Paediatric constipation and functional non-retentive faecal soiling

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Chapter 2

Childhood constipation: Is there new light in the tunnel?

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Constipation is a common phenomenon in childhood worldwide. The symptoms vary from mild and short-lived to severe and chronic with faecal impaction and encopresis. Although our understanding of pathophysiology has grown rapidly in recent decades, the causes and management of constipation in childhood remain obscure. This review begins with the current opinion concerning the definition of constipation as stated by a group of experts in the field of paediatric gastroenterology. Physiology of normal defecation, pathophysiological mechanisms, clinical features, and diagnostic work up for constipation then are addressed. Finally, an extensive overview is given concerning the treatment options and long-term outcome in these children.

Definition

One of the key problems in studies concerning the management of childhood constipation is the lack of a generally accepted definition for paediatric constipation. This derives mainly from the fact that constipation is a symptom rather than a disease. Constipation is often differently interpreted by patients and physicians (1). In children it is even more difficult to define, because, the physician must rely upon the interpretation of symptoms as told by the parents (2).

In the last two decades, the Iowa-criteria (3) have often been used in large randomised controlled trials. These criteria are based on the most common features of childhood constipation, i.e. infrequent defecation, large stools, encopresis and faecal impaction found on physical examination. The criteria are straightforward, easy to work with and useful in evaluating endpoints of various treatment regimens. However, they do not include the whole spectrum of childhood defecation disorders. Recently a group of experts in the field of paediatric gastroenterology categorised childhood functional gastrointestinal disorders using symptom-based diagnostic criteria (4). These Rome-II criteria define defecation disorders in childhood based on presenting symptoms including infant dyschezia, functional constipation, functional faecal retention and functional non-retentive faecal soiling (FNRFS) (table 1). These criteria should help clinicians to standardize the definitions used to categorize constipation and encourage researchers from various fields to study the (patho-) physiology and treatment of similarly defined disorders from different points of view.

Functional non-retentive faecal soiling is a separate entity defined as encopresis in the absence of other clinical and physical signs of constipation. These children have normal total and segmental colonic transit time and normal rectal sensation
Table 1 Childhood functional defecation disorders: ROME II – criteria (4).

<table>
<thead>
<tr>
<th>Diagnostic criteria</th>
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<tbody>
<tr>
<td><strong>Infant dyschezia</strong></td>
</tr>
<tr>
<td>At least 10 minutes of straining and crying before successful passage of soft stools in an otherwise healthy child</td>
</tr>
<tr>
<td><strong>Functional constipation</strong></td>
</tr>
<tr>
<td>In infants and pre-school children at least 2 weeks of:</td>
</tr>
<tr>
<td>1. Scybalous, pebble like, hard stools for a majority of stools, or</td>
</tr>
<tr>
<td>2. Firm stools two or less times/week, and</td>
</tr>
<tr>
<td>3. No evidence of structural, endocrine, or metabolic disease</td>
</tr>
<tr>
<td><strong>Functional faecal retention</strong></td>
</tr>
<tr>
<td>From infancy to 16 years old, a history of at least 12 weeks of:</td>
</tr>
<tr>
<td>1. Passage of large diameter stools at intervals &lt; 2 times/week, and</td>
</tr>
<tr>
<td>2. Retentive posturing, avoiding defecation by contracting pelvic floor and gluteal muscles</td>
</tr>
<tr>
<td><strong>Functional non-retentive faecal soiling</strong></td>
</tr>
<tr>
<td>In children older than 4 years, a history of once a week or more for the preceding 12 weeks of:</td>
</tr>
<tr>
<td>1. Defecation into places and at times inappropriate to the social context,</td>
</tr>
<tr>
<td>2. In the absence of structural or inflammatory disease, and</td>
</tr>
<tr>
<td>3. In the absence of signs of faecal retention</td>
</tr>
</tbody>
</table>

on anorectal function testing (5). The treatment of these patients consists of a strict toilet training regimen only without the use of laxatives (6). In this review on constipation, FNRFS will not be further discussed.

The universally accepted definition for encopresis (from kopros, Greek for stool) is the repeated expulsion of a normal bowel movement, whether involuntary or intentional, in inappropriate places (e.g. clothing, floor) in a child at least four years of age (or equivalent developmental level) (DSM-IV).

In a recent study, the prevalence and applicability of the definitions of defecation disorders in childhood according the paediatric Rome II criteria and according to criteria developed by dr. Loening-Baucke were evaluated in children with defecation disorders (7). According to the Rome-criteria, 64% and 18% of the patients fulfilled the criteria for functional constipation and functional faecal retention respectively, whereas 74% fulfilled the ‘Loening-Baucke’ criteria for paediatric constipation. The low prevalence of functional faecal retention (FFR) was recently confirmed by others (8). The low incidence of FFR might be a result of the subjectivity of the symptom of retentive posturing. Parents are often not able to determine reliably whether their child exhibits stool-withholding behaviour. Moreover, accuracy of responses depends greatly on the way questions are formulated by physicians and the way responses of parents are interpreted. We agree with Nurko that the current Rome-criteria are too restrictive and exclude too many children with constipation (9). The next Rome
criteria should include consideration of encopresis, the most important feature of constipation, encopresis, which is present in 84% of the patients. Uniform application of adequate definitions will allow for better understanding the pathophysiology of constipation, will enhance treatment monitoring and will allow comparison of the outcome of different treatment regimens. International collaboration is necessary to develop and validate standard constipation-questionnaires in which hard to quantify items as amount of stool, consistency of stool and retentive posturing are defined.

**Epidemiology**

Population based studies in adults in Westernized societies and in Asia have estimated that approximately 10-20% of otherwise healthy people report one or more symptoms of constipation (10-13). Little is known about the prevalence of constipation in developing countries (14,15).

To date, the worldwide prevalence figures for constipation in children varies widely and is estimated to range between 0.3 - 28% (16-19). This large range is likely due to the differing criteria used to define constipation and to differing cultural norms regarding acceptable bowel habits. Thirty-four percent of British children 4-11 years of age are reported to have had constipation. Of these, 5% had complaints for more than 6 months (20).

The prevalence of childhood constipation seems to be rising in the last decades (10). In one study of children between 0-9 years of age, the increase in physician visits for constipation was most marked in children less than 2 years of age (21). Whether this was a true increase in prevalence or a result in differences in the rate of seeking medical advice is unclear (22). Others have suggested that the increase in constipation in childhood is due to a decreased fibre intake (23).

Constipation is diagnosed in 3% of all children referred to a general paediatrician (24,25) and this percentage increases to 25% of all children referred to a paediatric gastroenterologist (26-28). Approximately 45% of children referred for gastrointestinal problems to our tertiary hospital in The Netherlands have constipation. In children with cerebral palsy or autism constipation is reported in from 26%-74% (29,30). In very low birth weight infants (<750 g) constipation is very common (32%). When evaluated between 10-14 years of age, these children continue to experience higher
rates of toileting problems such as encopresis and withholding behaviour, and neurodevelopmental impairment when compared with age matched children of higher birth weight (31).

Constipation is usually reported to be more common in boys than in girls, with a 2:1 ratio (32,33). Some studies report an equal prevalence between the sexes (10,19,34,35). In adults, significantly more women than men suffer from constipation and the ratio of women to men increases with age (36,37). In a large population based study from Australia, low-socio-economic status was strongly related to symptoms of constipation (38).

Encopresis is reported in 1.5 – 2.8 % of children older than 4 years. In 10-30% of these children, encopresis is not secondary to constipation but is a manifestation of FNRFS (4). In this group of children boys are more likely to experience this frustrating symptom than girls at a ratio of 9:1 (6,39).

**Physiology of defecation**

Normal anorectal function depends on the complex interplay between muscles of the pelvic floor, the autonomic and somatic nervous system and the group of muscles controlling the anal sphincters. Defecation is elicited by presence of faecal material in the rectum due to peristaltic propagation. Sensory stimuli in the anal canal provoke a sudden drop in the tone of the internal anal sphincter, the recto-rectal inhibitory reflex (RAIR). Recently studies in term and pre-term infants have shown that the RAIR is present in infants older than 26 weeks postmenstrual age (40). The voluntary defecation process is initiated relaxation of the puborectalis and levator ani muscles. Rectal distension induces contractions of the rectum and defecation can be completed by voluntary increase in intra-abdominal pressure. Triggering of receptors in the anal canal by faeces will result in the sensation of imminent faecal loss, giving the person the ability to prevent this loss of faeces 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 (due to rectal compliance) the rectal wall has adapted (distension) to the increased rectal volume. Many children achieve voluntary bowel control around 18 months, but the age at which complete control is attained is variable. Around the age of 3
years, 98% of the children are toilet trained (41). Girls appear to attain both bowel and bladder control earlier than boys (41). Development of bowel and bladder control is a maturational process, which cannot be accelerated by early onset and high intensity of potty-training (42). The child’s initiative proves to be a reliable indicator that the child is developmentally capable of being clean and dry. In one study, bowel and bladder control in term and prematurely born infants were attained at the same age (corrected for prematurity) and the timing was not affected by adverse perinatal events or mild to moderate neurological impairment or psychomotor development (43).

More than 99% of term infants pass the first stool within 48 hours (44). Weaver et al. found an inverse relation between gestational age and the day of the first bowel movement (45). In contrast to term infants, 35% of the infants with a birth weight between 1000–1500 g had delayed passage of the first stool (45).

Stool frequency declines from more than four per day during the first week of life to 1-2 per day at four years of age with a corresponding increase in stool size and weight (46). Approximately 97% of 1-4 year old children pass stool from 0.5 to 3 times daily (47). Black children show higher defecation frequencies and shorter transit times than white children (48).

Another study indicates that defecation frequency in children is highly variable, ranging between 1.4 to 4 times daily in the first weeks of life to 1.2 daily at 4 years of age (49). In the first year, the defecation frequency is higher in breastfed children and children on a diet rich in fibre (45). This is probably due to a difference in fat digestion and absorption between breast and formula fed infants (50). By 16 weeks of age however, both breast-fed and formula-fed children pass an average of 2 stools per day (46,51). The slow decrease in defecation frequency with increasing age suggests a maturation of water conserving ability of the colon (52).

In a sample of 350 children (1-4 years) from a general practice, 85% of children defecated once or twice daily and 96% fell in the range between 3 times per day to once every other day with a mean stool volume of 25 ml (53). In healthy African children aged 6 months to 5 years, 95% defecated one to three times a day with a mean volume of 50-75 ml per stool (54). In comparison to Western children, Non-Western children pass larger, softer, and more frequent stools (54-56). Generally, at the age of 4 years the defecation frequency of children equals that of adults and ranges from three bowel movements per day to 3 per week (46,57).
Table 2 The ‘Loening-Baucke criteria’ (3).

<table>
<thead>
<tr>
<th>Paediatric Constipation</th>
<th>At least two of the following criteria,</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Defecation frequency less than 3 times a week</td>
<td></td>
</tr>
<tr>
<td>2. Two or more encopresis episodes per week</td>
<td></td>
</tr>
<tr>
<td>3. Periodic passage of very large amounts of stool once every 7-30 days</td>
<td></td>
</tr>
<tr>
<td>4. A palpable abdominal or rectal mass at physical examination.</td>
<td></td>
</tr>
</tbody>
</table>

(The criterion of a large amount of stool is satisfied if it is estimated to be twice the standard amount of stool, shown in a clay model, or if stools are so large that they clog the toilet.)
Chapter 2

Pathogenesis

The pathophysiology of functional constipation is undoubtedly multi-factorial, and not well understood. Difficulties with defecation can result from abnormal function of the different players involved, including the colon, the rectum and the sphincter complex and not least the will of the child. Severe behavioural problems do occur in constipated children, but they are usually mild and seem to be secondary to bowel dysfunction (58-60).

Table 3 summarizes the most common causes of constipation in infants, toddlers and adolescents. In more than 90% of all age groups no obvious cause can be identified. In some babies, an acute episode of constipation may occur associated with a change in diet (i.e. human to cow’s milk) (61). Passage of dry and hard stools may cause anal fissures and pain. In ‘infant dyschezia’ it is hypothesized that neonates fail to coordinate increased intra-abdominal pressure with relaxation of the pelvic floor (4). This phenomenon is part of the child’s learning process for which no intervention is indicated. Genetic predisposition may play a role since constipation often dates back to the first months of life, and many patients have a positive family history of constipation (62-65). Recently, delayed maturation of the interstitial cells of Cajal was suggested to be involved in two neonates with constipation and abdominal distension (66). The most common condition in infancy that must be differentiated from idiopathic constipation is Hirschsprung’s disease (66).

Retentive posturing is probably the major cause for the development and/or persistence of constipation in the toddler period (17). The time of toilet training is an especially critical period when constipation may occur as a consequence of a struggle between child and parents (67). Interestingly, Borowitz et al., found no association between the development of early childhood constipation and the timing, style or techniques used for toilet training (68). Other causes of stool withholding are: 1) the previous passage of large, hard or painful stools, 2) anal fissures, 3) significant behavioural problems, 4) lack of time for regular toileting and 5) distaste for toilets other than the child’s own (22). When the retentive toddler experiences the urge to defecate, he assumes an erect posture and holds the legs stiffly together to forcefully contract the pelvic and gluteal muscles. Consequently the rectum accommodates to its content and the urge to defecate disappears. The retained stools become progressively more difficult to evacuate leading to a vicious circle in which the rectum is increasingly distended by large faecal contents. Finally chronic
rectal distension may cause overflow soiling, loss of rectal sensitivity and in the end loss of normal urge to defecate. This aberrant behaviour may lead to the unconscious contraction of the external sphincter during defecation (also known as anal sphincter dyssynergia) (32). Approximately 50% of children and adults with constipation have this abnormal defecation pattern. This paradoxical contraction of the anal sphincter complex has been considered by some to be the major pathophysiological mechanism of childhood constipation. However, normalization of this pattern with biofeedback training does not correlate with successful treatment outcome (32,69).

It is not clear that chronic postponement of defecation with rectal accumulation of faeces actually produces subsequent abnormalities in rectal sensation, compliance and motility, or whether these abnormalities are primary to the condition (69).

An overall delay in colonic transit time, slow transit constipation, objectified by colonic transit time measurements, is described in a minority of young women and adults with chronic constipation (70,71). This might be due to dysfunction of the muscles of the colonic wall (resulting in non-powerful contractions) or to dysfunction of the enteric nervous system (resulting in non-coordinated motor activity) (72). In children however, it might also be possible that delay in colonic transit time is also a phenomenon secondary to massive faecal retention in the rectum.

Some histopathologic studies in adults with slow transit constipation have suggested that decreased numbers of argyrophilic neurons are found in colonic tissue. Other studies have suggested that there is dysfunction of the intrinsic neural control secondary to alteration of the colonic cholinergic activity or to non-specific abnormalities of axonal structures, ganglion cells and the neuronal plexus (73,74). Recently, a reduction in the number of interstitial cells of Cajal was suggested to play a role in the pathophysiology of gastrointestinal motility in adults with slow transit constipation and in one child with severe constipation (75-77). However, Hasler suggested that the reduction of ICC’s might be secondary to an undefined injury and not the cause of slow transit constipation (78).
### Table 3 Etiology of constipation.

<table>
<thead>
<tr>
<th>Infants &amp; toddlers</th>
<th>Adolescents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Anal fissures</td>
<td>Inadequate food intake</td>
</tr>
<tr>
<td>Breast Feeding &amp; Bottle feeding</td>
<td>Anorexia nervosa</td>
</tr>
<tr>
<td>Cow’s milk allergy</td>
<td>Slow transit constipation</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>Diabetes Mellitus</td>
</tr>
<tr>
<td>Stool withholding behaviour</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td>Lack of fibres</td>
<td>Hypercalcaemia</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>Sexual abuse</td>
</tr>
<tr>
<td>Pseudo-obstruction</td>
<td>Drugs:</td>
</tr>
<tr>
<td>Hirschsprung's disease</td>
<td>Opiates</td>
</tr>
<tr>
<td>Neuronal intestinal dysplasia</td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Anorectal malformations</td>
<td>Antidepressants</td>
</tr>
<tr>
<td>Spina Bifida</td>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td></td>
<td>Scleroderma</td>
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<tr>
<td></td>
<td>Amyloidosis</td>
</tr>
<tr>
<td></td>
<td>Neoplasia</td>
</tr>
<tr>
<td></td>
<td>Parkinson’s disease</td>
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<tr>
<td></td>
<td>Depression</td>
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</table>
Clinical signs and symptoms of constipation
The majority of children with constipation have reduced frequency of defecation, in combination with encopresis, passage of large stools, hard stools, retentive posturing and painful defecation (21,71,79,80)(Table 4). The involuntary leakage of faeces may occur several times a day and in some severe cases with large rectal impactions it may also occur at night (71). Encopresis is a source of considerable embarrassment for the child who must deal with taunting by peers (80). Parents often feel that the child is to blame for encopresis citing such behavioural aspects as laziness, carelessness, immaturity and emotional problems as important factors. Encopresis is associated in the child with low self-esteem, depression, social withdrawal, shame, fear of discovery and anger. Although children chronically deny the problem, recent reports indicate that the overt denial is decreasing and that fewer children hide their soiled underwear (80). It is not surprising that children with constipation and encopresis have more behavioural problems than healthy controls. The behavioural problems, however, are usually mild, and referral to mental health services is rarely needed. Moreover, behavioural profiles in these children significantly improve after successful treatment (39).

In children with very infrequent passage of stool, there may be a pattern of intermittent passage of huge volume stools which may obstruct the toilet.

Table 4 Common clinical presentation of constipation (21,33,57,71,79,207).

<table>
<thead>
<tr>
<th>Feature</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soiling / encopresis</td>
<td>75-90</td>
</tr>
<tr>
<td>Defecation frequency &lt; 3/wk</td>
<td>75</td>
</tr>
<tr>
<td>Large stools</td>
<td>75</td>
</tr>
<tr>
<td>Straining during defecation</td>
<td>35</td>
</tr>
<tr>
<td>Pain during defecation</td>
<td>50-80</td>
</tr>
<tr>
<td>Retentive posturing</td>
<td>35-45</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>okt-70</td>
</tr>
<tr>
<td>Anorexia</td>
<td>okt-25</td>
</tr>
<tr>
<td>Vomiting</td>
<td>10</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>25</td>
</tr>
<tr>
<td>Enuresis / Urinary tract infection</td>
<td>30</td>
</tr>
<tr>
<td>“Psychological problems”</td>
<td>20</td>
</tr>
<tr>
<td>Physical examination</td>
<td></td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>20-40</td>
</tr>
<tr>
<td>Abdominal mass</td>
<td>30-50</td>
</tr>
<tr>
<td>Anal prolapse</td>
<td>3</td>
</tr>
<tr>
<td>Fissures / haemorrhoids</td>
<td>mei-25</td>
</tr>
<tr>
<td>Faecal impaction</td>
<td>40-100</td>
</tr>
</tbody>
</table>
evacuation of these large stools is often preceded by an increase in encopresis frequency and by complaints of abdominal pain and poor appetite. These symptoms disappear immediately after defecation. Between 10–70% of children with constipation complain of non-specific abdominal pain (32). Urinary tract infections and enuresis are reported in 30% of constipated children. The majority of constipated children have palpable abdominal masses and/or faecal impaction of the rectum on physical examination (7). Although at least one digital examination is recommended by experts in the field, this procedure is not performed routinely since many paediatricians consider repeated rectal examinations invasive and unethical (81,82).

Investigations
A careful medical history together with a thorough physical examination is all that is needed for diagnosis and treatment of most children with constipation. Symptom diaries (for diagnostic evaluation and monitoring treatment); colon transit studies (to confirm the patient’s complaints and to assess slow transit and regional delay) and anorectal manometry (to exclude Hirschsprung’s disease) are sometimes useful. In a recent study, MRI of the spine revealed spinal abnormalities in 10%. Follow-up of these children indicated that constipation improved after neurosurgical treatment (83).

Medical history
The medical history of children with constipation should include questions about the time after birth of the first bowel movement to discriminate functional constipation from Hirschsprung’s disease. Often one elicits a history of constipation beginning when an infant was weaned from breast feeding to a cow milk-based infant formula. Subsequently, age of onset of bowel problems, stool frequency, the consistency and size of stools, whether defecation is painful, whether blood has been present on the stool or the toilet paper and retentive posturing are issues to be questioned. Information about the encopresis frequency, the time of occurrence (day and/or night) and the situation in which encopresis occurs (behind the computer, when playing outside) is of major importance. Abdominal pain, loss of appetite, urinary tract problems, fever, nausea, vomiting, weight loss or poor weight
gain, neuromuscular development and psychological or behavioural problems should be assessed. Dietary history and the history of previous treatment strategies for constipation should also be determined. Finally, it is essential to ask for life events, such as death in the family, birth of a sibling, school problems and sexual abuse which might contribute to the development of retentive behaviour.

A stool diary is helpful to obtain reliable information from the patient, although the reliability of the recall of bowel habits is still under debate (84,85). One study in children with constipation suggested that the recall of the child and/or the parent is adequate and provides a good basis to evaluate treatment (86).

Physical examination
Complete physical and neurological examination should be performed in all children with defecation disorders. Abdominal examination sometimes gives valuable information concerning accumulation of gas or faeces. Perianal inspection provides information about the position of the anus, perianal faeces, redness, dermatitis, eczema, fissures, haemorrhoids and sexual abuse (scars). The anorectal digital examination assesses perianal sensation, anal tone, the size of the rectum, the amount and consistency of stool in the rectum, the voluntary contraction and relaxation of the anal sphincter and the presence of an anal wink.

Anorectal manometry
Anorectal manometry measures pressures in the anorectal region and is used to obtain selected information concerning anorectal function in children with constipation. Many investigators perform these studies, but lack of standardization in methods (open-tipped perfusion, closed triple-balloon, pressure transducers) has resulted in conflicting data (2,87). The main indication to perform anorectal manometry is to demonstrate the presence of the recto-anal inhibitory reflex (RAIR). The presence of the RAIR (relaxation of the internal sphincter induced by transient distension of the rectum) excludes Hirschsprung’s disease. False positive results may be due to technical factors such as insufficient insufflation of the distending balloon or an incorrect position of the catheter in the sphincter complex. The RAIR might also be absent in children with megarectum (88). In crying infants, artefacts
are common and results should be interpreted with caution. Rarely, the absence of the RAIR in the presence of ganglion cells is indicative for internal anal sphincter achalasia (89). Compared to functional constipation children with internal anal achalasia have less encopresis and less withholding behaviour. In this small group of children, botulinum toxin (15-25 U per quadrant) may be a safe and effective short-term treatment (89).

Studies using anorectal manometry have shown an increased threshold for rectal sensation in up to 70% of constipated children, particularly those with megarectum (90-93). The finding that the afferent pathway from the rectum is abnormal in constipated children further underscores that impaired rectal sensation should be considered as an important pathophysiological mechanism in childhood constipation (94). Compliance of the rectum and the age of the child will significantly influence the threshold for sensation measured as volume. Therefore, children with an increased rectal compliance will be incorrectly considered to have an increased threshold for sensation. The rectal volume at which sensation is perceived strongly depends on rectal compliance. A recent rectal barostat study using pressure controlled distension showed decreased rectal sensation in only 7% of the children with constipation (95). More than 50% of these children had an abnormal compliance. Surprisingly rectal faecal impaction was not predictive for an abnormal compliance.

Some studies have found no significant difference in the anal sphincter resting tone of constipated children and controls (32,34,91), while others found a significantly higher or significantly lower resting anal sphincter pressure in constipated children (27,96). External anal sphincter pressures change during expulsion of an anorectal catheter can be used to investigate the existence of pelvic floor dyssynergia. Pelvic floor dyssynergia occurs in more than 50% of the constipated children (32,33,69). It is, however, doubtful whether a manometric pattern indicative of dyssynergia alone is a sufficient diagnostic criterion. In a study in adults, when manometry indicated dyssynergia, defecography was in agreement in only 36% of patients. On the contrary, when manometry indicated normal expulsion, defecography could only confirm this in 88% of the time (97). No relationship between dyssynergia patterns and colonic transit times or patients complaints of infrequent defecation or defecatory difficulty was found in a study in constipated children (58,98).
Colonic manometry
Although colonic manometry is not any longer an experimental technique (81), and is considered an appropriate diagnostic modality for childhood defecation disorders, only one paediatric group has long standing experience with this procedure (99). Colonic manometry can be used to discriminate between functional and the rare neuromuscular causes of severe and therapy resistant constipation (99). Markers for normal motility are the presence of High Amplitude Propagated Contractions (HAPC's) and the presence of a gastro-colonic response to a meal. HAPC's are well organised peristaltic sequences important in the propulsion of colonic contents.

In patients with functional constipation, colonic motility is normal. Children with absent or weak colonic contractions, in the absence of generalised colonic dilatation, are more likely to have a colonic myopathy. In patients with colonic neuropathy the gastro-colonic response is absent and HAPC's are abnormal, disordered or absent (100).

In 146 children with chronic defecation disorders, 4 main indications for colon manometry were identified: clarifying the pathophysiology of lower GI symptoms in general (68%), clarifying the pathophysiology of persisting lower GI symptoms after surgery for Hirschsprung's disease, confirmation of the diagnosis intestinal pseudo obstruction (11%), and deciding about re-anastomosis of a diverted colon (7%) (99). Based on the results of the colonic manometry, recommendation to adjust therapy (mostly surgical) were made in 93% of these patients. A possible drawback of colonic manometry in paediatric patients is the lack of colonic motility data in healthy children. In addition, the procedure requires a lot of experience, which cannot be obtained in routine practice (101).

Abdominal X-ray and colonic transit studies
Conflicting data exist concerning the value of an abdominal x-ray in the diagnosis of constipation. Different scoring systems exist to assess faecal loading in constipated children (102-104). Inter-observer reliability has been variable in studies using x-ray to quantitate faecal retention (105-107). Although all referenced studies were performed by experienced paediatric and adult radiologists and paediatric gastroenterologists, the interpretation of radiological findings are difficult and subjective. An abdominal x-ray might only be helpful when there is doubt about whether a patient is constipated, in a child who is obese or refuses a rectal
examination, or in whom there are psychological factors such as sexual abuse that make rectal examination inappropriate and traumatic.

Assessment of total- and segmental colonic transit time (CTT) using radio-opaque markers more accurately and reliably provides information about colorectal motor function in defecation disorders (108). The marker technique is used to localise the delay in colonic transit and is helpful if bowel history is unreliable. In adults as well as in children, a good relation is found between symptoms of constipation and colonic transit time (CTT) (98,109,110). We use the Bouchoucha method, in which a segmental and total CTT is calculated from a single x-ray obtained on day 7 after ingestion of markers on the previous 6 consecutive days (111). Segmental transit time is obtained by multiplying the number of markers in the segment of interest (the numbers of hours in a day divided by the number of markers ingested). Before the study, the child should be on a high fibre diet but should not take oral or rectal laxatives that may affect bowel function.

Several studies have reported normal values for CTT in healthy children (34,108,112-115). Two Italian studies reported short values for the upper limit for total CTT based on the mean plus 2 SD (25 and 32 hours), whereas a recent study from the UK using the Bouchoucha method reported 84 hours as upper limit (34,114,115).

Studies in adults and children with constipation show different colonic transit patterns 1) normal colonic transit time: normal transit through all colonic segments, 2) outlet obstruction: delayed transit through the anorectal region and 3) slow transit constipation: prolonged transit through the entire colon. Normal CTT's are measured in 39% to 58% of constipated children (96,106,116). The most common type of delayed CTT in children is outlet obstruction at the level of the rectum (106,117).

The marker test is useful to differentiate between children with constipation and children with functional non-retentive faecal soiling (4). Children with FNRFS have a normal CTT and have normal values upon anorectal manometry. A normal CTT in combination with a normal defecation frequency without a rectal mass on physical examination confirms the diagnosis FNRFS (5). These children are best treated with a strict toilet training program and should not be treated with oral laxatives since it increases the encopresis frequency (6).
Treatment

Although childhood constipation is the most common complaint in childhood gastrointestinal disease, no large, randomised, placebo controlled trials are available (118,119). Currently, there is no information concerning the maximum dose, duration and long-term side effects of any compound used in the treatment of childhood constipation. Therefore, the treatment of these children is mainly based on clinical experience and usually consists of a behavioural strategy and oral and sometimes rectal laxatives. The behavioural component usually includes structured toilet training and keeping a bowel diary. At this time, the conditions characterised in the Rome-II criteria as functional constipation and functional faecal retention are not known to respond differently to therapy.

The treatment of acute simple constipation consists of dietary advice, review of a diary and appropriate toilet training. The treatment of chronic constipation in childhood is based on 4 important phases: 1) education, 2) disimpaction, 3) prevention of re-accumulation of faeces and 4) follow up.

It is important to treat constipation early in childhood to prevent development of severe constipation or encopresis or both (17). Large studies in the US and Great Britain showed that constipated children < 2 years of age responded better to treatment than children > 2 years of age.

Treatment of acute simple constipation

Dietary measures

For most infants with acute simple constipation, dietary measures, including an increase in fluid and carbohydrate intake often correct the problem. Toddlers and older children usually respond to an increase in fluid and fibre intake (120).

Diary

The child, with help of the parents, fills out a diary to objectify complaints, to quantify therapeutic progress and to enhance motivation. This stresses once more that the child is responsible for his/her own defecation problem. The diary chart is linked to a rewarding system.
Toilet training
Another simple general measure to normalize defecation is toilet training. The child is instructed to attempt to defecate after meals three times daily for 5 minutes. The child is stimulated to strain actively while placing his feet on a footrest. This is important to flatten the anorectal angle, which facilitates faecal expulsion. In one study, 15% (54 children) with constipation referred to a tertiary hospital was successfully treated by a combination of counselling, education and toilet training (86).

Treatment of chronic constipation
Counselling and education
Intensive support, education, and reassurance of the children and parents in combination with a non-accusatory approach of the physician and parents is crucial at the beginning of medical treatment for defecation problems (121). Counselling should be provided regarding normal bowel movements and its huge range within the population, the aetiology of constipation, and its prevalence in childhood. The caretaker should explain that a delay in bowel movements for several days or weeks causes discomfort for the child and often results in the involuntary loss of faeces in the underwear. Before treatment is started, it should be stressed that progress of treatment is often irregular and marked by periods of improvement alternating with deterioration while the duration of maintenance therapy usually requires 6 to 24 months (63,122).

Dietary measures
There are no large randomised controlled trials proving efficacy of increased fluid intake, non absorbable carbohydrates or oligosaccharides in infants and children with chronic constipation. In two small studies in 11 healthy children and 15 adults, an increase in fluid intake (1.5 l/day) resulted only in an increase in urine production and had no impact on consistency or frequency of the stools (123,124).

Some practitioners feel that feeding formula without iron-fortification prevents the development of constipation. However, a randomised controlled trial in 93 term infants showed no difference in the number of stools per day, the consistency
of the stools or gastrointestinal side effects such as abdominal cramps receiving formula with and one without iron fortification (125).

In a double blind cross-over study of 65 infants between 11 and 72 months, Iacono et al. showed disappearance of symptoms of constipation in 65% of cases after a switch from cow’s milk to soy milk (61). Symptoms reappeared within 5 to 10 days when 44 of the infants switched back to cows milk a month later. It is unclear from this study if constipation is a manifestation of intolerance to cow’s milk. It might be that lactose malabsorption leads to loose stools, perianal erythema with pain which finally leads to withholding behaviour and constipation. These interesting findings by Iacono et al. have to be confirmed in larger samples before elimination of cow’s milk becomes a routine procedure in children with constipation. In our daily practice, we rarely observe the relation between cow’s milk protein allergy and constipation.

The recommended fibre intake in children over 2 years of age is calculated as the age in years plus 5 grams/day (126). The association between fibre intake and constipation is still controversial. Two case control studies in children showed a lower fibre intake in constipated children compared to healthy controls (127,128). Discriminant analysis showed that only fibre intake was independently correlated with constipation (127). On the other hand it has been demonstrated that constipated children do generally not consume less fibres than healthy persons and treatment with increased fibre intake did not result in large clinical effects (56,129-131). Side effects such as intolerance, tastelessness of the fibre product may lead to poor compliance.

Recently, two small double-blind placebo controlled trials in 20 neurologically impaired constipated children and in 31 otherwise healthy constipated children showed beneficial effects of glucomannan (a fibre gel polysaccharide from the tubers of the Japanese Konjac plant that has no unpleasant taste or smell) 100mg/kg body weight (maximum 5 g/day) on defecation frequency, stool consistency, soiling episodes, suppository use and side effects (131,132). Although the defecation frequency significantly increased after glucomannan intake, no correlation between fibre intake and transit time was shown. Although the authors suggest continuing to recommend increasing the fibre intake in children with constipation, larger clinical trials have to confirm the outcome of these studies.
Chapter 2

Disimpaction
Rectal disimpaction prior therapy is generally accepted to be necessary before other maintenance therapy can be effective. If initial disimpaction is omitted, treatment with oral laxatives will paradoxically result in an increase in encopresis due to overflow diarrhoea and an increase in abdominal pain and bloating. Uncontrolled trials have described successful disimpaction by the oral route, the rectal route or a combination of the two (133-136).

PEG at a dose of 1.5g/kg/d for 3-4 days has been successfully and safely used for faecal disimpaction in children (135,136)(Table 5). No abnormalities in the electrolyte profile, serum osmolality or renal function tests were reported. In our own practice, patients with severe rectal impaction are initially treated by administering enemas for 3 consecutive days before oral laxatives are started (63). In practice, enemas with lower volumes will be prescribed to children less than 10 kg of bodyweight, whereas older children receive larger volume enemas (sodium-dioctylsulfosuccinate and sorbitol or phosphate-enema) (Table 5). In rare cases in which the defecation frequency does not normalize with adequate oral treatment, and in those patients with untreatable encopresis, the regular use of enemas is sometimes needed. The effect, however, of long-term administration on the rectal mucosa has never been studied properly (137). A report on side effects of commonly used laxatives, indicated that sodium docusate enema can produce structural changes in the gut mucosa in humans and even damage to the myenteric plexus in an animal model (138). However, the clinical significance of these observations is still not known. The application of Fleet enema (sodium biphosphate) can result in serious hyperphophataemia and hypocalcaemia, especially in younger children (139,140) and can also alter the appearance of the rectal mucosa (141).

Maintenance therapy (prevention of re-accumulation of faeces)
Once disimpaction has been achieved, it is essential to begin an oral daily laxative immediately and continue treatment for months or longer to prevent re-accumulation of retained stools and recurrence stool withholding behaviour. The correct dose is that which produces a daily soft stool without side effects.

Osmotic laxatives
There are no placebo-controlled trials of osmotic laxatives in children (119). The
<table>
<thead>
<tr>
<th>Laxative</th>
<th>Dosage</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactulose</td>
<td>1-3 ml / kg 1 or 2 times daily</td>
<td>Flatulence, abdominal pain</td>
</tr>
<tr>
<td>Lactitol</td>
<td>5-40 gr / 1 or 2 times daily</td>
<td>Flatulence, abdominal pain</td>
</tr>
<tr>
<td>Magnesium oxide</td>
<td>500-2000 mgr / day</td>
<td>Hypermagnesaemia, due to concurrent renal failure</td>
</tr>
<tr>
<td>Milk of Magnesia</td>
<td>&gt; 6 months: 1-3 ml / kg / day (divide into 1-2 doses)</td>
<td>See Magnesium oxide</td>
</tr>
<tr>
<td>PEG 3350 - 4000 Maintenance</td>
<td>0.26 - 0.84 / gr / day</td>
<td>Loose stools, bad taste (PEG + additional electrolytes)</td>
</tr>
<tr>
<td>PEG 3350 Disimpaction</td>
<td>1-1.5 gr / kg / day (3 to 4 days)</td>
<td>Loose stools, bloating/flatulence, nausea, vomiting</td>
</tr>
<tr>
<td>Mineral oil (liquid paraffin)</td>
<td>&gt; 12 months: 1-3 ml / kg / day (maintenance)</td>
<td>Bad taste, anal leakage, aspiration pneumonia (&lt; 12 months, dysphagia)</td>
</tr>
<tr>
<td></td>
<td>Disimpaction: 30ml/10 kg body weight</td>
<td>Flatulence, bloating, nausea</td>
</tr>
<tr>
<td></td>
<td>Or: 15-30 ml orally per year of age per day</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Max.: 240 ml 1 or 2 times daily for 3 days</td>
<td></td>
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<tr>
<td>Barley Malt extract</td>
<td>5-10 ml in 60-120 ml of water / juice 2 times daily (breast fed infants)</td>
<td>Abdominal cramps, abdominal pain, diarrhoea</td>
</tr>
<tr>
<td></td>
<td>2-10 ml per 240 ml of milk / juice (bottle fed infants)</td>
<td></td>
</tr>
<tr>
<td>Bisacodyl Oral</td>
<td>5 mg every other day-10 mg daily</td>
<td>Abdominal cramps, anal irritation abdominal pain</td>
</tr>
<tr>
<td>Bisacodyl Rectal</td>
<td>5 mg suppositories (3 days)</td>
<td></td>
</tr>
<tr>
<td>Glycerin suppositories</td>
<td>&lt; 6 years: 1 paediatric supp. (1 gr)</td>
<td>Anal irritation</td>
</tr>
<tr>
<td></td>
<td>≥ 6 years: 1 adult supp. (2 or 3 gr)</td>
<td></td>
</tr>
<tr>
<td>Sodium docusate + sorbitol enema 'Klyx'</td>
<td>&lt; 6 year: 60 ml, &gt; 6 years: 120 ml</td>
<td>Abdominal cramps</td>
</tr>
<tr>
<td>Sodium bisphosphate enema 'Fleet'</td>
<td>&gt; 20 kg, adult size enema</td>
<td>In case of renal problems or M. Hirschsprung: Hyperphosphataemia, other electrolyte disturbances</td>
</tr>
</tbody>
</table>
Table 5 continued

<table>
<thead>
<tr>
<th>Laxative</th>
<th>Dosage</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium laurylsulfoacetate enema</td>
<td>Infants &lt; 10 kg</td>
<td>Anal irritation</td>
</tr>
<tr>
<td>'Microlax'</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Senna</td>
<td>1-5 years: 5 ml 1 to 2 times daily</td>
<td>Abdominal cramps, melanosis coli, yellowish-brown urine</td>
</tr>
<tr>
<td>Senokot syrup</td>
<td>&gt;5 years: 10 ml/day</td>
<td></td>
</tr>
<tr>
<td>(granules/tablets)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lavage PEG 3350</td>
<td>15.5-183 ml/kg</td>
<td>Nausea, vomiting, abdominal cramps, pulmonary aspiration/ oedema</td>
</tr>
<tr>
<td>orally/NG-tube</td>
<td>first stool after 2.8 hours</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1-1.5 g /kg/day (3 to 4 days)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>first stool after 1.89 days</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from: (122,134-137,147,148,151,158,165,166,208-210).

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). The adequate dose should be continued for at least 3 months (142). Long-term administration in adults appears to have no adverse effects and a ‘rebound effect’ is not described (143) although repeatedly expressed by parents of children using synthetic disaccharides (137).

Two small randomised controlled trials compared lactitol and lactulose, both disaccharides derived from lactose (144,145). Both compounds were equally effective in increasing defecation frequency and normalizing stool consistency. Perkins et al. compared the effect of lactulose with senna (146). In this unblinded small crossover study both compounds proved to be effective in improving the defecation frequency, although senna had a higher rate of side effects, particularly abdominal pain and diarrhoea.

Other frequently prescribed osmotic laxatives are magnesium hydroxide, and to a lesser extent, magnesium sulphate. These poorly absorbed salts act either by osmosis or by a secretory effect on prostaglandins or gut hormones (CCK) thereby enhancing colonic motility (137,147). In the US the prescription is referred to as ‘milk of magnesia’ and the recommended dose ranges from 1-2 ml/kg bodyweight (148).

For a decade polyethylene glycol electrolyte solutions have been successfully and safely used to rapidly clean the colon of adults and children with refractory constipation (134,149-151). Therefore, it was used as a lavage solution in patients.
undergoing an endoscopy (152,153). More recently, small doses of polyethylene-glycols (PEG's) have been suggested as alternative laxative in adults as well as in children with constipation.

PEG's are non-absorbable compounds with high molecular mass, and are not metabolised by colonic bacteria. They act by osmosis and volume expansion in the large intestine (154). PEG appears safe as the polyethylene glycol recovery in urine is minimal and similar for normal (0.06%) and inflammatory bowel subjects (0.09%) (155). Small enteric losses of electrolytes have been observed, but only amount to a small fraction of normal daily dietary intake (156). It is proposed that PEG's are effective compared to other laxatives. Because no colonic metabolisation or fermentation is to be expected it is assumed that PEG's exert their function with fewer side effects.

In children, uncontrolled (148,157,158) and unblinded (159) studies have been performed assessing the effect of PEG. These studies report the effect of PEG at low doses; with mean effective doses ranging from 0.6 to 0.8 g/day (158). One study comparing PEG to lactulose in children reported an equal effect on stool frequency, stool consistency and straining in both groups. The encopresis frequency was not mentioned in this study (159). Parents rated the improvement of their child higher while receiving PEG compared to lactulose as 87% vs. 46%. Side effects are mild in all paediatric studies, with excessively loose stools being the most frequent side effect.

Besides the effects of PEG in daily use, it has also been studied for the removal of faecal impaction in severely constipated children (134,135,150). In a study by Ingebo et al. full colonic clean out was achieved without clinically important changes in laboratory values. This result was confirmed by Tolia et al. who compared PEG with mineral oil. A more recent study showed that a three day course of PEG 3350 was safe and effective in the treatment of childhood faecal impaction at doses between 1 and 1.5 g/day (135).

In adults, four large randomised controlled and double blinded trials compared PEG to placebo (149,160-162). Three studies (149,160,162) showed that PEG was superior to placebo with respect to defecation frequency and mean stool consistency. Different dosages are provided as proper dose, when given once: 68 g, another study suggested 223-446 g/day. Only the Andorsky et al. trial showed difference in side effects between both groups.
Two studies compared PEG to lactulose and showed that overall improvement was higher in the PEG group. Clinical tolerance was similar in both groups (163). Freedman et al. (164) showed that both lactulose and PEG were effective in reducing the number of hard stools in opiate induced constipation. Moreover, although not statistically significant, placebo reduced constipation as well (when compared to baseline).

In children one double blinded, randomised controlled trial has been performed (165) showing that PEG and lactulose both significantly increase defecation frequency and decrease encopresis frequency. Success (defined as a defecation frequency of 3 or more / week together with an encopresis frequency of once per 2 weeks or less) was more present in the PEG group (56% vs. 29%) after 8 weeks. Abdominal pain, straining, and pain on defecation were reported significantly less, however more children on PEG complaint about the bad taste. In the children who were successful on PEG the dosage was 0.26 ± 0.11 g / kg /day.

There is evidence that PEG is of value in the treatment of constipation in children. Most data come from uncontrolled studies. The randomised controlled studies show that PEG is at least as potent as lactulose. More randomised controlled trials have to confirm these observations (166).

**Stimulant laxatives**

An osmotic laxative as mono-therapy for chronic constipation is often not sufficient, and additional medication, such as the stimulant laxative bisacodyl or senna may be useful. Again there are no placebo controlled RCT’s which evaluate the efficacy of stimulant laxatives in constipated children (119). Sondheimer et al. compared senna with mineral oil and showed that 11 of 19 children treated with mineral oil discontinued regular medication after 6 months compared to only 4 of 18 using senna (167). Long term use of stimulant laxatives in adults has been associated with apoptosis of colonic epithelial cells with accumulation of phagocytic macrophages containing cellular remnants, but these are not pigmented (168). Apart from these changes, there does not appear to be any evidence that that long-term treatment with stimulant laxatives causes adverse effects on colonic motility in rats (169). Although infrequent, small doses of stimulant laxatives are unlikely to cause significant harm, it is wise to avoid long-term use of these compounds. In contrast to earlier believes mineral oil is inadequate to deplete
tissue stores of fat soluble vitamins (170). Mineral oil is contraindicated in children less than 12 months and in children with a risk for pulmonary aspiration (171).

Prokinetics
Good results of the prokinetic cisapride (4 dd 0.2 mg/kg) have been reported in small randomised studies (172) with a significant higher success percentage compared to placebo (76% vs. 37%) (172). However, since serious side effects, such as prolonged QTc-interval have been described the use of Cisapride in the treatment of childhood constipation is rare.

Behavioural therapy
The aim of a combination of behavioural treatment (toilet training in combination with a rewarding system, diminishing of toilet phobia), cognitive (psychotherapy, cognitive therapy and family therapy, or educational intervention) and laxative treatment is to lower the level of distress and develop or restore normal bowel habits by positive reinforcement, preservation of self-respect and encouragement of the child and parents during the treatment (173).

In a large prospective randomised controlled trial in 162 constipated children, a higher cure rate was found in children receiving behavioural intervention (toilet training, positive reinforcing scheme and dietary advice) plus laxatives (microlax, oral and rectal bisacodyl, followed by a long-term treatment of mineral oil plus phenolphthalein compared to those receiving behavioural intervention alone at both 6 and 12 month of follow-up. In a randomised controlled trial in 87 constipated children (8.6 ± 2.0 years) enhanced toilet training (intensive medical treatment plus behaviour management) was although not statistically significant more effective than either intensive medical treatment or biofeedback training (174). There is some evidence that enhanced toilet training (promoting regular toilet visits combined with education and reinforcement) via internet in combination with laxatives results in more success (less encopresis and higher defecation frequency) than is unspecified routine medical care only (175,176).

Psychological referral is indicated in children who fail intensive medical treatment and in those with severe emotional problems or serious family problems. In these patients it is preferred to combine psychiatric and paediatric treatment strategies.
Biofeedback training

It has almost been 25 years since the publication by Olness et al of their experience with biofeedback training to treat constipation and faecal incontinence in childhood (177). Biofeedback is a habit training, based on reinforcement and derived from a psychologic learning theory (178). Biofeedback devices in children with defecation disorders use anorectal monitoring instruments to amplify selected physiological processes to make previously unavailable physiologic information accessible to the subjects' consciousness. In constipated patients biofeedback is proposed to enhance rectal sensation in patients with sensory deficit, to strengthen and improve control of the external anal sphincter and to better coordinate muscle contraction and relaxation to achieve continence and adequate defecation. In more than 50% of children with defecation disorders, the external anal sphincter and puborectalis muscle contracts instead of relaxes during defecation (32,69,179).

Many uncontrolled studies in children with constipation show that adequate contraction of the external sphincter or normalisation of abnormal defecation dynamics can be achieved by biofeedback training (90,180-182). These studies suggest that normalisation of abnormal sphincter contraction results in the remission of constipation. (90,180-184). The success rates of biofeedback training in these studies vary between 50-100%. However, these small studies with selection bias often have no clear definitions to define constipation or successful outcome. Moreover, some investigators have suggested that non-specific factors associated with biofeedback training such as the intensity of treatment, the relationship with the investigator and patient and the professional attention, bias the outcome of treatment. To date, five controlled studies have been performed in constipated children (3,32,179,185,186). Two of these studies included very small numbers of children (185,186). A study by Loening-Baucke showed a significant short-term effect of biofeedback but the follow-up in these constipated children did not support an additional effect of biofeedback compared to conventional treatment. We previously showed that normalisation of defecation dynamics is not related to successful outcome in a large randomised, controlled study with 192 constipated patients (32). The improvement of the sensation of urge did not lead to a higher success rate compared to children receiving medical therapy only. The role of biofeedback training in the treatment of defecation disorders in children therefore seems limited.
Surgery

The majority of children and adolescents with constipation are successfully treated with a conventional regimen as described earlier. However, some patients with long-lasting medically resistant constipation requiring manual evacuations and hospitalisations, patients who refuse medication and those with documented abnormalities in colonic motility may benefit from surgery (187,188). Anorectal myectomy, antegrade continence enema (ACE), partial colon resection and colectomy are surgical procedures which are used in the treatment of these children.

In one study, only 30% of the constipated patients had long-lasting improvement after anorectal myectomy, and faecal incontinence was an important complication (189). Sphincterotomy appears only to be indicated as a primary or secondary procedure in children with Hirschsprung’s disease (190). In recent years, the appendico-caecostomy (Malone stoma) through which the appendix can be intermittently catheterised for administration of an antegrade enema has proved to be safe and effective in constipated children with spina bifida or anorectal malformations. Youssef et al showed significant improvement in neurologically intact children with severe constipation (191). However, follow up data on 300 ACE procedures in the United Kingdom showed only 52% success in children with functional constipation with a failure rate of 38% (192). Complications included stomal stenosis, leakage of the irrigation solution, granulation tissue, and tube dislodgement. Other side effects were abdominal cramping and soiling after administration of the antegrade enema. In our experience, a high failure rate is observed in children under the age of 5 years, children in whom previous normal bowel washouts were unsatisfactory and in those patients who were noncompliant to therapy.

Only few data exist on the effect of colostomy or (sub)total colectomy in children with severe constipation. Woodward et al. described a high success rate, with minimal complications of a standard Hartman procedure in 10 patients with long-standing constipation. In this report, children underwent formation of proximal sigmoid colostomy with limited anterior resection of hypertrophic proximal rectosigmoid. Two patients underwent “reversal” surgery without success. The authors suggest retaining the colostomy throughout life in children with neurodevelopment impairment. Stoma reversal using the Duhamel technique with a simultaneous ACE might be useful in neurologically intact children (193). Youssef
and colleagues describe a 90% success rate of sub-total colectomy in 19 children without neurodevelopmental impairments with longstanding therapy resistant constipation (191). The major drawback of this study was that the type of surgery was mainly based on the results of colonic manometry which showed partial or total motility abnormalities of the rectosigmoid and colon. Colonic motility disturbances should at least be confirmed by a positive transit study using either radiopaque markers or isotope scintigraphy (194,195). Patients with isolated rectosigmoid retention of markers and pelvic outlet obstruction confirmed by anorectal manometry or defecography are highly unlikely to benefit from colectomy (196). In adults, diminished rectal sensation in patients with slow transit constipation was adversely related to treatment outcome (197). Upper gastrointestinal motility studies should be performed in children with pancolonic motility disturbances. In adults, the presence of upper gastrointestinal dysmotility is a contraindication to surgical intervention because of both the high risk postoperative complications and long-term failure rates (198).

Surgery for children with longstanding constipation should be only considered in a highly selected group of patients who fulfil strict clinical, physiological and psychological criteria.

**Follow up and prognosis**

The general belief that children with constipation “just grow out of it” has been recently re-evaluated (63). A large cohort of 418 Dutch children with constipation older than 5 years at intake (279 boys, median age 8.0 years) was prospectively followed using a standardized questionnaire. All patients were intensively treated in a tertiary hospital with oral and rectal laxatives with or without biofeedback training / anorectal manometry. The median duration of follow-up was 5 years (range: 1-8). Approximately 60% of the patients had achieved success by 1 year. This finding is in accordance with a complete remission rate between 60-90% by one year of treatment, in earlier studies evaluating long-term outcome in children with constipation (25,62,79,120,199-205). However, both the van Ginkel et al. and Staiano et al. studies showed that despite intensive initial medical and behavioural treatment, 30-50% of these children persist to have severe symptoms of constipation after 5 years of
follow up and these symptoms are even present beyond 18 years of age (63,201). Another important finding of the van Ginkel study was that 50% of the children had at least one relapse within the first 5 years after initial treatment success, underscoring the need to continue frequent follow-up visits for at least 1 year after successful treatment to prevent or treat with laxatives a possible relapse.

Early onset of constipation (< 1 year) and the presence of encopresis at the time of initial presentation seem to be predictors of poor outcome (79,201). Sutphen et al. reported the association between persistence of complaints of constipation and behavioural problems such as trouble with peer relationships, school attendance and home conflicts with peers or siblings. Conflicting data exist concerning the relation between outcome and relevant co-factors such as clinical parameters (abnormalities found on physical examination), anorectal parameters (abnormal contraction of the external sphincter), sex, positive family history and the duration of symptoms before intake (63,69,79,181,201,203,206).

It should be acknowledged that the populations studied had long standing constipation in the majority of cases and were referred and treated in specialized tertiary care centres. This implies that these patients are unlikely to represent most children seen in a general population. Other drawbacks of the majority of these studies are a retrospective data collection, the use of cross-sectional instead of a longitudinal follow-up, low follow-up percentages and small numbers of patients (207-210).
Summary

Constipation is a very common problem in childhood and occurs world wide. It has great psychological impact on the child and its family. Its treatment is often long lasting and approximately 30% of the children still suffer from constipation beyond puberty. This frustrating phenomenon deserves much more attention than it receives to date. International collaboration is necessary to develop and validate standard constipation-questionnaires in which items as encopresis and soiling, large amounts of stool, consistency of stool and retentive posturing are clearly defined. This standard questionnaire will form the basis for the next Rome-criteria, recognizing different groups of children with different symptomatology of constipation and might lead to different therapeutic approaches. Future research should focus on better understanding of the physiology involved in defecation, withholding and rectal sensation. Large double-blind randomised controlled trials with well defined outcome measures should be performed and are necessary to compare the safety and efficacy of different laxative regimens in children with mild and severe constipation. These studies should cover longer follow-up periods and include socially (quality of life, scholastic performance, and family history) as well as clinical relevant outcomes.

Revised Rome-criteria enhanced rectal function testing (barostat) and new therapeutic options (polyethylene glycol) have shed a little more light on this common problem in childhood. However, there is still a long way to go before we reach the end of the tunnel.
References


