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UROLOGY REVIEW

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Vesicoureteral reflux in infants

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Abstract Grade 5 vesicoureteral reflux (VUR) is almost exclusively seen in male infants, and in one-third of cases occurring with a generalized small kidney with decreased renal function without a previous history of urinary tract infection. In females, however, high-grade reflux is rare and kidney damage almost always less severe and of the focal type, as in older children. Assessment of the bladder function with urodynamic and free voiding studies also indicates a difference between male and female reflux during infancy. Half of the males with dilating reflux initially have a hypercontractile urodynamic pattern indicating small functional capacity with high voiding pressures and often instability during filling. This pattern changes during the first couple of years to high-capacity overdistended bladders, often with incomplete emptying. In females, hypercontractility is seldom seen, but bladder function is characterized by high capacity and there is an increase in residual urine from presentation. The pathogenesis of VUR has also been suggested to differ between the sexes. Transient anatomical obstruction during fetal life has been proposed as the cause of gross VUR in males. The spontaneous resolution rate of dilating infant VUR seems to be significantly higher than in older children. A resolution of 40% of grades 4 and 5 has been reported during the first couple of years in prenatally diagnosed cases, suggesting that antireflux surgery should be postponed until after the infant year.

Key words Vesicoureteral reflux · Infants · Spontaneous resolution

Introduction

Gross vesicoureteral reflux (VUR) during infancy is mainly seen in male infants, is often bilateral, and has until recently been considered a malformation of the vesicoureteral junction. The less-severe reflux in female infants has not been possible to explain. Although reflux in older children is often seen with bladder dysfunction, the causal connection is poorly understood, except in those with nonneurogenic-neurogenic bladder dysfunction, where an increased outflow obstruction during voiding (detrusor-sphincter dyscoordination) is thought to induce the reflux [1]. This mechanism is similar to that seen in neurogenic bladder dysfunction, in which a causal connection is well established [2].

Recent reports also suggest bladder dysfunction in infants with dilating reflux, in addition to congenital malformation of the vesicoureteral junction [3–5]. The prevalence and pathogenic significance of the abnormal bladder function during early infancy, however, is still unknown. Although the role of bladder dysfunction in the pathogenesis of VUR in nonneurogenic bladders is debatable, detrusor-sphincter dyscoordination with or without overdistention and/or instability is closely connected to the reflux-urinary tract infection (UTI) complex, and must therefore always be considered in the treatment of VUR.

Grades of VUR and gender

Dilating reflux in infants is more common in males than females, with a ratio of between 3 and 5:1 [6–11], in contrast to older children, where most affected children are girls and have milder forms of reflux [12–14]. The higher predominance of males during infancy is seen both in series where the reflux is diagnosed prenatally [6–9, 11] and in those detected after UTI [10, 12, 15]. Grade 5 reflux, often concomitant with dilatation of the upper urinary tract, is almost exclusively seen in male infants [7–11, 16]. The gross reflux in infants is predominantly bilateral, with a reported frequency between 55% and 82% [7–9, 11, 16, 17]. A preponderence of bilateral reflux (72%) has also been shown for dilating reflux grades 3 and 4 in older children in the International Reflux Study in Children (IRSC) [18].

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Although high-grade reflux is more common in male infants, there is evidence from a recent study that the total numbers of refluxing male and female infants are equal. In a series of infants admitted for primary UTI (*n*=158) from an unselected population in the city of Gothenburg, the total number of refluxing male (*n*=14) and female (*n*=17) infants did not differ, even though the total number of male patients admitted was higher [19]. The reflux grades differed slightly in this small but population-based study, with a tendency towards more grade 4 reflux in the males and with mainly grade 3 as the highest grade in the females. No grade 5 reflux was seen in this small series, indicating that severe reflux during infancy is uncommon. In the study by Yeung et al. [11], the female patients also mainly had mild reflux (grades 1–3). In their series, however, the male infants also mainly had mild reflux, which can probably be attributed to selection of the patients according to prenatal dilation.

The total number of females with reflux presenting with UTI before 1 year of age was also greater (*n*=86) than the number of males (*n*=49) in the IRSC study, in which only reflux grades 3 and 4 were included [20]. However, of the total number of male children included in the study, two-thirds were under 1 year of age. Furthermore, of the total number of children of all ages, males constituted only 25%, showing that reflux is far more common in females of all ages, except for the grade 5 reflux seen in males in early infancy.

Kidney damage, grade of VUR, and gender

With the advent of prenatal diagnosis of dilating reflux it became possible to investigate infants with severe reflux before UTI. From 1987 several centers have reported prenatally diagnosed infants with VUR. While some have considered fetal VUR to be a benign disorder not often associated with kidney damage, others have reported congenital renal malformations in male infants [6, 8, 9, 16, 17, 21, 22]. The differences can probably be attributed to the fact that the series are small, and male infants with congenital malformations and gross reflux constituted a minor proportion of the total population of infants with VUR. It has now been confirmed in several studies [4, 8, 9, 16, 21, 22] that in about 20%–30% of cases, dilating infant reflux in males occurs with a generalized small kidney with a smooth outline and with decreased renal function without a previous history of UTI.

Yeung et al. [11] recently presented one of the largest series of prenatally diagnosed dilating reflux (155 infants) and found that 28% of all male infants had such generalized kidney damage, whereas it was rarely found in female infants (5%). The small kidney was almost always related to severe reflux. He also found focal kidney damage, but less commonly in males (12%). Altogether about 40% of all included patients, males and females, had kidney damage. In other series of infants with dilating VUR, the prevalence of kidney damage of all categories varies from 17% to 60% [9, 21, 22]. The variation can probably be attributed to the small numbers of infants included.

The generalized type of kidney damage in infant boys with gross reflux was recognized as long ago as 1970 by Rolleston et al. [15]; of 130 renal units with dilating reflux, 29 were damaged (22%), of which 26 had generalized changes. In this and other earlier studies [10, 12], however, the investigations were performed after presentation of UTI, and thus the damage could not be recognized as a congenital lesion.

Studies of noninfected male infants with dilating reflux diagnosed prenatally indicate that the generalized small kidney with a smooth outline represents maldevelopment that occurs in utero. Histological evidence of renal dysplasia was found in such infants subjected to unilateral nephrectomy in a study by Risdon et al. [23]. What is less clear is whether VUR is an important factor in the development of renal dysplasia or whether it is an unrelated phenomenon occurring in a markedly malformed urinary tract. In favor of the former are studies with a fetal lamb model in which obstruction created early in fetal life induces renal dysplasia [24]. Mackie and Stephens [25], however, suggest that the position of the ureteric orifice on the bladder trigone determines the degree of associated renal maldevelopment.

In female infants with reflux, generalized kidney damage is almost never seen [10, 11]. High-grade reflux is also very rare in female infants. The kidney damage seen is focal, as in older children and male infants with milder forms of reflux.

Urinary tract infection

Infants with gross reflux must be considered a high-risk group for UTI, and it is generally agreed that prophylactic antibiotics should be instituted as soon as possible [26]. Breakthrough UTIs are a problem in these infants with gross reflux, although the majority have no recurrences. This was conclusively shown in the IRSC study, in which recurrent UTI was mainly a problem in males with refux during the 1st year, but the prevalence was practically zero in males with reflux over 1 year [20]. In females, however, the recurrence rate was slightly lower during the 1st year, but stayed at a higher level during follow-up [20]. It was also shown in the same study that instrumentation of the urethra increases the risk of recurrences, which was also noted in other studies of infants with reflux, which reported infections in 4%–18% of patients after such procedures [9, 11]. A single dose of antibiotics at the time of instrumentation minimizes the risk of infection [26].

Breakthrough infections have also been reported in infants with prenatally diagnosed dilating VUR treated with prophylactic antibiotics without a primary infection. The proportion of infants with such breakthrough infections varies between 4% and 28% [8, 9, 11, 16]. The variation can probably be attributed to differences in follow-up time and severity of reflux.

When breakthrough infections occur, each patient needs individual treatment. Although we do not know why occasional patients develop recurrent UTI, the solution has often been surgery, even in small infants, either

vesicostomy or neoimplantation of the refluxing ureter. The possibility of bladder dysfunction with incomplete emptying has been suggested [3, 4, 10], and if this is correct, investigation and treatment of bladder function would be the logical step before recommending surgery.

Bladder dysfunction in infants with VUR

Background: bladder dysfunction in older children with VUR

VUR and bladder function are closely related. The most-obvious examples are seen in children with neurogenic bladders [2] and in boys with posterior urethral valves [27]. The common feature of importance for the occurrence of reflux in these two groups is the outflow obstruction; in neurogenic bladders the obstruction is functional, due to the detrusor-sphincter dyssynergy, and in valve bladders the obstruction is anatomical. There is also increasing evidence that dysfunction of the bladder/sphincter complex in otherwise healthy children after toilet training is related to reflux [28–30] and might even be of pathogenetic importance for the occurrence of reflux.

In these older children there are basically two bladder dysfunction patterns that have defined urodynamic findings and which have been reported in patients with VUR: (1) the unstable bladder and (2) the dyscoordinated bladder [28–30]. Both dysfunctional voiding patterns share a common urodynamic feature in that they produce functional urinary tract obstruction, although they represent completely different urodynamic entities. The unstable bladder is characterized by urinary obstruction during bladder filling due to voluntary sphincter constrictions in an appropriate attempt to maintain continence during an uncontrolled contraction of the bladder. In contrast, the dyscoordinated bladder is characterized urodynamically by obstruction during voiding due to involuntary constriction of the urinary sphincter during the voiding contraction. This is believed to be an acquired disorder, learned in response to uncontrolled bladder contractions, becoming manifest at some point after the toilet-training period [31, 32].

Both dysfunctions are often seen together, and unstable contractions have been reported in 75% of dyscoordinated bladders [33]. Both are accompanied by voiding symptoms, such as urinary incontinence and urgency, whereas incomplete emptying and UTI are mainly a problem of the dyscoordinated bladder. However, the voiding against an obstruction, as in the dyscoordinated bladder, is the most-serious dysfunction, since it has been reported that patients with this dysfunction and reflux often have injured upper urinary tracts, unlike those with an unstable bladder dysfunction. The dyscoordinated bladder also regularly decompensates with a weak contraction and high capacity (lazy bladder), although the voiding contraction can be strong, with high pressure levels before decompensation. Constipation and encopresis also occur regularly in children with dyscoordinated bladders [31].

Recently, a significant proportion of infants and children with grade 3 and 4 reflux were reported to have big bladders in the IRSC study [34]. Whether this bladder overdistention should be regarded as a separate bladder dysfunction pattern in children with reflux or due to dyscoordination is unclear, as bladder capacity was measured by voiding cystourethrography and not urodynamic assessments.

However, functional bladder disturbances in neurogenically healthy infants have not been considered possible because of the reflex-induced autonomous voiding in this age group. Furthermore, the gross bilateral reflux seen in this age group, particularly in males, has been considered to be due to a congenital malformation of the vesicoureteral junction.

Studies of bladder function in infants with VUR

Urodynamic studies

It was recently shown [3–5] that infant boys with gross bilateral reflux were often urodynamically abnormal, at least compared with older children. The majority (50%) of infant boys with reflux had very high pressure levels at the voiding contraction, the bladder capacity was low, and instability was seen in the majority of cases (hypercontractile bladder) [10, 35]. A minority had overdistended large-capacity bladders (25%), with normal pressure levels at contractions, but instability was often seen in those cases. Increased activity in the pelvic floor during voiding measured with electromyographic surface electrodes was registered in about 80% of the hypercontractile and in all the overdistended bladders, indicating dyscoordination. There was also a small group (25%) who could be regarded as urodynamically “normal”, but with voiding pressure levels above those regarded as normal in older children. The acceptance of higher pressure levels during infancy results from urodynamic studies of non-refluxing infants [5, 19, 36]. In infant girls the hypercontractile urodynamic pattern was not identified. The limited number of females investigated to date have an overdistended high-capacity bladder with incomplete voiding [10, 35].

Free voiding studies

Whether those infants with reflux and abnormal urodynamics really have bladder dysfunction is not proven by these invasive urodynamic investigations, at least not in those 50% of male infants with a hypercontractile bladder [10, 35], since very little is known about normal urodynamic parameters in this age group. The 25% of male infants and the females with a high-capacity bladder [10, 35], however, can more easily be accepted as having bladder dysfunction, since this is similar to the pattern of the dyscoordinated bladder/sphincter dysfunction seen in older children with reflux [28–30]. Furthermore, bladder dysfunction during infancy cannot be recognized from symptoms, since urgency, frequency, and day-time incontinence have no relevance in this age group. The only

parameter of importance for treatment of bladder dysfunction in infants is poor emptying of the bladder.

A noninvasive voiding observation test for infants in which the ability to empty the bladder can be studied, but which also describes the voiding pattern ("the 4-h voiding observation"), is now available [37]. The advantage of this noninvasive method is the fact that controls are available through studies of the voiding pattern of healthy infants [37], and thus pathology, both regarding emptying ability and the voiding pattern, can be recognized.

The refluxing infant boys with very high pressure levels and low capacity on urodynamic investigation (hypercontractile bladder) were shown to have a different voiding pattern from healthy infants of comparable age [35, 38]. The number of voidings was increased during the observation period, as was the number of interrupted voidings; two to four voidings with less than a 10-min interval and with low residual urine after the last voiding. Such interrupted voiding was seen in 20% of normal healthy infants [37], but in 60% of the refluxing infants with instability and high pressure [35, 38]. In those few infants with high-capacity, low-pressure bladders, both male and females, the high frequency of interrupted voidings was not seen. These children voided infrequently compared with normals, and residual urine volumes exceeded the amount of reflux urine, as measured by videocystometry. Abnormalities in both the urodynamic and the voiding pattern in these refluxing infants makes it highly probable that the findings really represent a bladder dysfunction.

Follow-up studies

In urodynamic follow-up studies of infant boys with reflux [5, 39], the hypercontractile high-pressure, low-capacity bladders change in most cases to high-capacity, low-pressure bladders with incomplete emptying during the first couple of years. These results suggest that infant boys with gross VUR might be the same as older boys with VUR who also had high-capacity, high-residual volume after voiding due to urethral overactivity, often with renal damage [30].

Relationship between bladder dysfunction in infants and older children with VUR

Thus, both instability and dyscoordination were seen in infant boys, but they could not be separated into groups as clearly as in older children. Most of those with dysfunction seem to have increased outflow resistance, as judged from both the high pressure levels initially and the high-capacity bladders, both early and particularly later. Since dyscoordination and other forms of increased outflow resistance can have a short primary period with increased work in the detrusor muscle recognized by high voiding pressure levels, both the hypercontractility seen early and the high-capacity bladders with high residual urine seen both early and later can have the same pathogenesis. Whether this suggested increase in outflow resistance is due to dyscoordination between the detrusor and the sphincter is speculative.

In these young infants, the increased sphincter activity of unstable contractions during filling and the voiding contraction cannot possibly be a learned response, but is rather congenital. This theory is supported by the finding of Noe [40] that not only reflux without bladder dysfunction (35%) but also reflux with overt bladder dysfunction (20%) are genetically determined. These results suggest that the bladder dysfunction in children with reflux can be hereditary and thus congenital, and is not always an acquired disorder, as is generally believed.

Treatment of bladder dysfunction in infants with VUR

Nothing has yet been reported about treatment of bladder dysfunction in infants with VUR. The correlation between spontaneous resolution of the reflux and bladder dysfunction is not known, and whether treatment of the latter influences the resolution is also unknown. However, we have recently summarized our experience of treatment of bladders with overt dysfunction (unpublished data). The treatment was mainly directed towards incomplete emptying with the use of clean intermittent catheterization (CIC), which almost only affects the high-capacity bladders with high residual urine. Some of the hypercontractile bladders also have increased residual urine, but to a lesser degree and with frequent voidings, making CIC an unsuitable treatment. Treatment of the reactivity in the detrusor muscle (hypercontractility) with detrusor relaxing drugs is also an option, but has not yet been tried in our institution.

During infancy, incomplete emptying can only be treated with CIC. Institution of CIC during the infant year is often easy, whereas after 1 year of age it is often troublesome, simply because the child is suspicious of unfamiliar events, especially if they are associated with pain. Therefore, from the age of 1.5 years we recommend early toilet training as a first step, since we have noticed that the emptying ability of the bladder is often improved after toilet-training (unpublished data). After training we also emphasize to the parents the importance of frequent, regular voidings during the daytime, in accordance with what is known about bladder retraining in older children. Sometimes it is also important to wake the child for voiding during the night, because many of these children become dry very early at night-time. Since they sleep 12 h a night and often drink a bottle of milk just before falling asleep, the urinary volume in the bladder in the morning is sometimes very high. In those with pronounced kidney damage and decreased ability to concentrate the urine, the nightly volume is always a problem. Since the bladders of the refluxing children after the age of 1 year are often big, these high nightly volumes contribute to a further increase in bladder capacity.

Noninvasive studies of the free voiding pattern with the "4-h voiding observation" have been used in reflux-

ing infants for diagnosing those with high levels of residual urine. Our policy to date has been to use CIC during the infant year, not because of high volumes of residual urine per se, but only when seen in combination with recurrent UTI and especially in those with poor kidney function.

Of 50 male and 20 female infants with dilating VUR, 11 and 4, respectively, have been treated with CIC since 1993. Most of the infants were started on CIC during the second half of the infant year, after the gradual change in bladder function pattern towards high-capacity, high-residual bladders. Two male infants, however, were started at an early age after 3 months of continuous drainage of the bladder with a suprapubic tube, because of severe dilatation of the upper urinary tract with bilateral maximal reflux. These two infants would have been subjected to vesicostomy in many other institutions [7, 8, 17].

Pathogenesis of infant reflux

Gross, often bilateral, reflux in male infants with generalized renal damage must be regarded as a separate group in the reflux family [11, 23]. It seems highly likely that the renal changes represent in utero maldevelopment. The reason for the more-severe reflux in male infants is not known and can only be speculated upon. The bladder dysfunction suggested by urodynamic investigations in some of these male infants [3, 5] and the increased bladder wall thickness [4] both suggest an increased outflow resistance. The male urethra is likely to be the culprit. A transient bladder outlet obstruction during fetal life is an attractive explanation. The resemblance to the bladder and upper urinary tract in infant boys with posterior urethral valves is another factor indicating earlier obstruction, dilated upper urinary tracts, kidney damage, bladder wall thickness, and bladder dysfunction with hypercontractility [41]. Of course the valve patients have much more-pronounced damage both of the kidneys and of the bladder, because of a more-severe and permanent obstruction. The transient bladder outlet obstruction during gestation suggested in these refluxing male infants has been suggested to be due to abnormal angulation during embryogenesis [42], Cowper's gland cyst [43], and posterior urethral membranes [44].

A congenital form of functional outlet obstruction (detrusor-sphincter dyscoordination) is another plausible explanation. An argument against this theory is the congenital functional obstruction seen in infants with neurogenic bladder (mainly myelomeningocele), who very seldom present with severe reflux at birth [2].

The results from prenatal investigation of the bladder in an infant boy with dilating reflux lend further support to the theory of a congenital bladder dysfunction [45]. Fetal examination with ultrasonography showed higher bladder volume compared with that expected at that gestational age. The residual urine was also significantly higher after voiding. Postnatally this boy was shown to have a small bladder with high pressure levels. This is similar to the bladder in patients with posterior urethral valves: big during fetal life, but when investigated with urodynamics after birth the bladder is hypercontractile, with even higher pressure levels than observed in those with reflux [41]. The high-capacity bladders with incomplete emptying in female infants, however, might have a different etiology than the dysfunction seen in male infants.

Resolution of infant reflux

The spontaneous resolution rate of dilating infant reflux seems to be higher than in older children. Yeung et al. [11] recently reported a resolution rate of 44% after 15 months of follow-up of grade 4 and 5 reflux in 55 infants (50 males, 5 females) prenatally diagnosed and primarily assessed at a mean age of 2.3 months. The mild reflux (grades 1–3) in this study (47 males, 27 females) had a resolution rate of 73% during the 1st year. Such high rates of spontaneous resolution were also reported earlier by Schulman et al. [46].

Although Yeung et al. [11] did not separate grades 4 and 5 reflux, there seems to be a difference in resolution rate between grade 5 and 4 from the results of other studies. In grade 5 reflux a relatively low resolution rate has been reported, between 0% and 30% during a follow-up of 2–5 years, whereas grade 4 was often reported to have a resolution rate of more than 50% (47%–67%) [7, 8, 15, 16]. However, small numbers of infants were included in the studies. In these studies the prognosis for resolution of mild grades of reflux was also excellent (67%–100%).

The spontaneous resolution rate in older children as judged from the IRSC study was only 16% in both grades 3 and 4 reflux [47]. However, in this study there was also a group of 80 patients with a spontaneous resolution rate of 43%. This group consisted of patients who were not included due to downgrading of reflux during the 6-month observation period before the study, and they were also younger than the study population. Males less than 2 years with grades 3 and 4 reflux had a resolution rate of 12%, which was half the total rate for males (24%). The corresponding figures for females were 1% and 25%. The reason for the difference between the resolution rates in the prenatally diagnosed cases of grades 3 and 4 reflux [11] and those of corresponding age and grades in the IRSC study can only be speculated upon. It is unlikely that the presentation of the reflux with UTI as opposed to prenatal diagnosis is the only reason. More probable is that there is a selection of "hard core" infants in the IRSC study.

Treatment of infant reflux

In 1970 Rollstone et al. [15] advocated surgery for gross reflux in infants, since he found a high frequency of progressive kidney damage in infants with gross reflux and also an insignificant resolution rate of grade 5 reflux. The present consensus, however, is that antireflux sur-

gery or endoscopic injection treatment should be postponed until after the infant year. The recently published studies showing a high resolution rate not only of mild but also gross reflux in infants have contributed to this view [7, 8, 11, 16, 48, 49]. The fact that most of the kidney damage seen in male infants is congenital and not acquired has also been of importance for treatment. Furthermore, successful reimplantation of a wide ureter into the small bladder of an infant is technically challenging and gives less-predictable results than ureteric reimplantation in later childhood.

Recurrent breakthrough UTIs are by many considered an indication for surgery in infants with VUR. According to the recent results concerning bladder function during the infant year [10, 35, 38], the first step in that situation should rather be investigation of the bladder function, especially evaluation of the emptying ability of the bladder. In cases of residual urine which significantly exceeds the reflux urine, measures to treat the bladder should be taken rather than treating the reflux surgically. In cases without breakthrough UTIs, however, there is no evidence for further development of new renal scars necessitating surgery during early infancy [50, 51].

In cases where surgery has to be performed many authors advocate vesicostomy as the procedure of choice during early infancy [7, 8, 17], with delayed neoimplantation. Gordon et al. [8] described two infants subjected to vesicostomy early during the infant year, neither of whom needed neoimplantation when the stoma was closed during the 2nd year of life. Whether this was an effect of the diversion per se or of the time elapsed with spontaneous resolution of the reflux can not be judged from the study. Others, on the other hand, prefer primary neoimplantation. In series presented by Anderson and Rickwood [9] and Greenfield et al. [52] no significant increase in postoperative complication rate after neoimplantation during early infancy was found. In the IRSC study [50], however, an increase in complication rate was noted in the younger children. The median age in those with postoperative obstruction (n=9) and persisting reflux (n=8) was only 1.5 years, compared with 3.5 years for the complete surgical group (n=151).

In conclusion, neonatal reflux differs significantly between males and females. In males the reflux is often severe and bilateral and combined with generalized kidney damage in one-third of cases without a previous history of UTI. In females the grade of reflux is mild to moderate and only with focal damage of the kidneys as in older children with reflux.

Further evidence for differences in the cause of reflux between males and females comes from recent investigation of the bladder function. Males initially have a urodynamic pattern typical for a congenital obstruction with very small functional bladder capacity and high voiding detrusor pressure levels (hypercontractility) in half of the cases, whereas females have an overdistended bladder dysfunction with incomplete emptying. An interesting observation is, however, the urodynamic pattern change in the males to an overdistended bladder dysfunction with incomplete emptying during the first couple of years, i.e., a pattern very similar to that seen in the females. This high-capacity bladder dysfunction has been reported earlier as most common in older children, both males and females [30, 34].

It is well known that dilating reflux in some infants is seen together with bladder dysfunction. Whether the bladder dysfunction is the primary cause of the reflux or is secondary, e.g., to transitory anatomical urethral obstruction during fetal life, similar to that seen in bladders of patients with posterior urethral valves, is not known.

About one-fifth of our infants with dilating reflux needed treatment for bladder dysfunction, which mainly included CIC. This treatment was instituted for prevention of recurrent UTI, and hence further kidney damage. However, in our small series we did not observe any significant influence on the reflux resolution rate (unpublished data). The explanation for the lack of spontaneous resolution might be that the anatomical structures at the vesicoureteral junction were irreparably damaged, which could be explained by the fact that the most-severe reflux was seen in those with the most-pronounced bladder dysfunction. Furthermore, the results suggest that pronounced bladder dysfunction is a negative prognostic factor for spontaneous resolution of gross reflux in this age group. There are also cases in the infant reflux population with normal bladder function, but the proportion is still unclear, partly due to the fact that there is no general agreement of what is a normal urodynamic pattern in early infancy.

Since it appears that infant reflux is not entirely a congenital malformation of the vesicoureteral junction as thought earlier, early antireflux surgery should be avoided if possible. This is further strengthened by recent studies showing a high spontaneous resolution rate of high-grade reflux during the first couple of years, a phenomenon which is more seldom seen in older children.

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