Initial management of complex pediatric disorders: prunebelly syndrome, posterior urethral valves

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Prunebelly syndrome (PBS) and posterior urethral valves (PUV) are conditions with impaired voiding proficiency caused by abnormal bladder development. Although infants with these conditions appear different, they may all present with respiratory distress, profound renal insufficiency, severe hydronephrosis (HUN), and bladder wall thickening. Infants with PBS also exhibit bilateral intra-abdominal cryptorchidism and a characteristic lax abdominal musculature. The incidence of PUV (1 case per 5000 to 8000 male births) [1] is roughly five times greater than that of PBS (1 case per 29,000 to 40,000 male births) [2]. Histologic studies of fetal bladder specimens have demonstrated an increase in bladder muscle thickness in infants with both of these conditions, implicating early urinary tract obstruction in the etiology [3].

The ultimate pattern of detrusor dysfunction results from differences in the onset, severity, and duration of urethral obstruction in PBS and PUV. Urethral obstruction is thought to occur earliest in PBS, causing massive distension of the bladder followed by urinary ascites [4–6]. The severity and early onset of urethral obstruction in PBS promote extensive renal dysplasia, persistence of a patent urachus, and myogenic bladder failure (similar to the end-stage detrusor dysfunction evident in PUV [7]). Massive bladder distension and ascites combine to degenerate the abdominal wall muscles and prevent testicular descent. Rupture of the obstructing membrane just proximal to the membranous urethra [2] occurs most often before birth.

These events account for the recognized spectrum of urethral profiles in PBS ranging from widely patent to stenotic [8]. Although urethral obstruction in PUV is persistently evident postnatally, a spectrum of severity exists. Another mechanism involving a primary mesodermal defect is also suspected in PBS, because fetal bladder histology ranges from thin muscle walls with increased collagen (no evidence of obstruction) to detrusor hypertrophy with a normal ratio of connective tissue (less severe but similar to the findings in PUV, indicating urethral obstruction) [3]. Abnormal banding of the ejaculatory ducts and agenesis of the seminal vesicles are found only in PBS (Fig. 1), further supporting a fundamental difference in the embryologic development of these two entities [8]. Genital duct abnormalities are detected when PBS presents in female infants [9–12].

Antenatal ultrasonography reveals similar findings in infants with PBS and PUV, including severe bilateral HUN, a dilated posterior urethra, and a large bladder that empties poorly during monitoring. Increased renal parenchymal echogenicity, cystic changes, and poor corticomedullary differentiation are signs of dysplasia [13,14]. Antenatal intervention by vesicoamniotic shunt [4,15,16] or pregnancy termination [17,18] has been considered for both conditions when severe oligohydramnios is present. Relief of urinary obstruction antenatally often fails to correct renal insufficiency [15,19]; however, pulmonary function and survival may be improved if oligohydramnios is reversed [20].

Renal dysplasia imparts a background of irreversible renal insufficiency in infants with PBS and PUV. Hyposthenuria (obligate polyuria) induced by renal tubular injury results in excessive...
clearance of free water and sodium. Severe HUN and urinary stasis increase the risk for urinary infection and urosepsis, which can incite severe dehydration and electrolyte disturbances. Preservation of renal function depends on early and effective relief of urinary obstruction and prevention of renal damage from pyelonephritis. Recognizing the severity of bladder dysfunction present is crucial to attain this goal. The incidence of renal failure continues to be 25% to 30% among children with PBS and severe PUV [21,22]. Appropriate initial evaluation and treatment for infants with PBS and PUV may help to avoid or postpone the need for renal transplantation [23], or at least improve graft survival when transplantation becomes necessary [24,25].

Prunebelly syndrome

Previously called the absent abdominal muscle syndrome [26–28] or its less offensive moniker, the triad syndrome [29], PBS [30] presents as a spectrum of involvement in the anterior abdominal wall, in the urinary tract, and in the degree of descent of the testes [31] (Fig. 2). Other serious anomalies outside the genitourinary tract are common (Fig. 3). The most severe abdominal wall defects exhibit complete absence of muscle ventral to the midaxillary line [12], which allows the entire abdominal wall to be lifted and palpated. Some infants present with more substantial or even normal abdominal wall thickness, especially in the upper quadrants [32]. The degree of abdominal wall involvement does not correlate with the severity of urinary tract impairment [31].

The ureter in PBS demonstrates gross, microscopic, and ultrastructural changes. These dilated and tortuous ureters exhibit wall thickening, which correlates with an increase in collagen deposition between muscle bundles [33]. Electron microscopy identifies massive replacement of smooth muscle architecture with fibrous and collagenous tissue, with progressive collagen deposition evident in the wider more distal ureter [34]. Clinical observation confirms that the best functioning ureter is nearest to the kidney [35]. Although ureteral dilatation is suspected to result primarily from inefficient peristalsis, distal ureteral obstruction can occur [36,37].

The bladder in PBS is vertically enlarged with an increased wall thickness but is typically not trabeculated. The dome of the bladder often exhibits a pseudodiverticulum at the urachal attachment, which may generate a patent urachus when urethral stenosis or atresia is present [38]. The trigone is broad, with the ureteral orifices displaced laterally, and vesicoureteric reflux (VUR) is detected in approximately 85% of infants with PBS [39]. The bladder outlet expands during voiding, exposing a characteristic tapered appearance on voiding cystourethrography (VCUG), even though intravesical pressures usually remain normal [40]. Inefficient bladder emptying with significant postvoid residual volumes
occurs in most children with PBS, independent of their voiding pattern (and independent of prior reduction cystoplasty) [41–43]. Although abdominoplasty improves the efficiency of bladder emptying for most children with PBS, residual volumes typically remain greater than 10% of bladder volumes [42].

Urethral obstruction from stenosis, valves, megalourethra, or atresia is recognized in as many as 25% of infants with severe renal impairment [12,44]. Stenosis can be demonstrated at autopsy as an angulation in a short segment of the prostatic urethra just above the membranous urethra [8,45,46]. This pattern, in which the membranous urethra exits from anterior wall of the prostatic urethra, can be associated with a normal or narrow caliber or with a “high takeoff” imparting relative obstruction (Fig. 4) [8]. Anterior folds of the prostatic urethral mucosa are suspected to cause obstruction when they overlap the urethral outlet (type IV valves) [8,33]. Variations on Young’s type I and III urethral valves are also recognized on postmortem examination in infants with PBS [8]. Although both types of megalourethra may occur, infants with PBS account for half the reported cases of the scaphoid type [47]. The absence of tissue in all three corporal bodies (fusiform megalourethra) or merely the corpora spongiosum (scaphoid megalourethra) occurs along with urethral obstruction in a spectrum of severity, which blurs the distinction between these two types [48,49]. Fusiform megalourethra is strongly linked to severe renal impairment and neonatal demise (Fig. 5) [47]. Absence of the entire penis and urethra has been observed in infants with PBS [50].

Bilateral nonpalpable undescended testes are a characteristic feature of PBS. The testes are intra-abdominal and mobile on a long mesorchium, and both testes are typically present and viable [51]. Although the testes are generally found overlying the dilated ureters at the level of the iliac vessels, their position can span the entire course of the ureter. The vas deferens can be tortuous and thin walled with segmental atresia [52,53], and the epididymis can be detached entirely from the testis [54]. In the prepubertal period, these testes may be

Fig. 4. Voiding cystourethrogram in a neonate with PBS and a patent urachus, demonstrating an elongated and dilated prostatic urethra with a high takeoff of the membranous urethra exiting anteriorly (white arrow).
histologically indistinguishable from normal immature testes, with no difference in germ cell counts detected [55,56]. Testis biopsies may also reveal tubules lined by only Sertoli cells [57], or Leydig cell hyperplasia with hypospermatogonia [58]. Infantile PBS germinal epithelium demonstrates morphologic and histochemical similarity to embryonic germ cells and intratubular germ cell neoplasia, suggesting that a developmental arrest occurs in these testes, and that children with PBS may be at a higher risk for germ cell tumors [59].

Associated anomalies can involve the respiratory tract, gastrointestinal tract, cardiovascular system, and musculoskeletal system. Respiratory impairment results from pulmonary hypoplasia (in utero oligohydramnios) and from mechanical factors (flattened diaphragm associated with rib flaring and weakened abdominal musculature). The resultant poor expiratory effort may only become apparent clinically during postoperative recuperation [60,61]. Although a wide spectrum of rare gastrointestinal maladies have been recognized (malrotation, volvulus [62], gastrochisis [63], omphalocele [64], Hirschsprung’s disease [65], and imperforate anus [39,66]), the most common manifestation is chronic constipation secondary to poor peristalsis and a generalized lack of intra-abdominal pressure [21]. Abdominoplasty and an ongoing bowel regimen are beneficial for the management of constipation [21]. Cardiovascular anomalies, most commonly septal defects (atrial and ventricular) and tetralogy of Fallot, occur in approximately 10% of infants with PBS [67]. Correction of these defects supersedes urologic reconstruction. Orthopedic abnormalities, which result from fetal compression, affect half of all infants with PBS. Common abnormalities include developmental dislocation of the hip, scoliosis, pectus excavatum, clubfeet, and muscular torticollis [68–70]. Many infants with PBS exhibit dimples on the lateral aspects of their knees without any functional orthopedic limitations (Fig. 6).

Initial evaluation

Before 1970, half of all infants with PBS died within the first 2 years of life [71]. The current prognosis and clinical management are determined primarily by the degree of renal impairment present (severe, moderate, or mild) [72,73]. When severe renal dysplasia is present, neonatal mortality generally follows acute respiratory distress owing to pulmonary hypoplasia or urosepsis [21,74]. Progression to renal failure is strongly correlated with bilateral abnormalities noted on renal ultrasonography or renography and a nadir serum creatinine level greater than 0.7 mg/dL [74]. Some infants with nearly normal urinary tracts and preserved renal function may only require surveillance, whereas others require active intervention to relieve urinary stasis and to prevent urinary infection.

Early assessment of infants with PBS is essential so that treatment can be individualized. Physical examination can reveal a palpable kidney, ureter, or bladder, suggesting that significant urinary obstruction is present. Urinalysis and urine cultures, along with assays for serum creatinine and electrolytes, can identify urinary infection or metabolic problems early enough for intervention and should be performed at regular intervals determined by their trend. Serial ultrasonography

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Fig. 5. Severe fusiform megalourethra in premature infant with PBS. Note the left leg behind the megalourethra with the heel at end of the penis.

Fig. 6. Dimple without underlying subcutaneous fat on the lateral aspect of the right knee in 6-month-old infant with PBS.
reveals the amount of renal parenchyma present and aids in the detection of progressive HUN. This preliminary investigation in the first few days of life will determine whether the infant needs only prophylactic antibiotic therapy and routine surveillance. VCUG can be postponed in infants with stable renal function to avoid introducing bacteria into a stagnant urinary system [75,76]. Infants with poor renal function, massive ureteral dilatation, a patent urachus, and high bladder residual volumes need additional investigation. VCUG will delineate urethral abnormalities, the degree of bladder distension, the extent of VUR, and the presence of urachal abnormalities. Concomitant antibiotic administration may mitigate the risk of urinary infection associated with catheterization. Nuclear renography (99mTcDMSA or 99mTcMAG3) aids in confirming functioning renal tissue; however, 99mTcMAG3 Lasix washout renography is unreliable for the detection of obstruction in the presence of extreme ureteral dilatation and tortuosity (with or without VUR), especially in the setting of poor renal function.

Initial treatment

Specific treatment of the dilated urinary tract in PBS has remained controversial for the past 25 years. Massively dilated, poorly functioning lower ureters may predispose the infant to stasis and infection with further renal deterioration [31]. Nonetheless, more than half of children with PBS who are followed up with only minimal surgical intervention (urethrotomy for urethral obstruction) have demonstrated a satisfactory outcome with stable renal function [75,77,78]. Cutaneous vesicostomy may be beneficial when poor bladder emptying leads to urinary infection, especially if urethral stricture, valves, or atresia is detected. Although a patent urachus may initially be present in this setting, bladder drainage is unreliable, because the urachus often closes within the first several weeks of life. Urethral atresia or stenosis can also be managed successfully with progressive soft dilation of the urethra, yielding a normal caliber urethra [79].

Urinary tract decompression may be indicated when progressive azotemia occurs, especially when in utero oligohydramnios was recognized. In these cases, bilateral open nephrostomies and renal biopsies have been advocated to differentiate between renal obstruction and renal dysplasia [75]. An alternative approach advises early supravesical diversion by pyelostomy followed by total reconstruction in a single stage (bilateral tapered ureteroneocystostomy, reduction cystoplasty, bilateral orchiopexy, and abdominoplasty) [80]. Loop ureterostomy should be avoided, because it may compromise the best portion of the ureter [35,75]. Temporary end cutaneous ureterostomy may offer temporary relief of obstruction and may promote a decrease in the overall caliber of the severely dilated ureter [75], but this approach should be used with caution in infants with PBS owing to poor ureteral peristalsis and a propensity for stomal stenosis. Percutaneous nephrostomy should be reserved for infants with severe azotemia or infection requiring exigent direct renal drainage to allow survival. Although primary newborn reconstruction for PBS has been completed with excellent results [72], the use of radiographic surveillance and antibiotic prophylaxis for several months is now considered preferable to lower the risk for postoperative pulmonary complications [81]. Ureteroneocystostomy with extensive tapering is technically feasible in infants with PBS because bladder volumes tend to be substantial [31], but coincident vesicostomy or, preferably, appendicovesicostomy should be considered to minimize the risk for postoperative obstruction.

Although abdominal wall laxity may improve somewhat with age, beneficial effects from abdominoplasty are suspected to include improved respiratory and bowel function and enhanced urinary tract emptying [42]. Regrettably, increased pressure on the flattened diaphragm in these infants in the immediate postoperative period contributes to restriction of pulmonary excursion and retention of secretions. Randolph and associates recognized that the upper abdominal musculature was predictably more normal on abdominal wall electromyography; therefore, they recommended a transverse lower abdominal incision for abdominoplasty, removing the lower abdominal musculature in continuity with the peritoneum and skin [32,80]. Ehrlich and associates use a midline incision, extensive dissection of the skin, and overlapping of the anterior abdominal wall fascia along the anterior axillary lines when performing abdominoplasty [82,83]. Abdominoplasty can also be completed by the formation of two longitudinal fascial pleats that are folded medially and secured at the bases of the folds and at the midline of the abdomen [84]. This approach, espoused by Furness and associates, provides more secure suture fixation when the abdominal wall fascia is severely attenuated. A novel repair promoted by Monfort and associates
using two laterally placed longitudinal incisions in the fascia, with subsequent closure in the midline, allows preservation of the umbilicus and offers excellent cosmetic results. Extensive ureteral mobilization and transabdominal orchiopexy are easily accomplished with the generous surgical exposure afforded by this technique [86].

Although transabdominal orchiopexy (without division of the spermatic vessels) can often be completed successfully in the neonate [72], achieving adequate spermatic vessel length for orchiopexy in the older infant or child with PBS may be problematic. A single-stage laparoscopic orchiopexy may be useful in select infants [87] when abdominoplasty is extraneous. A two-stage, vasal-pedicle orchiopexy [88] affords excellent success (>90%) [89], and the first stage can be completed safely using a laparoscopic approach [90].

In a comprehensive approach to reconstruction in PBS, preliminary laparoscopy is performed at approximately 6 months of age, along with a single-stage laparoscopic orchiopexy or a first-stage orchiopexy (laparoscopic division of the spermatic vessels) (Fig. 7). Ureteral dilatation, especially in infants without VUR, should be examined carefully during laparoscopy, because persistent tense distension of the distal ureter, despite the external pressure associated with pneumoperitoneum, strongly suggests distal ureteral obstruction (Fig. 8). After 2 months, the Monfort abdominoplasty with tapered ureteroneocystostomy (for persistent VUR or obstruction) and second-stage orchiopexy can be completed. The urachal diverticulum should be removed if present, but reduction cystoplasty [91] is no longer indicated. Appendicovesicostomy with an umbilical stoma facilitates intermittent catheterization to allow efficient bladder emptying and to prevent urinary infection [41]. Monitoring in an intensive care unit setting is preferable to manage the pulmonary compromise anticipated postoperatively.

**Posterior urethral valves**

In 1919, Young et al [92] described three distinct types of posterior urethral valves based on their cystoscopic appearance. Type I valves account for most (95%) posterior urethral obstructions, ranging from mild to severe depending on their configuration within the urethra. Abnormal insertion of the mesonephric ducts into the fetal cloaca is thought to generate obstructing fibrous stromal membranes in the place of the normal plicae colliculi [33]. Type II valves are considered artifact, resulting from muscular hypertrophy of the superficial trigone extending toward the verumontanum. The type III valve (5%) is a transverse concentric membrane distinct from the verumontanum that results from incomplete dissolution of the urogenital portion of the cloacal membrane (also found in PBS). Both types of valves (I and III) can be thick or thin, but a classic windsock appearance generally results from distension of a thin membrane. Dewan and associates [93] believe that these different types of valves actually represent varied manifestations of a congenital obstructing posterior urethral membrane.

High pressure during the storage and voiding of urine increases the workload on the distended bladder, yielding detrusor hypertrophy and an ingrowth of collagen in infant [94] and fetal [3] bladder specimens. Resultant detrusor hyperreflexia and loss of compliance promote the development of HUN, VUR, and renal damage (renal dysplasia, glomerular and tubular dysfunction). Concentration defects lead to a hyposthenuria with urine volumes large enough to impair voiding efficiency, further challenging the compliance of the ureters and bladder [95,96]. The most serious renal impairment occurs when bilateral VUR is present, forcing both kidneys to develop in a high-pressure setting [95,97]. A high risk for progression to renal failure has been recognized when renal dysplasia and bladder dysfunction exist [97]. The degree of renal dysplasia present at birth is irreversible and determines the potential for growth and function of the kidney. A nadir serum creatinine level greater than 0.8 [98] to 1.0 mg/dL [99] also suggests an impaired glomerular filtration rate (GFR) (<70 mL/min/1.73m²) [14,100] and poor long-term renal function. Proteinuria during infancy, which indicates significant hyperfiltration, also heralds eventual renal failure [14,101].

Mitigation of urinary tract pressures during development allows amelioration of impaired kidney and bladder function. Unilateral VUR may act as a pressure vent, leading to ipsilateral (usually left-sided) dysplasia but allowing better function to develop in the contralateral kidney (VURD syndrome) [102]. Similarly, urinary extravasation (with or without ascites), a patent urachus, and a large bladder diverticulum are protective factors preserving renal function [103–107]. A spectrum of protection clearly exists; however, some children with PUV experience an unfortunate progression toward renal insufficiency despite these protective effects. Bilateral VUR
predisposes to worse overall renal function in comparison with unilateral VUR [95,97] (Fig. 9), but renal function also steadily declines in boys with the VURD syndrome when observed for their first decade [108]. Although any single prenatal pressure vent promotes improved bladder function, indicated by favorable postnatal urodynamic parameters (mean end-filling pressures <30 cm H$_2$O, and total capacity at least equal to that predicted for age), additional pressure pop-offs afford cumulative benefits [103]. Isolated antenatal urinary ascites, speculated to result from extreme bladder pressure leading to rupture, is associated with poor overall
renal function (mean GFR, 29 mL/min/1.73m²). Better function follows unilateral urinoma in the absence (54 mL/min/1.73m²) and presence (70 mL/min/1.73m²) of ascites, with the best overall renal function occurring when bilateral urinomas appear (105 mL/min/1.73m²) [109]. A patent urachus may be considered beneficial [103] but is most often associated with poor overall renal function [110]. The degree of bladder dysfunction without antenatal pressure pop-offs may be severe, with children exhibiting poor urodynamic characteristics (mean end-filling pressures >40 cm H₂O, and bladder capacity <75% of that predicted for age) and a greater requirement for anticholinergic therapy and bladder augmentation [103].

**Initial evaluation**

Currently, most infants with PUV are detected on antenatal ultrasonography. This discovery allows early postnatal treatment and clinical surveillance in a tertiary care center. Nevertheless, some infants with PUV continue to escape fetal diagnosis, because only half are detected by ultrasonography before 24 weeks' gestation [111], and the most unfortunate of these infants present clinically with acidosis, uremia, urinary retention, and urrosepsis [97]. Early detection of PUV by 24 weeks' gestation identifies a high-risk group with a 50% chance of death or chronic renal failure [111]. Infants with severe PUV presenting with favorable urinary electrolytes, oligohydramnios, and fetal growth retardation before 24 weeks' gestation may undergo urinary tract decompression by vesico-amniotic shunt placement, but no long-term renal protection is usually achieved [112]. Progressive changes noted on second-trimester sonography can further delineate the postnatal prognosis. Poor postnatal outcomes (chronic renal failure or death) are predicted in 89% of infants who are found to have moderate or severe HUN (renal pelvic anteroposterior diameter ≥10 mm) and increased renal echogenicity or cystic changes, in contrast to 25% of infants lacking these ominous findings [113].

Ultrasonography performed in the neonatal intensive care unit remains fundamental to monitor the clinical progress of neonates with PUV, providing a measure of the amount of renal parenchyma and the severity of HUN. Perinephric urinoma or ascites evident on ultrasonography suggest prenatal renal or bladder rupture. Perinephric urinomas may be diffuse or localized, and the degree of hydronephrosis present may vary widely [114]. Poor corticomedullary differentiation with increased renal parenchymal echogenicity is the hallmark of renal dysplasia [13,14]. Detection of this finding bilaterally is considered a more meaningful indicator of the degree of infravesical pressure elevation than is detection of bilateral high-grade VUR [13]. HUN, urinary extravasation, and dysplasia are products of pervasive bladder pressure transmission to the upper urinary
tracts. Detection of an increased bladder wall thickness indexed to bladder filling (bladder diameter) reproducibly identifies infravesical obstruction present in children with PUV [115].

When this diagnosis is suspected in a newborn, urethral catheterization should be performed directly to allow bladder decompression until the child is able to undergo radiographic evaluation. Significant postobstructive diuresis from tubular dysfunction can ensue in cases of severe obstruction. Catheters that function poorly may actually be curled within a distended prostatic urethra, or may have entered a gaping ureteral orifice. In extreme cases, inflation of a catheter balloon may completely fill the bladder lumen and cause ureteral obstruction [116]. Radiographic confirmation of catheter position and even a prefatory VCUG can be performed in the neonatal intensive care unit using portable radiography. Voiding cystourethrosionography using echo contrast can also be used as the initial diagnostic examination to detect reproducibly the presence of PUV and VUR [117].

Fluoroscopic VCUG with views of the urethra during voiding is diagnostic for PUV. The posterior urethra is markedly dilated, and the valve appears as a thin linear defect in the column of radiocontrast. The bladder neck is narrowed and thickened, with the urinary channel displaced anteriorly. Contrast may fill the urethra, causing the appearance of a small diverticulum, or may reflux into the seminal vesicles and ejaculatory ducts. The bladder may appear diminutive because of extreme detrusor thickening when compared with the distended prostatic urethra and massively refluxing ureters (Fig. 10). VUR is usually high-grade and occurs in half the affected infants at initial VCUG, with half of these infants exhibiting unilateral involvement and half bilateral involvement [102,118]. Serial VCUG studies are useful to evaluate improvement or resolution of VUR and to confirm complete relief from obstruction following endoscopic valve incision.

Nuclear renography is essential in determining differential renal function. Use of $^{99m}$TcMAG3 provides functional data along with clear visual images of the renal parenchyma and the urinary collecting system [119]. The bladder must be decompressed adequately with a catheter (gravity drainage and aspiration) to avoid overestimation of function in refluxing renal units. The combination of $^{99m}$TcMAG3 renography and indirect radionuclide cystography (evaluation without urinary catheterization, before and after spontaneous micturition) aids in the detection of VUR but also provides a measure of bladder function [119]. An alternative radiotracer, $^{99m}$TcDMSA, which binds to the proximal tubules and provides images of only the renal parenchyma, provides the most accurate assessment of differential renal function.

Initial treatment

Infants with PUV may exhibit severe respiratory distress and metabolic acidosis that requires aggressive intensive care. After the diagnosis is made and the infant is stabilized, durable relief of urinary obstruction can be achieved by endoscopic incision of the PUV. For term infants, this procedure is frequently completed under general anesthesia using an 8F infant resectoscope and a sickle blade with little risk for urethral injury. This approach has few complications, especially when compared with the high rate of urethral stricture (50%) previously reported at the site of fulguration and in the bulbar urethra while employing a 10F resectoscope and electrocautery in infants during the first year of life [120]. Selective disruption of the obstructing valves either anterioely (1974) [121] or posteriorly (1985) [122] was formerly advocated when limitation from available endoscopic equipment was significant. Incision of the valves should be completed in the posterolateral positions (4:00 and 8:00 o’clock positions) and anteriorly (12:00 o’clock position)
to ensure complete relief from obstruction. In milder cases, fusion of the valves anteriorly may not be evident. Urethral catheter placement is rarely necessary following valve incision.

Premature or small infants may require a modified approach for the treatment of obstruction. A 7F cystoscope and a hook electrode (crafted from a 3F catheter and stylet) can be implemented for these infants, but this technique mandates extreme accuracy because it employs electrocautery and an unwieldy electrode in a diminutive space. The neodymium: yttrium-aluminum-garnet (Nd:YAG) laser can also be used to perform valve ablation [123]. Disruption of the PUV under C-arm fluoroscopic guidance may be accomplished with retrieval of a 6F Whitaker hook [124,125] or a No. 4 Fogarty balloon [126]. Although these methods offer little accuracy, excellent results following valve ablation using a 4F Fogarty balloon catheter under fluoroscopic guidance have been reported, achieving full resolution of obstruction without urethral injury in 34 of 35 (97%) infants studied [127]. Antegrade cystoscopy through the percutaneous sheath and valve incision can also be employed [128] and affords a unique perspective on the anatomy of the obstructing PUV. Urinary diversion by cutaneous vesicostomy may be prudent in select neonates, but vesicostomy cannot be proposed as an advantage over primary valve ablation when comparing mortality, preservation of renal function, or postoperative complications [129,130].

Surveillance ultrasonography performed after transurethral incision of PUV will help direct further treatment. HUN that improves after valve incision without a corresponding improvement in serum creatinine strongly suggests that significant renal dysplasia is present. These infants progress to renal failure despite urinary tract diversion. Vesicostomy should be considered when bladder emptying is incomplete despite valve incision, especially if HUN and azotemia (serum creatinine >1.8 mg/dL) are persistent. Vesicostomy has also been advocated in infants with severe bilateral VUR [129,131], because the worst overall renal function is often evident in these infants [97,132]. Ureterostomy or pyelostomy may be beneficial in atypical cases when azotemia and HUN are persistent or progressive despite efficient bladder emptying [133]. Pyelostomy or open nephrostomy provides the most certain urinary tract emptying and allows concomitant renal biopsy to be completed. This approach may be considered when the serum creatinine level fails to decrease by 10% daily to a nadir of less than 0.8 mg/dL (by day 5) [118,130] but is often the most useful when renal deterioration coexists with accumulation of perinephric urinoma or ascites after initial percutaneous drainage. High-loop cutaneous ureterostomy offers a simple and effective option for upper tract diversion [96] but also risks damage to the most normal portion of the distended ureter [134].

Despite reports supporting the concept that supravesical diversion preserves renal function in infants with severe PUV [118,135–137], it has been strongly suggested that a high incidence of renal dysplasia in this population limits any durable benefit beyond childhood [14,130,138–140]. In a group of 26 infants treated by supravesical diversion for persistent azotemia (median serum creatinine, 2.5 mg/dL), renal dysplasia was detected on biopsy in 85%. Despite diversion and a decrease in the median nadir serum creatinine at 1 year to 1.0 mg/dL, 58% of the infants subsequently progressed to renal insufficiency or failure, with 42% reaching end-stage disease at a median surveillance interval of 9 years [138]. Demonstrable ureterovesical junction obstruction was detected only rarely (4%) by antegrade pressure perfusion study performed through the supravesical diversion [138].

Most cases of unimproved HUN after valve incision are caused by severe detrusor dysfunction. An increase in bladder wall tension with high bladder filling pressures causes a functional obstruction at the ureterovesical junction and a corresponding increase in renal pelvic pressures. This valve bladder dysfunction [141] in children with thick-walled and poorly compliant bladders is accentuated by hyposthenuria and by rapid refilling of the bladder as urine in the ureters drains directly after voiding. Prolonged bladder decompression is also deleterious by disruption of normal bladder cycling, which negatively impacts bladder rehabilitation and ultimate capacity and compliance [139,140,142,143]. A critical balance exists in efforts to rehabilitate the kidneys and the bladder in children with PUV. Resolute efforts directed at preserving renal function might yield diminished bladder capacity and compliance and ultimately provoke deterioration of renal function. The Sober-en T ureterostomy has been offered as an option to preserve renal function without compromising bladder function, presupposing that ureteral peristalsis will actively fill the partially defunctionalized bladder [144].

Treatment should be designed to provide low-pressure urinary storage and complete emptying...
of the bladder with voiding. Poor bladder compliance and capacity in children with severe PUV leads to more frequent bladder augmentation to achieve adequate volumes and safe storage pressures [103,139,140]. Primary valve incision tends to preserve bladder capacity and compliance and should be pursued as an initial treatment for infants with PUV. VUR resolves spontaneously in approximately 30% of infants after valve incision, indicating improved bladder pressures [122,145]; however, valve incision alone may also create a hostile situation, with excessive storage pressures when bladder volume is severely compromised. Chronically increased bladder pressure promotes progressive deterioration of renal and bladder function and favors the formation of urinary infection. Pooling of significant volumes of urine in a massively refluxing and nonfunctional collecting system (VURD syndrome) further compounds this risk.

Concern for the detrimental effects of urinary diversion may be supplanted by regard for the importance of preventing urinary infection and renal injury. Secondary vescostomy was found to be useful in a select group of children with unrelenting sepsis despite valve ablation and aggressive medical therapy [130]. Persistent urinary infection despite vescostomy indicates inefficient clearance of urine, most likely from a distended refluxing ureter. End-cutaneous vescostomy of the refluxing ureter has been used in an effort to improve voiding dynamics and to aid in determination of differential renal function in these children [146]. Ureteral reimplantation of the nonfunctioning renal unit [147] has also been advocated as an alternative to nephroureterectomy [102]. Unfortunately, all of these interventions disallow bladder cycling at normal bladder pressures and disrupt rehabilitation of developing bladder function.

Use of a novel incontinent bladder pressure vent allows complete bladder emptying at safe pressures. A series of 10 infants with severe PUV and recurrent urinary infection despite vescostomy and aggressive medical therapy have been managed at Children’s Medical Center of Dallas over the last 8 years employing this principle. An incontinent ureterovesicostomy (Fig. 11) was created from the refluxing ureter in eight infants with VURD syndrome, and an incontinent appendicovesicostomy was constructed in two others. Nonfunctioning kidneys were removed by open (2) and laparoscopic (6) nephrectomy. Refluxing stomas were positioned in the diaper region. Further urinary infection was subsequently prevented in all infants. Urodynamic evaluation indicated normalization of bladder capacity and compliance over the subsequent 3-year interval in all but one child. In that case, the refluxing pressure vent was removed after only 1 year, and progressive deterioration of bladder compliance ensued. Augmentation cystoplasty was ultimately required owing to recurrent urinary infection and marked HUN.

Videourodynamic evaluations revealed ureteral leak pressures ranging from 15 to 20 cm H$_2$O and filling of the pressure vent to the level of the rectus fascia before urinary leakage. Appendicovesicostomy channels reached a higher pressure of 30 cm H$_2$O before venting occurred. These results suggest that an enhanced level of intrinsic luminal resistance is provided by using appendix versus the ureter, reminiscent of the urodynamic findings reported in continent Mitrofanoff conduits in children, also comparing the appendix and ureter [148]. Urinary continence and a normal voiding pattern were achieved in five boys after bladder venting was eliminated by ureteral reimplantation (2) and endoscopic injection therapy (3). One boy with severe developmental delays and three with less than 3 years’ surveillance continue bladder cycling with their pressure vents intact. The remaining boy is continent with intermittent catheterization following augmentation cystoplasty.

These findings suggest that the most effective use of the refluxing ureter in the VURD syndrome may be for bladder rehabilitation rather than
Fig. 12. Proposed management scheme for infants with PUV incorporating the use of a temporary incontinent bladder pressure vent to aid in bladder rehabilitation when progressive hydronephrosis or recurrent urosepsis is present. UTI, urinary tract infection.
bladder augmentation. Use of the appendix as an incontinent pressure vent may be even more beneficial by allowing a higher bladder storage pressure to enhance the effectiveness of bladder cycling and rehabilitation. These pressure vents, which are considered to act as temporary "training wheels" for the bladder allowing effective bladder cycling at safe pressures, may be incorporated into the management scheme for infants with severe PUV (Fig. 12).

Summary

A comprehensive approach must be pursued when treating infants with PBS and severe PUV to preserve renal and bladder function. Because the degree of renal dysplasia present is determined antenatally and is not reversible, preservation of renal function requires optimal bladder rehabilitation and prevention of urinary infection. Infants with PBS and PUV demonstrate impaired voiding proficiency. Those with PBS exhibit myogenic failure with incomplete emptying. Ensuring effective bladder emptying is crucial and can be aided by incorporating an appendicovesicostomy in reconstruction for infants with PBS. Infants with severe PUV typically possess small capacity bladders with poor compliance, which also promotes progressive renal deterioration. Rehabilitation of bladder function can be achieved by creating an incontinent bladder pressure vent allowing effective bladder cycling at safe pressures. This approach is especially appealing in the setting of recurrent urosepsis.

References


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