Voiding Dysfunction: What Can Radiologists Tell Patients and Pediatric Urologists?

Stephen A. Zderic[1,2]
Dana A. Weiss[1,2]

OBJECTIVE. Imaging children with dysfunctional voiding remains a challenge because 98% of these children have normal anatomy. Identifying the 1–2% of children who do have an anatomic basis for incontinence is important; this article focuses on how pediatric urologists use imaging for the evaluation of patients with this condition.

CONCLUSION. Imaging a patient with dysfunctional voiding can provide findings that will allow an accurate diagnosis and lead to optimal management. The key for the pediatric urologist is using imaging studies judiciously because the diagnostic yield is low. If every patient with dysfunctional voiding who presents to the clinic undergoes imaging, there will be little gain. Understanding in which patients to try imaging sooner versus trying medical and behavioral management first is a function of experience.

Keywords: bladder physiology, detrusor sphincter dyssynergia, ectopic ureter, pediatric urology

DOI:10.2214/AJR.14.14019

Received October 28, 2014; accepted after revision January 20, 2015.

Based on a presentation at the Society for Pediatric Radiology 2014 annual meeting, Washington, DC.

[1]Department of Surgery, Division of Urology, The Children's Hospital of Philadelphia, 34th and Civic Center Blvd, Wood Bldg, 3rd Fl, Philadelphia, PA 19104. Address correspondence to S. A. Zderic (zderic@email.chop.edu).

[2]Department of Urology, The Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA.

This article is available for credit.

WEB
This is a web exclusive article.

AJR 2015; 205:W532–W541

0361–803X/15/2055–W532

The most important information a radiologist can tell a patient, parent, and urologist about dysfunctional voiding is that there is an anatomic basis for the child's incontinence. Although this statement seems obvious, the reality is that pediatricians and pediatric urologists see many patients with problems of bowel and bladder control; epidemiologic survey data suggest that 3% of 5- to 7-year-old children experience diurnal incontinence. However, the incidence of an abnormal anatomic finding among all these children with bladder or bowel dysfunction is low—ranging from 1% to 2% [1]—even at a center where many pediatric patients are referred. Diagnosing a structural anomaly that accounts for urinary incontinence is even less likely today than it was 30 years ago because of early detection on prenatal sonography.

In this article, we aim to delineate the role that imaging plays in the evaluation of otherwise healthy children who present with dysfunctional voiding. These patients present with a variety of symptoms, and thus the indications for imaging will vary according to the mode of presentation (i.e., a presentation centered around incontinence vs infection). Children with known anatomic diagnoses such as spina bifida or spinal cord injury have voiding dysfunction, but their imaging requirements have already been well described.

The Embryologic and Neural Basis for Normal Micturition

A discussion of abnormalities of micturition should begin with a review of the voiding cycle, an explanation of how this complicated reflex changes during the course of normal development, and then an explanation of how it is altered in response to specific pathologic stresses. We will begin with a brief overview of the embryologic development of the bladder and colon at the 4th–6th weeks of fetal development [2]. During this critical time frame, the embryo undergoes a critical partition of the cloaca into the bladder and the rectum. The bladder begins to develop in the anterior half of the former cloaca, whereas the rectum develops in the posterior half. In addition, during this time frame, the urethra begins its migration to the normal perineal position in females. In males, the urethra elongates and ultimately reaches its final anatomic location at the tip of the glans in a process that is androgen dependent. At the same time that this partition is developing, the wolffian ducts serve as the origin of the ureteral buds, which make contact with the primitive metanephric blastema. As a result of complex reciprocal cytokine signaling between the ureteral bud and the blastema, the ureter, collecting system, and kidney develop [3, 4]. A ureteral bud that takes off too far from its normal spot on the wolffian duct will be more likely to insert abnormally into the

urinary tract and may result in either high-grade reflux or an ectopic ureter [5].

This brief summary of embryology is important to understanding pediatric voiding dysfunction for two important reasons. First, the common embryologic origin of the bladder and the rectum mean that these organs also share some overlapping neural pathways. Second, the embryologic origin of the ectopic ureter is important to keep in mind especially in the evaluation of the incontinent female. An ectopic ureter that leads to incontinence is seen only in women because the wolffian duct bypasses the external striated sphincter in its path along the lateral wall of the vagina.

Both the bladder and the rectum have sensory and motor functions that are derived from S2, S3, and S4 sacral segments. This shared sensory overlap accounts for the relationship between constipation and voiding dysfunction. The scientific basis for this association may be found in experimental and clinical studies. Dual fluorescent studies have been performed in rodents to perform retrograde neural tracing. In one such experiment, examination showed that half of the neurons within Barrington's nucleus have an origin in the bladder and one fourth have a rectal origin but that one fourth have sensory input from both the rectum and the bladder [6] (Fig. 1). Similar findings have been noted in the sensory afferent neurons within the dorsal horns of S2, S3, and S4 sacral segments. Although such a study describes the anatomic circuit, other studies show the neurophysiology of the relationship between a distended rectum and bladder function. In an experimental study of a rat model, investigators placed a balloon catheter in the rectum and a suprapubic tube to allow cystometry [7]. They found that inflation of the balloon led to rectal wall distention that, in turn, altered the cystometry and resulted in urinary frequency and a diminished voiding pressure [7]. Similar findings were noted in a human study in which rectal distention by a balloon altered the urodynamic tracing [8].

A basic review of the neural circuitry that regulates the lower urinary tract during the filling phase of the voiding cycle is shown in Figure 2. In 1925, Barrington [9] described a cluster of neurons within the brainstem that served to coordinate the firing of the detrusor muscle. During filling, the afferent neuron signals from the bladder that are activated with bladder distention send projections to the dorsal horn of the second, third, and fourth spinal cord segments [10–12]. Some of these neurons also project to higher centers in the brainstem (Barrington's nucleus) and cerebral cortex. These fibers convey the sense of fullness that trigger a desire to void. Some of these sensory neurons also synapse with an interneuron in the S2, S3, and S4 sacral segments that serves to connect the sensory neurons in the dorsal horn with the motor neurons in the anterior horn of these same segments and complete a classic reflex circuit. However, during the filling cycle, the interneuron's ability to fire is suppressed by a steady stream of tonic inhibitory signaling that emanates from the neurons in Barrington's nucleus. The primary inhibitory neurotransmitter released by Barrington's nucleus is glutamate [13, 14], although experimental studies suggest that other neurotransmitters play a role. The stress neuropeptide corticotrophin-releasing factor may also serve to inhibit the voiding reflex [15, 16].

In addition to the suppression of the voiding reflex arc during filling, there is also a simultaneous activation of neurons that stimulate the striated external sphincter complex and the smooth muscle of the bladder neck. These sphincter complexes will gradually tighten with bladder filling and thus prevent inadvertent leakage. The external striated sphincter is under volitional control and is innervated by the pudendal nerve, which also arises from the S2, S3, and S4 sacral segments. In contrast, the smooth-muscle fibers of the bladder neck, which form a shutterlike sphincter, are under control of sympathetic neurons that emanate from the thoracolumbar chain of ganglia. All of these nerves are active during bladder filling and signal these striated (external sphincter) or smooth (internal sphincter) muscles to generate tension and thus contribute to outlet resistance.

These relationships change during the voiding phase of the cycle as shown in Figure 3. As the child reaches a point at which the sensory signals alert the cortex that it is time to void, the cortex initiates a signal to Barrington's nucleus that removes the tonic inhibitory output that has suppressed the activity of the sacral interneuron. As this interneuron is activated and becomes capable of firing, the sacral reflex arc is completed, and the motor neurons found in the anterior horn of the S2, S3, and S4 sacral segments are activated. These parasympathetic cholinergic neurons give rise to motor fibers within the pelvic nerve that travel to peripheral ganglia within the bladder wall. Cholinergic postganglionic fibers travel to the motor endplate that impinges on the smooth muscle and deliver acetylcholine into the cleft. On binding to the muscarinic receptors expressed on the surface of the smooth-muscle fibers, contraction is initiated and maintained.

Categories of Voiding Dysfunction

Normal efficient voiding takes place when the firing of the detrusor muscle is coordinated with the simultaneous relaxation of the striated external and the smooth-muscle internal sphincters. Failure of either of these two sphincters to relax results in less efficient voiding. Children with voiding dysfunction present with a broad spectrum of symptoms and the incontinence may be associated with symptoms ranging from constipation to severe fecal soiling, cystitis, or even pyelonephritis [1]. On occasion, these patients present with intermittent lower abdominal pain that is caused by underlying constipation.

The rare presentation of a failure to relax the internal sphincter in conjunction with the firing of the detrusor muscle will be discussed first. This voiding phenotype has been well described by Combs et al. [17] and accounts for less than 5% of the patients evaluated in our voiding clinic [17]. These patients are typically adolescents who are very anxious and present with a prolonged urinary stream. A uroflow study will show a steady but very prolonged void with a diminished peak flow. If videourodynamic studies of these patients are performed, the following findings will be present: First, there will be an elevated voiding pressure; second, the electrical motor activity of the pelvic floor will be silenced during voiding as measured by surface patch electrodes (because by definition the striated external sphincter is relaxed during voiding); and, third, the bladder neck will fail to open and funnel during voiding (Fig. 4A). Because the bladder neck fibers are under the control of adrenergic neurons, these patients respond nicely to medical management with α-blockers and many clinicians may opt to try this therapy first. In managing males with this suspected diagnosis, it is essential to distinguish this subset of patients from those who have an underlying anatomic diagnosis such as a urethral stricture (Fig. 4B). Some urologists may opt to treat with an α-blocker first to see if there is improvement. If there is no change in the flow rate, then retrograde urethrography or voiding cystourethrography (VCUG) is indicated to rule out a urethral stricture.

The failure to relax the striated external sphincter that results in the classic picture of the neurogenic bladder is typically seen in patients with anatomic abnormalities such as spina bifida, a spinal cord injury, or bladder compression by a tumor. These patients often present with incontinence or urinary tract infections, and the bladder often undergoes significant hypertrophy. This hypertrophy results from the work done as the bladder attempts to empty against the resistance arising from the external sphincter that is firing simultaneously. This hypertrophy can ultimately result in severe bladder wall fibrosis and a loss of bladder compliance, which results in high storage pressures that compromise the upper urinary tract and that, in extreme cases, can lead to end-stage renal disease. However, a failure to relax the striated external sphincter can also be seen in dysfunctional voiding in the absence of any overt spinal cord abnormality and is a common finding in children presenting with urinary incontinence.

Hinman and Baumann [18] first described a population of patients with extreme voiding dysfunction who presented with urinary and fecal incontinence associated with bladder wall hypertrophy. They reported that a subset of these patients showed compromise of their upper urinary tracts. Later, Allen and Bright [19] described urodynamic patterns of dysfunctional voiding in otherwise neurologically intact children. These patients were observed to be high achievers who exhibited a tendency toward perfectionism. An example of such a patient is shown in Figure 5A, which shows the external sphincter is firing in conjunction with voiding. The postvoid image of this patient shows a highly trabeculated bladder and left-sided reflux (Fig. 5B). Ochoa and Gorlin [20] described a population of patients with a voiding phenotype that resembled that described by Hinman and Baumann [18], but this group of patients were characterized by two distinct features: first, their attempts to smile resulted in a grimace (and hence this constellation is referred to as the "Ochoa urofacial syndrome"); and, second, this voiding phenotype is inherited following Mendelian genetics [20, 21]. Genetic mapping studies performed of the original patient cohort described by Ochoa [21] in Columbia have shown that this gene is found in the region of the human genome where the proteolytic enzyme heparanase is localized [22, 23]. Familial cohorts have been described in other geographic areas [24].

Because the external striated sphincter is under volitional control in patients with no spinal cord abnormalities, urologists came to understand that the treatment of these patients should aim to teach patients how to relax their external sphincter in conjunction with voiding and should treat the underlying constipation. From this work came the realization that biofeedback therapy has a role in treating children with dysfunctional voiding who have no underlying anatomic basis for their presentation.

Wenske et al. [25, 26] have also pointed out that not all children with dysfunctional voiding who present with an intermittent urinary flow rate will prove to have detrusor sphincter dyssynergia. They reported evidence showing that some of these patients may present with an intermittent urinary flow rate and a normal relaxation of the external sphincter, which led them to conclude that these patients may have an underpowered detrusor sphincter. This hypocontractile detrusor muscle has been given several eponyms such as the "lazy bladder" or the "bladder holder." Typically, patients will present with urinary incontinence. This subset of patients will void infrequently (1–3 times per day), will often present with urinary tract infections or incontinence, and will have a large bladder capacity [27].

Diagnosis and Measurement

The diagnosis of pediatric dysfunctional voiding is primarily based on a careful history and physical examination in conjunction with a urinalysis. For many children, a urinary tract infection will be the primary mode of presentation and is a manifestation of the underlying voiding dysfunction. In particular, the history should focus on whether the child has ever achieved continence, the frequency of urination, the pattern of wetting, and whether the child has a history of urinary tract infections or a history of underlying constipation. Numerous studies point to the strong association between constipation and urinary tract infection and dysfunctional voiding [27]. It is common to see children present to our voiding dysfunction clinic with urinary incontinence that responds quickly when the underlying constipation is treated successfully.

In recent years, we have modified our approach to these patients by incorporating a symptom score sheet that the child and parents fill out together. This questionnaire was developed by Akbal et al. [28] and with some slight modifications was validated in our patient population [29]. This voiding symptom score has been used in our Dysfunctional Outpatient Voiding Education (DOVE) Center to grade and follow voiding dysfunction symptoms. The score can range from 0 (normal) to 35 (severe voiding dysfunction); when validated in our patient population, the average score at presentation was 12.4 points and 30% of the patients had a score of less than or equal to 8 points. This measurement tool is important for several reasons. First, it can serve to function as a resource allocator in terms of the patient's time and effort needed to achieve continence. The cohort of patients whose score is less than or equal to 8 points at presentation can often be successfully managed with a single visit that involves education about how the bladder works, treatment of low-grade constipation, and a recommendation of timed voiding with good water intake. If this group of patients can be successfully managed with one office visit in 80% of the cases, then the clinician has more time to focus on the more challenging subset of patients whose scores are higher. We also think that the score serves as a valuable tool for deciding which patients need to undergo imaging and when imaging should be performed. Patients who respond to the simple treatment and whose scores drop to normal will be spared imaging studies. On the other hand, patients for whom simple treatment fails to yield an improvement are exactly the group of patients in whom the yield for diagnostic imaging will be higher.

Another useful objective measure in the evaluation of these patients is urinary flow rate. Obtaining a urinary flow rate is a simple noninvasive test performed by having the child void in a commode equipped with a digital scale that drives its output to a computer. The resulting flow pattern is helpful in establishing whether there is a rise and fall in the flow rate that might be indicative of striated external sphincter dyssynergia. The postvoid residual can also be assessed noninvasively using a bedside bladder scanner.

Treatment of Voiding Dysfunction

Patients will respond to a spectrum of treatments that includes timed voiding, antibiotic prophylaxis, treatment of constipation, anticholinergic medication, and biofeedback. Biofeedback is an office-based procedure that is performed by placing patch electrodes over the perineum and teaching the child how to squeeze and then relax these muscles; the child is then coached to void while focusing on relaxation of this

muscle group. In recent years, the biofeedback system contains a video screen with an interactive game to capture the child's attention and reward the successful void that is accompanied by relaxed perineal musculature [30]. Does this therapy work? Our recent review of 55 patients who underwent biofeedback in our voiding dysfunction clinic revealed that the average daytime voiding symptom score dropped by 4.3 points and that 50% of the patients developed a normal bell-shaped uroflow curve after an average of 2.5 sessions [31]. Despite this improvement, it is important to remember that biofeedback requires time and effort on the part of the patient and family. We must remember that if a child is entered into a biofeedback treatment regimen but in fact has an anatomic abnormality, valuable time and resources will be lost. Although the yield for anatomic diagnoses at imaging may be low, there is a time when these patients should undergo imaging.

In extreme cases that fail to respond to simple treatment, it may be necessary to start clean intermittent catheterization (CIC) to teach the child how to optimally relax the striated external sphincter [32]. A case study of CIC management is shown in Figure 6 in which a 9-year-old girl presented with recurrent urinary and fecal incontinence. Findings on an initial ultrasound were normal. However, despite multiple rounds of biofeedback therapy and treatment of her constipation, the urinary incontinence persisted with a voiding symptom score of 27. An MRI examination of her spine showed normal findings. A videourodynamic study showed elevated storage pressures and a high voiding pressure of close to 100 cm H_2O, and active electromyography activity was seen during voiding. Fluoroscopy showed the classic "spinning top" findings, which are characteristic of detrusor sphincter dyssynergia. At this point, the decision was made to teach the patient CIC; with CIC treatment, her voiding symptom score improved from 27 to 1.

For some of our patients, CIC is used as a temporary measure and normal voiding function returns as the child learns to spontaneously relax the external sphincter. Although this invasive approach to achieving continence is needed in few patients, it is in exactly this group of resource-consuming patients for whom imaging is most indicated to rule out all other possible anatomic causes of incontinence.

Which Patients With Voiding Dysfunction Should Undergo Imaging and When and How to Image?

Healthy children with no other comorbidities and voiding dysfunction do not need to undergo imaging at presentation. The likelihood of finding abnormal anatomy that is responsible for urinary incontinence is between 1% and 2% [1]. Hence, imaging these children as soon as they present to the voiding dysfunction clinic is likely to result in many low-yield studies that do not add value. On the other hand, it is even more worrisome to see patients who have been treated with behavioral or medical management for years who are then shown to have an anatomic basis for incontinence. So how does one approach these patients when patients with aberrant anatomy present as the proverbial needle in the haystack?

We begin an evaluation with a basic history and physical examination and measurement of the voiding symptom score. For patients with a low score (≤ 8 points) with no history of urinary tract infections, one may treat clinically with education about how the bladder works, timed voiding, increased water intake, and treatment of constipation and safely omit imaging studies. In these cases, it is critical to ensure that the family understands that the child must return to the clinic if this simple treatment fails to yield progress and achieve continence. However, sometimes imaging the urinary tract is important in terms of achieving "buy in" from the parent who, after months or even years of frustration, is convinced that there must be something physically wrong with the child. Normal imaging findings help these parents accept the fact their child does not have an anatomic abnormality and can respond to the more time-consuming behavioral and medical management strategies.

Some patients need imaging soon after presentation to the voiding dysfunction clinic. These patients are children with a history of urinary tract infection. Imaging these patients is needed to rule out structural anomalies such as reflux that would alter medical management.

Another group for whom imaging is indicated is young females who by history have never achieved continence and whose family notes continuous wetting. These complaints should trigger clinical suspicion of an ectopic ureter; in most of these patients, ultrasound will suffice as the screening study. Patients are less likely to present with these findings today because prenatal sonography will detect the hydroureteronephrosis associated with an ectopic ureter, and these children are managed starting in the neonatal period. When imaging an older patient with a history that is suspicious for an ectopic ureter, findings of hydroureteronephrosis that extend below the bladder neck or the finding of a duplex system indicates the need for additional imaging.

It is also important to remember that, in rare cases, ultrasound may fail to detect an ectopic ureter especially if it is linked to an atrophic poorly functioning kidney. This failure of ultrasound happens rarely but is illustrated by the case presented in Figure 7. This patient presented as a 7-year-old girl with a long-standing history of day and night wetting and a voiding symptom score of 21. Although she was constipated, she and her family described her as voiding at regular intervals without urgency. Findings on renal bladder ultrasound were normal, and her uroflow rate was a perfect bell-shaped curve with no postvoid residual noted. At the clinic, she was prescribed polyethylene glycol 3350 (MiraLAX, Bayer HealthCare) for constipation and given voiding logs. Because her symptoms persisted, MR urography was performed: It revealed a right upper pole duplication with a dysplastic segment that was contributing a filtrate, which entered a nondilated ureter that ultimately terminated in the urethra and accounted for her symptoms (Figs. 7A and 7B). After undergoing a right upper pole partial nephrectomy and distal ureterectomy, she became continent.

Another indication for imaging early is the patient who presents with a sudden onset of wetting or a patient who shows other comorbidities. Figure 8 shows images of a 7-year-old boy with mild autism who had achieved daytime continence at 4 years old but had never achieved nighttime control. In recent months, his parents had noted polydipsia and polyuria, and he progressively lost daytime urinary control. His voiding symptom score was 12 at presentation. Given this constellation of findings, ultrasound was performed at the first visit. Ultrasound revealed bilateral hydroureteronephrosis (Figs. 8A and 8B) and a thickened bladder wall. He underwent VCUG, which revealed a highly trabeculated bladder wall and poor visualization of the urethra (Fig. 8C). These findings suggest the possible diagnoses of posterior urethral valves or Hinman syndrome. On the basis of these imaging findings, the decision was made to perform a cystoscopic evaluation,

and the diagnosis proved to be posterior urethral valves. One year later, he was continent day and night with a voiding symptom score of 0, and imaging showed a complete return to normal. We were able to evaluate his prenatal imaging, and there were no findings on that study to suggest any anomalies of the urinary tract. This case serves to remind us that we can place only so much reassurance on the statement that prenatal imaging findings were normal; in most of these types of presentations, the prenatal imaging is normal. Some lesions such as posterior urethral valves are progressive, so the ultrasound findings will become apparent only once the hydronephrosis has developed. In our series of patients with posterior valves, almost one fourth presented with postnatal clinical findings of infection or incontinence [33].

Some patients undergo imaging for a febrile urinary tract infection and that imaging examination reveals reflux, which suddenly becomes the central focus of physicians. In fact, most cases of reflux are low grade (grades I–III) and reflux often is associated with constipation and voiding dysfunction. It is critical to remember that treating the underlying voiding dysfunction is actually going to treat the reflux in most of these cases [34, 35]. Numerous studies have also shown that reflux surgery carries a higher failure rate if there is underlying voiding dysfunction [36, 37]. These concepts are illustrated in the case presented in Figure 9: a 6-year-old girl who presented with a clinical history of daytime wetting, constipation, and a febrile urinary tract infection. Her initial VCUG study showed a spinning-top urethra (Fig. 9A) (implying underlying detrusor sphincter dyssynergia), signs of bilateral high-grade reflux (Figs. 9B and 9C), and mild bladder wall trabeculation and constipation. This group of radiographic findings should encourage a urologist to start antibiotic prophylaxis (which has been shown to be beneficial especially in cases of bowel and bladder dysfunction [38]), treat the underlying constipation, obtain a urinary flow study, and consider the use of biofeedback therapy if the urinary flow rate is interrupted. With these measures, this patient's reflux resolved 1 year later (Fig. 9D).

It is also important to detect the presence of spinal cord abnormalities such as a tethered cord. Tethered cord often is not detected in young patients because of "normal" findings on physical examination of the spine, and patients present later with urinary incontinence or constipation. Obviously it is easier for the clinician to order MRI with confidence when the incontinent child presents with a markedly aberrant sacral finding, but even in the setting of a normal spine, history must be considered as well. If behavioral modification and anticholinergic medication fail, the patient may be found to have cord tethering on MRI of the spine. If a tethered cord is detected on MRI, cystometry may show uninhibited contractions, and neurosurgical release of the cord tether will often improve the voiding dysfunction. The diagnostic yield of spinal MRI in the setting of a normal physical examination is extremely low [39]; however, in a highly selected series, there will be a yield of positive findings despite normal findings on sacral examination [40]. We must stress that these studies are ordered for patients years after initial presentation and are not appropriate for the individual who presents to the voiding clinic for the first time.

Conclusions

In summary, imaging children with dysfunctional voiding can provide findings that will allow an accurate diagnosis and lead to optimal management. The key for the pediatric urologist is using imaging studies judiciously because the diagnostic yield is low. If every patient who presents to the clinic undergoes imaging, there will be little gain. Understanding in which patients to try imaging sooner versus trying medical and behavioral management first is a function of experience. We hope that an algorithm will be developed in the years ahead that will optimize the use of imaging in the management of these patients. For now, we must be content with the illustrations of individual cases of when imaging should be considered and how helpful it can be in select circumstances.

References

1. Franco I. Functional bladder problems in children. *Pediatr Clin North Am* 2012; 59:783–817
2. Lambert SM, Zdreic SA. Chapter 21: embryology of the female urogenital system and clinical applications. In: Cardozo L, Staskin D, eds. *Textbook of female urology and gynecology*, vol. 1. Abingdon, UK: Taylor and Francis, 2009:172–184
3. Shah MM. Branching morphogenesis and kidney disease. *Development* 2004; 131:1449–1462
4. Viana R, Batourina E, Huang H, et al. The development of the bladder trigone, the center of the anti-reflux mechanism. *Development* 2007; 134:3763–3769
5. Mackie GG, Stephens FD. Duplex kidneys: a correlation of renal dysplasia with position of the ureteral orifice. *J Urol* 1975; 114:274–280
6. Rouzade-Dominguez ML, Pernar L, Beck S, Valentino RJ. Convergent responses of Barrington's nucleus neurons to pelvic visceral stimuli: a juxtacellular labeling study. *Eur J Neurosci* 2003; 18:3325–3334
7. Miyazato M, Sugaya K, Nishijima S, Ashitomi K, Ohyama C, Ogawa Y. Rectal distention inhibits bladder activity via glycinergic and GABAergic mechanisms in rats. *J Urol* 2004; 171:1353–1356
8. Panayi DC, Khullar V, Digesu GA, Spiteri M, Hendricken C, Fernando R. Rectal distension: the effect on bladder function. *Neurourol Urodyn* 2011; 30:344–347
9. Barrington FJ. The lesions of the hind and mid brain on micturition in the cat. *J Exp Phsyiol* 1925; 15:81–102
10. Fowler CJ, Griffiths D, de Groat WC. The neural control of micturition. *Nat Rev Neurosci* 2008; 9:453–466
11. de Groat WC, Yoshimura N. Neurophysiology of micturition and its modification in animal models of human disease. In: Maggi C, ed. *Nervous control of the urogenital system.* Chur, Switzerland: Harwood Academic Publishers, 1993:227–290
12. de Groat WC, Yoshimura N. Mechanisms underlying the recovery of lower urinary tract function following spinal cord injury. *Prog Brain Res* 2006; 152:59–84
13. Sugaya K, de Groat WC. Inhibitory control of the urinary bladder in the neonatal rat in vitro spinal cord-bladder preparation. *Brain Res Dev Brain Res* 2002; 138:87–95
14. de Groat WC, Araki I. Maturation of bladder reflex pathways during postnatal development. *Adv Exp Med Biol* 1999; 462:253–263
15. Kiddoo DA, Valentino RJ, Zderic S, et al. Impact of state of arousal and stress neuropeptides on urodynamic function in freely moving rats. *Am J Physiol Regul Integr Comp Physiol* 2006; 290:R1697–R1706
16. Wood SK, Baez MA, Bhatnagar S, Valentino RJ. Social stress-induced bladder dysfunction: potential role of corticotropin-releasing factor. *Am J Physiol Regul Integr Comp Physiol* 2009; 296:R1671–R1678
17. Combs AJ, Grafstein N, Horowitz M, Glassberg KI. Primary bladder neck dysfunction in children and adolescents. I. Pelvic floor electromyography lag time: a new noninvasive method to screen for and monitor therapeutic response. *J Urol* 2005; 173:207–210; discussion, 210–211
18. Hinman F, Baumann FW. Vesical and ureteral damage from voiding dysfunction in boys without neurologic or obstructive disease. *J Urol* 1973; 109:727–732
19. Allen TD, Bright TC 3rd. Urodynamic patterns in

children with dysfunctional voiding problems. *J Urol* 1978; 119:247–249
20. Ochoa B, Gorlin RJ. Urofacial (Ochoa) syndrome. *Am J Med Genet* 1987; 27:661–667
21. Ochoa B. The urofacial (Ochoa) syndrome revisited. *J Urol* 1992; 148:580–583
22. Wang CY, Hawkins-Lee B, Ochoa B, Walker RD, She JX. Homozygosity and linkage-disequilibrium mapping of the urofacial (Ochoa) syndrome gene to a 1-cM interval on chromosome 10q23-q24. *Am J Hum Genet* 1997; 60:1461–1467
23. Pang J, Zhang S, Yang P, et al. Loss-of-function mutations in *HPSE2* cause the autosomal recessive urofacial syndrome. *Am J Hum Genet* 2010; 86:957–962
24. Garcia-Minaur S, Oliver F, Yanez JM, Soriano JR, Quinn F, Reardon W. Three new European cases of urofacial (Ochoa) syndrome. *Clin Dysmorphol* 2001; 10:165–170
25. Wenske S, Van Batavia JP, Combs AJ, Glassberg KI. Analysis of uroflow patterns in children with dysfunctional voiding. *J Pediatr Urol* 2014; 10:250–254
26. Wenske S, Combs AJ, Van Batavia JP, Glassberg KI. Can staccato and interrupted/fractionated uroflow patterns alone correctly identify the underlying lower urinary tract condition? *J Urol* 2012; 187:2188–2193
27. Van Batavia JP, Ahn JJ, Fast AM, Combs AJ, Glassberg KI. Prevalence of urinary tract infection and vesicoureteral reflux in children with lower urinary tract dysfunction. *J Urol* 2013; 190:1495–1499
28. Akbal C, Genc Y, Burgu B, Ozden E, Tekgul S. Dysfunctional voiding and incontinence scoring system: quantitative evaluation of incontinence symptoms in pediatric population. *J Urol* 2005; 173:969–973
29. Schast AP, Zderic SA, Richter M, Berry A, Carr MC. Quantifying demographic, urological, and behavioral characteristics of children with lower urinary tract symptoms. *J Pediatr Urol* 2008; 4:127–133
30. Combs AJ, Glassberg AD, Gerdes D, Horowitz M. Biofeedback therapy for children with dysfunctional voiding. *Urology* 1998; 52:312–315
31. Berry A, Rudick K, Richter M, Zderic S. Objective versus subjective outcome measures of biofeedback: what really matters? *J Pediatr Urol* 2014; 10:620–626
32. Silay MS, Tanriverdi O, Karatag T, Ozcelik G, Horasanli K, Miroglu C. Twelve-year experience with Hinman-Allen syndrome at a single center. *Urology* 2011; 78:1397–1401
33. Pulido J, Furth SL, Zderic SA, Canning DA, Tasian GE. Renal parenchymal area and risk of ESRD in boys with posterior urethral valves. *Clin J Am Soc Nephrol* 2014; 9:499–505
34. Koff SA. Relationship between dysfunctional voiding and reflux. *J Urol* 1992; 148:1703–1705
35. Koff SA, Wagner TT, Jayanthi VR. The relationship among dysfunctional elimination syndromes, primary vesicoureteral reflux and urinary tract infections in children. *J Urol* 1998; 160:1019–1022
36. Hinman F, Baumann FW. Complications of vesicoureteral operations from incoordination of micturition. *J Urol* 1976; 116:638–643
37. Noe HN. The role of dysfunctional voiding in failure or complication of ureteral reimplantation for primary reflux. *J Urol* 1985; 134:1172–1175
38. RIVUR Trial Investigators; Hoberman A, Greenfield SP, Mattoo TK, et al. Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med* 2014; 370:2367–2376
39. Broughton GJ, Clayton DB, Tanaka ST, et al. The usefulness of lumbosacral magnetic resonance imaging in the management of isolated dysfunctional elimination. *J Urol* 2011; 186(suppl 4):1715–1720
40. Satar N, Bauer SB, Shefner J, Kelly MD, Darbey MM. The effects of delayed diagnosis and treatment in patients with an occult spinal dysraphism. *J Urol* 1995; 154:754–758
41. Rouzade-Dominguez ML, Miselis R, Valentino RJ. Central representation of bladder and colon revealed by dual transsynaptic tracing in the rat: substrates for pelvic visceral coordination. *Eur J Neurosci* 2003; 18:3311–3324
42. Zderic SA, Canning DA. Posterior urethral valves. In: Canning DA, Docimo S, Khoury A, eds. *The Kelalis-King-Belman textbook of clinical pediatric urology*, 6th ed. Boca Raton, FL: CRC Press, 2016 (in press)

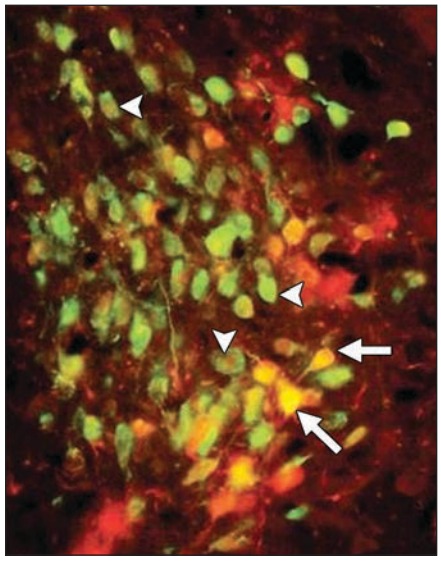

Fig. 1—Division of cloaca by urorectal septum gives rise to bladder and rectum, but there is overlap in sensory output from these organs. This overlap is shown on fluorescent photomicrograph obtained at retrograde tracing study in rat model in which modified pseudorabies virus–expressing green fluorescent protein is injected in bladder, and modified pseudorabies virus–expressing β-galactosidase is injected in rectum. Beta-galactosidase expression is detected with antibody coupled to red fluorophore. Sensory projections to Barrington's nucleus can be seen: About half stain green (*arrowheads*) (bladder afferent neurons), one fourth stain red (rectal afferent neurons), and one fourth stain yellow (*arrows*) (common afferent neurons). These results show that neurons are receiving afferent input from both rectum and bladder. (Reprinted with permission from [41]: Rouzade-Dominguez ML, Miselis R, Valentino RJ. Central representation of bladder and colon revealed by dual transsynaptic tracing in the rat: substrates for pelvic visceral coordination. *Eur J Neurosci* 2003; 18:3311–3324)

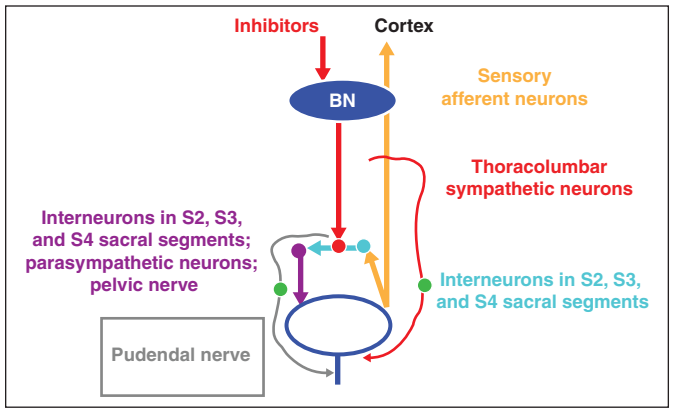

Fig. 2—Chart shows bladder filling phase of voiding cycle. During bladder filling phase, afferent neurons from bladder sense bladder distention and convey these signals to interneurons in S2, S3, and S4 sacral segments; Barrington's nucleus (BN), which is located in pons; and cortex. During filling phase, interneurons are shut down by neural input from Barrington's nucleus. Cortical inhibition drives Barrington's nucleus during this phase. As a result of this inhibition, there is no stimulation of parasympathetic neurons that give rise to pelvic nerve. Bladder storage is also facilitated by stimulation of pudendal nerve, which stimulates striated external sphincter and sympathetic nerves arising from lumbodorsal ganglia that stimulate bladder neck. Green dot = facilitation of neurotransmission, purple dot = pelvic nerve, red dot = inhibition of neurotransmission, blue dot = interneuron.

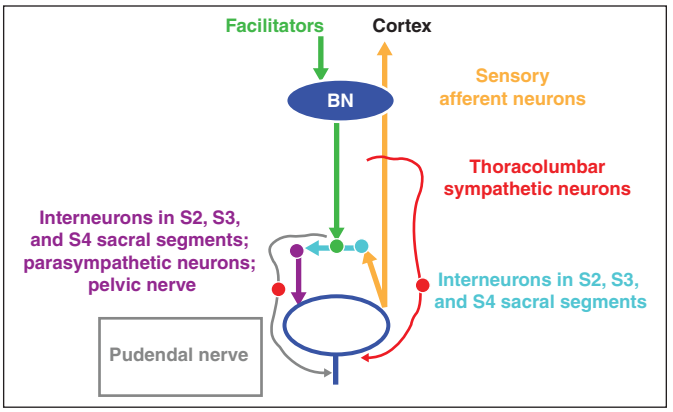

Fig. 3—Chart shows bladder emptying phase of voiding cycle. During emptying phase, afferent neurons from bladder sense bladder distention and convey these signals to cerebral cortex. Cerebral cortex emits signal to Barrington's nucleus (BN). Barrington's nucleus removes inhibitory signal to interneurons in S2, S3, and S4 sacral segments, which completes sacral reflex arc and allows voiding to proceed once motor neurons of pelvic nerve are activated. In coordinated manner, there is also simultaneous inhibition of pudendal nerve (to relax external striated sphincter) and of sympathetic fibers (to allow relaxation and funneling of bladder neck). Red dot = inhibition of neurotransmission, purple dot = pelvic nerve, green dot = facilitation of neurotransmission, blue dot = interneuron.

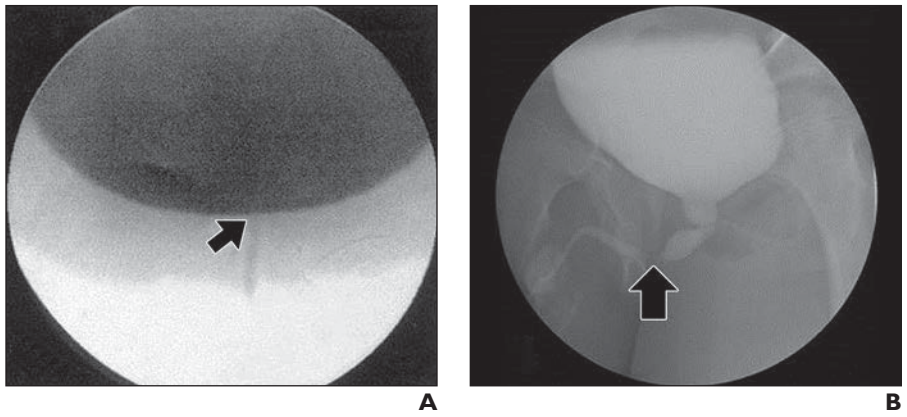

Fig. 4—Dyssynergia of bladder neck smooth muscle during voiding is rare cause of voiding dysfunction. (Reprinted from [17]: *The Journal of Urology*, Vol. 173 [issue 1], Combs AJ, Grafstein N, Horowitz M, Glassberg KI, "Primary bladder neck dysfunction in children and adolescents. I. Pelvic floor electromyography lag time: a new noninvasive method to screen for and monitor therapeutic response," pages 207–210, Copyright 2005, with permission from Elsevier)
A, Fluoroscopic image obtained during urodynamic study of 14-year-old girl with dyssynergia (*arrow*) of bladder neck smooth muscle.
B, Fluoroscopic image of 9-year-old boy with dyssynergia of bladder neck smooth muscle. In males, dyssynergia (*arrow*) of bladder neck smooth muscle must be differentiated from urethral stricture, which can present in similar manner.

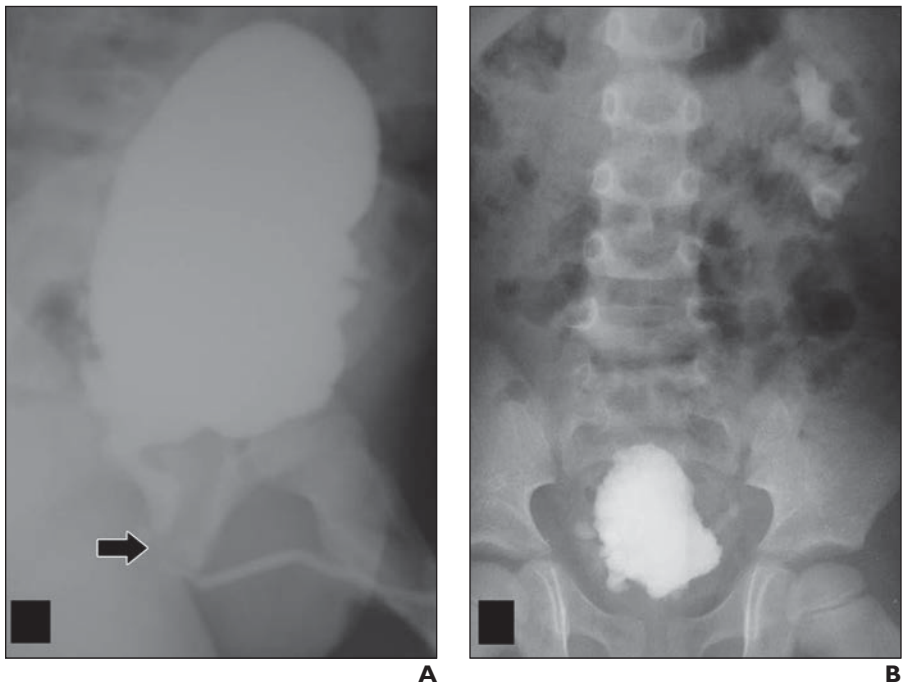

Fig. 5—Radiographic findings in 8-year-old boy with Hinman syndrome.
A, Fluoroscopic image during voiding cystourethrogram. Large trabeculated bladder results from repeated episodes of voiding against contracting external sphincter (*arrow*).
B, Postvoid fluoroscopic image, bladder trabeculations and diverticula suggest high-pressure voiding. In addition, there was reflux into left system late in voiding phase (not shown).

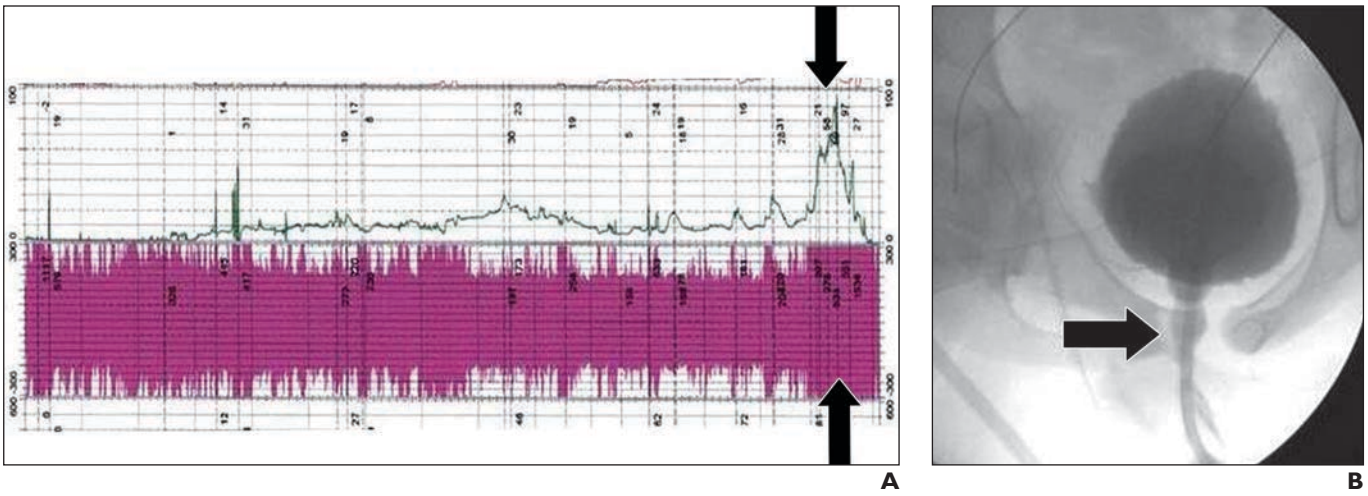

Fig. 6—9-year-old girl who presented with chronic wetting and constipation. Videourodynamic study revealed high voiding pressure of nearly 100 cm H_2O.
A, Electromyogram shows very active pelvic floor (*arrows*).
B, Activity detected at electromyography correlated with simultaneous firing of external sphincter (*arrow*) noted on fluoroscopic image. Multiple rounds of biofeedback failed; continence was ultimately achieved with regimen of clean intermittent catheterization. Before initiation of this aggressive approach, patient underwent MRI of urinary tract and lumbar spine to rule out tethered cord. This case is less severe form of Hinman syndrome.

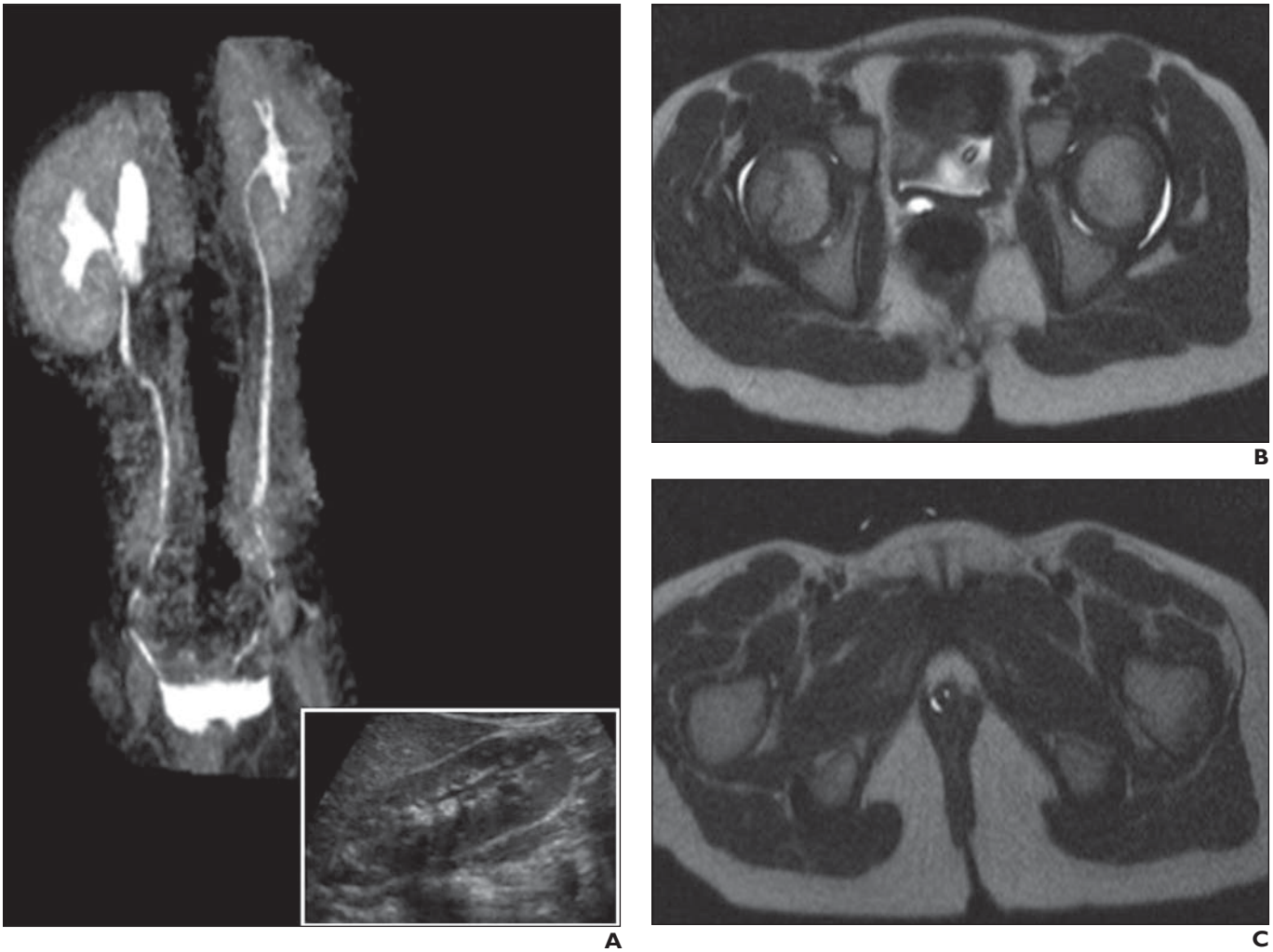

Fig. 7—Ectopic ureter in 7-year-old girl with normal ultrasound findings. Most ectopic ureters will present with abnormal ultrasound findings. Ultrasound typically shows hydroureteronephrosis and dilated ureter dropping below bladder neck. (Reprinted with permission from [2]: Lambert SM, Zdreic SA. Chapter 21: embryology of the female urogenital system and clinical applications. In: Cardozo L, Staskin D, eds. *Textbook of female urology and gynecology*, vol. 1. Abingdon, UK: Taylor and Francis, 2009:172–184)
A, Ultrasound image of right kidney. Ultrasound image shown in inset depicts normal findings. Because this child was continuously wet but had normal voiding diary and normal urinary flow rate, decision was made to perform MR urography.
B and **C,** MR urographic images show small dysplastic right upper pole segment that drains into hypoplastic ureter; hypoplastic ureter inserts into urethra.

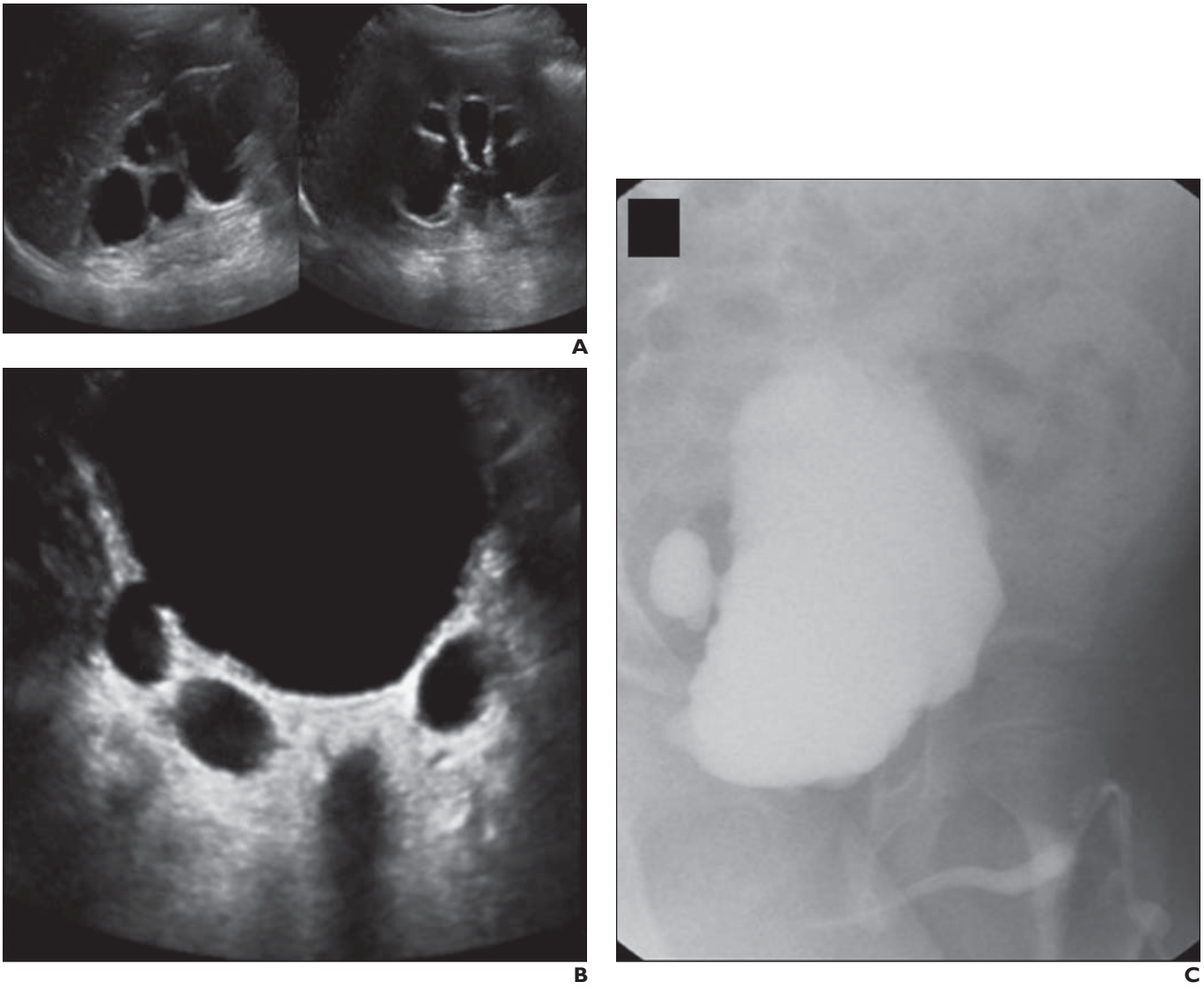

Fig. 8—In evaluating young males with incontinence, radiologists should consider posterior urethral valves in differential diagnosis. This 7-year-old boy with mild autism presented with worsening daytime incontinence, polyuria, and polydipsia. (Reprinted with permission from [42]: Zderic SA, Canning DA. Posterior urethral valves. In: Canning DA, Docimo S, Khoury A, eds. *The Kelalis-King-Belman textbook of clinical pediatric urology*, 6th ed. Boca Raton, FL: CRC Press, 2016 [in press])
A and **B,** Ultrasound images show bilateral severe hydroureteronephrosis.
C, Voiding cystourethrogram shows findings suggestive of either severe Hinman syndrome or posterior urethral valve: trabeculated bladder, small diverticulum, and poor opacification of urethra. Cystoscopy was performed and proved valve was incised. One year after cystoscopy, patient was continent day and night, and ultrasound showed complete resolution of hydronephrosis.

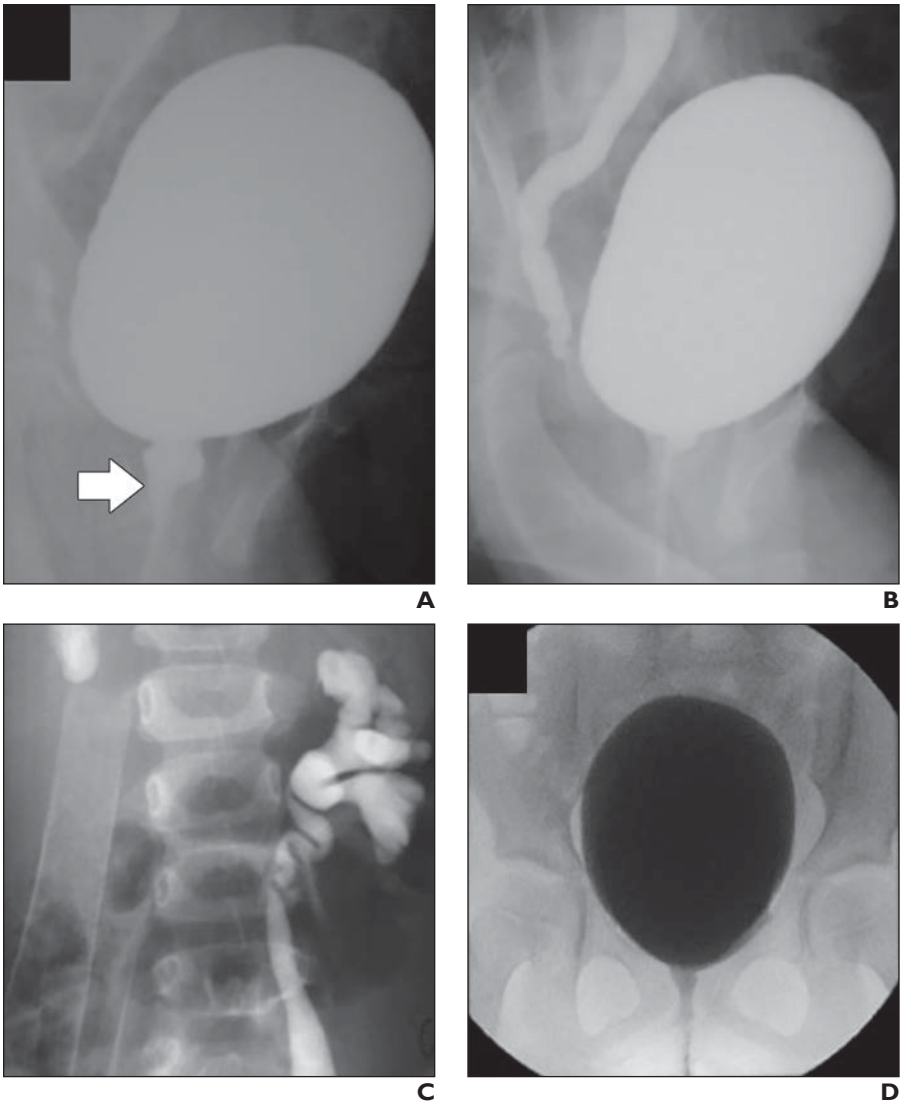

Fig. 9—6-year-old girl who presented with clinical history of daytime wetting, constipation, and febrile urinary tract infection. Dysfunctional voiding and vesicoureteral reflux are often seen together, and vesicoureteral reflux is critical diagnosis to make. Patients with reflux and voiding dysfunction are highest risk for recurrent urinary tract infections and benefit most from prophylaxis.
A, Voiding cystourethrogram shows that voiding is associated with firing of external sphincter (*arrow*).
B and **C,** Fluoroscopic images during voiding show bilateral high-grade reflux results from high-pressure voiding.
D, Fluoroscopic image during videourodynamic imaging obtained 1 year after antibiotic suppression, treatment of constipation, and biofeedback shows that reflux has resolved.

FOR YOUR INFORMATION

This article is available for CME and Self-Assessment (SA-CME) credit that satisfies Part II requirements for maintenance of certification (MOC). To access the examination for this article, follow the prompts.