Urinary Tract Infection

Color code: Dr. Khalid Alhasan (notes)

الصورة بكندا يا بنات، وروحوا لها بعد التخرج وبعد كورونا ان شاءالله

- Urinary tract infection (UTI) is a leading cause of serious bacterial illness in febrile infants, because they have specific issues compared to adults.
- Throughout childhood the cumulative incidence is approximately 10% in girls and 3% in boys, more common in girls due to short urethra.
- Urinary infection usually is ascending, with inoculation of fecally derived organisms from the urethra and peri-urethral tissues into the bladder. Rarely hematogenous.

- The most prevalent pathogens in several recent pediatric studies were

  Escherichia coli (54%-67%) E. coli is gram negative, it surrounds the perineal area with other G-ve organisms.
  Klebsiella (6%-17%)
  Proteus (5%- 12%)
  Enterococcus (3%-9%)
  Pseudomonas (2%-6%), unfortunately.

- Among patients with urinary tract anomalies or impaired immune systems, less virulent organisms, such as Staph epi, H influenzae, and group B Strept, may be responsible.

- The hematogenous route of infection is far less common with generally different causal organisms, such as Staph aureus, Candida (so bad), and Salmonella; Pseudomonas aeruginosa and Proteus can infect by either route.

Signs and symptoms

Non-toilet-trained and non-vocalized child.	Toilet-trained and verbalized child
General symptoms; fever, lethargy, irritability. Therefore, u don't know does the child have UTI? Or meningitis? Or bacteremia? When they have the bug in the urinary tract it can easily go to the blood or seed to the brain (meningitis) or to the bone (osteomyelitis). It is sometimes very serious especially in little children.	Like adult symptoms more or less. Dysuria Frequency Urgency Flank pain (pyelonephritis) Fever and vomiting Easier to pick-up than younger children

we start to train the child for toilet at 18 months but we don't force him/her. After five years, if still wet it is enuresis.

CLINICAL PRESENTATION

- Young infants often present with fever alone (≥38°C); irritability, vomiting, lethargy, or poor feeding variably may be present.
- For those younger than 3 months there is an increased risk of bacteremia and a greater possibility of undiagnosed congenital urologic malformations.
- Older children generally have more explicit symptoms of bladder inflammation and/or flank pain.

- For infants, any of the following increased the positive likelihood ratio of UTI to 2 or more: history of prior UTI, fever of more than 24 hours' duration or higher than 40°C, absence of circumcision in males, and suprapubic tenderness.
- Combinations of these findings amplified probability.
- For verbal children, the following symptoms were most reliable: abdominal pain with fever higher than 38°C, back pain), new-onset urinary incontinence, dysuria, and frequency.

DIAGNOSIS OF UTI :

- Specimen Collection :A non contaminated urine sample is fundamental.
- For older children: Midstream urine collection.
- For infants and non–toilet-trained children, the most accurate method of collection is suprapubic bladder aspiration, however, it rarely is practical. It is safe but
- Urethral catheterization or spontaneously voided clean catch midstream samples (usually obtained as you change the diaper “if lucky” the baby starts passing urine) are the most reliable alternatives.

- Perineal urine bag collection has a high rate of contamination and should be avoided for culture, but may help in screening infants for suprapubic bladder aspiration or urethral catheterization.
- For toilet-trained children, appropriate cleansing of the perineal/genital area before midstream urine collection is essential.
- You do urinalysis, gram stain, and culture.

Urinalysis :

- Although urine culture is the gold standard for UTI diagnosis, more rapid screening may be required for preliminary clinical decision making. Start empirical treatment once you take the sample.
- Urine Gram stain is the single most sensitive and specific test.
- For older infants and children, urine **dipstick** testing for both leukocyte esterase (means there is WBCs) and nitrites may be used if microscopy is unavailable, however, urine still must be sent for culture and symptomatic children must be treated pending the results because the dipstick false-negative rate is high (if negative nitrite doesn't exclude UTI as not all bacteria produce nitrite. Also babies pass urine frequently it's not kept in the bladder, thus nitrate is not reduced to nitrite).
- No role of RBC as it doesn't role in or role out.

Urine Culture

- Bacterial colony count criteria to distinguish urine infection from contamination are optional, not absolute.
- Although 10^5 colony forming units (CFU) per mL (10^8 CFU/L) is the generally accepted diagnostic cut-off level for midstream urine samples, true infection with a lower colony count occurs (eg, reduced bladder incubation time owing to urinary frequency or high urine flow rate, presence of an antibacterial agent in the urine). In children with clear symptoms we diagnose even if CFU is < 10^5
- For small babies (<1 year) you have to do full septic analysis, blood culture and LP because symptoms are cot specific. Then admit and start broad spectrum Abx. Treatment (cefotaxime and ampicillin).

Table 2. Urine Culture: Diagnostic Criteria for Urinary Tract Infection

Urine Collection Technique	CFU/mL (pure growth)	Probability of Infection
Suprapubic aspiration	Gram negative rod, any	>99%
	Gram positive cocci, more than a few thousand	>99%
Catheterization	$>10^5$	95%
	10^4-10^5	Likely
	10^3-10^4	Suspicious
Clean void (male)	$>10^4$	Likely
Clean void (female)	3 samples $>10^5$	95%
	2 samples $>10^5$	90%
	1 sample $>10^5$	80%

The doctor didn't read the pic. Just said that this is why we don't rely on the CFU > 10^5 cut-off.

TREATMENT

Younger than 3 months of age :

- All febrile neonates should be treated with IV antibiotics pending urine, blood, and CSF culture results.

Older than 3 Months :

- 10 to 14 days of oral treatment with cefixime, or amoxicillin/clavulanic acid is effective as 2 to 4 days of intravenous therapy followed by oral, to complete 7 to 21 days of antibiotic treatment (discharged if blood culture is negative).

- For older stable children no need for admission (oral Abx.)
- Final antibiotic choice should be based on culture and sensitivity results. Nitrofurantoin is used for prophylaxis. We usually give 3rd generation cephalosporin, if not available, Augmentin.
- Prompt antimicrobial therapy generally is believed necessary to diminish risk of renal scarring

UTI RECURRENCE

- You have to investigate further in boys and recurrent infection in girls.
- Recurrent UTIs develop in approximately 75% of children whose first infection occurs before the age of 1 year, and in about 40% of girls and 30% of boys presenting after this age (more in girls)
- Risk factors identified include dilating VUR, family history of UTI, infrequent voiding, and inadequate fluid ingestion.
- Strategies that may help prevent recurrence include management of voiding dysfunction and increased fluid intake.
- Do US looking for hydronephrosis, MCUG for posterior urethral valve and VUR (it cause recurrent UTI and deteriorating renal function by scarring (especially pyelonephritis)).

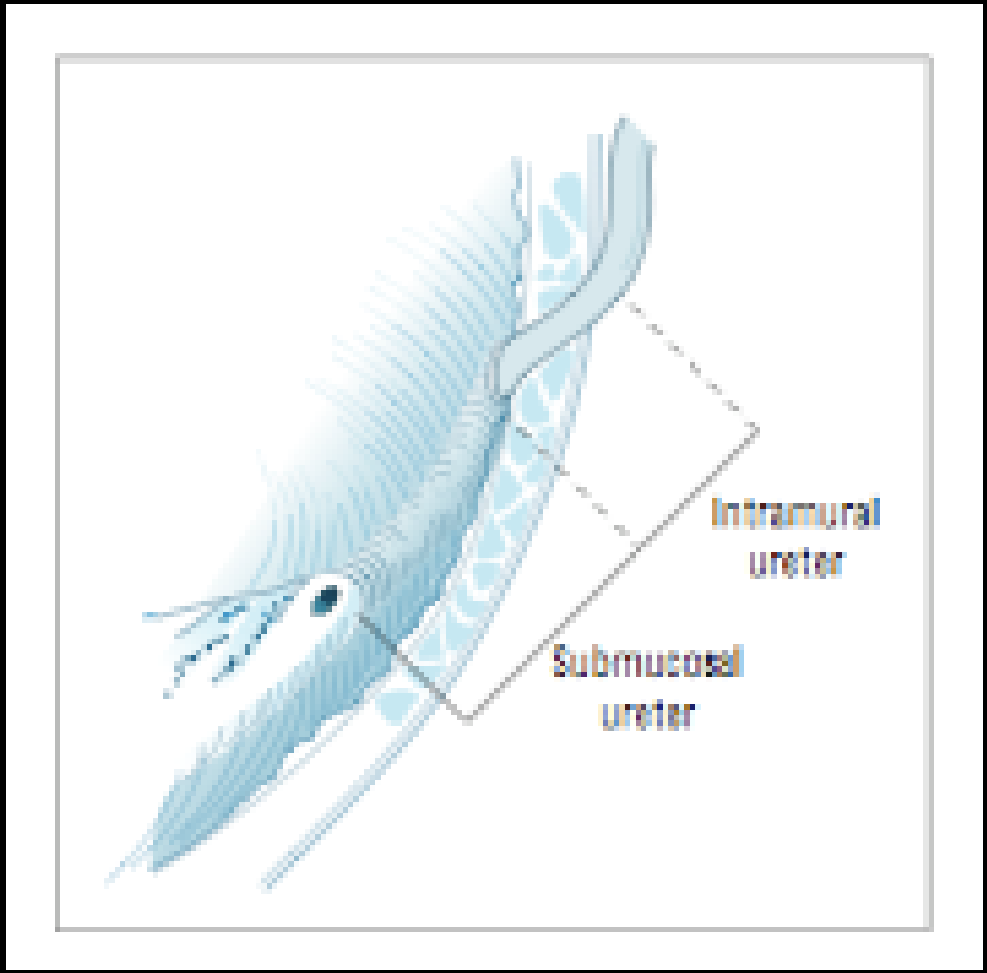
LONG-TERM OUTCOME

- Approximately 70% of infants and children with their first febrile UTI have pyelonephritis and renal scars may follow in 15% to 30%.
- With timely appropriate therapy most infants and children recover promptly without major long-term sequelae, but a small number are at risk for significant morbidity, progressive renal damage, and renal insufficiency

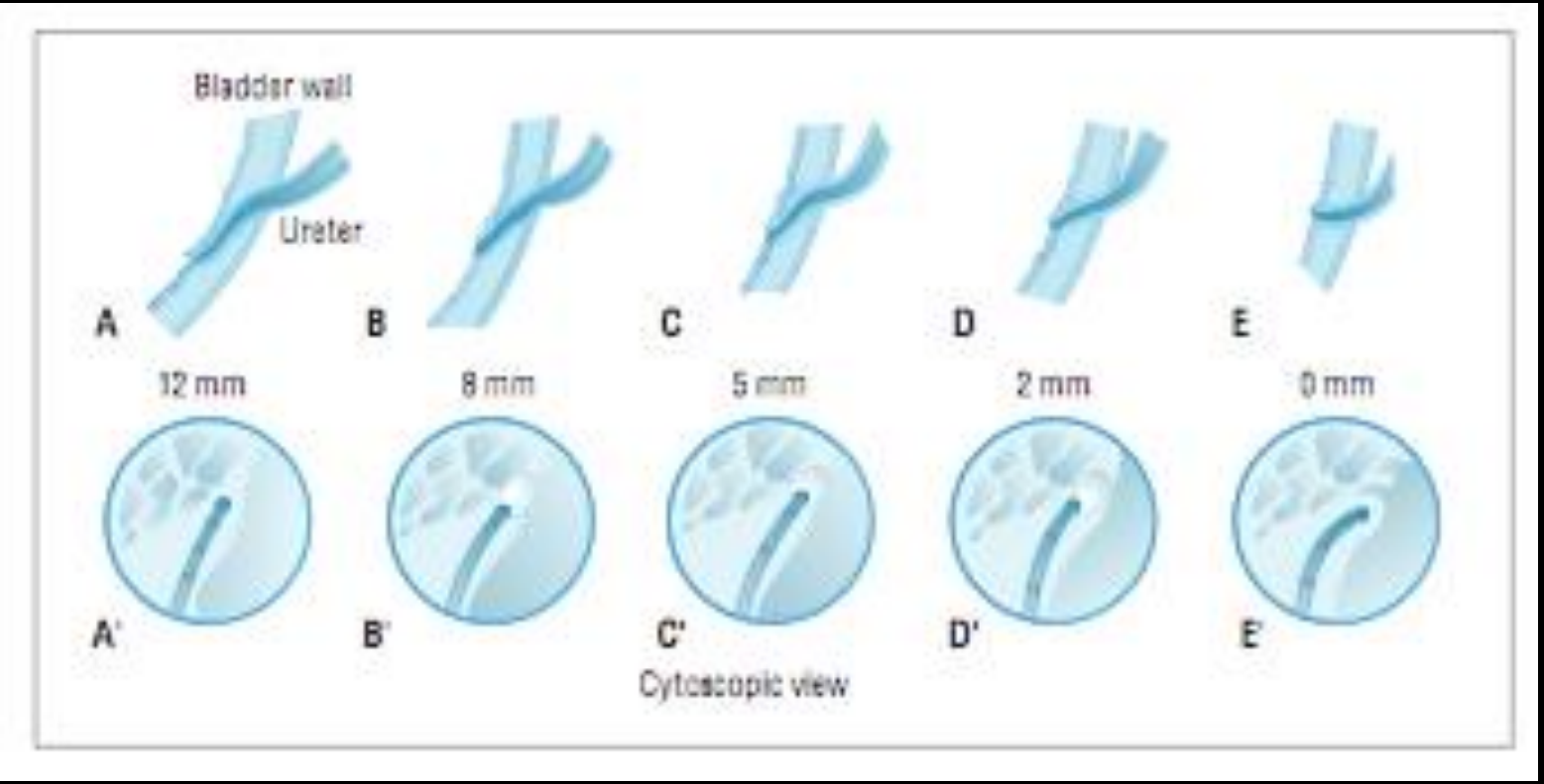
Vesicoureteral Reflux

- Retrograde flow of the urine from the urinary bladder into the ureters is prevented during micturition by a functional valve mechanism at the level of the ureterovesical junction (UVJ). Incompetence of the UVJ valve leads to flow of urine upstream into the ureter and the kidney, a condition known as vesicoureteral reflux or VUR.

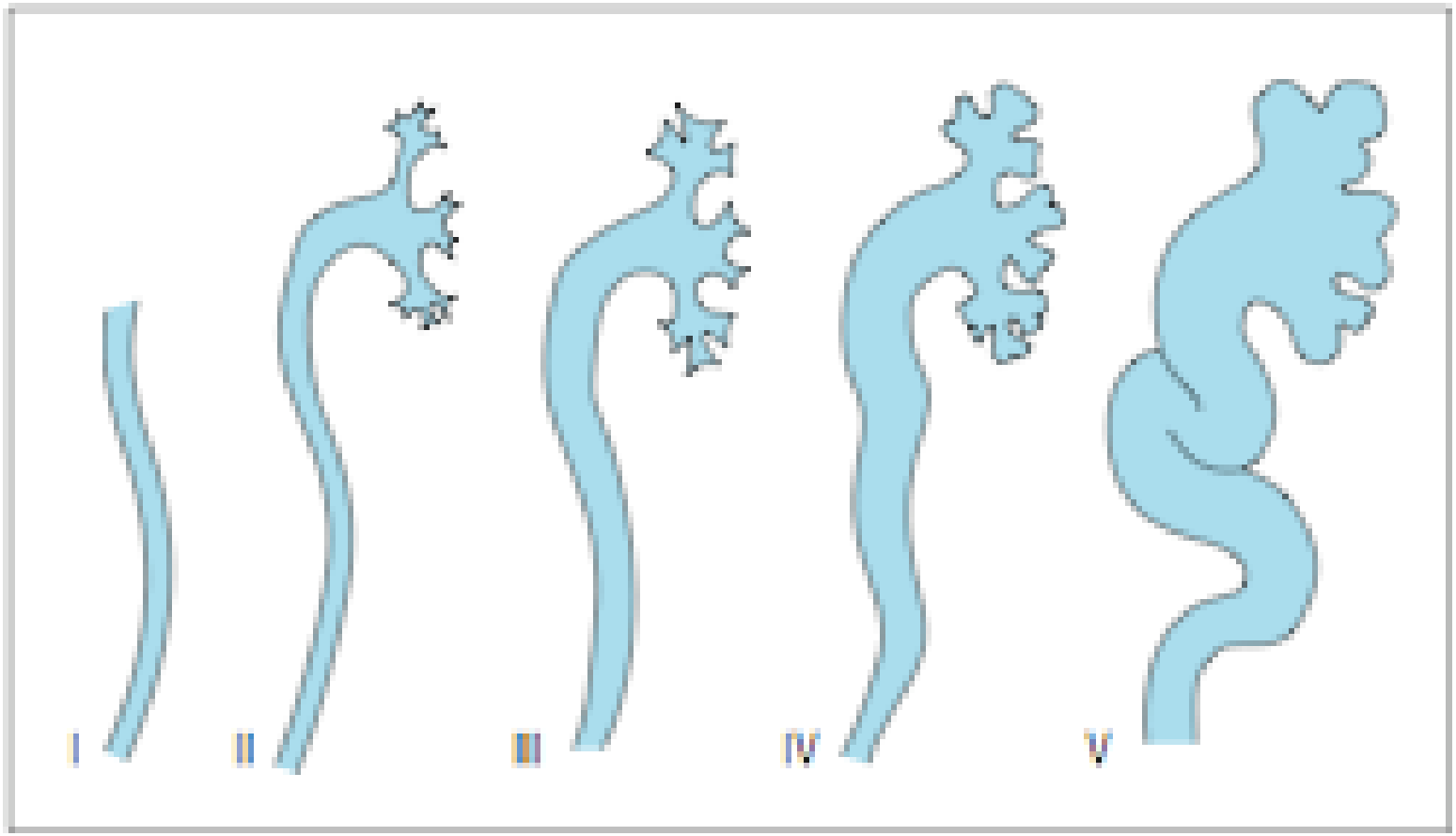
- The association of VUR and predisposition to UTI is well established.
- Functional anatomy the UVJ lacks a traditionally defined valve to prevent retrograde flow of urine from the bladder into the ureter.
- The antireflux mechanism operative at this location is dependent on the unique anatomic configuration of the ureteral insertion into the bladder .



A part of the ureter is in the wall of the bladder before opening. Once the bladder is full, the increased pressure pushes and closes the valve.



Staging; A: normal, E: when the bladder is full urine will go up (very high stage of reflux.



Grade 1: retrograde flow to half of ureters.
Grade 2: backflow up to pelvis.
Grade 3: up to pelvis with dilation of ureters.
Grade 4: up to pelvis with torturous dilation of ureters.
Grade 5: torturous dilation, hydronephrosis and blunting of the calyces.

•Primary VUR is the commonest congenital anomaly affecting the urinary tract.
•VUR can be seen in 25–50% of asymptomatic siblings of index children diagnosed as having VUR.
•The familial pattern of VUR have been well documented, but the mode of inheritance is unclear.
•It is well known that the prevalence of VUR decreases with increasing age of children, suggesting that there is a trend towards improvement of VUR, even without any intervention throughout the child- hood age spectrum
•Secondary is usually secondary to obstruction.

Table 36.1 Classification of vesicoureteral reflux (VUR)

Primary
Congenital VUR resulting from malimplantation of the ureter in the bladder – associated with urinary tract infection

Secondary
Bladder outlet obstruction:
- Posterior urethral valves
- Bladder neck obstruction
- Severe urethral stricture

Neurogenic bladder:
- Spina bifida–meningomyelocele

Chronic bladder inflammation
Urinary tract infection
Traumatic:
- Following bladder surgery
- Following ureteral calculus extraction

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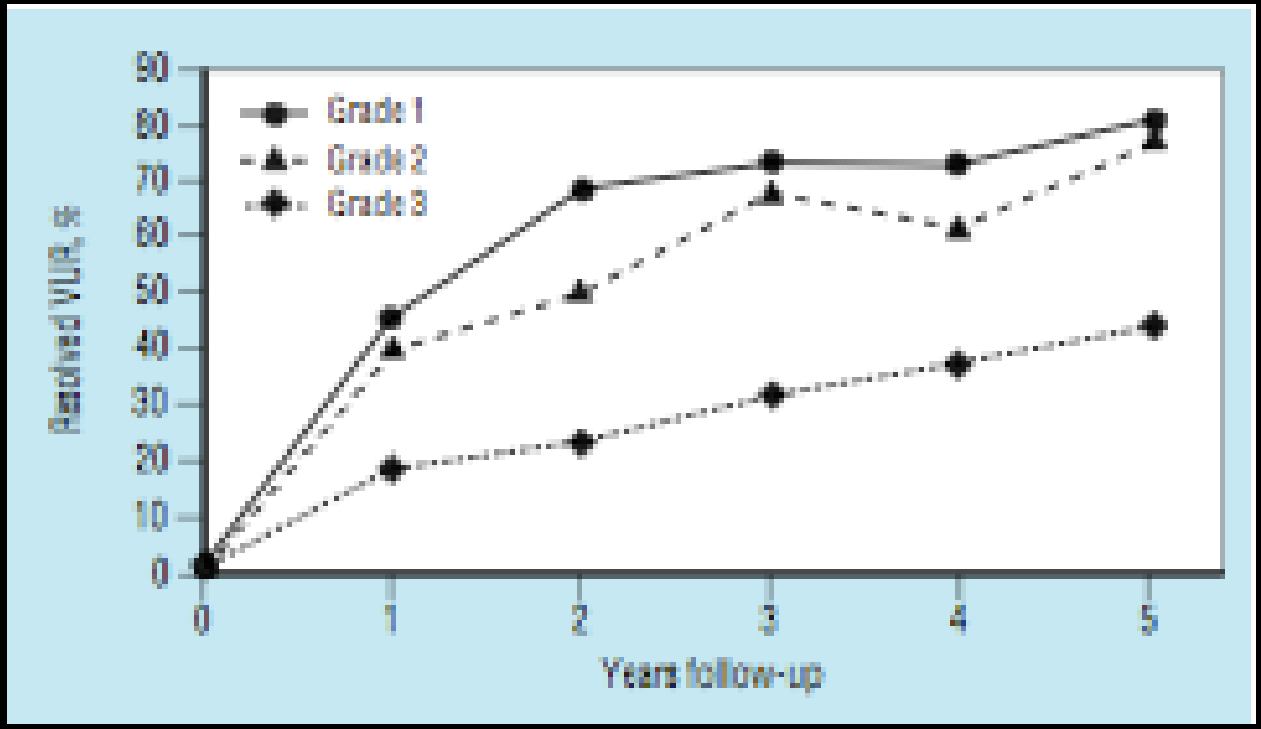
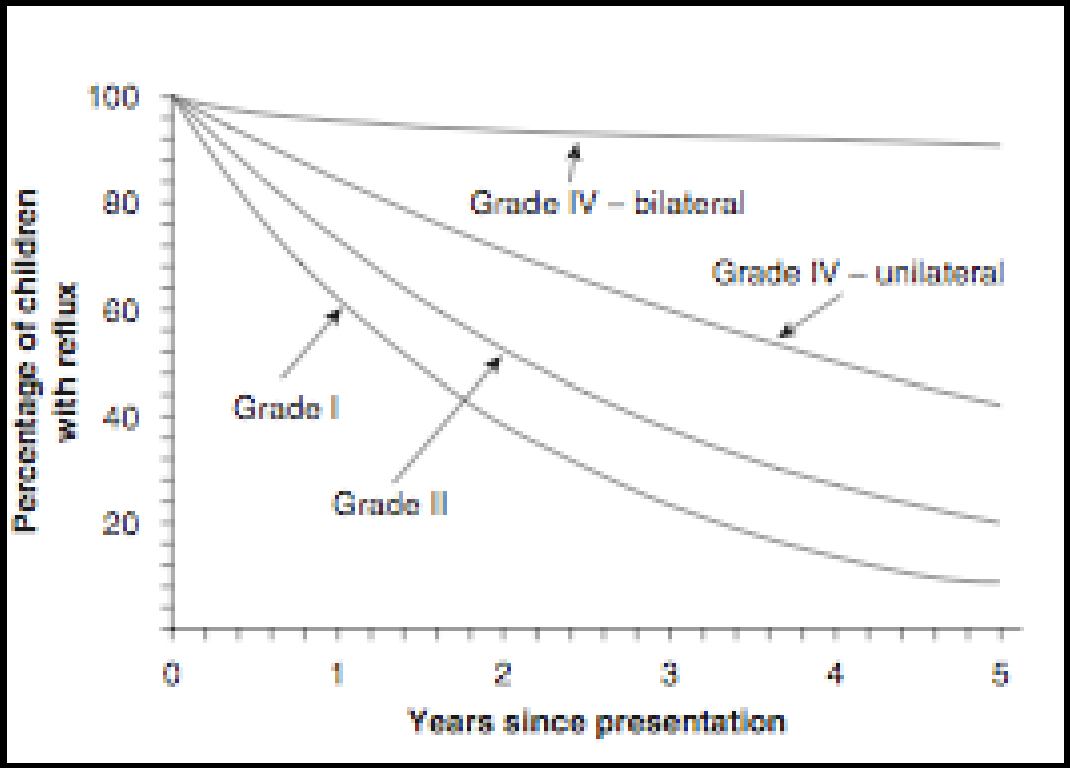
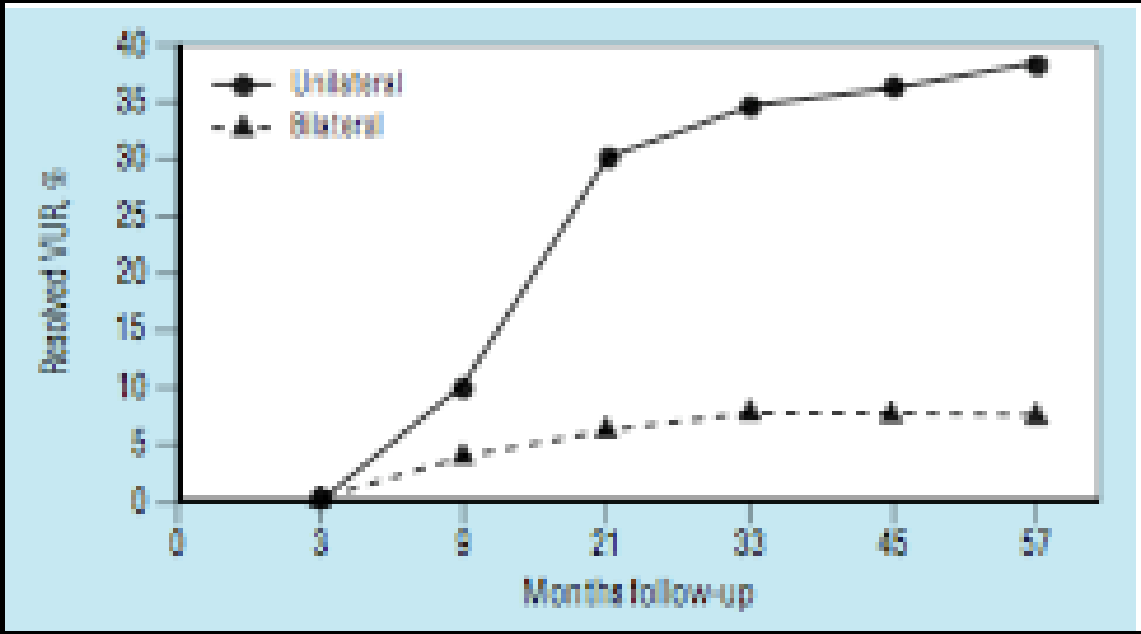


Do they outgrow VUR? Yes, but not always.
This graph shows the number of resolved VUR cases by years of follow up.
Grade 1 85-90% of them almost always resolve.
It's much less as the grade is more.



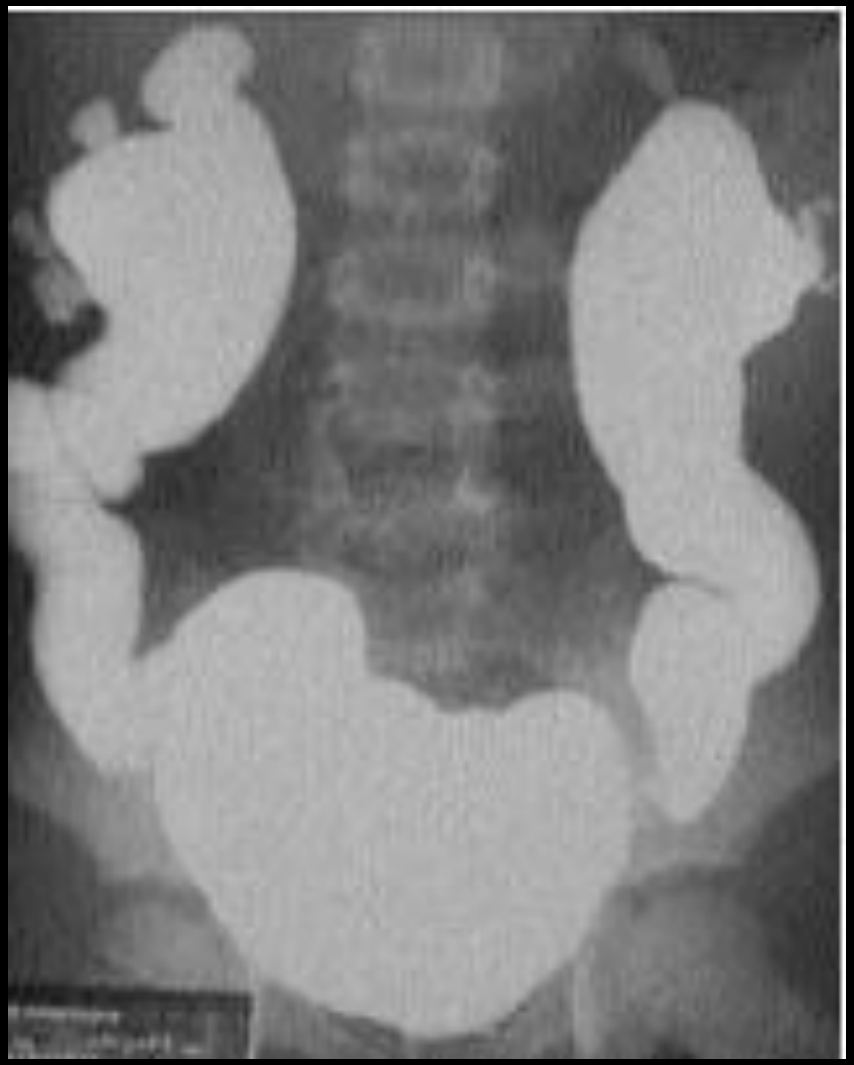
The other important thing is unilateral vs. bilateral. If it's bilateral VUR the chances it gets resolved is less, especially if it's high grade.



Unilateral vs Bilateral Resolution of grades III to V vesicoureteral reflux (VUR)

Unilateral and low grade reflux= very likely to resolve

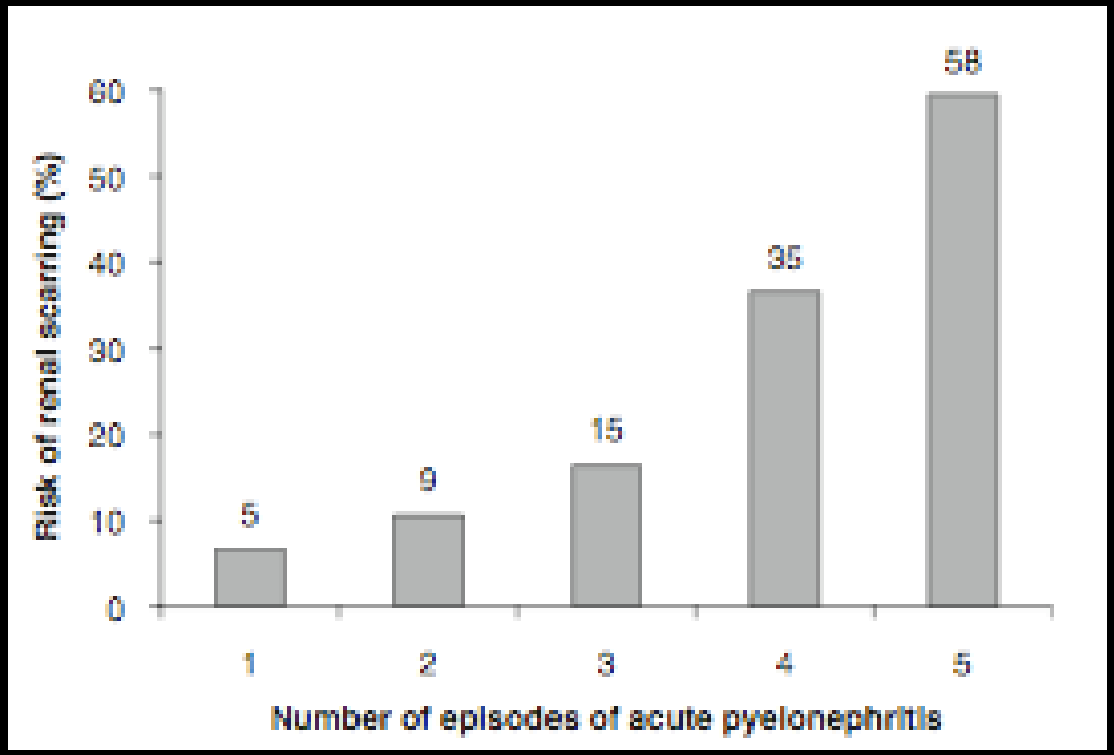
- The gold standard for evaluation of children for VUR is contrast vesicocystourethrography (VCUG), especially in male children, but nuclear cystogram is recommended in females.



Grade 5 bilateral reflux on MCUG. The ureters are dilated up to the pelvis and tortious ureter with blunting of calyces.

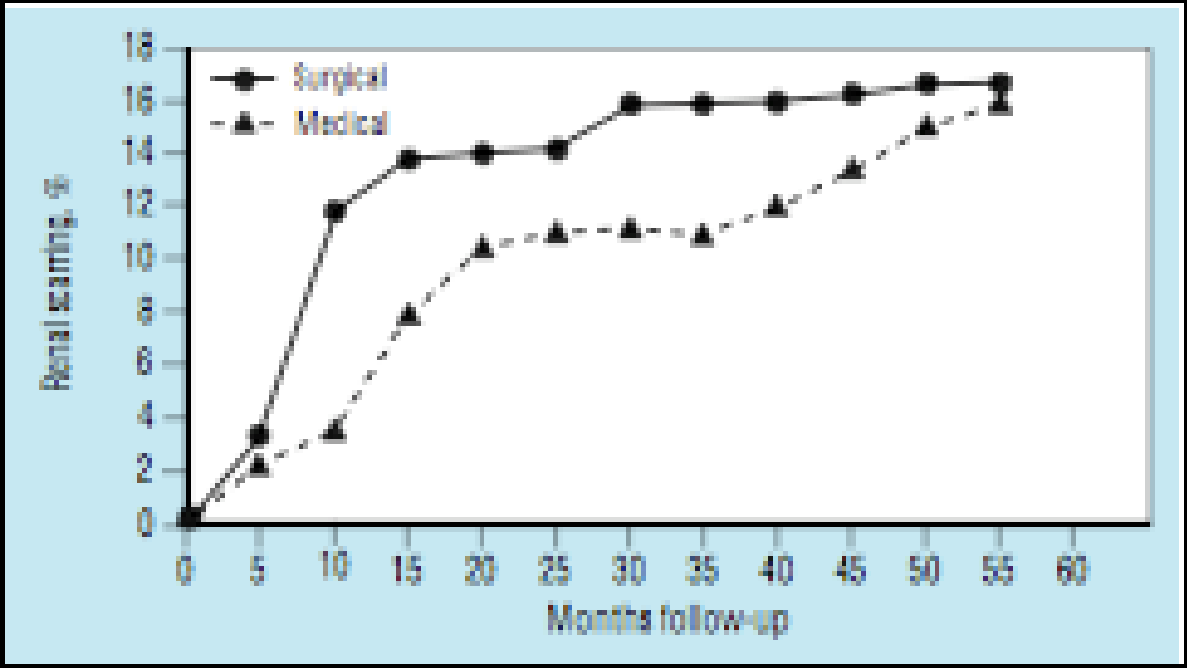
Renal scarring and VUR :

- VUR is well recognized to be associated with renal scar formation.
- Renal scar is diagnosed using DMSA. But you have to wait 3 months after the UTI resolves because if there is pyelonephritis it can be mistaken as scar.
- In general, the incidence and severity of renal scars associated with VUR increase with the grade of VUR.
- The incidence of renal parenchymal scars is also higher in those with recurrent febrile UTIs
- Such renal scars were termed 'reflux nephropathy' as a designation for renal scars associated with VUR and pyelonephritis.
- Unfortunately we still see it either delayed diagnosis or the patient in a rural area and the family is not compliant with treatment or follow-up. A patient may need dialysis.



More pyelonephritis = more scarring.
Almost 60% scarring when you have 5 pyelonephritis.

Management of VUR



Effectiveness of medical versus surgical treatment: new scar formation at follow-up examinations over 5 years in children with high-grade VUR

By the end of follow up (60 months) there is no difference in outcome! So I'd go with non-invasive.

Management of VUR

Medical:

- Prophylaxis Abx. Usually 1/3 of the dose, once per day, at night, usually ceftrine or Nitrofurantoin. It usually resolves because the angulation of the ureter to the bladder changes as the child grow up.

Surgery:

reserved for patients with **high grade and bilateral** reflux, or having **breakthrough** in any grade (infection continues despite giving Abx.)

- De-flux injection (inject bulking agents to the wall to change the angulation, unfortunately these agents get absorbed after few months and thus you have to inject twice)
- Ureteral reimplantation (very invasive, you have to cut the ureter and reimplant it in a de-reflux way. Last choice)

Congenital Anomalies of the Kidney and Urinary Tract (CAKUT)

- Congenital anomalies of the kidney and urinary tract (CAKUT) constitute approximately 20 to 30 % of all anomalies identified in the prenatal period.
- Defects can be bilateral or unilateral, and different defects often coexist in an individual child (multiple level: kidney, UPJ, ureter, UVJ obstruction, bladder, urethra “PUV”). Thus if there is a defect look for another defect and also look at the other side.
- The overall rate of CAKUT in live and stillborn infants is 0.3 to 1.6 per 1000 .

- The incidence is higher in women with a family history of CAKUT.
- Of all antenatal renal anomalies, the most frequent abnormality is hydronephrosis, (ie, upper urinary tract dilatation).
- Renal malformations are associated with non-renal congenital anomalies in about 30 % of cases, classically periauricular tags.

A- Kidney

Renal hypoplasia	Renal dysplasia
Low number of nephrons	Normal number of nephrons
Structurally normal kidney	Structurally abnormal kidney

1-Renal hypoplasia :

- A lower number of structurally normal nephrons, is a distinct entity separate from renal dysplasia
- Unknown causes
- Normally there is 1 million nephron in one kidney.

- The clinical diagnosis of renal hypoplasia is suggested when all of the following criteria are met :

  * Reduction of renal size by 2 standard deviations for the mean size by age

  * Exclusion of renal scarring by 99mTc-dimercaptosuccinic acid (DMSA) radionuclide scan. Reflux > UTI > multiple scars > the scarred area will not grow, this is not hypoplasia!

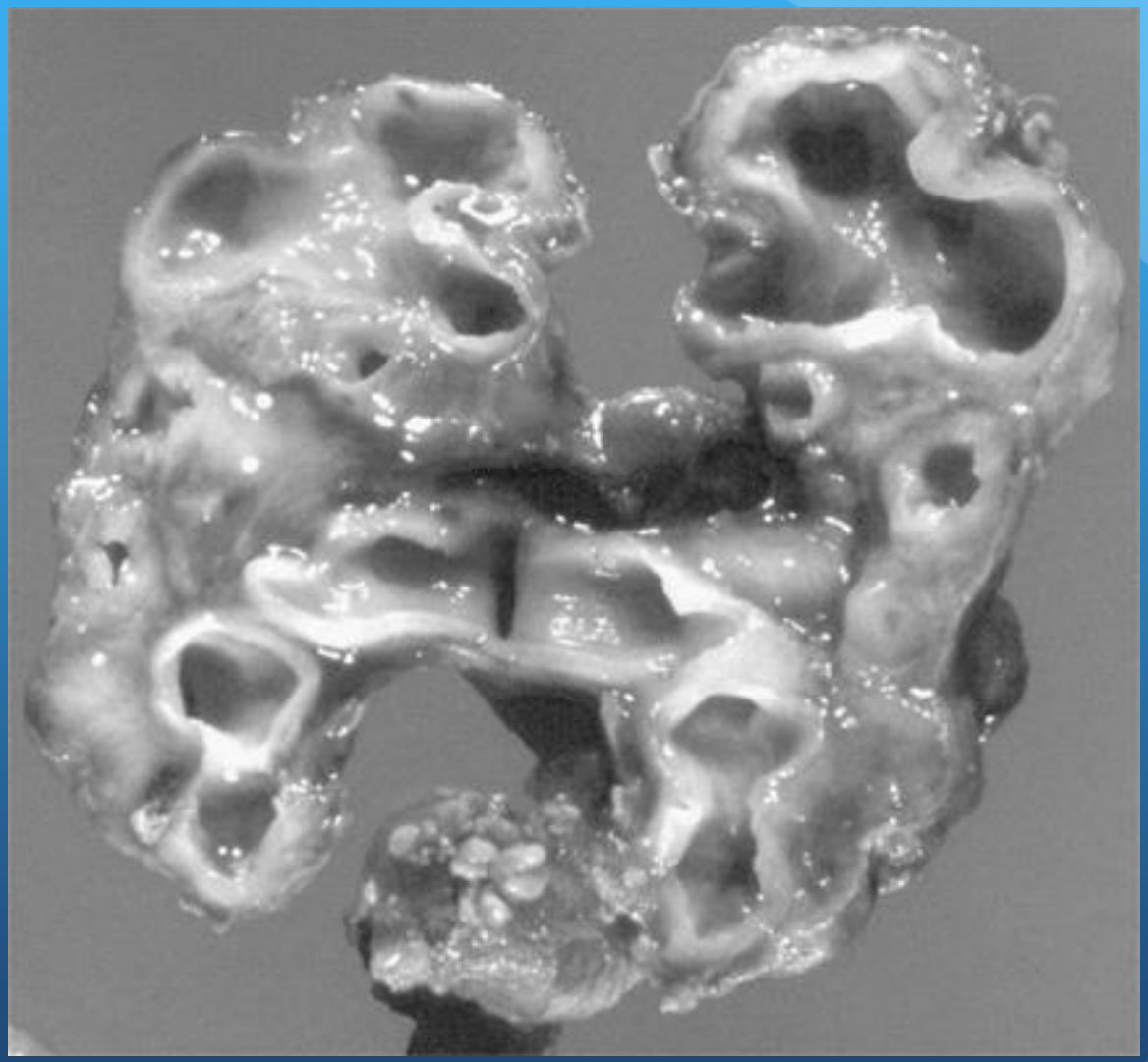
  * In cases of unilateral renal hypoplasia, compensatory hypertrophy of the contralateral kidney

من رحمة الله تعالى الكلية الثانية تكبر وتعوّض

2-Renal dysplasia:

- Renal dysplasia is characterized by the presence of malformed kidney tissue elements
- Dysplastic kidneys are variable in size but most are smaller than normal. Size is often determined by the presence or absence of cysts.
- Renal dysplasia may be unilateral or bilateral

- Renal dysplasia may be discovered during routine antenatal screening or postnatally when renal ultrasonography is performed in a dysmorphic infant.
- Bilateral dysplasia is likely to be diagnosed earlier than unilateral dysplasia especially if oligohydramnios is present.
- The classical example of renal dysplasia is MCDK (Multicystic dysplastic kidney).



- Many think that MCDK is secondary to renal obstruction.
- Investigate the other side and multilevel defects.
- Infants with bilateral dysplasia may have impaired renal function at birth and subsequent progressive renal failure may occur.
- Associated urological findings include abnormalities of the renal pelvis and calyces (congenital hydronephrosis) and ureters (duplicating collecting system), megaureter, ureteral stenosis, and vesicoureteral reflux (VUR).

- Because of the frequent association of renal dysplasia with a collecting system anomaly, voiding cystourethrography should be considered in all patients with renal dysplasia.
- The prognosis of renal dysplasia depends on whether there is unilateral versus bilateral disease. In general, the long-term outcome of unilateral renal dysplasia is excellent, particularly if there is a normal contralateral kidney.

3-Multicystic dysplasia :

- Multicystic dysplastic kidney (MCDK) is a nonfunctioning dysplastic kidney with multiple cysts, which is thought to arise from an alteration in renal parenchymal differentiation. MCDK consists of a nonreniform mass of cysts and connective tissue, and is most commonly detected by routine antenatal screening.

4-Renal agenesis:

- Renal agenesis is defined as congenital absence of renal parenchymal tissue and results from major disruption of metanephric development at an early stage.
- Unilateral RA accounts for 5 percent of renal malformations .
- The incidence of renal agenesis is approximately 1 per 2900 births
- Usually unilateral. Can live normal if the other kidney is normal.

- Cause: usually congenital, sometimes environmental, sometimes due to drugs like retinoic acid (used for acne) and cocaine. *important*
- Multiple factors are thought to be implicated in the pathogenesis of renal agenesis including mutations in genes important in renal development, and teratogenic and environmental agents (eg, retinoic acid and cocaine exposure)

The doctor skipped this slide

- Other urological abnormalities have been reported in up to 33 to 65 percent of unilateral cases
- Vesicoureteral reflux (VUR) is the most commonly identified urological abnormality,
- Nonrenal associated anomalies include cardiac anomalies (most commonly septal anomalies), genital tract, and gastrointestinal, respiratory, and skeletal malformations

Autosomal recessive PCKD	Autosomal dominant PCKD
AR= pediatrics age group	AD = ADults
Each have different genetic mutation	

5-Genetic cystic diseases :

- Genetic cystic renal diseases are disorders of terminal epithelial differentiation

A-Autosomal recessive polycystic kidney disease (ARPKD):

- It is caused by mutations in the PKHD1 gene, which codes for fibrocystin.
- ARPKD is characterized by multiple microscopic cysts, principally involving the distal collecting ducts Of both kidneys
- Kidneys are usually greatly enlarged and contain small cysts; renal failure is common in childhood. The baby born can't breath due to huge kidneys.

- The liver is enlarged and has periportal fibrosis and scattered cysts.
- Fibrosis produces portal hypertension by age 5 to 10 yr.
- Disease severity and progression vary. Severe disease may manifest prenatally or soon after birth or in early childhood with renal-related symptoms; less severely affected patients present in late childhood or adolescence with hepatic-related symptoms.

- Severely affected neonates commonly have pulmonary hypoplasia secondary to the in utero effects of renal dysfunction and oligohydramnios (potter's symdrome).
- If the patient presents in adolescence, nephromegaly is less marked, renal insufficiency may be mild to moderate, and the major symptoms are those related to portal hypertension.

- Diagnosis may be difficult, especially without a family history. Ultrasonography may demonstrate renal or hepatic cysts; definitive diagnosis may require biopsy.
- Ultrasonography in late pregnancy usually allows presumptive inutero diagnosis.
- Clinical manifestations include oligohydramnios, pulmonary hypoplasia, hypertension, congestive cardiac failure, liver disease, and renal failure.
- The perinatal prognosis depends on the pulmonary status.

B-Autosomal dominant polycystic kidney disease (ADPKD)

- ADPKD is characterized by bilateral renal enlargement secondary to multiple cysts.
- It is caused by mutations in either PKD1 (85 percent of patients) or PKD2 genes (15 percent)
- There is a greater variability in clinical manifestations of ADPKD with most patients having significant clinical findings only in adulthood.

- There are a subset of children who have an early onset of disease (in utero or in the first year of life) with symptoms similar to those with ARPKD.
- These include gross or microscopic hematuria, hypertension, proteinuria, cyst infection, and renal insufficiency
- What distinguishes it from recessive is that is has extra-renal manifestations. First, they will have cysts everywhere; cysts in the ovaries, pancreas, liver… everywhere. Also, they have cranial aneurysms as well as mitral valve prolapse. So, in the history of autosomal dominant, you have to ask about sudden death in the family. Sudden death would indicate CVA due to aneurysms. What is important in the autosomal recessive history? Skipped generations. Autosomal dominant does not skip generations; AD will be in every generation.

Table 17.4 Extrarenal manifestations of autosomal dominant polycystic kidney disease

Cardiovascular
Mitral valve prolapse
Aortic aneurysms
Hypertension
Intracranial aneurysms

Extrarenal cysts
Hepatic cysts:
Pancreatic cysts
Ovarian cysts
Testicular cysts:
Arachnoid cysts
Splenic cysts
Pineal cysts
Seminal vesicle cysts

Other
Hernias
Colonic diverticula
Cholangiocarcinoma
Congenital hepatic fibrosis

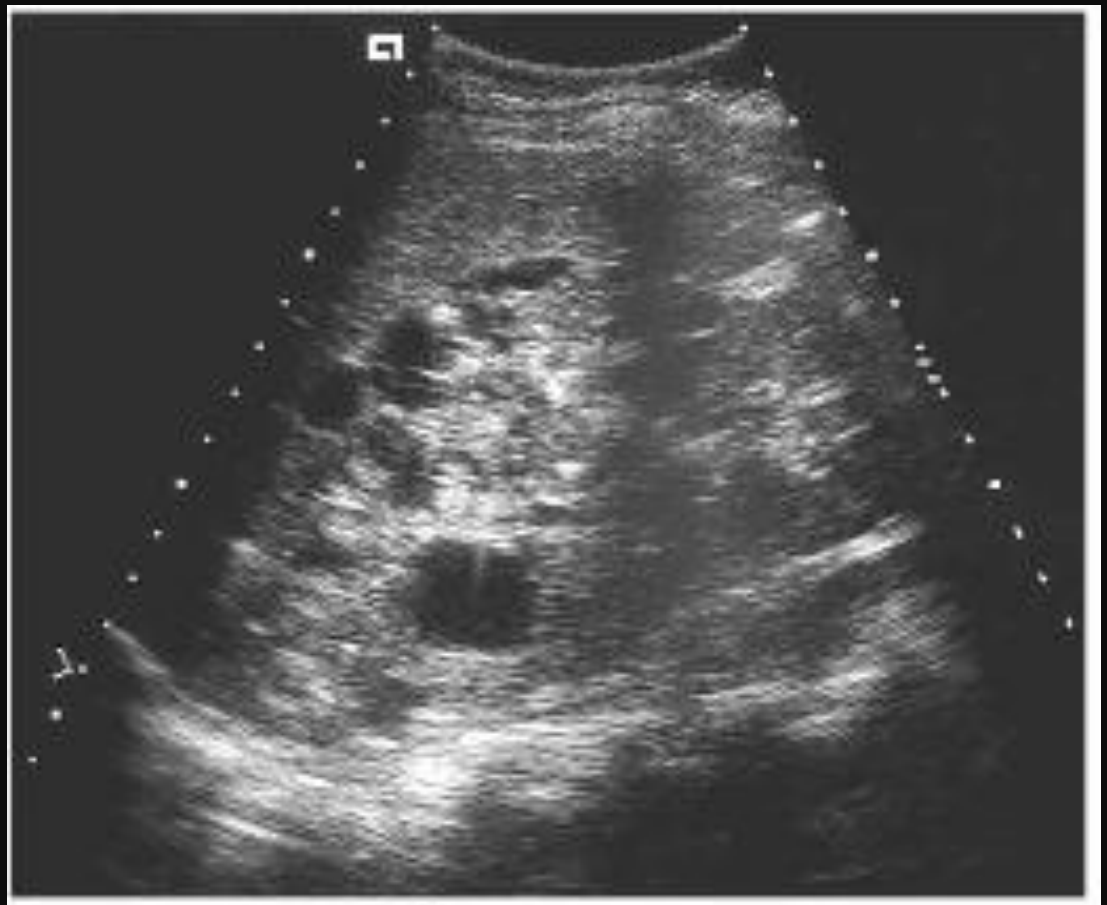
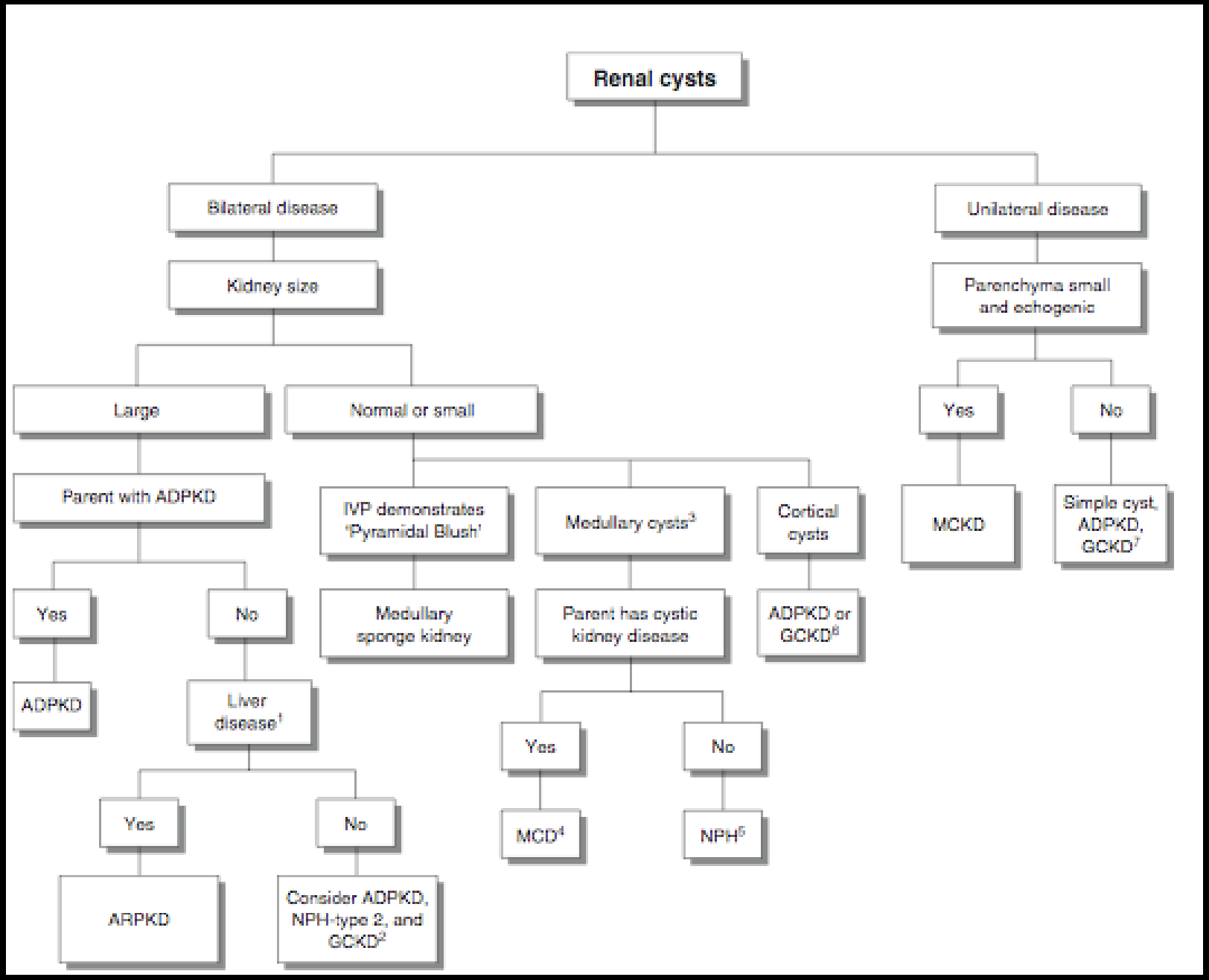


Figure 17.2 Sonogram of a 17-year-old patient with autosomal dominant polycystic kidney disease. Cysts of varying sizes are located in the cortex and the medulla.


Renal cysts
Bilateral disease
Unilateral disease
Kidney size
Parenchyma small and echogenic
Large
Normal or small
Yes
No
Parent with ADPKD
IVP demonstrates 'Pyramidal Blush'
Medullary cysts3
Cortical cysts
MCKD
Simple cyst, ADPKD, GCKD7
Yes
No
Medullary sponge kidney
Parent has cystic kidney disease
ADPKD or GCKD6
ADPKD
Liver disease1
Yes
No
MCD4
NPH5
Yes
No
ARPKD
Consider ADPKD, NPH-type 2, and GCKD2

RENAL ECTOPY:

- Renal ectopy occurs when the kidney does not normally ascend to the retroperitoneal renal fossa (level of the second lumbar vertebra).
- Simple congenital ectopy refers to a kidney that lies on the correct side of the body but lies in an abnormal position.

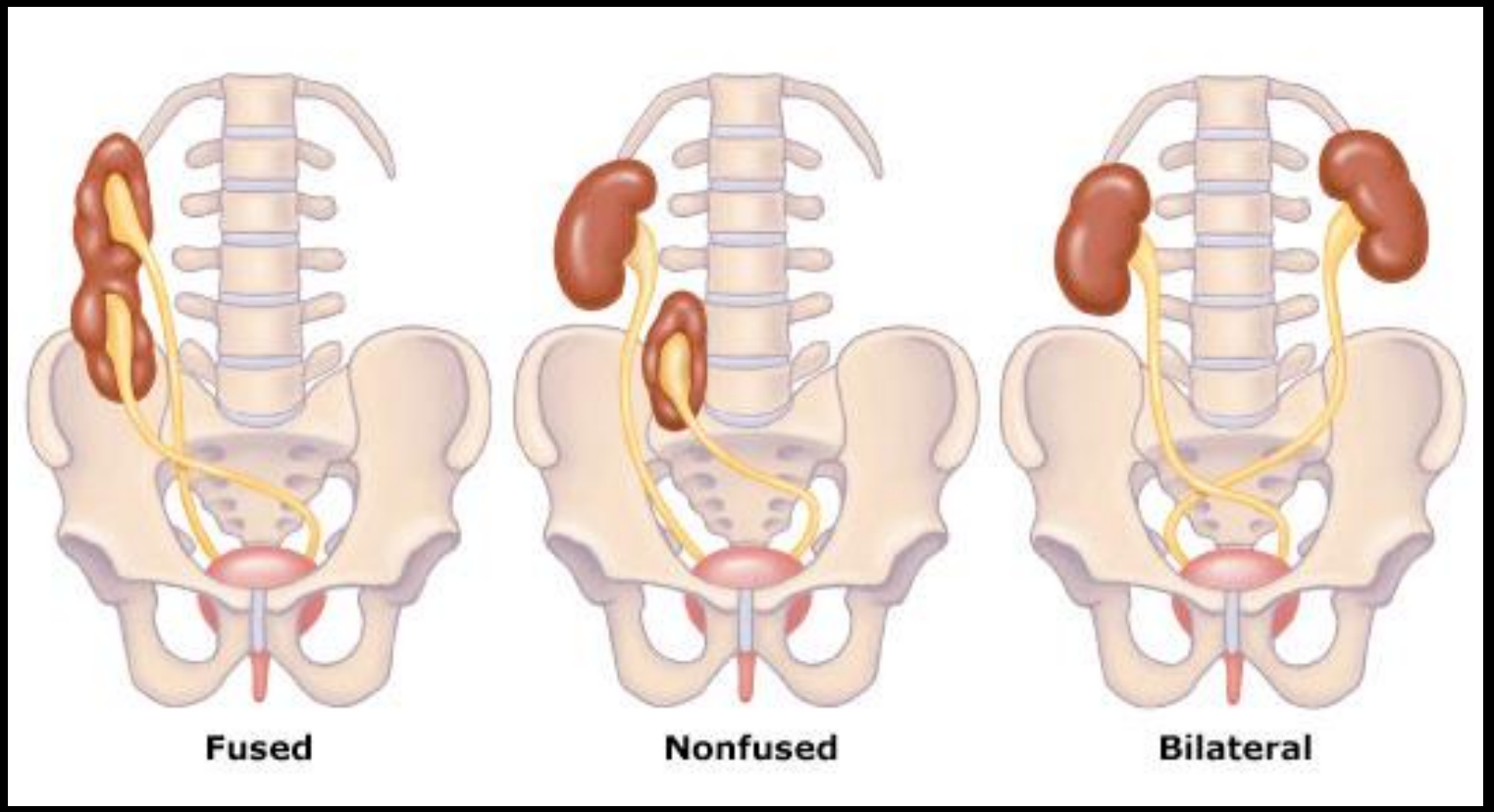
Crossed renal ectopia

- Different forms of crossed renal ectopia

  1- Fused: Ectopic kidney moves across the midline and fuses to the lower pole of the normally positioned contralateral kidney.

  2-Nonfused: Ectopic kidney moves across the midline without fusion and positioned at the rim of the pelvis (pelvic kidney).

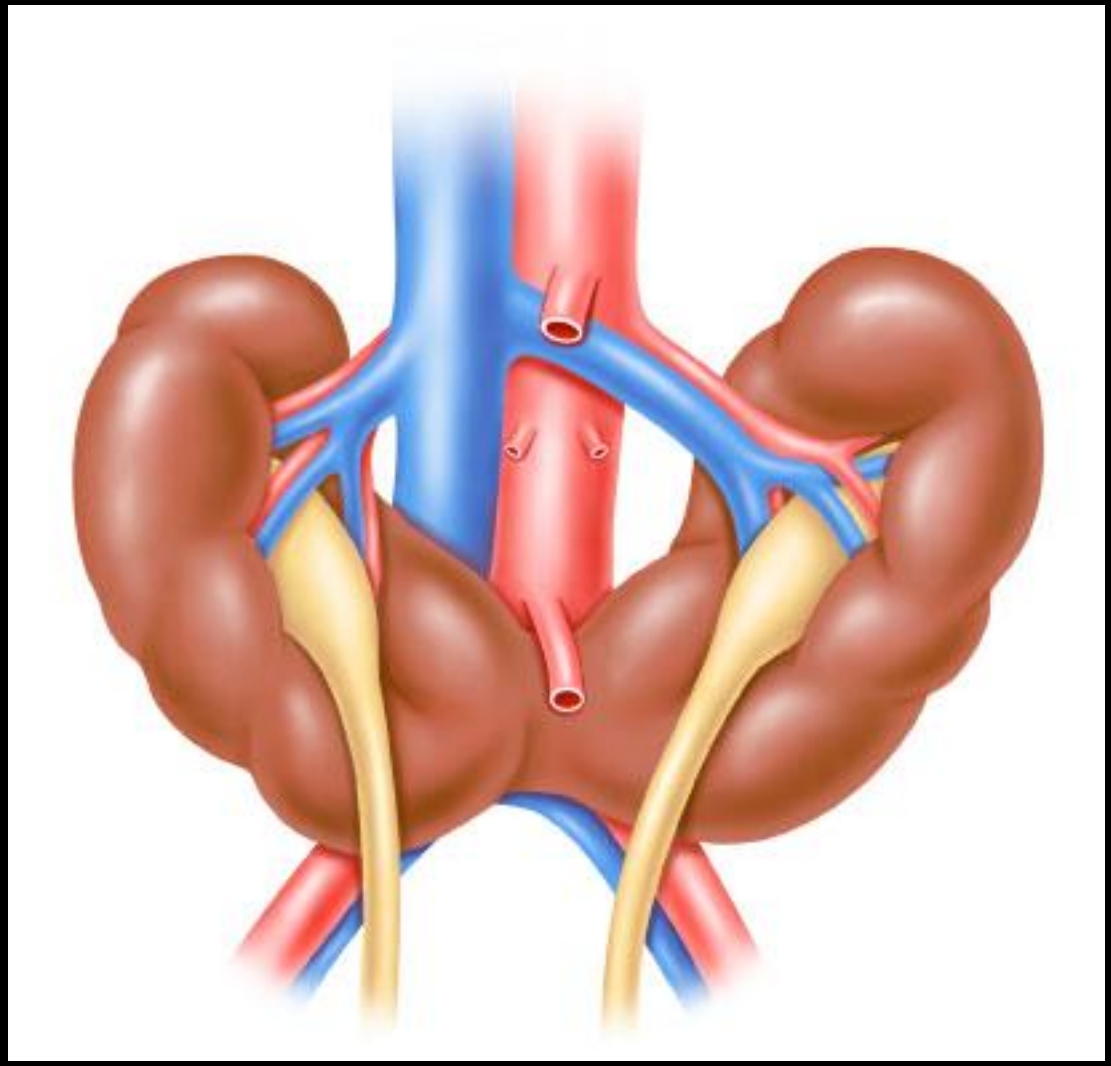
  3-Bilateral: Both kidneys are ectopic and cross the midline with the ureters maintaining their normal bladder insertion.



Let’s begin from the first on the left…
The left is crossed and fused.
The middle is crossed non-fused.
The right is bilateral crossing.

RENAL FUSION:

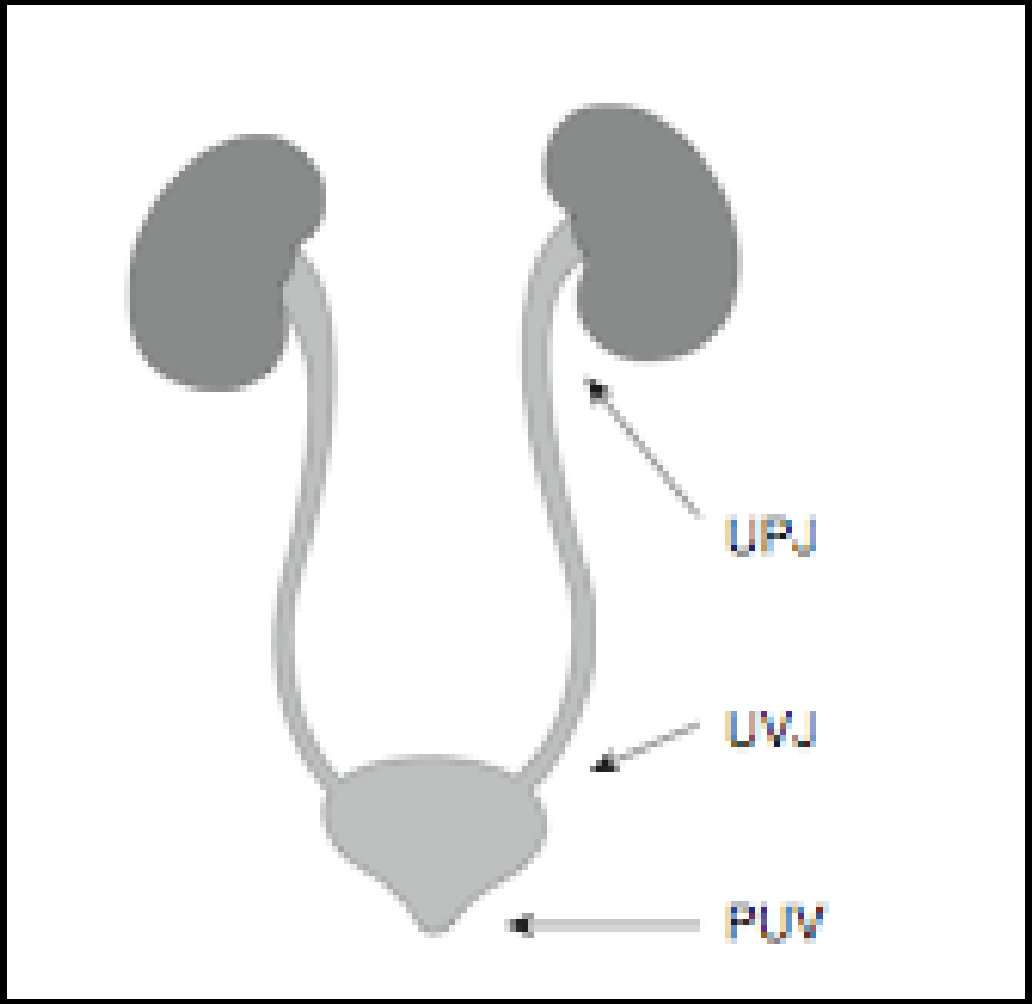
- Renal fusion occurs when a portion of one kidney is fused to the other.
- The most common fusion anomaly is the horseshoe kidney, which involves abnormal migration of both kidneys (ectopy), resulting in fusion.
- This differs from crossed fused renal ectopy, which usually involves abnormal movement of only one kidney across the midline with fusion of the contralateral noncrossing kidney.



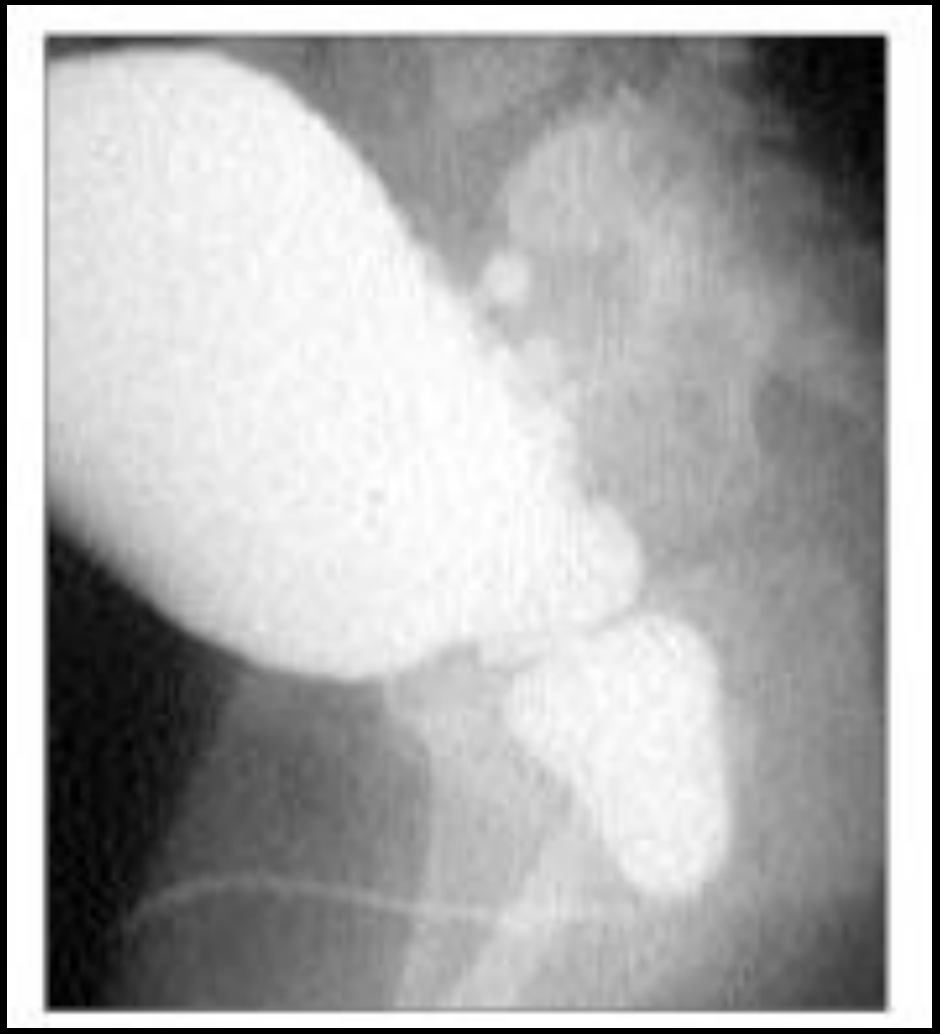
- Horseshoe kidney can be a feature of many syndromes including genetic disorders such as Turner syndrome, Trisomy 13, 18 and 2
- Patients with a horseshoe kidney appear to have an increased risk for Wilms tumor (not 100% of course).

- Most patients with an ectopic or fused kidney(s) are asymptomatic and are diagnosed coincidentally, often by antenatal ultrasonography. No hydronephrosis, no reflux.
- In patients diagnosed symptomatically with either anomaly, symptoms at presentation are generally related to associated complications including urinary tract infection (with or without VUR), obstruction, and renal calculi.

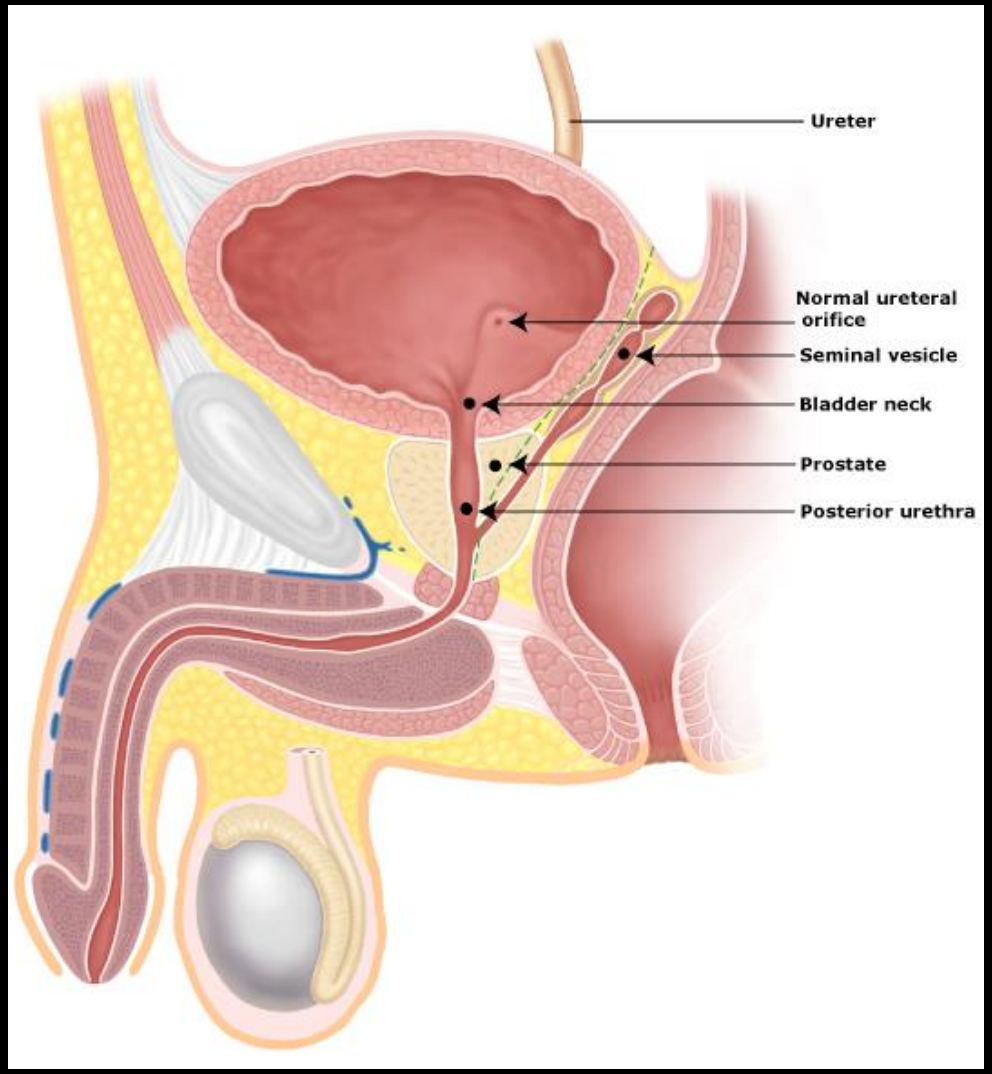
B-Ureter & Bladder



UPJ and UVJ Obstruction, diagnosed using:
US (hydronephrosis)
DTPA (like DMSA but DMSA shows anatomy while DTPA is excreted and thus shows the function especially in older children)
Complete obstruction > pyeloplasty



Posterior urethral valve: 1/3rd are born with bilateral renal failure. Few centers do intrauterine shunting of urine to amniotic fluid
Dx. MCUG done in lateral position with removed catheter (old keyhole sign)
Gold standard is scope

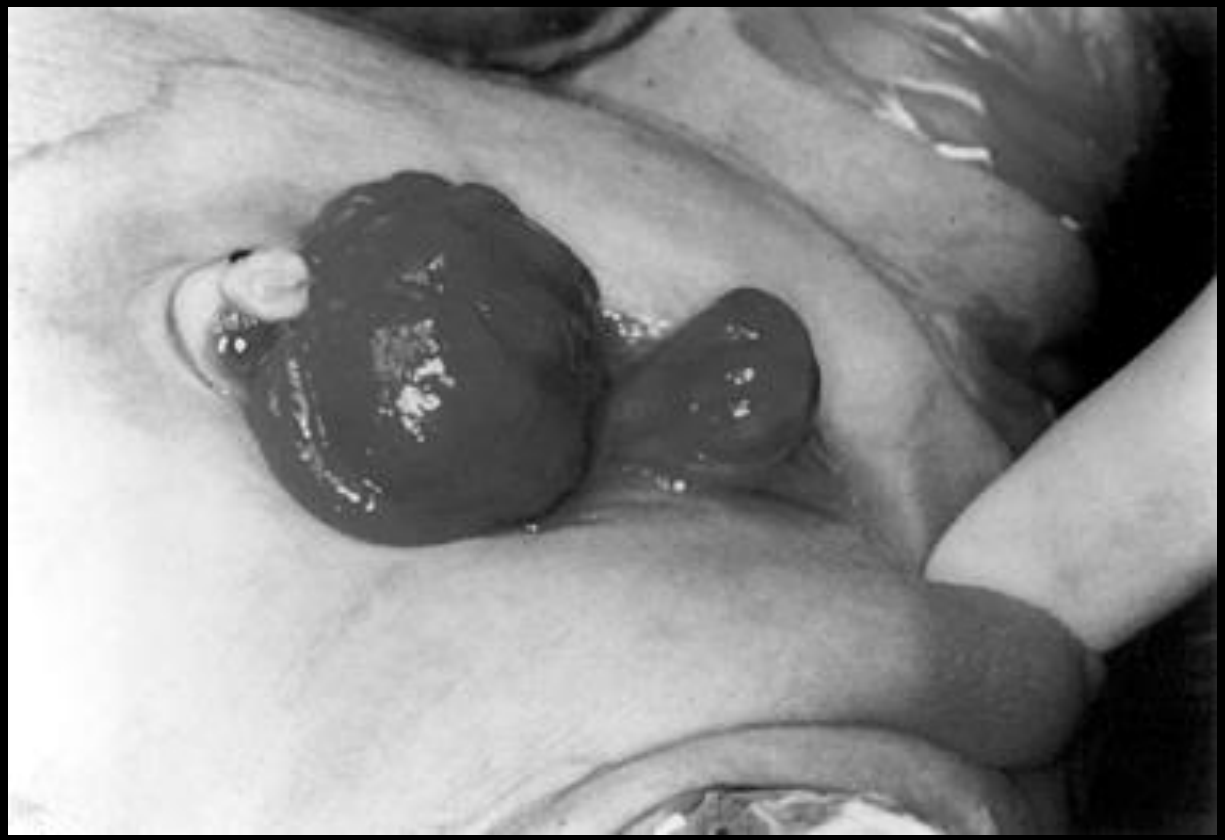


Location of ectopic ureteral orifices in boys

Bladder Extrophy (rare)

Physical findings characteristic of bladder exstrophy in both boys and girls include:

* Open bladder plate
* Low set umbilicus
* Diastasis of the symphysis pubis
* Anteriorly displaced anus
* Inguinal hernia



وكذا ختّمنا كلية الطب، مبروك يا خريجات♥