

Various Concepts in the Aetiology of Recurrent Urinary Tract Infections in Girls

PART I

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SUMMARY

Parents, patients and practitioners referring cases are often highly critical in their attitude and reluctant to have various diagnostic procedures instituted for the proper evaluation of recurrent urinary tract infections. Repeated follow-up examinations and protracted treatment prescribed are often frowned upon or completely ignored. It is also not generally realised that chronic pyelonephritis is more often a slow, insidious process. It is human to expect a quick solution to our problems, but in the great majority of cases it is of very little use in the long run to treat repeatedly the result of a urine culture and sensitivity without proper diagnostic evaluation.

In this article an attempt is made to give a clearer insight into this vast and complex problem of recurrent urinary tract infections in female children and young girls, with special reference to some of the more controversial concepts of various possible aetiological factors. It is admitted that it is often difficult for even the most experienced urologist to keep a balanced appreciation of what is fact or mere fantasy; parents and their private doctors are sometimes also the victims of interprofessional rivalry.

In a general classification of urinary tract infections one can state that infections are perpetuated by the following factors:

1. Foreign bodies, i.e. stones. This is, however, very rare in Western countries and will not be discussed.
2. Inability of the urinary tract to empty itself completely. Under this heading we find: (i) obstructive lesions—the urinary tract above the obstruction cannot empty completely; (ii) neurogenic lesions—ineffective detrusor function leaves residual urine in the bladder; (iii) vesico-ureteric reflux—part of the bladder urine flows back into the ureter and renal pelvis. This infects the kidneys, and when the reflux urine returns to the bladder, the bladder infection is perpetuated.
3. Various forms of vulvovaginal irritation, infection, or anomalies.

This article will be published in 3 parts. In part I some concepts regarding possible obstructive lesions and neurogenic lesions will be discussed.

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It is estimated that non-specific urinary tract infection is 9-14 times more common in females than in males.¹ It is now generally acknowledged that the majority of urinary tract infections occur by the ascending route, but it is also agreed that the normal bladder has an inherent resistance against infection and that normal voiding is an important physical mechanism by which the bladder maintains itself in the uninfected state, despite the fact that it has been proved many times that there is never a lack of available pathogens in the urethra. Cox *et al.*² for instance, have demonstrated bacterial populations in the midportion of the urethra in more than 80% of patients, and in the most proximal portion in more than 50%.

An abnormality must exist, either permanent or transient, systemic or local, if infection is to occur. It is thus understandable that the urethra has been the focus of attention for many investigators.

It has been said, and with good reason, that the last 5-6 cm of the female urinary tract, that is from the ureterovesical junction downwards, is one of the most controversial and bewildering subjects in the whole field of urology. The female urethra, especially, has been over-treated, over-stretched, over-cauterised, over-operated and over-evaluated in a frantic effort to relieve patients of a most distressing symptom complex.

In their endeavours to clarify this confusing subject, many investigators have used various techniques and sophisticated equipment, sometimes with contradictory results and conclusions. For example, Weiss and associates³ found that urethral stenosis could always be predicted from the cysto-urethrogram. Conversely, Shopfner⁴ states that, 'there are no valid roentgen criteria for a diagnosis of bladderneck obstruction, meatal stenosis or distal urethral stenosis'. He appears to conclude that since urethral or vesical neck obstruction cannot be determined radiographically, it does not exist.

In a recent article, Turner-Warwick *et al.*⁵ have emphasised the fundamental importance of recognising the limitations of our individual methods of assessment. The evaluation of urodynamic function by symptomatology, clinical examination, static radiography and endoscopy is considerably less reliable than is sometimes appreciated.

Infravesical Outflow Obstruction

Many urologists have constantly stressed the importance of infravesical obstruction in the aetiology of chronic

cystitis, but some observers, especially in more recent years, have considered it of minor importance. Between these conflicting views, a voluminous literature has accumulated. Deeply ingrained in urological thinking, is the basic concept that obstruction and stasis lead to infection.

In the early 1960s vesical neck obstruction was considered an important cause of lower urinary tract infection. The relief of the assumed vesical neck obstruction by various operative procedures did not give uniformly good results in the management of recurrent infection and there was a gradual swing away from incrimination of the vesical neck.

The Lyon Ring

In 1963 Lyon and Smith⁶ reviewed 100 girls with recurrent urinary tract infections. A point of consistent narrowing was found in the distal third of the urethra in as many as 90% of the girls studied. The ring was identified by means of the *bougie à boule* calibrator (Fig. 1). In a report 2 years later by Lyon and Tanagho⁷ they described the ring of distal urethral stenosis as a histologically proven structure composed primarily of collagenous tissue. Four types of urethrographic outlines were discussed and even urethras with outlines said to be characteristic of vesical neck obstruction often res-

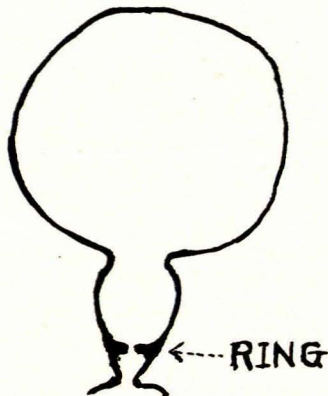


Fig. 1. The Lyon ring of distal urethral stenosis. It produces the so-called 'spinning-top' or 'carrot'-shaped urethra on urethrographic examination.

ponded to dilatation alone. Urethral dilatation with sounds up to 32F was carried out and an over-all rate of cure of 70% was achieved in follow-up study over an average of 2.2 years. They also noted that stenosis did not appear to recur after urethral dilatation.

In their frustration and dissatisfaction with the treatment of recurrent urinary tract infections, many urologists eagerly embraced the newer concept of the Lyon ring, and in the literature various operative procedures on the urethra were encouraged for the cure of a wide spectrum of symptomatology as well as infection.

In 1967 Immergut *et al.*⁸ measured the urethral calibre of 128 normal girls. At that time they were of the opinion that the normal urethral calibre could be computed in terms of age. In a second study, however, they found that in girls with urinary tract infections, the urethral calibre was actually larger than it was in girls of the same age who were uninfected and otherwise normal.

In a study by Halverstadt and Leadbetter⁹ urethral calibration was done on 106 children aged 1½ - 15 years. A range of sizes was encountered at each age level; from 12F to 18F was found at age 2 years, 14F to 22F at 11 years, and corresponding ranges at interval ages. They concluded that the absolute urethral calibre does not seem to be the most important single consideration. Bladder tone and function are additional factors; what may be an adequate urethral calibre in one child may be a relative obstruction in another of the same age who has an infection. They supported the concept that either an urethral constriction or meatal stenosis is an important cause of recurrent infection, but became dissatisfied with the results of urethral dilatation alone. Subsequently internal urethrotomies were done on all cases; it was considered of real value in the treatment of recurrent infection in female children.

Laminar Flow Versus Turbulent Flow

Halverstadt and Leadbetter proposed a possible mechanism whereby this improvement might be achieved. Perhaps, when the proximal urethra becomes dilated above the distal stenosis, the urine flow is turbulent during micturition and bacteria in the distal urethra are washed back into the bladder (Fig. 2). After dilatation or urethrotomy, and in the normal urethra, laminar flow is achieved and this rapidly washes bacteria away.

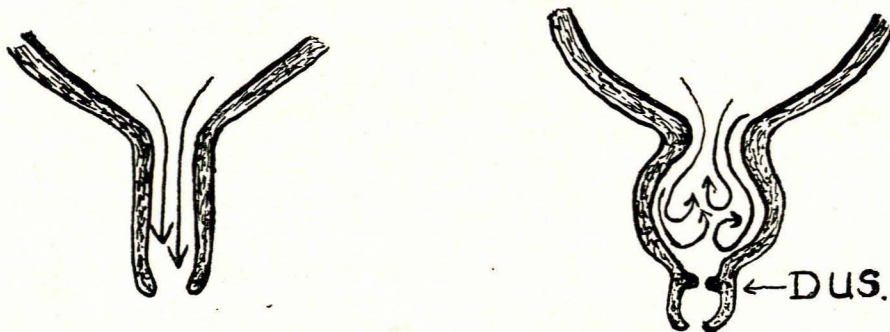


Fig. 2. Schematic presentation of laminar urethral flow versus turbulent flow due to distal urethral stenosis (DUS).

Graham and associates¹⁰ also discussed the significance of distal urethral narrowing in girls. They concluded, however, that normal girls have urethral calibres and palpable distal urethral narrowings of about the same range as children suffering from attacks of urinary tract infection.

Detrusor - Urethral Imbalance

In a subsequent article Immergut and Gilbert¹¹ supported the idea of Halverstadt and Leadbetter; they came to believe that children who have recurrent urinary tract infections have an imbalance involving the detrusor muscle contraction and the resistance in the distal urethra. In the years after their report in 1967, they have come to the conclusion that there is no normal urethral calibre for a specific age. Thus, it is possible for a 4-year-old girl to have an urethral calibre of 26F and still not empty the bladder if the detrusor muscle contraction is ineffective or relatively atonic. They have continued to perform internal urethrotomy to decrease intra-urethral resistance. Of 57 young girls with recurrent infections treated by internal urethrotomy and antimicrobial therapy for 4 weeks, 86% demonstrated either excellent response or improvement when followed for 6 months, and 67% had no further urinary tract infections.

Reflex Spasm of the Striated External Sphincter

In a recent article Hendry *et al.*² discussed the effects of urethral dilatation in recurrent urinary infections in girls. The results of a retrospective study confirmed that about 65% of girls with no serious vesico-ureteric reflux showed improvement in their recurrent urinary infections when they were treated with a single urethral dilatation and long-term antibiotic therapy. They concluded that the degree of dilatation and the addition of meatotomy appeared to be unimportant, and there was no evidence that repeated dilatation was any more effective than a single dilatation.

They also did urethral pressure profile studies and found that the results before and after treatment were virtually identical in dilated and undilated cases. However, there was a highly significant drop in urethral pressure after induction of general anaesthesia; this effect is not seen in adult women.

Tanagho *et al.*¹³ attributed high urethral pressure to reflex spasm of the striated external sphincter, which was corrected by urethral dilatation. They suggested that the spasm was induced by sensitisation of the distal urethral ring by vulvovaginal infection or irritation.

Deficient Bladder Sensation

In 1968 Motzkin¹⁴ drew attention to the fact that occult deficient bladder sensation can produce urological disorders which commonly have been attributed to bladder outlet obstruction. He pointed out that deficient bladder sensation is often the first manifestation of diabetes melli-

tus, even in children. The youngest patient with a positive glucose tolerance test was 4 years old.

'Deficient bladder sensation appears to be an independent facet of the diabetic syndrome, and much like nephropathy, retinopathy, complications of pregnancy and vascular degenerative phenomena, may appear years before there is any manifest diabetes.'¹⁴

The Uninhibited Neurogenic Bladder

In 1969 another aetiological concept flashed across the dark and controversial field of urinary tract infections in girls. Already in 1966 Lapedes theorised that the most common entity associated with urinary infection in girls is not infravesical obstruction in any form, but the uninhibited neurogenic or infant-type bladder. In a later study in a group of 250 females he found that 1 of every 6 patients demonstrated an uninhibited neurogenic bladder.

More recently Lapedes and Diakno¹⁵ reported their study involving 71 girls with documented urinary infection. The patients ranged from less than 1 year to 16 years old. They found the infant type of bladder in 61% of this series. Fifteen girls, i.e. 30%, had abnormally large-capacity bladders, the so-called 'infrequent voiders'. Six girls had normal values, 3 a motor paralytic bladder, and 1 a reflex neurogenic bladder. Obstructive disease was only demonstrated in 3% of cases. Ureteric reflux was demonstrated in 9 cases.

The Basic Neurological Defect

'As the child's nervous system matures, cortical control over both bladder smooth muscle and periurethral striated muscle is gained by the age of 2-3 years. In some girls cortical control over bladder smooth muscle is not attained at the age of 3 as evidenced by uninhibited contractions on cystometric examination. However, voluntary control of the periurethral striated muscle is developed. Thus, when the bladder of one of these children fills with urine, uncontrolled contractions of the detrusor occur, associated with a desire to void. If the child voids immediately, intravesical pressures remain low and no urinary infection occurs. But should she attempt to prevent urination and hold her urine, a marked rise in intravesical pressure will occur. The increase in intravesical pressure develops because the bladder muscle is contracting forcefully and involuntarily in an attempt to evacuate the bladder while simultaneously the child is trying to prevent incontinence by voluntarily contracting the periurethral striated muscle to cause elongation and constriction of the posterior urethra or urinary sphincter. Under these circumstances trabeculation of the bladder wall, diverticula, urinary tract infection, ureteric reflux, hydro-ureter, etc., may develop. It is postulated that the high intravesical pressure decreases blood flow to the bladder tissue and makes it susceptible to bacterial invasion'.¹⁵

Some children may have complete control by the age of 3-5 years, while others may not have full control

until the age of 14-16 years and some individuals may never develop voluntary control of the detrusor.

In the infrequent voider or the partial motor paralytic bladder, overdistension occurs with relative ischaemia of the bladder wall and with an increased susceptibility to bacterial invasion.

Patients with uninhibited neurogenic bladders were placed on a frequent voiding schedule (at least every 2 hours during the day and to awaken once or twice at night). Infrequent voiders also received Urecholine therapy. Children with severe urgency were given anticholinergic medication in the form of bantline or similar drugs.

None of the children in Lapide's series demonstrated any other type of concomitant neurological deficit.

Anal Electromyography

Various other investigators recently drew attention to the fact that occult or subclinical neurogenic vesical dysfunction can exist, which can be missed by standard urological and neurological investigative techniques. Such children often present with complaints entirely similar to those with simple obstructive problems—enuresis, diurnal incontinence and recurrent infection.¹⁶⁻¹⁸

Some cases had markedly dilated bladders and others spastic bladders. More precise and sensitive methods are necessary to reveal the extravesimal neurological abnormalities necessary to the diagnosis.

Dorfman *et al.*¹⁶ found electromyography of the anal sphincter of great value in providing objective evidence of neurological deficit in the sacral cord segments. They proposed that a group of children exist in whom a triad of findings strongly suggest subclinical congenital neurogenic bladder. This triad includes (i) chronic vesical dysfunction or infection, or both conditions; (ii) minor defects in the lumbosacral laminae; and (iii) an abnormal electromyogram of the anal sphincter.

Voiding Patterns

It is recognised that in comparison with men, women as a rule void far less frequently. Many young women or girls teach themselves, because of social circumstances or the type of work they do, to hold urine for long periods. It is often found in office girls, shop assistants, telephonists and so on. They are sometimes even proud of the fact that they only void twice or thrice daily.

A similar state of affairs is often found in otherwise completely normal children; they are so busy with their toys or occupied by some game that the normal urge to urinate is constantly suppressed, with the result that the bladder can become enormously distended. The stage is then set for increased susceptibility to bacterial invasion

by decreased blood flow to the bladder as described by Lapides and associates.

According to Harrow¹⁹ the bladders of normal children can be distended to an enormous size, especially under anaesthesia. Capacities of 400-500 ml are not unusual, but the ability to empty the bladder is completely normal.

The Megacystis Syndrome

The megacystis syndrome was discussed by Paquin and associates.^{20,21} The syndrome is characterised by repeated urinary tract infections in children who have dilated, refluxing ureters and a large, thin-walled bladder. Harrow, after his gratifying results with ureteric reimplantation, was convinced that the main defect was primary ureteric reflux. The so-called megacystis, the thin-walled distended bladder, was an illusion arising from the easy distensibility of the bladder.

Another writer²² has also emphasised that the primary defect is a short or absent intravesical ureter resulting in an orifice which is gaping or 'golf-hole' in configuration and more laterally placed. This is by far the most frequent congenital anomaly resulting in reflux and is often termed primary reflux or 'uretera ectopia lateralis'. Reflux from this cause is seen in conjunction with the non-neurogenic megacystis syndrome, but they consider it to be a pathological entity probably derived from a generalised detrusor hypoplasia. Reflux of this type affects girls far more often than boys (by a ratio of 8 or 10 to 1) and is clearly hereditary. In addition, reflux of this type is apparently very rare in Blacks.

(To be continued)

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