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

PART II

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SUMMARY

The important role that vesico-ureteric reflux plays in the perpetuation of urinary tract infections has become increasingly evident. There is general agreement on the importance of its early detection and treatment. It is also evident that the vast majority of children with reflux have congenital anatomical abnormalities of the ureterovesical junction. There are, however, controversial views on the subject, and various concepts of the mechanism responsible for the competency of the ureterovesical junction. The important anatomical factors are the length and diameter of the intravesical (submucosal) ureter, the ratio of length to width, the pliability of the roof of the submucosal ureter and the integrity of the underlying detrusor.

Reflux is not a single disease and the aetiology may vary. It is but a radiographic sign common to several pathological processes.

There is also still considerable debate as to whether primary reflux can maturate and disappear with age. This has an important bearing on the formulation of any prognostic and therapeutic programme.

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The subject of vesico-ureteric reflux has been studied widely, both experimentally and clinically, since it was first demonstrated experimentally in 1898 by Semblinow. In 1916 Kretschmer was able to demonstrate reflux radiographically. In 1924, Bumpus had already reviewed 1 035 cystograms and found reflux in 89 (8,6%). He associated reflux with infection of the upper urinary tract and claimed that such infection caused rigidity of the ureteric valve.[1] Talbot and Bunts,[2] in 1949, reported 337 paraplegic patients of whom 16 had associated hydronephrosis and hydro-ureter. Fifteen of these 16 patients were subjected to cystographic studies and 10 demonstrated regurgitation. Following this report many papers appeared concerning the relationship between reflux, infection and dilatation of the upper urinary tracts. In 1948 Stewart introduced the 'delayed cystographic technique', and still later, the conventional voiding cystogram, after having demonstrated that reflux is sometimes revealed only during voiding. The whole subject of vesico-ureteric reflux gathered new momentum in 1952 when Hutch[3] described the pathology of reflux occurring secondary to obstructive and neurological disease, and his observations have stood the test of time.

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The Vesico-ureteric Junction Mechanism

There is still not complete agreement on the mechanism responsible for competency of the ureterovesical junction, despite the advent and wider availability of cine radiography and electronic pressure and flow-measuring devices.

Bell's Muscle

As long ago as 1812 Charles Bell described the trigonal muscles which 'are attached to the orifices of the ureters and are seated in the bladder'. These structures were said to descend from the ureteric orifices towards the vesical neck where they unite and run towards the prostate gland. 'The use of these muscles is to assist in the contraction of the bladder and at the same time to close and support the mouths of the ureters.'

Bell also emphasised the importance of the oblique passage of the ureter through the bladder wall: 'It will be observed that the orifices of the ureters are not closed by the contraction of the muscular fibres around them. They are defended against the return of urine by the obliquity of their passage through the coats of the bladder.'

There are many staunch supporters of the original concept of Bell's muscle. According to their studies of the anatomy of the human ureterovesical junction, Tanagho and Pugh[4] concluded that the ureter does not end at the ureteric orifice. It loses its lumen at this level but its musculature, without interruption, continues downward as the superficial trigone to end at the verumontanum. In addition, Waldeyer's sheath, which surrounds the distal end of the ureter, does not end at the ureteric hiatus but proceeds downward and medially under the superficial trigone. These 2 layers together constitute the trigone of the bladder, which is embryologically, anatomically and functionally a direct continuation of the ureter. Furthermore, the ureter is an outgrowth of the Wolffian duct and mesodermal in origin, as opposed to the bladder, which

arises from the endoderm.[5] It has been shown by earlier investigators that the trigonal muscle is supplied by the sympathetic nerves, while the detrusor muscle is innervated by the parasympathetic fibres.

After a series of experimental studies on dogs, Tanagho *et al.*[6] concluded that active contraction of the trigonal muscle tightens the intravesical ureter with firm coaptation of its lips. The trigonal muscles are stretched when the bladder is distended and this increases their tone and their occlusive effect on the intravesical ureter. During micturition the trigonal muscles contract actively to open the bladderneck and simultaneously to occlude firmly the intravesical ureter to prevent reflux, as the intravesical pressure rises sharply due to active contraction of the detrusor muscle.

In an earlier paper, Stephens and Lenaghan[7] of Australia stated that they believe that the ureteric orifice ordinarily is held closed by the action of longitudinal fibres in the roof of the intramural and submucosal portions of the ureter, and they have demonstrated that these fibres may be either deficient or that the entire distal portion of the roof of the ureter is completely absent in many cases with reflux.

Ratio of Length to Width

Paquin[8] believed that the diameter-to-length ratio of the intracystic ureter played a significant role in ureteric valvular competence. Included in the length of the ureterovesical valve are both the intravesical and intramural ureters. The normal ratio in human subjects was found to be 6,7 : 1, and if this ratio were reduced beyond 2,5 : 1, reflux is more likely to occur.

The Submucosal Ureter as a Passive Leaflet Valve

In a recent article Politano[9] reported studies and measurements made of the bladder trigone and ureterovesical junction in more than 200 autopsy specimens. A distinction was made between the submucosal or intravesical part, and the intramural part. The intravesical portion constitutes about two-thirds of the length of the entire ureterovesical junction. Observations made in more than 500 patients with reflux have disclosed the absence or near-absence of the intravesical segment of the ureterovesical junction. Politano also quoted the experimental studies of Gruber,[10] and more recently Witherington,[11] who suggest that the intravesical portion of the ureter is of the utmost importance in the prevention of reflux. Destruction or shortening of this portion produces immediate reflux. Apparently, Politano also does not consider the function of the trigonal muscle to be of much importance in the prevention of reflux. He wrote: 'The exact role of these structures in the prevention of vesico-ureteric reflux is not clearly understood. There is considerable experimental and clinical evidence to suggest that such isolated structures are not truly significant in the prevention of reflux. It is more likely that these structures act as anchoring points, attachments or areas of reinforcement for the ureter.'

In conclusion, he postulated that the submucosal (intravesical) ureter functions as a passive leaflet valve. The ureterovesical junction is visualised as a collapsible tube (ureter) which penetrates bladder muscle and passes beneath the urothelium for a short distance. When the bladder is filling, the ureter becomes elongated and is compressed against a firm bladder musculature. During micturition, the detrusor contracts around the intramuscular portion of the ureter, compressing or constricting this segment. The intravesical portion shortens, thickens and is thrown into multiple convoluted folds, thus acting as an obstacle to the reflux of urine.

The Ureteric Orifice, its Configuration and Competency

Lyon and associates[12] believe that the ureteric orifice, rather than the tunnel, controls valvular competency.

Follow-up studies by means of endoscopic evaluation and motion-picture recordings were done on 330 girls with recurrent urinary tract infection or difficult urination, or both. These studies were continued for 3 months to 12 years.

Ureteric orifices were graded on the basis of configurations and positions. Four configurations were described, i.e. the cone-shaped (54% of cases), the football-stadium-shaped (23%), and horseshoe-shaped (15%) and the well-known golf-hole-shaped (8%) (Fig. 1). These various shapes have been graded as 0, 1, 2 and 3, respectively. Three positions within the trigone have been described, i.e. the A position or the usual midtrigonal position, the B position, more lateral than A, and the C position at the junction of the trigone and the lateral wall of the bladder. The percentage reflux varies from 4% in the case of the usual cone-shaped midtrigonal A position up to 100% in the case of the far laterally-situated, golf-hole type of ureteric orifice.

Lyon supported the concept that the trigone acts as a supporting structure for the ureter, particularly in its intracystic portion. Developmental deficiency and weakness of the trigone cause lack of support and a lateral shift of the ureteric orifice with an increased tendency towards reflux. He believes that reflux cannot be predicted on the basis of tunnel length alone. Reflux was demonstrated in tunnels as long as 2,5 cm, and yet no reflux was found in some tunnels as short as 1 cm.

Spontaneous Improvement of Vesico-ureteric Reflux

According to Hutch[13] the intravesical ureter gains length with age, thereby providing competence. This contention has been endorsed by other investigators. Lyon and associates reported that 93% of their cases with a cone-shaped ureteric orifice gained complete competence, 70% with a football-shaped orifice, 19% with a horseshoe-shaped orifice, and none of their cases with a golf-hole-shaped orifice. All their cases initially received only antibiotic treatment and urethral dilatation. All children who stopped demonstrating reflux under conservative manage-

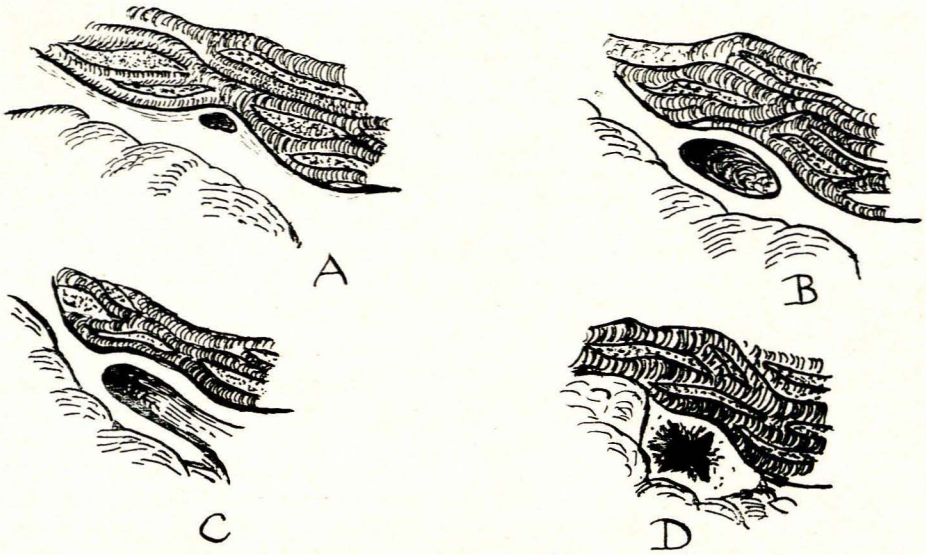

Fig. 1 Various ureteric orifice configurations (modified after Lyon *et al.*[12]): A—usual cone-shaped orifice, incidence of reflux 4%; B—oval or 'football-stadium-shaped' orifice, reflux incidence, 28%; C—'horseshoe-shaped' orifice, reflux 83%; D—'anal' or 'golf-hole-shaped' orifice, reflux 100%.

ment did so in less than 2 years. It was noted that although the original configuration of the ureteric orifice had been maintained, those that did not allow reflux appeared to be under less tension and tended to remain closed. They concluded, however, that due to the fact that there was no change in the general configuration of the orifice in patients in whom reflux stopped, and because this occurred in less than 2 years under conservative management, it raises serious questions regarding maturation as a basis for cure of reflux.

After discussing their experiences and their results with conservative management of vesico-ureteric reflux, Politano and Harper[14] were of the opinion that only in about one-third of cases can symptomatic improvement be expected from conservative management (urethral catheter drainage, urethral dilatations or transurethral resection of the vesical neck). Disappearance of reflux seems unrelated to age and growth. It seems unlikely that any magical maturation of the trigone takes place with the ageing process.

Reflux and Ureteric Peristalsis

Melick *et al.*[15,16] consider active ureteric peristalsis of primary importance in the prevention of reflux. 'The laws of hydrodynamics demand that for a reservoir (the bladder) to fill, the filling pressure must be greater than the pressure in the reservoir. Furthermore, if the reservoir is to be emptied by an additional force, backflow must be prevented. If it is not prevented, ureteric reflux will occur. Backflow into the pump (the ureters) can be prevented in only 2 ways: a constantly greater pressure in the pump or a valve mechanism between the pump and the reservoir or bladder.'

According to Melick, they could show almost without exception a correlation between pressure deficiencies in the ureter and the severity of reflux. The worst cases of ureteric reflux with the most dilation and damage had the lowest intra-ureteric pressures. Some severely dilated ureters seemingly had good active peristalsis by direct vision on a television screen, and confirmed later by cine radiography, but when the intra-ureteric pressures were measured they were found to be exceedingly low.

Since they believe that the basic cause of ureteric reflux lies within the peristaltic mechanism of the ureter which produces lower intra-ureteric pressure, they have done almost no operative procedures on the ureterovesical junction, since to their way of thinking, it is mechanically impossible to restrict or prevent reflux without also impeding efflux.

Vesical Pressure at which Reflux Occurs

In an excellent contribution, Lattimer and associates[17] gave a lucid, logical and well-motivated approach to the problem of vesico-ureteric reflux. Based on the premise that reflux tends to be reversible and that it is due most likely to anatomical deficiencies in the terminal portion of the ureters, as suggested by Stephens and other investigators, they proposed a classification of cases with reflux according to the intravesical pressures at which reflux occurs.

Patients are classified according to whether they have reflux at (*i*) high intravesical voiding pressures; (*ii*) lower pressures, but high intravesical volumes; and (*iii*) low pressures and low volumes.

If the intravesical voiding pressure is very high, this is most often brought about by obstruction or relative

Acute or chronic cystitis may cause secondary reflux. Oedematous fluid at the ureteric hiatus prevents the normal movement of the ureter through the hiatus, thus hampering the intravesical ureter from adapting to changing conditions in the bladder, increasing the possibility of reflux. This may occur in an otherwise normal ureterovesical junction.

Reflux can occur secondary to congenital anomalies of the ureter, such as ectopic orifices or duplication with or without ureteroceles. Fehrenbaker and associates[18] found ureteric reflux in 72% of children who had complete ureteric duplication investigated for urinary infection.

Reflux may follow on any type of surgical procedure that damages the ureterovesical junction. It has been described after transurethral resections of the bladder neck, removal of submucosal ureteroceles, cauterisation or resection of tumours near the ureteric orifices, and so on.

Reflux and Infection

Few conditions in urology have stimulated more interest than the problem of vesico-ureteric reflux. Some of the more controversial aspects of vesico-ureteric reflux regarding basic defects and the formulation of prognostic and therapeutic programmes have been highlighted in this article, but in conclusion one can say, without fear of an argument, that there is general agreement that reflux is one of the most important causes of the perpetuation of infection in unobstructed urinary tracts. Hutch[19] has emphasised that about 50% of children (and at least 10% of adults) with urinary tract infection, have reflux. It is also in those with reflux that pyelonephritic changes develop.[20]

It was recently stated: 'The recent recognition of the importance of vesico-ureteric reflux and the need for its early detection and treatment will surely be marked as one of the great milestones in urology.'[21]

(To be continued)

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