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. always check the other side, and check different level
- 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

extrarenal manifestation > preauricular tag

A- Kidney

1-Renal hypoplasia : smaller kidney > less number of nephrons

- A lower number of structurally normal nephrons, is a distinct entity separate from renal dysplasia
- Unknown causes

small kidney by US it may be a scar or hypoplasia (you can't tell)

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

2-Renal dysplasia: non functional

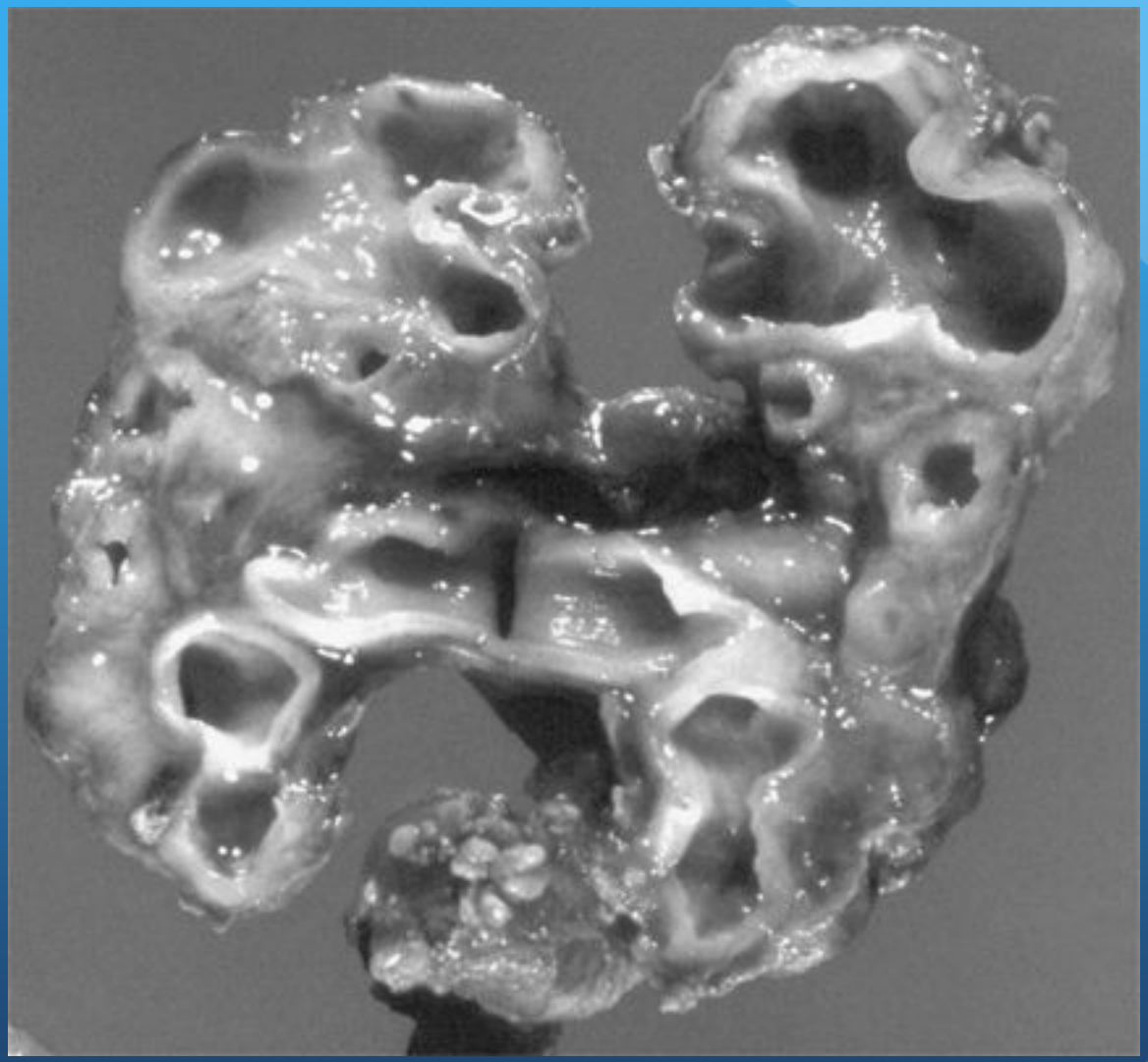
- Renal dysplasia is characterized by the presence of malformed kidney tissue elements
- Dysplastic kidneys are variable in size but most are smaller than normal. Size is often determined by the presence or absence of cysts.
- Renal dysplasia may be unilateral or bilateral

in the past they used to do nephrectomy to the dysplastic kidney because they thought it has a relation to tumor but now we don't do it

- 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.

these type of patient will have lung hypoplasia + renal dysplasia > potter syndrome

dysplasia



- 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

- 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)

- 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 dominant : adult type - they have more extrarenal manifestation > they can have ovarian cyst- liver cyst, cysts everywhere. they also may have aneurysm and mitral prolapse
easier in diagnosis > in each generation they will have a family member with the same problem
autosomal recessive : children - harder to diagnose (skipped generation)

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 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.
- 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 in utero 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

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

communicating cyst > hydronephrosis
noncommunicating > just a cyst

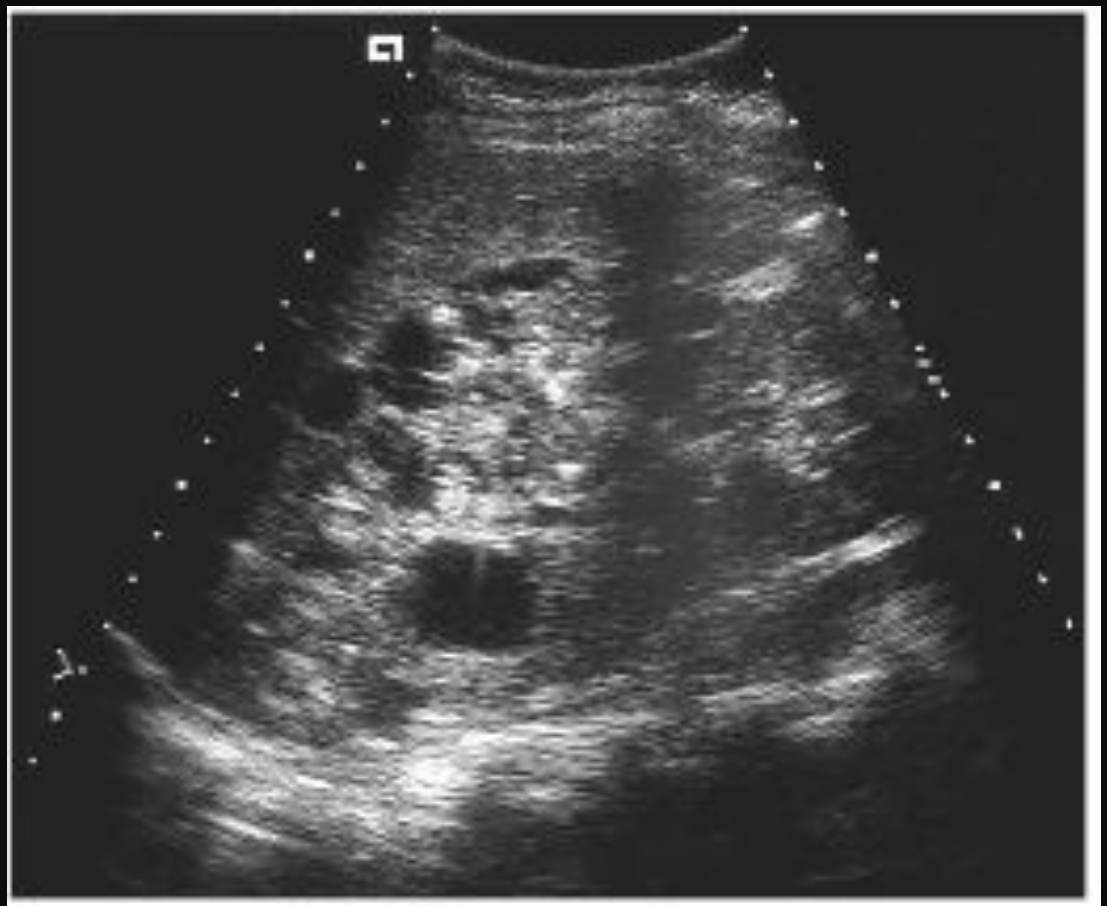
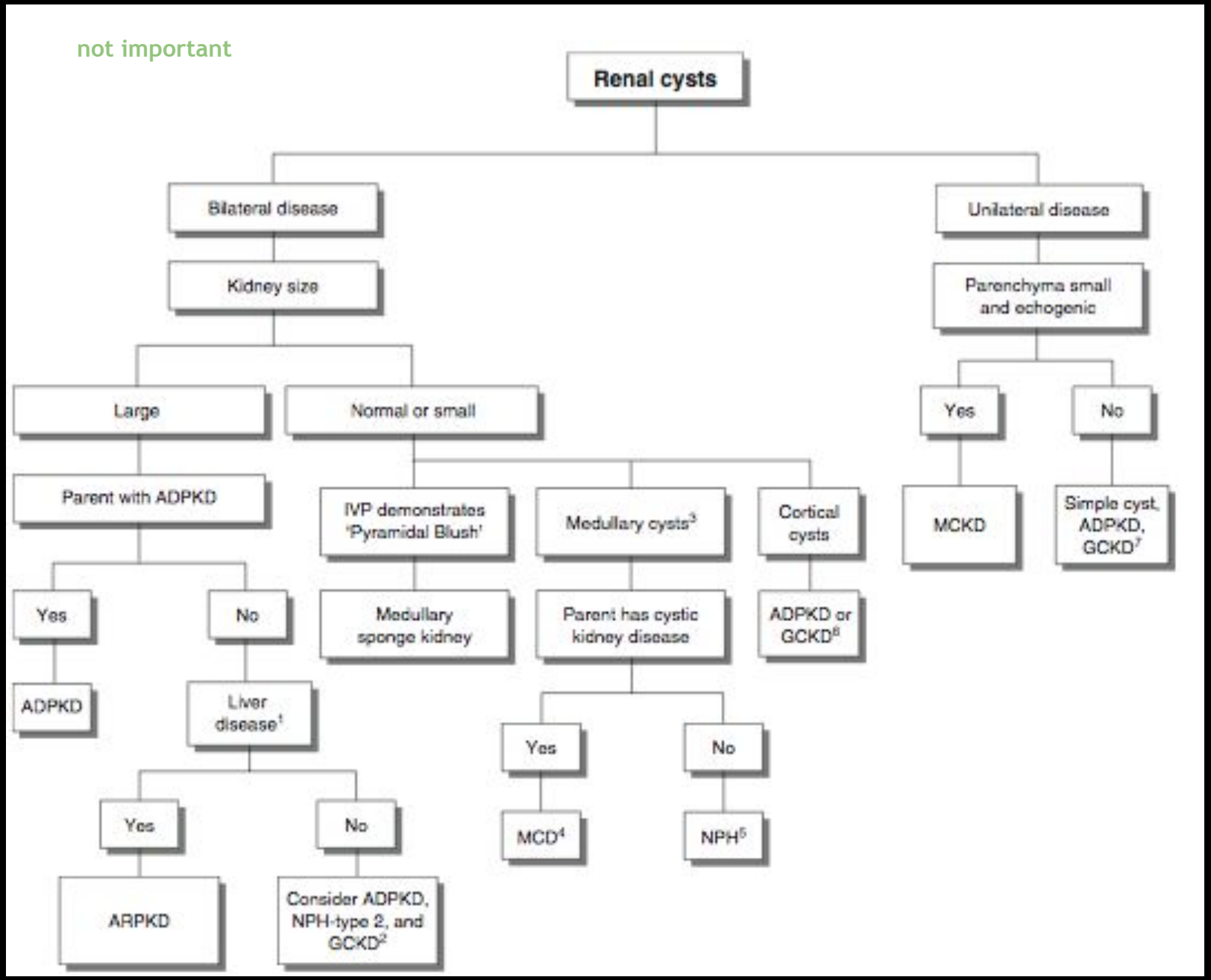


Figure 17.2 Sonogram of a 17-year-old patient with autosomal dominant polycystic kidney disease. Cysts of varying sizes are located in the cortex and the medulla.

not important



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.

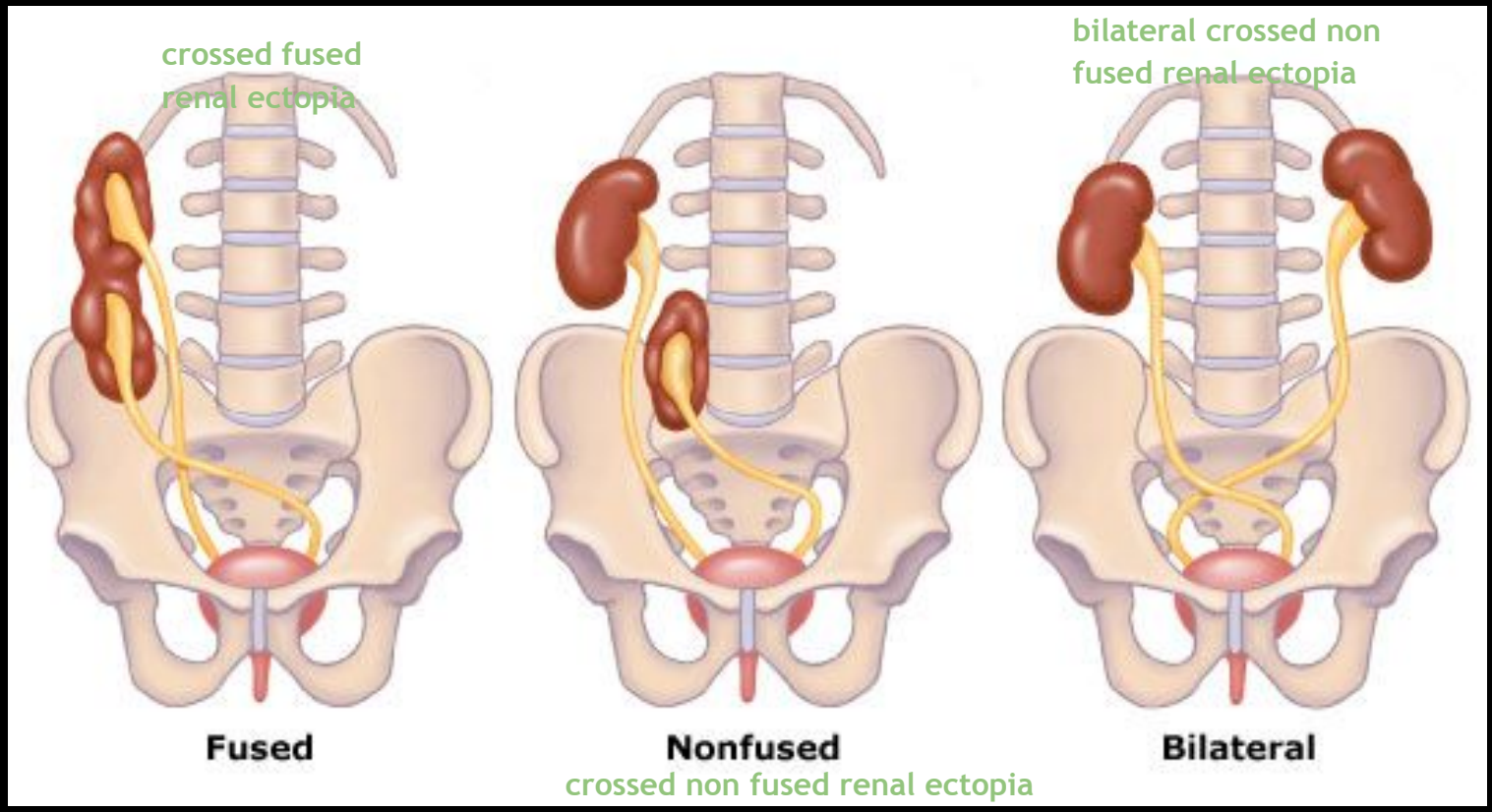
Crossed renal ectopia

- 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).

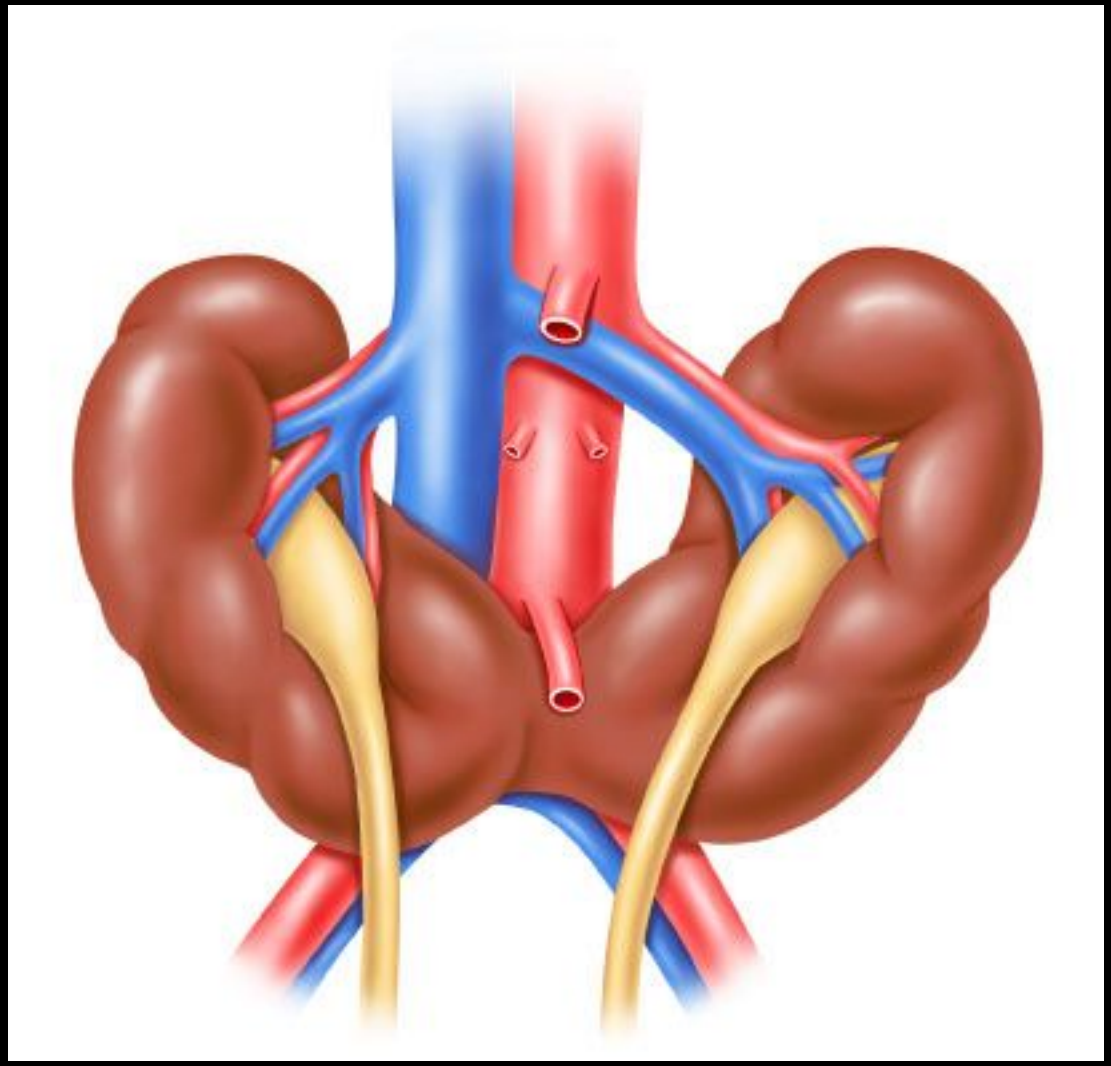
3-Bilateral: Both kidneys are ectopic and cross the midline with the ureters maintaining their normal bladder insertion.


crossed fused
renal ectopia
bilateral crossed non
fused renal ectopia
Fused
Nonfused
crossed non fused renal ectopia
Bilateral

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.

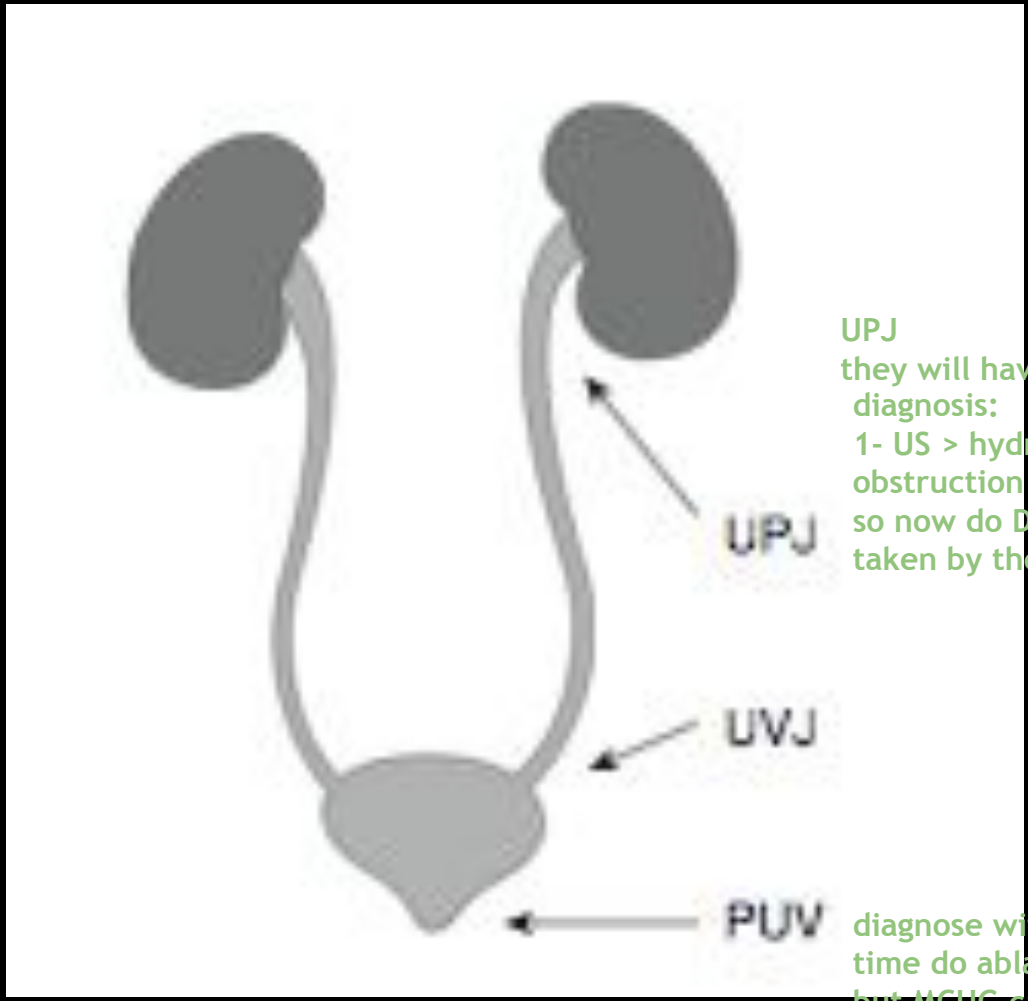
horseshoe kidney
come in association of turner's syndrome pancake kidney > when the fusion occur in the upper< middle and lower parts of the kidney (rare)



- 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.

- Most patients with an ectopic or fused kidney(s) are asymptomatic and are diagnosed coincidentally, often by antenatal ultrasonography.
- 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.

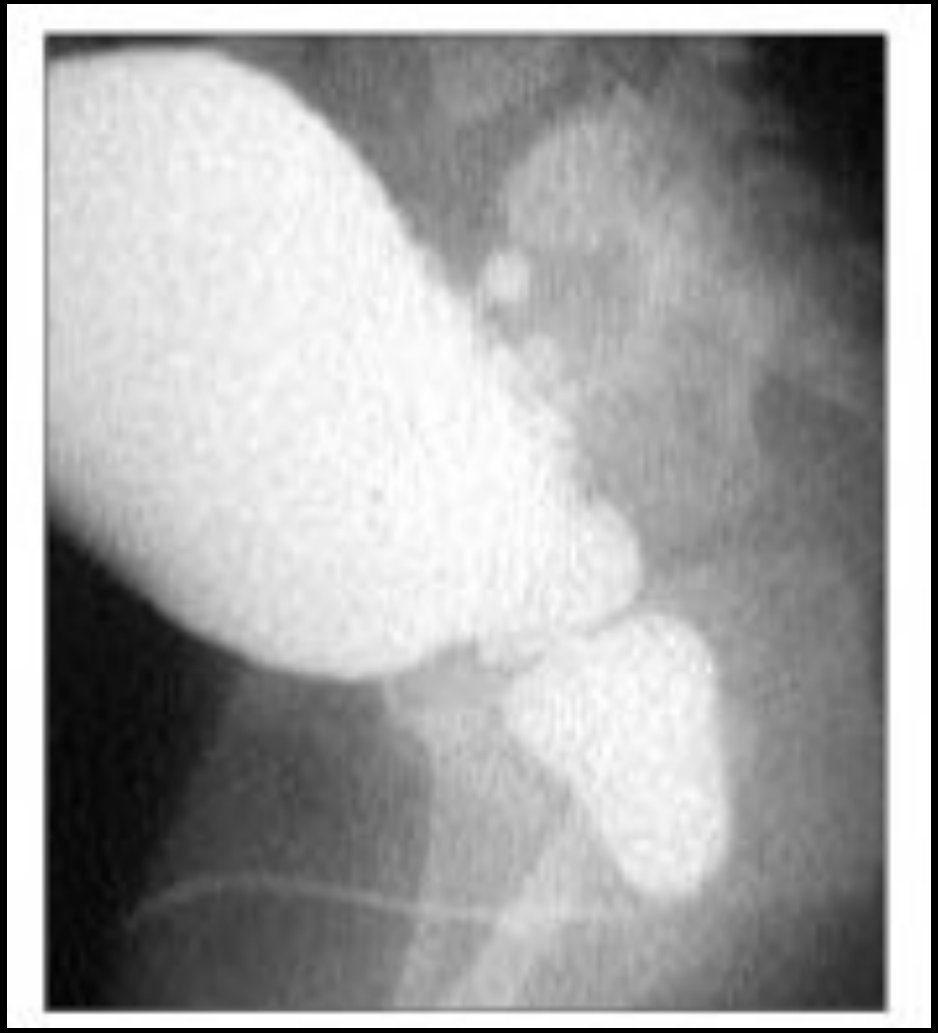
B-Ureter & Bladder

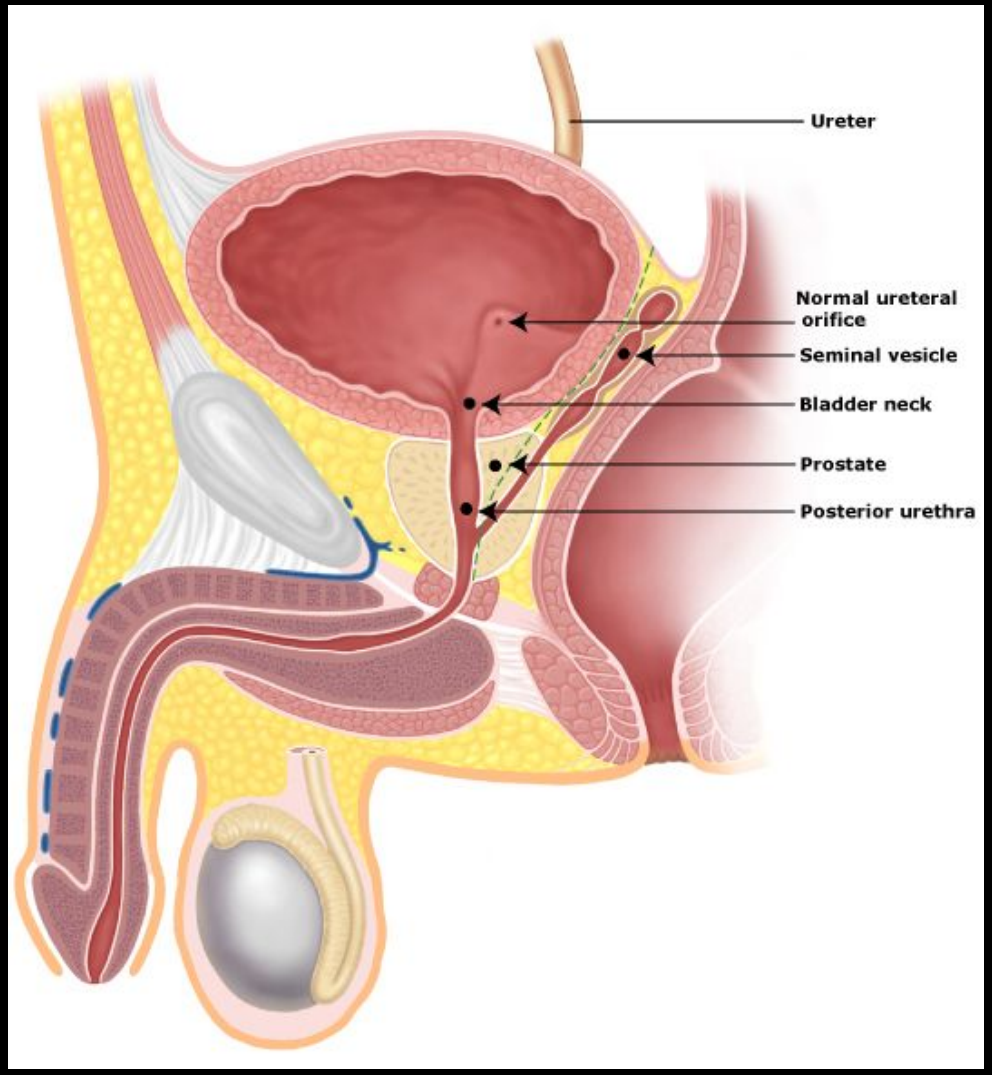


UPJ
they will have hydronephrosis
diagnosis:
1- US > hydronephrosis only do VCUR > no r
obstruction
so now do DTPA or MAG3 (a dye injected in
taken by the kidney but will not be execrat

diagnose with scope and in the same time do ablation to the valve to treat
but MCUG can give you a hint

old keyhole sign
proximal dilatation

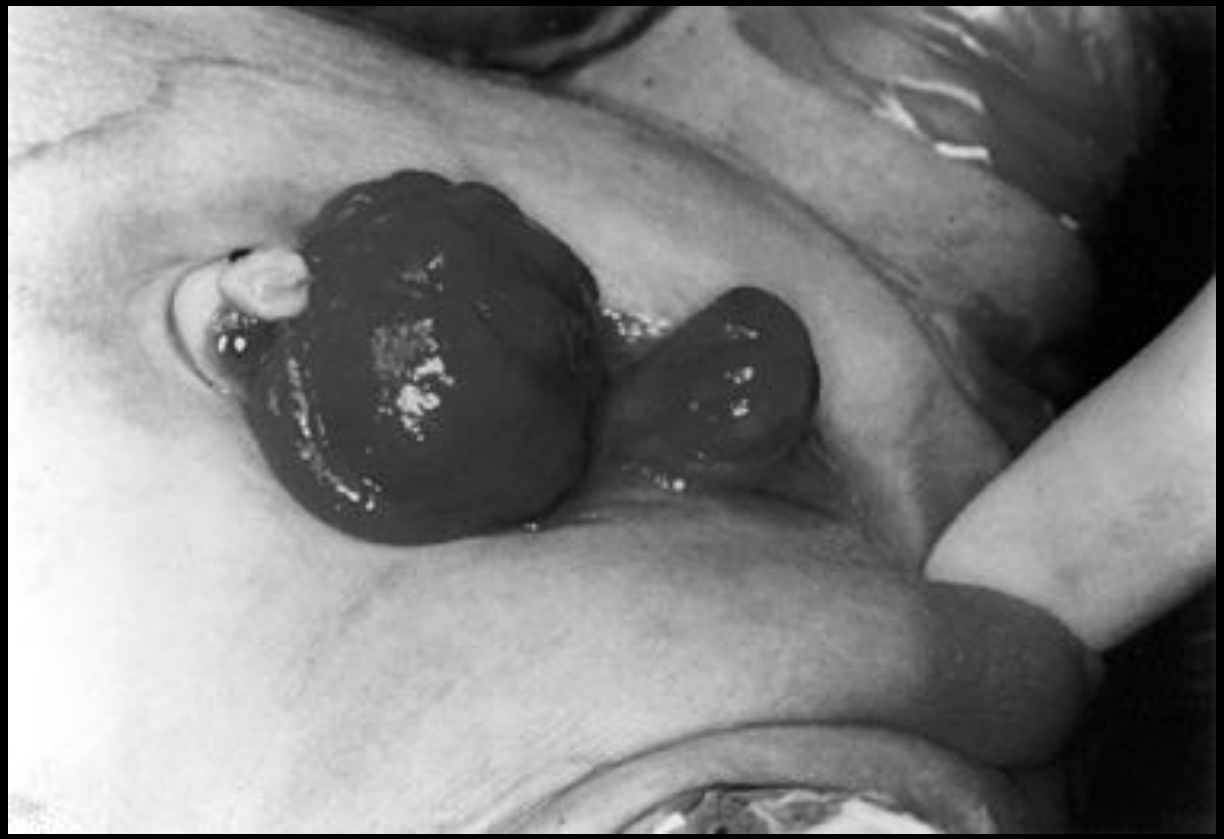




Location of ectopic ureteral orifices in boys

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



bladder exstrophy


Urinary Tract Infection

- Urinary tract infection (UTI) is a leading cause of serious bacterial illness in febrile infants

when the patient is younger UTI will be more dangerous and serious if you didn't treat it early
why?
once it invade the blood it can go to so many places, for example to meninges and causes meningitis, or to joints and causes septic arthritis
or to bone and causes osteomyelitis so in young children we get worry whenever these babies are having bacteremia so treat early.

- Throughout childhood the cumulative incidence is approximately 10% in girls and 3% in boys.

because of short urethra

- Urinary infection usually is ascending, with inoculation of fecally derived organisms from the urethra and peri-urethral tissues into the bladder

- **The most prevalent pathogens in several recent pediatric studies were** for ascending infection

  Escherichia coli (54%-67%)

  Klebsiella (6%-17%)

  Proteus (5%- 12%)

  Enterococcus (3%-9%)

  Pseudomonas (2%-6%)

- 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, and Salmonella; Pseudomonas aeruginosa and Proteus can infect by either route.

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.

clinical presentation varies in different age group
unverbalized children will have general s&s
verbalized children will present UTI symptoms like 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 (sterile) urine sample is fundamental.
- For infants and non–toilet-trained children, the most accurate method of collection is suprapubic bladder aspiration (it is invasive they don't prefer it), however, it rarely is practical.
- Urethral catheterization or spontaneously voided clean midstream samples (usually obtained) are the most reliable alternatives.

why we don't take first part of urine?
it will be contaminated

- 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.

  the problem here that there is chance of contamination, so if it came -ve there is no infection but if it came +ve you don't know if it UTI or contamination

- For toilet-trained children, appropriate cleansing of the perineal/genital area before midstream urine collection is essential.

Urinalysis :

- Although urine culture is the gold standard for UTI diagnosis, more rapid screening may be required for preliminary clinical decision making.
- Urine Gram stain is the single most sensitive and specific test.
- For older infants and children, urine dipstick testing for both both leukocyte esterase 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.

sometimes you have -ve nitrate while patient is still having UTI
because it depend on the organism not all the organism can change nitrate to nitrite
the other reason is : because babies pass urine immediately they don't wait so the nitrate will not have time to react
sometime even in older children the urine is really irritant so the pass urine immediately that's why they have frequency and urgency

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 small children blood culture is mandatory (<3 months)
if they present with meningitis signs and symptoms do lumbar puncture.
in those children you have to do full septic workup

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%

to have multiple colonies we need time but the will pass urine immediately so sometime even if the colonies are low we diagnose UTI if the patients had the classical s&s of UTI

- (don't wait for the result, start empirical treatment(something that cover gram -ve like 3rd generation cephalosporins > cefixime) immediately then change it to definitive treatment to prevent pyelonephritis it may cause renal impairment (by scar)

TREATMENT

Younger than 3 months of age :

- All febrile neonates should be treated with IV antibiotics pending urine, blood, and CSF culture results.
  - if the fever subside ad patient can eat and looks well and with -ve urine culture and can take abx, you can discharge him

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.
  - if the patient is not dehydrated and stable with no vomiting you can treat him as an outpatient with oral abx

- Final antibiotic choice should be based on culture and sensitivity results.
- Prompt antimicrobial therapy generally is believed necessary to diminish risk of renal scarring

if you treat it the patient as outpatient give him an appointment after 3 days to make sure the abx is sensitive to the organism (culture)

UTI RECURRENCE

- 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
- Risk factors identified include dilating VUR, family history of UTI, infrequent voiding, and inadequate fluid ingestion. +hypospadias +uncircumcised and voiding dysfunction especially in girls > they hold urine to much >urine stagnant which is a good media for bacteria > bladder will try to hold urine this will cause thick bladder wall and this will cause discoordination of urine accomodation and also the contraction of the bladder will be disrupted this will cause dysfunction

  and decreased fluid intake will also cause UTI
- Strategies that may help prevent recurrence include management of voiding dysfunction and increased fluid intake.

LONG-TERM OUTCOME

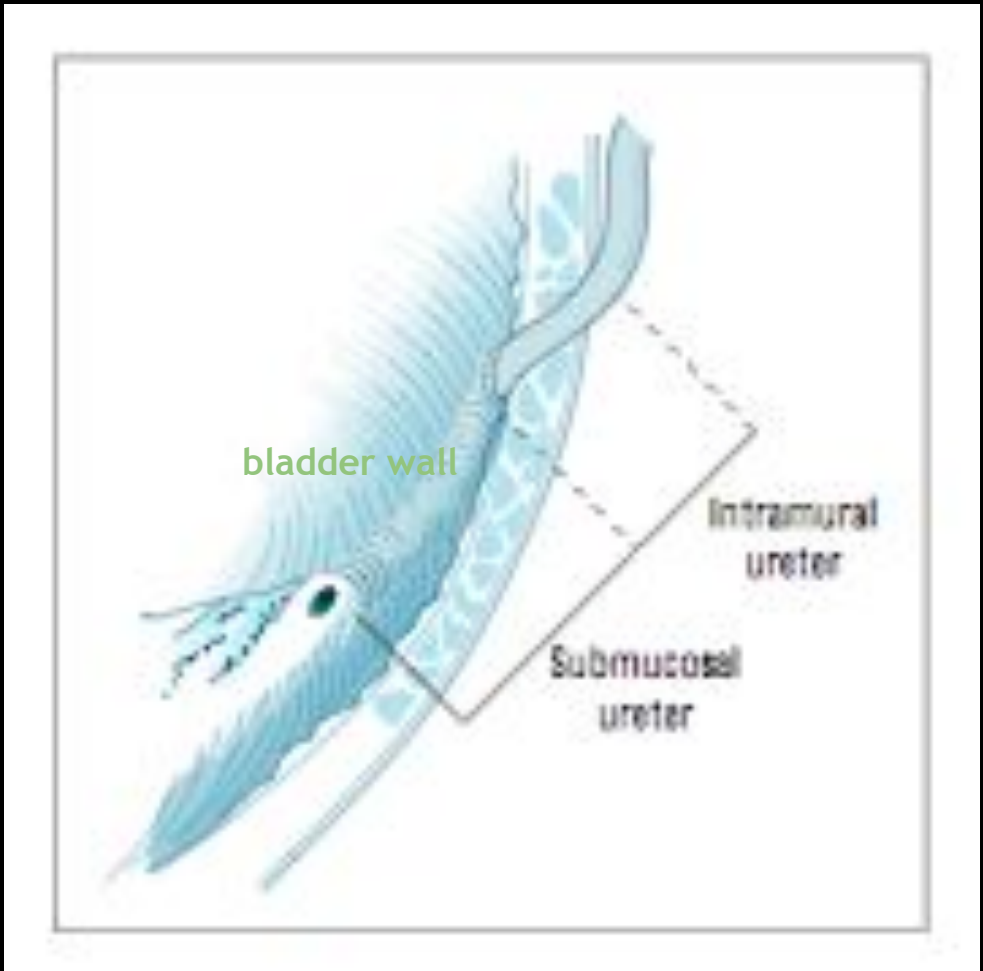
- Approximately 70% of infants and children with their first febrile UTI have pyelonephritis and renal scars may follow in 15% to 30%.
- With timely appropriate therapy most infants and children recover promptly without major long-term sequelae, but a small number are at risk for significant morbidity,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

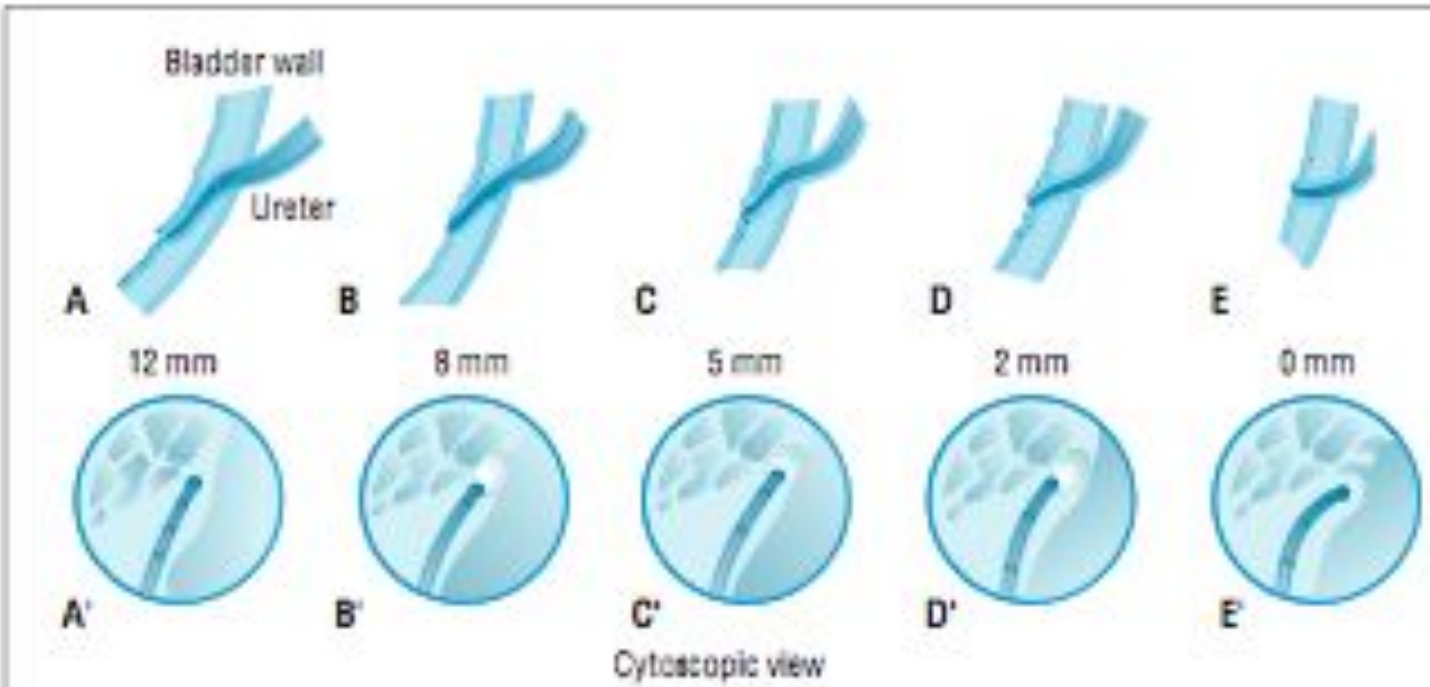
Vesicoureteral Reflux

- 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.

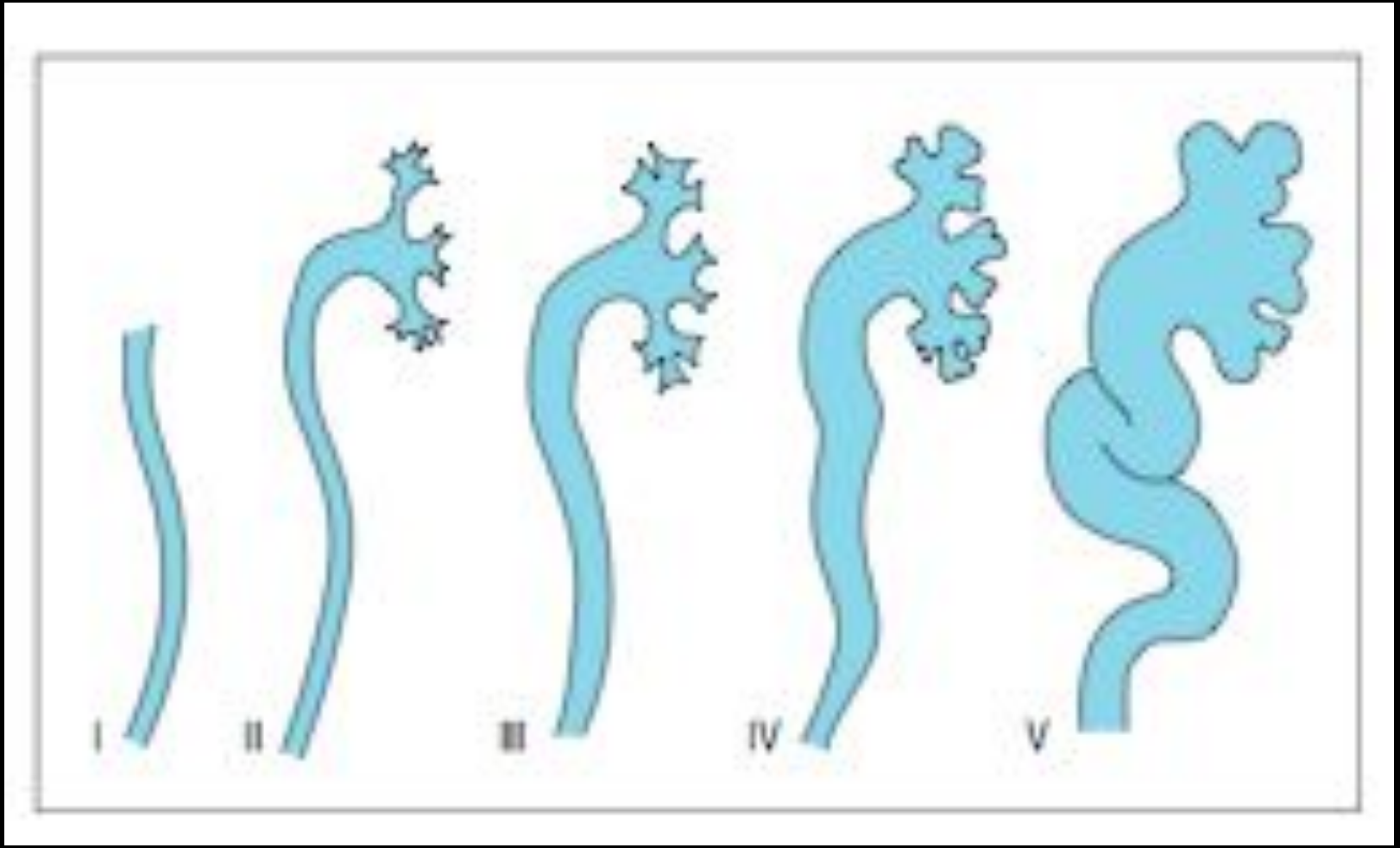
- The association of VUR and predisposition to UTI is well established.
- Functional anatomy the UVJ lacks a traditionally defined valve to prevent retrograde flow of urine from the bladder into the ureter.
- The antireflux mechanism operative at this location is dependent on the unique anatomic configuration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

normally the ureter will go through bladder wall so when the bladder is full of urine this will cause pressure on the ureter which will prevent the urine reflux this is a functional valve not a real valve




Bladder wall
Ureter
A
B
C
D
E
12 mm
8 mm
5 mm
2 mm
0 mm
A'
B'
C'
D'
E'
Cytoscopic view

there is 5 grades of of VUR, we diagnose it using VcUG
we insert catheter to the bladder then we inject dye to fill the bladder (full) after that with older children, they will be asked to pass urine to increase the pressure inside the bladder and we detect the retrograde flow



grade 1: retrograde of urine to half of the ureter or more than half
grade 2: tell the pelvis
grade 3: tell the pelvis + ureter dilatation
grade 4: dilatation + vertoucity
grade 5 : hydronephrosis + complete blunting of 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

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

doctor went through it

Secondary

Bladder outlet obstruction:

- Posterior urethral valves
- Bladder neck obstruction
- Severe urethral stricture

Neurogenic bladder:

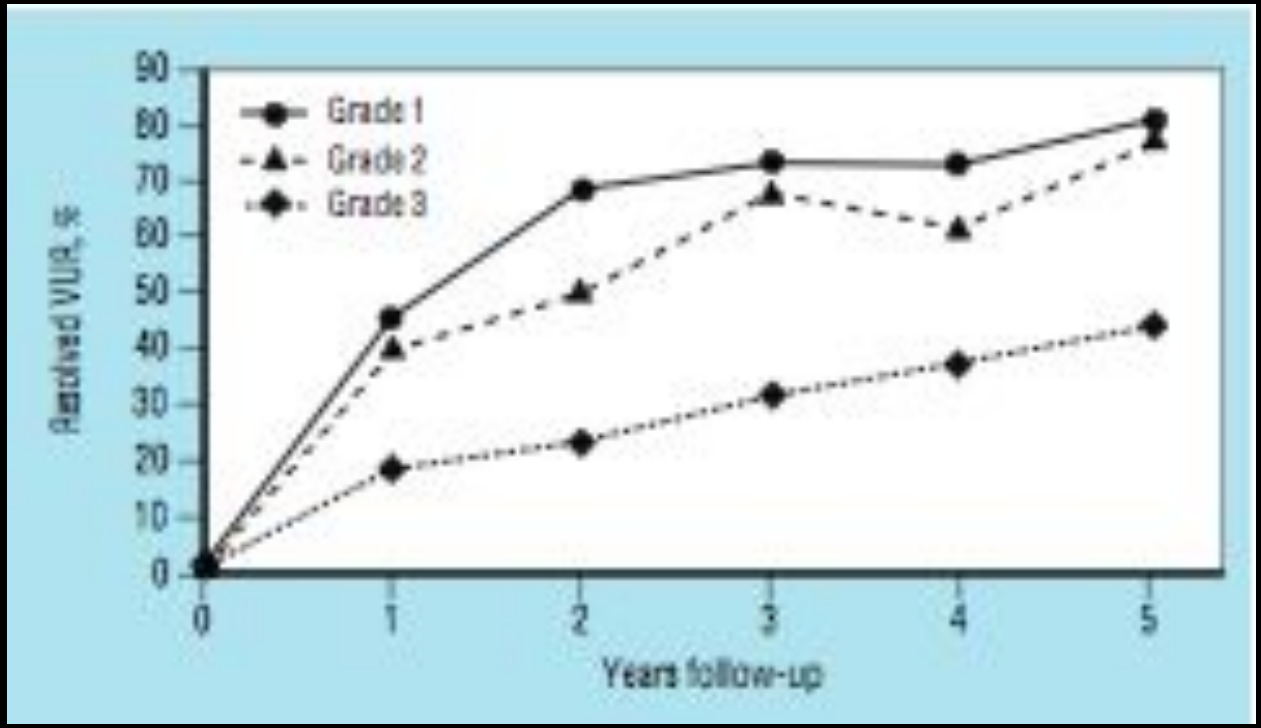
- Spina bifida–meningomyelocele

Chronic bladder inflammation

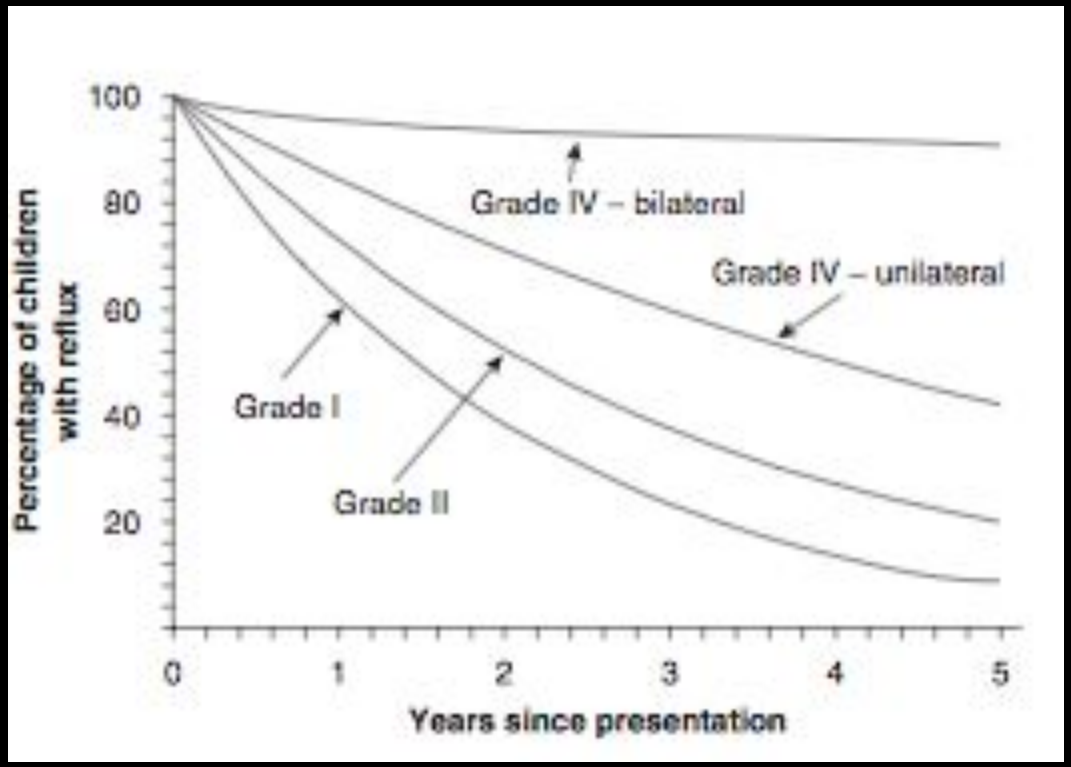
Urinary tract infection

Traumatic:

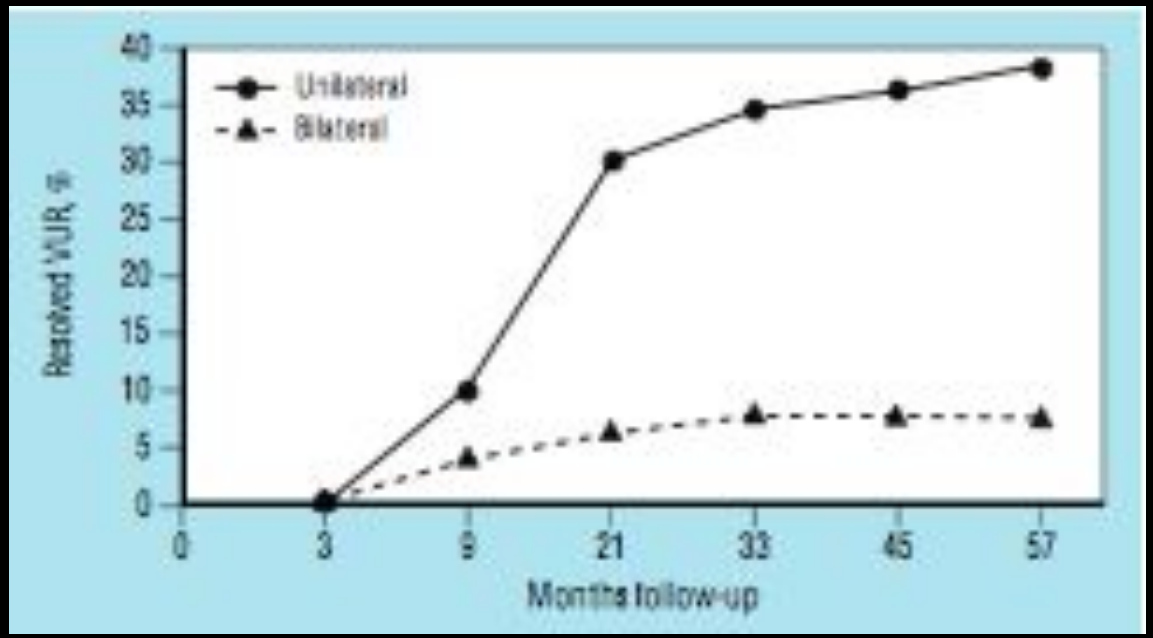
- Following bladder surgery
- Following ureteral calculus extraction



VUR could disappear with time, (when the child grow up and get taller the angle of the ureter changes and this will resolve VUR.



the probability of resolution depend on the grade
lower grade = high resolution rate
and also uni/bi lateral play a role in the resolution
unilateral = high rate of resolution than bilateral

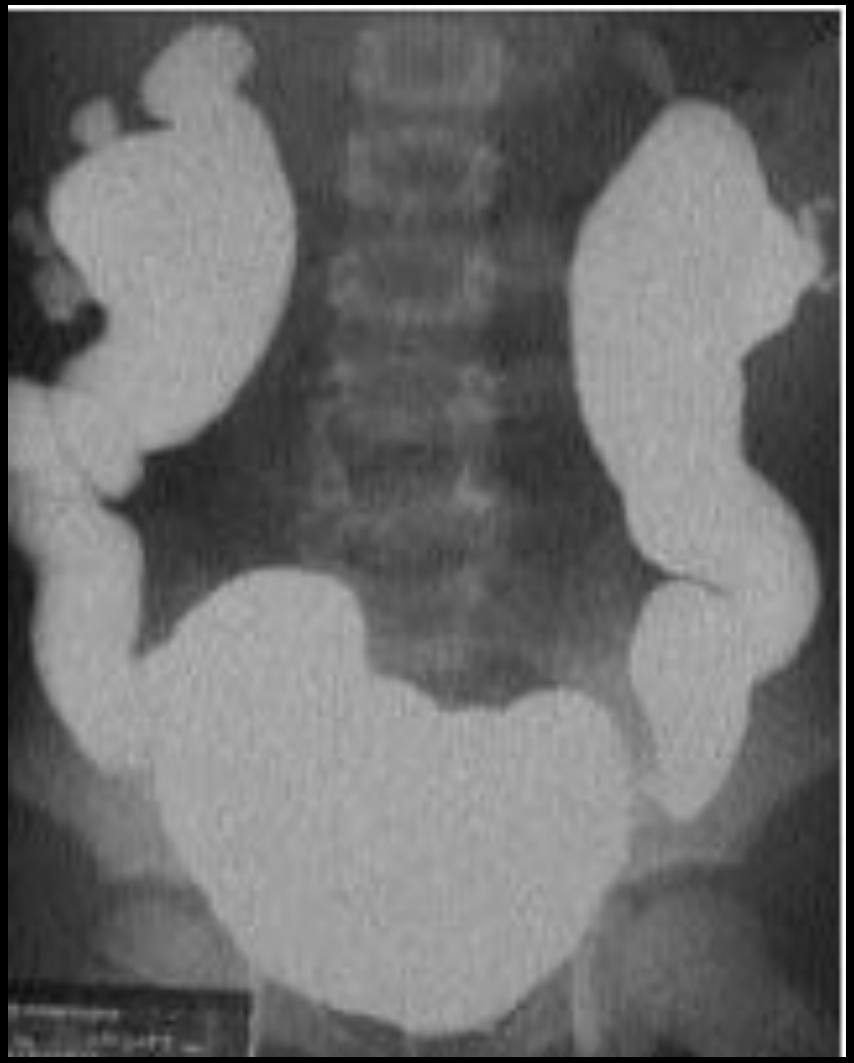


Unilateral vs Bilateral Resolution of grades III to V vesicoureteral reflux (VUR)

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

VCUG IS A DYNAMIC STUDY sometimes we can use US
don't use VCUG unless the urine culture is -ve because if you do it the infection will go to the kidney causing pyelonephritis

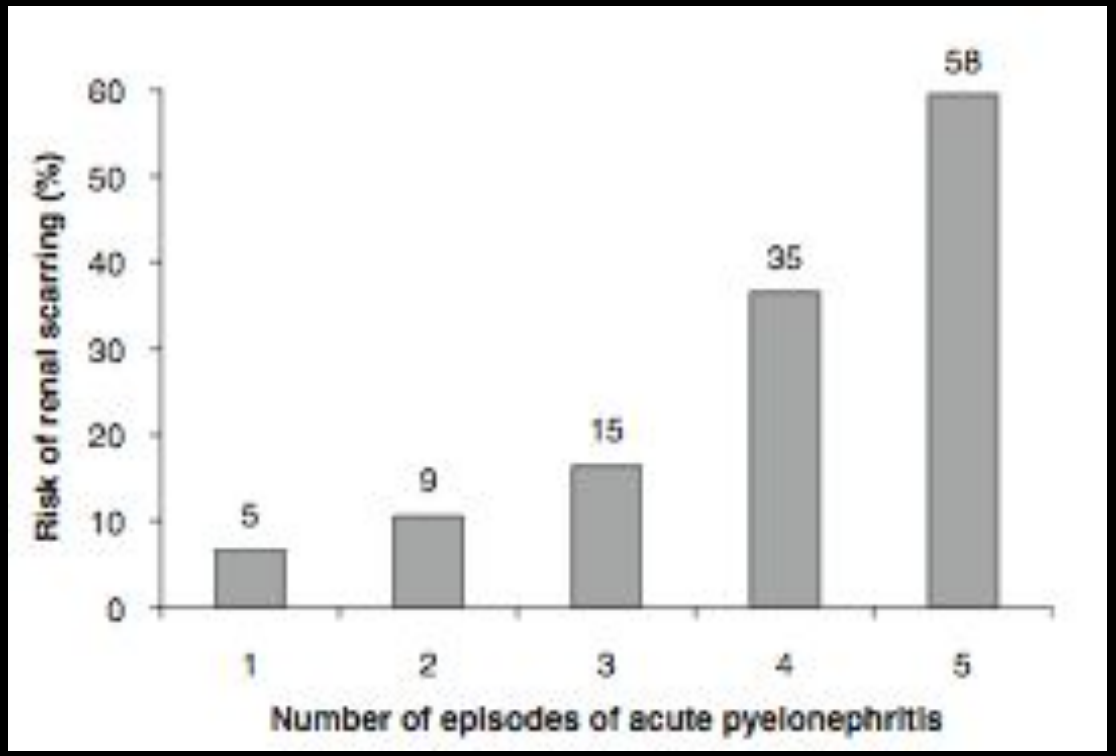
this is a VCUG, you can see bilateral grade 5 VUR



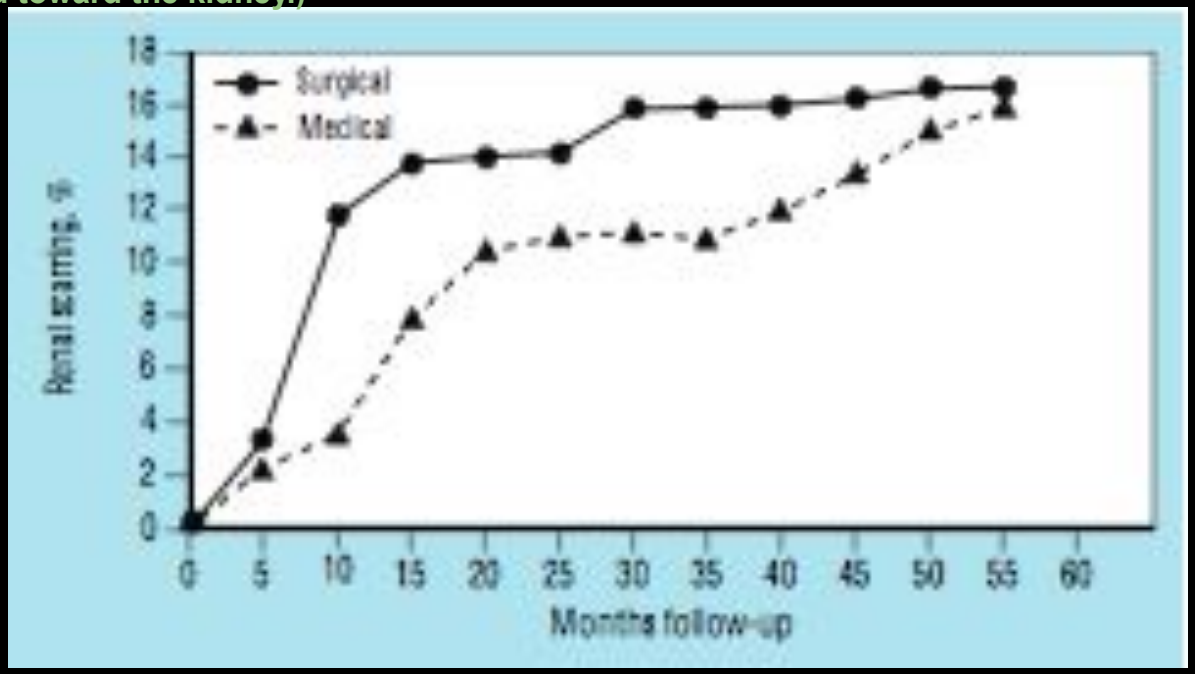
Renal scarring and VUR :

- VUR is well recognized to be associated with renal scar formation.
- 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.

as the number of pyelonephritis increases the risk of scarring increases as well
so you need to treat it early to prevent scarring



treatments :
1- medical > give prophylactic ABx for 2 years then repeat VCUG (lower grades), for the prophylactic dose we give one third of the treatment dose usually we use nitrofurantoin (bad taste they can't tolerate it) so we give bactrien as replacement also we can use cephalosporins(1st or 2nd generation) but they develop resistance easily
start prophylactic ABx on all patients and wait for the resolution
but you have to tell the patients with higher grades or bilateral VUR that most likely will not work and they may need surgery, the aim of of ABx is to prevent pyelonephritis and scarring.
2- surgical intervention
higher grade of VUR and bilateral > unlikely to resolve by itself
(ureteral reimplantation - the other surgery is less invasive (injects a small amount of gel-like material under the opening of the ureter. The injected material partially closes the opening and prevents the urine from going backward toward the kidney.)



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