic drug (neostigmine or prostigmine) or a gut relaxant (pethidine or glucagon) are studied (191;212).

Very often a recording period of 30 min is practised with an adaptation period of 15 min before the recordings start (198; 200; 202; 204; 205; 210).

9/ Pain-pressure correlation. The present author is interested in the correlation between pressure recording and pain sensations. Is the pain correlated to a particular sigmoidal contraction? (213).

1.3.4 Radiologic investigation of colonic physiology

1.3.4.1 Radiologic investigation

On November 8, 1895, W.C.Röntgen discovered the X-rays (214). In 1898 the first report was published about the movements of the stomach in humans studied by means of the X-rays (215). Soon the studying of the movements of the colon, in cats, followed (216). Peristalsis (and antiperistalsis in the right colon), was observed. In 1909 and 1911 further observations on the motility of the colon, in humans, were published (217;218). In 1945 the influence of rage on the motility was established. A contraction of a lengthy segment was observed in a rat that was in a rage. The same rat, later and calm, showed no contraction (219).

Other authors described the alterations in motility of the sigmoid, seen during a barium enema, thought to be characteristic of IBS: segmentation and/or contraction of lengthy segments (26;87-89;164-171) (see section 1.2.3.1).

It was suggested that these peculiar states of contraction of the sigmoid could be caused by castor oil, used in the cleansing of the colon (220) or by a barium suspension at low temperatures (170). The castor oil is not the only cause because the present author also sees these contraction patterns nowadays, and his patients don't use castor oil (221). The bariumsulphate should be at bodytemperature.

It seems possible to recognize this functional abnormality

during a barium enema. It is, however, not possible to quantify these data (189;190;222;223). The development of image intensifiers reduces the dose of radiation, so that a more prolonged examination can be undertaken. These developments have extended the scope of radiology in the study of gut motility.

The pain from which the patients suffer can also be studied. There may be a correlation between the abnormal contraction of the sigmoid, as seen during the barium enema, and the left abdominal pain (87-89). It has to be avoided to suggest to the patient that she/he has to feel the pain during the barium enema.

The present author disagrees with another author (224) who stated that the radiologist must not be aware of the clinical diagnosis. The radiologist has to know what the thoughts of the clinician are in order to perform the most appropriate examination. The radiologist has to have interest in the study of functional abnormalities and has to perform the suitable examination.

The present author agrees with others that there is a need for studies employing simultaneous radiography and pressure recording to elucidate the colonic motility (186) and to get more information about the cause of the pain in painful IBS. It is necessary to measure the height of the waves which correlate with the patients' pain. Is the intrasigmoidal pressure of such a height that the receptors in the wall are triggered to send a pain stimulus centripetally?

1.3.4.2 Radiologic investigation combined with pressure recording

In pressure recording it is thought that the rise in pressure is an active contraction (9). But is it indeed an active contraction ? In 1961 the first systematic study of colonic motility by the combined method of radiologic study and pressure registration was published; cineradiography was applied (191). The types of movements were bowel shortening or luminal narrowing or combinations. Shortening was present when the haustral configurations moved towards each other. Narrowing was observed as a reduction in the width of the bowel while maintaining parallelism of the walls. This narrowing could be multihaustral or singlehaustral. Other manifestations were segmentation: local contractions that deepened the haustral folds (192). The shortening is caused by a contraction of the longitudinal muscles. The narrowing and segmentation is caused by a contraction of the circular muscles.

Earlier interpretations of pressure changes in terms of motility appeared to be misinterpretations (183;206). It was discussed in section 1.3.3.2 that it may be more appropriate to consider pressure as resulting from a resistance to flow. In investigations, combining radiologic technics and pressure recording, it appeared that if the flow was not resisted there was colonic motility and movement of the contents without an increase of the pressure (isotonic contraction (106)). If the flow was resisted and there was colonic motility (as is the case in a segmental contraction of the sigmoid) the pressure became

elevated. Other authors also found that not all radiologically observed movements had pressure recording counterparts in cineradiology (192;225). It was concluded from these studies that pressure recording may be a recording of the resistance to flow.

1.3.5 Methods of analysing pressure recordings (table 2)

1.3.5.1 Introduction and history

Most motility studies in humans have been confined to the rectum and rectosigmoid areas (27). The analysis of physiologic records is complex and time consuming. Colonic recordings are among the most difficult because of their variability and of our incomplete knowledge about their meaning (32). The scoring should be done in such a way that the investigator is not biased. There must be clearly defined scoring criteria. Only a few of the existing studies met these requirements (32). The records have largely been scored visually. Visual methods vary considerably from one study to another as there is no universally accepted scoring convention.

Earlier workers described three types of waves (82;183). Other authors have questioned its usefulness and categorized the waves in their own way. Some authors (99) discerned:

a/ simple wave: monophasic and approximately symmetrical;

b/ complex wave: two or more waves together, the line does not return to the baseline;

c/ repetitive wave: a sequence of two or more waves, the curve returns to the baseline. It is possible to discern the single wave.

Other authors described peak waves and base line shifts (192). Peaks were identified by a rapid change in up- and downstrokes, baseline shifts exhibited slow up- and downstrokes. Pattern interpretation has not progressed far because a wide variety of wave forms is recorded (130). It is a subjective form of interpretation.

1.3.5.2 Characteristics of the waves

Most investigators now prefer to describe the overall degree of activity (27). The term "motility index" is used to describe the total change in intraluminal pressure per unit of time.

The motility index is the sum of the products of the amplitude and duration for each wave, expressed per period of time (19;27;191). Some authors, however, multiply the mean amplitude and the percentage duration of activity (203); others use for this product the term index of total activity (202); others even use the term motility index, for that product (205). Very confusing.

A wave is defined as a curved line placed upon a baseline with an amplitude and a duration.

The amplitude is the vertical distance between the basal pressure line and the highest point of the wave or curve (211). The positive pressure deviation from baseline must be of at least 2 mm Hg (99). The amplitude can be expressed, in mm Hg or in Pascal according to the S.I. (Système International in French) agreements (table 2).

1/ Incidence: the number of waves per period of time.
2/ Amplitude of the waves, 1 mm Hg is about 133.3 Pa (Pascal).
3/ Duration of the wave in second (s).
4/ Motility index = the sum of the products of the amplitudes + the duration of each wave per period of time. formula: Σ (amplitude x duration) in t min/t min
5/ Area under the curve.
6/ Mean numbers ± SEM (standard error of the mean).
7/ Statistical analysis.

Table 2 Methods of analysis and characteristics of the waves

The duration is measured in seconds from the point of deflection from the baseline to the return (192). The baseline of the recorder has to be stable (211). The recording paper has to move at a standard speed so that the duration of any pressure wave can be measured.

In case of complex waves it is difficult to know what the duration is. No criteria could be find in the literature to solve this problem.

The incidence of the wave is the number of waves ocurring in a period of time.

As many waves are far from sinusoid, but have irregular shapes, it is debatable if it is correct to take the motility index as the index of the change in pressure . So some investigators estimate the area under the curve to describe that change (32;200;210). It is possible to calculate that area with the aid of a computer. One can trace the pressure waves on paper of uniform standard weight and cut them out (210). Another possibility is to count the squares under the curves on the recording paper.

A study in which a comparison is made between motility index calculations and area under the curve estimations could not be found in the literature.

Of each characteristic the mean numbers and the SEM (standard error of the mean) are calculated. After this a statistical analysis must be done. Some authors have applied this analysis to their numbers (199;200;204;205).

1.4 Terminology

1.4.1 Introduction

Consideration of bowel habit may include six parameters (9;65;226) (table 3). Traditionally one bowel movement per day is thought to be ideal. Of 1500 interviewed healthy persons 99% had bowel movements within the frequency limits of every third day and three times a day. Nevertheless, some regarded themselves constipated and took laxatives (65;227). Stool

1 Stool frequency
2 Stool consistency
3 Stool weight
4 Ease of defecation
5 Sensation of rectal emptiness
6 Transit time measurements

Table 3 Some parameters of bowel habit

frequency differs whether the information is obtained from recall or from a prospective diary (9).

In order to provide more objective evidence of stool consistency a penetrometer has been devised and gone into production (228). Penetrometry consists of measurement of the distance travelled into the stool of a standard, pointed, inverted cone, dropped from a standard height.

Stool weight may range from 35 to 225 grams per stool, there are age and geographic variations (9;226). The average normal stool weight in Western society is between 100 and 150 grams daily (9).

Difficulty in evacuating stools is even more difficult to evaluate. How does one define straining ?

Patients suffering from diverticulosis complain of sensations of non-emptiness after a bowel movement. It is speculated that some feces is retained in the diverticula which is expelled afterwards, filling the sigmoid with stools again. Patients with IBS may complain of an incomplete evacuation. This may be caused by the hypersegmentation of the sigmoid as is demonstrated during the barium enema (fig 2, section 1.2.3.1). It may be that the bariumsulphate is trapped in saccules (89). Another explanation may be that there is a tendency to prolapse formation or an incipient anal prolapse.

Transit time is the time required for a meal to pass through the gastrointestinal tract. It varies widely in different populations with different fiber consumptions. Fluids and solids have different rates of transit. The mean transit time through the human colon measured with the aid of radiopaque markers in food in normal adults is about four days and in normal children two and a half day (226).

A high fiber diet favors fast transit times (185). The Ugandans have a transit time of 36 hours as opposed to 83 hours for fiber deficient British individuals. The average African daily diet contains about 60 grams of dietary fiber, its British counterpart 12 grams (65).

In considering bowel habit it is necessary that the doctor personally examines the stool in difficult cases of persisting complainers in order to objectify the quality and the quantity of the stools.

The definition of normal bowel habits is difficult because these habits are related to many factors, among others the social habits of people, the geographic variations, the kind of food that is taken (fiber consumption) and the age of the studied people. It is important that the doctors ,concerned with patients with problems with their stools, come to an agreement about definitions.

1.4.2 Constipation

One of the characteristics of constipation (constipare = to crowd together) may be a number of stools of less than three per week (9;229). The stools are hard, lumpy, scybalous or pelletal. Constipation may be defined as straining at stool for more than 25% of occasions; thus defined 6% of apparently healthy British people has to be considered as constipated (9). Patients complaining of "constipation" may mean: infrequent or difficult defecation or abdominal discomfort, distension or "wind". The sensation of rectal emptiness is not spoken about

(9;65;229). The transit time in these patients is suspected to be above the mean time.

1.4.3 Diarrhea

Diarrhea (dia rhein = to flow through, Greek) can be defined as four or more defecations daily. The consistency of the stool is watery or semi-solid on more than 25% of occasions (9;229). The transit time is shortened as most time of the bowel contents is spent in the colon.

Diarrhea may occur paradoxically in impacted patients. This is not recognized unless digital rectal examination is performed. Only fluid finds its way around the solid fecal mass in the rectum.

In the literature it is stated that a complaint is worthy of medical consideration by the very fact that the patient has come forward with the complaint to the doctor (9;226). In the author's opinion the doctor must have the knowledge to sort out these complaints into pathologic and non-pathologic ones. Moreover she/he should have the courage to tell the patient what has been found. If the cause of the complaint is not found, that must be told instead of "it must be nervousness".

1.4.4 IBS

Concerning IBS there has been a verbal debris (165) almost likening the diarrhea sometimes met in this condition.
The following terms have been found in the literature: adaptive colitis, ataxic colon, autonomic imbalance of the colon, chronic catarrhal colitis, chronic spasmodic affections of the colon, colica or colitis mucosa, colicky sigmoid syndrome, colon or colonic neurosis, colon hyperirritabile, colonic enterospasm, dyskinesia or dyssynergia of the colon, endocrine imbalance of the colon, functional enterocolonopathy, functional diarrhea, functional disorders of the colon, glarry enteritis, glutinous diarrhea, instable colon, intestinal croup, irritable bowel syndrome (IBS), irritable colon, irritable colon syndrome, irritable gut syndrome, lienteric diarrhea, membranous catarrh of the intestine, membranous enteritis or colitis, muco-membranous colic or colitis, mucous colitis or colic, myxoneurosis or myxoneurosis intestinalis membranacea, nervous diarrhea, neurogenic mucous colitis, nonspecific diarrhea, spasmodic stricture, spasmomyxorrhea, spastic colon, tender colon syndrome, tubular diarrhea, unhappy colon, unstable colon, vagotonia of the colon and vegetative neurosis of the colon (9;23;26;32;80;82;168;205;230-232).

The Germans and the French have their own special names. In German there are :Reizcolon (16) and decompensiertes Colon (26). In French the names almost sound like songs: colopathie fonctionelle douloureuse (15) or l'entérocolite muco-membraneuse.

It seems as if the gaps in our knowledge (228) are filled up with an overwhelming number of names.

The first description of IBS in the literature was, as far as could be checked, in 1820 (233). Other publications followed in 1830 (quoted by 65); 1849 (234) and in 1871 (235). In those

days the malady was called membranous enteritis or spasmodic stricture. A peculiar discharge of membranous matter or jelly casts was noted; this material resembled ordinary mucus. Some patients suffered from attacks of abdominal pain, also called spasmodic or colicky pain (233-235).

Later on it was thought that IBS was a clinical picture of a dysfunction of the bowel that includes some combination of three symptoms: colonic pain; upset bowel habit and hypersecretion of mucus (236). Other authors mentioned: a/ pain and/or alternating bowel habits; b/ diarrhea or alternating diarrhea and constipation, no pain; c/ no identifiable anatomic abnormality (17;20;24;26;27;50;53;58). Some authors call the malady spastic colon if pain is concerned, which is relieved with bowel movement (9;11;50;226;235). The spastic colon may be associated with constipation (9;23;24;65;226), or there may be no disturbance of bowel habit (237). Pain is the cardinal, commonest and most distressing symptom of IBS (9;33;34;233-235;238). The pain may be located in the left lower abdomen and may be colicky, in bouts or sharp piercing knife like (23;33;34; 206;237). The diarrhea mostly is painless (17;20;24;26;27;50;53; 58;206;226).

Physical examination of the abdomen may reveal little, but a surgical scar is common. The colon may be palpated, rope like, and tender, especially in spastic cases. Another author describes more and other physical signs: a/systemic signs: cool, clammy hands and flushing of the skin of the face and neck; b/ abdominal signs: an excessively palpable and tender colon and scars c/ rectal signs: increased clinically assessed anal sphincteric tone; a positive mucosal tap sign (pain on tapping the finger, during rectal examination, against the mucosa on the sacral side of the rectum) ; an empty or nearly empty rectum and the presence of hard or firm feces (9). Patients with the painful IBS were said to have more backpain and a constant feeling of tiredness than matched controls (239).

The third characteristic of the syndrome is the absence of any identifiable anatomic abnormality. A barium enema examination and a sigmoidoscopy must show no anatomical abnormalities; a biopsy must be within normal limits; blood tests including haemoglobin, ESR (erythrocyte sedimentation rate), serum albumin, and liver function tests must also be within normal limits; there must be no blood in the stool (19;20;32;55-58;238).

It recently appeared that even computed tomographic studies of the painful abdomen were carried out and interpreted as normal in 40 patients (240). A CAT-scan investigation is not indicated in such cases.

As there are no positive diagnostic criteria for the IBS (6), the syndrome remains ill defined (64;241-243). Thus, arbitrary decisions in diagnosing a painful IBS cannot be eliminated (2;244). Exclusion of organic diseases remains necessary.

1.4.5 Secondary IBS

The term secondary IBS may be misleading. On one side it means that IBS may coincide with other illnesses, on the other side that other illnesses may mimic the symptoms of IBS. The

consequence may be that patients, suffering from IBS, who appear to have gallstones too, and who are treated by a cholecystectomy, may have an improvement of the symptoms of the IBS whereas other patients may not improve. Especially female persons, with IBS, still suffer with it when the stone-filled gallbladder or appendix (with or without histologic evidence of inflammation) is removed or when a gynaecological operation has been performed (23;32;76;245). In one series 40% of new referrals of patients with IBS had undergone previous abdominal surgery and 33% had lost their appendices without a clear alleviation of their symptoms (23;32;54;76).

The other side of the problem is that some patients are thought to have functional symptoms of a painful IBS, but no diagnostic tests are performed to exclude an organic disease. Too many anxious patients with colonic cancer may wait overlong, because their symptoms are thought to be functional, before the correct anatomic diagnosis is made (23;32;231;246).

It is time to develop a test so that the disorder in painful IBS can be diagnosed positively.

1.4.6 Lactase deficiency

Some patients with diarrhea, thought to have an IBS, may have a lactase deficiency. This deficiency leads to a lactose malabsorption and diarrhea (247;248). It was advised to perform the lactose tolerance test in IBS patients. However, hypolactasia appears to play only a minor role in the etiology of the IBS, especially in the group without painless diarrhea (249). Recently, the lactose tolerance test was carried out only in those IBS patients who complained of diarrhea (5). Yet, rarely, a patient with constipation who has a hypolactasia may be encountered.

1.5 Etiology and pathogenesis of painful IBS and diverticulosis

1.5.1 Introduction

Etiology (aetia = cause; logos = science) describes the cause of a disease. Pathogenesis (pathos = disease; genein = to produce) explains in wich way the cause leads to a disease (188). Sometimes the terms etiology and pathogenesis are used interchangeably (250). In this section we will discuss both items together.

1.5.2 Etiology and pathogenesis of painful IBS

Three main factors are important: increased sigmoidal motility, possibly congenital; dietary; psychological (250).

1.5.2.1 Increased sigmoidal motility

According to the literature, the sigmoidal motility may be increased in patients with abdominal pain (191;197-200;204;205). Other authors found no increased motility in such patients with a spastic colon (99). Others found a normal motility if they had no symptoms (203). One author stated, in a review, that the data obtained by pressure recording, so far, is conflicting (97).

Some investigators studied the relationship between pain and sigmoidal motility. One investigation showed a correlation between hypermotility and pain sensations in 5 of 7 painful IBS patients (100). Others insufflated balloons in the rectosigmoid to evoke pain sensations (94) or to reproduce the patients' pain (83;84). During sigmoidoscopy or barium enema it is also possible to elicit pain (85-89;251). The source of the pain may be hypersegmentation or an unusually strong contraction (32). Is there an increased tension in the colonic wall or a colonic hyperalgesia (91-94)?

A correlation between pain and hypermotility could not be found in one investigation (99). Nevertheless, it was suggested that the painful IBS might be rather functional than psychological (251;252).

1.5.2.2 Low fiber diet

A high fiber diet (HFD) may result in a marked decrease of pain or cramps in patients with painful IBS (5;25;54;57;65;253-256). So fiber deficiency may be important. A carefully controlled clinical trial demonstrated that 20 grams of wheat bran (or four slices of whole meal bread) daily improved IBS symptoms, especially pain (57). Wheat bran is currently being used by 93% of British gastroenterologists.

1.5.2.3 Psychologic factors

The psychologic or psychosomatic etiologic factor in IBS is a big problem. Excitement resulted, in a case report, in evacuation of feces from a transverse colostomy (257). Patients with IBS may have more motility of the sigmoid colon because they are frequently emotionally aroused or they may mislabel normal physiological activity because they are neurotic (238). Unsympathetic discussion of certain emotional conflicts led to hypomotility in 18 patients with diarrhea whereas pain stimulus led to hypermotility in seven volunteers (258;259). Diarrhea predominant IBS may be related to anxiety (260;261). A positive association between psychoneurotic disorders and IBS was shown (262;263). Irritable colon was thought to be a bodily change accompanying emotional conflict in response to environmental stress (264;265). Pain prone patients were assumed to choose suffering as their way of life (266). There might be a genetic predisposition to neuroticism which predisposes to IBS (267). It is said that the causation of disease by psychosocial stimuli is unproven, but at a high level of suspicion (268).

According to another author, however, all diseases are multicausal, the relative contribution of the somatic, psychologic or social component varies from disease to disease (269). Anxiety is a part of the illness experience in all patients (270).

The present author agrees with the following statement : "Even under ideal research conditions, it is wise to remember how difficult it is to prove the absence of a relation " (271). The evidence of the relations between psychologic phenomena and functional alterations in the colon is anecdotal (65) and the role of psychosocial factors in patients with the IBS is controversial (9).

1.5.3 Etiology and pathogenesis of diverticulosis

The three factors which are mainly of concern are: congenital; dietary and increased sigmoidal motility.

1.5.3.1 Congenital factors

Patients with congenital abnormal collagen, as in cases with Ehlers-Danlos syndrome (272), Marfan's syndrome (273) or neuromuscular disorders of the gut (274) may have colonic diverticula in an early stage of life.

It is suggestive that congenital factors play a role in the resistance of the colonic wall against intraluminal pressures.

1.5.3.2 Low fiber diet

A low fiber diet fed to rats or rabbits led to the formation of colonic diverticula (275;276). Hemicellulose in the form of psyllium was found to prevent the development of diverticula (275). In humans it is reported that a low fiber diet (Western society) leads to a higher incidence of diverticulosis compared to people with a high fiber intake (tropical or African society) (41;277-281). It was found that the tensile strength of the sigmoid was smaller in a Western group than in an African group (282). Diverticulosis may be a deficiency disease, there is a lack of fiber (283-285). New support was published for this idea. The paleolithic diet might have included more nondigestible fiber than the Western society diet (286).

A low fiber diet, producing small stools, may lead to intermittent distension of the sigmoid so that an increased uptake of elastin may be triggered (149) (see section 1.2.2). A low fiber diet may also cause a narrowing of the sigmoid so that segmentation is more prominent and high pressures can be produced more frequently (147;287). The relationship between fiber diet and intrasigmoidal pressures has been demonstrated (276;288-291).

1.5.3.3 Increased sigmoidal motility

Diverticula appear to occur in other sites in the body, there are some hypotheses about the etiology. It is thought that Zenker's diverticulum of the esophagus is caused by a dyskinesia of the cricopharyngeal muscle (78). After endoscopic treatment of such diverticula, the resting pressures were decreased (292). Ureteral diverticula may be caused by an increased pressure in the ureter (293).

The role of smooth muscle hyperactivity in diverticulosis of the sigmoid was also acknowledged in radiology. By hypotonic barium enema, with the aid of probanthine, retrograde sigmoid obstruction could be evaluated, and the true diagnosis of diverticulosis could be made (294).

Investigators, recording motility in the sigmoid of patients with diverticulosis, found, in comparison to controls, higher activity (202;210). Others found this after morphine and prostigmine administration (147;211;212) or if these patients had symptoms (205).

1.6 Reproduction of abdominal pain in painful IBS and diverticulosis

1.6.1 Introduction

According to Webster's dictionary to reproduce means: to make a copy or duplication (of a picture, or the like) or to repeat. To repeat means: to do or make again. A correlation means: a close or mutual relation or relationship between two phenomena.

In the present study the term to reproduce is used when a correlation, between a subjective phenomenon (pain) and an objective phenomenon (sigmoidal contraction), as seen during the barium enema investigation, is observed again during the pressure recording study. This reproduction confirms a correlation between pain and sigmoidal contraction. The contraction must coincide correlatively, and not accidentally, with the pain, so that it may explain the pain. Is it possible to reproduce the correlation pain-contraction during the pressure recording so that it is clear that the observed correlation is real ? A substrate of the pain has to be looked for, be it pathologic in anatomy or in function.

It is the objective of the present author to try to find an X ray film of the problem in the patients with a painful IBS. The pain and the abnormal function have to be reproduced. The present author wants to produce it in a photograph.

1.6.2 The relationship: motility-pain

When a patient is investigated ,she or he tells us when pain is felt. When we palpate the right upper abdomen in a patient with gallstones, having a painful attack, this is painful. If there is no attack, there may be no pain, although the gallstones are in situ. Normally the contractions of smooth muscle of the gallbladder or of the sigmoid are not painful. However, if there is an impaction, the contractions are very painful and are called cramps or spasms (78;106).

Is it possible to objectify this pathologic function ? It is possible to objectify the pathologic anatomy (calculi) in the gallbladder.

1.6.2.1 Sigmoidoscopy and pain

During sigmoidoscopy (in painful IBS patients) a correlation may be noted between spasms and pain (9;80;85). Others found that injection of air might reproduce some of the patient's symptoms (251).

1.6.2.2 Barium enema and pain

It is the rule, in patients thought to have a painful IBS, to have a barium enema done to exclude other diseases (78;191). So it is logical to see if it is possible to find the cause of the pain during this investigation.

It appeared possible, according to some authors, to reproduce the patient's characteristic pain during a barium enema (88;89). Other authors, describing the radiologic signs

of IBS, did not look for a reproduction of the pain (164-171). It was stated, that the radiologic method is a reliable technic with which it is possible to reproduce the pain and to correlate the pain with the functional state of the sigmoid (87).

1.6.2.3 Pressure recording and pain

In investigations in animals it was shown that pressure above the physiological limit, applied to the gallbladder, evoked a painful stimulus in the splanchnic nerve (106;108;114). It is known that a high pressure in the gallbladder leads to pain in patients: a gallstone colic.

In the small intestine a correlation between pain and disordered motility was suggested during pressure recording (90;295).

Some authors, recording sigmoidal pressure and pain in painful IBS, could not find a correlation between pain and pressure (98;99;187). Others noted an abnormally increased sigmoidal motility in such patients (20;191;197-199;204) or higher amplitudes of the waves if they had symptoms (191;204;206). These authors did not write about a correlation between a painful event and a particular wave. Some authors found an intersegmental incoordination coinciding with cramping pain in stoma patients (81;82).

In another study it was noted that the onset of abdominal pain coincided correlatively with a marked increase in the motor activity of the colon in 5 out of 7 investigated painful IBS cases (100). The pain may be functional and caused by contractions of the sigmoid (9;251;252).

However, it is possible to prove that the contractions are painful: if a correlative coincidence of pain and contractions is evident and can be reproduced, the proof is there.

1.7 Electromyography

A firm foothold on a slippery slope ?
(Almy 1980)

For the sake of completeness a short review of this subject will be given.

Colonic smooth muscle, like muscle in other parts of the gut, generates electrical signals that are responsible for the pacing of contractions. These electrical signals can be recorded during electromyography with the aid of mucosal suction electrodes (130). Two wave forms have been demonstrated: slow waves and spike potentials. The slow waves are phasic undulations in electrical potential of the smooth muscle membrane. The spike potential is characterized by a rapid deflection of the electrical recording (27).

Four types of colonic myoelectrical activity have been described in in vivo studies of normal subjects (238;296-300).

1/ Slow waves occur at a frequency of up to 13 cycles/min. These waves are called electrical control activity (ECA), basic electrical rhythm (BER) or simply slow waves. Slow waves originate in the circular muscle. The dominant frequency of slow waves may depend on the location in the distal bowel from which it is recorded: rectal sites may show six cycles/min in approximately 90% of activity; at 25 cm from the anus the

three to four cycles/min may be seen in about 97% of activity.

2/ Short spike bursts consist of two to ten seconds (s) bursts of potentials, they are also termed discrete electrical response activity (DERA). They are associated with contractions in 44% of cases.

3/ Long spike bursts or continuous electrical response activity (CERA) consist of trains of spikes lasting 6.4 s or longer. They are associated with lumen-occluding, segmenting contractions on 60% of occasions and cause the to and fro movement of the colonic contents.

4/ Contractile electrical complexes (CEC) are bursts of electrical oscillations in 25 to 40 cycles/min. They are associated with lumen occluding contractions in 55% of occurrences. It was said that these bursts may be responsible for contractions leading to transport of colonic contents. They may originate in the longitudinal muscle.

Regarding painful IBS it appeared in studies, which used slow waves as a dependent measure, that these slow waves occurred at two frequencies: six and three cycles/min. The former was the dominant frequency in control groups as well as in IBS groups, but the three cycle/min frequency appeared to be significantly more frequent in the IBS patients than in controls (296;297;301). Other authors found in controls slow wave frequencies of 6.2 waves/min and in IBS patients frequencies of 3.1/min (302). Conflicting results were found by other investigators: they could not establish unique myoelectrical characteristics in patients with the IBS (32). Others found an abnormal spike burst in patients with the IBS (238;300). It was stated that these discrepancies have not yet been explained (239).

Discrepancies between investigators may be due to differences in the part of the gut from which is recorded, or to differences in filter and amplifier characteristics , or to differences in patient population. Neither the recording technics nor the methods of analyzing myoelectrical data have, as yet, been standardised (238).

The relationship between the electrical and motor activities of the human colon is said to be poorly understood (303). In an editorial the hope was expressed that the IBS might be recognized by his pattern of myoelectrical activity, so that we would have gained a firm foothold on a slippery slope (304). So far, this hope remains.

1.8 Differential diagnosis, therapy and prognosis

1.8.1 Differential diagnosis

The differential diagnosis is restricted to the left lower abdominal pain, the diarrhea and constipation are not included. In the first place we have to differentiate between painful IBS and diverticulosis. A barium enema is necessary to make the right diagnosis. This examination and/or a sigmoidoscopy are indicated to exclude colonic tumors (10;246). Left renal colic may also simulate the painful IBS (10;78;80;170).

Other conditions which must be distinguished are inflammatory, infectious and ischemic colitis, and lactase deficiency. In cases of female patients one must bear in mind the possibility of dysmenorrhoea, endometriosis or left-sided

salpingitis (10;80;170). Rare diseases we may have to think of are porphyria and tabetic crises.

1.8.2 Painful IBS: therapy and prognosis

In 1905 it was thought that the treatment was to keep the colon empty (230). In 1928, however, it was written that fruit and vegetables had been excluded too rigorously (80). Later on, it was assumed that relief of symptoms, especially of pain, might be possible in three ways: by a high fiber diet, gut relaxants and/or psychotropic drugs and psychotherapy.

1.8.2.1 High fiber diet

Your baker, your doctor:
the "drug" is whole meal bread.

Some of the features of fiber have been discussed in section 1.3.1.2. Nonstructural polysaccharides appeared to have water holding and gelling effects (25). Bran softens the stool. Unprocessed bran has much more effect than fine bran. Pectin is digested and has thus little effect on fecal bulk.

Patients may respond to an increased amount of dietary fiber (54;250). Twenty grams of bran, or four slices of whole meal bread, daily, improved the symptoms (57). In placebo-controlled trials of bran, however, the placebo gave good results too (5;9;253;254;305). It might be possible that the composition of the placebo was not good; one of the constituents was polyvinyl pyrrolidone. This is inert, but it is not absorbed, so that it has bulking properties and may have therapeutic effects in painful IBS patients (306;307).

1.8.2.2 Gut relaxants

As the cholinergic part of the neurogenic system predominantly increases the motility, it is logic to use anticholinergics, if a hypermotility is suspected. These drugs have been advised and were thought to be of benefit (308-314).

A peripheral dopamine antagonist (domperidone) was compared in a double-blind study with a placebo in patients with the IBS (315). The placebo gave as good results as the drug.

1.8.2.3 Psychotropic drugs and psychotherapy

In a study phenobarbital was preferred to placebo, subjectively (313). A significant difference between diphenylhydantoin and placebo could not be demonstrated in another study (316). Psychotherapy has been tried out, success was claimed (317-321).

Some authors combined high fiber diet, a gut relaxant and/or a psychotropic drug, sometimes with alleviation (312;322-324). The use of alternative medicine appeared to be common in patients with the IBS (325).

Thanks to methods for the measurement of motility therapeutic steps can be taken on a rational basis (326). The results can be objectified.

1.8.2.4 Conclusions

IBS is difficult to treat so that many treatments are recommended. Few good double-blind studies have been done, too few. Dietary fiber may lower pressures in the sigmoid (9). Pain is relieved by high fiber diet, be it a placebo effect or a real medical result. It is best to start with whole meal bread or brown bread and other foods rich in natural fiber before prescribing bran (9).

As IBS is a chronic illness drugs should be prescribed with great precaution. Instead of trying a psychotropic drug, it is better to try to reassure the patient (10;80).

The best way to reassure is to explain what the cause of the pain is. This is another argument for the finding of a positive diagnostic criterion in painful IBS and to find the cause of the pain.

1.8.2.5 Prognosis of painful IBS

The prognosis appears to be, in so far as cure is concerned, not good. Few people become and remain symptom-free, although subjective release may be obtained (17;54;78;327-330).

It was suggested that longstanding painful IBS might lead to diverticulosis (26;46;330). This item is discussed in the following section.

1.8.3 Diverticulosis: therapy and prognosis

Once diverticula are formed, they cannot be cured. The mere existence of diverticula does not justify the excision of the affected sigmoid (331). Attention should be directed towards the prevention.

High fiber diet may prevent the formation of diverticula as bran leads to lower intrasigmoidal pressures (276;289;290). This diet led to a normal bowel habit and a relief of pain (147;284;285). Two patients have been described who might have shown, radiologically, a reversibility of incipient diverticula, after a year of treatment with a high fiber diet (332). This diet may prevent further complications of diverticulosis (291).

In the past decade sigmoid myotomy came into the picture. As inadvertent perforation during the operation often occurred, reoperation was regularly required (42). This may be the reason why the operation is no longer performed nowadays. The eating of brown bread is much safer.

The prognosis of diverticulosis is, concerning cure, not good, they do not disappear. The complications are diverticulitis with narrowing and perforation, as discussed in section 1.2.4.

1.9 Possible links between IBS and diverticulosis

1.9.1 Introduction

Many authors asked the question if there are links between painful IBS and diverticulosis. Are these two conditions different phases of a single entity (26)? Is there a gradual development from one disease to the other (205;333)? Is there

one hypermotile state in these conditions (334;335)? Other authors included diverticulosis in their group of patients with IBS (336).

1.9.2. Sequence of events? Correlation with age

The mean age in patients with an IBS is lower than that of patients with a diverticulosis (26;32;172;337). This sequential order will not directly mean a causal one. A longlasting longitudinal investigation of a large group of patients with a painful IBS is necessary to prove that.

1.9.3 Prevalence

The prevalence (the proportion of cases in a defined population in a period of time (188)) of both conditions is high (27-30;41). Thus, a coincidence is easily misinterpreted as a correlation. In a report the development of diverticulosis in patients with a painful IBS was 24%, in the general population it was 12% (46;330). Erroneously these authors concluded that diverticulosis in IBS was twice the occurrence of diverticulosis in the general population. Perusing their articles made clear, however, that the occurrence of diverticulosis in both conditions is the same in patients of the same age.

A different prevalence between female and male has been reported in the diseases (31;32;40-43) (section 1.1.2).

1.9.4 Similarity in etiology

1.9.4.1 Lack of fiber

A low fiber diet plays an important role in the etiology of painful IBS and diverticulosis (see section 1.5.2.2 and 1.5.3.2). It may be assumed that painful IBS is caused by a colon "that is struggling with our modern fiber-deficient diet" (241).

1.9.4.2 One hypermotile state ?

1.9.4.2.1 Pressure recording

In painful IBS and diverticulosis a hypermotility in the sigmoid may be found (see section 1.5.2.1 and 1.5.3.3). It was thought that the colonic changes in painful IBS might facilitate the development of diverticula (334;335).

There may be two forms of diverticulosis (338;339):

A/ Simple massed diverticulosis. In this condition it was assumed (338) that the narrowing and shortening of the colon was caused by a shortness of mucosa caused by the numerous pockets. This form may show a diverticulosis in the entire colon. There are mostly few symptoms of pain (339).

B/ Diverticulosis with spastic colon resulting in the heaping up of big muscular folds and narrowing of the lumen. Form B could support the idea of a relationship between painful IBS and diverticulosis. These patients show the actual presence of the combination of painful IBS and diverticulosis (339).

Some similarities between the two diseases have been found in pressure recording after food and cholecystokinine (340;341).

1.9.4.2.2 Electromyography

The myoelectric activity in the two diseased states has been studied. One researcher found a myoelectrical evidence to link them; others could not find that (334;342).

1.9.4.2.3 Radiologic findings

The relation between painful IBS and diverticulosis had also been studied radiologically. Diverticula may be caused, as appears in barium enema investigation, cineradiography and pressure recording (343), by a hypersegmentation. They originate in the grooves between the thick muscular rolls. In one patient, serial radiologic observations showed that the appearance of diverticula occured after a period of eleven years after the demonstration of the hypersegmentation (338).

The radiologic signs of hypersegmentation of the circular muscle of the sigmoid, seen both in painful IBS and diverticulosis are an indication that in both conditions a hypermotility exists.

1.9.5 Similarity in symptoms and radiologic signs

Both conditions may be accompanied by recurring episodes of left lower abdominal pain and/or disturbed bowel habits (26;33; 34;37).

Radiologically, it appears that both conditions show a contractile sigmoid on barium enema study. In IBS the contractile state is more pronounced than in diverticulosis (26). Two cases who showed radiologic signs of irritable colon and incipient diverticula were described (332). Are these cases patients with an IBS or a diverticulosis or are these patients illustrating the link between the two conditions?

1.9.6 Similarity in treatment

High fiber diet is of great significance in the treatment of both conditions (see section 1.8.2 and 1.8.3).

1.9.7 Conclusion

It may be that IBS is not the only one etiologic factor in diverticulosis, but it seems evident that IBS could be one of them. This probability would be approaching proof if more evidence could be gathered that in both conditions hypermotility exists.

2

OBJECTIVES OF THE STUDY

Patients were studied who had a history, symptoms and medical workup compatible with painful irritable bowel syndrome (IBS). The patients felt, during a single and double contrast barium enema investigation, their own characteristic pain and showed, simultaneously, a contraction of the sigmoid. These patients underwent a second radiological study, with a barium enema of smaller volume, and, simultaneously, a continous recording of the intra-sigmoidal pressure.

The same investigations were performed in a control group and in two groups of patients with diverticulosis: one without and one with IBS-like pain. All the characteristics of the waves, including the area under the curve and the motility index were estimated in the four groups.

The aims of the study:

1/ The first objective was to obtain information about the reproducibility of the correlation of the characteristic pain and visible contractions of the sigmoid. Such reproduction would mean that it is possible to recognize a painful IBS by one careful, physiologically directed single and double contrast barium enema examination.

2/ The second objective was to answer the question whether all muscular activity of the sigmoid, as demonstrated by movements of the sigmoidal wall, is expressed by a change in the intraluminal pressure.

3/ The third objective was to compare the basal, postprandial and post-glucagon pressure recordings in the four groups, paying special attention to pressure changes during the characteristic pain.

4/ The fourth objective was to formulate accurately considerations about the mechanism of that characteristic pain.

5/ The fifth objective was to reconsider the hypothesis that painful IBS and diverticulosis are expressions of one hypermotile state. Is painful IBS an etiologic factor of diverticulosis?

6/ The sixth objective was to answer the question whether it is necessary to estimate the area under the curve as well as the motility index in evaluating the results of the pressure recordings.

3
PATIENTS AND METHODS

3.1 Patients and selection criteria.

3.1.1 Definitions and inclusion criteria for the pressure recording investigation.

In this study four groups of patients were studied: a control group, a painful IBS group, a diverticulosis group and a painful IBS with diverticulosis group. The patients in the various groups were defined as follows:

A/ a control case:

a/ has no anatomic abnormality in a barium enema nor in a sigmoidoscopy , no painful contractions are encountered;
b/ may have vague discomfort in the upper abdomen or blood in the stool;
c/ has a normal blood chemistry.

B/ a patient with the painful IBS:

a/ shows a correlation of the characteristic pain with a sigmoid contraction during the barium enema (contraction causes pain; relaxation relieves the pain). The term characteristic pain means: the pain which forced the patient to visit the doctor.
b/ has a discontinuous pain in the left lower abdomen;
c/ has pain for longer than three months;
d/ may have, in the history, alternating bowel habits, (diarrhea and, at another time, constipation);
e/ has deterioration of the pain in correlation with a meal or a defecation and may have pain relief by a bowel movement;
f/ has no anatomic abnormality in a barium enema nor in a sigmoidoscopy;
g/ has no blood in the stool;
h/ has a normal blood chemistry.

C/ a patient with a diverticulosis:

a/ has a diverticulosis of the sigmoid colon;
b/ may or may not have vague pain in the abdomen.

D/ a patient with a painful IBS with diverticulosis:

a/ shows a correlation of the characteristic pain with a sigmoid contraction during the barium enema examination;
b/ has a diverticulosis of the sigmoid colon.

3.1.2 Data of the patients who underwent a pressure recording investigation

During his daily work as a general practising radiologist the author selected the cases for the pressure recording. A protocol was used (table 4). Directly after the barium enema examination the patients were placed, according to the results, in one of the four groups. Informed consent was obtained.

```
Patient: name                                          date:
         sex: female/male
         date of birth
History: pain:kind: vague/ colicky/ knife like/ discontinuous
               like labour pains   yes/no
               localization: left lower abdomen/ elsewhere
               duration:< 3 months; 3 months-1 year; 1 year-5 years;
                        5-10 years; >10 years
               correlation with meal                yes/no
               correlation with defecation          yes/no
                 pain leads to urge                 yes/no
                 defecation leads to pain release   yes/no

         defecation: alternating:                   yes/no
                     incomplete emptying:           yes/no
                     blood:                         yes/no
barium enema examination:
     single-contrast : reproduction of the pain          yes/no
                       urge to defecate                  yes/no
     x-ray film      : segmentation of sigmoid           yes/no
                       contraction of lengthy segment    yes/no
     after defecation: segmentation of sigmoid           yes/no
     double-contrast : relaxation of the contracted part yes/no
                     : relief of the pain                yes/no
                       1 mg glucagon i.v.                yes/no
     diverticulosis of the sigmoid colon                 yes/no

Diagnosis:  Control/ painful IBS/ diverticulosis/
            painful IBS with diverticulosis/ other.
```

Table 4 Protocol form for the barium enema examination

The three groups of 15 patients included 11 female and four male patients each. The fourth group of eight patients included six female and two male patients.

The mean age ± the SEM (standard error of the mean) was:
A/ in the control group: 48.7±1.7 years (range: 38-59 years)
B/ in the painful IBS group: 43.6±2.2 years (31-60 years)
C/ in the diverticulosis group: 53.9±1.6 years (36-60 years)
D/ in the painful IBS with diverticulosis group: 49.5±2.4 years (range: 36-58 years).

The control cases were significantly younger than the diverticulosis patients ($p<0.05$, Student's t test), the painful IBS patients were also younger than the diverticulosis cases ($p<0.001$). The other differences in age were not significant.

3.1.2.1 Data from history and referring physicians (item and number of patients).

```
A/ control group: N = 15
     occult blood in stool                 : 5
     vague pain in upper abdomen           :10
     duration: <3 months          : 3
               3 months to 1 year: 4
               1-5 years          : 3
     correlation with meal and defecation : 0
     defecation: alternating          : yes: 0     no:15
```

B/ painful IBS group: N = 15
discontinuous pain localised in the left lower abdomen: 15
colicky/labourlike pain: 12
duration: 3 months to 1 year: 1
1-5 years : 5
5-10 years : 6
>10 years : 3
correlation with meal : 6
correlation with defecation :12 (some patients showed a correlation with both a meal and a defecation).
defecation: alternating : yes: 10 no: 5
incomplete emptying: yes: 6 no: 9

C/ diverticulosis group: N = 15
vague or continuous pain: 11
localisation in the left lower abdomen : 6
duration: <3 months : 2
3 months to 1 year: 4
1-5 years : 5
correlation with meal : 2
correlation with defecation : 1
defecation: alternating : yes:3 no:12
incomplete emptying: yes:5 no:10

D/ painful IBS with diverticulosis group: N = 8
localisation in left lower abdomen: 8
duration: 1-5 years : 1
5-10 years: 4
>10 years : 3
correlation with meal: 3
correlation with defecation: 5
defecation: alternating: yes:5 no:3
incomplete emptying: yes:6 no:2

3.1.2.2 Results of the barium enema examination (table 5)

The three patients in the control group who showed a segmentation of the sigmoid had only minor symptoms, no pain was elicited and the mild discomfort disappeared spontaneously.

The main complaint of the patients in the painful IBS group was a characteristic pain, which pain was reproduced during the enema. The patient recognized the pain which mostly occurred at the moment of segmentation or lengthy contraction of the sigmoid. Two patients presented a reproduction of their pain during air insufflation, when the sigmoid was expanding.

Twelve patients of the group with a diverticulosis showed, during the enema, some segmentation or lengthy contraction of the sigmoid. This disappeared after reassurance. These patients did not experience pain.

Eight patients with a diverticulosis of the sigmoid presented the same pain-pattern as the patients in the painful IBS group. They had pain with a mean duration of about nine years. Their pain was reproduced during the barium enema examination and was relieved after a relaxation of the sigmoid.

Group	C	I	D	ID
Pain during enema	0	15	0	8
Reproduction of the characteristic pain	0	15	0	8
Urge to defecate	3	12	11	5
Segmentation or lengthy contraction of sigmoid	3	15	12	8
Relaxation after glucagon	0	10	0	7
reassurance	0	5	12	1
Pain relief		15		8

Table 5 Results of the barium enema examination.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

3.2 Methods

3.2.1 Unbiased observer.

During the pressure recording as well as during the subsequent analysis of the data and the calculation of the numbers the author was unbiased.

3.2.2 Preparation.

In preparing the patients a clean sigmoid was preferred in order to make it possible to visualize the sigmoid with the aid of barium-sulphate. The colon was cleansed prior to the pressure study in the same way as it was cleansed prior to a barium enema examination (221). In a preparation-period of two days the patients observed the following instructions: a/ a low residue diet, b/ drinking of at least 3 liters of water per day, c/ 2x15 grams of magnesium-sulphate per day, d/ 2x10 milligrams of bisacodyl (Dulcolax) per day. The magnesium sulphate and the bisacodyl were to be taken in the morning before the breakfast and in the night two hours after dinner.

Besides the usual blood chemistry the serum potassium level was also estimated, as it has been published that the diarrhea, ocurring during the cleansing period, could lead to a hypokaliemia, especially in patients who use diuretics and digitalis (344). Hypokalaemia may lead to a hypo-activity of the sigmoidal musculature.

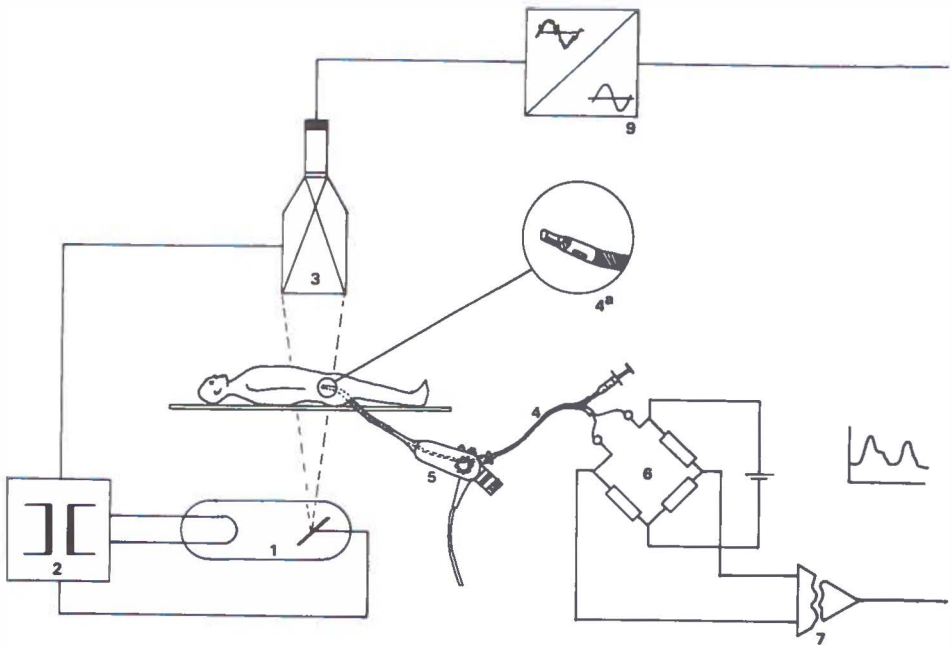
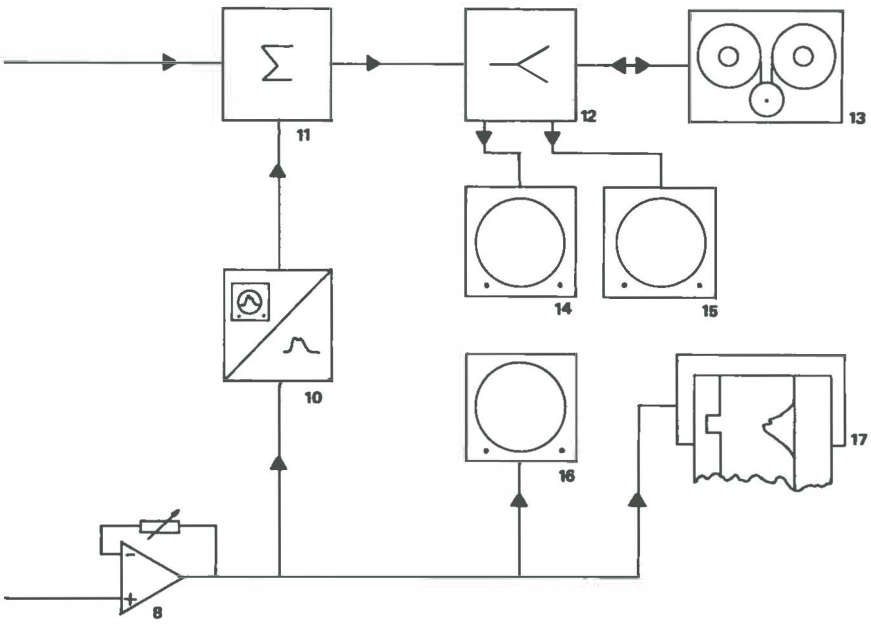


fig. 13 Devices used 1/ X-ray tube ,2/ high-voltage generator, 3/ image intensifier (1-3: Optimus M200 (Philips)); 4/ micro transducer catheter with lumen and pressure sensor; 4a/ microtip of catheter (fig.14) the catheter is a PC-471-A (Millar); 5/ flexible sigmoidoscope, TCF 1S (Olympus), 6/ strain gauge bridge with excitation supply, 7/ input amplifier with isolation barrier,



8/ output amplifier with gain control; 6-8: CGR 1000 Catheterisation system (CGR Biomedical); 9/ video image processor, VIP 300 (Pie Data Medical); 10/ analog video convertor, AVC 800 (Philips); 11/ videomixer, VMC 81 (Satco); 12/ video distribution box and recorder control VDB 01 (Kemptronics); 13/ video production recorder, VPR 1, Ampex corporation; 14 and 15/ video monitor, 9807 (Philips), 16/ analog monitor, CGR 1000, 17/ fluid jet recorder, Oscillomink 8 (Siemens).

3.2.3 Devices and catheter.

The devices used in this study are shown in figure 13 and 14.

Previously, open ended tubes have been used, which need flushing to keep them open. The flushing would have washed out the radiologic contrast, rendering the sigmoidal wall invisible. That's why an electronic microtransducer catheter, a new pressure recording device, was employed. These catheters do not need flushing so that the motility of the sigmoidal wall remains visible.

The technical specification of the electronic microtransducer catheter: the type of sensor is a silicon strain gauge; the pressure range is from -300 up to +400 mm Hg; the sensitivity is 3.1 mV/V/100 mm Hg ; the temperature error band is 3 mm Hg maximal shift from 23 degrees to 38 degrees Celsius; the linearity & hysteresis is ±0.5% of full scale; the drift is less than 12 mm Hg in 12 hours; the natural frequency is 25 to 40 kHz, the bridge resistance is 1300 to 2000 Ohm. The reference pressure is the atmospheric pressure.

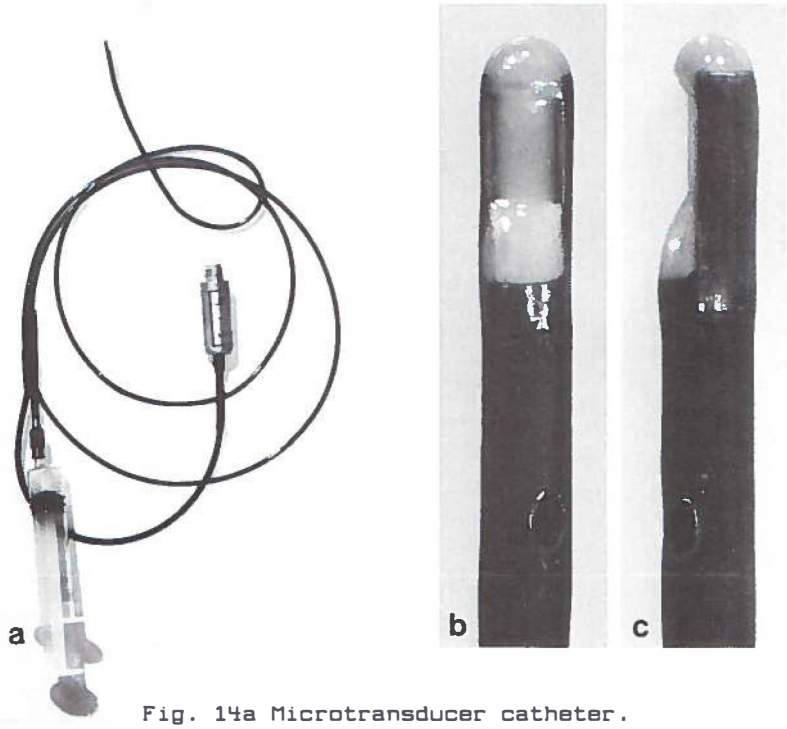


Fig. 14a Microtransducer catheter.

Fig. 14b Microtip of catheter, face-on view.

Fig. 14c Microtip of catheter, seen in profile.

The noise in the system appeared to be of no significance. The effective window of the microtransducer is 1.1x0.575 mm. The drift for the period of time that the investigation lasted was 4 mm Hg, a negligible influence as the study concerns a comparative one in which a control group is included.

3.2.4 Sigmoidoscopy, calibration, introduction of the micro transducer catheter.

Immediately prior to the pressure recording a sigmoidoscopy was performed with the aid of a flexible sigmoidoscope. The endoscopist looked for anatomical abnormalities. If these were encountered the patient could not be incorporated in the study except if diverticula were seen.

The equipment was calibrated with the aid of a blood pressure clock. The calibration pressure was 100 mm Hg. A deflection of the pen by 1 mm on the recording paper of the fluid jet recorder corresponded to a pressure rise of 1 mm Hg. In patients with pressures of more than 60 mm Hg 1 mm corresponded to 2 mm Hg, in the rare cases in which the pressures exceeded 120 mm Hg, 1 mm corresponded to 4 mm Hg. No basal pressure was recorded as we were interested in the changes of the intrasigmoidal pressure.

The catheter was introduced through the biopsy channel of the flexible sigmoidoscope into the sigmoid to a distance of 30 cm from the anal verge. After the introduction of the catheter, the sigmoidoscope was withdrawn until it lay outside the patient. The position of the microtransducer was checked fluoroscopically. The air, which was incidentally inflated during the sigmoidoscopy, was drained through a small tube which was introduced into the rectum and remained there for 10 min.

Through the central lumen of the catheter, 20-40 ml of a 20% suspension of barium-sulphate, at body temperature, was injected into the sigmoid. In this way the position of the microtransducer was checked and the motility of the sigmoidal wall became visible.

3.2.5 Procedure.

The small tube through which the air had escaped, was removed. The patient rested for 15 min.

It was explained to the patient that the pressure and the motility of the sigmoidal wall were recorded. If pain was felt, the patient had to tell that. Nothing was suggested to the patient. The recordings were performed in a quiet room. The patient lay at ease in a supine position on a couch. Close contact was kept.

At regular intervals the proper functioning of the system was checked by having the patients cough which gave a steep and well recognizable rise in the pressure recording (fig 15).

The pressure was recorded during 3 periods of 30 min each:

A/ The fasting period. The procedure started at 12h30 p.m.. After the low residue dinner and the laxatives of the regime taken the night before, the patients were not permitted to eat or drink until they were offered the standard meal during the pressure study.

B/ The standard meal. It is reported in the literature that a meal may give a hyperactivity of the sigmoid (204;208;210). Formerly this reactive hyperactivity was called: gastro-colic response. However, the response also occurred after total gastrectomy. Another name was suggested: colonic response to eating (345). The means by which eating a meal produces an increase in motility of the colon is, up until now, unresolved (345). Neurotensin might mediate the postprandial induced changes in the motility pattern: an endocrine-mediated effect (346). The fat component of the diet was suggested to be the predominant stimulus of colonic motor activity (347). In another study it was found that the response to a meal was cholinergically mediated (348). In patients with an electrophysiologically documented complete thoracic spinal cord injury, it became evident that the Central Nervous System is essential for the postprandial increase in activity (349). Shamfeeding (spitting the masticated food into a cup without swallowing) did not stimulate the colon (350). OP-CCK (an octapeptide of cholecystokinin) had a minor role in this response.

Some researchers use a standard meal of 1000 kcal or 4000 kjoule (348), others use a 2400 kjoule meal (351). In this study it was decided to give a standard meal of intermediate calorie-load. A meal of 3200 kjoule (consisting of one egg of about 50 grams, 250 ml milk, 4 slices of cheese,(each of about 15 grams), 1 role of bread and about 20 grams of butter) was offered.

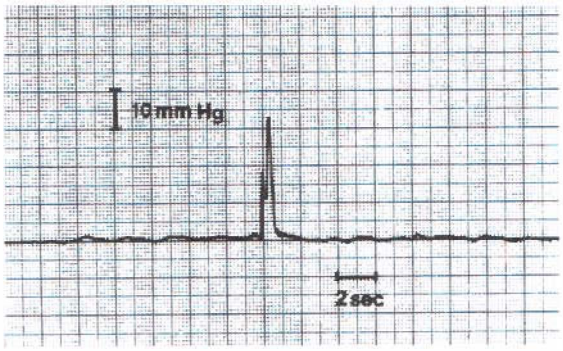


Fig. 15 Coughing: a steep rise in pressure is caused.

C/ The post-glucagon period. Glucagon has metabolic as well as gastrointestinal actions (352). In the metabolic action the output of glucose from the liver is increased, in the gastrointestinal action the motility of, among others, the colon is inhibited. Doses of 0.2-1.4 mg have been used in the literature (353;354). Glucagon brought about an intensive relaxation of the smooth muscle; it was suggested that it might be used in the treatment of spastic pain (355). Other authors found that barium enema studies performed with glucagon produced significantly less spasm and discomfort (356). It was also found that glucagon caused an inhibition of food induced motor activity (357).

In this study crystalline pancreatic glucagon (Glucagon "Lilly") was used in a dose of 1 mg (1 U) of glucagon hydrochloride to which 49 mg of lactose was added. This powder was dissolved and intravenously administered, half an hour after the start of the postprandial period.

3.2.6 Pressure recording

The recorded pressure waves were written, with the aid of the fluid jet recorder, on paper which was divided in squares of 1 by 1 mm , 5 by 5 mm and 10 by 10 mm, so that it was possible to count the squares under the curve. The paper speed was 5 mm per second , so that each curve could be measured: its height, its length and its area under the curve.

Patient: name: date:
sex: female/male
birth date:
Sigmoidoscopy.

Recording: a/ the sigmoidal pressure
b/ the contractions of the sigmoidal wall
c/ the pain of the patient

Fasting period:	pain	yes/no
	reproduction of pain	yes/no
	contractions of sigmoid	yes/no
	correlation: pain-contraction sigmoid	yes/no
Postprandial period:	pain	yes/no
	reproduction of pain	yes/no
	contractions of sigmoid	yes/no
	correlation: pain-contraction	yes/no
Postglucagon period:	relief of pain	yes/no
	decrease of contractions	yes/no
	correlation: relief of pain and decrease of contractions	yes/no

Table 6 Protocol-form used during the pressure recording studies

During the pressure study fluoroscopy was incidentally performed in order to see what happened to the sigmoidal wall in rest and in activity. If indicated these fluoroscopic images were recorded on videotape.

This method enabled us to record three items:

a/ the motility of the sigmoidal wall
b/ the pain of the patient and
c/ the wave which correlated with the pain

A protocol was used (table 6).

3.2.7 Analysis of the data.

A wave was defined as a curved line placed on a baseline with a/ an incidence; b/ an amplitude; c/ a duration; and d/ an area under the curve.

a/ The incidence of the waves was expressed in the number of waves per minute.

b/ The amplitude is the vertical distance between the basal line and the highest point of the curve and is expressed in mm Hg (fig 16). The positive pressure deviation from baseline has to exceed 2 mm Hg, smaller waves were not counted. Negative pressures were seldomly seen and were not counted, as was done by other researchers (99;211). The mean amplitude of the waves was obtained by adding the amplitude of all waves and dividing the sum by the number of the waves.

As no criterion concerning the definition of a complex wave (in which the tracing does not return to the baseline, fig 17a, b) could be found in the literature, the following criterion was developed: if the duration of such a complex wave was longer than 43 s (being the width of one sheet of our recording paper) the wave was considered to end as the pressure line approached the baseline at a distance of 10 mm Hg or less. This separation of waves is arbitrary. However, without a clear definition it is impossible to achieve reproducible results.

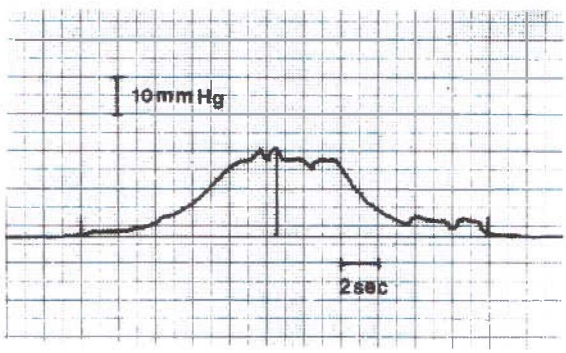


Fig. 16 The amplitude and the duration. The two vertical lines indicate the endpoints of the wave.

c/ The duration of the wave is measured from the point of deflection of the curve from the baseline to the return and expressed in seconds (s) (fig 16). The mean duration was calculated by dividing the sum by the number of the waves.

d/ The area under the curve was estimated by counting, manually and visually, the squares under the waves, as seen on the recording paper. These squares could correspond to 1, 25 or 100 square mm. The mean area of the curves was estimated by adding the area of all waves and dividing the sum by the number of the waves.

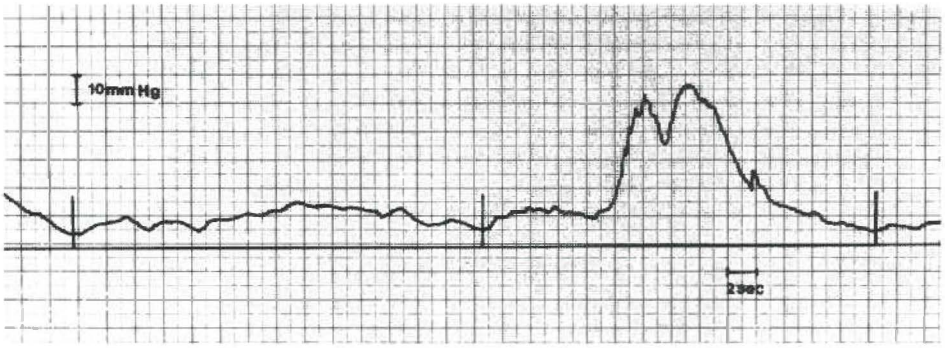


Fig. 17a Complex wave: the tracing does not return to the baseline. The duration of this wave exceeds 43 s. The wave is considered to end when the pressure line approaches the baseline at a distance of 10 mm or less.

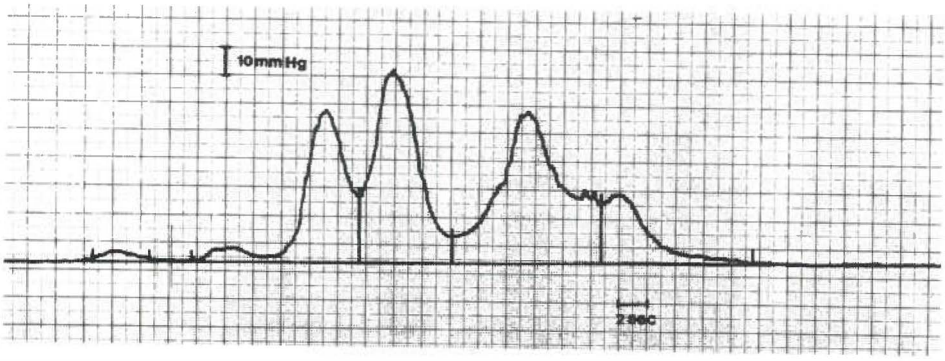


Fig. 17b Complex wave: The duration of this wave does not exceed 43 s. The 2 vertical lines at the beginning and at the end of this wave indicate the endpoints. The additional four vertical lines illustrate where, accidentally, the endpoints could have been laid if the definition was not clearly stated.

Of these items the mean and the standard error of the mean (SEM) was calculated with the aid of a calculator. These numbers were estimated per period (fasting, postprandial or postglucagon) and over all three periods together (overall), per patient and per group. Special attention was given to the correlation between pain and pressure waves. The results of the three groups were compared.

The motility index (MI) is a derived number as it is the sum of the products of amplitude and duration of each wave. The MI was calculated, and expressed in mmHg.s. The same calculations as with the other items were carried out.

Finally a statistical analysis was performed.

3.2.8. Statistical analysis.

This analysis is obligatory to establish whether the differences found are accidental or correlative.

Various tests have been performed (chapter 4). The two-sided Mann-Whitney (or Wilcoxon rank sum) test (distribution-free or non-parametric i.e the distribution of the variables is not as in a Gauss' curve), corrected for ties, is applied in the tables 7-13 and 27. The two-sided Student's t-test (assuming unequal variances) is used in the tables 23, 25 and 26. The Wilcoxon matched pairs signed rank test is applied in the mean values in figure 25.

The figures are not significant (indicated as NS) if the results of the analysis is that p (probability) is > 0.05. If they are significant this is indicated by *, ** or ***. One * means $p < 0.05$: the chance that the results are mistakenly interpreted as really different is less than 5%. In the same way ** means: $p < 0.01$ and ***: $p < 0.001$.

RESULTS 4

The mean numbers with the standard error of the mean (SEM) are shown in the figures 18-24. The results of the statistical analysis are tabulated (tables 7-13). The numerical findings are tabulated in the appendix (tables 16-22).

The term "overall" is used to indicate that the figures of the three periods are taken together.

4.1 Characteristics of the waves.

4.1.1 Incidence.

The number of waves per min is about 1. The incidence appeared to be significantly higher only in the fasting and the postglucagon period of the painful IBS with diverticulosis group compared to the control group (fig 18 and table 7 and 16).

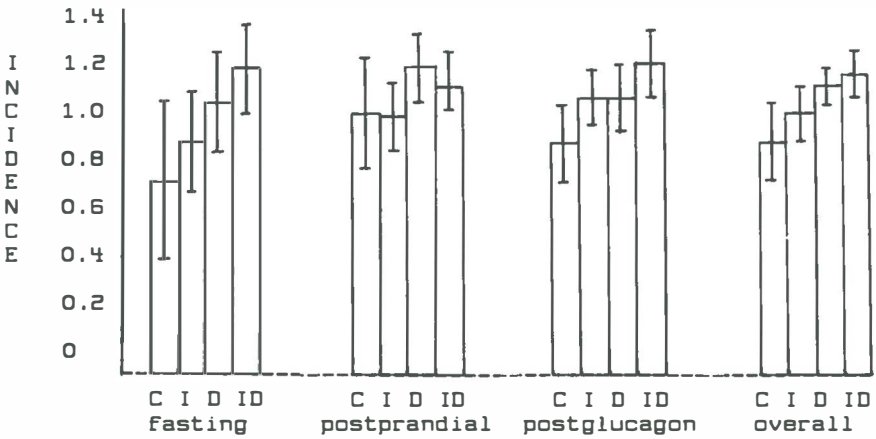


Fig 18 The mean incidence (with SEM) in waves/min in the four groups and in the three periods. C = control; I = painful IBS; D = diverticulosis; ID = painful IBS with diverticulosis.

Compared groups	C-I	C-D	C-ID	I-D	I-ID	D-ID
Fasting	NS	NS	*	NS	NS	NS
Postprandial	NS	NS	NS	NS	NS	NS
Postglucagon	NS	NS	*	NS	NS	NS
Overall	NS	NS	NS	NS	NS	NS

Table 7 Incidence: statistical analysis (Mann-Whitney test) of the differences between the groups in the three periods and overall.
NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

4.1.2 Amplitude.

Only after the administration of glucagon the amplitudes were statistically significantly higher in the painful IBS group, in comparison to the controls. In the diverticulosis group the amplitudes were higher in all three periods in comparison to the controls. The painful IBS with diverticulosis patients showed significantly higher amplitudes in comparison to the three other groups in all periods (fig 19, table 8 and 17).

The highest amplitude in the control group was 116 mm Hg (15.5 kPa), in the painful IBS group it was 108 mm Hg (14.4 kPa), in the diverticulosis group it was 164 mm Hg (21.9 kPa) and in the painful IBS with diverticulosis group the highest pressure measured 224 mm Hg (29.9 kPa).

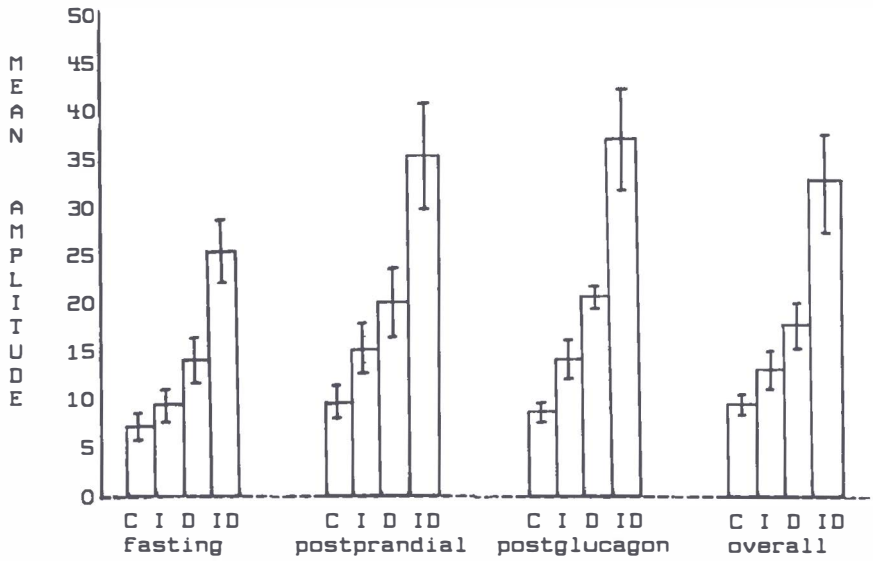


Fig 19 The mean amplitude (with SEM) in mm Hg in the four groups and in the three periods. 1 mm Hg = 133.3 Pa.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

Compared groups	C-I	C-D	C-ID	I-D	I-ID	D-ID
Fasting	NS	*	***	NS	***	**
Postprandial	NS	**	***	NS	**	*
Postglucagon	*	***	***	*	**	*
Overall	NS	***	***	NS	***	**

Table 8 Amplitude: statistical analysis (Mann-Whitney test) of the differences between the groups in the three periods and overall.
NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

4.1.3 Duration.

The duration in painful IBS, diverticulosis and painful IBS with diverticulosis compared to the controls was significantly longer in many periods. The duration in painful IBS in comparison to diverticulosis was not significantly different. The waves also did not last longer in the painful IBS with diverticulosis patients compared to the painful IBS and the diverticulosis patients (fig 20, table 9 and 18).

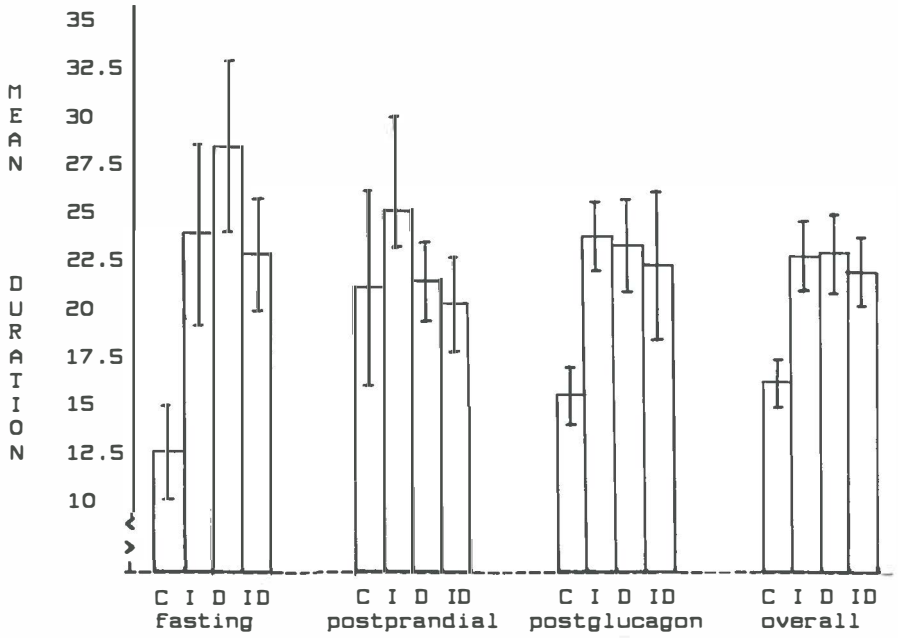


Fig 20 The mean duration (with SEM) in s, in the four groups and in the three periods.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

Compared groups	C-I	C-D	C-ID	I-D	I-ID	D-ID
Fasting	*	***	**	NS	NS	NS
Postprandial	NS	NS	NS	NS	NS	NS
Postglucagon	***	**	*	NS	NS	NS
Overall	***	**	**	NS	NS	NS

Table 9 Duration: statistical analysis (Mann-Whitney test) of the differences between the groups in the three periods and overall.
NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

4.1.4 Total area under the curve

The total area under the curves is the sum of all areas under the curves of each patient. This item was almost always greater in the painful IBS group, the diverticulosis group and the painful IBS with diverticulosis group compared to the control group. The comparison painful IBS and diverticulosis did not reveal a higher period. The total area was always greater in painful IBS with diverticulosis in comparison to painful IBS. Only the "overall" total area was higher in painful IBS with diverticulosis compared to diverticulosis (fig 21, table 10 and 19).

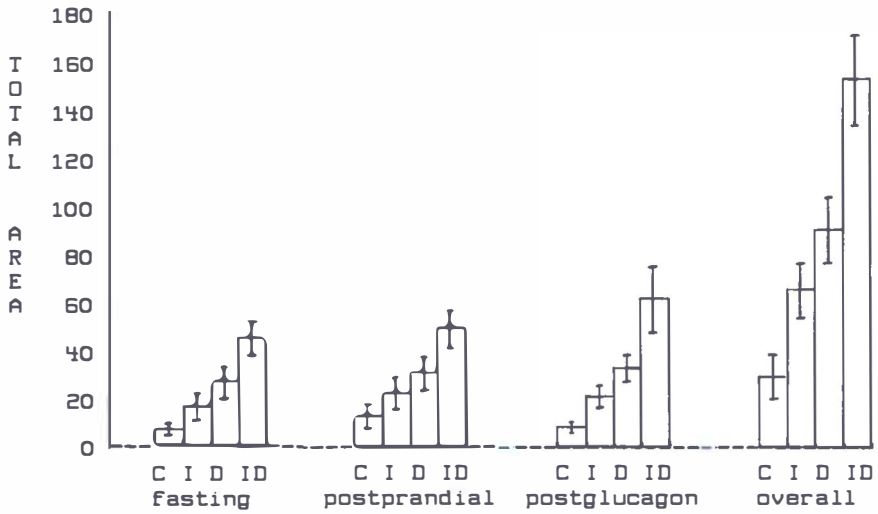


Fig 21 The total area under the curve (with SEM) in square mm x 1000 in the four groups and in the three periods. C = control; I = painful IBS; D = diverticulosis; ID = painful IBS with diverticulosis.

Compared groups	C-I	C-D	C-ID	I-D	I-ID	D-ID
Fasting	NS	***	***	NS	**	NS
Postprandial	NS	**	**	NS	*	NS
Postglucagon	**	***	***	NS	**	NS
Overall	*	***	***	NS	***	**

Table 10 Total area under the curve: statistical analysis (Mann-Whitney test) of the differences between the groups in the three periods and overall.
NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$;
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

4.1.5 Mean area under the curve

The calculations of the significant differences with the mean area show almost the same outcome as the calculations with the total area (table 10 and 11). See also fig 22 and table 20.

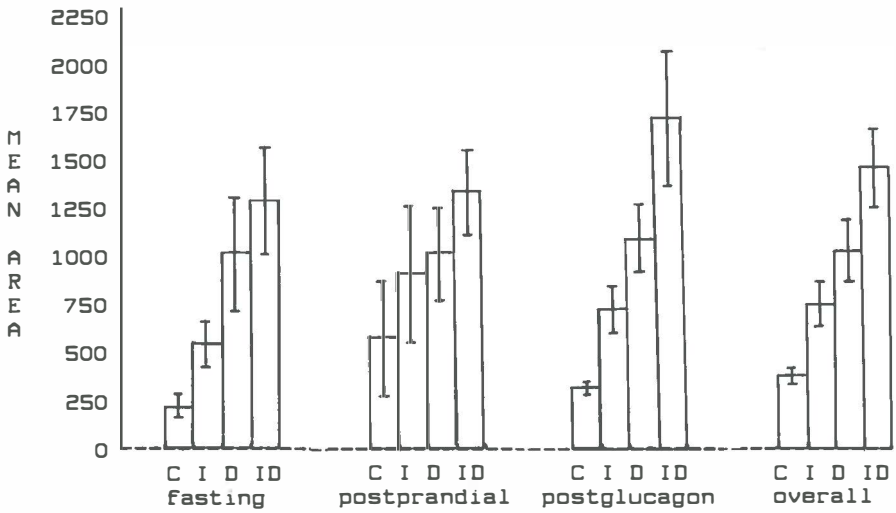


Fig 22 The mean area (with SEM) in square mm in the four groups and in the three periods.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

Compared groups	C-I	C-D	C-ID	I-D	I-ID	D-ID
Fasting	*	***	***	NS	**	NS
Postprandial	NS	**	**	NS	*	NS
Postglucagon	***	***	**	NS	**	NS
Overall	**	***	***	NS	**	*

Table 11 Mean area under the curve: statistical analysis (Mann-Whitney test) of the differences between the groups in the three periods and overall.
NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

4.1.6 Total motility index

The significant results of the total motility index are almost the same as the results of the total area under the curve (table 10 and 12). See also fig 23 and table 21.

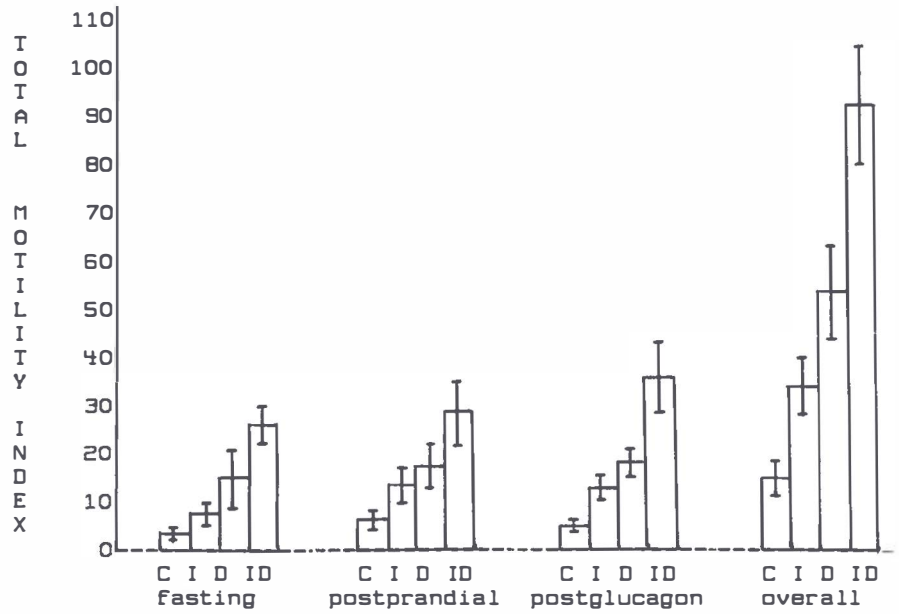


Fig 23 The total motility index (with SEM) in mm Hg.s x 1000 in the four groups and in the three periods.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

Compared groups	C-I	C-D	C-ID	I-D	I-ID	D-ID
Fasting	NS	***	***	NS	**	NS
Postprandial	*	**	***	NS	*	NS
Postglucagon	**	***	***	NS	**	NS
Overall	**	***	***	NS	**	*

Table 12 Total motility index: statistical analysis (Mann-Whitney test) of the differences between the groups in the three periods and overall.
NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

4.1.7 The mean motility index

The calculations with the mean motility index show almost the same significant result as the calculations with the total and the mean area under the curve and as the total motility index (table 10, 11 and 12). See also fig 24 and table 22.

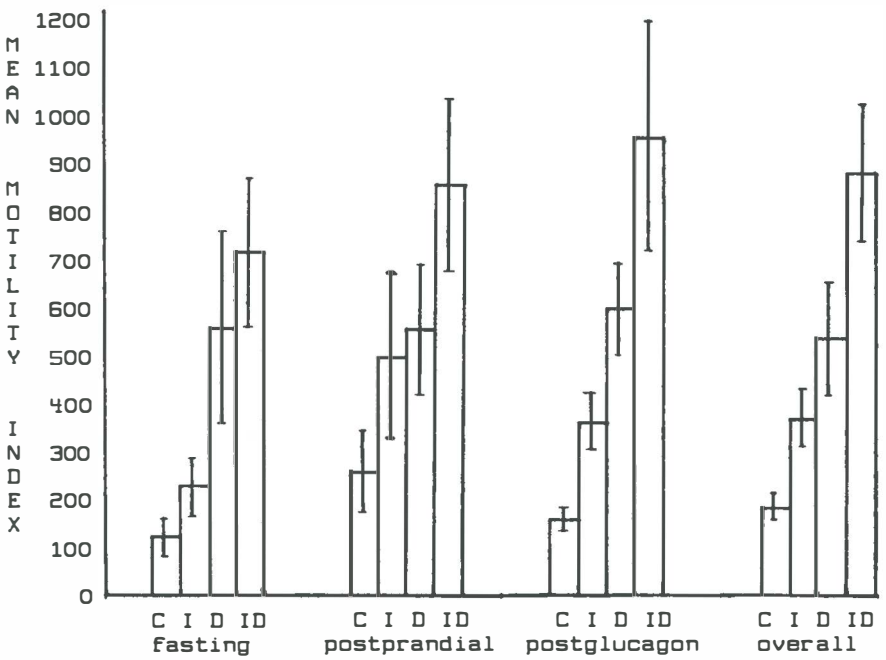


Fig 24 The mean motility index (with SEM) in mm Hg.s in the four groups and in the three periods.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis.

Compared groups	C-I	C-D	C-ID	I-D	I-ID	D-ID
Fasting	NS	***	***	NS	***	NS
Postprandial	*	**	**	NS	*	NS
Postglucagon	***	***	***	*	**	NS
Overall	**	***	***	NS	**	*

Table 13 Mean motility index: statistical analysis (Mann-Whitney test) of the differences between the groups in the three periods and overall.
NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$.
C = control; I = painful IBS; D = diverticulosis;
ID = painful IBS with diverticulosis

4.2 The correlation pain-wave.

4.2.1 The characteristics of the painful waves in the painful IBS group and in the painful IBS with diverticulosis group

During the pressure recording investigation a repeated reproduction of the characteristic pain of the patients, as observed during the barium enema examination, was seen in 14 of the 15 patients with painful IBS and in seven of the eight patients with painful IBS with diverticulosis. Totally, a reproduction was seen in 21 of 23 patients (about 90%). The two patients who did not show a reproduction suffered from discontinous pain, not real colicky, in the left lower abdomen, for shorter than 1 year.

Three patients showed one painful wave. It is not possible to make statistical calculations in these cases. The other patients demonstrated this phenomenon mora often. The average number of painful waves per patient is: 7.4 ± 1.3 (table 23, appendix). About 7 % (89/1249) of the waves in painful IBS and about 8% (66/841) of the waves in painful IBS with diverticulosis appeared to be painful.

Table 23 (appendix) shows the mean values of the amplitudes of the waves during which the patients did not feel pain (their pain was not reproduced during these waves), and, on the right side, the mean amplitudes of the waves which were accompanied by their pain. The amplitude of these painful waves is significantly higher in comparison with the waves which did not cause pain, in most patients. In the patients with a painful IBS the mean amplitude of the painless waves is 12.3 mm Hg (1.6 kPa), in the painful waves this mean value is 28.2 mm Hg (3.8 kPa). These mean values are, in the painful IBS with diverticulosis group, 30.7 mm Hg (4.1 kPa) in the painless waves and 61.3 mm Hg (8.2 kPa) in the painful waves (see also fig 25). Statistically these numbers are significantly different.

Conclusion: pressure waves with significantly higher amplitudes correlate with pain.

Table 24 (appendix) makes clear that the duration does not play a role in the evoking of pain. No significant differences are found, except in patient number 50 in whom the duration of the painful waves is even shorter.

Table 25 (appendix) shows that the mean area under the curve is significantly greater in the painful waves in eight patients with a painful IBS and in two patients with a painful IBS with diverticulosis, compared to the painless waves. In the painful IBS group the mean value of the painful waves is significantly higher in comparison to the mean value of the painless waves (see also fig 25).

Table 26 (appendix) demonstrates that the mean motility index in the painful waves is significantly greater than the mean MI of the painless waves in six patients with a painful IBS and in two patients with a painful IBS with diverticulosis. The mean value of the painful waves is significantly greater than that of the painless waves in the painful IBS group (fig 25).

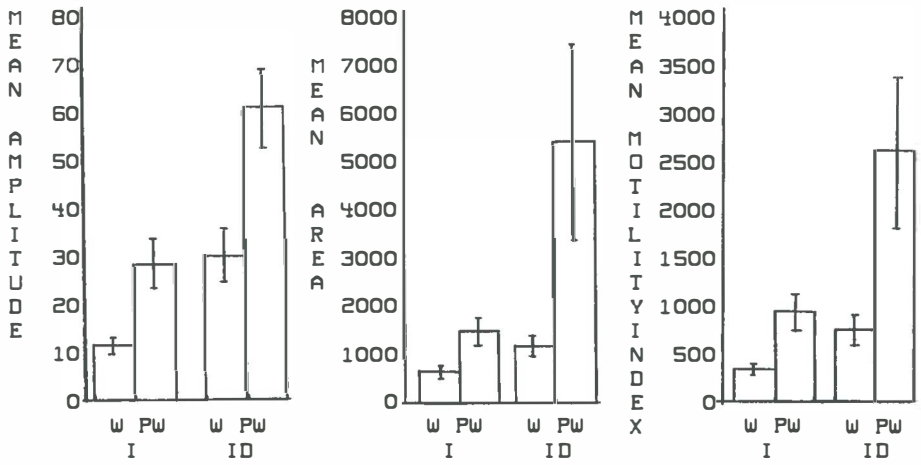


Fig 25 The characteristics of the painless waves (W) and of the painful waves (PW) in painful IBS (I) and in painful IBS with diverticulosis (ID). Amplitude in mm Hg; area under the curve in square mm; motility index in mmHg.s. Mean values with SEM (derived from the tables 23, 25 and 26, appendix)

4.2.2 Pain versus no pain in diverticulosis.

The results of the two groups with diverticulosis are compared in table 27 (appendix).

The mean amplitude of the seven patients with a painful IBS with diverticulosis and with a reproduction of their characteristic pain during the pressure recording investigation is in every period, significantly, greater than the mean amplitude of the 15 patients with a diverticulosis without pain.

The duration of the curves shows no statistically significant differences. The areas under the curve and the motility indices are not often, statistically, greater in the patients with a painful IBS with diverticulosis.

Conclusion: significantly higher amplitudes are correlated with pain experiences.

4.3 Concluding comments on the results

The results from the tables 7 through 13 are summarized in table 14. Only the statistically significant differences are mentioned here.

The incidence is not different except on two occasions (table 7 and 14).

The mean amplitude is higher in the diverticulosis group compared to the controls and in the painful IBS with diverticulosis group compared to the controls and the diverticulosis group (table 8 and 14).

The duration is longer in some periods in the groups with patients in comparison to the group with controls, but not in the groups with patients compared to one another (table 9 and 14).

The areas under the curve increase from controls to the painful IBS with diverticulosis (table 10, 11 and 14 and fig 21 and 22). In painful IBS with diverticulosis the greatest resistance to flow was found.

The motility indices show almost the same outcome as the areas under the curve (table 10-13): the resistance to flow increases: controls < painful IBS < diverticulosis < painful IBS with diverticulosis.

	C < I	C < D	C < ID	I < D	I < ID	D < ID
In			F;PG			
A	PG	F;PP;PG;O	F;PP;PG;O	PG	F;PP;PG;O	F;PP;PG;O
Du	PG;O	PG;O	F;PG;O			
TAr	PG;O	F;PP;PG;O	F;PP;PG;O		F;PP;PG;O	O
MAr	PG;O	F;PP;PG;O	F;PP;PG;O		F;PP;PG;O	O
TMI	PG;O	F;PP;PG;O	F;PP;PG;O		F;PP;PG;O	F;PG
MMI	PG;O	F;PP;PG;O	F;PP;PG;O	PG	F;PP;PG;O	O

Table 14 Summary of statistically significant differences, from the tables 7 through 13.

The characteristics of the waves are statistically significant in the mentioned period.

C = control; I = painful IBS; D = diverticulosis; ID = painful IBS with diverticulosis.
In = incidence; A = amplitude in mm Hg; Du = duration in s
TAr = total area under the curve in mm Hg.s; MAr = mean area;
TMI = total motility index; MMI = mean motility index.
F = fasting; PP = postprandial; PG = postglucagon; O = overall.

The impression is created that the patients with a painful IBS have a position in between the control cases and the patients with a diverticulosis cases and that the patients with a diverticulosis are positioned in between the patients with a painful IBS and a painful IBS with diverticulosis.

Of the 23 patients with a reproduction of their characteristic pain during the barium enema examination 21 cases showed a second time a reproduction during the pressure recording investigation : 90%.

It appeared in our study that the amplitude is very often significantly greater in the painful waves in comparison to the painless waves (table 23, appendix). Is the high amplitude responsible for the experienced pain?

The duration is of no significance (table 24). The mean area and the mean motility index are less often significantly different (table 25 and 26).

4.4 Fluoroscopy during the pressure recording

During fluoroscopy the author did not see contractions of the sigmoid when there were no pressure recordings. Especially during the postglucagon period it became clear, in the five to ten min rest of the sigmoid immediately following the administration of glucagon, that there are no pressure tracings when the sigmoidal wall does not move.

On the other hand it became evident that there sometimes might be seen contractions of the muscular wall of the sigmoid colon at the site of the microtransducer, without measurable changes in the pressures. This was especially observed when the sigmoid was not segmented. The impression was gained that the contents of the colon could move freely.

Conclusion: not all muscular activity has counterparts in the tracings, but there are no tracings without activity. In this aspect it must be admitted, however, that the observer is not unbiased in this observation, so that a subjective component cannot be excluded completely.

4.5 Cyclic contractions

Some authors (19) described in their pressure recording study, using balloons, slow, isolated, contractions lasting about 15 s or longer. These contractions correspond, according to the authors, to the three to four cycle/min contractions reported in electromyography.

The author found, visually, in the present pressure recordings, cyclic waves on 20 occasions in the 15 patients of the control group, and of 35 occasions in the 15 patients of the painful IBS group. These prevalences are, in comparison with the sum of about 1190 waves in the whole control group and the sum of about 1340 waves in the whole painful IBS group, very low. They seem of no significance.

5

DISCUSSION

5.1 Pressure recording is resistance recording.

> Experimental physiology conjoined with clinical observation may determine the true nature of many morbid states.
> (Clark 1859; 79)

The present pressure recording study was combined with fluoroscopy. The impression was created that not all muscular activity of the sigmoid had counterparts in the pressure waves. No pressure waves, however, were seen without activity. Other authors found the same (183;191;193;225). Propulsive contractile activity is preceded by a wave of relaxation (27;32;78;106;117). In propulsion the resistance to flow therefore is minimal, thus the pressure waves are minimal too (isotonic contraction).

Some authors did not observe a movement of the contents of the bowel in one-third of the pressure waves (192). They, however, employed radiotelemetric capsules which move freely in the gut, and which may show a pressure wave every time they meet the wall of the bowel.

Contraction of the circular muscle layer of the colon leads to a segmentation as can be seen during a barium enema examination. Very strong contractions of the circular muscle, called hypersegmentation, give rise to a constriction of the bowel lumen. This hypersegmentation results in an impedance to the flow in anal direction. In the right colon this hypersegmentation is physiologic. Hypersegmentation, results in an increase of pressure as recorded in our study. Another researcher found the same (106).

Conclusion: Absence of waves during the pressure recording means either propulsion or absence of contractile activity. Presence of waves means contraction plus resistance to flow. Essentially, the recording of pressure is the recording of resistance.

5.1.1 The solution to a paradox.

Several authors have been puzzled by noting a hypermotility in constipated IBS patients and a hypomotility in diarrheal IBS patients. They called this finding paradoxical as they thought that constipation ought to show a low activity and diarrhea a high activity (9;204;229;358;359).

The present author agrees, with Christensen (96), that the hyperactivity in constipation is caused by the non-propulsive or segmenting activity of the sigmoid resulting in a resistance to net flow in anal direction. The segmentation leads to the formation of sealed off chambers in which high pressures can be built up, if the contraction of the circular muscles goes on. This was demonstrated in the present study. The author also agrees with Tucker and Schuster (27) that diarrhea may be associated with a loss of the segmenting contractility.

Thanks to the combination of fluoroscopy and pressure recording it became clear that the recording of the pressure is

a recording of the resistance to flow. High recordings mean high resistance to flow and constipation, low recordings mean low resistance to flow and diarrhea. That is the solution to the paradox.

5.2 The reproduction of the correlation: pain-contraction.

Twenty one of the 23 painful patients, with IBS-like pain, who felt a reproduction of their characteristic pain during a sigmoidal contraction in the barium enema examination, showed a second reproduction of the correlation pain-experience and sigmoid-contraction during the pressure recording study.

Especially when studying a patient with a painful abdomen the radiologist has to be perceptive to the complaints of the patients during the barium enema examination. The subjective discomfort must be noted and a reproduction, if any, of the characteristic pain must be perceived. A segmentation of the sigmoid may correlate with that pain. The radiologist should be interested in the study of functional disorders.

Lumsden, Truelove and Chaudhary (88;89) reported their findings during barium enema studies in painful IBS patients. They noted a correlation between the experience of abdominal pain, identical with the previous complaint, and a radiologically observable contraction of the colon. Haubrich (85) observed, during colonoscopy, spasms which might simulate the pain of the patients. He pleaded that the radiologist also seek positive evidence for the diagnosis of a painful IBS in a radiographic configuration. In this way the barium enema examination can be more conclusive than "negative".

In this study it became clear that the radiographic configuration which the radiologist has to seek is a segmentation or a contraction of a lengthy segment (fig 2-4). Besides that, however, a reproduction of the patient's own characteristic pain during the barium enema examination must occur.

It is further necessary:

a/ to make the sigmoid relax (with the aid of a bowel relaxing drug (glucagon or butylscopolamine) or reassurance),
b/ to see the decrease of the contraction and
c/ to note a simultaneously occurring relief of the pain.

In this way the correlation pain-contraction is observed twice during the barium enema examination: contraction elicits the pain, relaxation relieves the pain.

The radiologist has to search for such a correlation, or no correlation will be found.

5.3 The recognition of a painful IBS case by a barium enema examination. Sensitivity, specificity, accuracy, predictive value.

Let us take the diagnosis, as obtained by the pressure recording, as the "golden" standard, and the barium enema examination as the test. The diagnostic value (360) of the radiologic investigation is shown in table 15.

Sensitivity =TP (True Positive) = T+/D+	= 21/21 X 100%	=	100%
Specificity =TN (True Negative) = T-/D-	= 30/32 X 100%	=	94%
False Positive ratio = T+/D-	= 2/32 X 100%	=	6%
False Negative ratio = T-/D+	= 0/21 X 100%	=	0%
Predictive Value+Test = TP/(TP+FP) = 100/(100+6) X 100%		=	94%
Accuracy = TP+TN/all patients = (21+30)/53 X 100%		=	96%

Table 15 The diagnostic value of the detection of the pain reproduction with the aid of a single and double contrast barium enema examination. N = 53.

These figures may be impressive but the group of patients is small and the interest of the researcher in this subject is great; so the value of these figures is limited. Besides that, it was the barium enema examination that indicated if a case underwent a pressure recording study or not, so the true positive ratio could be nothing less than one hundred percent and the false negative ratio nothing more than nil percent.

One question, however, can be answered clearly: it is possible to recognize a painful IBS patient with a barium enema examination. The author agrees with Bockus (87) that the barium enema study is a reliable and reproducible technic for the search of a correlation between symptom patterns and functional derangements. The radiologist must have interest in functional pathology and search for it.

5.4 The cause of the pain.

> The pathogenic spotlight is brought to bear on the disordered sigmoidal motility (Almy 335).

The patient wants to know what the cause of the pain is (69) (section 1.1.4). Tucker and Schuster (27) wrote in 1981: " More recently, attempts have been made to correlate these changes in intraluminal pressure with patients' symptoms of pain....". The question is, as ten Thije wrote (78): "Why are contractions of the colon painful ?" These pains can be elicited during a barium enema examination, as discussed in section 5.2 and 5.3, but also during a sigmoidoscopy.

In accordance with the suggestion of Thompson (9) the present author has investigated the pain of the IBS patients and has put it into a separate category, apart from the diarrhea and the constipation.

Some authors noted a cramping pain, in stoma patients, coinciding with an intersegmental incoordination (81;82) or in patients during an operation under local anaesthesia when the bowel was contracting (136).

Ritchie (94), Swarbick e.a. (84) and Dworken e.a. (83) induced colonic pain by inflating balloons. In 29 of the 48 patients the pain induced was the same pain in quality and site as their present complaint (84). Ritchie (94) hypothesized a

colonic hyperalgesia in his patients ; he also thought, on the other hand, that the pain could be caused by an increased tension in the colonic wall (33;94).

Hertz (91-93) assumed, as far back as 1911, that the sensation of visceral pain was due to an increase in tension on the fibers of the muscular coat of the colon. Later on it appeared, in pressure recording studies, that in painful IBS patients colonic motility was abnormally increased (197-200;204). In this study the same was found (table 19).

Wangel and Deller (204) and Connell e.a. (198) found higher amplitudes in painful IBS patients, in the present study the same was found. Those authors (204, 198), however, did not look for a correlation between high amplitudes and pain experiences as the author in this study did. The mean amplitude in the painful IBS group of the present study was in the fasting period 9.8 mm Hg and in the postprandial period 15.3 mm Hg (table 17); Connell e.a. (198) found 10.9 and 16.7 mm Hg respectively. These results are well comparable.

Chaudhary and Truelove (191) found high amplitudes, and Parks and Connell (340) as well as Misiewicz e.a. (203) found hyperactivity in the painful IBS patients only if they had complaints. These findings may seem a little enigmatic, but in the author's opinion they are not. They point into the physiological direction. In contrast with anatomical abnormalities, physiological or functional abnormalities are not permanently "at hand". If there are no pains, there are no functional problems and no functional pathology can be found.

The correlation of pain and contraction was sought for by Holdstock, Misiewicz and Waller (100). They found that the onset of abdominal pain coincided with a marked increase in the motility of the colon in five out of seven patients with a painful IBS. They did not correlate the pain experience with the amplitudes of the waves.

Harvey and Read (252) reproduced the pain through an intravenous injection of cholecystokinin in four of eight patients who complained of attacks of abdominal pain after food, The researchers noted a typical attack of the patients' usual pain, at a time when there was a hypermotility. These authors did not study the relationship of amplitude of the wave and pain experience either.

From the present study, in which the amplitudes of the painful waves were correlated with the pain experiences, it became clear that the painful waves are associated with statistically significantly higher amplitudes (table 23). The mean amplitude of the painful waves in painful IBS patients is 28.2 compared to 12.3 mm Hg in the waves without pain. Ritchie (236) regarded some pain in painful IBS cases as due to contraction waves which averaged 45 mm Hg. He did not compare this finding with the results in controls. He thought that this amplitude was not high enough to cause the pain. The patients in the present study did feel pain with mean amplitudes of 28 mm Hg, so their pain experiences appear to be at variance with the thoughts of Ritchie.

Bloom e.a. (99) studied ten IBS patients with diarrhea and/or constipation. They found lower amplitudes in these cases with the aid of telemanometric capsules. No clear relationship could be observed between the occurrence of pain and any particular wave form. It is logical that Bloom e.a. (99) found

lower amplitudes, in comparison to controls, as it has been observed that there is a hypomotility in diarrhea (9;204;229;359).

In section 5.1 it was discussed that pressure recording is resistance recording and that patients with a diarrhea "just let the contents flow through", as the Greek meaning of the term diarrhea indicates. The explanation, why Bloom e.a. (99) could not find a correlation between pain and wave form may be that a telemetric pill moves too freely in the colon to be able to establish the high waves which correlate with pain and contraction, as was found in the present study.

Misiewicz (187) found, on pressure recording investigation, in the "true" sigmoid (the pressure sensors had been introduced through a flexible sigmoidoscope; as was done in this study) a hyposegmentation. This observation is, together with the study of Bloom e.a., at variance with almost all previous studies (191;197-200;204;340) in which a hypermotility was found. In the present study the same found. It may be that Misiewicz's patients (187) were symptomless, as they were in one of his other studies (203). As discussed earlier in this section: a functional pathology is not constantly present.

Fig. 26a Segmenting contraction of the sigmoid.

Fig. 26b The patient indicates where the pain is felt.

Fig. 26c The pain has disappeared. The patient and the sigmoid are relaxed.

5.4.1 Conclusion

In the present study a correlation of three signs was found:
a/ a radiologically visible segmentation of the sigmoid (fig 26)
b/ high amplitudes (fig 27)
c/ pain sensations of the patient.

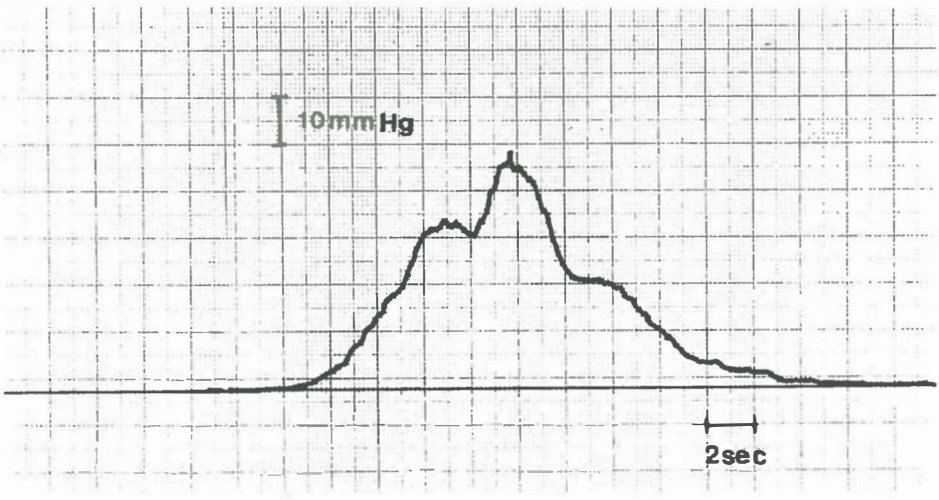


Fig. 27a No pain is felt during this wave of 48 mm Hg.

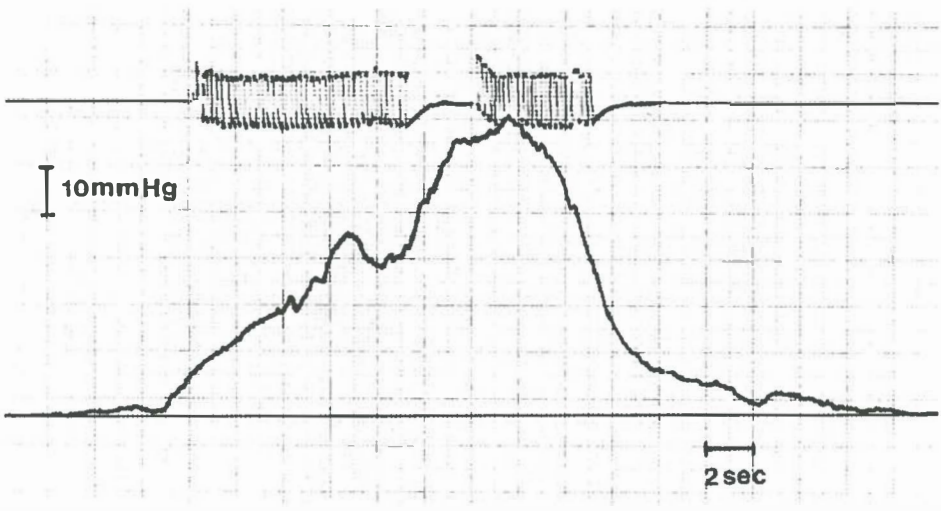


Fig. 27b The characteristic pain is felt (as indicated by the spikes) during this wave of 63 mm Hg.

The author is tempted to call the correlation: sigmoidal contraction and pain reproduction, as occurring during the barium enema examination, "the painful IBS phenomenon". The correlation of relaxation of the sigmoid and decrease of the discomfort must also be established, whereas it also must be made clear that the patient's characteristic pain, which urged her/him to visit the doctor, is reproduced during the barium enema study. The patient has to feel her/his pain and to report about it without the suggestion or influence of the radiologist.

The correlation contraction and pain was again reproduced in 90% of the patients during the pressure recording study.

5.4.2 Colonic colic.

In former days (361;362) the term colic was used to indicate pain in the colon. As discussed in section 1.1.5.2 such powerful contractions, as have been recorded in this study, can be evoked by an obstruction of the forward movement of the contents of the colon. In patients with a painful IBS or a painful IBS with diverticulosis this obstruction may be caused by a hypersegmentation: a colic-like contraction of the smooth muscle of the colon. There seem to be a colonic colic. Another name used is spastic colon. The best name is painful IBS.

About the cause of the hypersegmentation knowledge is scanty; a low fiber diet may play an important role. Pressure recording in patients who have used a high fiber diet can reveal more about this question.

5.4.3 Pain experiences.

From this study of the pathophysiology of the sigmoid one factor which influences the pain experiences has been revealed:

1/ the evoked amplitudes are above the normal physiologic range.

The study of the literature (see section 1.1.5) revealed three factors:

2/ the varying responding thresholds of the receptors;
3/ the plasticity of the nociceptive system;
4/ the emotional influence through the limbic system.

The explanation why two of the 23 patients with a "painful IBS phenomenon" did not experience a reproduction of their pain may be sought in one of these factors.

5.5 Hypermotile state in painful IBS and diverticulosis.

Are both conditions different phases
of one single entity ? (Thijn 1973; 26)

Several researchers found higher activity in diverticulosis compared to controls (202;205;210-212;the present study).

Parks and Connell (202), using perfused open ended tubes, found higher amplitudes in diverticulosis. They found in the fasting period a mean pressure of 5.8 mm Hg in their controls and 7.9 mm Hg in the diverticulosis group. After the meal these pressures measured respectively 6.6 and 12.2 mm Hg. In the

present study higher amplitudes were measured (table 17): controls: 7.6 mm Hg in the fasting and 9.9 mm Hg in the postprandial period; diverticulosis: 14.8 mm Hg if fasting and 21.0 mm Hg post-prandial. A strain gauge microtransducer, with central lumen, was applied in this study so that the values may be different. The results, however, point into the same direction.

Weinreich and Andersen (205) calculated the product of the mean amplitude and activity percentage and found higher figures in painful diverticulosis patients, if they had pain, than in controls. In this study the same was found (table 14; 21 and 22).

Arfwidsson and Kock (210) found more milligrams of activity in diverticulosis than in controls. They cut out the paper on which the individual pressure waves above the basal line were written and weighed the paper. This result is comparable to the findings of the present study (table 14,19, and 20).

Painter published much about diverticulosis patients (47; 147; 211 e.a.;212 e.a.; 241; 283 e.a.; 284 e.a.; 285; 287; 343 e.a.). He called diverticulosis a deficiency disease. In pressure recording, using open ended tubes, he found, after prostigmine, higher amplitudes and longer durations in the diverticula bearing region of the sigmoid (212).

In studies combining pressure recording and cineradiography Painter (287) observed that the diverticula varied in size according to the pressure in the bowel. The segmentation narrowed and at times occluded the colonic lumen, in which way high intraluminal pressures could be generated. During fluoroscopy the investigator did not clearly observe this in the present study. In one case Painter recorded a pressure of 60 mm Hg. In this study an amplitude of 224 mm Hg (29.9 kPa) was recorded as the highest pressure (section 4.1.2).

Painter and Burkitt (343) suggested that the high pressures "blew up" a segment (formed by the constricting or segmenting circular muscle) so that the mucosa penetrated through the weak spots in the muscular layer. In the present study support for this assumption was found as significantly higher amplitudes in the two groups with a diverticulosis were measured (table 17).

Eastwood e.a. (201) found results which raised some doubts about the raised intraluminal pressures in patients with a diverticulosis. They used open ended tubes but do not mention if they perfused these tubes, this fact may explain their different findings.

As already was discussed in section 5.4, it became clear that painful IBS patients were more active in their sigmoid colon than controls (89;191;197-200;204;252;340; the present study)

5.5.1 Reactions to drugs

Parks and Connell (340) and Chasen e.a. (341) found higher responses of painful IBS and diverticulosis patients to drugs. The present author found the same. After the injection of glucagon a period of inactivity of about five to ten min was seen, other authors found the same (352-355). After this, more activity was observed in the patients in comparison with the controls (table 8-14). It seems as if the sigmoid has gained energy during the 5 to 10 min "rest" after the administration of

glucagon, which energy facilitates the hypermotility.

5.5.2 Conclusion

The conditions painful IBS, diverticulosis and painful IBS with diverticulosis show a hypermotile state. The three conditions react in the same way to drugs. Snape (334) asked in 1984: " Are there hypermotile states in these conditions ?". The results of the present study show that there are.

5.6 The distribution of age and resistance to flow

As the ages were significantly different in some of our cases (section 3.1.2) one might assume that the different ages led to different motilities and amplitudes. In fig 28 it is demonstrated that there is no correlation between the mean age of the groups and the overall total motility indices. The mean age does not increase in the same way as the motility index.

The resistance to flow is independent of the age of the patients.

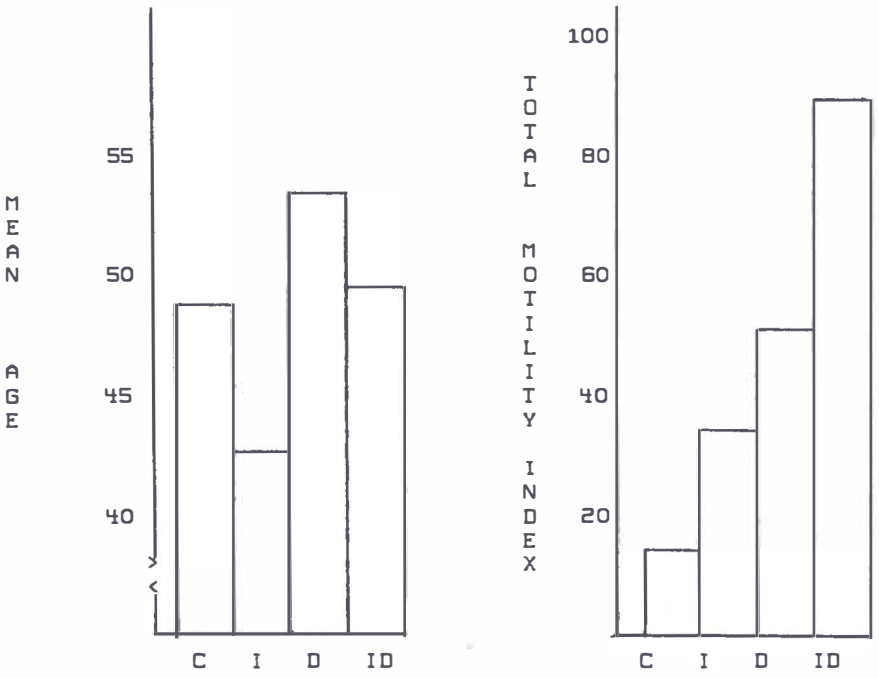


Fig 28 Comparison of the mean ages (in years) of the four groups with the overall total motility index (in mm Hg.s x 1000) (compare table 21 and fig. 23). C = control; I = painful IBS; D = diverticulosis; ID = painful IBS with diverticulosis.

The colon of the painful IBS patients has to endure the high pressures for a long period as it became clear that these patients may have pain for a long time (section 1.8.4). After many years of high pressures diverticula may become manifest in the older patient. Thijn (26) suggested this possibility.

5.7 Area under the curve or motility index ?

In the present study the area under the curve and the motility index were estimated in order to see if both variables have to be calculated in the evaluating of the results of pressure recording studies. When the results of the tables 10 through 13 are compared, it becomes clear that the significant outcome is almost comparable (see also table 14). The results are only different in the comparison of the groups diverticulosis and painful IBS with diverticulosis.

As far as the author could check no other researchers did all these calculations. Some calculated only the motility index (19;191), others determined the area under the curve by an integrator (200) or a balance (210).

From the results of the present study it appears that it is not necessary to establish both the motility index and the area under the curve. It is, however, necessary to measure the amplitude of the wave, as that characteristic has appeared to be of importance for the explanation of the pain.

It seems sufficient to establish the amplitude and the duration of the waves so that the motility index (table 2) can be calculated.

5.8 Contractions: three to four cycles per minute ?

Whitehead, Engel and Schuster (19) described, as was discussed in section 4.5, in their pressure recording study, slow contractions which might correspond to the three to four cycle/min contractions reported in myoelectrical investigations (296;297;301;363). The present pressure recordings did not show that. The findings of Whitehead e.a. (19) could not be confirmed, neither could Latimer (32). Whitehead e.a. recorded at nine to 14 cm from the anus, and thus in the rectum. In the present study the author recorded 30 cm from the anus, and thus in the sigmoid. This may be the explanation for the difference.

The present author agrees with Huizinga e.a. (303) that the relationship between the electrical and motor activities, so far, is poorly understood.

5.9 Some hypotheses about the pathophysiology of painful IBS, diverticulosis and painful IBS with diverticulosis.

As discussed in section 1.2.2 there is a contracted state of the longitudinal muscle in diverticulosis, and probably, in painful IBS. In these contracted muscles elastin is deposited in a contracted state (149). The contracted state of the longitudinal muscles is maintained through these elastin deposits. The consequence is that the longitudinal muscle cannot properly contract so that the propulsion must be done almost alone by the circular muscle. This leads to a hyperactivity of the circular muscle as has been demonstrated. But the hyperactivity of the circular muscle also leads to a

segmentation or a hypersegmentation as has been observed during the barium enenma examination of the sigmoid (concertina-like sigmoid). This hypersegmentation can result in a constriction of the colonic lumen so that sealed off chambers can be formed and high amplitudes can be generated, as was demonstated in our study.

It was discussed in section 1.1.5 that mechano-sensitive or pressure-sensitive fibers in the colon in mammals (113;121;122) and sensory fibers in the biliary tract (114) respond to high pressures (107;124-126) and contraction (110;121). Higher pressures give rise to higher stimuli (106;127). The result is a sensation of pain caused by the high amplitudes in the sealed off chambers in the segmented sigmoid, as was found in the present study.

But the nociceptive system is plastic so that the pain is no longer felt by the patients and disappears. This may be the explanation why some patients with a diverticulosis do not appear to have felt much pain in the history. The high pressures, however, remain.

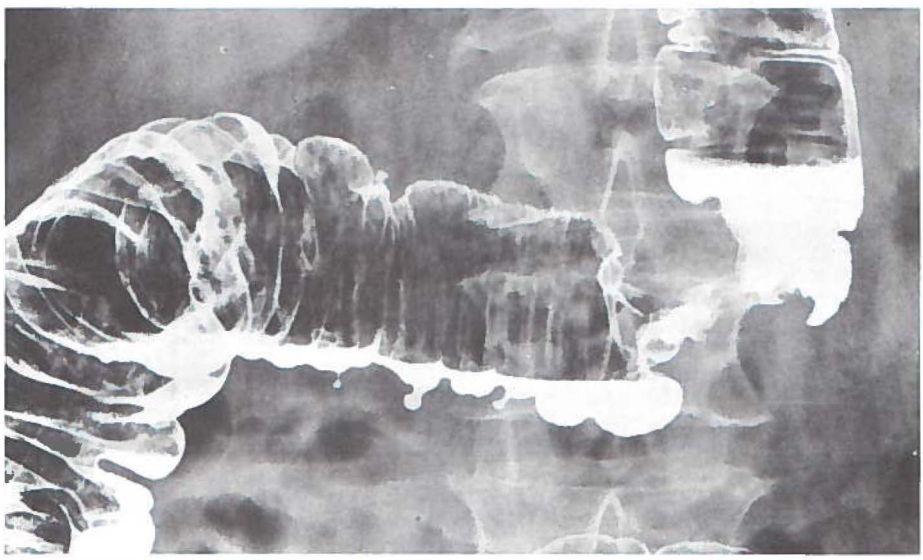


Fig. 29 This patient shows an obstructing colonic tumor. Proximal to this tumor tiny herniations of the mucosa can be seen. There were no diverticula elsewhere in the colon. This film seems to demonstrate the assumption that high amplitudes cause diverticula (courtesy of Prof. Dr. C.J.P. Thijn).

After years of high amplitudes the mucosa begins to herniate through the corrugated muscular wall, and incipient herniations can be seen during the barium enema examination as tiny mucosal herniations (fig 5). After many years of disordered motility and increased resistance to flow with high amplitudes, diverticula may be formed.

Radiologically the assumption of the formation of diverticula through high pressures seem to be visualised in a patient with an obstructing tumor in the colon (fig 29). Proximal to this obstruction tiny herniations of the mucosa are visible.

Thijn (332) described two patients in whom the tiny diverticula apparently were reversible after a year of a high fiber diet. Further radiologic investigation is necessary to confirm these findings. Nevertheless, Thijn's observation opens the way to a further revealing of the secrets of the etiology of diverticulosis with the aid of the X-rays. It was reported that a high fiber diet decreased the hyperactivity (289;290) so that the radiologically observed reversibility has a pathophysiologic base.

The amplitudes were very high in the patients with a painful IBS with diverticulosis and lower in the patients with a diverticulosis (table 17). It seems as if the diverticula are being formed in the patients with a painful IBS with diverticulosis and have been formed in the patients with a diverticulosis. It may be hypothesized that the process of diverticula formation may be burnt out: the amplitudes are decreasing, the pains are decreasing too.

The pain in painful IBS is a noxious stimulus as, in the long run, the high amplitudes lead to a damage of the sigmoid with herniations of the mucosa as the consequence. The reaction to this painful stimulus ought to be a protective one: a high fiber diet.

It is the author's opinion that a low fiber diet plays an important role in the etiology of painful IBS. This diet leads to an intermittent distension of the sigmoid resulting in a deposition of contracted elastin in the contracted longitudinal muscle. The circular muscle shows a hypersegmentation resulting in a resistance to the distal flow of the contents and in high amplitudes felt by the patients as pain. The prevention of pain must be sought in a high fiber diet.

In the etiology of diverticulosis the low fiber diet as well as the painful IBS are of great importance. The author is convinced, however, that both conditions are determined multifactorially and that of these factors just one (in painful IBS) or two (in diverticulosis) have been revealed.

In former days the painful IBS was named: spasmodic stricture. It now appears that the pain, in the patients with a painful IBS and in the patients with a painful IBS with diverticulosis, is caused by a constricting or segmenting contraction of the sigmoid, resulting in high amplitudes. The patient feels a spasm i.e. a cramping pain (78). It was stated (364) that in cases in which no specific cause for the pain could be found these people had to be considered to have functional pain. The present study makes clear that this "functional pain" is a pain caused by a disordered function of the sigmoid in these patients, which can be demonstrated by a

barium enema examination.

The present author disagrees with others (365) who thought that the abnormal activity probably was not the cause of the pain.

5.10 Differentiating painful IBS and diverticulosis: therapeutical use ?

The reason why a patient seeks medical advice is that she/he wants an explanation of the cause of the pain and relief of the pain.

It became clear from the results of this study that the cause of the pain must be sought in an increased resistance to flow with high amplitudes.

In section 1.9 the possible links between painful IBS and diverticulosis were discussed. The clinical presentation of both diseases is similar: pain and disturbed bowel habit (26;33;34). Radiologically both conditions may show a contractile and segmenting sigmoid.

From the literature it appeared that both conditions are treated with a high fiber diet (section 1.8.2 and 1.8.3). Patients with a painful IBS found relief of their pain with high fiber diet as well as with placebo-diets (5;9;253;254;305). In diverticulosis patients high fiber diet led to a normal bowel habit and relief of the pain (Painter: 147;241;285), to prevention of complications (291), to a standardizing of the resistance to flow in humans (289;290), and to a decrease of incipient or tiny diverticula as diagnosed by radiology (Thijn:332).

The immediate therapeutical relevance of the differentiating is debatable as both conditions are treated in the same way, by a high fiber diet. Clinically, of course, it is necessary to know which of the two conditions we are dealing with, as a diverticulosis can lead to a life threatening perforation. A physiologically directed barium enema examination must be done, in painful patients, in order to try to establish a correlation between the characteristic pain and a sigmoidal contraction, so that the diagnosis of a painful IBS can be objectfied and made on positive grounds. Further it must be established if diverticula or a colonic tumor or another anatomical abnormality are present.

5.11 Future developments

Patients with a discontinuous abdominal pain ought to have a physiologically directed single and double contrat barium enema investigation of the colon in order to establish if they have a painful IBS or a painful IBS with diverticulosis. It is important to recognize these patients so that they can be treated by a high fiber diet and the development of diverticula and their complications can be prevented.

Patients from general practitioners and medical specialists, among others gastroenterologists but also gynaecologists, with undiagnosed pain ought to have a physiologically directed single and double contrast barium enema investigation in order to avoid a "Homeric peregrination" in the

health care (366).

In the pressure recording studies of IBS patients it is important to differentiate between painful IBS patients, IBS patients with diarrhea, IBS patients with constipation or IBS patients with alternating diarrhea and constipation. It was found in this study that the painful IBS shows a hypermotility with high amplitudes. It may be assumed that the IBS patients with a diarrhea show a low motility, the IBS patients with a constipation show a high motility and that the patients with an alternating bowel habit show a state of motility according to the state of their defecation. Further research can confirm these assumptions.

In those patients with a painful IBS or a painful IBS with diverticulosis in whom the pain cannot be reproduced and correlated with a segmenting contraction, ways have to be sought to make it possible to objectify such a correlation during a barium enema examination, e.g. with parasympathomimetic drugs (prostigmine or neostigmine) or cholecystokinin.

It is necessary to do pressure recording studies in patients with a painful IBS after a high fiber diet in order to objectify the subjective relief of the patients. Are the amplitudes lower? If these amplitudes are lower it may be expected that diverticula formation can be prevented by a high fiber diet.

6
CONCLUSIONS OF THE STUDY

In chapter 2 the objectives of the study were formulated. The results of the present pressure recording investigation lead to the answers:

1/ The first objective was to obtain information about the reproducibility of the correlation of pain and contraction so that it may be possible to recognize a painful IBS or a painful IBS with diverticulosis patient with one barium enema study.

The correlation pain-experience and sigmoid-contraction was reproduced in 14 of 15 patients with a painful IBS and in seven of eight patients with a painful IBS with diverticulosis during the pressure recording investigation.

This correlation was observed, for the first time, during the single and double contrast barium enema and, several weeks later, for the second time during the pressure recording investigation, in which the sigmoid was made visible by barium sulphate.

Thus a patient with a painful IBS can be recognized by a barium enema study alone, be it that such an examination must be physiologically directed. The radiologist must be informed by the patient about her/his characteristic pain, must be perceptible to the patient's pain and must have knowledge of the physiology of the colon. The reproduction of the patient's own, characteristic pain, during the barium enema examination, in combination with a segmentation of the sigmoid, as well as the relief of the pain with a relaxation of the sigmoid is a positive diagnostic criterion and may be called "a painful IBS phenomenon".

2/ The second objective was to answer the question whether all muscular activity of the sigmoid, as demonstrated by movemens of its wall, is expressed by a change in the intraluminal pressure.

Not all muscular activity, as seen by the investigating radiologist, was expressed in pressure waves: a part of the visible contractions was not accompanied by discernable waves. The area under the curve and the motility index, strictly spoken, measure the degree of the resistance to flow of the sigmoidal contents.

3/ The third objective was to compare the pressure recordings in the four groups, paying special attention to pressure changes during the characteristic pain.

It was possible to correlate the amplitude of the pressure waves with the pain sensations of the patients. Painful waves had statistically significantly higher amplitudes than painless waves.

4/ The fourth objective was to formulate considerations about the mechanism of that characteristic pain.

The observation that the pain is accompanied by amplitudes above the range of controls, is compatible with the hypothesis that increased intraluminal pressures (and compression of mucosal and submucosal structures) are the cause of the pain. There appears to be a "colonic colic". A triad of pain-experience, sigmoid-contraction and high-amplitude-wave was established.

5/ The fifth objective was to reconsider the hypothesis that painful IBS and diverticulosis are expressions of one hypermotile state, painful IBS being an etiologic factor of diverticulosis.

In the investigated groups of patients the sigmoidal motility, or rather the pressures, increased in the following order: controls, painful IBS, diverticulosis and painful IBS with diverticulosis. This supports the hypothesis that these diseases are part of one hypermotile state. Painful IBS may be one of the etiologic factors of diverticulosis.

6/ The sixth objective was to answer the question whether the area under the curve as well as the motility index ought to be estimated in evaluating the results of the pressure study.

Strong evidence was gained that it is sufficient to estimate the motility index, being the sum of the products of the amplitude and the duration of each wave. It is not necessary to estimate the area under the curve as well.

SUMMARY

Radiological and motility studies of the sigmoid are described in three common conditions: painful irritable bowel syndrome (IBS), diverticulosis without and diverticulosis with IBS-like pain. The phenomenon, especially studied in these patients and compared with a control group, was their left lower abdominal pain and its correlates. IBS patients with painless diarrhea and/or painless constipation were not considered. It was hoped that collection and comparison of the data might improve the diagnostic possibilities of the radiologist and might elucidate the cause of the pain and possible links between the three conditions.

The review of the literature

In chapter 1 the literature is reviewed.

A positive diagnostic criterion is lacking in patients with a painful IBS. The diagnosis is, traditionally, made by exclusion. Pain is a subjective phenomenon. The doctor wants an objective, reproducible, phenomenon. Is the pain caused by an abnormal sigmoid function? A reproduction of the patient's own characteristic pain is necessary during an investigation. An examination must be performed in which the characteristic pain as well as the sigmoidal contractions simultaneously can be recorded so that they can be correlated. An abnormal function of the sigmoid can be examined by pressure recording. Sigmoidal contractions can be visualized with the aid of radiologic methods. Can the diagnosis painful IBS be made with the aid of a barium enema examination?

In section 1.1.5 it appeared, neurophysiologically, that powerful contractions may cause high pressures in the colon which can evoke afferent discharges from specific nociceptors or mechanoreceptors. The responding thresholds of these receptors vary. The sensory pathways in the case of colonic pain are along the splanchnic nerve, the spinothalamic tract, and the connections between the thalamus and the somatosensory cortex of the postcentral gyrus. Motivational and emotional dimensions can be added to the pain experience. The nociceptive system is plastic.

In section 1.2 it is discussed that diverticula are thought to be herniations of the mucosa at weakened sites in the sigmoidal wall. No evidence is found for a hypertrophy or a hyperplasia of the longitudinal muscles. Their thickening is caused by a contracted state, which is maintained by deposits of elastin. Intermittent segmental sigmoidal contraction, as caused by small stools which are the consequence of a low fiber diet may trigger an increased deposition of, among others, contracted elastin.

In section 1.3 it is described that in the motility of the colon (the movements of the colonic wall) four patterns were observed: 1/ the basic tone; 2/ the nonpropulsive segmental contraction or segmentation which increases the resistance to anal flow; 3/ the propulsive contraction and 4/ the retropulsive contraction.

The motility has mostly been recorded with the aid of

intraluminal pressure recording alone. The combination with radiologic methods, with the aid of which the movements of the wall can be visualized, provides the best method for studying the sigmoidal motility.

The etiology of the painful IBS is discussed in section 1.5. There may be a hypermotility of the sigmoid wich may be caused by a low fiber diet. The correlation of experiences of pain and amplitudes of waves has not been studied. The etiology of diverticulosis is also sought in a low fiber diet. It has been called a deficiency disease.

In section 1.8 the differential diagnosis, therapy and prognosis are discussed. High fiber diet, but also placebo-diets relieve the pain in patients with a painful IBS and decreases the motility in patients with a diverticuliosis. Few good double-blind studies have been performed. Painful IBS is a longstanding disease.

In section 1.9 possible links between painful IBS and diverticulosis are discussed. The diseases may both show a hypermotility. One hypermotile state is hypothesized.

The present pressure recording investigation.

In chapter 2 the aims of the study are mentioned. First a single and double contrast barium enema examination was performed to select the patients. Secondly a pressure recording investigation was carried out, several weeks later.

Six questions were posed: 1/ Is it possible to reproduce the correlation pain-contraction for the second time during the pressure recording study? Is it possible to recognize a painful IBS patient by a physiologically directed barium enema study? 2/ Is all muscular activity of the sigmoid, as demonstrated by movements of its wall, expressed by a change in the intraluminal pressure? 3/ Are there special pressure changes during the characteristic pain experiences? 4/ Is it possible to formulate considerations about the mechanism of such pain? 5/ Are painful IBS and diverticulosis expressions of one hypermotile state and is painful IBS an etiologic factor of diverticulosis? 6/ Is it necessary to estimate both the area under the curve and the motility index in evaluating the results of the pressure recording?

In chapter 3 the patiens and methods are discussed.

Four groups were studied: a control group, a painful IBS group, a diverticulosis group and a painful IBS with diverticulosis group.

The cases are defined in section 3.1:

A/ A control case has an anatomically and functionally normal barium enema examination. A sigmoidoscopy does not reveal any abnormality. There may be some pain in the upper abdomen or blood in the stool.

B/ A patient with a painful IBS has a discontinuous pain in the left lower abdominal quadrant for longer than 3 months. The reproduction of the pain, correlated to a sigmoidal contraction, is established during the barium enema study. The barium enema study and the sigmoidoscopy does not reveal any anatomic abnormality. There is no blood in the stool. There may be

alternating bowel habits and deterioration of the pain in correlation with a meal or a defecation. There is a normal blood chemistry.

C/ A patient with a diverticulosis has a diverticulosis of the sigmoid with or without some vague pain.

D/ A patient with a painful IBS with diverticulosis showes a reproduction of the pain, correlated to a sigmoidal contraction during the barium enema study. There is a diverticulosis of the sigmoid.

The patients were selected with the aid of an interview and a single and double contrast barium enema examination. Radiologically a patient with a painful IBS may be recognized by a segmentation of the sigmoid. For the purpose of our study it was obligatory to reproduce the pain of the patients with a painful IBS or a painful IBS with diverticulosis during the barium enema study. The observed sigmoidal contraction and relaxation had to be correlated to the characteristic pain-experience. These patients underwent a pressure recording study in order to see if the correlation pain-experience and sigmoid-contraction could be reproduced. The correlation of the experience of the pain and the character of the simultaneously occurring pressure waves was also studied. The characteristics found in the four groups were compared.

The methods of the pressure recording examination are discussed in section 3.2. 1/ A preparation was given so that the sigmoid was empty. 2/ Fifteen patients were studied in the control, painful IBS and diverticulosis group , eight patients were investigated in the painful IBS with diverticulosis group. 3/ The recording took place at 30 cm from the anus. 4/ A strain gauge microtransducer was used. 5/ The catheter was introduced through the biopsy channel of a flexible sigmoidoscope. 6/ One mm deflection of the pen on the recording paper was mostly calibrated to be 1 mm Hg. 7/ Radiologic technics were applied. The paper speed was 5 mm/sec. 8/ The pressure was recorded during a fasting, a post-prandial and a post-glucagon period, each lasting 30 min. 9/ The pain-pressure correlation was studied.

The results are shown in chapter 4. Only the statistically significant figures are reported here:

1/ The incidences (waves per min) were almost comparable between the four groups. 2/ The amplitudes were higher in diverticulosis and in painful IBS with diverticulosis compared to controls and in painful IBS with diverticulosis compared to diverticulosis. The amplitudes were also higher in the painful waves compared to the painless waves in the painful IBS group and in the painful IBS with diverticulosis group. 3/ The duration of the waves was longer in the three groups of patients compared to the controls. 4/ The motility index (being the sum of the products of the amplitude and the duration of each wave per period of time) and 5/ the area under the curve (estimated by counting the squares under the curve) increased in the following order: controls, patients with painful IBS, diverticulosis and painful IBS with diverticulosis. The mean motility index and mean area under the curve were greater in

some patients with painful waves in the group with painful IBS and in the group with painful IBS with diverticulosis.

The discussion is given in chapter 5 and the conclusions from the investigation are drawn in chapter 6.

The answers to the questions posed in chapter 2 are:

1/ In about 90% of the cases it was possible to reproduce for the second time the pain-contraction correlation (first observed during the barium enema examination) in the pressure recording investigation. The patient must be examined during a period of pain. A patient with a painful IBS can be recognized by a barium enema study if the radiologist is perceptible to the patient's pain and has knowledge of the (patho)physiology of the sigmoid.

The positive diagnostic criterion sought for in the painful IBS is a segmenting sigmoidal contraction correlated to a reproduction of the patient's pain experience.

2/ Not all muscular activity is expressed by a change in the intraluminal pressure. Pressure recording, usually considered to quantify motility, is a recording of resistance.

3/ The pain-experiences correlated with high amplitudes of the waves.

4/ The pain seems to be caused by pressures with a very high amplitude. The amplitudes of the painless contractions are not different from the amplitudes observed in controls. There is a disordered function of the sigmoid, in patients with a painful IBS and with a painful IBS with diverticulosis. The result is a segmenting contraction which leads to high pressures and pain: a "colonic colic". The reproducible correlation between pain and contraction which was observed, may be called "a painful IBS phenomenon".

Methods must be sought to evoke this IBS phenomenon. Patients with undiagnosed abdominal pain ought to have a physiologically directed barium enema examination performed by a perceptive radiologist.

5/ The results can support the hypothesis that painful IBS and diverticulosis are part of one hypermotile state. Painful IBS can be one of the etiologic factors of diverticulosis.

The high amplitudes, occurring especially during the painful waves in the groups with painful IBS and painful IBS with diverticulosis, may cause the formation of diverticula. When the amplitudes in the painful IBS with diverticulosis group are compared to the amplitudes in the diverticulosis group it is clear that the amplitudes are highest in the painful IBS with diverticulosis group. It may be suggested from this finding that, when the diverticula are present, the amplitudes become lower. Is the group with the painful IBS with diverticulosis, in the present study, the linking condition between painful IBS and diverticulosis?

6/ The significant results in pressure recording can be obtained by the calculation of the motility index alone. As the amplitude is important for the study of the cause of the pain, this variable has to be measured. Moreover, the amplitude and the duration can easier be estimated than the squares under the curve can be counted.

The following hypotheses can be formulated: a low residue diet may give rise to raised amplitudes in the sigmoid colon. These high amplitudes can be felt as a painful event, as was found in the present study in the patients with a painful IBS and a painful IBS with diverticulosis. These high amplitudes result in pulsion-diverticula so that a diverticulosis is the consequence.

SAMENVATTING

In dit proefschrift worden de resultaten beschreven van een radiodiagnostisch - en een motiliteitsonderzoek van het sigmoid bij drie veel voorkomende ziektebeelden: het pijnlijk Irritable Bowel Syndrome (IBS) en de diverticulosis zonder en met een zelfde pijn als bij het IBS. Het onderzoek was speciaal gericht op het symptoom van de pijn in de linker onderbuik en haar correlaties met sigmoid contracties en drukgolven. De bevindingen bij de patienten werden onderling, en met een controlegroep, vergeleken. Patienten met het IBS en een veranderd defaecatiepatroon (diarree en/of obstipatie) maar zonder pijn werden niet in het onderzoek betrokken.

Het doel van het onderzoek was om na te gaan of de verzameling en de onderlinge vergelijking van de gegevens zou kunnen leiden tot een verbetering van de diagnostische mogelijkheden van de radiodiagnost. Daarnaast bestond de hoop meer inzicht te krijgen zowel in de oorzaak van de pijn bij deze ziektebeelden als ook in hun eventuele onderlinge relaties.

Het literatuur onderzoek.

In hoofdstuk 1 worden de bevindingen uit de literatuur besproken.

Bij het onderzoek van patienten met een pijnlijk IBS is er geen positief diagnostisch criterium. De diagnose wordt "per exclusionem" gesteld. Pijn is een subjectieve belevenis. De arts wil een objectieve en te reproduceren waarneming. Wordt de pijn veroorzaakt door een abnormaal functionerend sigmoid ? Een herhaling van de eigen karakteristieke pijn van de patient tijdens het onderzoek is nodig. Er moet een onderzoek gedaan worden waarbij de karakteristieke pijn als ook het functioneren van het sigmoid tegelijkertijd worden geregistreerd zodat ze met elkaar gecorreleerd kunnen worden. Door drukmeting in het sigmoid kan een afwijkende functie worden vasgesteld. Met radiologische methoden kunnen sigmoid contracties zichtbaar gemaakt worden. Kan de diagnose pijnlijk IBS gesteld worden met behulp van een radiologisch colon onderzoek?

Uit paragraaf 1.1.5 blijkt dat krachtige contracties van de colon musculatuur hoge drukken kunnen veroorzaken. Hierdoor kunnen afferente ontladingen in specifieke nociceptoren of in mechanoreceptoren opgewekt worden. De reactie drempels van deze receptoren variëren. In geval van pijn geleiding uit het colon, bestaan de sensibele banen uit verbindingen tussen neuronen in de nervus splanchnicus, de tractus spinothalamicus en de connecties tussen de thalamus en de somatosensibele cortex in de gyrus postcentralis. Neurofysiologisch werden aanwijzingen gevonden dat motivatie en emotie de pijn ervaring beinvloeden. Het nociceptief systeem is plastisch: chronische pijn wordt op den duur minder gevoeld.

Diverticuli worden beschouwd als herniaties van de mucosa door zwakke plaatsen in de sigmoid wand (paragraaf1.2). Er zijn geen aanwijzingen gevonden voor een hypertrofie of een hyperplasie van de longitudinale spierlaag in het sigmoid. De vastgestelde verdikking wordt veroorzaakt door een gecontraheerde toestand, in stand gehouden door afzetting van elastine. Inter-

mitterende verwijding van het sigmoid, zoals veroorzaakt door weinig ontlasting die het gevolg is van een vezelarme voeding, zou een verhoogde afzetting van elastine in gang kunnen zetten.

In paragraaf 1.3 wordt beschreven dat bij de motiliteit van het colon (ook wel genoemd de bewegingen van de colon wand) vier patronen kunnen worden onderscheiden: 1/ de basale tonus; 2/ de niet-propulsieve segmenterende contractie of segmentatie die de weerstand van de anaalwaarts gerichte stroom verhoogt; 3/ de propulsieve contractie en 4/ de retropulsieve contractie.

De motiliteit van het sigmoid wordt meestal alleen geregistreerd door intraluminale drukmeting. De combinatie hiervan met radiologische methoden, waardoor de bewegingen van de wand zichtbaar gemaakt kunnen worden, biedt echter de beste mogelijkheid om dit te doen.

De etiologie van de pijn bij het pijnlijk IBS wordt besproken in paragraaf 1.5. Er zou een verhoogde motiliteit van het sigmoid kunnen bestaan die veroorzaakt kan worden door een voedingspatroon waarbij vezelarme voeding wordt gebruikt. De correlatie tussen de pijn belevenis en de amplitudes van de golven bleek niet onderzocht. De etiologie van de diverticulosis wordt ook gezocht in een vezelarme voeding. Het is een deficientie ziekte genoemd.

In paragraaf 1.8 worden de differentiaal diagnose, de therapie en de prognose besproken. Een vezelrijk dieet, maar ook een placebo-dieet, verminderden de pijn bij patienten met een pijnlijk IBS. Er blijken weinig goede dubbel-blinde onderzoekingen gedaan te zijn. Bij patienten met een diverticulosis bleek een vezelrijke voeding de motiliteit te verminderen. Pijnlijk IBS is een chronische ziekte.

In paragraaf 1.9 worden de mogelijke verbanden tussen het pijnlijk IBS en de diverticulosis besproken. Beide kunnen een verhoogde motiliteit van het sigmoid laten zien. Het bestaan van één hypermotiele toestand wordt wel verondersteld.

Het motiliteitsonderzoek.

In hoofdstuk 2 wordt het doel van het onderzoek besproken. Eerst werd er een enkel en dubbel contrast colon inloop onderzoek gedaan om de patienten te selecteren. Vervolgens werd, na enkele weken, een drukmetingsonderzoek gedaan.

Er werden zes vragen gesteld: 1/ Is het mogelijk de correlatie pijn en contractie voor de tweede keer te reproduceren gedurende het drukmetingsonderzoek? Is het mogelijk een patient met een pijnlijk IBS te herkennen met een fysiologisch gericht colon inloop onderzoek? 2/ Wordt alle musculaire activiteit van het sigmoid, zoals deze waargenomen kan worden door bewegingen van de wand, uitgedrukt in een verandering van de intraluminale druk? 3/ Zijn er speciale drukveranderingen tijdens de karakteristieke pijn belevenissen? 4/ Kunnen wij meer te weten komen over de oorzaak van de pijn? 5/ Zijn pijnlijk IBS en diverticulosis onderdeel van één hypermotiele toestand en speelt de eerste afwijking een rol in de etiologie van de laatste? 6/ Is het nodig zowel de oppervlakte onder de curve als de motiliteitsindex te bepalen bij de beoordeling van de resultaten van de drukmeting?

In hoofdstuk 3 worden de patienten en de methoden besproken. Er werden vier groepen onderzocht: een controle groep, een groep met een pijnlijk IBS, een groep met een diverticulosis en een groep met een pijnlijk IBS met diverticulosis.

De groepen worden gedefinieerd in paragraaf 3.1:

A/ Een controle persoon mocht vage pijn in de bovenbuik hebben. Er mocht bloed in de ontlasting zijn. De bloedchemie echter moest normaal zijn. Het radiodiagnostisch colon onderzoek en de sigmoidoscopie mochten geen anatomische of fysiologische afwijkingen tonen.

B/ Een patient met een pijnlijk IBS had een discontinue pijn, langer dan 3 maanden bestaand, in de linker onderbuik. De correlatie tussen de pijn (de karakteristieke pijn van de patient) en een sigmoid contractie moest tijdens het radiodiagnostisch colon onderzoek vastgesteld zijn. Er was geen bloed in de ontlasting. Eventueel was er een intraindividueel wisselend defecatie-patroon of trad een verergering op van de pijn in correlatie met een maaltijd of een defecatie. De bloedchemie was normaal. Een colon inloop onderzoek en een sigmoidoscopie toonden geen anatomische afwijkingen.

C/ Een patient met een diverticulosis had een diverticulosis van het sigmoid al of niet met vage pijn.

D/ Een patient met een pijnlijk IBS met diverticulosis toonde een reproductie van de pijn, gecorreleerd aan een sigmoid-contractie, tijdens het colon inloop onderzoek. Tevens waren er diverticuli in het sigmoid.

De patienten werden geselecteerd op basis van een anamnese en een colon inloop onderzoek uitgevoerd zowel met enkelvoudig als met dubbelcontrast. Bij het radiologisch onderzoek van het colon zou een patient met een pijnlijk IBS herkend kunnen worden aan een segmentatie van het sigmoid. Het was voor het doel van het onderzoek obligaat dat de pijn van de patienten met een pijnlijk IBS of een pijnlijk IBS met diverticulosis reproduceerbaar bleek tijdens het radiologisch colon onderzoek. De waargenomen contractie en relaxatie van het sigmoid moesten gecorreleerd zijn aan de karakteristieke pijn belevenis van de patient.

De aldus geselecteerde patienten ondergingen een motiliteits onderzoek door middel van drukmeting ten einde na te gaan of de correlatie tussen de pijn belevenis en de sigmoidcontractie eveneens reproduceerbaar was tijdens dit tweede onderzoek. Ook het karakter van de drukgolven, die simultaan met de pijn optraden, werd bestudeerd. De variabelen, gevonden bij de vier groepen, werden onderling vergeleken.

De methoden van het drukmetingsonderzoek worden besproken in paragraaf 3.2. 1/ Er werd een voorbereiding gegeven zodat het colon schoon was. 2/ Het aantal patienten per groep was 15 in de controle, pijnlijk IBS en diverticulosis groep en acht in de pijnlijk IBS met diverticulosis groep. 3/ Er werd gemeten in het sigmoid op 30 cm van de anus. 4/ Er werd een microtransducercatheter gebruikt. 5/ De catheter werd via het biopsie kanaal van een flexibele sigmoidoscoop ingevoerd. 6/ Een mm uitslag van de schrijver op het registratie papier was meestal gelijk aan 1 mm Hg. 7/ Radiodiagnostische methoden werden toegepast. De papier snelheid was vijf mm/sec. 8/ Registratie vond plaats gedurende een nuchtere periode, een periode direct na de maaltijd en een periode direct na toediening van glucagon. Elke

periode duurde 30 min. 9/ De correlatie pijn-ervaring en drukgolf werd bestudeerd tijdens het drukmetingsonderzoek.

De resultaten worden in hoofdstuk 4 vermeld. Alleen de statistisch significante uitkomsten worden hier genoemd. 1/ De incidentie van de golven per minuut was vrijwel vergelijkbaar tussen de vier groepen. 2/ De amplitudes waren hoger bij patienten met een diverticulosis en met een pijnlijk IBS met diverticulosis in vergelijking met de controles en eveneens hoger bij patienten met een pijnlijk IBS en diverticulosis in vergelijking met alleen diverticulosis. De amplitudes van de golven die met pijn gepaard gingen waren ook hoger in vergelijking met de golven die niet met pijn gepaard gingen bij de patienten met het pijnlijk IBS en met het pijnlijk IBS met diverticulosis. 3/ De duur van de golven, in seconden, was langer bij de patienten in vergelijking met de controles. 4/ De motiliteitsindex, zijnde de som van de producten van de amplitude en de duur van elke golf, per tijdsperiode en 5/ de oppervlakte onder de curve, bepaald door het tellen van de vierkantjes onder de curve, werden bij de vier groepen berekend en onderling vergeleken. Beide stegen in deze volgorde: controlepersonen, patienten met een pijnlijk IBS, patienten met diverticulosis en patienten met een pijnlijk IBS met diverticulosis. De gemiddelde motiliteitsindex en de gemiddelde oppervlakte onder de curve waren groter bij sommige patienten met pijnlijke golven uit de pijnlijk IBS groep en de pijnlijk IBS met diverticulosis groep.

In hoofdstuk 5 volgt de bespreking. De conclusies zijn in hoofdstuk 6 vermeld. De antwoorden op de in hoofdstuk 2 gestelde vragen zijn:

1/ Bij 90% van de patienten werden de correlatie pijn en contractie (voor het eerst gezien tijdens het colon inloop onderzoek) gereproduceerd tijdens het drukmetingsonderzoek. De patient moet worden onderzocht in een periode met pijnklachten. Een patient met een pijnlijk IBS kan herkend worden met het radiodiagnostisch colon onderzoek, mits de radiodiagnost ontvankelijk is voor de pijn klachten van de patient en kennis heeft van de pathofysiologie van het sigmoid.

Het positieve diagnostische criterium waarnaar, in dit onderzoek, is gezocht, is, bij een patient met een pijnlijk IBS, een segmenterende sigmoid contractie gecorreleerd aan de karakteristieke pijn ervaring van de patient.

2/ Niet alle musculaire activiteit van het sigmoid bleek een verandering in de intraluminale druk teweeg te brengen. Zonder deze activiteit werden er echter geen drukgolven gezien. Het is, uit dit onderzoek, gebleken dat bij drukmeting de weerstand tegen de voortgang van de darminhoud wordt gemeten. Drukmeting, beschouwd als een parameter van de motiliteit, is meting van de weerstand.

3/ De beleefde pijnklachten correleerden met golven met hoge amplitudes.

4/ De pijn lijkt te worden veroorzaakt door drukgolven met een zeer hoge amplitude. De amplitudes waargenomen bij pijnloze contracties verschillen niet van de amplitudes bij controle personen. Er bestaat een stoornis in de functie van het sigmoid bij patienten met een pijnlijk IBS en een pijnlijk IBS met

diverticulosis. Het gevolg is een segmenterend contraherend sigmoid, gepaard gaand met hoge drukken en pijn: een "colon koliek". De reproduceerbare waarneming van de correlatie tussen de pijn belevenis en de contractie zou het "pijnlijk IBS symptoom" genoemd kunnen worden. Het is noodzakelijk te zoeken naar methoden om dit IBS symptoom uit te lokken.

Patienten met onverklaarde, discontinue buikpijn behoren een fysiologisch gericht radiologisch colon onderzoek te ondergaan.

5/ De resultaten steunen de hypothese dat het pijnlijk IBS en de diverticulosis deel zijn van één hypermotiliteitstoestand. Pijnlijk IBS kan één van de etiologische factoren van diverticulosis zijn. De hoge amplitudes, die vooral optreden tijdens de pijnlijke golven bij de groepen met een pijnlijk IBS en een pijnlijk IBS met diverticulosis, kunnen de vorming van diverticuli veroorzaken. De amplitudes in de pijnlijk IBS met diverticulosis groep zijn hoger dan de amplitudes in de groep met alleen een diverticulosis. De amplitudes lijken lager te worden wanneer de diverticuli eenmaal zijn ontstaan. De vraag doet zich voor of de patienten met een pijnlijk IBS met diverticulosis de overgang vormen tussen de patienten met alleen een pijnlijk IBS en de patienten met alleen een diverticulosis.

6/ De significante resultaten van een drukmetingsonderzoek kunnen verkregen worden door de berekening van de motiliteitsindex alleen. Daar de amplitude belangrijk blijkt voor het onderzoek naar de oorzaak van de pijn, moet deze variabele zeker gemeten worden. Het berekenen van de motiliteitsindex verdient de voorkeur boven het bepalen van de oppervlakte onder de curve.

De volgende hypothesen kunnen geformuleerd worden: Een vezelarm voedingspatroon kan leiden tot verhoogde amplitudes van de motorische golven in het sigmoid. Deze hoge druk golven leiden tot pijn lijden, zoals bij dit onderzoek werd vastgesteld bij patienten met een pijnlijk IBS en met een pijnlijk IBS met diverticulosis. De hoge druk golven resulteren in pulsiediverticuli leidend tot een diverticulosis.

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APPENDIX

Table 16 Incidence: number of waves per min in the four groups, in the three periods and overall.

A/ Control

pat.	fasting	postprandial	postglucagon	overall
01	0.77	0.80	1.37	0.93
02	0	0.37	0.20	0.19
03	0.43	2.27	0.87	1.19
04	0.13	0.40	0.47	0.33
05	0.33	1.90	0.77	1.00
06	1.13	2.23	1.53	1.63
07	0.10	0.10	0.53	0.24
08	0.20	1.03	1.07	0.77
09	4.10	0.43	2.47	2.33
10	0	0.40	0.50	0.30
11	1.77	0.43	0.40	0.87
12	0.20	1.20	0.83	0.74
13	1.30	2.13	0.90	1.44
14	0.57	0.70	0.80	0.69
15	0.33	0.67	0.50	0.50
MEAN	0.76±0.27	1.00±0.20	0.88±0.15	0.88±0.15

B/ Painful IBS

pat.	fasting	postprandial	postglucagon	overall	painful wave
16	0.20	0.47	0.27	0.31	0.02
17	0.90	0.50	1.37	0.92	0.04
18	1.40	0.90	1.07	1.12	0
19	0.90	1.13	1.23	1.09	0.04
20	0.17	0.50	1.17	0.61	0.22
21	0.40	0.63	1.47	0.83	0.02
22	0.20	0.67	1.13	0.67	0.13
23	0.97	0.67	0.73	0.79	0.01
24	1.50	0.57	1.43	1.17	0.01
25	0.50	1.60	0.50	0.87	0.14
26	2.53	1.37	1.70	1.87	0.09
27	2.03	0.93	0.97	1.31	0.01
28	0.23	1.83	1.27	1.11	0.12
29	0.90	2.07	1.47	1.48	0.04
30	0.90	0.73	0.53	0.72	0.06
MEAN	0.92±0.18	0.97±0.13	1.09±0.11	0.99±0.10	0.06±0.01

Table 16 Incidence (continued)

C/ Diverticulosis

pat.	fasting	postprandial	postglucagon	overall
31	0.87	0.57	0.63	0.69
32	0.23	1.87	1.13	1.08
33	1.73	0.60	0.50	0.94
34	0.70	1.93	1.53	1.39
35	0.73	1.13	0.97	0.94
36	1.03	1.13	1.27	1.14
37	0.17	1.37	1.63	1.06
38	1.20	1.67	0.70	1.19
39	1.23	1.47	1.07	1.26
40	1.30	0.57	2.13	1.33
41	0.13	0.73	1.40	0.76
42	2.27	1.43	1.10	1.60
43	1.40	1.27	0.87	1.18
44	0.87	0.83	0.67	0.79
45	2.40	1.60	0.70	1.60
MEAN	1.08±0.18	1.21±0.12	1.09±0.12	1.13±0.07

D/ Painful IBS with diverticulosis

pat.	fasting	postprandial	postglucagon	overall	painful wave
46	1.47	0.90	1.47	1.28	0.03
47	2.07	1.13	0.90	1.37	0.18
48	1.40	0.87	1.10	1.12	0.03
49	0.63	0.90	0.80	0.78	0.20
50	0.87	0.83	0.93	0.88	0.04
51	1.10	1.20	1.57	1.24	0.18
52	0.93	1.50	1.54	1.32	0
53	1.40	1.70	1.50	1.43	0.07
MEAN	1.23±0.16	1.13±0.11	1.23±0.12	1.18±0.08	0.10±0.03

Table 17 Mean amplitude of the waves in mm Hg(±SEM) in the four groups, in the three periods and overall.

A/ Control

pat.	fasting	postprandial	postglucagon	overall
01	14.0±1.6	12.0± 1.2	15.3±1.9	14.0±1.0
02	0	5.7± 0.7	5.3±0.7	5.6±0.5
03	5.3±0.7	21.2± 2.0	9.2±1.3	16.4±1.5
04	13.6±6.1	19.0± 3.5	7.9±1.3	13.1±1.9
05	18.2±4.2	11.5± 1.3	5.4±0.5	10.7±1.0
06	9.9±0.9	11.3± 0.7	18.9±1.9	13.3±0.8
07	5.0±1.5	3.7± 0.7	8.3±1.1	7.2±0.9
08	7.5±2.7	7.5± 0.6	14.2±1.4	10.6±0.8
09	9.7±0.8	8.9± 1.2	13.8±1.4	11.1±0.7
10	0	9.3± 1.6	6.3±0.9	7.6±0.9
11	5.5±0.4	3.8± 0.2	3.8±0.1	4.9±0.3
12	4.3±0.8	4.5± 0.7	8.8±1.7	6.0±0.7
13	7.6±0.6	6.7± 0.4	10.4±0.9	7.7±0.3
14	8.9±2.5	18.0± 3.0	7.3±1.3	11.4±1.4
15	4.7±0.5	4.9± 0.4	9.1±1.9	6.2±0.7
MEAN	7.6±1.3	9.9± 1.5	9.6±1.1	9.7±0.9

B/ Painful IBS

pat.	fasting	postprandial	postglucagon	overall	painful wave
16	3.3±0.2	3.9± 0.3	5.2±0.8	4.1±0.3	7.3± 0.3
17	6.9±2.4	9.5± 1.5	14.8±1.5	11.3±1.2	31.5± 3.3
18	6.3±0.2	9.4± 1.3	13.1±0.5	9.3±0.7	0
19	16.0±2.2	27.9± 2.8	24.4±1.4	23.2±1.4	41.3± 7.7
20	8.4±3.2	8.5± 1.9	11.5±1.2	10.4±0.9	14.2± 1.6
21	4.2±0.9	8.6± 1.6	16.6±1.5	12.6±1.1	34.5±12.5
22	10.8±3.2	24.2± 1.9	21.0±2.4	21.1±1.6	29.1± 2.9
23	4.7±0.6	5.7± 0.8	6.9±1.0	5.7±0.5	13.0
24	8.4±0.9	14.9± 2.9	12.7±1.4	11.2±0.9	29.0
25	12.2±3.0	31.2± 3.7	7.5±1.0	23.1±2.7	59.3± 7.4
26	9.8±0.7	12.5± 0.9	10.7±0.8	10.7±0.5	21.8± 2.5
27	23.1±2.0	29.1± 4.9	23.6±4.5	24.7±1.9	57.0
28	2.9±1.2	14.6± 1.0	12.1±1.6	13.2±0.9	24.6± 2.7
29	19.3±1.8	16.6± 1.4	25.4±3.2	20.1±1.3	38.5± 1.9
30	10.2±1.4	14.3± 1.4	11.6±1.6	11.9±0.9	21.7± 3.0
MEAN	9.8±1.5	15.3± 2.3	14.5±1.7	14.2±1.7	28.2± 4.3

Table 17 Mean amplitude (continued)

C/ Diverticulosis

pat.	fasting	postprandial	postglucagon	overall
31	35.2±9.0	54.8±14.0	30.7±7.7	39.2±5.9
32	14.4±1.4	10.4± 1.1	14.1±1.7	12.0±0.9
33	14.6±1.5	13.9± 2.9	13.7±3.0	14.3±1.2
34	10.0±2.1	10.1± 0.8	7.8±0.8	9.2±0.6
35	8.5±0.9	11.4± 1.4	35.7±5.1	19.0±2.3
36	15.6±2.5	23.8± 3.2	22.4±3.6	20.6±2.3
37	25.8±2.5	15.8± 2.2	20.9±1.8	18.9±1.4
38	23.6±1.7	35.8± 1.9	29.6±2.5	30.5±1.3
39	8.3±1.3	16.5± 2.1	21.5±1.4	15.2±1.1
40	9.8±2.2	10.6± 1.7	19.3±2.1	15.0±1.4
41	5.8±1.5	21.4± 2.5	26.3±3.1	23.5±2.1
42	16.2±0.9	18.9± 2.0	20.7±2.5	18.0±0.9
43	17.9±2.4	15.0± 2.5	9.8±1.7	14.9±1.4
44	8.4±1.1	35.4± 5.5	37.2±5.2	26.0±2.9
45	7.6±0.8	21.6± 2.7	14.0±2.4	13.2±1.2
MEAN	14.8±2.1	21.0± 3.2	21.6±2.3	19.3±2.0

D/ Painful IBS with diverticulosis

pat.	fasting	postprandial	postglucagon	overall	painful wave
46	15.3±1.8	15.8±3.0	23.8± 2.7	18.7±1.5	52.3± 1.8
47	21.4±3.4	35.2±5.3	15.4± 2.5	24.1±2.4	55.4± 7.9
48	25.5±4.6	43.3±5.3	18.7± 1.5	27.9±2.6	71.7± 2.6
49	27.2±4.5	20.0±3.9	45.3± 6.9	30.6±3.3	55.6± 5.3
50	42.3±5.0	49.9±4.8	79.0±14.6	57.7±5.9	33.5± 5.3
51	27.5±4.7	48.1±5.6	40.3± 5.3	39.3±3.2	93.6± 5.3
52	32.4±3.3	47.2±4.3	48.7± 6.0	43.1±5.5	0
53	25.5±2.3	36.4±3.4	37.1± 4.5	32.8±3.6	66.7± 5.1
MEAN	27.1±2.8	37.0±4.6	38.5± 7.2	34.3±4.3	61.3± 7.1

Table 18 Mean duration of the waves in s (±SEM) in the four groups, in the three periods and overall.

A/ Control

pat.	fasting	postprandial	postglucagon	overall
01	11.0± 1.1	13.1± 1.2	14.6± 1.2	13.3±0.7
02	0	10.5± 0.9	13.5± 2.3	11.6±1.0
03	11.8± 1.5	16.7± 0.7	11.4± 1.2	14.5±0.6
04	10.9± 1.4	28.7± 6.8	27.0± 5.6	22.6±3.0
05	25.9± 2.2	13.8± 0.9	7.8± 0.6	13.6±0.8
06	13.8± 1.1	12.4± 0.9	14.9± 0.9	13.5±0.6
07	5.2± 1.2	28.2± 9.1	21.9± 5.8	20.7±4.5
08	13.0± 4.1	13.6± 1.5	12.7± 1.4	13.1±1.0
09	9.8± 0.6	76.2±32.4	10.0± 0.8	14.0±2.3
10	0	21.3± 2.3	20.6± 2.7	20.9±1.8
11	9.4± 0.9	12.3± 2.0	18.8± 3.1	11.4±0.9
12	21.2± 2.8	20.1± 1.3	18.7± 1.8	19.6±1.0
13	24.7± 1.8	18.3± 0.9	13.8± 0.8	19.3±0.8
14	15.7± 2.6	19.1± 1.8	10.2± 1.8	14.7±1.3
15	14.3± 2.1	12.9± 1.2	12.6± 1.5	13.1±0.9
MEAN	12.5± 2.0	21.1± 4.2	15.2± 1.3	15.7±1.0

B/ Painful IBS

pat.	fasting	postprandial	postglucagon	overall	painful wave
16	10.1± 2.3	17.1± 1.6	18.4± 3.1	16.0±1.4	13.5±1.5
17	22.9± 7.0	16.2± 1.3	16.7± 1.4	18.6±2.4	16.8±1.3
18	11.1± 0.9	17.6± 3.4	17.9± 2.4	15.0±1.3	0
19	20.2± 1.9	24.3± 2.5	25.2± 1.8	23.5±1.2	20.2±1.3
20	75.0±30.8	15.0± 5.2	31.9± 2.1	36.9±3.6	33.8±2.8
21	12.1± 2.6	19.2± 1.7	25.9± 1.3	22.0±1.1	30.2±9.8
22	18.5± 7.0	30.5± 2.5	34.1± 2.5	31.3±1.9	38.3±3.8
23	8.2± 1.3	22.1± 3.0	31.3± 4.9	17.8±2.1	28.0
24	8.7± 0.7	80.0±33.6	28.2±11.5	28.2±7.5	88.4
25	36.9± 7.4	19.0± 1.8	21.8± 2.6	23.0±2.0	25.5±2.9
26	18.1± 1.9	25.6± 1.9	27.9± 1.4	22.9±1.1	25.8±4.2
27	25.1± 1.9	17.7± 1.3	17.3± 1.3	21.4±1.1	28.0
28	24.5± 7.4	21.1± 1.0	20.5± 2.0	21.1±1.1	23.8±2.9
29	29.6± 2.5	17.9± 0.9	17.7± 1.0	20.2±0.8	19.1±3.7
30	33.2± 3.9	25.9± 2.3	28.3±10.7	30.2±3.1	31.0±6.0
MEAN	23.6± 4.3	24.6± 4.1	24.2± 1.5	23.2±1.6	28.2±4.9

Table 18 Mean duration (continued)

C/ Diverticulosis

pat.	fasting	postprandial	postglucagon	overall
31	49.4± 7.4	25.4± 1.9	12.3± 1.3	31.5±3.8
32	63.6±26.8	16.6± 1.6	25.1± 4.0	23.0±2.7
33	17.4± 1.7	21.1± 3.2	24.1± 7.3	19.4±1.8
34	18.6± 2.6	14.8± 1.1	18.4± 1.9	16.8±1.0
35	17.2± 1.0	23.6± 1.4	28.5± 2.2	23.6±1.1
36	28.0± 2.8	18.3± 1.4	11.8± 3.3	19.0±1.3
37	34.9± 7.1	23.4± 1.8	25.7± 2.3	25.2±1.5
38	46.3± 3.6	37.1± 2.4	34.4± 2.8	39.7±1.8
39	14.0± 1.8	23.6± 2.1	41.4± 4.1	25.5±1.8
40	22.6± 1.7	16.9± 2.7	15.9± 2.7	18.2±1.0
41	34.8± 5.2	21.2± 1.9	25.2± 1.5	24.5±1.2
42	26.7± 1.3	25.6± 2.0	28.7± 2.3	26.8±1.0
43	28.7± 1.7	15.2± 0.8	19.1± 1.5	21.5±1.0
44	20.6± 1.9	28.3±10.8	25.6± 2.3	24.7±3.9
45	8.9± 0.5	9.6± 0.7	17.6± 2.3	10.5±0.5
MEAN	28.8± 3.8	21.4± 1.7	23.6± 2.1	23.3±1.7

D/ Painful IBS with diverticulosis

pat.	fasting	postprandial	postglucagon	overall	painful wave
46	18.9±2.5	13.4±1.5	24.9± 3.9	19.9±1.9	76.4±40.5
47	16.9±1.7	14.8±1.1	6.5± 1.7	14.0±1.0	20.0± 4.8
48	17.7±2.6	20.8±2.5	24.2± 2.1	20.6±1.4	31.9± 8.8
49	24.1±1.7	17.9±1.8	30.9± 2.8	24.0±1.4	29.2± 1.9
50	35.7±5.1	26.1±1.9	16.5± 1.4	25.8±2.0	4.2± 2.5
51	12.2±0.9	25.3±2.1	20.2± 1.4	19.7±1.0	25.7± 3.2
52	28.3±2.7	26.8±1.5	18.8± 2.4	25.4±1.3	0
53	27.4±0.4	14.7±1.2	35.9±10.3	26.1±2.7	126.2±68.0
MEAN	22.7±2.7	20.0±2.0	22.2± 3.2	21.9±1.5	44.8±15.9

Table 19 Total area under the curve in square mm (x 1000) in the four groups, in the three periods and overall.

A/ Control

pat.	fasting	postprandial	postglucagon	overall
01	7.9	8.6	17.8	34.4
02	0	1.9	1.2	3.1
03	1.8	48.6	5.9	56.4
04	1.4	9.6	5.2	16.2
05	6.5	21.5	1.9	29.8
06	9.4	22.8	26.5	58.7
07	0.3	0.8	7.3	8.3
08	2.0	9.8	15.5	27.3
09	37.6	53.3	25.9	116.7
10	0	5.4	5.0	10.4
11	6.2	1.6	2.2	10.0
12	1.2	6.9	7.0	15.1
13	19.0	19.1	9.3	47.4
14	4.3	12.1	4.6	20.9
15	1.6	3.2	3.6	8.4
MEAN	6.6±2.6	15.0±4.2	9.3±2.1	30.9±7.7

B/ Painful IBS

pat.	fasting	postprandial	postglucagon	overall	painful wave
16	0.4	2.1	1.6	4.1	0.4
17	11.0	4.1	17.7	32.8	4.0
18	7.0	9.9	18.2	35.1	0
19	16.2	43.1	42.6	102.0	8.6
20	6.0	8.2	24.7	38.9	17.4
21	1.5	6.2	32.2	39.9	2.8
22	2.8	24.5	56.7	83.9	24.4
23	3.0	5.6	9.1	17.7	0.6
24	8.0	84.2	54.0	146.2	3.1
25	13.7	59.8	5.3	78.8	37.7
26	26.3	24.2	31.5	82.0	7.6
27	84.9	24.0	21.7	130.6	3.2
28	2.5	33.0	19.3	54.8	11.3
29	27.4	38.4	34.2	100.0	5.4
30	18.2	13.3	8.5	40.0	6.1
MEAN	15.3±5.4	25.4±6.0	25.2±4.3	65.8±10.7	8.8±2.7

Table 19 The total area under the curve (continued)

C/ Diverticulosis

pat.	fasting	postprandial	postglucagon	overall
31	63.9	46.0	13.8	123.7
32	25.7	22.8	23.2	71.7
33	34.3	11.1	16.2	61.6
34	9.8	20.2	12.7	42.7
35	6.9	15.2	68.7	90.7
36	27.9	25.9	36.5	90.3
37	8.3	29.2	59.4	97.0
38	72.9	104.6	34.6	212.1
39	13.1	41.6	62.7	117.4
40	19.3	6.3	43.5	69.1
41	1.6	21.2	42.2	65.1
42	75.1	42.4	38.1	155.6
43	31.8	19.1	10.6	61.5
44	9.4	68.2	36.4	113.9
45	12.2	26.6	11.6	50.4
MEAN	27.5±6.3	33.3±6.5	34.0±5.0	94.9±11.6

D/ Painful IBS with diverticulosis

pat.	fasting	postprandial	postglucagon	overall	painful wave
46	34.1	19.0	100.4	153.5	33.9
47	60.8	38.8	6.2	105.8	39.0
48	50.3	46.4	35.0	131.6	13.7
49	25.5	20.5	54.1	100.1	47.1
50	71.2	52.7	71.7	195.7	4.6
51	20.9	68.4	60.8	150.0	59.2
52	42.2	66.1	57.9	166.2	0
53	46.3	66.4	128.0	240.7	79.2
MEAN	43.9±6.0	47.3±7.1	64.3±13.2	155.5±16.4	39.5±9.7

Table 20 The mean area under the curve in square mm (±SEM) in the four groups, in the three periods and overall.

A/ Control

pat.	fasting	postprandial	postglucagon	overall
01	345± 52	359± 49	435± 55	391± 32
02	0	175± 27	198± 50	183± 24
03	139± 19	715± 85	228± 42	527± 60
04	260± 150	801± 224	371± 71	541±103
05	647± 133	377± 58	81± 9	332± 43
06	275± 33	341± 38	575± 55	399± 27
07	83± 38	265± 77	454±171	378±127
08	341± 235	316± 47	484± 80	396± 47
09	305± 40	4100±2037	349± 46	559±140
10	0	453± 71	330± 85	384± 57
11	117± 13	121± 24	184± 37	128± 11
12	119± 38	192± 14	280± 41	226± 18
13	487± 36	298± 20	343± 32	364± 17
14	251± 20	576± 98	190± 60	338± 50
15	161± 27	159± 20	237± 65	186± 24
MEAN	235± 46	617± 254	316± 35	355± 34

B/ Painful IBS

pat.	fasting	postprandial	postglucagon	overall	painful wave
16	69± 17	149± 19	202± 38	147± 17	208± 8
17	407± 179	274± 71	431± 47	395± 64	995± 12
18	166± 13	366± 78	570±116	347± 46	0
19	601± 82	1268± 140	1152±121	1040± 75	2160±185
20	1207± 438	544± 150	705± 71	707± 74	871±113
21	125± 35	326± 61	731± 59	532± 48	1403± 23
22	466± 227	1225± 122	1666±208	1399±134	2031±353
23	103± 30	281± 49	412± 82	249± 35	630
24	177± 21	4950±3370	1257±847	1392±654	3080
25	911± 297	1247± 199	353± 54	1010±140	2902±443
26	346± 33	590± 51	617± 37	488± 24	956± 61
27	1391± 119	856± 127	749±129	1107± 80	3195
28	363± 106	599± 43	508± 76	548± 38	1031±141
29	1015± 78	619± 53	777± 89	752± 43	1345±111
30	673± 153	605± 78	529±115	615± 74	1013±196
MEAN	534± 109	927± 302	711± 99	715±102	1455±259

Table 20 Mean area under the curve (continued)

C/ Diverticulosis

pat.	festing	postprandial	postglucagon	overall
31	2456± 614	2555± 470	727±181	1995±346
32	3671±2343	406± 68	682±127	739±188
33	659± 99	618± 145	1081±463	725±106
34	469± 90	347± 50	276± 43	341± 32
35	313± 35	445± 42	2367±472	1067±190
36	911± 162	762± 100	960± 95	877± 78
37	1668± 303	713± 132	1212±190	1021±117
38	2025± 199	2092± 154	1647±138	1982±102
39	353± 71	946± 120	1958±163	1039± 91
40	495± 89	373± 65	680±108	576± 65
41	407± 36	964± 167	1006±130	957± 98
42	1105± 87	985± 124	1156±147	1080± 65
43	758± 80	503± 82	407± 58	580± 48
44	360± 48	2728±1586	1819±268	1605±569
45	169± 22	567± 95	484±108	360± 41
MEAN	1055± 256	1000± 205	1097±158	996±133

D/ Painful IBS with diverticulosis

pat.	festing	postprandial	postglucagon	overall	painful wave
46	775±158	702±186	2283± 667	1334±273	11305±7597
47	980±206	1142±194	228± 46	860±120	2437± 629
48	1198±298	1786±240	1061± 112	1305±145	4580±2689
49	1341±245	760±173	2256± 376	1430±175	2618± 295
50	2740±480	2110±279	2561± 530	2477±259	1155± 300
51	632±106	1899±277	1293± 188	1293±126	3698±1562
52	1563±526	1469±127	1259± 287	1402±157	0
53	1102±208	1151± 81	2843±1081	1793±273	13196±7013
MEAN	1291±232	1377±186	1723± 317	1487±168	5570±1783

Table 21 Total motility index: in mm Hg.s (x 1000) in the four groups, in the three periods and overall.

A/ Control

pat.	fasting	postprandial	postglucagon	overall
01	3.9	4.0	10.1	18.0
02	0	0.7	0.5	1.2
03	0.8	26.4	3.0	30.2
04	0.7	7.0	3.1	10.8
05	4.5	10.5	1.0	16.1
06	4.3	10.1	13.3	27.7
07	0.1	0.3	3.3	3.7
08	0.9	3.2	6.0	10.1
09	17.4	13.7	12.6	43.7
10	0	2.4	2.2	4.7
11	2.9	0.7	0.9	4.4
12	0.5	3.3	3.7	7.6
13	7.7	7.9	3.9	19.4
14	3.7	8.3	2.9	14.9
15	0.7	1.3	1.9	3.8
MEAN	3.2±1.2	6.7±1.8	4.6±1.1	14.4±3.1

B/ Painful IBS

pat.	fasting	postprandial	postglucagon	overall	painful wave
16	0.2	1.0	0.7	1.9	0.2
17	5.3	2.5	10.9	18.7	2.1
18	3.1	5.1	8.5	16.7	0
19	9.2	23.2	23.8	56.2	3.3
20	2.3	6.3	13.2	21.8	10.5
21	0.7	3.6	18.6	22.9	1.8
22	1.9	15.3	26.0	43.2	13.5
23	1.6	2.8	5.9	10.2	0.6
24	3.8	40.4	20.0	64.2	2.6
25	6.9	31.6	2.4	40.9	19.9
26	13.8	13.0	15.1	41.9	4.0
27	34.8	16.5	13.2	64.5	1.6
28	1.2	17.6	11.1	29.9	6.5
29	14.6	18.9	21.5	55.0	3.1
30	9.7	8.8	5.1	23.6	4.4
MEAN	7.3±2.3	13.8±3.0	13.1±2.0	34.1±5.1	4.9±1.4

Table 21 Total motility index (continued)

C/ Diverticulosis

pat.	fasting	postprandial	postglucagon	overall
31	68.7	25.2	9.4	103.4
32	6.6	11.7	12.2	30.6
33	18.7	7.2	8.0	33.9
34	4.1	11.2	8.3	23.6
35	3.3	8.5	33.8	45.6
36	9.8	16.6	20.3	46.7
37	4.7	17.0	32.1	53.7
38	40.8	69.0	21.5	131.4
39	5.1	17.6	27.4	50.1
40	9.3	3.4	26.1	38.8
41	0.7	11.4	28.5	40.6
42	31.2	24.3	22.2	77.6
43	21.1	9.6	5.4	36.1
44	4.5	31.5	21.5	57.5
45	5.5	12.4	6.1	24.0
MEAN	15.6±4.8	18.4±4.1	18.9±2.5	52.9±7.8

D/ Painful IBS with diverticulosis

pat.	fasting	postprandial	postglucagon	overall	painful wave
46	17.1	8.4	35.3	60.7	12.3
47	30.3	23.1	3.6	57.0	20.7
48	28.0	25.8	15.1	68.9	7.8
49	13.8	11.7	41.0	66.4	30.0
50	40.5	33.6	45.8	119.9	2.6
51	11.5	48.1	44.5	104.1	43.0
52	24.7	53.9	41.9	120.5	0
53	29.8	26.6	60.6	117.0	34.5
MEAN	24.5±3.5	28.9±5.6	36.0±6.4	89.3±10.1	21.6±5.6

Table 22 Mean motility index in mm Hg.s(±SEM) in the four groups, in the three periods and overall.

A/ Control

pat.	fasting	postprandial	postglucagon	overall
01	17± 3	169± 2	246± 35	205± 20
02	0	62± 11	78± 20	68± 10
03	59± 8	388± 52	115± 20	282± 36
04	175± 89	582± 149	223± 53	360± 72
05	467±105	184± 29	44± 7	179± 25
06	128± 16	150± 18	289± 33	187± 15
07	28± 11	93± 20	206± 72	166± 54
08	148±105	104± 15	188± 29	147± 18
09	142± 21	1050± 549	170± 25	208± 39
10	0	203± 42	151± 42	174± 30
11	54± 7	51± 11	72± 13	56± 5
12	89± 14	93± 9	150± 25	114± 11
13	197± 24	123± 9	144± 14	150± 9
14	218±105	396± 85	120± 43	240± 46
15	66± 13	64± 8	127± 39	85± 14
MEAN	129± 30	247± 69	155± 17	175± 21

B/ Painful IBS

pat.	fasting	postprandial	postglucagon	overall	painful wave
16	34± 8	70± 11	92± 17	69± 8	98± 14
17	197± 88	168± 38	266± 39	226± 35	519± 44
18	74± 7	88± 48	264± 54	165± 23	0
19	305± 52	684± 88	642± 66	574± 44	822±142
20	575±225	422± 158	377± 48	407± 56	525± 87
21	56± 22	189± 48	422± 41	305± 32	919± 39
22	308±212	766± 101	765±123	720± 81	1126±172
23	54± 17	139± 28	268± 79	144± 28	630
24	84± 12	2378±1534	464±214	611±269	2564
25	460±135	658± 105	160± 22	524± 73	1528±249
26	181± 20	318± 31	296± 24	249± 15	500± 58
27	570± 54	590± 115	455± 95	546± 45	1596
28	175± 49	320± 28	291± 52	299± 25	592±110
29	19± 2	305± 30	488± 78	413± 32	770±148
30	360± 66	399± 74	319± 78	363± 41	733±229
MEAN	230± 49	506± 145	371± 45	374± 49	861±166

Table 22 Mean motility index (continued)

C/ Diverticulosis

pat.	fasting	postprandial	postglucagon	overall
31	2643±965	1483± 411	496±218	1667±436
32	949±391	208± 41	360± 62	315± 46
33	359± 57	401± 122	533±234	399± 59
34	194± 42	193± 34	180± 35	189± 21
35	152± 20	249± 27	1166±237	536± 95
36	316± 90	487± 77	534± 95	453± 57
37	938±229	414± 84	655± 98	566± 65
38	1134±145	1381± 123	1024±127	1228± 80
39	137± 33	401± 56	858± 86	444± 43
40	238± 50	201± 44	408± 83	323± 48
41	181± 26	517± 95	679±102	597± 71
42	459± 48	565± 89	671±108	539± 43
43	503± 70	253± 48	207± 49	341± 37
44	173± 29	1261± 584	1075±179	810±217
45	76± 12	264± 47	290± 83	173± 22
MEAN	563±172	552± 115	609± 80	572±103

D/ Painful IBS with diverticulosis

pat.	fasting	postprandial	postglucagon	overall	painful wave
46	389± 99	309± 90	802±224	528± 97	4111±2272
47	488±116	679±130	134± 41	463± 71	1291± 373
48	666±161	994±177	456± 50	682± 84	2592±1333
49	726±135	432±105	1707±324	949±139	1667± 233
50	1559±276	1342±169	1637±346	1518±160	638± 169
51	385± 78	1373±242	947±156	933±107	2689± 357
52	880±162	1198±172	908±246	1093±187	0
53	710±124	521± 26	1346±505	861±125	5753±3387
MEAN	725±134	856±150	992±195	878±119	2677± 666

Table 23 Mean amplitude in mm Hg.(±SEM) of the painless and painful waves apart. (N = number of the waves). Student's t test; NS = not significant; * = p<0.05; ** = p<0.01; *** = p<0.001.

Painful IBS

pat.	painless waves	N	painful waves	N	stat. analysis
16	3.9±0.3	26	7.3± 0.3	2	**
17	10.3±1.1	79	31.5± 3.3	4	**
18	9.3±0.7	101	0	0	
19	13.0±1.4	94	41.3± 7.7	4	*
20	8.2±1.0	35	14.2± 1.6	20	**
21	12.0±1.1	73	34.5±12.5	2	NS
22	19.0±1.7	48	29.1± 2.9	12	*
23	5.6±0.5	70	13.0	1	
24	11.0±0.9	104	29.0	1	
25	15.8±2.5	65	59.3± 7.4	13	***
26	10.2±0.4	160	21.8± 2.5	8	**
27	24.4±1.9	117	57.0	1	
28	11.7±0.8	89	24.6± 2.7	11	**
29	19.5±1.2	129	38.5± 1.9	4	***
30	10.9±0.8	59	21.7± 3.0	6	*
MEAN	12.3±1.4		28.2± 4.3		***

Painful IBS with diverticulosis (8 pat.)

pat.	painless waves	N	painful waves	N	stat. analysis
46	17.8±1.4	112	52.3± 1.8	3	***
47	19.4±2.3	107	55.4± 7.9	16	**
48	26.3±2.3	98	71.7±17.2	3	NS
49	22.0±3.2	52	55.6± 5.3	18	***
50	59.0±5.9	75	33.5± 5.3	4	NS
51	30.3±3.1	100	93.6± 5.3	16	***
52	40.8±1.3	108	0		
53	29.6±0.6	123	66.7± 5.1	6	***
MEAN	30.7±4.8		61.3± 7.1		***

Table 24 Mean duration in s (±SEM): overall and painful waves apart. Student's t test; NS = not significant; * = p<0.05; ** = p<0.01 *** = p< 0.001.

Painful IBS

pat.	overall	painful waves	stat.analysis
16	16.0±1.4	13.5± 1.5	NS
17	18.6±2.4	16.8± 1.3	NS
18	15.0±1.3	0	
19	23.5±1.2	20.2± 1.3	NS
20	36.9±3.6	33.8± 2.8	NS
21	22.0±1.1	30.2± 9.8	NS
22	31.3±1.9	38.3± 3.8	NS
23	17.8±2.1	28.0	
24	28.2±7.5	88.4	
25	23.0±2.0	25.5± 2.9	NS
26	22.9±1.1	25.8± 4.2	NS
27	21.4±1.1	28.0	
28	20.2±0.8	23.8± 2.9	NS
29	20.2±0.8	19.9± 3.7	NS
30	30.2±3.1	31.0± 6.0	NS

Painful IBS with diverticulosis

pat.	overall	painful waves	stat.analysis
46	19.9±1.9	76.4±40.5	NS
47	14.0±1.0	20.0± 4.8	NS
48	20.6±1.4	31.9± 8.8	NS
49	24.0±1.4	29.2± 1.9	NS
50	25.8±2.0	4.2± 2.5	**
51	19.7±1.0	25.7± 3.2	NS
52	25.4±1.3	0	
53	26.1±2.7	126.2±68.0	NS

Table 25 Mean area under the curve (±SEM): painless and painful waves. Student's t test: NS = not significant; * = p<0.05; ** = p<0.01; *** = p<0.001.

Painful IBS

pat.	painless waves	painful waves	stat. analysis
16	143± 92	208± 8	**
17	364± 64	995± 12	***
18	347± 46	0	
19	995± 75	2160± 185	**
20	613± 94	871± 113	NS
21	508± 48	1403± 23	***
22	1250±135	2031± 353	NS
23	243± 35	630	
24	1376±644	3080	
25	632±140	2902± 443	**
26	465± 23	956± 61	***
27	1089± 80	3195	
28	488± 36	1031± 141	**
29	733± 41	1345± 111	**
30	574± 77	1013± 196	NS
MEAN	655± 95	1455± 259	***

Painful IBS with diverticulosis

pat.	painless waves	painful waves	stat. analysis
46	1067±263	11305±7597	NS
47	624±115	2437± 629	*
48	1204±145	4580±2689	NS
49	1019±175	2618± 295	**
50	2548±259	1155± 300	**
51	908±126	3698±1562	NS
52	1320±153	0	
53	1237±261	13196±7013	NS
MEAN	1241±202	5570±1783	NS

Table 26 Mean motility index in mm Hg.s (±SEM): painless and painful waves. Student's t test; NS = not signifcant; * = p<0.05; ** = p<0.01; *** = p<0.001.

Painful IBS

pat.	painless waves	painful waves	stat. analysis
16	67± 9	98± 14	NS
17	211± 35	519± 44	***
18	165± 23	0	
19	550± 45	822± 142	NS
20	340± 70	525± 87	NS
21	288± 31	919± 39	**
22	618± 86	1126± 172	*
23	141± 27	630	
24	592±269	2564	
25	324± 69	1528± 249	**
26	237± 15	500± 58	**
27	537± 44	1596	
28	263± 23	592± 110	*
29	402± 32	770± 148	NS
30	326± 37	733± 229	NS
MEAN	337± 44	861± 166	***

Painful IBS with diverticulosis

pat.	painless waves	painful waves	stat.analysis
46	432± 97	4111±2272	NS
47	339± 69	1291± 373	NS
48	623±130	2592±1333	NS
49	701±156	1667± 233	*
50	1565±186	638± 169	**
51	615±102	2689± 357	***
52	1066±181	0	
53	622± 63	5753±3387	NS
MEAN	745±139	2677± 666	NS

Table 27 The mean values (±SEM) of the characteristics of the waves in the four periods in diverticulosis and in painful IBS with diverticulosis.
Statistical analysis: Mann-Whitney test: NS = not significant; * = $p<0.05$; ** = $p<0.01$; *** = $p<0.001$.

	diverticulosis	painful IBS with diverticulosis	statistical analysis
Amplitude in mm Hg (from table 17)			
fasting	14.8± 2.1	27.1± 2.8	**
postprandial	21.0± 3.2	37.0± 4.6	*
postglucagon	21.6± 2.3	38.5± 7.2	*
overall	19.3± 2.0	34.3± 4.3	**
Duration in seconds (from table 18)			
fasting	28.8± 3.8	22.7± 2.7	NS
postprandial	21.4± 1.7	20.0± 2.0	NS
postglucagon	23.6± 2.1	22.2± 3.2	NS
overall	23.3± 1.7	21.9± 1.5	NS
Total area under the curve in square mm (x 1000) (from table 19)			
fasting	27.5± 6.3	43.9± 6.0	NS
postprandial	33.3± 6.5	47.3± 7.1	NS
postglucagon	34.0± 5.0	64.3±13.2	NS
overall	94.9±11.6	155.5±16.4	**
Mean area under the curve in square mm (from table 20)			
fasting	1055± 256	1291± 232	NS
postprandial	1000± 205	1377± 186	NS
postglucagon	1097± 158	1723± 317	NS
overall	996± 133	1487± 168	*
Total motility index in mm Hg.s (x 1000) (from table 21)			
fasting	15.6± 4.8	24.5± 3.5	NS
postprandial	18.4± 4.1	28.9± 5.6	NS
postglucagon	18.9± 2.5	36.0± 6.4	*
overall	52.9± 7.8	89.3±10.1	NS
Mean motility index in mm Hg.s (from table 22)			
fasting	563± 172	725± 134	NS
postprandial	552± 115	856± 150	NS
postglucagon	609± 80	992± 195	NS
overall	572± 103	878± 119	*

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