Defecation disorders and chronic abdominal pain in children. Pathophysiology and treatment
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Chapter 1

Introduction to defecation disorders and chronic abdominal pain in children

*Based on three articles*

Functionele gastrointestinale ziektebeelden op de kinderleeftijd: Chronische buikpijn
Rijk van Ginkel, Hans A. Büller, Hugo S.A. Heymans, Jan A.J.M. Taminiau, Marc A. Benninga

accepted for publication in the Nederlands Tijdschrift voor Geneeskunde.

Functionele gastrointestinale ziektebeelden op de kinderleeftijd: Obstipatie en solitaire encopresis; deel I: fysiologie en pathofysiologie
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1. General introduction

The second Rome criteria for functional gastrointestinal disorders in adults were published in 2000. For the first time a chapter was included on childhood functional gastrointestinal disorders, based on the expert opinion of pediatric gastroenterologists and psychologists. A functional gastrointestinal disorder is defined as ‘a variable combination of chronic or recurrent gastrointestinal symptoms not explained by structural or biochemical abnormalities’. This widely used, but unclear term ‘functional’ was originally adapted from the Freudian psycho-analytic field, pointing to e.g. an isolated paralysis of an arm, without any sign of neurological involvement. This so-called functional paralysis was explained to represent an expression of unconscious anger against a parent, withholding the patient to do this parent any physical harm. In the medical literature, the use of the word ‘functional’ is broadened to describe every symptom for which no somatic, organic or psychiatric explanation can be found.

When functional symptoms become chronic or recurrent, they are classified as a functional disorder. In the Rome-II paper, four groups of functional pediatric gastrointestinal disorders are distinguished: 1) vomiting, 2) abdominal pain, 3) functional diarrhea and 4) disorders of defecation.

This thesis focuses on two disorders of defecation, namely functional constipation and functional non-retentive fecal soiling and on two abdominal pain disorders, namely irritable bowel syndrome and functional abdominal pain. These disorders are very common in daily clinical practice, but most importantly, they are difficult to treat, often leading to misunderstanding and frustration of the treating physician, the children and their parents.

The aim of this introduction is to give a global overview of the current views on anorectal physiology and especially on the underlying pathophysiology and the treatment of these disorders. As an introduction to the following chapters, inconsistencies in the literature or open questions that in our view definitely require further investigation will be identified and discussed against the current knowledge. As such, this chapter will set the stage for the following chapters, in which some of these open questions will be addressed.
2. Anatomy and physiology of anorectal function

2.1 Anatomy

The anatomy of the anorectum is schematically represented in figure 1.

The upper end of the rectum is located at the third sacral vertebra. At the distal end, it bends abruptly along the upper surface of the coccyx and levator muscle, forming the anorectal angle. Comparable to other parts of the gastrointestinal tract, the rectal wall is composed of several layers, including the mucosa, the submucosa with the submucosal nervous plexus, the circular smooth muscle layer and the longitudinal muscle layer with the myenteric plexus in between these two muscular layers and the outer adventitia.

The most distal part of the gastrointestinal tube is formed by the anal sphincter complex, separating the internal milieu from the outside and is the most important player responsible for maintaining fecal continence. This sphincter complex is embedded in the striated pelvic floor, of which the puborectalis muscle joints the upper part of the external anal sphincter. The anal sphincter complex consists of two components, the smooth muscle component or the internal anal sphincter and the striated muscle component or the external anal sphincter. The internal anal sphincter surrounds the proximal part of the anal canal. It is tonically contracted generating 85% of the anal resting pressure. This smooth muscle is innervated by the enteric nervous system located within the gut wall and is thereby not under voluntary control. Stimulation of mechanoreceptors located in the rectum, and to some degree in the sigmoid, leads to activation of intramural inhibiting neurons, leading to relaxation of the internal anal sphincter, the so-called inhibition reflex.
In contrast to the internal sphincter, the external anal sphincter consists of striated muscle and is innervated by the pudendal nerve and under voluntary control. As such, this muscle can be contracted on demand, for example when defecation needs to be postponed.

The muscles of the pelvic floor are also involved in the maintenance of continence. Especially the puborectal muscle, which originates from the pubic bone, loops around the caudal part of the rectum at the junction with the anal canal and ends again at the os pubis. This muscle, also under voluntary control, is tonically contracted and mainly responsible for the formation of the anorectal angle, a mechanism thought to act as a valve and closing of the distal rectum during episodes of increased abdominal pressure. Finally, when needed, the pelvic floor and glutei muscles can assist the anal sphincter complex.

Sensation arising from the anorectal area is of great importance to detect the presence, the volume and consistency of feces in the rectum. Both mucosal and intramuscular receptors are involved to fulfill this task. The anal canal is covered with nerve endings detecting the nature of the anal content discriminating between gas, liquid and feces. Clearly, this is of great importance in the entire process of defecation. On the other hand, intramural stretch and/or pressure receptors will detect the degree of rectal filling giving rise to sensations of desire to defecate and urgency. Finally, receptors, most likely located in the pelvic floor and/or the pelvis detect increases in intra-abdominal pressure, which may indeed represent a challenge for the anal sphincter complex leading to expulsion of rectal contents. In the latter case, compensatory reflexes will be activated to increase anal sphincter pressure ensuring fecal continence.

Sensations arising from the anorectal area are transported via afferent neural pathways to the spine. Via ascending nerves in the spinal cord (the spinothalamic tract) the information is transported to the thalamus. Only when the sensory information is transferred to the limbic and somatosensory areas of the cerebrum, sensations as flatus and desire to defecate will be perceived. Comparable pathways are responsible for the sensation of gastro-intestinal pain.

2.2 Physiology

Normal anorectal function strongly depends on the complex interplay between the different anorectal and pelvic anatomical structures (Fig. 1). Principally, the main task of the anorectum is to continuously ascertain absolute fecal continence. The only moment that the anorectum is dismissed of this task is during defecation, whereby defecation in fact can be considered as a controlled episode of incontinence at a socially acceptable moment. It should be stressed though that normal defecation is not simply a transient 'failure' of the sphincter complex, but is also a complex mechanism depending not only on normal sensation and motility of the anorectal area, pelvic floor, sigmoid and descending colon, but also involving the abdominal and respiratory muscles. Furthermore, one should realize that also psychological factors may have a major impact on these pathways underlying normal defecation.

Fecal continence is warranted by different mechanisms. First of all, the caudal end of the rectum is closed by the anal sphincter complex, creating an anal sphincter resting pressure of circa 40 mm Hg, which is build up by both the internal (for 85%) and external anal sphincter. This pressure increases by a reflex contraction of the external anal sphincter complex when an acute increase of intra-abdominal pressure occurs, thus counteracting the imminent loss of feces.
This is an important mechanism in normal daily life when intra-abdominal pressure is increased during coughing, laughing, bending, sneezing, etc. This function of the anal sphincter to get the ‘gate closed’ is supported by rectal motility, which is directed to keep the rectum empty, transporting feces back towards the sigmoid, thus keeping the feces separated from the anal canal\(\textsuperscript{1}\). A final mechanism taking care for continence is the sensation in the cranial part of the anal sphincter. Triggering of receptors in the anal canal by feces will result in the sensation of imminent fecal loss, giving the person the ability to prevent this loss of feces by contracting the pelvic floor muscles. When defecation is not desirable, the external sphincter complex, with the help of the pelvic floor, remains contracted, until the rectal wall has adapted to the increased rectal volume. When the intra-rectal pressure decreases, the sensation of urge will disappear. In addition, retrograde contractions of the caudal part of the rectum may occur, transporting the feces back into the sigmoid colon.

The interplay of all these mechanisms starts when feces enters the rectum, e.g. due to increased propulsive activity of the colon following ingestion of a meal. Filling up the rectal vault with feces leads to an increase in intra-rectal pressure. Triggering of receptors located in the rectal wall induces 2 mechanisms: 1) the inhibition reflex, leading to a decrease in anal sphincter pressure (internal sphincter), which is the more pronounced when rectal filling increases. 2) Above a certain threshold in rectal pressure, the perception of urge occurs. At that time, due to a reflex triggered by this sensation of urge, the external anal sphincter complex contracts for a short time, preventing immediate loss of feces, thus creating time to consider if the pelvic floor has to be contracted to stop imminent defecation or to permit the defecation process to continue.

Defecation occurs when there is enough difference in pressure in the rectum at one hand (rectal contractions and straining) and the pelvic floor at the other hand (relaxation of the anal sphincter complex and pelvic floor and flattening of the anorectal angle). Straining is essential when a child tries to defecate without the sensation of urge (e.g. during toilet training). During the process of toilet training the child starts to get grip on these complex mechanisms to control the defecation process. The will of the child seems to be a crucial factor in this process.

Aberrations in these complex interplaying mechanisms might lead to clinical signs and symptoms of constipation and fecal incontinence. Pathophysiologic mechanisms of these clinical entities are largely unknown. The last decades, only little progress has been made in resolving these mechanisms. Large lacunas are also still present in anorectal (dys)functioning.

The physiology of pain is extremely complex. Pain is the subjective response of an individual to the perception of noxious stimuli. The noxious stimulus is sensed by a peripheral receptor and a pain message is then transmitted via afferent fibers to the spinal cord. After entering the central nervous system, the signal is passed up via ascending tracts in the spinal cord to synapses in specific areas of the midbrain, pons, and diencephalons. At any point along the path, reflex arcs may be stimulated to initiate aversion responses to the noxious event. From these lower brain centers, the nociceptive information may or may not be forwarded to the limbic and somatosensory areas of the cortex where the subjective, conscious experience of pain resides\(\textsuperscript{2}\). This conscious experience is influenced by psychological aspects.

So, different levels in the physiology of pain can be distinguished on theoretical grounds. However, the very complex interplay between these components makes it almost impossible to
isolate and study one single component. The experience of pain might be useful, informing the person of possible harm to his body, giving him the opportunity to prevent himself from further harm. However, when the 'pain-system' is activated by physiological stimuli or remains active when the harmful event has been treated, then this system generates symptoms and contributes to the genesis of symptoms and disease.

3. Constipation and functional non-retentive fecal soiling

3.1 Definitions

As described earlier, a panel of experts has reported definitions of pediatric functional bowel disorders, including defecation disorders. Of these, functional constipation and functional non-retentive fecal soiling will be discussed.

3.1.1 Constipation

The current Rome II criteria define childhood constipation based on a presenting symptom profile. Two subgroups, namely functional constipation and functional fecal retention are distinguished.

Functional constipation is defined as follows: 'In infants and children at least two weeks of 1) scybalous, pebble-like, hard stools for a majority of stools; or 2) firm stools 2 or less times/week; and 3) there is no evidence of structural, endocrine, or metabolic disease'.

Functional fecal retention is defined as follows: 'From infancy to 16 years old, a history of at least 12 weeks of: 1) passage of large diameter stools at intervals < 2 times/week; and 2) retractive posturing, avoiding defecation by purposefully contracting the pelvic floor. As pelvic floor muscles fatigue, the child uses the gluteal muscles, squeezing the buttocks together'.

The main difference between functional constipation and functional fecal retention is the occurrence of retractive posturing in the latter. Retentive posturing is the behavioral withholding of stool during sensation of urge, which according to the authors of the Rome criteria mostly results from painful defecation. However, the possible underlying mechanisms causing this painful defecation are not taken into account. While the Rome-group stresses the importance of retractive posturing, the very common and major symptom of constipation, namely fecal soiling, was not included in the definitions. As we feel that this is an important feature of constipation, a different definition for constipation (in children of > 4 years of age) has been used in the following chapters. In our view, at least two out of the four following criteria have to be fulfilled: 1) two or less bowel movements per week without laxatives, 2) two or more soiling episodes per week, 3) periodic passage of a very large amount of stool once every 7–30 days and 4) a palpable abdominal or rectal mass on physical examination.
3.1.2 Functional non-retentive fecal soiling

The Rome group defined functional non-retentive fecal as follows: Once a week or more for the preceding 12 weeks, in a child older than 4 years, a history of: 1) defecation into places and at times inappropriate to the social context; 2) in the absence of structural or inflammatory disease; and 3) in the absence of signs of fecal retention.

Almost all studies performed in the "encopretic" child assume that all these children are constipated. Therefore, a major benefit of this definition is, that there is a definition, for the first time clearly stating, that these children form a separate entity. Although in the current literature sometimes a difference is made between soiling (loss of small amount of feces due to 'overflow') and encopresis (normal bowel movement) the terms are used interchangeably. However most times the term encopresis is used, defined as 'the voluntary or involuntary passage of a quantitatively normal bowel movement in the underwear in children over the age of 4 years, occurring on a regular basis without any organic cause". Sometimes the term 'solitary encopresis' is used. It is not fully clear why the Rome group has chosen for the term soiling in the definition of these children. This might lead to some confusion, as it might refer to 'rectal overflow'. In addition, it is stated, without referring to medical literature, that the main cause of this symptom in unconscious anger. Research on behavior in children with functional non-retentive fecal soiling, however, suggest that aberrant behavior, which was found in 35% of these children, is secondary to the occurrence of encopresis.

3.2 Epidemiology and clinical presentation

3.2.1 Constipation

Constipation is mainly a problem in Western societies. It is diagnosed in 3% of the children referred to a pediatrician. Complaints related to defecation are responsible for 25% of outpatient visits to pediatric gastroenterologists. Estimations on the prevalence of constipation in the general pediatric population vary from 0-3.8%. In the Netherlands 1% of the children in the age range of 0-4 years, but hardly any in the range of 4-15 years visits the general practitioner for complaints of constipation. Constipation is more common in boys than in girls (2:1). In some studies however, also a 1:1 ratio is described. In only 10% of all children with defecation disorders, constipation is part of an organic disorder.

The most important complaint of constipated children is a combination of a low defecation frequency and soiling. Soiling often occurs several times a day and in case of severe fecal retention it occurs even at night. Another typical feature of functional constipation is the production of a large amount of stool, which may be so enormous that it may clog the toilet. This can occur once a week to once a month and is of course a very painful event. Often, the evacuation of such a large amount of stool is preceded by an increase of the soiling frequency and complaints of abdominal pain and poor appetite. These symptoms disappear immediately after the production of this large amount of stool. It is therefore not surprising that upon
physica examination constipated children might present with abdominal or rectal fecal impaction. With the help of bimanual palpation, it can sometimes be observed, that the fecal accumulation extends from the anal canal up to the flexura lienalis of the colon. Sometimes, the observed abdominal distention might also be due to accumulation of gas as a consequence of a high dose of lactulose, while rectal or abdominal scybala have not been removed. Finally, extraintestinal symptoms are reported such as complaints of urinary tract infections and enuresis in circa 30% of the children.

### 3.2.2 Functional non-retentive fecal soiling

Soiling is reported in 1.5 – 2.8 % of children older than 4 years. In 10-30% of these children the soiling is not secondary to constipation. Approximately 90% of the group of children with functional non-retentive fecal soiling consists of boys.

As already mentioned, children with functional non-retentive fecal soiling are devoid of any sign or symptom of constipation. The single complaint is soiling. These children hardly complain of abdominal pain and their appetite is normal. Some report an acute irresistible urge to defecate, showing resemblance with idiopathic fecal incontinence in adults. In circa 30% of children with functional non-retentive fecal soiling aberrant behavior is observed using the Child Behavior Check List. It is clear, that the occurrence of soiling has a large impact on normal daily life of the child (isolated position, ragged at school), but also strains the relationship between parents and siblings, interfering with and compromising normal family life.

### 3.3 Pathophysiology

#### 3.3.1 Constipation

The pathophysiology underlying functional constipation is undoubtedly multifactorial, and certainly not well understood. Clearly, functional constipation can result from abnormal function of the different players involved, including the colon, the rectum and the sphincter complex and not at least the will of the child. In general, the two subgroups slow transit constipation and outlet obstruction, leading to retention of feces in the rectum, can be distinguished. Most likely, different pathophysiological mechanisms underlie each of these different forms of constipation.

##### 3.3.1.1 Abnormal colonic motility

Slow transit constipation can be diagnosed by colonic transit time measurements showing an overall delay in colonic transit time. Both muscular (impaired contractility) and neural (uncoordinated motor activity) mechanisms may lead to impaired propulsion of fecal contents leading to slow transit and constipation. Mechanisms underlying this entity might be an impairment of neurotransmitter function, such as nitric oxide (NO) or substance P or aberrations in the interstitial cells of Cajal. However, it remains difficult whether observed abnormalities are primary or secondary to longstanding constipation.
In addition to neuromuscular dysfunction, constipation can also result from massive fecal retention in the rectum. It has been shown that voluntary retention of feces can cause a delay in colonic transit in healthy volunteers. Similarly, massive fecal retention in children can also inhibit colonic transit and thus indirectly lead to prolonged transit times.

### 3.3.1.2 Abnormal sphincter function

An alternative mechanism leading to constipation is so-called outlet obstruction or abnormalities in the dynamics underlying defecation. In these children, the delay in colonic transit is situated in the rectum \(^{29}\), a finding present in 40% of constipated children. The underlying mechanism of outlet obstruction is thought to result from abnormal defecation dynamics. Under normal circumstances, the pressure generated by the anal sphincter complex should drop during an attempt to defecate allowing expulsion of fecal contents. However, using anorectal manometry, a paradoxical contraction of the anal sphincter complex is observed \(^{32,4}\), in more than 50% of constipated children \(^{3,44}\). This contraction of the anal sphincter might disturb the normal defecation process, leading to fecal accumulation. For a long time, this abnormality was regarded as the major underlying pathophysiologic mechanism in childhood constipation, reflecting the often observed stool withholding behavior / retentive posturing. Possible causes leading to this behavior may be 1) pain resulting from the previous production of a large, hard stool, 2) anal fissures, 3) primarily behavioral mechanism, 4) not taking time to go to the toilet, 5) resistance to go to another toilet than their own.

If abnormal defecation dynamics are indeed an important mechanism leading to fecal retention and constipation, it is remarkable that this phenomenon is also observed in children with functional non-retentive fecal soiling \(^{7,14}\). In addition, a large study comparing conventional treatment with additional biofeedback training in constipated children showed that biofeedback training could normalize the aberrant sphincter contraction, however it did not lead to a larger success rate in children receiving additional biofeedback training. These findings argue against a major contribution of abnormal defecation dynamics.

### 3.3.1.3 Abnormal rectal sensation

As explained previously, arrival of fecal material in the rectum is sensed by different types of nerve endings giving rise to sensations of flatus, urge to defecate and pain. This sensory information is of great importance to initiate the defecation process. Abnormalities in rectal sensation are therefore believed to play an important role in the pathogenesis of constipation.

Several studies have investigated rectal sensitivity in children with constipation. In these studies, rectal sensation is determined with the help of rectal balloon inflation, measuring the volume at which e.g. sensation of urge is perceived. These studies showed impaired rectal sensation in a subgroup of patients with constipation. However, rectal volume might be age-dependent and no age-dependent normal values are available. Consequently, older children will be at risk to be classified as having abnormal sensation and in contrast, young children will be at risk to be unjustly classified as having normal rectal sensation. Moreover, rectal volume depends also on rectal compliance, which is not taken into account by volume measurement. Therefore,
the rectal barostat might be of great help in studying rectal sensation. This computer driven mechanical pump is able to inflate a rectal balloon, while at the same time rectal pressure and rectal volume is measured. Thus, the rectal threshold for sensation can be measured as pressure, which is more unlikely to depend on age than data derived from volume-driven distentions.

3.3.1.4 Abnormal motility/sensitivity parameters: primary or secondary?

Unraveling pathophysiologic mechanisms in constipated children are especially difficult as longstanding rectal accumulation of feces may lead to neuromuscular damage with abnormalities in rectal sensation, compliance and motility. It is currently unknown whether observed abnormalities in rectal function in constipated children, such as an increased rectal volume at first sensation of urge, are really causing constipation or whether they are secondary to fecal accumulation. Prospective studies evaluating early aggressive treatment are certainly required to further clarify this issue.

3.3.2 Functional non-retentive fecal soiling

The pathophysiological mechanisms underlying functional non-retentive fecal soiling are much less studied than those of constipation. Studies evaluating the underlying pathophysiology are rather scarce and limited to manometric studies (anal sphincter rest pressure, maximal squeeze pressure and rectal sensation) and colonic transit time measurements \(^{(5,11,15)}\). None of these studies show any abnormalities \(^{(6)}\), leading to the concept that the main problem in these children is most likely of psychological origin.

Although psychological issues will certainly contribute to the pathophysiology of this defecation disorder, it remains important to continue the search for new pathophysiological concepts. One so far neglected possible mechanism could be changes in rectal function. Not only alterations in reservoir capacity, but also abnormal rectal sensation and motility may lead to fecal soiling. Theoretically, impaired reservoir function with increased contractility of the rectum in response to arrival of stool or decreased rectal sensation might lead to uncontrollable expulsion of stool. So far, the role of the rectum has not extensively been studied in this defecation disorder. This can only be achieved using the rectal barostat, as described in one of the next chapters.

3.4 Treatment

During the last decades only a few randomized studies, most of them with small patient numbers, have been performed evaluating new treatments for children with defecation disorders. The treatment of constipation is mainly based on empirical experience, but not on placebo controlled randomized studies. The subdivision in functional constipation and functional fecal retention as suggested by the Rome II criteria has no therapeutic consequences at this time. Although functional constipation and functional non-retentive fecal soiling are completely
different entities, there is overlap in their treatment as far as it concerns treatment modalities influencing behavioral or psychological aspects, and will therefore be discussed together.

3.4.1 General measures

3.4.1.1 Education

As the will and motivation of the child are very important in the total therapeutic process, an extensive explanation of the disease has to be given and the possible consequences of stool withholding have to be discussed with the child and its parents. Therefore, after a thorough history taking and physical examination, it is very important to take ample time for education concerning constipation and soiling. Issues to discuss are: 1) prevalence of constipation and soiling, 2) the relationship between fecal impaction and overflow diarrhea (explaining with the help of drawings), 3) organic versus functional disease 4) therapy (stressing that this might not be easy and will be longlasting), 5) the responsibility of the child for its the treatment, 6) the struggle concerning the defecation problem, which does exist in nearly every family dealing with a constipated child.

3.4.1.2 Behavioral therapy

There are no randomized studies evaluating the effect of behavioral treatment in children with defecation disorders. In our experience, the psychological counseling of the child, but also of the total family, can be of great value, especially to support the initiated toilet training and to give structure and rest in the family. Most of the behavior modification programs do contain the following issues: positive reinforcement of defecation on the toilet and to be clean, ignoring or neutral attitude towards the child when it has soiled and send the children to the toilet 2-3 times per day \(^\text{21}\). It is all directed to give the defecation process its normal place in normal daily life.

3.4.1.3 Diary

Filling out a diary objectifies the complaints of the child, gives insight in the therapeutic progress and might motivate the child. Therefore, the child has to fill out the diary card itself. This stresses once more that the child is responsible for the defecation problem. The diary card is linked to a rewarding system.

3.4.1.4 Toilet training

Another simple general measure that may be of help to normalize defecation is toilet training. At the start of the treatment the child is instructed to attempt to defecate three times a day during 5 minutes after each meal. The child is stimulated to strain actively while placing its feet on a foot-rest. The latter is important to flatten the anorectal angle, facilitating fecal expulsion. Using this approach, the child is forced to focus on its bowel function. Furthermore,
in case of defecation, the rectum will be empty, reducing the risk of fecal soiling during the rest of the day.

These general measures in combination with medical therapy, is successful in 15% of children with severe constipation referred to a tertiary hospital. Clearly, additional treatment is required. One possible option would be more aggressive pharmacological treatment using laxatives and/or enemas.

**3.4.2 Pharmacotherapy**

So far, no double-blinded randomized studies on oral or rectal laxatives have been performed in children with constipation, except the use of cisapride. Even the effect of lactulose is hardly investigated. Therefore, the best “evidence-based” treatment can not be constructed and almost all advices concerning the use of oral or rectal laxatives are, at this moment, bases on clinical empirical experience. The major aim of medical therapy is to remove fecal accumulation and to prevent its recurrence, thus preventing prolonged rectal distention potentially leading to rectal damage.

**3.4.2.1 Oral laxatives**

Most often the initial treatment involves an osmotic laxative (e.g. lactulose or lactitol) in a dose of 6 gram per kg body weight, divided in two portions per day. The main function of the osmotic laxatives is to loosen stool consistency, thus facilitating transport and expulsion and rendering defecation less painful. The dose is increased until improvement is achieved (sometimes up to 2-3 times the starting dose). During the first days flatulence may occur whereas abdominal pain can increase, especially on higher doses of laxatives. The dose should be titrated based on the defecation frequency aiming at a frequency of ≥ 3x per week. In addition, fecal accumulation in the rectum should be prevented. This adequate dose should be continued for at least 3 months.

However, lactulose as mono-therapy is often not sufficient and additional medication is needed. When slow transit constipation is diagnosed, stimulative laxatives such as bisacodyl (5 mg every other day) might be useful. Alternatively, cisapride or Transipeg can be started. Good results of cisapride (4 dl 0.3 mg/kg) have been reported in small randomized studies with a significant higher success percentage compared to placebo (76% versus 37%) Transipeg (polyethylene glycol) has been shown to be useful in the treatment of constipation in adults and children in a dose of 0.8 g/kg/day once daily. However, when outlet obstruction is diagnosed, the use of enemas is unavoidable.

In contrast to constipation, colonic transit is normal in children with functional non-retentive fecal soiling. As such, in our opinion, there is no rational to treat these children with laxatives. Nevertheless, this therapy is often started in these children, although so far, no double-blinded randomized studies on oral or rectal laxatives have been performed in this subgroup of children. One might even speculate that prescribing laxatives will have a negative effect in children with fecal soiling. Therefore, it is important to study the effect of laxatives on successful outcome in these children.
3.4.2.2 Enemas

Impaired emptying of the rectum can lead to fecal impaction and fecal soiling. When fecal impaction is found on clinical examination, daily enemas for at least 3 days should be administered before oral laxatives are started. If the rectum is clogged with hard stool, treatment with oral laxatives, without removing these scybala with enemas, will paradoxically result in an increase in soiling due to overflow diarrhea. Moreover, children will report more side-effects such as abdominal pain and bloating.

In practice, enemas with lower volume will be prescribed to children less than 10 kg of body weight, whereas older children preferentially receive larger volume enemas (120 ml, Klyx®: sodium-dioctylsulfosuccinate and sorbitol or phosphate-enema). If the fecal mass has been removed successfully, but soiling relapses or the defecation frequency does not normalize with adequate treatment with oral laxatives, enemas are added to the long-term treatment.

3.4.3 Biofeedback training

In more than 50% of children with defecation disorders, the anal sphincter complex contracts instead of relaxes during defecation. It is possible to normalize this phenomenon with the help of biofeedback training. However, we previously showed that normalization is not related to successful outcome. Also the improvement of the sensation of urge with this technique did not lead to a higher success rate compared to children receiving only medical therapy. The role of biofeedback training in the treatment of defecation disorders in children seems therefore to be limited.

3.5 Prognosis

Although some follow-up studies have been performed in constipated children, many of them have disadvantages. Some studies had a cross-sectional instead of a prospective design, had low follow-up percentages or low patient numbers, had a follow-up only at 1 year after treatment or had vague inclusion criteria. Nevertheless, these studies show that a positive family history for constipation and an early age of onset of the complaints are negative prognostic factors for successful treatment. Furthermore, it is interesting that far more boys than girls present with constipation, whereas in adults the percentage of constipated woman is larger than that for man. This further stresses the need of a thorough long-term follow-up study.

In children with functional non-retentive fecal soiling, only one abstract concerning the prognosis of this patient group is available. It showed the persistence of complaints in 30% of the children attending secondary school. It persisted in 22% of the patients reaching young adulthood, whereas none of these children received any treatment anymore.
4. **Functional abdominal pain and irritable bowel syndrome**

4.1 **Definition**

In 1958 Appley defined *recurrent abdominal pain* as at least three episodes of abdominal pain severe enough to affect activities over a period of not less than three months. This definition has been used in children with chronic abdominal pain, over the past 5 decades. However, this definition neglected different clinical presentation forms of children with chronic abdominal pain and in addition, the development of more advanced diagnostic tools (such as endoscopy) required revision of this more general definition from Appley.

The Rome-group defined 5 different subgroups of children with functional abdominal pain on the basis of clinical criteria. All these definitions include the statement that the children should be mature enough to provide an accurate pain history. Moreover, the abdominal pain has to be present for a total period of at least 12 weeks, which needs not to be consecutive, in the preceding 12 months. The 5 groups are: 1) functional dyspepsia, 2) irritable bowel syndrome, 3) functional abdominal pain, 4) abdominal migraine and 5) aerophagia. The entities irritable bowel syndrome and functional abdominal pain will be discussed below.

Irritable bowel syndrome is defined as abdominal discomfort or pain that has two out of three features: 1) relieve with defecation; and/or 2) onset associated with a change in frequency of stool; and/or 3) onset associated with a change in form (appearance) of stool. Symptoms further supporting the diagnosis of irritable bowel syndrome are: abnormal stool frequency (> 3 bowel movements per day or < 3 bowel movements per week), abnormal stool form, abnormal stool passage, passage of mucus and bloating or feeling of abdominal distension.

Functional abdominal pain is defined as: 1) continuous or nearly continuous abdominal pain in a school-aged child or adolescent; and 2) no or only occasional relationship of pain with physiological events (e.g. eating, menses, or defecation); and 3) some loss of daily functioning; and 4) the pain is not feigned (e.g. malingering); and 5) insufficient criteria for other functional gastro-intestinal disorders that would explain the abdominal pain.

The main difference between these irritable bowel syndrome and functional abdominal pain is the absence of accompanying symptoms in children with functional abdominal pain, whereas in children with IBS, pain is accompanied by changes in defecation or symptoms related to defecation.

To prevent any misunderstanding, the definition recurrent abdominal pain has to be avoided in medical literature from now on. To be clear, the definition recurrent abdominal pain includes all sub-classifications as defined by the Rome II group. Therefore, functional abdominal pain is not the same entity as recurrent abdominal pain.
4.2 Epidemiology and clinical presentation

4.2.1 Recurrent abdominal pain

Recurrent abdominal pain, as described by Appleby was reported in more than 10% of school-aged children. In this classic study, only in 5-10% of these children with “recurrent abdominal pain”, an organic cause underlying the abdominal pain, was found. Forty years later an even higher percentage of chronic abdominal pain is reported in Swedish and American school-aged children (circa 20%).

Since the introduction of new diagnostic techniques (e.g. pH-monitoring and endoscopy) an organic cause is reported in 35-42% of the children with chronic abdominal pain. Inflammation of the stomach is reported in 12%, lactose malabsorption in 20% and chronic inflammatory bowel disease in 4% of children referred for chronic abdominal pain. These above mentioned studies, however, were performed in a tertiary center, probably leading to referral bias. Chronic abdominal pain is more common in girls than in boys (5:3).

The character of the pain is often dull, sometimes crampy and mostly localized around the umbilicus. The severity of the pain ranges from pain hardly influencing normal daily activities to a presentation resembling an “acute abdomen”. The duration of the pain varies from minutes to days.

4.2.2 Irritable bowel syndrome

No epidemiological data are available for the new defined Rome II criteria of irritable bowel syndrome. Some studies using definitions for IBS in adults, comparable with the Rome II criteria, showed that 52% of children older than 5 years of age visiting a clinic for abdominal pain had symptoms of IBS. Moreover 17% of high-school and 8% of middle-school students showed symptoms of IBS.

The clinical presentation is as described in the definition.

4.2.3 Functional abdominal pain

No epidemiological data are available in children with functional abdominal pain and the clinical presentation is described in the definition.

4.3 Pathophysiology

No data are available concerning pathophysiological mechanisms in children with irritable bowel syndrome or functional abdominal pain. Therefore, the following paragraph will briefly discuss the current views and hypotheses raised in adult literature. For a more extensive description of underlying pathophysiological mechanisms in adult IBS patients, we refer to a recent review in this field.
4.3.1 Visceral hypersensitivity

Visceral hypersensitivity seems to be an important pathophysiological mechanism in adults with functional abdominal complaints. Visceral hypersensitivity points to an increased sensitivity of the gastrointestinal tract for a normal stimulus. Such a stimulus (e.g., distension of the rectum) is perceived as a normal, non-painful sensation (e.g., sensation of urge) in healthy persons, while patients with visceral hypersensitivity interpret this stimulus as pain. More than 50% of adults with irritable bowel syndrome show alterations in rectal sensation. Theoretically, abnormal processing of the sensory signal can occur at any level in the neural pathway involved, from the mechanoreceptor in the gut wall to the brain centers involved in the central processing of gastrointestinal information. However, a review concerning visceral hypersensitivity questions the purely somatic interpretation of these results. The lowered threshold for pain is explained by an acquired fixed attention to gastrointestinal sensations.

4.3.2 Abnormal gastrointestinal motility

In adults with irritable bowel syndrome disturbances in gastrointestinal motility, such as a delayed, but pronounced rectal contractile response to a meal, are observed. However, although subgroups of IBS patients show altered responses in the small and large intestine to a broad spectrum of stimuli, such as diet, hormones and psychological stress, no test has been established as a diagnostic standard.

4.3.3 Psychological factors

There are no studies in children with IBS and functional abdominal pain evaluating the role of psychological factors. It is obvious though that alteration in the social situation (divorce of parents, migration, passing away of a family member) and the attitude of the parents towards the child with chronic abdominal pain will have a major psychological impact on the child. There is indeed a relationship between childhood abdominal pain and somatic complaints of the parents. Mothers of children with chronic abdominal pain show more complaints of anxiety, depression and somatisation compared to a control group of mothers not having children with chronic abdominal pain.

4.4 Treatment

The treatment of children with functional abdominal pain and IBS is often difficult and longlasting, mainly due to the lack of insight in the underlying pathophysiological mechanisms. The Rome II sub-classification has, so far, not resulted in a different general approach to children with functional abdominal pain and IBS. The treatment is often empirical and includes reassurance, education concerning the disease, filling out a diary, stimulation of daily (school) activities, food- and liquid advices and eventually prescribing medication.
4.4.1 General measures for functional abdominal pain and IBS

4.4.1.1 Reassurance and education

First of all it has to be stressed to the patient and its parents that the pain is real and largely influences daily functioning of the child and its family. In addition the high incidence of chronic abdominal pain in school-aged children is discussed, referring to the very low percentage of children in which an organic cause can be detected. The absence of ‘emergency symptoms’ such as rectal blood loss, fever, weight loss, etc. underlines the absence of a severe illness. It is important to ask the parents what diagnosis they have in mind. Moreover, the intensive relation between the brain and the gastrointestinal tract is discussed. It has to be stressed, that it is not really a disease, but a chronic problem.

When the child is complaining of abdominal pain, the parents and e.g. teachers are advised to pay attention to it, without reacting too strong to these complaints. Normalization of daily activities (playing, school, hobbies) plays an essential positive role in the treatment.

4.4.1.2 Fiber

An adequate liquid- and fiber intake is thought to be of some importance. Studies in adult IBS patients do not show a significant positive effect of dietary fiber. A double blind randomized study in children with recurrent abdominal pain showed a significant decrease in abdominal complaints with fibers compared to placebo. The effect of fiber is probably the most effective in those children with some complaints of constipation. The compliance concerning fiber intake, as studied in children with constipation, is not high.

4.4.1.3 Psychological intervention

Studies in adult patients with IBS show that a good doctor-patients relationship has a placebo response of 30%–80%. An important aspect for the caretaker in this relationship is the awareness that the patient or its parents might have particular ideas about the cause and consequences of the pain. Therefore it is important to discuss their major points of concern and to give a clear explanation of the disease. Furthermore, realistic goals have to be made. When the goal is to cure the patient totally, this might lead to disappointment for both the physician and the patient. A more realistic goal is e.g. the re-introduction of normal daily activities. It is essential, as it is for functional defecation disorders, to get the patient and its parents involved in the treatment strategy. A longstanding relationship, preferably with the general physician, to stress that there is no special (organic) cause for the disease, might be of great value.

Family therapy and the handling of stress and pain are the major cornerstones concerning psychological intervention. Referral to a psychologist or psychiatrist is indicated when there are signs of primary psychopathology (anxiety, depression, strong tendency to internalization) or when there are signs of a disturbed family structure (e.g. imitation of painful behavior). Structured family therapy in combination with teaching the child how to cope with his pain was effective in 55% of children with chronic abdominal pain.

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A positive effect of hypnotherapy is shown in adults with irritable bowel syndrome suggesting alterations in rectal perception in those patients with visceral hypersensitivity, however via an unknown mechanism. A pilot study using hypnotherapy in children seemed also to be successful in the 5 included patients.

4.4.2 Pharmacotherapy used in children with IBS

At present, there are no controlled studies evaluating the effect of drugs in children with IBS or functional abdominal pain. In general, treatment of these children mainly involves supportive measures as described above, and in our hands, medical therapy is not indicated. In the US on the other hand, sometimes tricyclic antidepressives are prescribed in children with functional abdominal pain or IBS, probably due to good results in adults with functional gastrointestinal disorders.

Spasmolytics, such as butylscopolamine (Buscopan) and mebeverine (Duspatal) lower the tone and motility of the gastrointestinal tract. Based on these properties, they may theoretically be effective in patients with chronic abdominal pain, but randomized placebo-controlled studies are lacking in children.

4.5 Prognosis

Little is known concerning long-term follow-up of children with chronic abdominal pain. Some studies suggest that 25-50% of children with functional abdominal pain still have abdominal pain in adulthood with features of irritable bowel syndrome. This seems to be especially the case in girls. However, a population based birth cohort study showed no prognostic value of childhood chronic abdominal pain concerning abdominal pain in adulthood. Two studies show a higher incidence of psychiatric disorders in adulthood in patients with chronic abdominal pain in childhood, compared to the normal population. A timely psychological intervention in a child with chronic abdominal pain from a “pain family” will probably prevent persistence of complaints in adulthood.

Conclusion

The functional gastrointestinal disorders, constipation, functional non-retentive fecal soiling, functional abdominal pain and irritable bowel syndrome are common disorders in children. Remarkably, little is known about the underlying pathophysiological mechanisms. In addition, evidence based treatment strategies are lacking leading, mainly due to this lack in pathophysiological insight. In this thesis, we therefore tried to gain more insight in the role of the anorectum in these disorders and evaluated the effect of some treatment strategies.
Reference List


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