Urinary Tract Obstruction and Dilatation

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Anju Goyal

Abstract

Congenital anomalies of the kidney and urinary tract (CAKUT) has an incidence of 3–6 per 1000 birth and is a common cause of chronic kidney disease in children. While most CAKUT are believed to be sporadic, recent studies have suggested a high incidence (upto 50%) of CAKUT in families of index cases of urinary tract anomaly (Renkema et al. Nephrol Dial Transplant. 26:3843–51, 2011; Bulum et al. Pediatr Nephrol. 28:2143–7, 2013). This suggest a genetic basis and various genes such as HNF1 β[beta], PAX2, RET and ROBO2 have been implicated. Commonly CAKUT result in dilatation and/or obstruction of the urinary tract anywhere from the kidney down to the bladder and urethra. There can be isolated dilatation of the pelvicalyceal system (hydronephrosis [HDN]) or associated ureteric dilatation (hydroureteronephrosis [HDUN]) with or without bladder abnormality. HDN/HDUN can be secondary to obstructive or non-obstructive pathology. Obstruction is defined as 'some impedence to the flow of urine, which causes gradual and progressive damage to the kidney' (Dhillon. Essentials of paediatric urology. Informa Healthcare, p. 133–42, 2008). The non-obstructive dilatation can be due to vesico-ureteric reflux (VUR) or it can be non-obstructive, non-refluxing dilatation. Non-obstructive non-refluxing pathology, which is usually due to inherent dysplasia of the developing urinary tract, is more difficult to define and to differentiate from obstruction. Occasionally obstruction and reflux can coexist.

Keywords

Urinary tract anomaly • Prenatal diagnosis • Investigations • Surgical management • Outcomes

A. Goyal, MCh, FRCS(Paed)
Royal Manchester Children's Hospital,
Manchester, UK
e-mail: anju.goyal@cmft.nhs.uk

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65.1 Introduction

Congenital anomalies of the kidney and urinary tract (CAKUT) has an incidence of 3–6 per 1000 birth and is a common cause of chronic kidney disease in children. While most CAKUT are believed to be sporadic, recent studies have suggested a high incidence (upto 50%) of CAKUT in families of index cases of urinary tract anomaly [1, 2]. This suggest a genetic basis and various genes such as HNF1 β[beta], PAX2, RET and ROBO2 have been implicated. Commonly CAKUT result in dilatation and/or obstruction of the urinary tract anywhere from the kidney down to the bladder and urethra. There can be isolated dilatation of the pelvicalyceal system (hydronephrosis [HDN]) or associated ureteric dilatation (hydroureteronephrosis [HDUN]) with or without bladder abnormality. HDN/HDUN can be secondary to obstructive or non-obstructive pathology. Obstruction is defined as 'some impedence to the flow of urine, which causes gradual and progressive damage to the kidney [3]. The non-obstructive dilatation can be due to vesico-ureteric reflux (VUR) or it can be non-obstructive, non-refluxing dilatation. Non-obstructive non-refluxing pathology, which is usually due to inherent dysplasia of the developing urinary tract, is more difficult to define and to differentiate from obstruction. Occasionally obstruction and reflux can coexist.

The landscape of neonatal urinary tract dilatation and obstruction anomalies has been transformed by the introduction of routine antenatal ultrasound (US) screening. A mid-trimester ultrasound scan to detect fetal structural anomalies has been undertaken in the UK since the 1980s. A fetal anomaly screening scan is offered to all pregnant women from 18 to 20(+6) weeks. High-resolution 2D ultrasound scan provides detailed assessment of urinary tract from early 2nd trimester onwards. It can detect renal pelvic (Fig. 65.1) and/or ureteric dilatation/anomaly and/or bladder distention (Fig. 65.2) along with other associated non urinary tract abnormalities. Many of the detected anomalies might never have come to attention clinically in childhood but often generates disproportionate parental anxiety during the pregnancy [4].

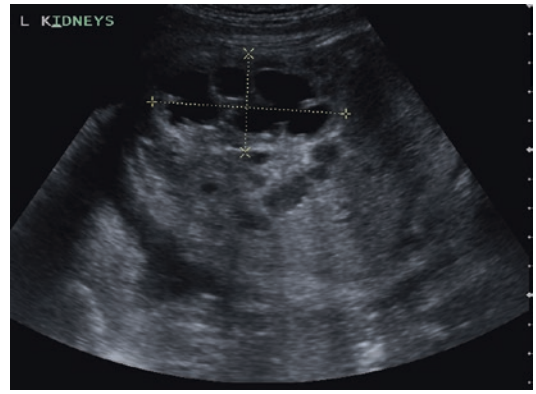

Fig. 65.1 Antenatal scan demonstrating left hydronephrosis

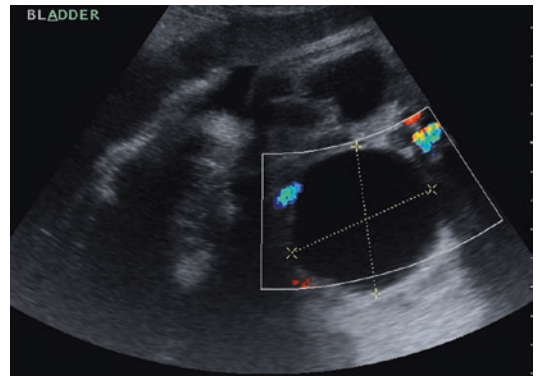

Fig. 65.2 Distended bladder on antenatal scan

Antenatal detection has created a whole new field in the practice of paediatric urology. It deals predominantly with healthy children with no obvious clinical problem who have a potential for morbidity in the form of urinary tract infection (UTI) and renal functional deterioration. There are management dilemmas as to how far to investigate in an apparently healthy child, especially where natural history of the abnormality is not clear and management may not yield satisfactory outcomes. This is especially brought to focus when managing cases with megaureter and non-specific renal pelvic dilatation. Natural history studies are limited. Some

anomalies such as antenatal HDN and megaureter are better studied than others and this has led to majority of these being managed conservatively with careful monitoring [5].

Most neonates are asymptomatic at birth and have a benign pathology, which needs antibiotic prophylaxis, careful and optimally timed investigations and monitoring. In the medium term, only 7% of these antenatally detected anomalies require surgery [5]. A recent long-term outcome study demonstrated that one third each showed normalization, need of surgery or persistence of anomalies without need of surgery [6]. And further few of these such as those with posterior urethral valves (PUV), severe pelvi-ureteric junction (PUJ) obstruction and obstructing duplex ureterocoele, will require intervention in the neonatal period.

The challenge for the medical community is to differentiate those, which need treatment to prevent renal deterioration from those that are unlikely to have any consequences. In order to make this differentiation, the optimum level of investigations that a child should be subjected to, continue to be refined. As demonstrated by trends in management of HDN, the pendulum has swung from aggressive surgical correction to non-interventional observation for majority [5, 7].

65.2 Antibiotic Prophylaxis

Urinary tract dilatation and obstruction, on account of stasis of urine predisposes the child to urinary tract infection. In some pathology, prophylaxis has been proven to be helpful where as in others, the benefit is debatable. Antibiotic prophylaxis reduces the risk of UTI and prevents renal scarring in selected cases [8, 9]. Regardless of the need for intervention, antibiotic prophylaxis is started in most neonates with suspected urological anomaly while awaiting investigations and it remains the mainstay of urological management in a significant number of refluxing, obstructive and non-refluxing, non-obstructive pathologies. In our practice, trimethoprim at 2 mg/kg is the most commonly used antibiotic, followed by cefalexin.

65.3 Prenatally Detected Urinary Tract Anomalies and Their Antenatal Management

65.4 Incidence

A significant proportion of congenital urinary tract anomalies are diagnosed antenatally on detailed fetal anomaly scan done at 20 weeks gestation. About 20% of the anomalies are detected at a later gestation scan despite an apparently normal 20 weeks scan [5]. A small proportion escapes antenatal detection and may present in early infancy with symptoms of abdominal mass or UTI.

The reported incidence of antenatal urological anomalies is increasing due to improved detection. A variable incidence has been reported depending upon the threshold for diagnosing pelvicalyceal dilatation with most citing incidence of 1 in 100 or higher [4, 5, 10, 11]. A consensus statement by the Society for Fetal Urology (SFU) suggests that up to 5% of fetuses might be affected by HDN [12]. Most of these are mild dilatation and incidence of significant uropathy is around 1 in 500 [4].

The most commonly detected anomalies are—non-specific dilatation (NSD) of pelvicalyceal system (48.6%), VUR (12%), PUJ obstruction (10.6%), multicystic dysplastic kidney (MCDK) (6%) [5]. Apart from urinary tract dilatation, antenatal screening may detect—absence of kidney, absence of bladder, renal dysplasia, amniotic fluid volume increase or decrease, associated other system anomalies such as haematocolpos, etc. (Table 65.1). Though antenatal findings suggest the possible diagnosis, it is not always accurate and hence prognostic predictions are fraught with pitfalls. Any advice about antenatal intervention or progression or otherwise of pregnancy has to be very cautious with recognition of limitations of imaging techniques [13].

Table 65.1 Features and possible aetiology of antenatally detected urinary tract dilatation/pathology

Pathology	Features on antenatal scans	Aetiology
Upper urinary tract pathology	Renal pelvic dilatation	Non specific dilatation, PUJ obstruction, duplex kidney
	Ureteric dilatation ± Renal pelvic dilatation	Megaureter (obstructed or non-obstructed), Vesico-ureteric reflux, duplex kidney
	Other renal pathologies	Renal aplasia, dysplasia, MCDK, duplex
Lower urinary tract pathology	Bladder distention ± renal pelvic and ureteric dilatation	PUV, Isolated Megacystis, Neuropathic bladder (unusual), urethral atresia
	Bladder not seen	Bladder exstrophy / Cloacal exstrophy
Entire urinary tract malformation	Renal pelvic and ureteric dilatation along with bladder distention	PUV, Prune belly syndrome, Megacystis megaureter syndrome, MMIHS
Associated with complex urogenital tract malformations	Usually renal pelvic and ureteric dilatation ± bladder distention	Cloacal anomaly, Vaginal atresia, Urogenital sinus, Imperforate anus

65.5 Antenatal Investigations

Most antenatally detected anomalies require monitoring during pregnancy with ultrasound scan. The frequency of monitoring depends upon the severity of pathology. In unilateral renal dilatation follow up scan at 30–32 weeks gestation would suffice but in bilateral PCS dilatation or solitary kidney, serial scans at 4 weekly intervals are required (see Fig. 65.3a). In case of associated oligohydramnios, referral to specialist fetal therapy unit must be made. In selected cases such as when kidneys are not seen clearly due to maternal habitus or low liquor volume, magnetic resonance (MR) scan of fetus may be helpful to assess anatomy. In some instances, when pathology detected might warrant consideration of termination, MR may be done to be absolutely sure of the pathology—such as in cloacal exstrophy [13]. Depending upon the findings of antenatal scan, other investigations such a karyotyping, amniotic fluid analysis might be required. There is up to 22% reported incidence of chromosomal abnormalities in antenatal lower urinary tract obstruction (LUTO) [14–17].

65.6 Antenatal Intervention

Intervention can be diagnostic or therapeutic. Alternatively it may be termination of pregnancy (TOP). TOP is recommended only if bilateral severe renal dysplasia/solitary dysplastic kidney with or without oligohydramnios or in very severe anomalies with poor quality of life such as cloacal exstrophy.

Antenatal intervention is most commonly considered in cases of LUTO because if untreated, it carries a mortality of up to 45% mainly due to the severe oligohydramnios and resulting pulmonary hypoplasia [18]. One third of survivors may develop end-stage chronic renal impairment [19]. Because of this prognosis, there is a termination rate of up to 50% in severe LUTO [20, 21]. LUTO is amenable to therapeutic fetal intervention and it is considered if there is predicted poor prognosis with some anticipated salvage consequent to intervention. The aim of therapeutic antenatal intervention is prevention of renal failure and pulmonary hypoplasia. The prognostic criteria for case selection for intervention include echogenicity of kidneys and liquor volume. Biochemistry of fetal urine gives information about the prognosis but a systematic review [22] demonstrated that none of the analytes of fetal urine yielded clinically significant accuracy to predict poor postnatal renal function. Also fetal urine for analysis is obtained by vesicocentesis, which carries its own risk; hence it is not routinely performed. As a preparation for therapeutic intervention, it is mandatory to perform a detailed anomaly scan, determine fetal sex and offer fetal karyotyping.

There are different modalities of therapeutic intervention. Though fetal cystoscopy, open shunt insertion and repeated vesicocentesis have been utilised [23, 24], percutaneous vesico-amniotic shunt (VAS) placement is the most commonly used modality. VAS involves the placement of a double pig-tailed catheter under ultrasound guidance and local anaesthesia, with the distal end in the fetal bladder and the proximal end in the amniotic cavity to allow drainage of fetal urine. Since the first report of VAS in human fetuses in 1982 [25], many case series have suggested that

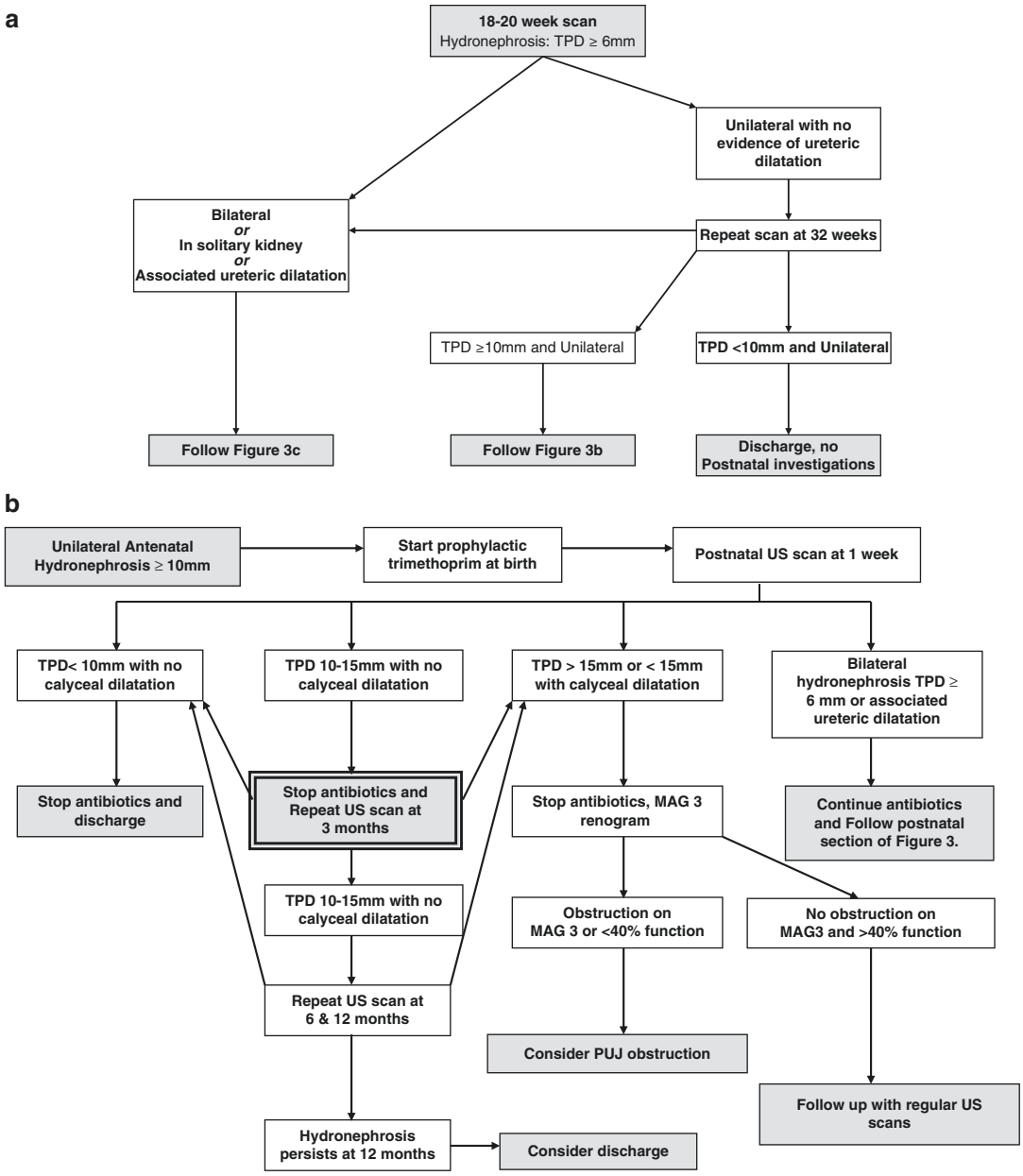

Fig. 65.3 Institutional management protocol for antenatal hydronephrosis. (**a**) Antenatal scan findings and pathway for management, (**b**) Postnatal management for unilateral hydronephrosis, (**c**) Pathway for bilateral hydronephrosis, hydronephrosis in a solitary kidney or associated ureteric dilatation

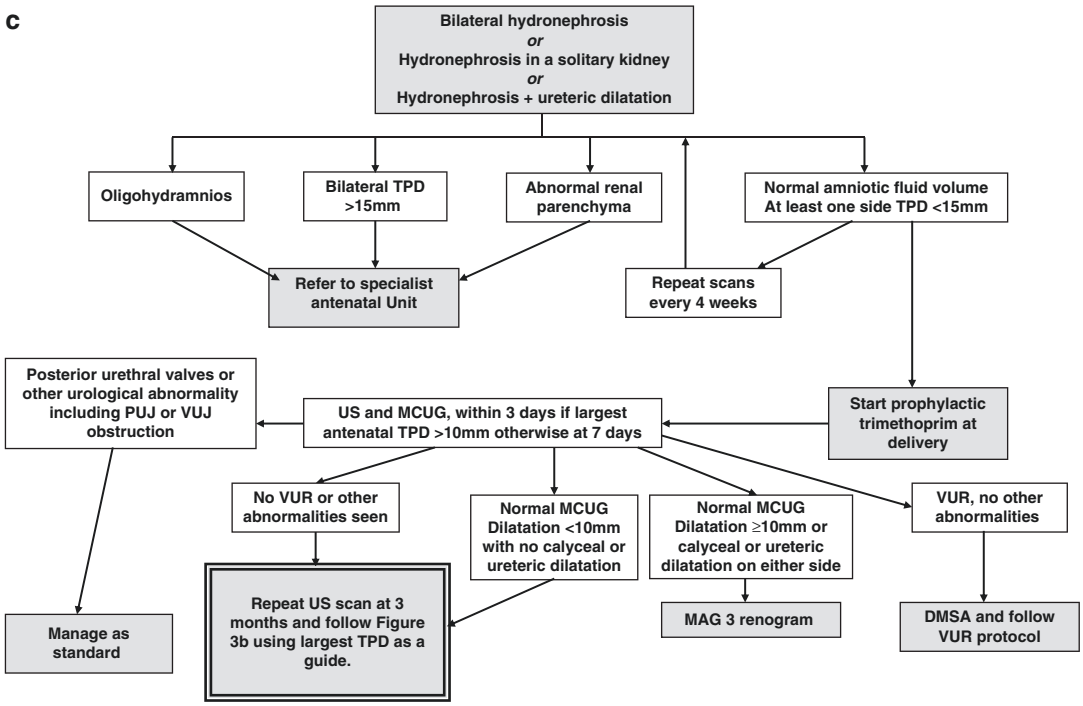

Fig. 65.3 (continued)

survival could be improved with this [26]. VAS has a significant incidence of complications: shunt displacement/occlusion (upto 34%), preterm labour, chorioamnionitis, traumatic injury and fetal/neonatal death [27]. Despite initial promise of good results, outcomes have not been very positive and VAS is not in vogue any more. Systematic review of observational studies showed a role for VAS in reduction of perinatal mortality but long-term mortality and morbidity remains high. It suggests that amelioration of oligohydramnios by shunting reduces mortality due to pulmonary hypoplasia, but the renal damage is not reversible [27]. A multi centre randomised controlled trial (PLUTO—The Percutaneous shunting in Lower Urinary Tract Obstruction) conducted by The University of Birmingham, UK compared in-utero VAS with conservative management [28]. The as-treated analysis of 31 pregnancies showed that fetuses that underwent bladder shunting had a three-time higher chance of postnatal survival than non-shunted fetuses, though very few survived with normal renal function. These findings are in line with results from studies in animals, which have shown that renal damage occurs rapidly after the onset of obstruction and might be only partly reversible [29]. The dysplastic changes seen in fetal kidneys are probably a different pathological process, rather than just a consequence of obstruction [30].

65.7 General Principles of Postnatal Management

A thorough clinical examination of the newborn remains very relevant. The necessity of investigations is clear when a neonate presents with symptoms of UTI or mass or urinary stream problems. However formulating a rational investigation protocol for antenatally detected anomalies that is appropriate and is tailored to the urgency of concerned pathology is more difficult. The aim is to investigate urgently those, which are likely to result in infection or nephron damage if left untreated. Others can be investigated at a pace that is suitable for the child, family and is likely to give best information. Fig. 65.3a–c shows the pro-

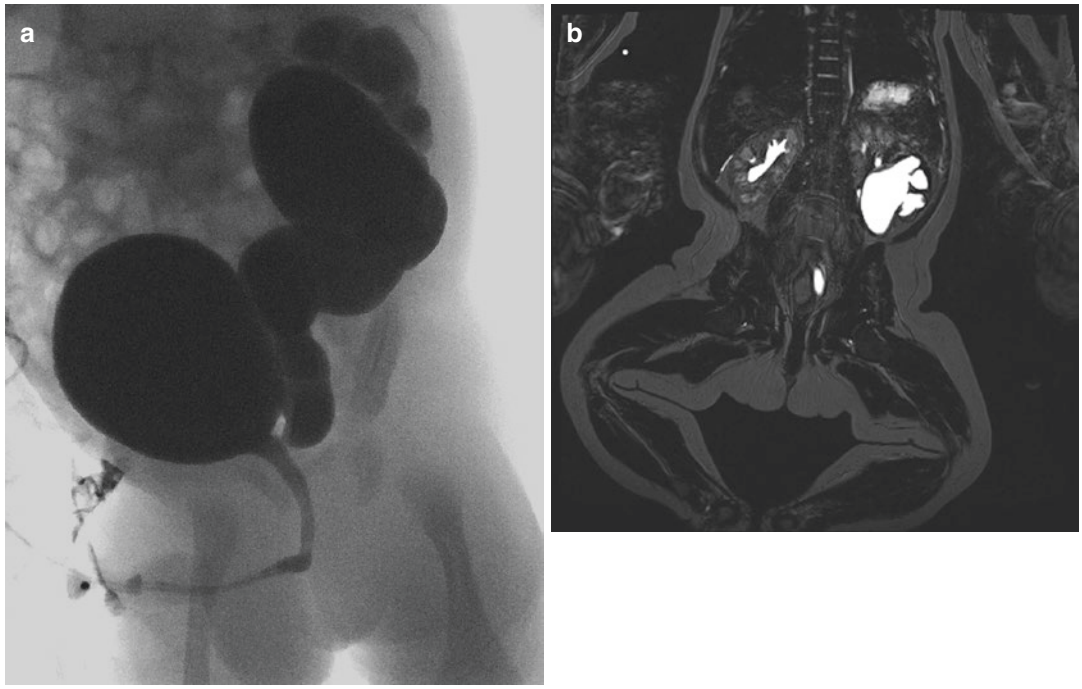

Fig. 65.4 (**a**) MCUG showing left VUR in an apparently simplex system but is actually lower pole reflux in duplex kidney, (**b**) MR scan showing left duplex in the same patient

tocol for investigation and management of antenatally detected hydronephrosis at our institute.

Due to renal immaturity, a nuclear medicine scan in first 2 months might not give accurate information about renal function and drainage. Similarly an ultrasound scan done in first 48 hours may miss important pathology as diuresis is not established as yet. Hence in most cases ultrasound should be delayed till at least 1 week of age. The indication for earlier ultrasound in first 2–3 days would be palpable mass, bilateral HDN or HDN in a solitary kidney or suspected LUTO. Micturating cystourethrogram (MCUG) is being used more selectively now whereas earlier it was performed in most cases with HDN and MCDK. MCUG is warranted in cases of suspected LUTO or if there is any ureteric dilatation. Bilateral HDN in boys even in the absence of ureteric dilatation could be due to LUTO and should be investigated with MCUG. An MR scan may be helpful to delineate anatomy in selected cases such as in duplex kidneys (Fig. 65.4a, b), horseshoe kidney, etc.

65.8 Multicystic Dysplastic Kidney

MCDK constitutes 6% of the antenatally detected anomalies. Overall Incidence has been estimated at 1 in 2400. Previously most common presentation was postnatally with abdominal mass but now most are detected antenatally.

MCDK develops due to failure of induction of metanephric blastema by the ureteric bud leading to replacement of whole kidney with multiple non-communicating cysts with no discernible parenchyma. There may be associated ureteric atresia, dilatation of ureter or ureterocoele. Confirmation is done with a postnatal ultrasound (Fig. 65.5a). If there are multiple cysts with big central cyst then a PUJ obstruction with huge pelvicalyceal dilatation (Fig. 65.5b) must be considered in differential diagnosis. Differentiation can be made with a DMSA scan which shows no function in a MCDK.

Natural history of MCDK is well documented [31]. Based on the natural history stud-

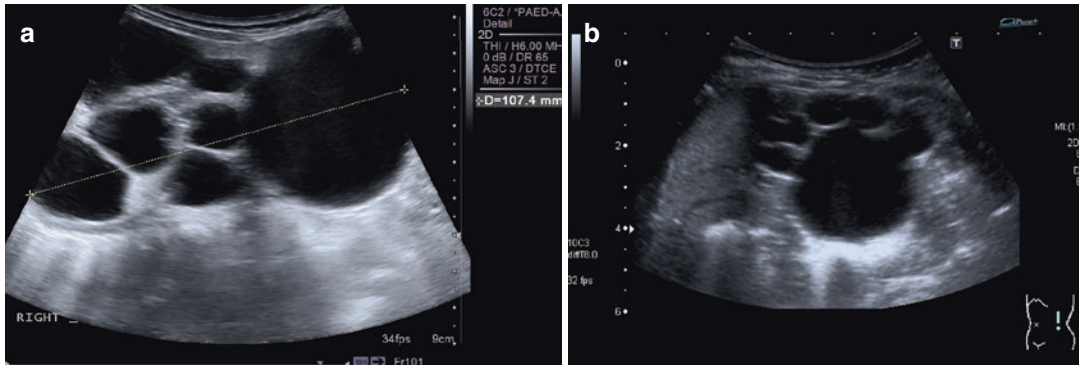

Fig. 65.5 (**a**) MCDK with multiple non-communicating cysts on US, (**b**) MCDK with dominant medial cyst mimicking severe PUJ obstruction

ies, significant changes in investigations and management have happened in last 2 decades. In MCDK there is associated VUR with reported incidence of contralateral reflux being 4.5–20% and ipsilateral reflux is present in 3–16%. It was a standard practice to do a MCUG to assess for reflux. However, it is an invasive investigation involving radiation and risk of UTI. Reflux is however low grade and mostly clinically inconsequential. Hence MCUG is no longer routinely recommended [31–34]. It may be considered in selected cases when there is contralateral kidney pathology or ureteric dilatation or family history of VUR or if there is UTI in infancy.

MCDK are managed conservatively with monitoring of blood pressure, urinalysis for protein, Glomerular Filteration Rate (GFR) estimation and follow up US to check for MCDK involution and contralateral kidney growth. Spontaneous complete involution rate is 60% at 10 years [31]. Nephrectomy is no longer recommended. Hitherto, one of the rationales for nephrectomy was to prevent risk of hypertension, malignancy and the argument that removing MCDK allowed child to be discharged from follow up. However large long-term studies have identified small but important risk of contralateral pathology (PUJ obstruction, Vesico-Ureteric Junction (VUJ) obstruction, VUR, abnormal echogenicity with low GFR) mandating follow up in early childhood regardless [29].

65.9 Isolated Pelvicalyceal Dilatation

Hydronephrosis in newborn does not equate with obstruction. Pelvicalyceal system (PCS) dilatation can be due to non-specific dilatation (NSD) or PUJ obstruction [5]. In NSD there is no hold up on MAG3 scan. While some NSD are result of fetal polyuria and resolve with time, others are consequent to kinks, folds and narrowings at PUJ, which straighten/settle over time. About 50% of antenatal PCS dilatation is transient and post natal ultrasound scan is normal. In PUJ obstruction there is delayed drainage on MAG3 scan. These are more difficult to manage, as they are a different entity to PUJ obstruction presenting later in childhood with symptoms. The standard investigations for diagnosing obstruction such as MAG3 scan and severity of dilatation on ultrasound are not applicable to this group [35, 36]. Evidence of obstructive injury to kidney in the form of decrease in function of >10% and increasing hydronephrosis, is currently the accepted way of differentiating between those needing surgery and those who can be managed conservatively. Only 22–30% of PUJ obstructions require surgical intervention [5, 35] and intervention is rarely required in neonatal period. Most neonates can be investigated as per the protocol shown (Fig. 65.3 b). Only indication for urgent investigations would be in cases of severe dilatation bilaterally or in a solitary kidney (Fig. 65.3c). Even severe unilateral hydronephrosis can be observed safely non-operatively with regular imaging (Fig. 65.6a, b)

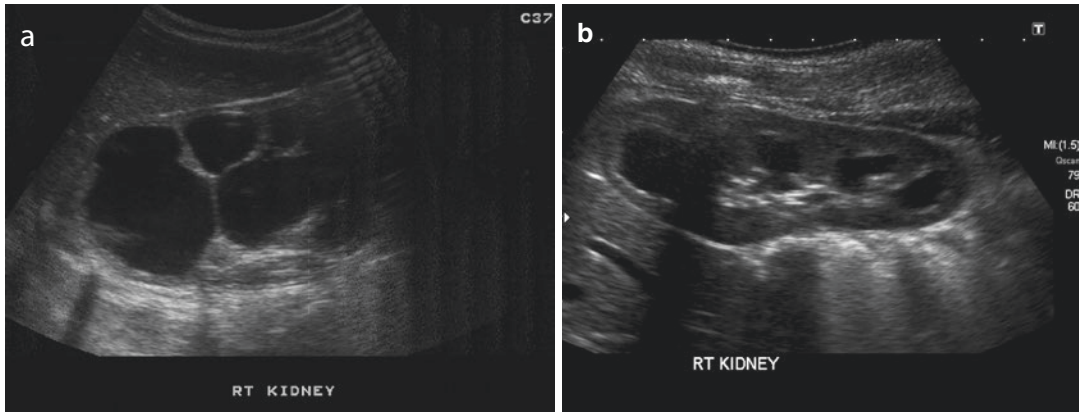

Fig. 65.6 (**a**) Severe PCS dilatation SFU grade 4, (**b**) Same patient, PCS dilatation now improved on conservative management

Table 65.2. SFU grading of Hydronephrosis

Grade	Characteristics of central renal echo complex
0	Closely apposed
1	Slight separation
2	Further separation; one or few calyces may be visualized
3	Pelviectasis and fluid filled calyces seen throughout kidney
4	Grade 3 with parenchyma over calyces thinned

and need for intervention seems to be independent of initial severity of HDN, degree of renal function and renogram pattern [35].

Thirty years after commencement of antenatal detection and management, we are still debating the indications and timing of surgical intervention. Protocols and guidelines in various centres are derived from natural history studies, which had arbitrary cut-off points for surgical interventions; hence many current indications continue to be arbitrary.

Hydronephrosis can be graded on the basis of pelvic dilatation assessed as transverse anteroposterior diameter (TAPD) with separate specific reference to calyceal dilatation and cortical thinning. Society for Fetal Urology (SFU) recommends grading on the basis of dilatation and renal cortex thickness [37] (Table 65.2). Only grades 3 and 4 are felt to be clinically significant with respect to obstruction. In our centre and in most UK centres, radiologists prefer to assess hydronephrosis with TAPD. A new classification system—Urinary Tract Dilation (UTD) Classification System has been proposed which can be applied both prenatally and postnatally [38].

Two most debated aspects of antenatal HDN are initial assessment protocol of antenatal HDN and indication for intervention in PUJ obstruction.

65.10 Assessment of Antenatal HDN

Different parameters have been proposed. The maximum antero-posterior diameter at the hilum in the transverse plane (TAPD) is the crucial measurement. After detection of isolated HDN on 20 weeks scan, it is recommended that repeat scan should be done around 30 weeks gestation. TAPD at this scan correlates closely with the need for surgery [39] and hence is the basis of postnatal management. Some including our institution protocol (Fig. 65.3a–c) recommend no postnatal scanning for those who have TAPD of less than 10 mm on >30 week scan. But with this cut-off parameter, a small proportion of urologically significant anomalies (mostly non-dilating reflux but some PUJ obstruction) may be missed. Hence some recommend at least one postnatal scan for those with TAPD more than or equal to 7 mm [5].

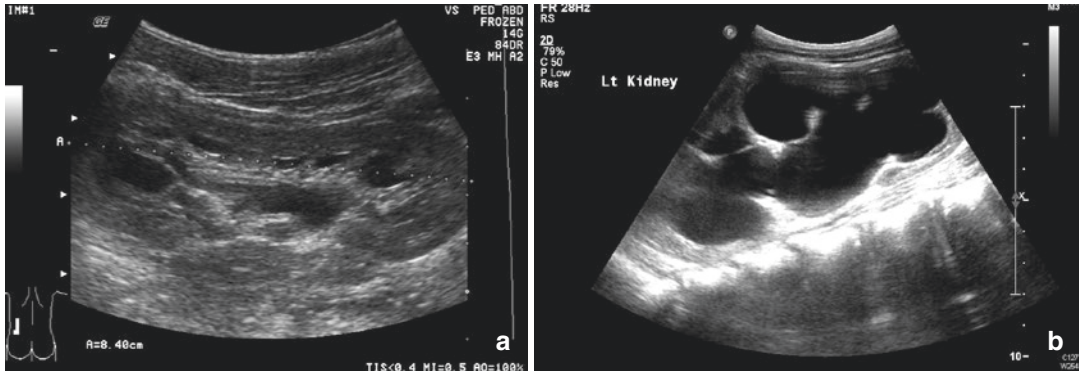

Fig. 65.7 (**a**) Ultrasound scan showing PCS dilatation which settled on conservative management and thus discharged, (**b**) Same patient presented 3 days later with acute obstruction and pain

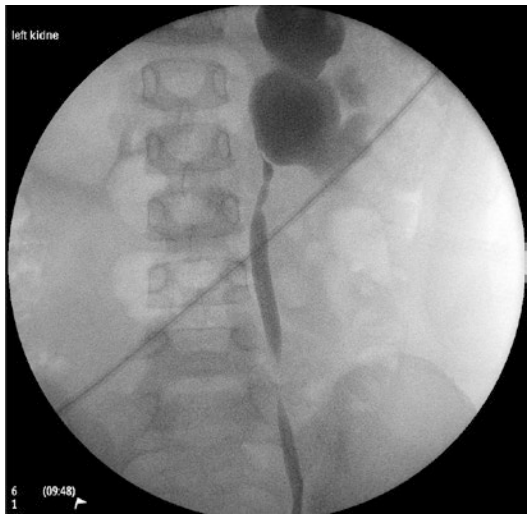

Fig. 65.8 Retrograde pyelogram demonstrating narrowing at the PUJ

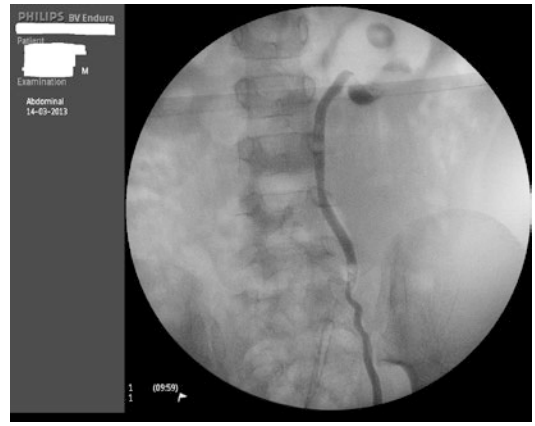

Fig. 65.9 Retrograde pyelogram showing a kink at the PUJ due to aberrant lower pole vessel

It is important that postnatal ultrasound should be viewed in light of antenatal scans. If antenatal scans showed huge dilatation but postnatal scans do not, they should be viewed with suspicion and a further ultrasound scan should definitely be performed. MCUG is usually indicated if there is any ureteric or bladder dilatation and is usually done few weeks after birth. An urgent MCUG should be considered in first week of life, in cases of bilateral dilatation or dilatation in a solitary kidney and should be adequately covered with antibiotics. When indicated, MAG 3 scan should be performed at 2–3 months of age. Again it may be indicated earlier in bilateral/solitary kidney cases.

Early natural history studies of PCS dilatation [35, 40–42] demonstrated that majority of these can be managed conservatively. A very small proportion of antenatal HDN that has resolved fully or partially may develop obstruction at a later date (Fig. 65.7a, b) and families should be counselled about it at the time of discharge from follow up.

65.11 Pelvi-Ureteric Junction Obstruction

PUJ obstruction is the most commonly detected anomaly on antenatal scans after NSD. It is defined as PCS dilatation with impaired drainage on MAG3 scans. It can be unilateral or bilateral. It is

more common in males and left side is more common. About 10% may be bilateral [5]. Occasionally there may be a familial predisposition with cases found in different generations and in siblings.

Usually there is an intrinsic PUJ narrowing of variable length (Fig. 65.8), rarely it may be due to aberrant lower pole vessel (Fig. 65.9). In intrinsic PUJ, the proximal ureter is bound to the lower renal pelvis by flimsy adhesions. Once the ureter is dissected free, it is usual to find a narrow segment, 2–10 mm in length immediately below the pelvi-ureteric junction and that urine does not escape from the renal pelvis until an incision is carried proximally above the narrow segment [43]. PUJ usually shows histological features of narrowing with decreased smooth muscle and increased collagen and elastin.

PUJ obstruction usually remains asymptomatic despite increasing dilatation. Very rarely it may present in infancy with mass, UTI, sepsis, hypertension or haematuria.

65.12 Diagnosis and Indication for Intervention in PUJ Obstruction

Initial assessment is with an US and MAG3. Delayed drainage pattern or a non-draining curve should not be taken as a mark of obstruction [36]. Peters [44] has defined obstruction as "a condition of impaired urinary drainage which, if uncorrected, will limit the ultimate functional potential of a developing kidney." The dilemma facing urologists managing these patients is that are we loosing nephrons because we are waiting for too long [45] or are we intervening when we did not need to. Certainly the trend over the years is more towards conservative management following results from natural history studies. Dynamic functional MR is being investigated for its utility to provide more accurate assessment of obstruction [46].

65.12.1 Management

The most commonly accepted indications for intervention are: serial ultrasound scans showing increasing PCS dilatation, MAG3 scan showing deterioration in kidney function by >10% and symptoms of UTI/haematuria or echogenic fluid in pelvis on US (Fig. 65.10). Intervention if the differential renal function on first assessment is below 40% is debatable [35].

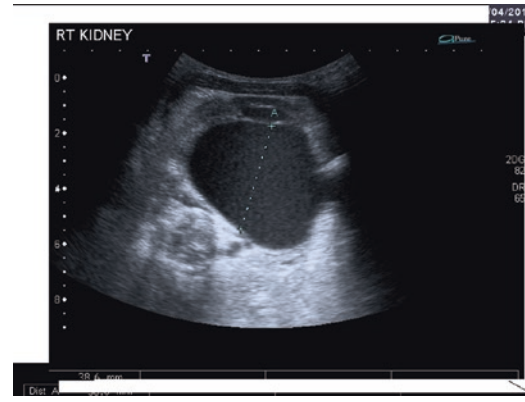

Fig. 65.10 Echogenic debris on US in a child with PUJ obstruction

Anderson Hynes pyeloplasty is the standard procedure performed. Occasionally if there is some uncertainty about the level of obstruction, a retrograde pyelogram can be done on the table to delineate anatomy better before proceeding to pyeloplasty (Fig. 65.11a, b). Though laparoscopic/robotic pyeloplasty is gaining acceptance and becoming more common in older children, open surgery is still the procedure of choice in infants. If there is massive pelvic dilatation, a reduction of pelvis is important to prevent kinking at the PUJ. In our practice, a transanastomotic stent is kept and patient is usually discharged the next day of the operation. Stent is removed approximately 6 weeks later.

A percuatenous nephrostomy may occasionally be done before pyeloplasty when there is poor function or if there is presentation with pyonephrosis. Post-nephrostomy nuclear medicine scan will provide better assessment of function to guide towards nephrectomy or pyeloplasty. If there is an acute presentation with pain which does not settle, emergency stent insertion might be considered but proceeding straight to emergency pyeloplasty is another option.

Post operative scans if done early often show preoperative level of PCS dilatation causing

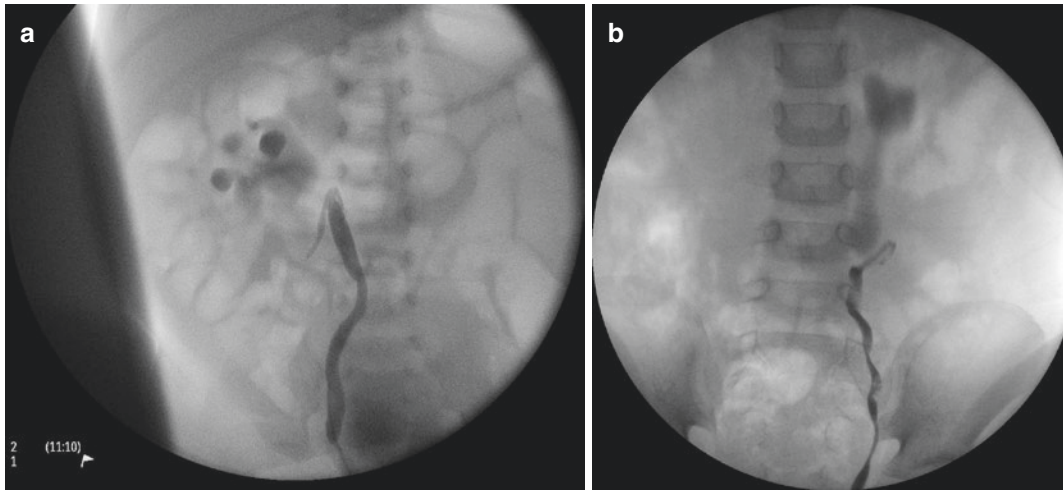

Fig. 65.11 Retrograde pyelogram. (**a**) narrowing at the PUJ, (**b**) mid-ureteric stricture

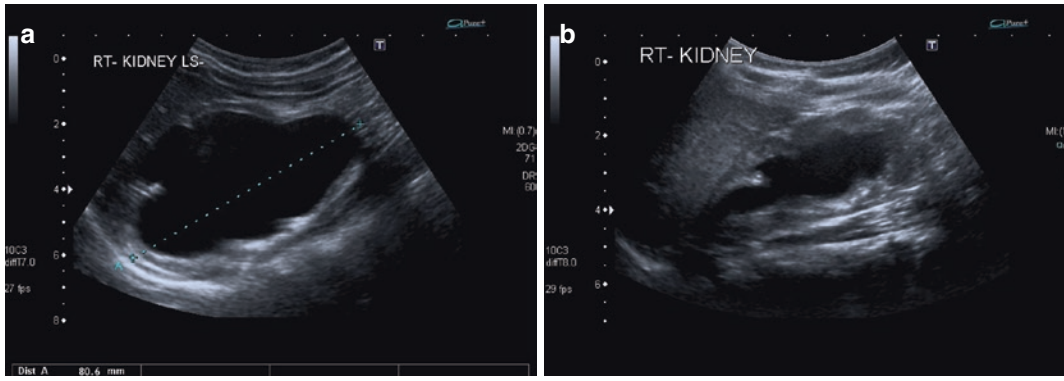

Fig. 65.12 Post pyeloplasty imaging. (**a**) US scan 4 weeks following stent removal demonstrating severe PCS dilatation, (**b**) repeat scan after 10 weeks showing that dilatation has settled without any intervention

unnecessary anxiety. It takes some time for dilatation to settle down. For this reason we defer follow up scan till about 3 months following removal of stent (Fig. 65.12a, b).

65.12.2 Vesico-Ureteric Reflux

Vesico-ureteric reflux is the retrograde flow of urine from the bladder up into the ureter and upper urinary tract. Postnatally VUR usually present as UTI. Prenatally diagnosed VUR refers to a diagnostic sequence in which the dilatation of the fetal urinary tract initiates postnatal investigations confirming VUR. An indicator of reflux on antenatal scan is ureteric dilatation. A significant proportion of infantile VUR escape antenatal detection and present with UTI [47]. Prenatal VUR constitutes 12–15% of all prenatal HDN and the protocol for investigation of antenatal HDN determines the proportion of VUR in any series. Prenatal VUR tends to be more in males and higher grade and bilateral and is known to follow a benign course [5, 48–51]. Approximately 80% is in males [51, 52]. Prenatal VUR is bilateral in 60–80% [47, 49, 51, 52]. Upto 50% VUR is grade IV and V [50, 52].

Bilateral high-grade reflux in boys is a distinct entity, which is known to have a high rate of spontaneous resolution. Up to 30% of grade 4 and 5 VUR resolve in first year of life. Transient functional urethral obstruction has been suggested as a

cause for high grade VUR in males [53]. VUR can be primary due to an anatomical abnormality of the vesico-ureteric junction, which weakens the normal anti-reflux mechanism. Secondary VUR is associated with abnormal bladder such as the neuropathic bladder, posterior urethral valves or anatomical variants such as duplex kidneys.

65.12.3 Investigations

MCUG is the gold standard investigation for VUR and allows grading (Fig. 65.13). A DMSA scan informs about the kidney function and any scarring or global dysplasia. Global atrophy might be seen without any UTI and is usually associated with high-grade reflux and is reflective of intrinsic developmental anomaly of the renal units [48, 50]. UTI usually results in focal scarring [51]. Follow-up is usually with US and DMSA. In our unit we do not do a formal assessment of VUR resolution. If the child is infection free on antibiotic prophylaxis, a trial of discontinuation is given at attainment of potty training. A proportion of HDN due to low grade VUR picked up antenatally may never have presented postnatally [54]. There is a trend towards a more select approach to MCUG in antenatal HDN due to low yield in NSD without ureteric dilatation. Rather than exposing every child with HDN to the invasive procedure of MCUG, indications have been rationalised and we advocate it only in cases with dilated ureter or bilateral HDN (see Fig. 65.3c). This approach tends to detect high grades of VUR which are clinically relevant [5].

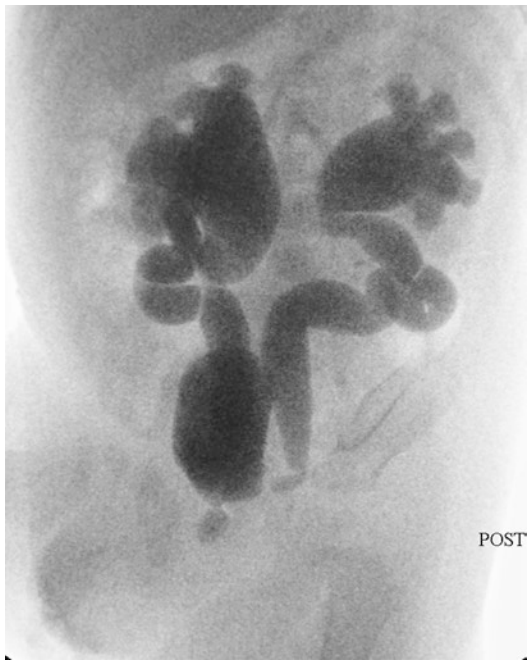

Fig. 65.13 MCUG demonstrating bilateral grade 5 VUR

65.12.4 Treatment

The goal of management of VUR is to prevent UTI. Antibiotic prophylaxis is the mainstay of VUR management for all grades. Evidence for this has been limited but some good observational, long term studies have provided insight into the best treatment options for VUR and provided evidence base for current management. In children with non-dilating reflux, antibiotic prophylaxis is an option but its efficacy is not established [55]. Recently Swedish reflux trial demonstrated that in dilating reflux, antibiotic prophylaxis result in a significant decrease in infection rate and scarring [8, 9].

All grades of VUR have a tendency for spontaneous resolution with up to 3/4th improving or resolving [47, 48, 50–52]. Recurrent UTI and bladder dysfunction predicts non-resolution [47, 48]. 16–52% breakthrough infection rate has been reported in prenatal VUR while on antibiotic prophylaxis [47, 48, 50, 51, 56]. Up to 20% have recurrent UTI.

A surgical intervention is rarely required in infancy. For recurrent UTI in boys, circumcision reduces the risk. An endoscopic correction of reflux may be done in cases of recurrent UTI. In high grade reflux—ureteric reimplantation can be done but is technically difficult in infants; ureterostomy or vesicostomy can be a temporary option [51].

65.12.5 Primary Non-refluxing Megaureter

Primary non-refluxing megaureter is mostly detected antenatally. It may be obstructed or non-obstructed and the distinction between them is very difficult. VUJ obstruction constitutes

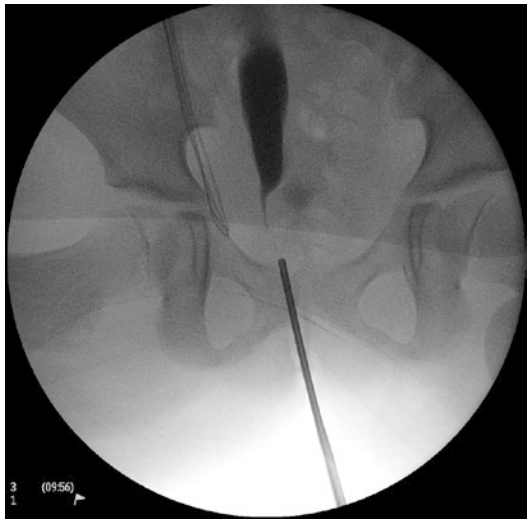

Fig. 65.14 Retrograde study showing an adynamic segment of the lower ureter in a megaureter

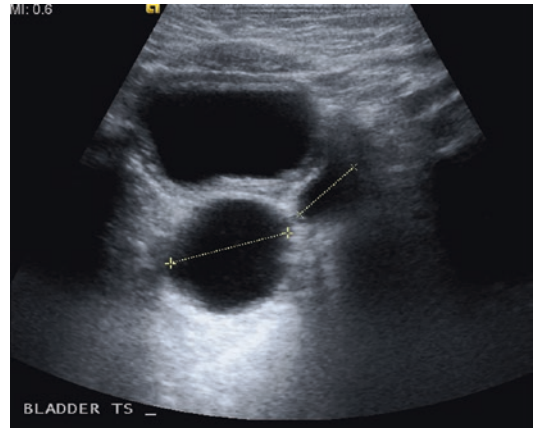

Fig. 65.15 Bilateral dilated ureters behind the bladder

2.3% of all antenatally detected urinary tract anomalies [5]. Most are asymptomatic but some may present with UTI. Non-refluxing megaureter has an incidence of about 1 in 1500 with a male preponderance and is more common on the left [57–59]. It can be bilateral in 13–42% of cases [58, 59].

The obstruction may be functional with an adynamic segment at the VUJ (Fig. 65.14) or may be due to narrow VUJ. Histological studies of the VUJ show increased collagen with reduction in muscle component [60]. The pathology is thought to result from congenital defective vascular development at the vesicoureteric junction [60]. Other mechanism might be dysplastic development of the entire ureter and PCS. Spontaneous resolution in majority supports a maturational causation [61, 62].

Ultrasound (Fig. 65.15) and MAG3 (Fig. 65.16) scans give anatomical and functional details. A MAG3 may show draining kidney in the presence of obstruction if area of interest in drawn over the kidney as the isotope is draining into the dilated ureter. A MCUG rules out VUR. An MR urogram might be done to evaluate further if needed. Similar to dilemmas in PCS dilatation management, the most important challenge is to define and identify obstruction in megaureter. Nevertheless, the relevant pathophysiology is stasis of urine. The walls of dilated ureter cannot coapt to generate effective peristalsis leading to stasis related complications such as infection and stone formation.

Antibiotic prophylaxis needs to be commenced at birth. The concept of management has changed from surgical intervention to close observation. Currently 70—90% can be managed conservatively [58, 63]. Conventional surgical option is ureteric reimplantation. However despite ureteric reimplant, the ureteric and PCS dilatation might not improve due to developmental dysplasia of the system. Minimally invasive procedures such as stent insertion, balloon dilatation and cutting balloon endoureterotomy of VUJ have been reported with variable success rates [64–69]. The rationale for stenting is that a period of drainage would allow the ureteric dilatation to come down to such an extent that following removal of the stent effective peristalsis would continue [58]. However, sometimes the narrow VUJ may not allow a guidewire insertion precluding endourological intervention. Occasionally an ureterostomy may be required if obstruction is leading to sepsis. A refluxing reimplantation is another option in infants [70]. There is a great debate on the best interventional modality.

Even more keenly debated is the indication for surgical intervention. Most commonly agreed indications include renal function deterioration on nuclear medicine scan and development of

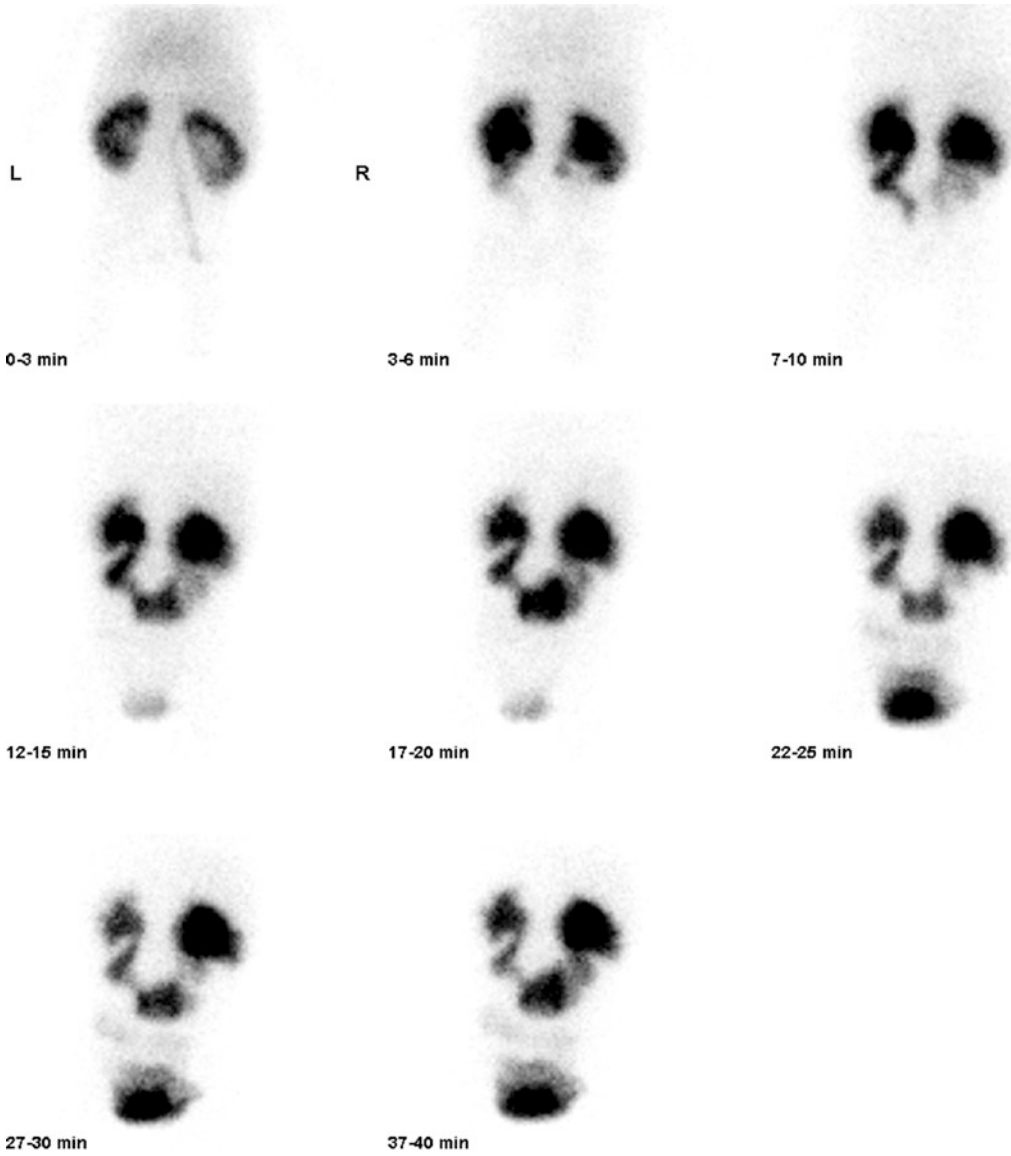

Fig. 65.16 MAG 3 scan showing bilateral megaureters

symptoms such as UTI or pain [57, 58, 63]. An increasing hydronephrosis or hydroureter can be monitored closely. A recent long term observational study from our institute [58] confirmed that conservative management is highly successful especially when the ureteric diameter was less than 10 mm with virtually all resolving completely. When ureter was more than 10 mm size, complete resolution is not common and 25% developed complications. Still the majority remains asymptomatic.

65.12.6 Duplication Anomalies

They constitute 2.6% of antenatally detected anomalies [5]. The commonly identified features are hydronephrosis, dilated ureter, duplex appearance and ureterocoele. But majority of duplication anomalies are uncomplicated where there is no associated dysplasia or dilatation and they remain undetected.

Those that are detected on antenatal scans or which present postnatally have either dysplastic/

dilated one moiety or both. Upper moiety is usually associated with obstruction due to ureterocoele or narrow VUJ. Upper moiety ureter may have an ectopic opening outside the bladder. Lower moiety is usually associated with VUR and rarely PUJ obstruction.

Duplication anomalies rarely cause symptoms in infancy. A large ureterocoele (Fig. 65.17) may give rise to obstructive bladder symptoms. Child may present with sepsis/pyonephrosis of the dilated obstructed upper pole or have UTI due to refluxing lower pole. Girls may present with wetting due to ectopic ureter opening in urethra, perineum or vagina but it is usually noted after potty training. Boys with ectopic ureter are never incontinent as opening is always above the sphincter but may present with UTI/epididymo-orchitis when ectopic ureter is opening into the vas/seminal vesicle.

Antibiotic prophylaxis is commenced at birth. Ultrasound delineates the anatomy. MCUG is done to assess for reflux. A MAG 3/DMSA scan should be done in 2–3 months time. In complex cases a MR scan may be done (Fig. 65.18).

Ureterocoele associated with a dilated upper pole may be non-obstructive and can be managed non-operatively [71]. Intervention is required early if the obstructed upper pole gets infected. An urgent endoscopic incision of ureterocoele relieves the obstruction [72–75]. Ureterocoele incision may prove to be the definitive management in 2/3rd of patients. In our series of 39 patients who had incision of ureterocoele, further surgery was necessary in only 13%. Incision may result in reflux into the upper pole. Heminephrectomy is the treatment of choice when the function of upper moiety is poor. If there is reasonable function then excision of ureterocoele with ureteric reimplantation is an option [75, 76]. If there is persistent obstruction/infection in infancy following incision of ureterocoele or if obstruction is due to narrow VUJ without associated ureterocoele, then an urgent ureterostomy may need to be done. Another option is to do uretero-ureterostomy but non-refluxing lower pole is the prerequisite [77].

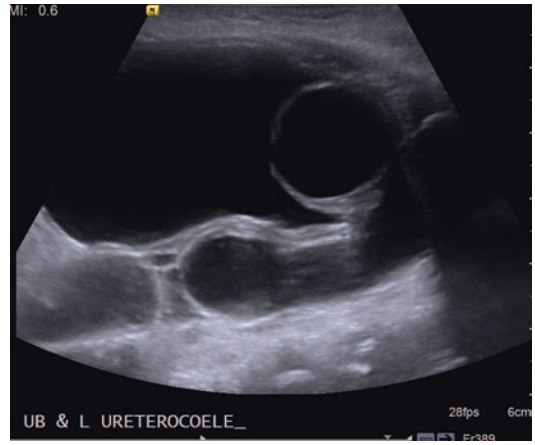

Fig. 65.17 A large ureterocoele obstructing the bladder neck on US

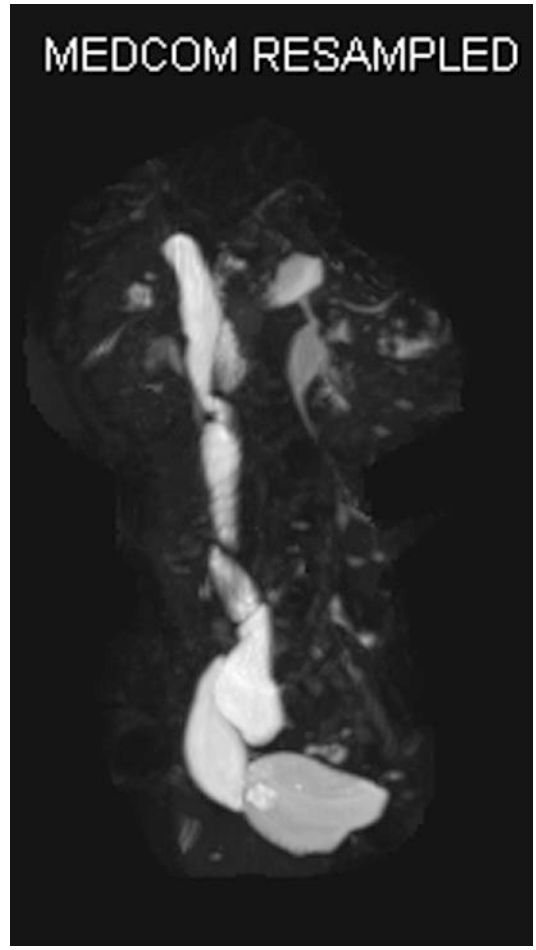

Fig. 65.18 MR urogram demonstrating an ectopic ureter associated with cryptic upper pole

VUR associated with lower pole is managed with antibiotic prophylaxis. It can be treated endoscopically or with ureteric reimplantation if there are recurrent UTI despite antibiotics. If lower pole is dysplastic with poor function then lower pole heminephrectomy can be carried out, preferably laparoscopically.

65.12.7 Megacystis

A large bladder may be detected on antenatal scans and its presence along with findings of HDN commonly suggest lower urinary tract obstruction, which is predominantly due to posterior urethral valves and urethral atresia. A small proportion is due to non-obstructive pathology such as isolated megacystis, megacystis associated with severe dilating VUR (also called Megacystis Megaureter Syndrome (MMS)) [74], Megacystis Microcolon Intestinal Hypoperistalsis Syndrome (MMIHS) and Prune Belly syndrome (PBS). Isolated megacystis is a distinct entity where a large bladder exists without VUR or any obstructive pathology (Fig. 65.19) and may be detected antenatally [78, 79].

The pathophysiology of megacystis in MMS is proposed to be consequent to the inability of the bladder to stay empty completely after voiding due to reflux into extremely voluminous ureters [78]. But existence of isolated megacystis without VUR and detection of large bladder in MMS as early as 15 weeks of gestation [80] contests this theory. An alternative hypothesis is that it is due to dysplasia of the developing urinary tract, which can range from involvement of the kidney (HDN), ureters (megaureter), bladder (isolated megacystis), whole urinary tract (MMS, PBS), to involving the gastrointestinal tract (MMIHS).

In megacystis, a MCUG to assess bladder volume and VUR is done (Fig. 65.20a, b). Urodynamic study gives information on bladder storage and emptying function. The bladder is usually large capacity, hypotonic and may have poor emptying (Fig. 65.21). DMSA scan informs about the degree of renal dysplasia.

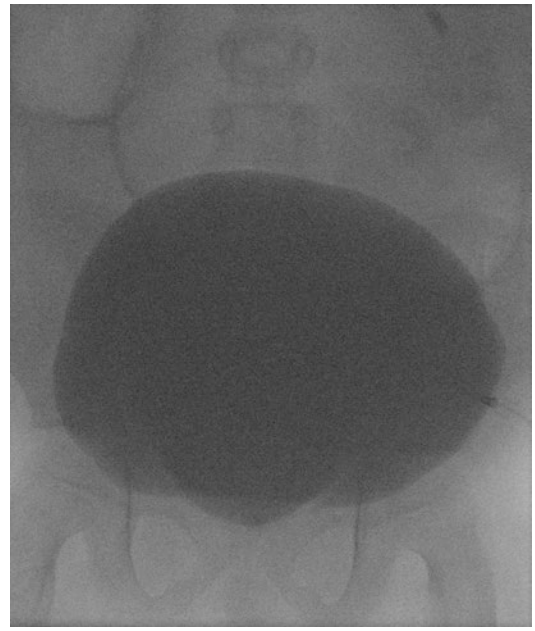

Fig. 65.19 Large bladder—isolated megacystis

65.12.8 Management

The concept of management has evolved from surgical reduction of bladder [81] to antireflux surgery [82] to conservative management. Long-term outcome series are lacking. The prognosis depends upon the extent of inherent dyplasia of the system including kidneys. Management goals are prevention of infection by ensuring complete bladder emptying. Surprisingly, a good proportion has good bladder emptying but a minority might require ISC. Our series [83] demonstrate that bladder dynamics tend to stabilise over time as long as UTI's can be prevented by antibiotic prophylaxis and complete bladder emptying. A few went on to develop deterioration of bladder dynamics and these had poor bladder emptying.

65.12.9 Posterior Urethral Valves

Posterior urethral valves are an important cause of antenatally detected and postnatally presenting lower urinary tract obstruction which carries a 50% fetal and neonatal mortality [18]. PUV is a congenital obstructive uropathy where there is

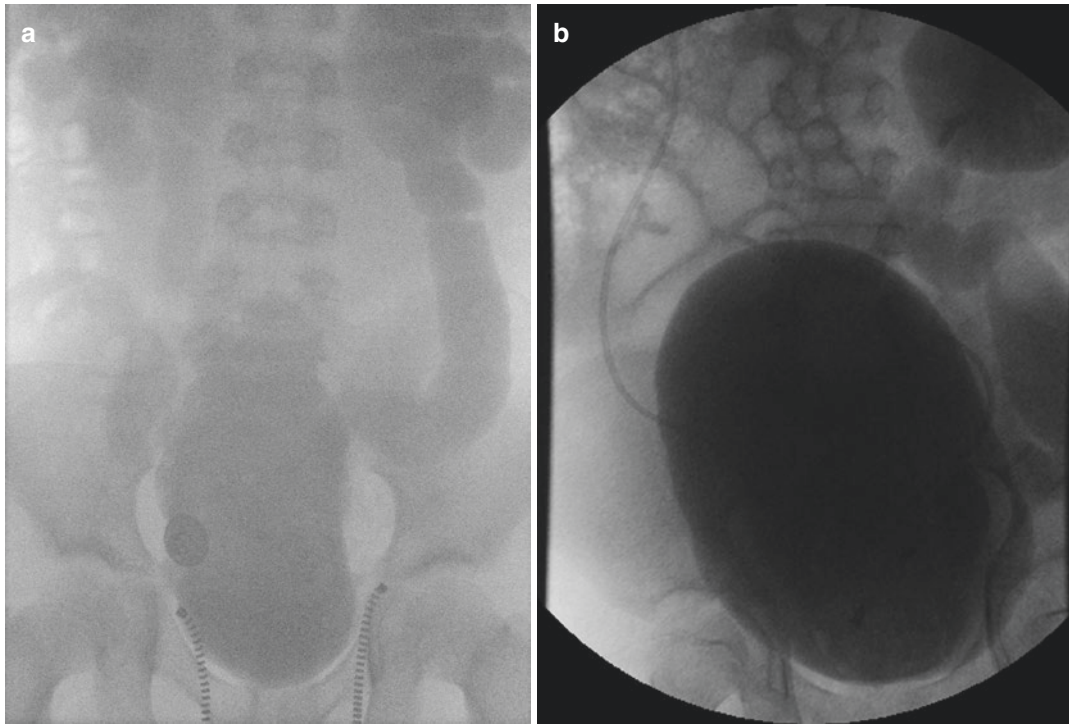

Fig. 65.20 Megacystis megaureter syndrome. (**a**) bilateral VUR, (**b**) unilateral VUR

obstruction in the posterior urethra and there is associated variable developmental dysplasia of the entire urinary tract. An incidence of 1 in 5000 live births has been reported. Anecdotally its incidence has been thought to be declining because of antenatal detection and subsequent terminations. But a recent study refutes this assumption [84]. It is an important cause of renal failure in paediatric population. UK Renal registry shows that obstructive uropathy accounts for 15% of end stage renal disease (ESRD) and that PUV is responsible for 25–30% of paediatric renal transplants [85]. There is a known association with Downs syndrome [86, 87]. A familial predisposition to PUV is rare but it may be associated with other CAKUT in family members [1, 2].

65.12.10 Pathology

Historically Young classified PUV into 3 types—Type 1, II and III [88]. But this classification is not accepted any more. Typical valves are mucosal folds, which arise from the lower end of verumontanum and go down to meet in midline anteriorly and cause obstruction to antegrade flow and correspond to type I valve. Rarely one may find a transverse membrane across the urethra immediately below the verumontanum with a centrally or eccentrically sited aperture (Type III). Type II valves are not recognized as a pathology. Dewan [89] postulated the concept of congenital obstructing posterior urethral membrane (COPUM) and proposed that typical configuration of valve results from rupture of this membrane by a catheter. But this configuration can be seen in uncatheterised urethra as well. Embryologically valves result from abnormal integration of wolffian ducts into the developing urethral wall. It is an early event and can be detected in early second trimester.

There may be minimal involvement of upper urinary tract or there may be associated disordered development of entire urinary tract resulting in dysplastic kidneys and ureters with thickened hypertrophied bladder. In some cases

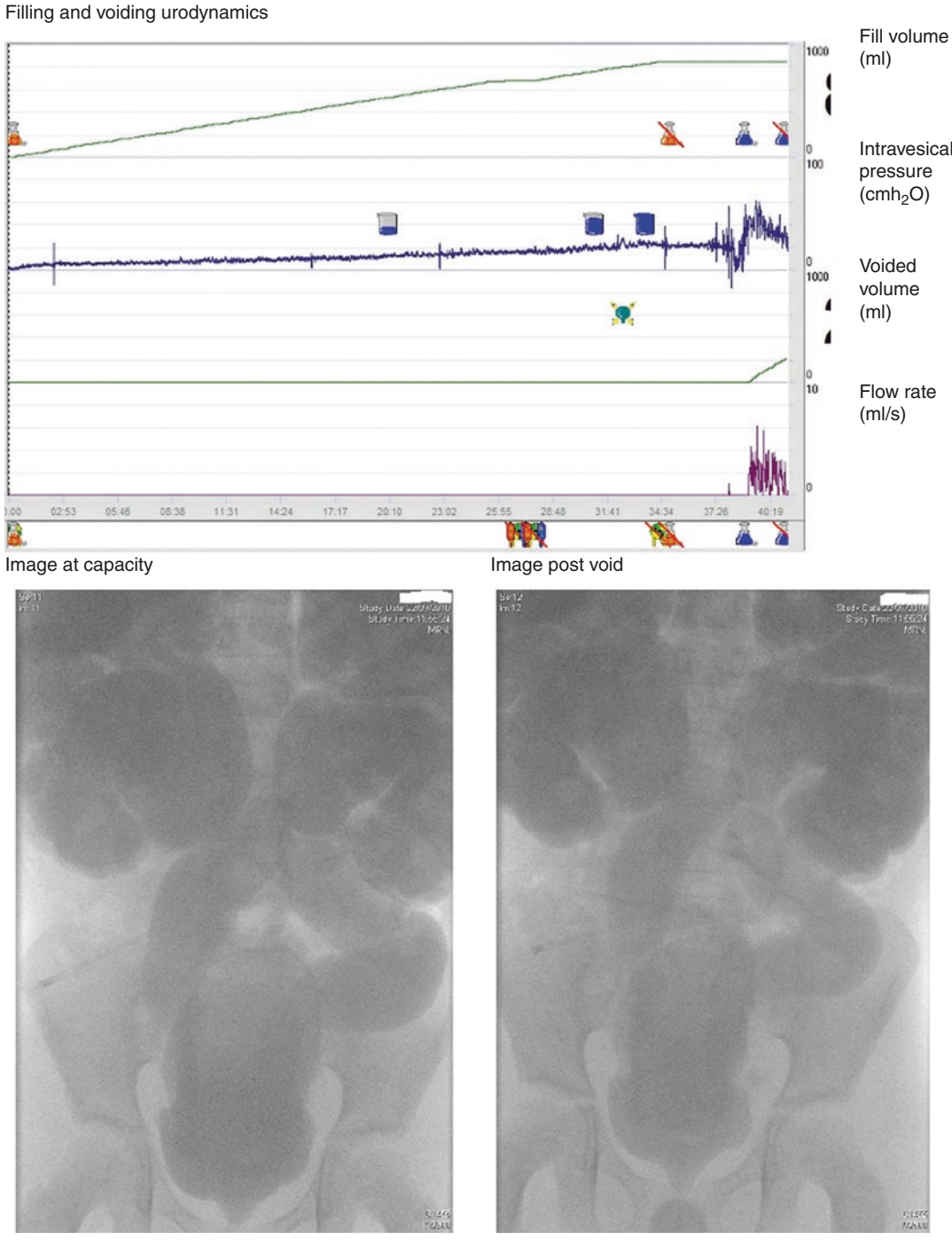

Fig. 65.21 Urodynamic study in a 7 year old boy with MMS showing 850 ml capacity with bilateral VUR, compliance of 55 mls/cm of H_2O and poor emptying

only one kidney might be dysplastic with very poor function and almost normal function on other side—termed Vesico-Ureteric Reflux and Dysplasia (VURD) syndrome. In mild variant of PUV, both kidneys might be well developed with only bladder distension. VUR is present in 40–60% cases and is bilateral in half of these.

65.12.11 Clinical Presentation

Antenatal detection is the most common presentation with two-third of PUV detected to have abnormal findings on prenatal scans though specific diagnosis of LUTO has been made in only 3/4th of these [90]. Rest present postnatally with poor urinary stream, large bladder, UTI's. A few still present with sepsis and renal failure. A good urinary stream does not exclude posterior urethral valves. Very occasionally child may present with urinary ascites either due to leak from bladder or more commonly from kidney and this is protective for renal development. Those who have had antenatal intervention may get ascites due to displacement of the bladder stent into peritoneal cavity.

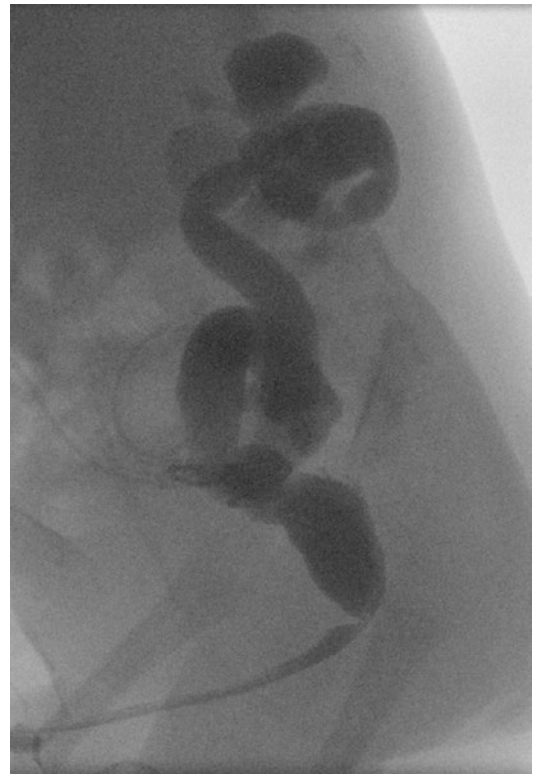

Fig. 65.22 Dilated and elongated posterior urethra along with VUR on MCUG in a neonate with posterior urethral valves

65.12.12 Diagnosis and Investigations

On antenatal scans, a keyhole sign is suggestive of PUV. Spectrum of findings may include bilateral HDUN, unilateral HDN, bilateral HDN with no ureteric dilatation or only bladder dilatation. Similar features on postnatal ultrasound supports diagnosis but definitive diagnosis is made on MCUG, which shows a dilated elongated posterior urethra with or without associated trabeculated bladder and VUR (Fig. 65.22). Bladder neck may be prominent leading to impression of constriction at the bladder neck.

Cystoscopy provides the final answer and the valves are best observed endoscopically with the tip of the cystoscope situated approximately 1 cm distal to the verumontanum. With antegrade flow through the proximal urethra obtained by opening the draining channel and stopping the flow of irrigation fluid, the valve margins can be seen to co-apt in the midline [43].

65.12.13 Management

Antibiotic prophylaxis is started after birth in antenatally detected or postnatally suspected cases. The urinary tract is obstructed from the first trimester of gestation and catheterisation can usually wait until transfer to a specialist paediatric surgical centre. Negotiation of catheter past the valves may be slightly awkward or more commonly it can curl in the dilated posterior urethra. It is not uncommon to damage the urethra when balloon is blown in the urethra by an inexperienced person. If it is imperative that child be urgently catheterised in the non-specialist unit to relieve obstruction, then a fine polythene catheter is safer than a balloon catheter.

These patients should be ideally be jointly managed along with a paediatric nephrologist as the neonate needs close monitoring of electrolytes, acid-base balance, fluid balance and renal function due to associated renal dysplasia and tubular dysfunction. Catheterisation results in post-obstructive diuresis and appropriate fluids should be supplemented, usually orally. A period of catheterisation stabilises the renal function. A MCUG under appropriate antibiotic cover should be done to confirm the valves and assess the bladder and VUR. If there is UTI or sepsis, appropriate antibiotic management should be instituted.

Once renal function is stabilised, resection can be attempted with a 9 Fr resectoscope and in older patients. 11/13 Fr resectoscope can be used. A diathermy hook or a cold knife may be used and valve may be ablated at 5 and 7 o'clock position or at 12 o'clock position. Nd YAG and Ho YAG [91, 92] laser have also been used for valve ablation with claims of lower risk of stricture. Where urethra does not accept a resectoscope or one is not available, a ureteric catheter or a cold knife can be utilised through a cystoscope to ablate the valves. Post-operative catheter drainage for a short duration may be employed if there is some trauma or oedema to urethra during the ablation but is not necessary. A post-operative MCUG or check cystoscopy to check completion of ablation is optional.

Further follow up is with regular monitoring of renal function, DMSA scan and US.

65.12.14 Bladder in PUV

Typically the bladder may be small capacity and poorly compliant with detrusor overactivity. Bladder dysfunction in PUV may progress from detrusor overactivity to normal function to low compliance and in later stages detrusor hypocontractility [93]. Short term anti-cholinergic therapy may be warranted in initial stages and usually results in improvement. Most bladders normalize with time. However some bladders go on to develop valve bladder syndrome. Valve bladder syndrome is characterized by persisting or progressive HDUN in the absence of obstruction [93–95]. This is attributed to constant bladder overdistention due to a combination of polyuria and incomplete emptying, bladder insensitivity and VUR. Polyuria due to renal dysplasia and consequent concentration defect is known to be present in 60% of PUV [96]. Resolution of valve bladder after renal transplant supports the role of polyuria in aetiopathogenesis of valve bladder. Where renal function dose not warrant transplant, ensuring effective bladder emptying by regular voiding, double voiding and overnight catheterisation has been reported to have good outcomes [94]. In severe cases, bladder augmentation or urinary diversion might be required.

65.12.15 Urinary Diversion

A short term urinary diversion may occasionally be required when a premature baby's urethra is unable to accept a resectoscope; a suprapubic catheter may be inserted or a temporary vesicostomy might be fashioned.

After valve ablation if there is recurring UTI and poor renal function and accurate assessment of obstruction at the VUJ is precluded by dysplastic dilated urinary tract, ureterostomy may provide relief. A low, loop ureterostomy can be done easily via a Pfannensteil incision and will allow some bladder cycling as well. It can be simply reversed. An end ureterostomy will warrant reimplantation at closure. A high ureterostomy may be preferred if very dilated tortuous ureters are causing stagnation of urine with recurrent UTI's, as it ensures the best unobstructed drainage of urine. Once done, ureterostomy is best left for at least 1 year or preferably 2 years to allow growth of kidney without any obstruction and UTI. There have been concerns about bladder dysfunction due to non-cycling of urine but in our experience bladder function quickly recovers after ureterostomies are closed. A vesicostomy has the advantage of bladder cycling and is preferable to ureterostomy under appropriate circumstances where obstruction at the VUJ is not an issue.

65.13 Long Term Outcomes

65.13.1 Renal Failure

Development of renal failure depends on the degree of urinary tract dysplasia at birth. If kidneys are dysplastic then they are more likely to develop ESRD. Further continuing damage may occur due to persistent obstruction, VUR, UTI or bladder dysfunction. Historically 1/3rd developed renal failure but better management has led to improved results with latest data suggesting that only 13% progress to ESRD [97, 98]. 31% of PUV have severe bladder dysfunction which can contribute to it [99].

65.13.2 Sexual Function and Fertility

Many factors in PUV can affect sexual function including renal failure, bladder neck procedure, abnormal reflux into ejaculatory system leading to epididymo-orchitis, and cryptorchidism. While concerns have been raised about fertility and sexual function, a recent long-term study of 67 adult PUV patients did not show any particular difference compared to normal controls regarding fertility, and erections [99, 100]. Again abnormal sperm parameters have been identified by few studies, but no significant semen abnormality has been identified and reported fertility is comparable to controls [101].

65.13.3 VUR

VUR tends to resolve after ablation of valve and is managed with antibiotic prophylaxis. Ureteric reimplantation is rarely required. Circumcision is protective against infection and should be considered as first line of management for recurrent UTI. But when VUR is associated with poorly functioning kidney as in VURD (Fig. 65.23a, b), it tends to persist causing recurrent UTI and requires nephrectomy.

65.13.4 Urinary Incontinence

Patients with posterior urethral valves achieve daytime and night-time urinary continence significantly later than their healthy peers [102]. Continued urinary incontinence might be a consequence of bladder dysfunction or rarely may be related to sphincter damage during valve ablation. Urethral stricture may also occur after valve resection.

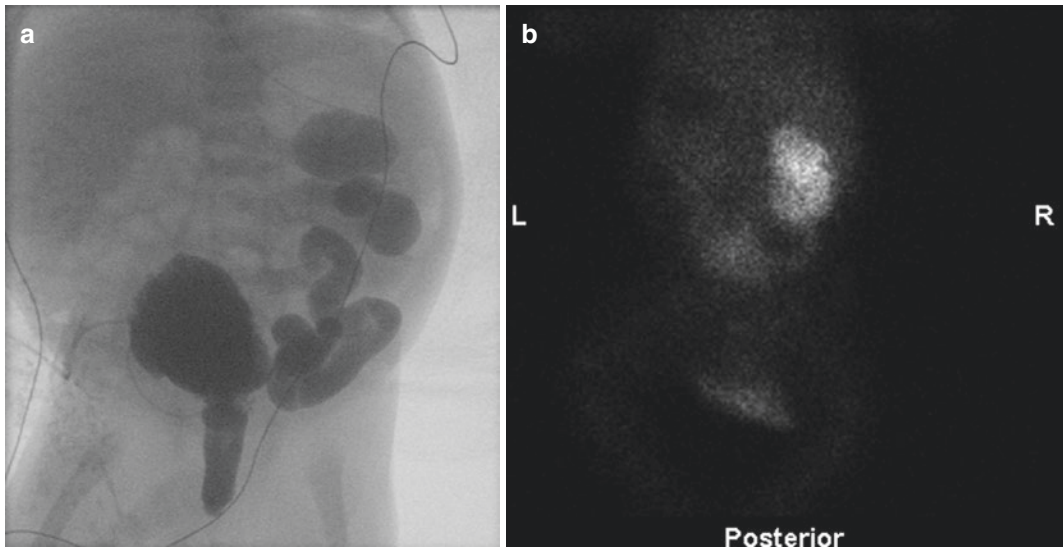

Fig. 65.23 VURD syndrome in PUV. (**a**) Left high grade reflux, (**b**) no function on the side of reflux on DMSA

References

1. Renkema KY, Winyard PJ, Skovorodkin IN, et al. Novel perspectives for investigating congenital anomalies of the kidney and urinary tract (CAKUT). Nephrol Dial Transplant. 2011;26:3843–51.
2. Bulum B, Ozçakar ZB, Ustüner E, et al. High frequency of kidney and urinary tract anomalies in asymptomatic first-degree relatives of patients with CAKUT. Pediatr Nephrol. 2013;28:2143–7.
3. DFM T. Upper tract obstruction (Chapter 6). In: DFM T, Duffy PG, AMK R, editors. Essentials of paediatric urology. 2nd ed. London: Informa Healthcare; 2008. p. 73–92.
4. Dhillon GK. Antenatal hydronephrosis (Chapter 10). In: DFM T, Duffy PG, AMK R, editors. Essentials of paediatric urology. 2nd ed. London: Informa Healthcare; 2008. p. 133–42.
5. Mallik M, Watson AR. Antenatally detected urinary tract abnormalities: more detection but less action. Pediatr Nephrol. 2008;23:897–904.
6. Nef S, Neuhaus TJ, Spartà G, et al. Outcome after prenatal diagnosis of congenital anomalies of the kidney and urinary tract. Eur J Pediatr. 2016;175:667–76.
7. James CA, Watson AR, Twining P, Rance CH. Antenatally detected urinary tract abnormalities: changing incidence and management. Eur J Pediatr. 1998;157:508–11.
8. Brandstrom P, Esbjorner E, Herthelius M, et al. The Swedish reflux trial in children: III. Urinary tract infection pattern. J Urol. 2010;184:286–91.
9. Brandstrom P, Neveus T, Sixt R, et al. The Swedish reflux trial in children: IV. Renal damage. J Urol. 2010;184:292–7.
10. Thomas DFM. Prenatal diagnosis. What do we know of long-term outcomes? J Pediatr Urol. 2010;6:204–11.
11. Hsieh MH, Lai J, Saigal CS. Urologic Diseases in America Project. Trends in prenatal sonography use and subsequent urologic diagnoses and abortions in the United States. J Pediatr Urol. 2009;5:490–4.
12. Nguyen HT, Herndon CD, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. J Pediatr Urol. 2010;6:212–31.
13. Goyal A, Fishwick J, Hurrell R, Cervellione RM, Dickson AP. Antenatal diagnosis of bladder/cloacal exstrophy: challenges and possible solutions. J Pediatr Urol. 2012;8:140–4.
14. Sebire NJ, Von Kaisenberg C, Rubio C, Snijders RJM, and Nicolaides KH. Foetal megacystis at 10-14 weeks of gestation. Ultrasound Obstet Gynaecol 1996: 8: 387–390
15. Favre R, Kohler M, Gasser B, Muller F, Nisand I. Early fetal megacystis between 11 and 15 weeks of gestation. Ultrasound Obstet Gynecol. 1999;14:402–6.
16. Liao AW, Sebire NJ, Geerts L, Cicero S, Nicolaides KH. Megacystis at 10-14 weeks of gestation: chromosomal defects and outcome according to bladder length. Ultrasound Obstet Gynecol. 2003;21:338–41.
17. Al-Hazmi H, Dreux S, Delezoide AL, et al. Outcome of prenatally detected bilateral higher urinary tract obstruction or megacystis: sex-related study on a series of 709 cases. Prenat Diagn. 2012;32:649–54.
18. Freedman AL, Johnson MP, Gonzalez R. Fetal therapy for obstructive uropathy: past, present, future? Pediatr Nephrol. 2000;14:167–76.
19. Parkhouse HF, Barratt TM, Dillon MJ, et al. Long term outcome of boys with posterior urethral valves. Br J Urol. 1988;62:59–62.
20. Cromie WJ, Lee K, Houde K, Holmes L. Implications of prenatal ultrasound screening in the incidence of major genitourinary malformations. J Urol. 2001;165:1677–80.
21. Lee J, Kimber C, Shekleton P, Cheng W. Prognostic factors of severe foetal megacystis. ANZ J Surg. 2010;81:552–5.
22. Morris RK, Quinlan-Jones E, Kilby MD, Khan KS. Systematic review of accuracy of fetal urine analysis to predict poor postnatal renal function in cases of congenital urinary tract obstruction. Prenat Diagn. 2007;27:900–11.
23. Ruano R. Fetal surgery for severe lower urinary tract obstruction. Prenat Diagn. 2011;31:667–74.
24. Morris RK, Malin GL, Khan KS, Kilby MD. Systematic review of the effectiveness of antenatal intervention for the treatment of congenital lower urinary tract obstruction. BJOG. 2010;117:382–90.
25. Robyr R, Benachi A, Daikha-Dahmane F, Martinovich J, Dumez Y, Ville Y. Correlation between ultrasound and anatomical findings in fetuses with lower urinary tract obstruction in the first half of pregnancy. Ultrasound Obstet Gynecol. 2005;25:478–82.
26. Harrison MR, Ross N, Noall R, de Lorimier AA. Correction of congenital hydronephrosis in utero. I. The model: fetal urethral obstruction produces hydronephrosis and pulmonary hypoplasia in fetal lambs. J Pediatr Surg. 1983;18:247–56.
27. Clark TJ, Martin WL, Divakaran TG, Whittle MJ, Kilby MD, Khan KS. Prenatal bladder drainage in the management of fetal lower urinary tract obstruction: a systematic review and meta-analysis. Obstet Gynecol. 2003;102:367–82.
28. Morris RK, Malin GL, Quinlan-Jones E, et al. Percutaneous vesicoamniotic shunting in Lower Urinary Tract Obstruction (PLUTO) Collaborative Group. Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial. Lancet. 2013;382:1496–506.
29. Kitagawa H, Pringle KC, Koike J, et al. Vesicoamniotic shunt for complete urinary tract obstruction is partially effective. J Pediatr Surg. 2006;41:394–402.

30. Berman DJ, Maizels M. The role of urinary obstruction in the genesis of renal dysplasia. A model in the chick embryo. J Urol. 1982;128:1091–6.
31. Aslam M. Watson AR; Trent & Anglia MCDK Study Group. Unilateral multicystic dysplastic kidney: long term outcomes. Arch Dis Child. 2006;91:820–3.
32. Ismaili K, Avni FE, Alexander M, Schulman C, Collier F, Hall M. Routine voiding cystourethrography is of no value in neonates with unilateral multicystic dysplastic kidney. J Pediatr. 2005;146:759–63.
33. Kuwertz-Broeking E, Brinkmann OA, Von Lengerke HJ, et al. Unilateral multicystic dysplastic kidney: experience in children. BJU Int. 2004;93:388–92.
34. Goyal A and Hennayake S. Routine voiding cystourethrogram in multicystic dysplastic kidney: Rationalising its use. Presented at British Association of Paediatric Surgeons, 54th Annual International Conference, Edinburgh, 2007.
35. Ulman I, Jayanthi VR, Koff SA. The long-term followup of newborns with severe unilateral hydronephrosis initially treated nonoperatively. J Urol. 2000;164:1101–5.
36. Gordon I, Dhillon HK, Gatanash H, Peters AM. Antenatal diagnosis of pelvic hydronephrosis: assessment of renal function and drainage as a guide to management. J Nucl Med. 1991;32:1649–54.
37. Fernbach SK, Maizels M, Conway JJ. Ultrasound grading of hydronephrosis: introduction to the system used by the Society of Fetal Urology. Pediatr Radiol. 1993;23:478–80.
38. Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). J Pediatr Urol. 2014;10:982–98.
39. Policiano C, Djokovic D, Carvalho R, Monteiro C, Melo MA, Graça LM. Ultrasound antenatal detection of urinary tract anomalies in the last decade: outcome and prognosis. J Matern Fetal Neonatal Med. 2015;28:959–63.
40. Gordon I, Dhillon HK, Peters AM. Prenatally diagnosed hydronephrosis: the Great Ormond Street experience. Br J Urol. 1998;81(Suppl 2):39–44.
41. Dhillon HK. Antenatal diagnosis of renal pelvic dilatation--the natural history of conservative management. Pediatr Radiol. 1991;21:272–3.
42. Ransley PG, Dhillon HK, Gordon I, Duffy PG, Dillon MJ, Barratt TM. The postnatal management of hydronephrosis diagnosed by prenatal ultrasound. J Urol. 1990;144:584–7. discussion 593-4
43. AMK R. Urinary tract obstruction and dilatation in the newborn (Chapter 45). In: Rickham PP, Johnston JH, Lister J, Irvine IM, Irving IM, editors. Neonatal surgery. 3rd ed. Boston: Butterworth-Heinemann; 1990. p. 656–77.
44. Peters CA. Urinary tract obstruction in children. J Urol. 1995;154:1874–83.
45. Thornhill BA, Burt LA, Chen C, et al. Variable chronic partial ureteral obstruction in the neonatal rat: a new model of ureteropelvic junction obstruction. Kidney Int. 2005;67:42–52.
46. Grattan-Smith JD, Jones RA. MR urography: technique and results for the evaluation of urinary obstruction in the pediatric population. Magn Reson Imaging Clin N Am. 2008;16:643–60.
47. Sjöström S, Sillén U, Bachelard M, Hansson S, Stokland E. Spontaneous resolution of high grade infantile vesicoureteral reflux. J Urol. 2004;172:694–8. discussion 699
48. Upadhyay J, McLorie GA, Bolduc S, Bägli DJ, Khoury AE, Farhat W. Natural history of neonatal reflux associated with prenatal hydronephrosis: long-term results of a prospective study. J Urol. 2003;169:1837–41.
49. van Eerde AM, Meutgeert MH, de Jong TP, Giltay JC. Vesico-ureteral reflux in children with prenatally detected hydronephrosis: a systematic review. Ultrasound Obstet Gynecol. 2007;29:463–9.
50. Penido Silva JM, Oliveira EA, Diniz JS, Bouzada MC, Vergara RM, Souza BC. Clinical course of prenatally detected primary vesicoureteral reflux. Pediatr Nephrol. 2006;21:86–91.
51. Gordon AC, Thomas DFM, Arthur RJ, Irving HC, Smith SE. Prenatally Diagnosed Reflux: a follow–up study. Br J Urol. 1990;65:407–12.
52. Farhat W, McLorie G, Capolicchio G, et al. The natural history of neonatal vesicoureteral reflux associated with antenatal hydronephrosis. J Urol. 2000;164:1057–60.
53. Avni EF, Schulman CC. The origin of vesico-ureteric reflux in male newborns: further evidence in favour of a transient fetal urethral obstruction. Br J Urol. 1996;78:454–9.
54. Ismaili K, Avni FE, Hall M. Results of systematic voiding cystourethrography in infants with antenatally diagnosed renal pelvis dilation. J Pediatr. 2002;141:21–4.
55. Garin EH, Olavarria F, Garcia NV, et al. Clinical significance of primary vesicoureteral reflux and urinary antibiotic prophylaxis after acute pyelonephritis: a multicenter, randomized, controlled study. Pediatrics. 2006;117:626–32.
56. Evans K, Asimakadou M, Nwankwo O, et al. What is the risk of urinary tract infection in children with antenatally presenting dilating vesico-ureteric reflux? Pediatr Urol. 2015;11:93.e1–6.
57. Hodges SJ, Werle D, McLorie G, et al. Megaureter. ScientificWorldJournal. 2010;10:603–12.
58. Ranawaka R, Hennayake S. Resolution of primary non-refluxing megaureter: an observational study. J Pediatr Surg. 2013;48:380–3.
59. Shukla AR, Cooper J, Patel RP, et al. Prenatally detected primary megaureter: a role for extended followup. J Urol. 2005;173:1353–6.
60. Payabvash S, Kajbafzadeh AM, Tavangar SM, et al. Myocyte apoptosis in primary obstructive megaureters: the role of decreased vascular and neural supply. J Urol. 2007;178:259–64.

61. Shokeir AA, Nijman RJ. Primary megaureter: current trends in diagnosis and treatment. BJU Int. 2000;86:861–8.
62. Wilcox D, Mouriquand P. Management of megaureter in children. Eur Urol. 1998;34:73–8.
63. Chertin B, Pollack A, Koulikov D, et al. Long-term follow up of antenatally diagnosed megaureters. J Pediatr Urol. 2008;4:188–91.
64. Christman MS, Kasturi S, Lambert SM, et al. Endoscopic management and the role of double stenting for primary obstructive megaureters. J Urol. 2012;187:1018–22.
65. Farrugia MK, Steinbrecher HA, Malone PS. The utilization of stents in the management of primary obstructive megaureters requiring intervention before 1 year of age. J Pediatr Urol. 2011;7:198–202.
66. Carroll D, Chandran H, Joshi A, McCarthy LS, Parashar K. Endoscopic placement of double-J ureteric stents in children as a treatment for primary obstructive megaureter. Urol Ann. 2010;2:114–8.
67. Romero RM, Angulo JM, Parente A, Rivas S, Tardaguila AR. Primary obstructive megaureter: the role of high pressure balloon dilatation. J Endourol. 2014;28(5):517–23.
68. García-Aparicio L, Blázquez-Gómez E, Martin O, et al. Use of high-pressure balloon dilatation of the ureterovesical junction instead of ureteral reimplantation to treat primary obstructive megaureter: is it justified? J Pediatr Urol. 2013;9:1229–33.
69. Smeulders N, Yankovic F, Chippington S, Cherian A. Primary obstructive megaureter: cutting balloon endo-ureterotomy. J Pediatr Urol. 2013;9:692.e1–2
70. Lee SD, Akbal C, Kaefer M. Refluxing ureteral reimplant as temporary treatment of obstructive megaureter in neonate and infant. J Urol. 2005;173:1357–60.
71. Han MY, Gibbons MD, Belman AB, Pohl HG, Majd M, Rushton HG. Indications for nonoperative management of ureteroceles. J Urol. 2005;174:1652–5.
72. Jayanthi VR, Koff SA. Long-term outcome of transurethral puncture of ectopic ureteroceles: initial success and late problems. J Urol. 1999;162:1077–80.
73. Chertin B, Fridmans A, Hadas-Halpren I, Farkas A. Endoscopic puncture of ureterocele as a minimally invasive and effective long-term procedure in children. Eur Urol. 2001;39:332–6.
74. Smith C, Gosalbez R, Parrott TS, Woodard JR, Broecker B, Massad C. Transurethral puncture of ectopic ureteroceles in neonates and infants. J Urol. 1994;152:2110–2.
75. Castagnetti M, El-Ghoneimi A. Management of duplex system ureteroceles in neonates and infants. Nat Rev Urol. 2009;6:7–15.
76. de Jong TP, Dik P, Klijn AJ, Uiterwaal CS, van Gool JD. Ectopic ureterocele: results of open surgical therapy in 40 patients. J Urol. 2000;164:2040–3.
77. Prieto J, Ziada A, Baker L, Snodgrass W. Ureteroureterostomy via inguinal incision for ectopic ureters and ureteroceles without ipsilateral lower pole reflux. J Urol. 2009;181:1844–8.
78. Williams DI. Megacystis and Megaureter in children. Bull N Y Acad Med. 1959;35:317–27.
79. Paquin AJ Jr, Marshall VF, McGovern JH. The megacystis syndrome. J Urol. 1960;83:634–46.
80. Mandell J, Lebowitz RL, Peters CA, Estroff JA, Retik AB, Benacerraf BR. Prenatal diagnosis of megacystis-megaureter association. J Urol. 1992;148:1487–9.
81. Welch KJ, Steward W, Leibowitz RL. Non obstructive megacystis and refluxing megaureter in preteen enuretic boys with minimal symptoms. J Urol. 1975;114:449–54.
82. Willi UV, Lebowitz RL. The so-called megaureter-megacystis syndrome. AJR Am J Roentgenol. 1979;133:409–16.
83. Angotti R, Lewis MA, Goyal A. Megacystis megaureter syndrome: 20 years experience. Presented at annual meeting of the European Society for Pediatric Urology 2014.
84. Lloyd JC, Wiener JS, Gargollo PC, Inman BA, Ross SS, Routh JC. Contemporary epidemiological trends in complex congenital genitourinary anomalies. J Urol. 2013;190:1590–5.
85. Lewis MA, Shaw J, Sinha MD, et al. UK Renal Registry 12th Annual Report (December 2009): Chapter 14: demography of the UK paediatric renal replacement therapy population in 2008. Nephron Clin Pract. 2010(115):c279–88.
86. Kupferman JC, Stewart CL, Kaskel FJ, Fine RN. Posterior urethral valves in patients with Down syndrome. Pediatr Nephrol. 1996;10:143–6.
87. Kupferman JC, Druschel CM, Kupchik GS. Increased prevalence of renal and urinary tract anomalies in children with Down syndrome. Pediatrics. 2009;124:e615–21.
88. Young HH, Frontz WA, Baldwin JC. Congenital obstruction of the posterior urethra. J Urol. 1919;3:289.
89. Dewan PA, Keenan RJ, Morris LL, Le Quesne GW. Congenital urethral obstruction: Cobb's collar or prolapsed congenital obstructive posterior urethral membrane (COPUM). Br J Urol. 1994;73:91–5.
90. Malin G, Tonks AM, Morris RK, Gardosi J, Kilby MD. Congenital lower urinary tract obstruction: a population-based epidemiological study. BJOG. 2012;119:1455–64.
91. Mandal S, Goel A, Kumar M, et al. Use of holmium: YAG laser in posterior urethral valves: Another method of fulguration. J Pediatr Urol. 2013;9:1093–7.
92. Bhatnagar V, Agarwala S, Lal R, Mitra DK. Fulguration of posterior urethral valves using the Nd: YAG laser. Pediatr Surg Int. 2000;16:69–71.
93. Koff SA, Mutabagani KH, Jayanthi VR. The valve bladder syndrome: pathophysiology and treatment with nocturnal bladder emptying. J Urol. 2002;167:291–7.
94. Capitanucci ML, Marciano A, Zaccara A, La Sala E, Mosiello G, De Gennaro M. Long-term bladder function followup in boys with posterior urethral

valves: comparison of noninvasive vs invasive urodynamic studies. J Urol. 2012;188:953–7.
95. De Gennaro M, Capitanucci ML, Mosiello G, Caione P, Silveri M. The changing urodynamic pattern from infancy to adolescence in boys with posterior urethral valves. BJU Int. 2000;85:1104–8.
96. Dinneen MD, Duffy PG, Barratt TM, Ransley PG. Persistent polyuria after posterior urethral valves. Br J Urol. 1995;75:236–40.
97. Smith GH, Canning DA, Schulman SL, Snyder HM 3rd, Duckett JW. The long-term outcome of posterior urethral valves treated with primary valve ablation and observation. J Urol. 1996;155:1730–4.
98. DeFoor W, Clark C, Jackson E, Reddy P, Minevich E, Sheldon C. Risk factors for end stage renal disease in children with posterior urethral valves. J Urol. 2008;180:1705–8.
99. Woodhouse CR, Reilly JM, Bahadur G. Sexual function and fertility in patients treated for posterior urethral valves. J Urol. 1989;142:586–8.
100. Taskinen S, Heikkilä J, Santtila P, Rintala R. Posterior urethral valves and adult sexual function. BJU Int. 2012;110:E392–6.
101. Caione P, Nappo SG. Posterior urethral valves: long-term outcome. Pediatr Surg Int. 2011;27:1027–35.
102. Jalkanen J, Heikkilä J, Kyrklund K, Taskinen S. Controlled outcomes for achievement of urinary continence among boys treated for posterior urethral valves. J Urol. 2016;196:213–8.