

INTRAMURAL URETER AND URETEROCELE

Alex Simpson Smith Memorial Lecture delivered at The Hospital for Sick Children, London, W.C.1

July 2, 1963

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DURING the past ten years much research has been directed to the study of the structure and function of the normal intramural part of the ureter. The anatomy of the uretero-vesical 'lock' mechanism of both the normal and abnormal variants of this part of the ureter is now more clearly understood. It is proposed to describe the short, the long, and the structurally abnormal intra-mural ureters, together with the physiological defects which they involve and which provoke clinical problems.

The Normal Intramural Ureter

The intramural ureter comprises that part of the ureter which lies within the bladder from its point of entry in the lateral wall to the orifice in the trigone. At first the ureter lies in the muscular tunnel of the bladder and there it rests on the muscle of the bladder under the vesical mucosa. Its length is variable, being only 4 to 6 mm. long in the infant and 10 to 19 mm. in the adult (Hutch, 1962).

The intramural ureter is slightly narrower in calibre than the extra-vesical ureter. Its muscle coat differs in that it is composed of longitudinally arranged muscle bundles only. The circular component of the extravascular ureter, which is its most conspicuous layer, is not continued into the wall of the intramural ureter.

The longitudinal muscle fibres of the roof of the intramural ureter insert into the rim of the orifice but the muscle of the floor of the ureter is prolonged into the trigone, where it is tethered. The function of the uretero-vesical valve, for reasons described elsewhere, is believed to depend on an intrinsic muscular mechanism of the intramural ureter (Stephens and Lenaghan, 1962). The eccentric tethering of the longitudinal muscle causes the roof and walls to press back upon the floor. This action is enhanced by intra-vesical hydrostatic pressures. The mechanism is thus an activated flap valve, which is dependent on muscle for its activation, and obliquity of course for its flap valve action.

Inspection of the orifice of the ureter at cysto-

scopy lends support to this theory of action. The orifice, in its resting state is a pit, slit, or falciform crescentic opening. Its walls and roof are approximated to the floor thus shutting the lumen from view. During expulsion of urine the ureteric orifice is expanded by the force of the jet, temporarily opening the lumen to view. After the jet has ceased, sudden transitory contraction of the longitudinal muscle jerks back the rim of the orifice, hurriedly occluding the lumen and re-setting the flap valve. The muscle then slackens to its tonic resting state. The longitudinal muscle animates and quickens the action of the flap valve.

Moreover obstruction of the urethra causes hypertrophy of the muscle of the intra-mural ureter, thereby strengthening its walls and maintaining efficiency in the uretero-vesical valve. The severest urethral obstruction will not impair the valve action provided that this segment of the ureter is normal in its structure.

The Abnormal Intramural Ureter

Numerous defects of the intramural ureter occur and impair its function. A defective ureter may be too short, too long, too wide, abnormal in structure, or associated with a diverticulum or a ureterocele.

(a) *The Short Intramural Ureter*

Absence in whole or in part of the submucosal segment is a common occurrence; the deficiency is more easily recognized when it is unilateral and the opposite side is available for comparison. The orifice of the short ureter issues into the bladder more laterally, with result that the trigone reaches out towards the lateral wall of the bladder at the expense of the submucosal segment. Deficiency in length of the submucosal ureter entails a corresponding reduction in its musculature and therefore in its efficiency.

(b) *Abnormal Structure of the Intramural Ureter*

The formation of muscle within this segment may be impaired. Defects of the muscle may take

the form of wedge or patchy deficiencies in the roof and walls. These may extend for a short or long distance, may perhaps involve the whole length of the intramural ureter, and may occur in an intramural ureter of the congenitally short type ((a) above). The effect is to render the flap valve inactive.

Furthermore, intramural segments of orthotopic and ectopic components of double ureters may be affected in the same way.

Appearances of the Impaired Valve. The orifice of the defective ureter is then patulous, flaccid, sluggish or immobile, or lies patent exhibiting irregular contractions. When the intramural channel is short, the orifice presents an appearance to the cystoscopist similar to that of a sloping tunnel entrance, and when the submucosal segment is absent, the ureteric orifice resembles the entrance to a rock face tunnel, vertical and sheer.

The phenomenon of vesico-ureteral reflux is often associated with megaureter, which is presumed to be an additional malformation (Stephens, 1963a). The ureteric orifice may then be correspondingly enlarged and may often be readily recognized as such by cystoscopy.

When these conditions prevail, the flocculent material in the urine can be seen to undergo a to-and-fro movement in and out of the orifice. This two-way flow can be confirmed by fluoroscopy. Some ureters exhibit reflux early, others late in the period of filling of the bladder, others again only during micturition.

The two-way flow of vesico-ureteral reflux promotes stasis, and stasis is the fore-runner of infection.

For many patients, especially those exhibiting megaureter in association with reflux, the elimination of stasis may be effected by the simple, regular faithful practice of multiple micturition (Stephens 1963b). It is indeed fortunate that such a simple trick of micturition can be invoked to prevent the infection which so commonly supervenes on impairment of valve function, an impairment which depends upon defects of its muscle component.

Furthermore, provided infection is eliminated by such a method it is safe to await spontaneous improvement or cessation of reflux such as was found to occur in two-thirds of the ureters of a series of 32 patients who were observed for periods of five to ten years.

(c) *Paraureteral Diverticula*

When a ureter lies in proximity to a vesical diverticulum vesico-ureteral reflux may occur. In the series of patients studied, it was possible to make a generalisation, namely, that if the urethral orifice lay within the diverticulum reflux was free. If the two orifices were separate, no reflux oc-

curred; if contiguous, reflux was limited to the lower reach of the ureter.

Diverticula result from deficiencies in the bladder muscle and exhibit a particular predilection for the zone near which the ureters enter the bladder.

Histological examinations of these zones reveal that ureters with orifices contiguous with diverticula exhibit patchy deficiency of muscle in their walls, whilst the engulfed ureters are almost totally deficient in muscle. The defect in common between the diverticulum and the ureter is muscle deficiency which accounts for the vesical bulge on the one hand and for vesico-ureteral reflux on the other.

The ureter with orifice adjacent but not contiguous with that of the diverticulum is competent, its muscle being adequate, though not always complete in its distal roofing. The presence of the diverticulum however, vicariously elongates the intramural ureter, and thus presents sufficient of the muscularized segment to the side-on position so essential to flap-valve function.

It is concluded that the chief factor which impairs the action of the uretero-vesical valve is the lack of the muscular component of the intramural ureter.

In addition to congenital muscular defect, acquired conditions such as inflammation or spinal trauma may result in impaired action of the muscle. Pyogenic or tuberculous infection involving the muscle of the ureter may inflict temporary or permanent damage on the uretero-vesical valve, and ureteritis, as distinguished from cystitis, may initiate or exaggerate reflux. Injuries of the spine not uncommonly provoke reflux, and though the mechanism is not fully understood, it seems probable that the innervation of the muscle is rendered defective.

(d) *The Long Intramural Ureter*

The long intramural ureter lies within the wall of the bladder and sometimes extends beyond the confines of the bladder into the wall of the urethra and vagina. All such described in this lecture are ectopic members of double ureter systems. The anatomical course of this part of an ectopic ureter, the changes in structure and the aetiology of ureteroceles, are pertinent to the theme of this paper.

Course of Ectopic Ureter

The ureter which issues from the caudal segment of the kidney is called orthotopic because it opens into the bladder in the usual situation. That which drains the cranial segment is the ectopic ureter. It terminates at an ectopic site, either in the orthotopic ureter or in the trigone, urethra

or genital tract. Both ureters enter the intramural tunnel of the bladder together, the orthotopic issuing into the lumen of the bladder after a short course beneath the vesical mucosa on to the lateral cornu of the trigone. The ectopic ureter runs a submucosal course which is short when it issues cranial or medial and close to the orthotopic orifice and long when distal to it. The ectopic ureter which issues into the urethra or genital tracts in its course through the submucosal plane must inevitably pass within and not through the sphincteric muscle coats of the urethra (Stephens, 1963c).

Position of Orifice and Leakage. The ectopic ureter that issues into the bladder does not create a wetting problem, but when the orifice lies in the urethra or in the vulva the circumstances are different and in some instances induce uncontrollable leakage.

It is well known that ectopia of the ureter in the male does not cause wetting. In the female, if the orifice is in the internal sphincter zone of the urethra, no wetting occurs: but if it is beyond this zone, wetting may occur.

When the orifice lies within the internal sphincter zone, it is as efficiently sealed as the bladder itself and no wetting occurs. The ureter contains the urine between the acts of micturition, until with relaxation of the sphincter it overflows into the bladder.

When the orifice lies in the external sphincter zone or beyond, the internal sphincter no longer acts upon the orifice but on the ureter which lies within its grip. Intermittent peristalsis in the ureter or the ureteral overflow pressure or both combined, predominate over the sphincter between the acts of micturition, thereby causing persistent wetting. Many examples of the long submucosal ureter were shown to lack muscle, and consequently power of peristalsis; the internal sphincter then outmatched the defective ureter and prevented leakage. In special circumstances, however, the ureter does leak; for example when the ureter overflows—nocturnal wetting, or when the patient stands and gravity exaggerates the pressure in the column of urine in the ureter, the 'vertical incontinence' of Higgins, Williams and Nash (1951). It has been reported that wetting first occurred in a woman after her first pregnancy. Here infection in an otherwise functionless ureter with discharge of mucopus is a likely explanation.

The Structure of the Long Intramural Ureter

Some hint as to the structure of this ureter may be obtained from a cystoscopic study of the ureteral orifice and the bladder base. The long ectopic ureters which issued by a normal orifice in the bladder were invisible beneath the trigone. They

contained in their intramural course a long but normal longitudinal coat. These ureters subserved normal ureteric function in the patients studied in this series. When the orifice was stenotic a ureterocele was visible at the base of the bladder.

Those ureters which issued into the urethra beyond, were all abnormal but conformed to a pattern distinguished by the appearances of the orifices and the calibre of the lumens. When the orifice was near normal in appearance the intramural ureter lay invisibly beneath the trigonal mucosa, its calibre normal or uniformly large in diameter. When the orifice was, on the one hand, large and patulous, or on the other hand, stenotic, undiscovered or absent, the ureter was generally expanded within the walls of the trigone to form a ureterocele. In some, active contractibility could be distinguished. In others, the ureterocele remained tense, flaccid, or inert (Stephens, 1963d).

All the long ectopic ureters which issued into the urethra were subjected to obstruction caused by the grip of the internal sphincter upon the orifice or upon the ureter itself. The way in which the ureteric structure reacted was variable.

(a) It appeared that the presence of a normal ureteric orifice presaged the association of an intramural ureter which exhibited a strong hypertrophic muscle coat. Furthermore, histological examination revealed that it was composed not only of the longitudinal muscle coat but possessed a hypertrophic circular coat as well. In other words, the intramural ureter resembled the extramural ureter in structure and was equipped to execute peristalsis.

One specimen however, revealed a normal calibre amuscular ureter. Presumably it was laid down in this calibre, and the absence of muscle accounted for the lack of hypertrophy. In another, thick adventitious tissue preponderated over the muscle components.

The two features which help the clinician in recognising the pathology of the ureter are the relatively normal ureteric orifice and the lack of trigonal deformation.

(b) An abnormally large orifice, usually situated in the upper one-third of the urethra, signifies ureterocele formation in the sub-trigonal space. Such orifices and associated ureteroceles behave differently according to their structure.

Some large orifices open widely to permit the flow of urine, and snuggle back into the wall of the urethra as the jet ceases. The ureterocele in its distended state occupies the trigonal area and obscures the view of other vesical landmarks, but when contracted it is invisible. On occasions, a sudden contractile wave, beginning posteriorly, shakes the ureterocele, converting it to a tenuous ridge under the trigone. This ridge remains

visible momentarily, and then vanishes from view. In this contracted state, the walls of the intramural ureter steer the ureteral catheter freely into the extramural zone.

Biopsy material from this type of ureterocele indicates that muscle, though sparse in the walls and roof, is arranged not only in longitudinal direction, but to some extent in circular or oblique distribution as well. This arrangement accounts for peristalsis, and active emptying of the ureterocele during micturition. The extreme thinness of the muscle in the roof however, accounts for inability to force the grip of the internal sphincter, the damming back of urine in the ureter, and the distension to maximum proportions of this weakly supported trigonal part of the ureter.

Other large orifices remained limp or immobile; the roof wavered in the fluid stream and the ureterocele remained immobile or sluggish. The roof merely collapsed, showing minimal intrinsic contractility. The ureteric catheter, in this type, wound up in the capacious ureterocele and would go no further.

Three unspoiled specimens obtained from post-mortem material confirmed the complete lack of muscle in the roof and sides of the distal half or more of the ureterocele. Lack of muscle explains the immobility of this type of ureterocele.

One patient exhibited a half-way stage between a hypertrophic tortuous ureter and a ureterocele. The tortuosities were recognisable as oval and crescentic filling defects in the cystogram. The oval filling defect was the end-on appearance of the ureter on the trigone and the crescents were tortuosities.

The muscular component of the ureterocele determines also the competence of its orifice. Reflux was demonstrable in a minority of the long intramural ureters; it is likely that reflux occurs when the distal part of the roof of the ureterocele is amuscular and hence not sphincteric, or when the ureterocele is thick-walled, and composed chiefly of fibrocytes, collagen and elastic tissue, with only a sprinkling of muscle. Here the reflux may be limited in proportion to the extent of muscular endowment of the wall.

It is presumed that the sphincteric mechanism is adversely affected by lack of or impairment of muscle action in the walls of the ureterocele. Even the continuation of a thick circular coat and excess fibrous tissue may impair the action of the longitudinal fibres which are the special activators of the sphincter mechanism of the ureter.

The large orifice, often ten times normal size, the capacious ureterocele which may be better described as a ureterobladder, and the abnormal mural components all point to a developmental

origin—an aberration of expansion of the ureteric bud—in this variety of ureterocele.

(c) A small or undiscovered ectopic orifice is also associated with ureterocele formation. The orifice and adjoining ureter are subjected to double obstruction indicated by the term sphinctero-stenotic as applied to the ureterocele. The orifice, being small is difficult to discover. It may lie in the urethra, hidden from view by the wall of the ureterocele, or in the ejaculatory duct, or be absent. Clues as to the sites of the orifices were forthcoming in two patients from examination of the vas and the scrotum. A thickened vas in one patient, and epididymal cysts in another indicated the association of malformations of both the Wolffian ducts and the ectopic ureter, which issued into the ejaculatory ducts.

The behaviour of this type of ureterocele is predictable but the structure is not: it remains distended; emptying is slow because of stenosis and is retarded further by the long continued grip of the sphincter.

The walls of all the ureteroceles which were subjected to distension were devoid of muscle rather than possessing excess hypertrophic muscle as would be expected. Histological studies of three totally occluded ureters revealed absence of muscle in the distal halves or more, and patchy distribution in the remaining portions. This distribution of muscle contrasts with that of the stenotic ureterocele, the orifice of which lies within the bladder. There the muscle is hypertrophic as one would expect; not thin, patchy, incomplete or absent as in those of the sphinctero-stenotic type.

The reason for the discrepancy of muscle clothing is found in the rudimentary nature of the deformity. The closer the orifice lies to the ejaculatory duct in the male or to the orifice of the Müllerian duct in the female, the more rudimentary and abnormal are the ectopic ureter and its metanephric cap. Furthermore, the size of the ectopic ureter and its transmural segment are dictated primarily by the developmental organization of the ureteric bud, which thus account for individual variation in size from borderline to big or ballooned. Furthermore, that part of the ureter which lies within the walls of the bladder may be subjected to the same growth stimulus which excites the tube-like structure to enlarge to form the bladder. Hence an ectopic ureter may be stimulated to form its own bladder (ureterocele) within the bladder.

Here again, the theme of intrinsic muscle endowment of the ureter is again invoked to explain the behaviour of ureteroceles and some facets of the leakage problem.

Prolapse of Ureterocele

Prolapse of the ureterocele may occur from the bladder into the urethra and cause obstruction for the duration of the prolapse. It involves only those instances in which the ureteric orifices lie in the urethra. It seems that factors conducive to maintaining distension of the ureterocele during voiding, together with the intrinsic encroachment of the ectopic ureter into the urethra are essential to prolapse. The factors are, firstly, refilling from below during voiding—urethro-ureteral reflux—an event ensuing on absence of muscle in the ureter; secondly, retention of urine induced by stenosis; and thirdly, rapid overfilling from above by active peristalsis of a large full ureter during the act of micturition.

In the female, the prolapsed ureterocele appears at the external urethral orifice and receives immediate treatment, but in the male prolapse or partial prolapse is occult and sinister and may be identified only by a filling defect in the posterior urethra on micturition cysto-urethrography. Reduction of the prolapse relieves the obstruction, though recurrence is likely. Insidious renal impairment ensues in the undiagnosed and untreated occult type.

Obstruction of the Ipsilateral Orthotopic Ureter and Contralateral Ureter

The orifices of both these ureters are liable to obstruction by the distended ectopic ureterocele. The ipsilateral orthotopic ureter is trapped and squeezed flat between the distended ectopic ureter and the mucous membrane of the trigone. The fuller the ureterocele and adjoining ureter, the greater the squeeze.

The opposite ureter may be drawn up onto the slopes of the ureterocele and its orifice and adjoining ureter pressed flat.

Histological studies of the orthotopic orifice and adjacent ureter have shown that here again, the muscle is deficient in many instances, with twofold effect. First reflux from the bladder occurs and secondly the terminal ureter being adynamic adversely affects the propulsion of urine into the bladder, thus aggravating obstruction.

In these ways, any or all orifices may be impaired causing deterioration in kidney function with concomitant depression in health.

Summary

The uretero-vesical valve which governs one-way flow of urine is intrinsic in that part of the ureter which lies in the submucous plane of the intramural course through the bladder wall. It relies for its action on its side-on position relative to the lumen of the bladder and on its longitudinal muscle component, which activates its flap valve.

Defects of this submucosal section of the ureter either of length, of muscle or both lead to a two-way flow, stasis and infection. The simple and faithful practice of multiple micturition by the patient, instructed by an informed paediatrician and supervised by the parent effectively overcomes stasis in the megaureter and eliminates infection.

When the submucosal segment is abnormally long, the muscle component may be defective rendering the valve incompetent. When this segment is of sufficient length to extend into the urethra ureterocele formation is not uncommon; defects in its muscle coat which impair emptying, permit refilling during voiding and promote prolapse of the ureterocele. If the ureter issues into the urethra beyond the internal sphincter zone, wetting ensues, but even this is capricious by nature of the varying degree of the muscle endowment of its walls.

REFERENCES

- HIGGINS, T. T., WILLIAMS, D. I., and NASH, D. F. E. (1951): 'The Urology of Childhood', p. 2. London: Butterworth.
- HUTCH, J. A. (1962): The Role of the Ureterovesical Junction in the Natural History of Pyelonephritis, *J. Urol. (Baltimore)*, **88**, 354.
- STEPHENS, F. D., and LENAGHAN, D. (1962): The Anatomical Basis and Dynamics of Vesicoureteral Reflux, *Ibid.*, **87**, 669.
- (1963a): 'Congenital Malformations of the Rectum, Anus and Genito-Urinary Tracts', p. 123. Edinburgh: E. & S. Livingstone.
- (1963b): *Ibid.*, p. 125 and 145.
- (1963c): *Ibid.*, p. 157.
- (1963d): *Ibid.*, p. 178.