Urological Issues in Pediatric Dialysis

8

Angus Alexander, Antoine E. Khoury, and Armando J. Lorenzo

Keywords
Pediatric dialysis • Urological issues • Chronic kidney disease • Posterior urethral Valves • Vesicoureteric reflux

Abbreviations

CIC	Clean intermittent catheterization
CKD	Chronic kidney disease
CRF	Chronic renal failure
ESRD	End-stage renal disease
FSGS	Focal segmental glomerulosclerosis
LUT	Lower urinary tract
PBS	Prune belly syndrome
PD	Peritoneal dialysis
PUV	Posterior urethral valves
PVRV	Post void residual volumes
UVJ	Ureterovesical junction obstruction
VCUG	Voiding cysto-urethrogram
VUR	Vesicoureteric reflux

A. Alexander (✉)
Senior Fellow, Division of Urology, The Hospital for Sick Children, Toronto, Canada
e-mail: armando.lorenzo@sickkids.ca

A.E. Khoury
Department of Urology, Children's Hospital of Orange County and University of California Irvine Medical Center, Orange, CA, USA

A.J. Lorenzo
Division of Urology, The Hospital for Sick Children, Toronto, Canada

Introduction

The prevalence of stage 5 chronic kidney disease (CKD) in the pediatric population is approximately 50 cases per million. It has been noted to be increasing in all age groups, but especially among older children [1]. In contrast to adults where glomerulopathy and vasculopathy are the major causes of disease, at least 40% of the CKD in children is due to congenital urological abnormalities [2–6]. As a result of this predominance of urological issues in the pediatric population, the urologist is an essential member of any team tasked with the management of pediatric CKD. Similarly, health care providers dealing with these patients benefit from understanding the urological management principles for this patient population.

In this chapter, we outline the common urological conditions that cause renal failure; we discuss their diagnosis, pathophysiology, and provide an overview of management from a urological perspective. Where relevant, we have highlighted any unique implications for the dialysis patient and/or the transplant recipient. Understanding that dialysis represents a treatment phase between the development of stage 5 CKD and renal transplantation, it is important to

B.A. Warady et al. (eds.), *Pediatric Dialysis*, DOI 10.1007/978-1-4614-0721-8_8,

discuss issues present prior to the initiation of dialysis and following renal transplantation. In addition to this, we will look at the indications for nephrectomy in the CKD patient and the urology specific pre-transplant workup.

Urological Causes of Chronic Kidney Disease

As with most pediatric pathology, the causes of CKD can be divided into congenital and acquired conditions [4, 7–16]. The causes have been listed by anatomical location in Table 8.1. The most important of these are highlighted and are the conditions that we have chosen to focus on in the chapter (Table 8.1).

Posterior Urethral Valves

Posterior urethral valves (PUVs) are abnormal membranous folds unique to the male prostatic urethra. While one must be aware of other causes of congenital lower urinary tract (LUT) obstruction, such as urethral atresia and obstructive ureteroceles, PUVs are undoubtedly the most common. They are encountered in 1 of 10,000–25,000 births [17–19].

Advances in antenatal diagnosis, better perinatal medicine and early PUV management have led to a decrease in the neonatal mortality rate associated with PUVs. In spite of these advances and the introduction of antenatal interventions, there has been little improvement in the proportion of these patients ultimately developing CKD [20]. Twenty to sixty percent of these boys will manifest with evidence of CKD in childhood and 11–51% will eventually progress to stage 5 disease during long-term follow-up [21–24].

Table 8.1 Urological causes of chronic kidney disease in children

	Causes
Congenital	*Renal dysplasia*
	Ureteropelvic junction obstruction
	Ureterovesical junction obstruction
	Ureteroceles
	Vesicoureteric reflux
	Neuropathic bladder
	Posterior urethral valves
	Prune belly syndrome
Acquired	Obstructing renal tract calculi
	Obstructing neoplasms
	Neuropathic bladder
	Urethral strictures

Increasingly, the diagnosis is being suspected in the antenatal period with typical ultrasound features that include oligohydramnios, bilateral hydroureteronephrosis, a thick-walled bladder, and a dilated posterior urethra (Fig. 8.1). Children who escape prenatal diagnosis present at different ages in the postnatal period with a variety of features that include respiratory insufficiency, renal insufficiency, urosepsis, failure to thrive, poor urinary stream, and urinary incontinence. This variety of presentations represents a spectrum of disease, where lesser forms of obstruction are often detected later in life and may be associated with less impact on overall renal function.

In an attempt to prevent or attenuate renal damage that occurs in utero, prenatal interventions have sought to bypass the urethral obstruction with open or percutaneous diversion of the fetal urinary system. The decision to attempt antenatal intervention is aided by the analysis of fetal urinary markers (sodium, chloride, osmolality, and B_2-microglobulin). Currently the favored and most common approach to the fetal lower tract obstruction is percutaneous placement of a vesicoamniotic shunt. This achieves the required supra-urethral diversion while being minimally invasive, obviating the need for a maternal hysterotomy and fetal vesicostomy. Although technically feasible, antenatal interventions have failed to reliably prevent renal insufficiency and are associated with a fetal mortality rate that ranges from 33% to 43%. Not all the reported deaths are directly related to the intervention, however, as many of the series include deaths that the intervention failed to prevent (pulmonary hypoplasia). These procedures are also associated with significant morbidity in the form of urinary ascites, visceral herniation, shunt malfunction, and migration [25–28].

Regardless of the timing of the postnatal presentation, an ultrasound of the kidneys, ureter,

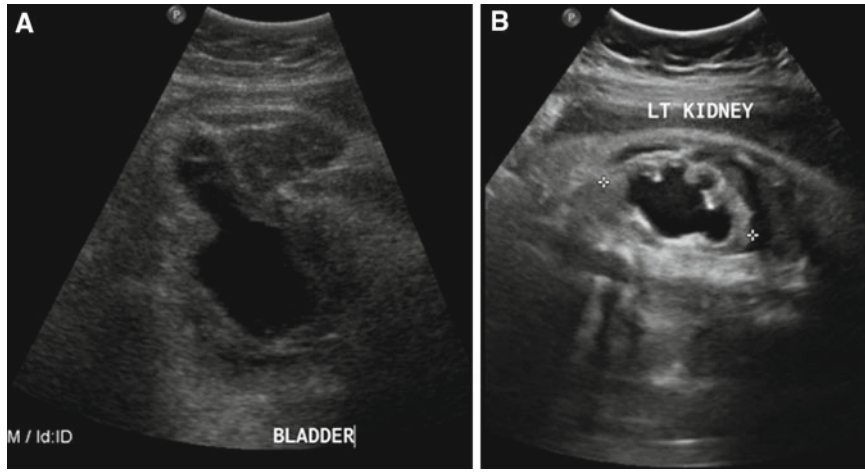

Fig. 8.1 Sonographic features suggestive of PUVs detected during antenatal evaluation: (**a**) thick-walled bladder with prominent posterior urethra, the "key-hole" sign; (**b**) high-grade hydronephrosis

and bladder is often the first imaging study requested, and will often demonstrate many of the above-mentioned ultrasonographic features. Following this, a voiding cysto-urethrogram (VCUG) is indicated to confirm the diagnosis. Typical features on VCUG include a dilated posterior urethra with a clear sharp transition to a normal distal channel, an associated valve cusp, thickened open bladder neck, and a trabeculated bladder. Vesicoureteric reflux (VUR) is also often present (Fig. 8.2). During the workup it is important to look for features that may be associated with a more favorable prognosis. Although not always predictive of a good outcome, the presence of a "pop-off" has been reported to be protective in some children. These include unilateral VUR into an ipsilateral dysplastic/nonfunctioning kidney, a perinephric urinoma, urinary ascites, and a patent urachus [29–34].

Accepting that we cannot alter preexisting renal dysplasia and understanding that many of these children will eventually develop CKD, our role in their management is to delay the onset of renal failure by optimizing the function of the ureters, bladder, and urethra. Management is initially directed at systemic stabilization and decompression of the urinary tract. Initial urological instrumentation usually involves urethral

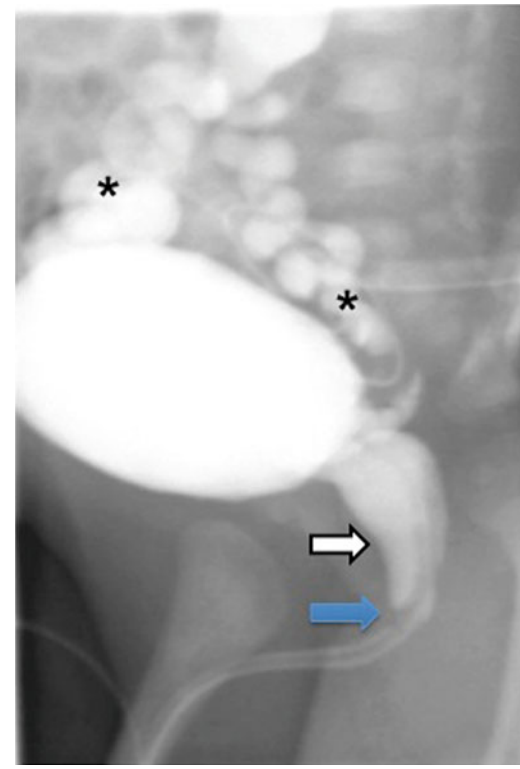

Fig. 8.2 Features of PUV on VCUG: prominent posterior urethra (*white arrow*) with a change in caliber compared with the anterior urethra at the site of the valves (*blue arrow*). Associated bilateral vesicoureteral reflux (*asterisk*)

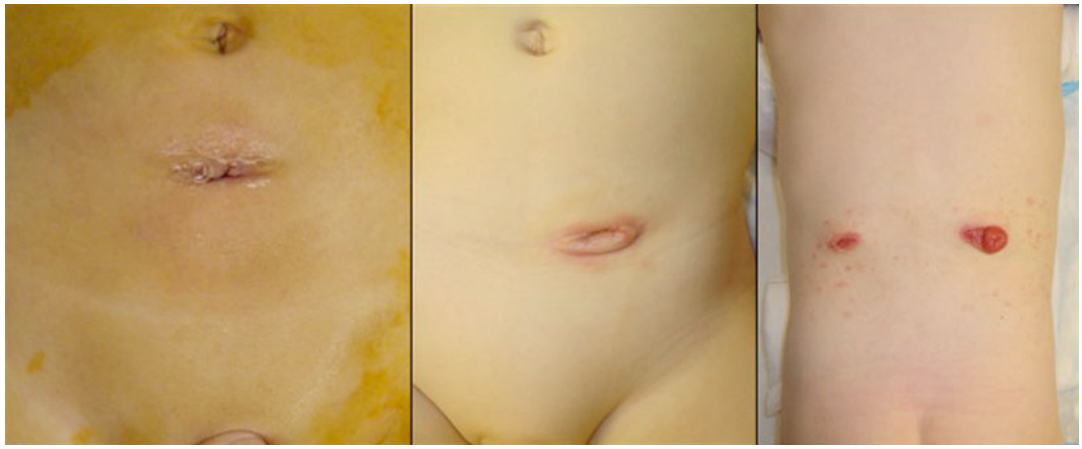

Fig. 8.3 Appearance on physical examination of different forms of cutaneous urinary diversion: (**a**) vesicostomy, (**b**) distal ureterostomy, and (**c**) bilateral pyelostomies (patient prone)

catheterization in the early neonatal period, even before the diagnosis has been confirmed. This simple intervention temporarily bypasses the obstruction, allows accurate monitoring of urine output, and helps avoid emergent surgical intervention while associated abnormalities are identified and their management optimized. Following this, a VCUG can be obtained by instilling contrast through the catheter. Subsequent definitive urethroscopic valve ablation can be attempted in all but the smallest infants. Premature or small infants whose urethras will not accommodate a scope are candidates for alternative forms of decompression. Similarly, in the occasional scenario where valve ablation does not achieve decompression of the upper tracts surgical diversion above the bladder outlet warrants consideration. This may be in part due to a functional ureterovesical junction (UVJ) obstruction as the ureter passes through a markedly thickened detrusor muscle. In such situations, segments of the urinary tract can be temporarily brought to the skin, in the form of a vesicostomy, ureterostomy, or pyelostomy (Fig. 8.3).

Many institutions will perform a circumcision at the time of the valve ablation or vesicostomy in order to decrease the risk of urinary tract infections (UTIs). A recent study by Mukherjee showed that there was an 83% reduction in the incidence of UTI in those children with valves who had been circumcised [35]. A more conservative approach would be to perform a circumcision only in the event of demonstrated predisposition to recurrent UTIs. This intervention is often heavily influenced by cultural and religious expectations.

Following valve ablation the obstructive process is usually relieved, yet the functional consequences are less predictably improved. Urodynamic findings in these boys remain highly variable and prone to change over time as renal function, growth, and the acquisition of continence further challenge the stability of the bladder [36, 37]. The primary goal of the urological management in PUVs is preservation of upper tract function. This is achieved by ensuring an infection-free urinary tract with a bladder that stores urine at low pressure and empties efficiently. The secondary goals would include continence and attaining an adequate lower tract for the effective drainage of a renal allograft in those that require it.

Lower tract dysfunction that is poorly controlled can adversely affect existing renal function. DeFoor and Ansari have demonstrated that residual bladder dysfunction is an independent risk factor for CKD [10, 22]. In 1980, Mitchell coined the term "valve bladder syndrome" identifying deleterious features of lower tract dysfunction that could reliably predict renal deterioration. The phrase describes the development or persistence of

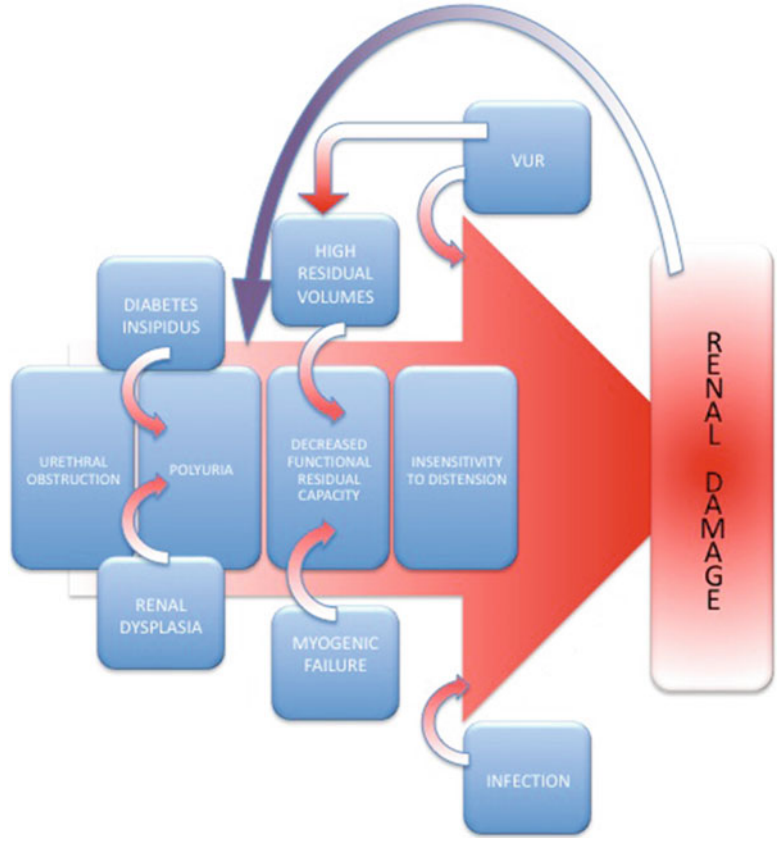

Fig. 8.4 Issues to consider in the monitoring of patients with PUV. Adequately addressing these problems helps prevent or slow renal deterioration, and provides a conceptual framework upon which to consider interventions and tailor treatment

hydroureteronephrosis in the presence of a poorly compliant, thick-walled bladder, incontinence, and polyuria [38]. Koff further clarified the role of the bladder in the deterioration of the upper tracts, suggesting that polyuria, insensitivity to overdistension, and high post void residual volumes were the three key factors contributing to renal deterioration in valve patients [39]. Looking at these three factors in more detail gives us a very plausible explanation for how an overwhelmed bladder, with borderline function, can facilitate rather than cause, upper tract damage: *Polyuria*, caused by nephrogenic diabetes insipidis, has the potential to overload the bladder of the most diligent voider. *Insensitivity to overdistension* contributes to the potential for bladder overload and injury. *High post void residual volumes* decrease the functional capacity of the bladder and are not necessarily the result of myogenic failure [40]. Pseudoresidual volumes can be generated by VUR when urine is refluxed into dilated ureters during filling and voiding, only to be dumped back into the bladder immediately post void. An additional source of pseudoresidual volume is found in the patients with a hypertrophied detrusor muscle. This hypertrophy creates a functional UVJ obstruction during bladder filling, an obstruction that is relieved in the post void period allowing for the retained urine to drain from the dilated ureters (Fig. 8.4) [41].

As a result of a better understanding of the condition, clinicians no longer accept hydroureteronephrosis as unavoidable in the upper tracts of valve patients. Management has become proactive and more aggressive, focused on achieving complete urinary tract emptying (double voiding, timed voiding, and clean intermittent catheterization [CIC]), optimizing detrusor function (with judicious use of anticholinergics) and the selective use of alpha-blockers to assist voiding. Where polyuria and decreased functional capacity are an issue, routine daytime interventions may be unable to prevent hydronephrosis. Nocturnal CIC or overnight indwelling catheterization have been

shown to reduce diuresis, decrease the incidence of UTIs, improve continence, and decrease upper tract dilation [39, 42, 43].

VUR in PUV children is found in 50–70% of patients and is usually secondary to the obstructed bladder outlet [44, 45]. Because of its association with worse renal dysplasia, high-grade reflux can predict higher morbidity and mortality [46, 47]. Adequate treatment of the valvular obstruction will lead to spontaneous resolution of VUR in most cases (62%), and, therefore, VUR should be treated as conservatively as possible [45, 48]. Rarely, surgical intervention is indicated for recurrent pyelonephritis in cases where LUT dysfunction has been ruled out or controlled.

The presence of persistent unilateral reflux into a dysplastic nonfunctioning kidney in males with PUVs has been associated with a better renal functional prognosis than standard valve patients [46, 49]. The reason for this is thought to be due to the dysplastic kidney's protective effect as the renal pelvis and ureter absorb most of the abnormal pressures generated by the bladder during voiding. However, Narasimhan and colleagues showed that while the syndrome did seem to favor a better outcome, half of their patients had some form of renal scarring, voiding dysfunction, UTIs, diurnal incontinence, and hydroureteronephrosis [49]. This data would support the contention that every boy with PUV, regardless of the presence of "favorable prognostic features," should have close multidisciplinary team follow-up in order to identify and appropriately treat potential threats to the remaining renal function.

Vesicoureteric Reflux in the Pediatric Dialysis Patient

Renal damage or abnormal development related to VUR (reflux nephropathy) is often congenital, representing renal dysplasia that is likely to coexist with reflux rather than be directly caused by it (Fig. 8.5). Subsequently, postnatal renal function may be further threatened by pyelonephritis, which is facilitated by reflux of infected urine into the abnormal renal unit [50–53]. As discussed in the previous section, secondary reflux can be associated with transmission of high bladder pressures to the upper tracts, which can further compromise the renal parenchyma. Differentiation between primary and secondary reflux has important therapeutic implications. In this section, we concentrate on primary VUR, while secondary reflux is discussed under the specific primary conditions.

Primary VUR accounts for 7–25% of pediatric CKD cases [4, 54, 55]. Ardissino looked at 343 patients who had VUR and CKD and found that almost 60% of his series required renal replacement therapy prior to the age of 20. Given this high incidence of end-stage renal disease, he suggests that children with reflux-associated CKD have a relatively poor renal prognosis and deserve particular attention [56]. Neither medical

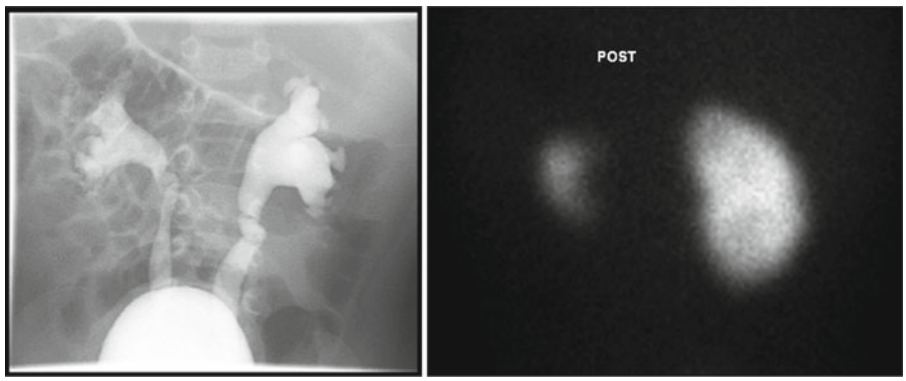

Fig. 8.5 Findings suggestive of renal dysplasia: (**a**) bilateral high-grade reflux detected in infant without a history of urinary tract infections; (**b**) DMSA scan demonstrates poor function of the left renal moiety and photopenic defects

nor surgical management can alter the function of a dysplastic kidney and should therefore concentrate on preventing further damage by early diagnosis and treatment of febrile UTIs (pyelonephritis) and the correction of bladder and bowel dysfunction (increased fluid intake, prophylactic antibiotics, treatment of constipation, biofeedback, and bladder training). By increasing fluid intake, more urine is produced. This in turn increases the volume and frequency of voiding, effectively flushing the LUT and mechanically clearing it of bacteria. Prophylactic antibiotics have long been held as the cornerstone of conservative management of VUR [57]. Recent large series have begun to question this conventional wisdom [58–60]. In the absence of more definitive data on the topic it would seem prudent to continue with the selective use of antibiotics based on a holistic assessment of individual patients and their parents.

Bladder training is aimed at those children with an element of dysfunctional voiding. The process involves the education and retraining of the voiding process to achieve a volitional, regular, and complete void. Emphasis is placed on awareness of the pelvic musculature and coordination of the detrusor muscle contraction with sphincter relaxation. This training can be enhanced by biofeedback technology that registers and rewards the correct identification and control of pelvic musculature. The effective elimination of urine is very closely tied to the effective elimination of feces (bladder and bowel dysfunction). Active management of constipation has been shown to improve voiding dysfunction, incontinence, enuresis, urgency, and UTIs [61–63].

The surgical approach to the child with VUR and recurrent pyelonephritis who fails to respond to medical management is usually a graded escalation in intervention that includes circumcision in males, endoscopic sub-ureteric injection of a bulking agent (such as dextronomer/hyaluronic acid), and ureteric reimplantation. Although surgical reimplantation is more invasive than endoscopic therapy, it carries a higher overall success rate in terms of reflux correction. This is an important distinction when considering the child with borderline renal function and a predisposition to recurrent scarring UTIs. An argument can be made for a more aggressive approach in these patients, consisting of early prophylactic circumcision and surgical reimplantation of the ureter.

In regard to the reflux patient with CKD who requires dialysis, the indications for medical management or surgical intervention are usually no different from those patients with normal renal function. One must be aware that once transplanted these children will be immunosuppressed and have an additional renal unit. Following renal transplantation, UTIs occur commonly in children with VUR; approximately 60% of these patients experience at least one episode [64, 65]. The risk is highest in the first year posttransplantation and then decreases over time [66]. Although VUR has not been documented as an independent risk factor for UTI in this population [67, 68], it has been associated with acute pyelonephritis in two pediatric studies [66, 68] and yet, has not been convincingly linked to graft loss [66, 68–70]. Thus, considering the potential for increased morbidity in the setting of immunosuppression, due consideration should be giving to addressing pre-transplant vesicoureteral reflux, particularly in patients with a history of multiple episodes of pyelonephritis. In cases with high-grade reflux and an associated poorly functioning kidney, performing a nephroureterectomy rather than reimplantation should be considered.

Following renal transplantation, VUR into the allograft is common and varies according to the ureteral implantation procedure used [66, 67, 71, 72]. As a result, it is not common practice to routinely "screen" for reflux posttransplant. Nevertheless, in the setting of recurrent UTIs posttransplant, a VCUG is warranted to exclude reflux into the native or transplanted kidneys. Treatment for posttransplant reflux–associated UTIs is initially conservative. Patients who fail to improve are candidates for surgical intervention. This may involve efforts to stop the reflux or remove a poorly functioning, refluxing native renal unit. Recently, the sub-ureteric injection of dextronomer/hyaluronic acid has gained wide acceptance as a minimally invasive method of correcting VUR. However, when compared to open reimplantation of the ureters, the success

rate of ureteric injection is lower and there is a lack of long-term follow-up. Cloix and Williams reported reflux resolution following ureteric injection in only 29% and 44% of their patients, respectively [73, 74]. Similarly, surgical reimplantation is not without problems in transplanted patients. Neuhaus reported transient obstruction and a persistent increase in serum creatinine in 60% of his reimplanted children [72]. Given the above issues combined with the efficacy of conservative management and the concept that adult donor kidneys are less susceptible to the effects of refluxed bacteriuria, we believe surgical intervention is rarely indicated in this patient population.

Neurogenic Voiding Dysfunction

Under normal circumstances the detrusor muscle and the sphincter complex function in a coordinated fashion that optimizes both storage and emptying. During the filling phase, the detrusor muscle is relaxed and said to be compliant as it fills without an increase in pressure. As capacity is reached, the compliance decreases. A full bladder is detected by stretch receptors and perceived centrally. If voiding is appropriate, the sphincteric mechanism relaxes in anticipation of a coordinated detrusor contraction, expelling urine from the bladder. If voiding needs to be delayed, afferent nerves stimulate sympathetic and pudendal outflow activity, initiating the guarding reflex which inhibits detrusor contraction and stimulates the rhabdosphincter to increase outflow resistance [75]. Disrupted innervation can lead to an alteration of this normal, coordinated interaction.

Neurogenic voiding dysfunction is an all-inclusive term that describes those vesicourethral units with abnormal neural anatomy or function. Neurological lesions vary considerably in their influence on the key bladder functions of storage and emptying. Upper motor neuron lesions tend to produce hyperreflexic bladders with sphincter dyssynergia. Lower motor neuron lesions tend to produce an areflexic bladder with variable sphincter function. Unfortunately, there is a huge range of neurological lesions that variably affect the detrusor muscle, striated urethral sphincter, and the smooth muscle of the bladder neck. This highly variable situation makes classification difficult; as a result, popular classifications tend to focus on the dysfunction rather than on the underlying cause [76]. Wein simplified the problem by describing the voiding dysfunction in two broad categories: a failure of storage and a failure of emptying [77]. Adequate storage requires bladder compliance, capacity, and an outlet resistance at the bladder neck. Efficient emptying requires a coordinated interaction of detrusor contraction and a lowering of the outlet resistance. Four broad, simplified, scenarios exist: (1) a bladder with adequate storage and an outlet with low resistance; (2) a bladder with adequate storage and an outlet with increased resistance; (3) a bladder with inadequate storage and an outlet with low resistance; and (4) a bladder with inadequate storage and an outlet with increased resistance (Fig. 8.6). Based on this understanding one can see how the neurogenic bladder may be incontinent, continent, or hypercontinent.

Regardless of the detrusor compliance, poor tone in the sphincter mechanism usually leads to incontinence. Provided it is associated with low leak point pressures, there should be no threat to the functioning of the upper tracts. The "hostile bladder" is found in situations where hyperreflexic, poorly compliant, small capacity bladders are combined with high outlet resistance. This resistance is caused by sphincter hypertonia and detrusor-sphincter dyssynergia (DSD). In these situations, high filling and voiding pressures are transmitted to the kidney, leading to dysfunction and, if not corrected, permanent damage [78].

Following the diagnosis of neurogenic voiding dysfunction, initial management is directed at maintaining acceptable bladder storage pressures, ensuring efficient emptying and preventing UTIs [79]. Early medical management and close monitoring are the cornerstones of a successful outcome for these children. Patients vary in their need for specific medical interventions but should be managed according to their unique urodynamic dysfunction. The basic concepts of this management are outlined in Table 8.2. The majority of children with "hostile bladders" are managed

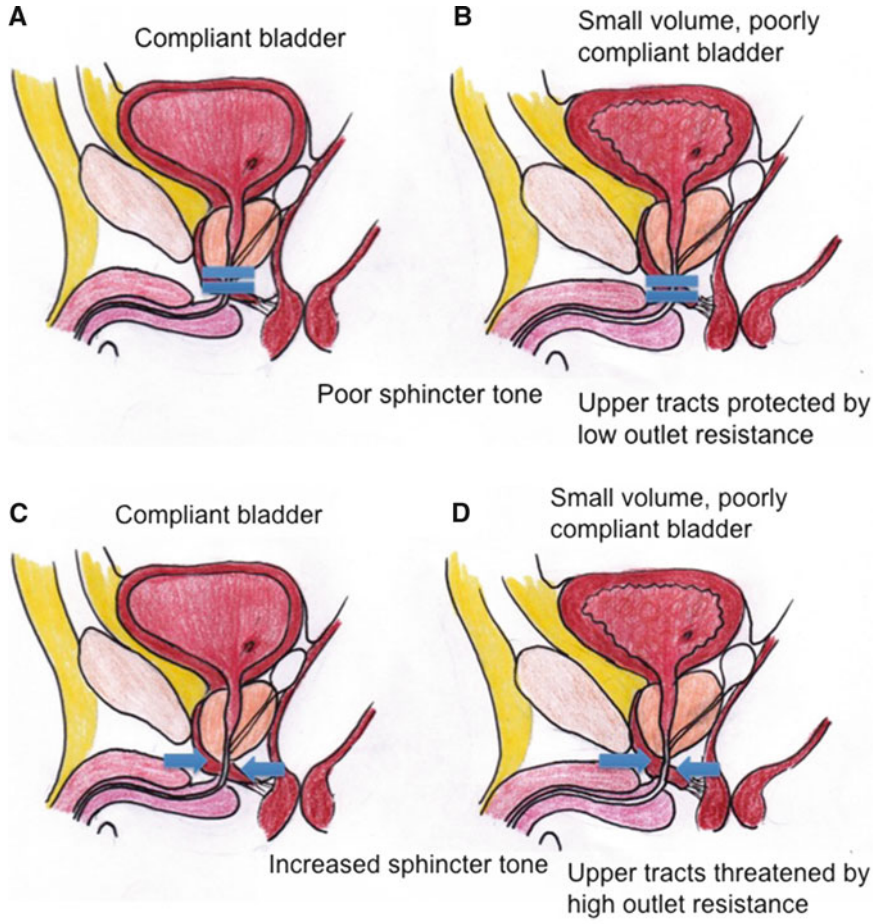

Fig. 8.6 The four broad scenarios created by bladder and sphincter neurology: (**a**) good bladder compliance with poor sphincter tone, (**b**) poor bladder compliance with poor sphincter tone, (**c**) good bladder compliance with increased sphincter tone, (**d**) poor bladder compliance with increased sphincter tone

Table 8.2 Basic concepts of management for neurogenic voiding dysfunction based on Wein classification

	Bladder	Outlet	Bypass
Facilitate storage	*Decrease tone* • Bladder muscle relaxants	*Increase resistance* • α-Agonists • Mechanical compression	CIC Diversion
	Increase capacity • Bladder augment		
Facilitate emptying	*Increase bladder pressure* • Crede maneuver • Trigger zones • Bladder training	*Decrease resistance* • α-Blockade • Sphincterotomy • Bladder neck disruption • Urethral dilation	CIC Diversion

with a combination of CIC (to ensure regular and complete emptying) [80–82], anticholinergics (to attenuate uninhibited detrusor contractions, increase capacity and decrease tone) [83, 84], α-Blockers (introduced to decrease the sphincter muscle tone) [85, 86], and prophylactic antibiotics (to prevent recurrent UTI).

Surveillance is a crucial component of the management of the neurologically impaired child. In myelodysplasia in particular, the neurological consequences are often dynamic, with changes taking place throughout childhood but particularly at puberty when linear growth is accelerated. The entire urinary system should be screened regularly for evidence of deterioration. Ultrasound of the kidneys, ureter, and bladder is useful in detecting renal growth failure, scarring, loss of corticomedullary differentiation, hydronephrosis, bladder wall thickening, and significant residual volumes. In the patients who are able to void, urinary flow rates demonstrate abnormal flow curves and combined with electromyography may demonstrate DSD. Urodynamic studies are useful in monitoring bladder dynamics during the filling and emptying phases. MRI is indicated for the initial workup of many of these patients and may be indicated during the surveillance period when changing clinical features suggest the development of a potentially correctable cause, as would be the case in a patient with a tethered cord.

In the event that the above medical management is ineffective or not tolerated, treatment will need to be escalated. Surgical strategies are mainly aimed at addressing three different issues: decreasing bladder outlet resistance, providing alternative access for catheterization, and enhancing bladder capacity and compliance. For patients in whom continence is not necessary, strategies aimed at reducing outlet resistance include urethral dilation [87, 88] and sphincterotomy (in older male patients) [89]. Vesicostomy produces an incontinent diversion, a safe and reliable method of decompressing the upper tracts in young children with neurogenic bladders [90].

When continence is a goal of treatment, bladder emptying aided by CIC through the urethra is favored. In some children this is not feasible as catheterization may be anatomically difficult or impossible (as seen in children with urethral strictures), poorly tolerated (in patients with a sensate urethra) or difficult to perform (related to body habitus and poor manual dexterity) [7]. These patients may benefit from a surgically constructed continent catheterizable channel, usually fashioned with the appendix (Mitrofanoff channel) or reconfigured small bowel (Monti channel) [91]. These conduits should be as short and straight as possible to avoid intubation issues, and run into the bladder from an easily accessible, cosmetically sensitive site. Accessibility is the principal goal and is ideally determined preoperatively by the surgeon, patient, and a stoma nurse. Cosmesis is a secondary concern to function, often best achieved with the stoma placed at the umbilicus (Fig. 8.7).

Fig. 8.7 Patient with an appendico-vesicostomy (Mitrofanoff channel), performing self-catheterization through stoma located at the umbilicus

When it comes to specific surgical interventions for improving compliance, increasing capacity and decreasing uninhibited detrusor contractions there are a number of surgical options that disrupt the detrusor muscle and augment the bladder. Enterocystoplasty is the most commonly used technique and it involves the use of a portion of the intestine that has been detubularized, reconfigured into a patch, and then sutured into the defect of a widely incised bladder. The intestinal

patch can be ileum, colon, or stomach but the most commonly used segment appears to be the ileum [92, 93]. Because of the absorptive and secretory functions of the gastrointestinal epithelium, metabolic abnormalities may develop over time and become clinically relevant in children with marginal renal function. In order to offset the metabolic impact of the intestinal segments the bladder can also be augmented using tissue naturally lined by urothelium. With the exception of ureterocystoplasty, the urodynamic results of these procedures are less reliable and associated with only a modest improvement in many cases. Ureterocystoplasty is, on the other hand, very effective and describes the use of the dilated tortuous ureter of a poorly functioning renal unit to augment the bladder [94, 95]. Auto-augmentation effectively creates a diverticulum of bladder mucosa that is allowed to protrude from a wide surgical incision in the detrusor muscle, thereby increasing compliance capacity.

A summary of the advantages and disadvantages of common bladder augmentation procedures is provided in Table 8.3

Table 8.3 A summary of the advantages and disadvantages of common augmentation procedures

Auto-augmentation
• Lined by urothelium
No metabolic sequelae
No bowel harvesting
Extraperitoneal approach
Not reliable at increasing volume
Ureterocystoplasty
• Native ureter
• Lined by urothelium
No metabolic sequelae
No bowel harvesting
Mucosa backed by muscle
Not always available
Not always sufficient
Additional exposure required (laparoscopic/open)
Colocystoplasty
• Sigmoid/ileo-colic
Large diameter
Reliable blood supply
Mobile segments
Ileocaecal valve can be used to prevent urinary reflux
Can be tunneled
Not always available
Can impact gut function
Bowel surgery required
Absorption of urinary waste
Lifelong alkanization required if renal function impaired
Mucus production +++
Bladder stone and UTI risks +++
? Higher perforation rate
? Tumor formation
Gastrocystoplasty
• Greater curvature of stomach
No absorption of urinary waste
Secretes acid ameliorating metabolic acidosis
Less mucus, stones, and infections
May facilitate emptying
Hematuria dysuria syndrome notable in sensate, incontinent patients
Caution in defunctioned bladders: bleeding, ulcers, and perforation
Less compliant
? turno formatio Less capacious
Ileocystoplasty
• Preterminal ileum
Reliable blood supply and length
Most compliant bowel segment
Hyperchloremic metabolic acidosis
Mucus production ++
Stones and infection
Vitamin B_{12} deficiency
? Tumor formation

Bladder Augmentation and End-Stage Renal Disease

It is reasonable to expect that if a severely dysfunctional bladder has caused or facilitated the failure of the native kidneys then a kidney transplanted into the same environment will be exposed to the same hostile forces and is therefore at risk. Initially severe bladder dysfunction was a contraindication to transplantation, but over time, effective reconstruction of the lower tract allowed for the creation of a safe reservoir for urine storage. This has allowed for successful renal transplantation in children with stage 5 CKD and severe LUT dysfunction.

The safety and timing of bladder augmentation in the child with stage 5 CKD (ESRD) has been the subject of a number of studies [96–103]. The cumulative graft survival rates for the children who underwent major LUT reconstruction seem favorable but are difficult to accurately

compare for a lack of standardized follow-up period [98, 100, 101, 104]. Having established the safety of transplantation in these patients, timing of the reconstruction in relation to the transplantation became the next important question. Basiri conducted a retrospective study looking at three groups of patients: those who underwent bladder augmentation *prior* to transplant, those who had augmentation *post* transplant, and those transplanted patients who did not require LUT reconstruction. Graft survival and incidence of symptomatic UTI were no different in the two augmented groups but the group that did not require augment did significantly better in both outcomes. Basiri suggested that the increased incidence of UTI could be the cause of lower graft survival rates in the augmented groups [99]. In additional studies, DeFoor acknowledged the high rate of posttransplant sepsis in the series by Koo [104] and Hatch [101] and contrasted this to his own report on a series of 20 patients who underwent enterocystoplasty pre-transplant. DeFoor suggested that prophylactic antibiotics and the predominance of gastrocystoplasty (85%) were likely contributors to the unusually low rate of UTI seen in his patients [98].

In summary major LUT reconstruction appears safe prior to renal transplantation. It should be remembered that these bladders are inherently dysfunctional and the augmentation cannot be expected to completely negate the consequences of that dysfunction. In conjunction with this, the reconstructive procedures carry with them inherent metabolic, functional, and surgical risks that often persist throughout life. It is unlikely, therefore, that graft survival can be expected to be as good or better than it is in children with normal bladders, but it is encouraging that results are seldom shown to be significantly worse.

Prune Belly Syndrome

Three abnormalities define prune belly syndrome (PBS): an absence or deficiency of abdominal wall musculature, bilateral cryptorchidism, and dilated uropathy involving the urethra, bladder, and ureters (Fig. 8.8). PBS has an incidence of 1 in 29,000 to 1 in 40,000 live births. The precise cause of PBS remains unknown [105, 106]. The full-blown syndrome is unique to the male patient; a "pseudoprune" disorder can occur in both males and females and describes the identical pathology to the PBS but lacking the complete triad of features [107–109]. Associated pulmonary, cardiac, orthopedic, and gastrointestinal abnormalities are relatively common and contribute to overall morbidity and mortality [110]. The underlying pathology and possible clinical presentation is summarized in detail in Table 8.4 [111, 112].

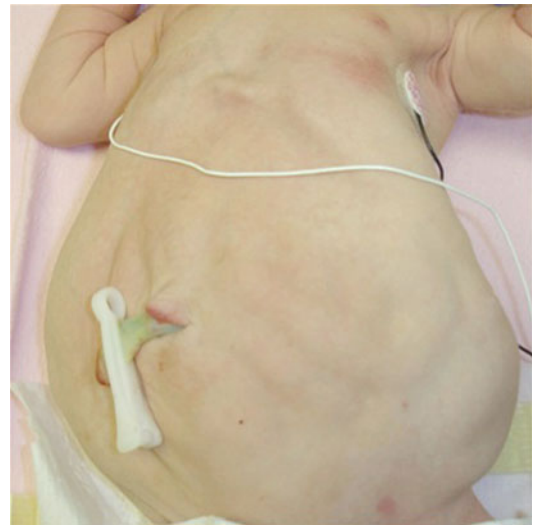

Fig. 8.8 Characteristic abdominal wall appearance in a newborn boy with prune belly syndrome

From a urological perspective, initial workup aims to exclude obstruction, VUR, and renal dysplasia. The passage of urine in these diffusely dilated urinary tracts is usually not obstructed but is often inefficient, a consequence of gross dilation. If obstruction is present, initial ultrasound may reveal an unusually thickened bladder wall or serial ultrasounds may reveal progressive dilation of the upper tracts. Furosemide washout studies are imperfect at diagnosing obstruction and should be interpreted with caution in the setting of gross distension. Thickening of the bladder wall should raise the suspicion of a urethral obstruction. A VCUG will define urethral and bladder anatomy, confirm VUR and as a result, should be done early in the workup of PBS patients. Where renal dysplasia is suspected or

Table 8.4 Clinical features of prune belly syndrome with pertinent urological issues highlighted

Anterior urethra	• Ranges from *urethral atresia* to fusiform megalourethra • Complete obstruction is lethal unless urachus is patent • Variably deficient corpora cavernosa and spongiosum
Testicles	• Bilaterally cryptorchid • Usually intra-abdominal location • Intrinsically abnormal testis with marked Leydig cell hyperplasia • Increased risk of malignancy • Decreased spermatagonia or azoospermia • Paternity may be possible with assisted reproductive techniques
Genital conduits	• Epididymal-testicular dissociation • Ectopic, thickened vas • Seminal vesicles are usually absent or atretic but may be ectatic in some cases • All contribute to infertility • Retrograde ejaculation
Prostate and prostatic urethra	• Prostatic hypoplasia • Epithelial glandular development consistently lacking – contributes to infertility • Prostatic urethra is dilated, in continuity with an open bladder neck and tapering to the membranous urethra • Utricular diverticulae common • Hypoplastic or absent verumontanum • Reflux into the vas can be seen • Obstructive prostatic urethral lesions are seen in 20% – poorer prognosis
Bladder	• *Grossly enlarged* • Trabeculation unusual • Pseudo-diverticulum or urachal remnant • *Urachus may be patent* • Widely separated ureteric orifices due to splayed trigone and *predisposing to reflux* • Open bladder neck • *Efficient storage with good compliance* • *Poor emptying due to hypo-contractility and VUR (CIC may be required)* • *Delayed sensation to void* • Instability and uninhibited contractions unusual • *Requires regular assessment for altered voiding efficiency*
Ureters	• *Elongated, dilated, and tortuous* • Lower third more severely affected • *Peristalsis present but ineffective* • *True obstruction rare* • *VUR present in 85%*
Kidneys	• *Variable renal dysplasia* • *Hydronephrosis* • May have hydronephrosis without renal dysplasia • Uretero pelvic junction obstruction has been reported
Abdominal wall	• *Variable deficiency of underlying anterior abdominal wall muscle* • Transversus abdominus most affected followed by infraumbilical rectus, internal oblique, external oblique, and the supraumbilical rectus abdominus • Can cause developmental delay due to axial instability (sitting and walking) • Can predispose to constipation and pneumonia as a result of poor valsalva

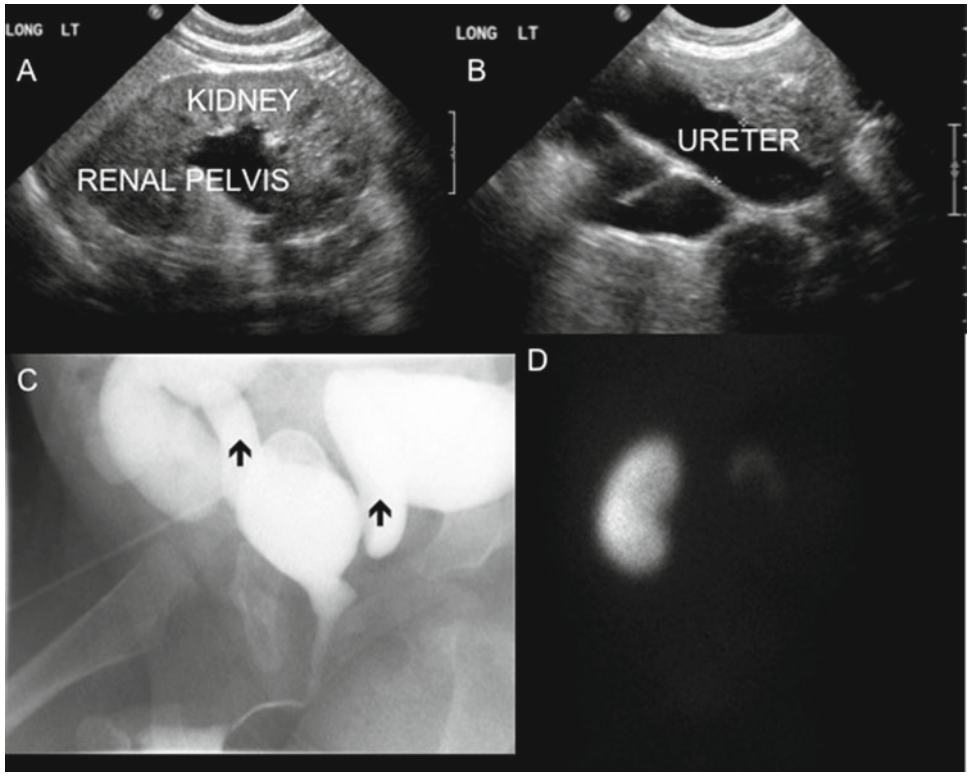

Fig. 8.9 Imaging studies in a patient with prune belly syndrome: (**a** and **b**) hydroureteronephrosis with dilated and tortuous ureter; (**c**) VCUG after vesicostomy creation demonstrating bilateral high-grade reflux into dilated distal ureters (*arrows*); (**d**) posterior view of a DMSA scan demonstrating poor right renal differential function

Table 8.5 Outcomes of prune belly syndrome based on salient features and Woodard category

Category	Salient features	Outcome
1	Severe renal dysplasia Pulmonary hypoplasia	Few survive beyond neonatal period
2	Mild to severe renal dysplasia No pulmonary hypoplasia	Survival with variably impaired renal function
3	No renal dysplasia No pulmonary hypoplasia	Excellent prognosis provided upper tracts are protected

there have been recurrent febrile UTIs, a nuclear medicine scan is indicated (Fig. 8.9).

As with many syndromes, PBS represents a spectrum of disease with a wide range of impairment due to the underlying congenital abnormalities. As a consequence, management has to be individualized. It is useful to consider the child with PBS as fitting into three broad categories as outlined by Woodard [113] (Table 8.5). Category 1 children have severe pulmonary and renal dysplasia and have a very poor prognosis. Outcome is largely determined by pulmonary function and possible associated cardiac defects. Urological management should aim to identify obstructing uropathy and, if present, may involve diverting the upper tracts if appropriate for the individual patient. Category 2 patients tend to have no immediate threat to life but renal dysfunction is significant. Baseline renal function has to be monitored and optimized. Management should involve a multidisciplinary team with active participation of pediatric nephrologists and urologists. The structural integrity of the renal tracts has to be regularly assessed and conditions that

threaten the kidneys need to be identified and treated early. Category 3 patients demonstrate good renal function despite their grossly dilated urinary tracts. They have a good prognosis, because they lack renal dysplasia, but they still require close monitoring for signs of deteriorating renal or urinary tract function.

Management of these complex patients is aimed at delaying the onset of renal failure. It should include prophylactic antibiotics because of the potential for VUR and urinary stasis. Timed voiding, double voiding, and CIC, when necessary, are recomended to facilitate complete bladder emptying. Pyleostomies, ureterostomies, or vesicostomies are unusual interventions that may be required to divert the urinary stream above an obstruction or poorly draining segment. Early orchidopexies are indicated to optimize spermatogenic potential and facilitate testicular examination. Abdominoplasty, where necessary, improves psychosocial well-being and has recently been shown to improve pulmonary function, defecation, and voiding efficiency [114, 115]. The timing of and indication for the above interventions vary with each patient and institutional protocols.

There is debate on the best management of children with PBS. Where the debate lingers is the question of how aggressive to be when considering surgery. Aggressive reconstruction involves simultaneous and early (3 months to 1 year of age) resection, tapering and reimplantation of the ureters, bilateral transabdominal orchidopexy, abdominoplasty, and may include reduction cystoplasty or resection of the urachal diverticulum [116]. With the lack of a clear benefit in bladder capacity or voiding efficiency[117], reduction cystoplasty is not recommended by all proponents of the more aggressive approach [118]. Conversely, the conservative approach argues that surgery cannot improve baseline renal function and should not be prophylactic but rather reserved for those patients in whom obstruction, stasis, or reflux is causing a problem [115, 119].

Regardless of how well we manage these children, some will progress to stage 5 CKD. In this event, PBS is not a contraindication to either peritoneal dialysis (PD) or renal transplantation. While PD does pose some unique challenges with respect to anchoring the PD catheter to the attenuated abdominal wall [120], it is successful at temporarily replacing renal function. Renal transplantation in children with PBS has not shown a statistically significant difference in graft or patient survival [121, 122].

Urological Issues in the Pre-transplant Workup

Unlike adult patients, pediatric transplant recipients often have urological issues that have caused or contributed to their renal failure. It is therefore imperative that the pediatric urologist is integrally involved in the pre-transplant workup and optimization of these patients. The pre-transplant assessment is aimed at identifying those factors that may complicate transplant surgery, as well as those factors that pose a potential threat to graft or patient survival following transplantation. These factors include previous surgeries and existing stomas, a history of a hypercoagulable state or inguinal vascular access (Fig. 8.10) and, in the case of a living donor, the renal and vascular anatomy of the donor allograft. All this information is necessary for planning the surgical approach, including the side and site of the transplant vascular anastomosis. With particular relevance to nephrectomy, the need for simultaneous or pre-transplant procedures should be established and well coordinated prior to the procedure.

The anatomy and functioning of the bladder and its outflow tract must be assessed for factors that could compromise postoperative graft survival. If there is voiding dysfunction or features of a hostile bladder, these need to be addressed prior to transplantation. In the case of a defunctionalized bladder or a bladder of an oliguric patient, it is important to ascertain the relative likelihood of underlying bladder dysfunction. Generally, a normal bladder that has been defunctionalized by diversion or anuria will reestablish normal function over time. This is in contrast to the dysfunctional bladder that could threaten the survival of the allograft if not addressed prior to surgery. In this regard, pre-transplant undiversion or sham bladder cycling via urethral or suprapubic catheter has been suggested as an important diagnostic step in the workup of these patients.

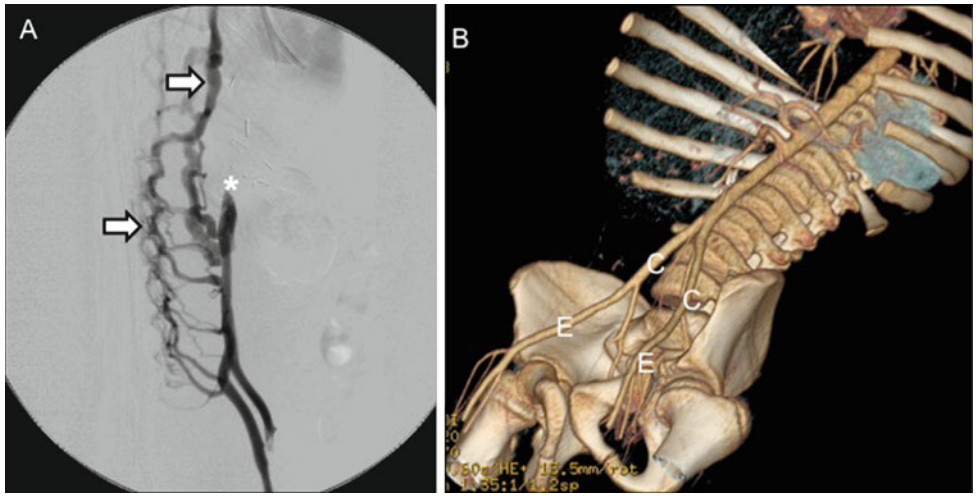

Fig. 8.10 Imaging studies used to further evaluate abdomino-pelvic vascular anatomy following abnormal Doppler ultrasound screening: (**a**) Venogram demonstrating occluded inferior vena cava (*) with prominent collaterals into lumbar veins and the azygos system (*arrows*). (**b**) CT scan reconstruction of arterial phase demonstrating acceptable targets for transplantation at the level of common (**c**) and external (**e**) iliac arteries

Conditions predisposing the immunosuppressed patient to infection could compromise patient survival. VUR into the native kidneys or the allograft has been associated with an increased incidence of UTI in graft recipients [66, 69]. This is especially true of patients with underlying voiding dysfunction and those with high-grade reflux (grade IV–V) [55, 69]. Basiri found that preemptive ureteral reimplantation failed to reduce the risk of infection in patients with VUR who underwent transplantation. However, subset analysis of patients with high-grade reflux did show a reduction in the incidence of UTI. Based on this observation, Basiri suggested that patients with high-grade reflux into native kidneys should be considered for pre-transplant, anti-reflux surgery or nephrectomy.

Among the many possible investigations of the potential transplant recipient's urinary tract, not all need be routinely performed. Urologic workup should be individualized with studies chosen according to their ability to define relevant anatomical or functional abnormalities. An ultrasound of the kidneys, ureters, and bladder is a very commonly performed, noninvasive investigation that will detect abnormalities in structure or position of the kidneys. A VCUG is indicated in patients with underlying urological abnormalities or where VUR was suspected. Additionally, the VCUG is able to assess bladder capacity, anatomy, and emptying efficiency. Where voiding dysfunction is suspected a urinary flow rate with or without electromyography can be done. Urodynamic studies are indicated if abnormal bladder function is suspected based on underlying pathology, preceding surgical interventions, or present clinical evidence. Computerized tomography would be indicated if native renal tumors or stones were suspected. Doppler ultrasound of the pelvic and abdominal vasculature is performed to confirm normal vascular anatomy where doubt of its patency exists.

Nephrectomy

As a general rule the kidneys of a stage 5 CKD patient should not be removed prior to transplantation. Even poorly functioning kidneys can provide a valuable homeostatic adjunct to dialysis. However, there are a number of situations in which nephrectomy is indicated (Table 8.6). Renin-dependent hypertension is common to focal segmental glomerulosclerosis (FSGS), hemolytic uremic syndrome, reflux nephropathy, and cystinosis. Pre-transplant nephrectomy may be indicated in these patients as steroid medication

Table 8.6 Indications for pre-transplant nephrectomy

Pathology	Systemic impact
Hypertension	• Lifelong antihypertensive medication • Potential for end-organ dysfunction
Proteinuria	• Immunosuppression • Hypercoagulable state • Malnutrition
Infection	• Urinary infections • Renal parenchymal infections (fungal infection)
Polyuria	• Dehydration • Electrolyte abnormalities • Inefficient voiding
Renal calculi	• Pain • Infections
Neoplastic potential	• Recurrence after previous partial nephrectomy • Genetic predisposition to renal malignancies (Beckwith Wiedemann)
Mass effect	• Lack of space for the allograft • Lack of peritoneal domain for PD

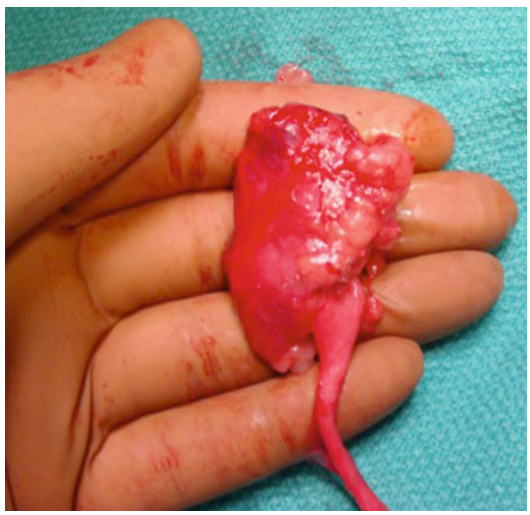

Fig. 8.11 A small atrophic kidney removed laparoscopically in a patient with stage 5 CKD and renin-mediated hypertension. Procedure performed in preparation for renal transplantation, with improvement in blood pressure control

and fluid overload could precipitate malignant hypertension in the postoperative period. In these particular children, nephrectomy is often curative and can obviate the need for long-term antihypertensive therapy (Fig. 8.11). Additionally, the vaso-active effects of hyperreninemia may decrease perfusion of the grafted kidney in the immediate postoperative period. Persistent proteinuria can lead to malnutrition, hypercoagulable states, and immune suppression. It can also confound the significance of proteinuria in the posttransplant urine. If the proteinuria is clinically significant, bilateral nephrectomy is indicated. Intractable polyuria can cause dehydration, electrolyte abnormalities, and renal tract dysfunction and, if present, is an indication for nephrectomy [123]. Massive native VUR not only predisposes to UTI, but can also cause bladder dysfunction as refluxed urine drains into the bladder post void, causing high residual volumes and decreasing functional bladder capacity. If this is the case nephrectomy with ureterectomy is curative. Prior to excising the ureters, one should exclude the need for a future bladder augmentation, as suitable ureters are an ideal material for augmentation cystoplasty. Tuberculosis, xanthogranulomatous pyelonephritis, and fungal infections are just some of the chronic or recurrent infections that are best treated with excision of the entire renal unit ahead of immunosuppressive therapy. The kidney that is predisposed to symptomatic stone formation should be removed. The risk of malignancy is an unusual indication for unilateral or bilateral nephrectomy. It is encountered in situations where genetic disorders predispose to malignancy (e.g., Denys-Drash and Beckwith Wiedemann Syndromes). Where a partial nephrectomy has been performed for malignancy, the remnant parenchyma should be removed before transplantation. Nephrectomy is further indicated in the case of multicystic dysplastic kidneys with significant parenchyma or demonstrable growth of the remnant [124]. Rarely one sees large, pathological kidneys that produce a significant mass effect. These kidneys may need to be removed to make space for the donor kidney or to facilitate PD (Fig. 8.12).

When nephrectomy is being considered in the child with stage 5 CKD (ESRD) one has to take many factors into account. In practice, the balance between the severity of native kidney dysfunction and the relative contribution of these failing kidneys to the management of the patient often dictates timing and staging of nephrectomy.

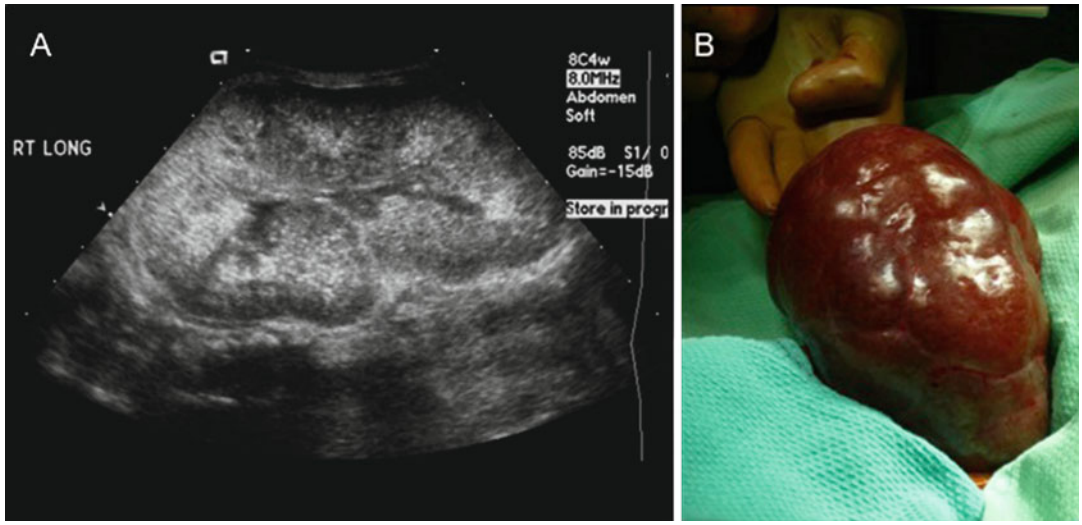

Fig. 8.12 Large kidney removed from patient with autosomal recessive polycystic kidney disease due to inability to effectively carry out peritoneal dialysis. Patient subsequently has been considered for deceased donor renal transplantation. Notice large size of the native kidney on ultrasound (**a**) and at the time of open nephrectomy (**b**, compare size to surgeon's hand in the background)

The likely time to transplantation and the possible need for PD should be included in any decision making.

Once the decision to perform nephrectomy has been made, the operational approach and technique are considered next. The nephrectomy can either be done laparoscopically or as an open procedure. The surgical approach can be transperitoneal or retroperitoneal. The technique and approach should be tailored to the individual patient and the relative skills of the surgical team. The goal is to have the safest, most efficient, least invasive operation that aims to preserve as much of the peritoneal domain as possible [123, 125, 126].

Any surgery is subject to complications, and nephrectomy is no different. CKD and dialysis can both predispose to perioperative bleeding. Immunosuppressive therapy can predispose to infections in the immediate postoperative period. Bowel injuries have been reported following nephrectomy, as have infections of incision sites. Some kidneys are notoriously difficult to remove (polycystic kidneys, chronic parenchymal infection/inflammation) and are often approached with an open technique to avoid the higher than usual complication rates that can be seen when minimally invasive techniques are used [127, 128].

Inguinal Hernias and Peritoneal Dialysis

The incidence of inguinal hernias developing in children while on PD ranges from 8% to 30%. The incidence is highest in patients under 2 years of age. Most of the hernias will develop within 3 months of the initiation of PD [129].

The persistence of a patent processus vaginalis is found in 90% of neonates and predisposes them to the development of an indirect inguinal hernia [130]. The processus vaginalis tends to close spontaneously during childhood and with this, the incidence of inguinal hernia drops. PD, however, creates an abnormal peritoneal fluid volume and consequently an increase in hydrostatic pressure within the peritoneal cavity. This pressure is amplified in sitting or ambulatory patients and is capable of exposing any weakness or potential space that exists in previous incisions, the umbilical remnant or the inguinal canals and is the most likely factor accounting for the higher incidence of inguinal, umbilical, and incisional hernias in PD patients [131]. Management of the inguinal hernia in the patient on PD depends on the surgical approach of the managing physicians. Preemptive diagnosis and prophylactic ligation of

the patent processus vaginalis is easily performed at laparoscopic catheter insertion and safely eliminates the problem before PD begins. However, many surgeons use an open technique for catheter insertion that does not allow for visualization of the internal ring. In this case one simply waits for the development of a hernia before repairing it via a standard inguinal approach. When suspicion of a hernia exists in a patient who is receiving PD, ultrasound and peritoneography can be effective at confirming the diagnosis prior to any surgical intervention [132]. Inguinal hernias are usually hydroceles (fluid hernia), but because there is always a risk of bowel herniation and incarceration, herniotomy is advocated. While timing of hernia repair is determined by the relative risk of bowel incarceration and the health of the patient, it should not be unduly delayed. While waiting for surgery, the patients and their families should be educated on the features of an incarcerated hernia so they can identify the problem and respond appropriately, should it occur. Because of the high incidence of recurrent inguinal hernias in young children on PD, the internal ring should be actively reinforced in addition to the standard high ligation of the hernia sac. Bilateral herniotomies should be performed in all cases because of the relatively high risk of developing a contralateral hernia [133, 134].

Stomas, Catheters, Vascular Access, and Incisions

Children with CKD frequently require multiple surgeries. Operations common to this group include ureteric reimplantation (pfannenstiel incision), nephrectomy (bilateral flank incisions), bladder augmentation (midline lower abdominal incision), PD catheter placement (horizontal paramedian incision), hernia repair (inguinal/umbilical incisions), ventriculo-peritoneal shunt placement (horizontal upper quadrant), and renal transplantation (Gibson/curved iliac fossa incision). In conjunction with this, they often require stomas (colostomy or vesicostomy). Catheterizable channels for bladder drainage or bowel irrigation are commonly placed in the iliac fossae or umbilicus (Fig. 8.13). Some children may have gastrostomy tubes in the epigastrium. The issue that arises from the multitude of possible surgeries that these patients undergo is the need for careful preoperative planning and careful consideration of the follow-up management that may be required. The potential for stomas to be too close to PD catheters or to be placed in the path of ideal surgical incision lines is high if they are not well planned. There is the potential to devascularize segments of the abdominal wall if care is not taken to avoid intersecting and parallel, horizontal incisions. Phlebotomy, temporary intravenous access, and hemodialysis catheters should avoid the groin vessels if possible as a small but significant number of patients will have obliterated iliac vasculature secondary to these interventions. This can make the vascular anastomosis at the time of transplant difficult or impossible, necessitating an alternate site for the implantation of the donor kidney.

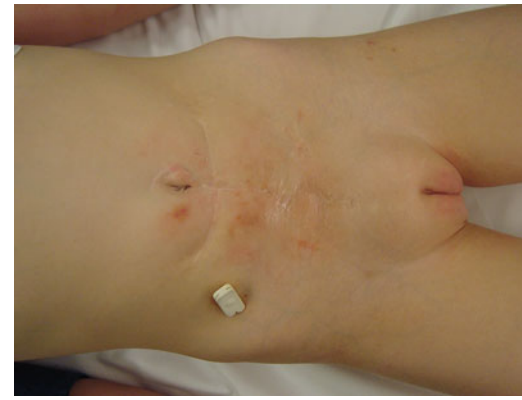

Fig. 8.13 The scarred lower abdomen of a patient with CKD following multiple surgical interventions

Summary

Pediatric patients with CKD and underlying urological issues are uniquely challenging and are ideally suited to management by a multidisciplinary team. It is unusual in modern practice to find urological issues destroying normal kidneys. It is far more common that renal dysfunction preexists as part of, or secondary to, early fetal

urological pathology. Despite fetal interventions, we are unable to alter this congenital renal dysfunction and are therefore restricted to prolonging native function by optimizing the drainage of urine from these kidneys in order to prevent infection and pressure from damaging them further. Additionally, we must be cognizant of the fact that many of these patients will require more than one major surgical intervention, including renal transplantation, during their lifetime and decisions made in their early management will have lifelong implications.

References

1. Orr NI, et al. Frequency, etiology and treatment of childhood end-stage kidney disease in Australia and New Zealand. Pediatr Nephrol. 2009;24(9):1719–26.
2. Deleau J, et al. Chronic renal failure in children: an epidemiological survey in Lorraine (France) 1975–1990. Pediatr Nephrol. 1994;8(4):472–6.
3. Neu AM, et al. Chronic dialysis in children and adolescents: the 2001 NAPRTCS annual report. Pediatr Nephrol. 2002;17(8):656–63.
4. Ardissino G, et al. Epidemiology of chronic renal failure in children: data from the ItalKid project. Pediatrics. 2003;111(4 Pt 1):e382–7.
5. Chesney RW, et al. Report of an NIH task force on research priorities in chronic kidney disease in children. Pediatr Nephrol. 2006;21(1):14–25.
6. Seikaly MG, et al. Chronic renal insufficiency in children: the 2001 annual report of the NAPRTCS. Pediatr Nephrol. 2003;18(8):796–804.
7. de Jong TP, et al. Treatment of the neurogenic bladder in spina bifida. Pediatr Nephrol. 2008;23(6):889–96.
8. Kari JA. Neuropathic bladder as a cause of chronic renal failure in children in developing countries. Pediatr Nephrol. 2006;21(4):517–20.
9. Kari JA, et al. Renal involvement in children with spina bifida. Saudi J Kidney Dis Transpl. 2009;20(1):102–5.
10. DeFoor W, et al. Risk factors for end stage renal disease in children with posterior urethral valves. J Urol. 2008;180(4 Suppl):1705–8. Discussion 1708.
11. Dik P, et al. Early start to therapy preserves kidney function in spina bifida patients. Eur Urol. 2006;49(5):908–13.
12. Coulthard MG, Keir MJ. Reflux nephropathy in kidney transplants, demonstrated by dimercaptosuccinic acid scanning. Transplantation. 2006;82(2):205–10.
13. Strand WR. Initial management of complex pediatric disorders: prunebelly syndrome, posterior urethral valves. Urol Clin North Am. 2004;31(3):399–415, vii.
14. Marra G, et al. Severe vesicoureteral reflux and chronic renal failure: a condition peculiar to male gender? data from the ItalKid project. J Pediatr. 2004;144(5):677–81.
15. Roth KS, et al. Obstructive uropathy: an important cause of chronic renal failure in children. Clin Pediatr (Phila). 2002;41(5):309–14.
16. Woolf AS, Thiruchelvam N. Congenital obstructive uropathy: its origin and contribution to end-stage renal disease in children. Adv Ren Replace Ther. 2001;8(3):157–63.
17. Casale AJ. Early ureteral surgery for posterior urethral valves. Urol Clin North Am. 1990;17(2):361–72.
18. Thomas DF, Gordon AC. Management of prenatally diagnosed uropathies. Arch Dis Child. 1989;64(1 Spec No):58–63.
19. Tsingoglou S, Dickson JA. Lower urinary obstruction in infancy: a review of lesions and symptoms in 165 cases. Arch Dis Child. 1972;47(252):215–7.
20. Roth KS, Carter Jr WH, Chan JC. Obstructive nephropathy in children: long-term progression after relief of posterior urethral valve. Pediatrics. 2001;107(5):1004–10.
21. Holmdahl G, Sillen U. Boys with posterior urethral valves: outcome concerning renal function, bladder function and paternity at ages 31 to 44 years. J Urol. 2005;174(3):1031–4. Discussion 1034.
22. Ansari M et al. Risk factors for progression to end-stage renal disease in children with posterior urethral valves. J Pediatr Urol. 2010;6:261–4.
23. Warren J, Pike JG, Leonard MP. Posterior urethral valves in Eastern Ontario – a 30 year perspective. Can J Urol. 2004;11(2):2210–5.
24. Smith GH, et al. The long-term outcome of posterior urethral valves treated with primary valve ablation and observation. J Urol. 1996;155(5):1730–4.
25. Holmes N, Harrison MR, Baskin LS. Fetal surgery for posterior urethral valves: long-term postnatal outcomes. Pediatrics. 2001;108(1):E7.
26. McLorie G, et al. Outcome analysis of vesicoamniotic shunting in a comprehensive population. J Urol. 2001;166(3):1036–40.
27. Salam MA. Posterior urethral valve: outcome of antenatal intervention. Int J Urol. 2006;13(10):1317–22.
28. Freedman AL, et al. Long-term outcome in children after antenatal intervention for obstructive uropathies. Lancet. 1999;354(9176):374–7.
29. Georgieva M, et al. Urinary ascites and perirenal urinoma – a renoprotective "complication" of posterior urethral valves. Aktuelle Urol. 2003;34(6):410–2.
30. Rittenberg MH, et al. Protective factors in posterior urethral valves. J Urol. 1988;140(5):993–6.
31. Oliveira EA, et al. Prognostic factors in prenatally-detected posterior urethral valves: a multivariate analysis. Pediatr Surg Int. 2002;18(8):662–7.
32. Mizra K, Onuora V, Al-Sowailem A. Protective factors in posterior urethral valves in Saudi children. Ann Saudi Med. 1998;18(3):263–5.

33. Kaefer M, et al. Posterior urethral valves, pressure pop-offs and bladder function. J Urol. 1995;154 (2 Pt 2): 708–11.
34. Silveri M, et al. Fetal monolateral urinoma and neonatal renal function outcome in posterior urethral valves obstruction: the pop-off mechanism. Pediatr Med Chir. 2002;24(5):394–6.
35. Mukherjee S, et al. What is the effect of circumcision on risk of urinary tract infection in boys with posterior urethral valves? J Pediatr Surg. 2009;44(2): 417–21.
36. De Gennaro M, et al. The changing urodynamic pattern from infancy to adolescence in boys with posterior urethral valves. BJU Int. 2000;85(9):1104–8.
37. Emir H, et al. Urodynamic findings of posterior urethral valve patients. Eur J Pediatr Surg. 2002;12(1): 38–41.
38. Mitchell ME. Valve Bladder syndrome. In: Presented at the annual meeting of the North Central Section, Hamilton: American Urological Association; 1980.
39. Koff S, Mutabagani K, Jayanthi V. The valve bladder syndrome: pathophysiology and treatment with nocturnal bladder emptying. J Urol. 2002;167(1):291–7.
40. De Gennaro M, et al. Detrusor hypocontractility in children with posterior urethral valves arises before puberty. Br J Urol. 1998;81(Suppl 3):81–5.
41. Glassberg KI, et al. Observations on persistently dilated ureter after posterior urethral valve ablation. Urology. 1982;20(1):20–8.
42. Nguyen MT, et al. Overnight catheter drainage in children with poorly compliant bladders improves post-obstructive diuresis and urinary incontinence. J Urol. 2005;174(4 Pt 2):1633–6. Discussion 1636.
43. Fumo MJ, McLorie GA. Management of the valve-bladder syndrome and congenital bladder obstruction: the role of nocturnal bladder drainage. Nat Clin Pract Urol. 2006;3(6):323–6.
44. Hassan JM, et al. Vesicoureteral reflux in patients with posterior urethral valves. J Urol. 2003;170(4 Pt 2): 1677–80. Discussion 1680.
45. Priti K, et al. Posterior urethral valves: incidence and progress of vesicoureteric reflux after primary fulguration. Pediatr Surg Int. 2004;20(2):136–9.
46. Cuckow PM, et al. Long-term renal function in the posterior urethral valves, unilateral reflux and renal dysplasia syndrome. J Urol. 1997;158(3 Pt 2): 1004–7.
47. Parkhouse HF, et al. Long-term outcome of boys with posterior urethral valves. Br J Urol. 1988;62(1): 59–62.
48. Heikkila J, Rintala R, Taskinen S. Vesicoureteral reflux in conjunction with posterior urethral valves. J Urol. 2009;182(4):1555–60.
49. Narasimhan KL, et al. The vesicoureteral reflux dysplasia syndrome in patients with posterior urethral valves. J Urol. 2005;174(4 Pt 1):1433–5. Discussion 1435.
50. Bailey RR. The relationship of vesico-ureteric reflux to urinary tract infection and chronic pyelonephritis-reflux nephropathy. Clin Nephrol. 1973;1(3):132–41.
51. Rolleston GL, Shannon FT, Utley WL. Relationship of infantile vesicoureteric reflux to renal damage. Br Med J. 1970;1(5694):460–3.
52. Roberts JA. Pathogenesis of pyelonephritis. J Urol. 1983;129(6):1102–6.
53. Roberts JA. Vesicoureteral reflux in the monkey: a review. Urol Radiol. 1983;5(3):211–7, 219.
54. Fenton S, et al. Renal replacement therapy in Canada: a report from the Canadian organ replacement register. Am J Kidney Dis. 1995;25(1):134–50.
55. Casale P, et al. Recurrent urinary tract infection in the post-transplant reflux nephropathy patient: is reflux in the native ureter the culprit? Pediatr Transplant. 2005;9(3):324–7.
56. Ardissino G, et al. Long-term outcome of vesicoureteral reflux associated chronic renal failure in children. Data from the ItalKid project. J Urol. 2004;172(1):305–10.
57. Williams GJ, Lee A, Craig JC. Long-term antibiotics for preventing recurrent urinary tract infection in children. Cochrane Database Syst Rev. 2001;4: CD001534.
58. Conway PH, et al. Recurrent urinary tract infections in children: risk factors and association with prophylactic antimicrobials. JAMA. 2007;298(2): 179–86.
59. Pennesi M, et al. Is antibiotic prophylaxis in children with vesicoureteral reflux effective in preventing pyelonephritis and renal scars? a randomized, controlled trial. Pediatrics. 2008;121(6):e1489–94.
60. Roussey-Kesler G, et al. Antibiotic prophylaxis for the prevention of recurrent urinary tract infection in children with low grade vesicoureteral reflux: results from a prospective randomized study. J Urol. 2008;179(2):674–9. Discussion 679.
61. Hadjizadeh N, et al. Association of voiding dysfunction with functional constipation. Indian Pediatr. 2009;46(12):1093–5.
62. Halachmi S, Farhat WA. The impact of constipation on the urinary tract system. Int J Adolesc Med Health. 2008;20(1):17–22.
63. Kasirga E, et al. Evaluation of voiding dysfunctions in children with chronic functional constipation. Turk J Pediatr. 2006;48(4):340–3.
64. Mathew TH, Kincaid-Smith P, Vikraman P. Risks of vesicoureteric reflux in the transplanted kidney. N Engl J Med. 1977;297(8):414–8.
65. Prat V, et al. Urinary tract infection in renal transplant patients. Infection. 1985;13(5):207–10.
66. Ranchin B, et al. Vesicoureteral reflux after kidney transplantation in children. Nephrol Dial Transplant. 2000;15(11):1852–8.
67. Fontana I, et al. Impact of vesicoureteral reflux on graft survival in paediatric kidney transplants. Transplant Proc. 1998;30(5):2000–1.
68. Dunn SP, et al. Pyelonephritis following pediatric renal transplant: increased incidence with vesicoureteral reflux. J Pediatr Surg. 1987;22(12): 1095–9.

69. Basiri A, et al. Does pre-transplantation antireflux surgery eliminate post-renal transplantation pyelonephritis in children? J Urol. 2006;175(4):1490–2.
70. Barrero R, et al. Vesicoureteral reflux after kidney transplantation in children. Pediatr Transplant. 2007; 11(5):498–503.
71. Engelstein D, et al. A critical appraisal of vesicoureteral reflux in long-term renal transplantation recipients: prospective study. Transplant Proc. 1997; 29(1–2):136–7.
72. Neuhaus TJ, et al. Pyelonephritis and vesicoureteral reflux after renal transplantation in young children. J Urol. 1997;157(4):1400–3.
73. Cloix P, et al. Endoscopic treatment of vesicoureteric reflux in transplanted kidneys. Br J Urol. 1993;72(1): 20–2.
74. Williams MA, Giel DW, Hastings MC. Endoscopic Deflux injection for pediatric transplant reflux: a feasible alternative to open ureteral reimplant. J Pediatr Urol. 2008;4(5):341–4.
75. Wan J, Park JM. Neurologic control of storage and voiding. In: Docimo SG, Canning DA, Khoury AE, editors. The Kelalis-King-Belman textbook of clinical pediatric urology. London: Informa Healthcare; 2007.
76. Neveus T, et al. The standardization of terminology of lower urinary tract function in children and adolescents: report from the Standardisation Committee of the International Children's Continence Society. J Urol. 2006;176(1):314–24.
77. Wein AJ. Classification of neurogenic voiding dysfunction. J Urol. 1981;125(5):605–9.
78. Joseph DB. Current approaches to the urologic care of children with spina bifida. Curr Urol Rep. 2008; 9(2):151–7.
79. Hopps CV, Kropp KA. Preservation of renal function in children with myelomeningocele managed with basic newborn evaluation and close followup. J Urol. 2003;169(1):305–8.
80. Kaefer M, et al. Improved bladder function after prophylactic treatment of the high risk neurogenic bladder in newborns with myelomeningocele. J Urol. 1999;162(3 Pt 2):1068–71.
81. Edelstein RA, et al. The long-term urological response of neonates with myelodysplasia treated proactively with intermittent catheterization and anticholinergic therapy. J Urol. 1995;154(4):1500–4.
82. Lapides J, et al. Clean, intermittent self-catheterization in the treatment of urinary tract disease. J Urol. 1972;107(3):458–61.
83. Goto M, et al. Clinical effects of oxybutynin hydrochloride in the treatment of unstable bladder and overactive neurogenic bladder: a long-term clinical trial. Hinyokika Kiyo. 1988;34(3):541–50.
84. Thompson IM, Lauvetz R. Oxybutynin in bladder spasm, neurogenic bladder, and enuresis. Urology. 1976;8(5):452–4.
85. Koyanagi T. Further observation on the denervation supersensitivity of the urethra in patients with chronic neurogenic bladders. J Urol. 1979;122(3): 348–51.
86. Takimoto Y, et al. Clinical effect of new alpha-adrenergic blocker on micturition disturbance of neurogenic bladder and lower urinary tract obstruction. Hinyokika Kiyo. 1983;29(2):255–63.
87. Wan J. The role of urethral dilation in managing pediatric neurogenic bladder dysfunction. Curr Urol Rep. 2009;10(2):153–8.
88. Park JM, et al. External urethral sphincter dilation for the management of high risk myelomeningocele: 15-year experience. J Urol. 2001;165(6 Pt 2): 2383–8.
89. Pan D, et al. Long-term outcomes of external sphincterotomy in a spinal injured population. J Urol. 2009;181(2):705–9.
90. Morrisroe SN, et al. Vesicostomy revisited: the best treatment for the hostile bladder in myelodysplastic children? BJU Int. 2005;96(3):397–400.
91. Lemelle JL, Simo AK, Schmitt M. Comparative study of the Yang-Monti channel and appendix for continent diversion in the Mitrofanoff and Malone principles. J Urol. 2004;172(5 Pt 1):1907–10.
92. Chen JL, Kuo HC. Long-term outcomes of augmentation enterocystoplasty with an ileal segment in patients with spinal cord injury. J Formos Med Assoc. 2009;108(6):475–80.
93. Gurocak S, et al. Bladder augmentation: Review of the literature and recent advances. Indian J Urol. 2007;23(4):452–7.
94. Churchill BM, et al. Ureteral bladder augmentation. J Urol. 1993;150(2 Pt 2):716–20.
95. Landau EH, et al. Bladder augmentation: ureterocystoplasty versus ileocystoplasty. J Urol. 1994;152 (2 Pt 2):716–9.
96. Capizzi A, et al. Kidney transplantation in children with reconstructed bladder. Transplantation. 2004; 77(7):1113–6.
97. Djakovic N, et al. Intestinal reconstruction of the lower urinary tract as a prerequisite for renal transplantation. BJU Int. 2009;103(11):1555–60.
98. DeFoor W, et al. Lower urinary tract reconstruction is safe and effective in children with end stage renal disease. J Urol. 2003;170(4 Pt 2):1497–500. Discussion 1500.
99. Basiri A, et al. Kidney transplantation in children with augmentation cystoplasty. J Urol. 2007;178(1): 274–7. Discussion 277.
100. Fontaine E, et al. Renal transplantation in children with augmentation cystoplasty: long-term results. J Urol. 1998;159(6):2110–3.
101. Hatch DA, et al. Kidney transplantation in children with urinary diversion or bladder augmentation. J Urol. 2001;165(6 Pt 2):2265–8.
102. Power RE, et al. Renal transplantation in patients with an augmentation cystoplasty. BJU Int. 2000; 86(1):28–31.
103. Rigamonti W, et al. Kidney transplantation into bladder augmentation or urinary diversion: long-term results. Transplantation. 2005;80(10):1435–40.
104. Koo HP, et al. Renal transplantation in children with severe lower urinary tract dysfunction. J Urol. 1999; 161(1):240–5.

105. Ives EJ. The abdominal muscle deficiency triad syndrome–experience with ten cases. Birth Defects Orig Artic Ser. 1974;10(4):127–35.
106. Williams DI, Burkholder GV. The prune belly syndrome. J Urol. 1967;98(2):244–51.
107. Rabinowitz R, Schillinger JF. Prune belly syndrome in the female subject. J Urol. 1977;118(3):454–6.
108. Aaronson IA, Cremin BJ. Prune belly syndrome in young females. Urol Radiol. 1979;1(3):151–5.
109. Bellah RD, States LJ, Duckett JW. Pseudoprune-belly syndrome: imaging findings and clinical outcome. AJR Am J Roentgenol. 1996;167(6):1389–93.
110. Ely B, Gustafson RA, Karnsakul W. Pseudoprune-belly syndrome in vertebral abnormalities, anal atresia, cardiac abnormalities, tracheoesophageal fistula and/or esophageal atresia, renal agenesis and dysplasia, and limb defects association. Clin Gastroenterol Hepatol. 2008;6(7):e26.
111. Woods AG, Brandon DH. Prune belly syndrome: a focused physical assessment. Adv Neonatal Care. 2007;7(3):132–43. quiz 144–5.
112. Ashcraft's Pediatric Surgery George Whitfield Holcomb III and J. Patrick Murphy (Editors) Saunders 5th edition Chapter 62: Prune Belly Syndrome by Romano DeMarco Pages 796–804.
113. Woodard JR. Prune belly syndrome. In: Kelalis PP, King LR, Belman AB, editors. Clinical pediatric urology. Philadelphia: WB Saunders; 1985. p. 805–24.
114. Smith CA, et al. Voiding function in patients with the prune-belly syndrome after Monfort abdominoplasty. J Urol. 1998;159(5):1675–9.
115. Diao B, et al. Prune belly syndrome: epidemiologic, clinic and therapeutic aspects. Prog Urol. 2008; 18(7):470–4.
116. Fallat ME, et al. The prune belly syndrome: a comprehensive approach to management. J Urol. 1989; 142(3):802–5.
117. Bukowski TP, Perlmutter AD. Reduction cystoplasty in the prune belly syndrome: a long-term followup. J Urol. 1994;152(6 Pt 1):2113–6.
118. Kinahan TJ, et al. The efficiency of bladder emptying in the prune belly syndrome. J Urol. 1992;148(2 Pt 2):600–3.
119. Hubinois P, Valayer J, Cendron J. A series of 34 cases of prune belly syndrome in children. Sem Hop. 1983;59(40):2769–77.
120. Crompton CH, Balfe JW, Khoury A. Peritoneal dialysis in the prune belly syndrome. Perit Dial Int. 1994;14(1):17–21.
121. Fontaine E, et al. Long-term results of renal transplantation in children with the prune-belly syndrome. J Urol. 1997;158(3 Pt 1):892–4.
122. Reinberg Y, et al. The outcome of renal transplantation in children with the prune belly syndrome. J Urol. 1989;142(6):1541–2.
123. Shoma AM, Eraky I, El-Kappany HA. Pretransplant native nephrectomy in patients with end-stage renal failure: assessment of the role of laparoscopy. Urology. 2003;61(5):915–20.
124. Broyer M. What are the indications for nephrectomy, either bilateral or unilateral, prior to transplantation in children? Pediatr Nephrol. 1991;5(1):11.
125. Gundeti MS, Taghizaedh A, Mushtaq I. Bilateral synchronous posterior prone retroperitoneoscopic nephrectomy with simultaneous peritoneal dialysis: a new management for end-stage renal disease in children. BJU Int. 2007;99(4): 904–6.
126. Doublet JD, et al. Retroperitoneal laparoscopic nephrectomy of native kidneys in renal transplant recipients. Transplantation. 1997;64(1):89–91.
127. Keeley FX, Tolley DA. A review of our first 100 cases of laparoscopic nephrectomy: defining risk factors for complications. Br J Urol. 1998;82(5): 615–8.
128. Dunn MD, et al. Laparoscopic nephrectomy in patients with end-stage renal disease and autosomal dominant polycystic kidney disease. Am J Kidney Dis. 2000;35(4):720–5.
129. von Lilien T, et al. Hernias: a frequent complication in children treated with continuous peritoneal dialysis. Am J Kidney Dis. 1987;10(5):356–60.
130. White JJ, HaIler JA. Groin hernia in infants and children. In: Nyphus LM, Condon RE, editors. Hernia. Philadelphia: Lippincott; 1978.
131. Aranda RA, et al. Intraperitoneal pressure and hernias in children on peritoneal dialysis. Pediatr Nephrol. 2000;14(1):22–4.
132. Wetherington GM, et al. Abdominal wall and inguinal hernias in continuous ambulatory peritoneal dialysis patients. Am J Surg. 1985;150(3): 357–60.
133. Khoury AE, et al. Hernias associated with CAPD in children. Adv Perit Dial. 1991;7:279–82.
134. Tank ES, Hatch DA. Hernias complicating chronic ambulatory peritoneal dialysis in children. J Pediatr Surg. 1986;21(1):41–2.