Childhood disorders of the urinary tract

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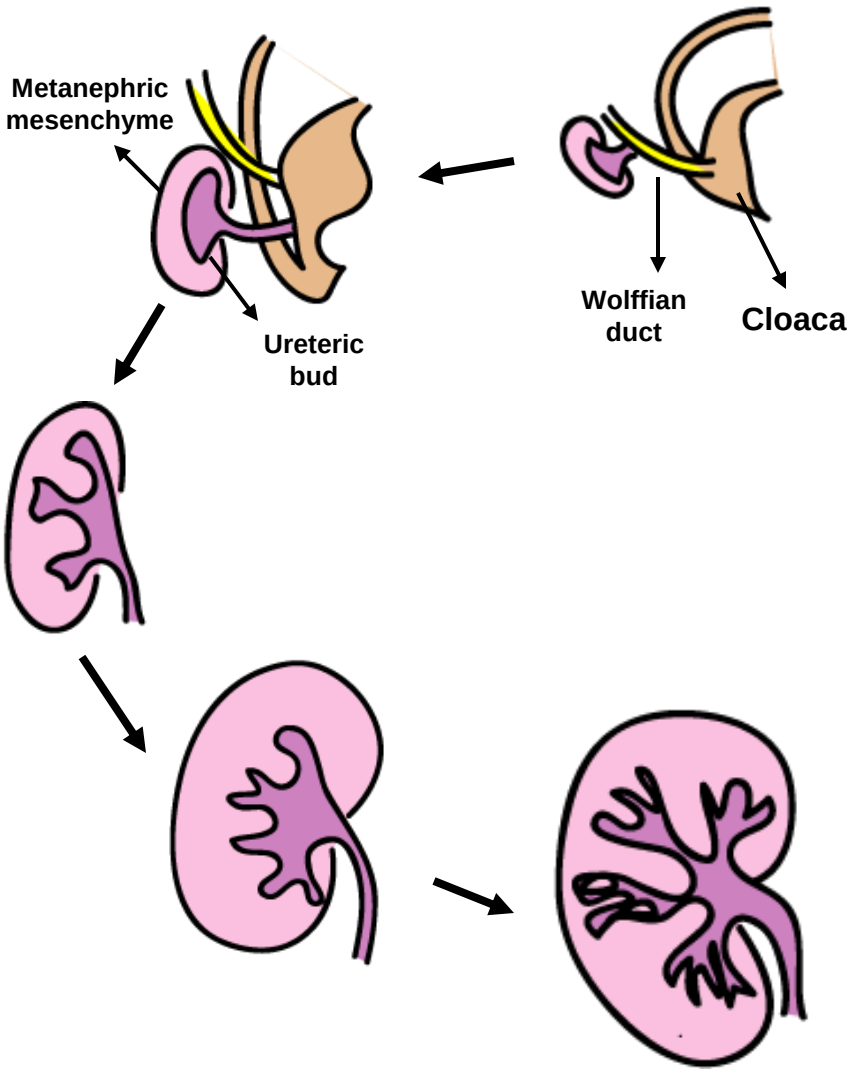
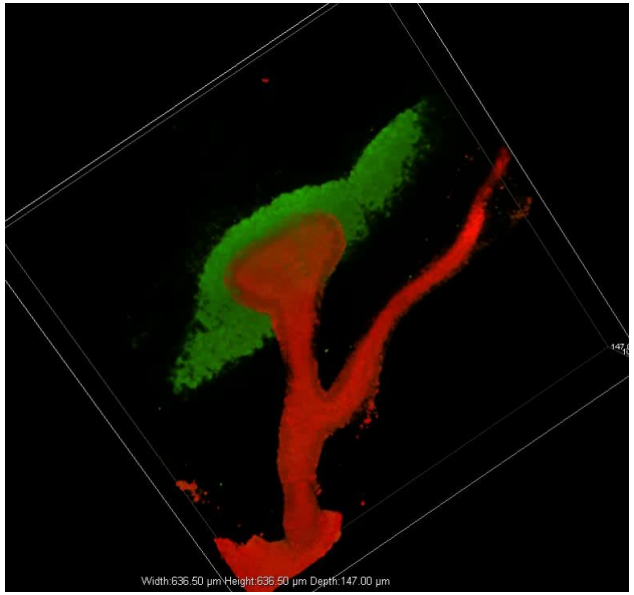
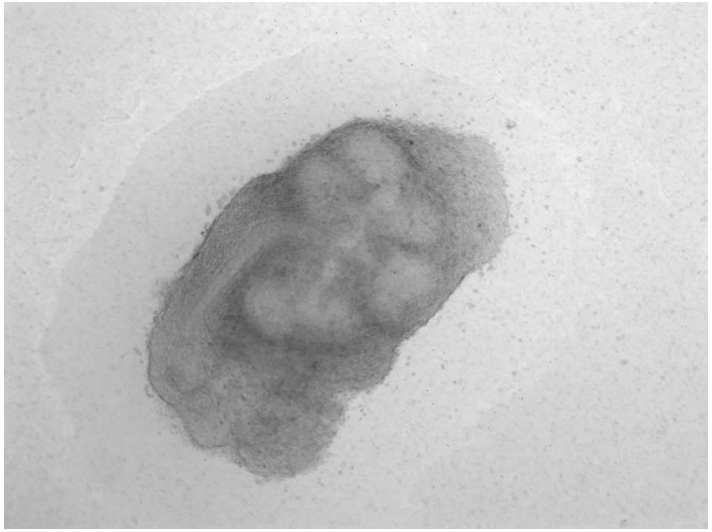
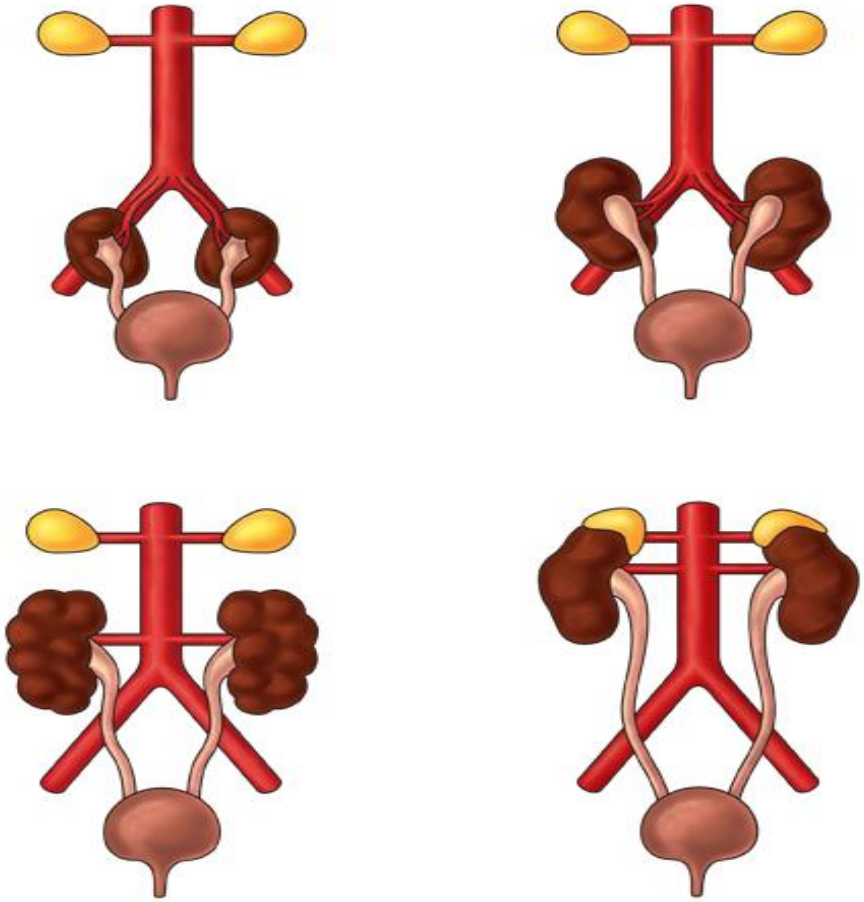
Kidney development







Migration of kidneys



Major disorders of the urinary tract

- Obstruction
- Reflux
- Voiding dysfunction

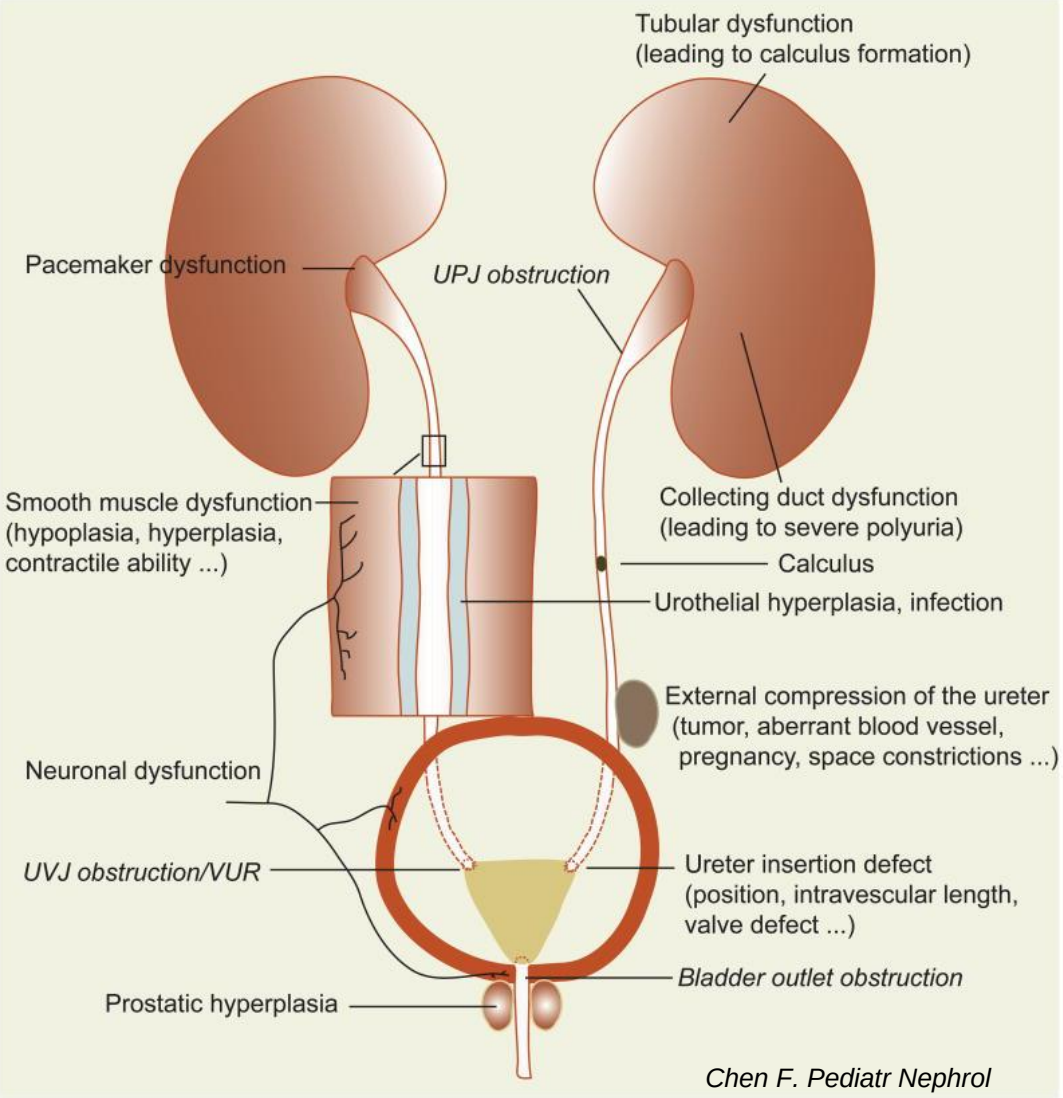
Causes of urinary tract obstruction

Definition: Impaired urinary drainage

Causes:

1. Congenital : most common cause in the pediatric population (1:1000 live births)

2. Acquired (stones, trauma, clots, tumor)



Chen F. Pediatr Nephrol (2009) 24:1621–1632

Clinical presentation

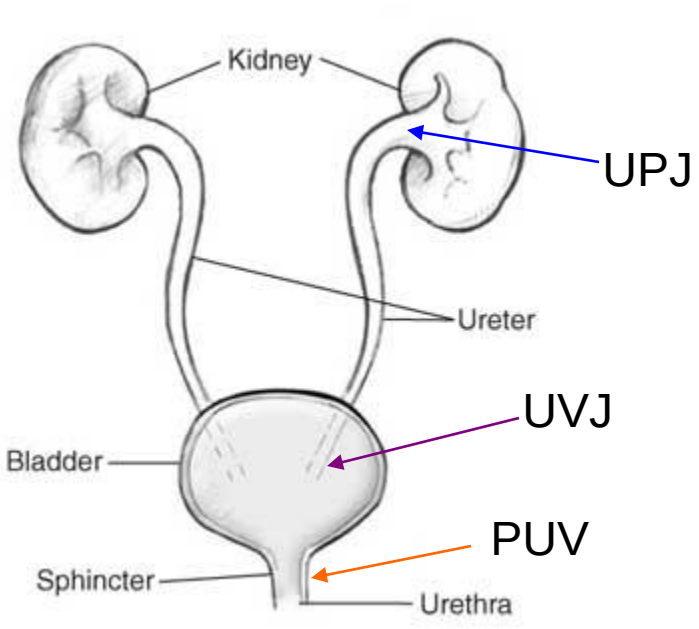
- Palpable abdominal mass (m/c in children)
- In boys, obstruction below level of bladder results in palpable walnut-sized mass representing bladder above the pubic symphysis
- Flank pain (m/c in adults), incontinence, urinary tract infection (due to urinary stasis), hematuria
- Urinary stream may be weak with bladder outlet obstruction
- Resulting renal insufficiency can manifest as failure to thrive, vomiting, diarrhea

Common sites of congenital urinary tract obstruction

• UPJ: Ureteropelvic junction (ureter-renal pelvis) 1:1500, m/c cause of hydronephrosis detected prenatally

• UVJ: Ureterovesicular junction (ureter-bladder) 20% of prenatal hydronephrosis

• PUV: posterior urethral valves (urethra: bladder outlet) 1:5000



UPJ obstruction

- m/c obstructive lesion

- Male: female ratio 2:1

- Presents as:

1) Fetal hydronephrosis on maternal US
2) Palpable renal mass in newborn or infant
3) Abdominal, flank or back pain
4) Febrile UTI
5) Hematuria after minimal trauma

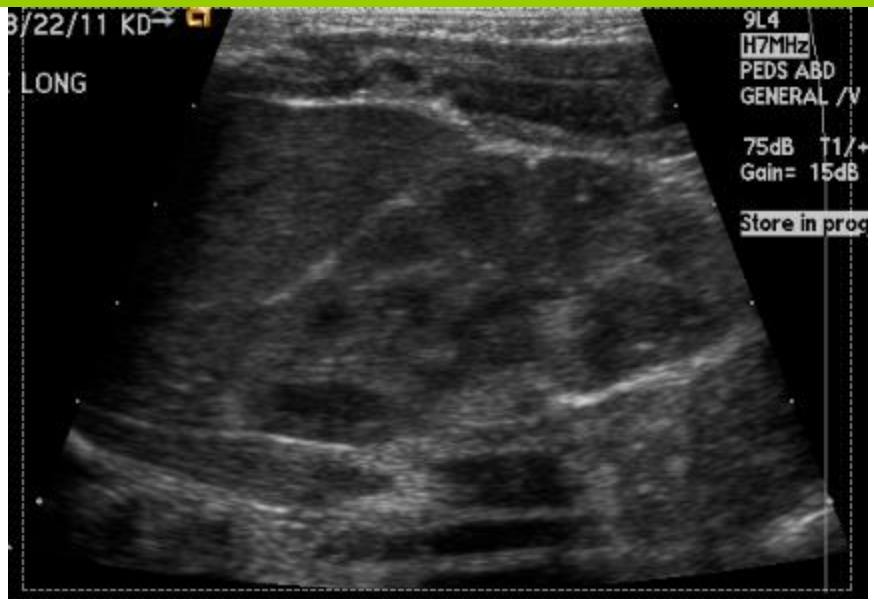
- 10-15% of patients have ipsilateral vesicoureteral reflux

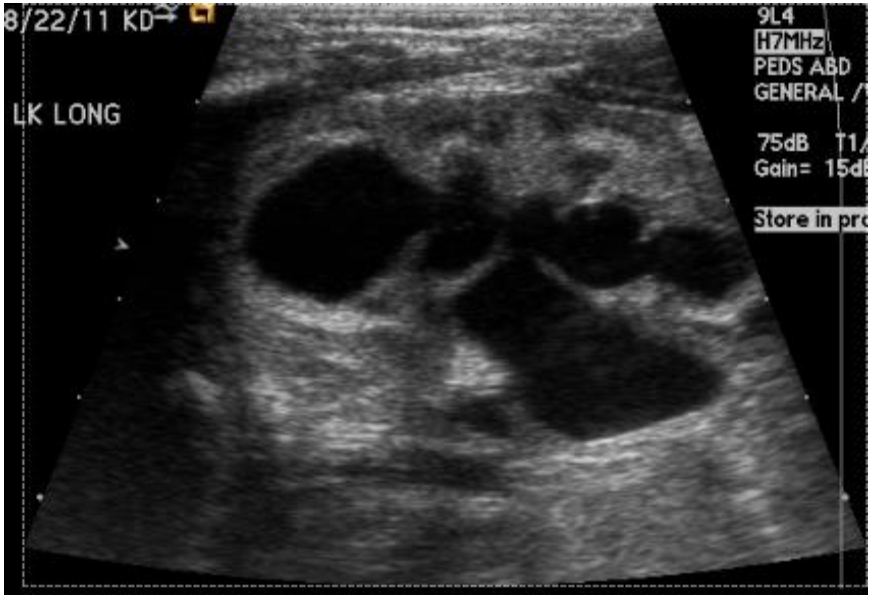
Posterior urethral valves

- m/c cause of severe obstructive uropathy
- Prevalence: 1/5000 males
- Tissue leaflets fanning distally from the prostatic urethra to external urinary sphincter
- 50% of patients have vesicoureteral reflux
- 30% of patients progress to end stage renal disease

Imaging studies: Ultrasound

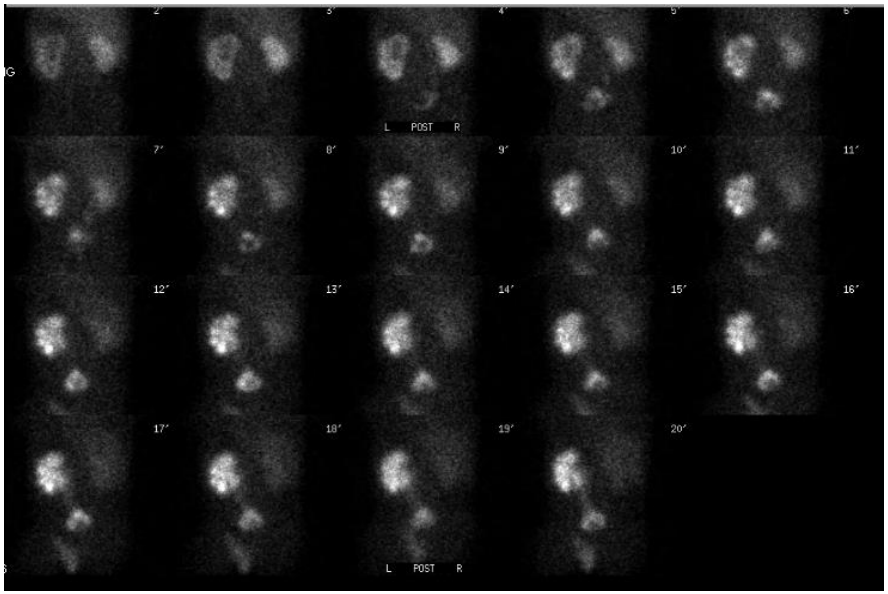
- Dilated urinary tract
- May persist after surgical correction of obstruction
- In acute or intermittent obstruction, dilatation of the collecting system may be minimal
- Dilated urinary tract may also result from VUR, abnormal formation of urinary tract, polyuria

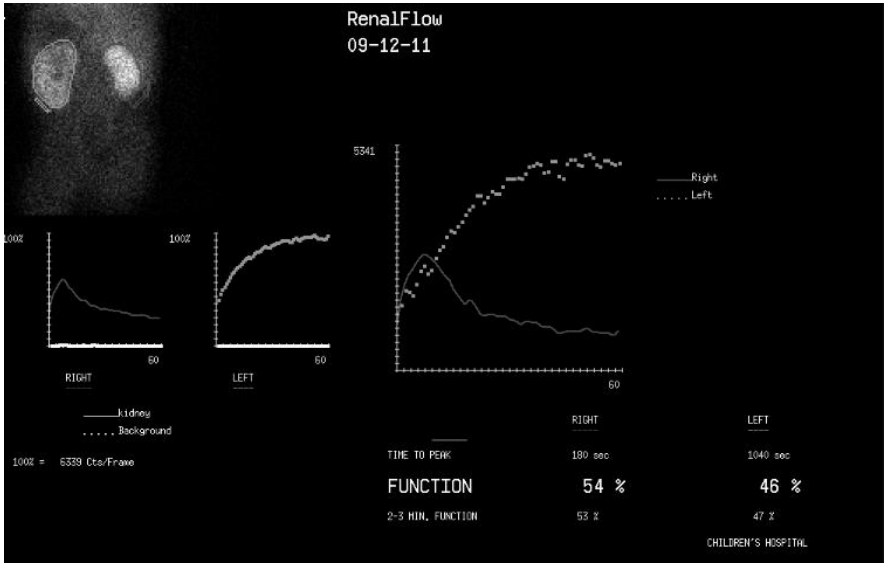




Imaging studies: MAG3 scan

- MAG-3 (mercaptoacetyl triglycine) scan determines the relative contribution of each kidney to total renal function
- Shows location of functional obstruction
- MAG-3 excreted by renal tubular secretion
- Small dose injected intravenously
- During first 2-3 mins, renal parenchymal uptake analyzed and compared
- After 20-30 mins, furosemide given and rapidity of drainage to the bladder analyzed
- Half of the radionuclide should be cleared from the renal pelvis within 10-15 mins
- >20mins indicate obstruction

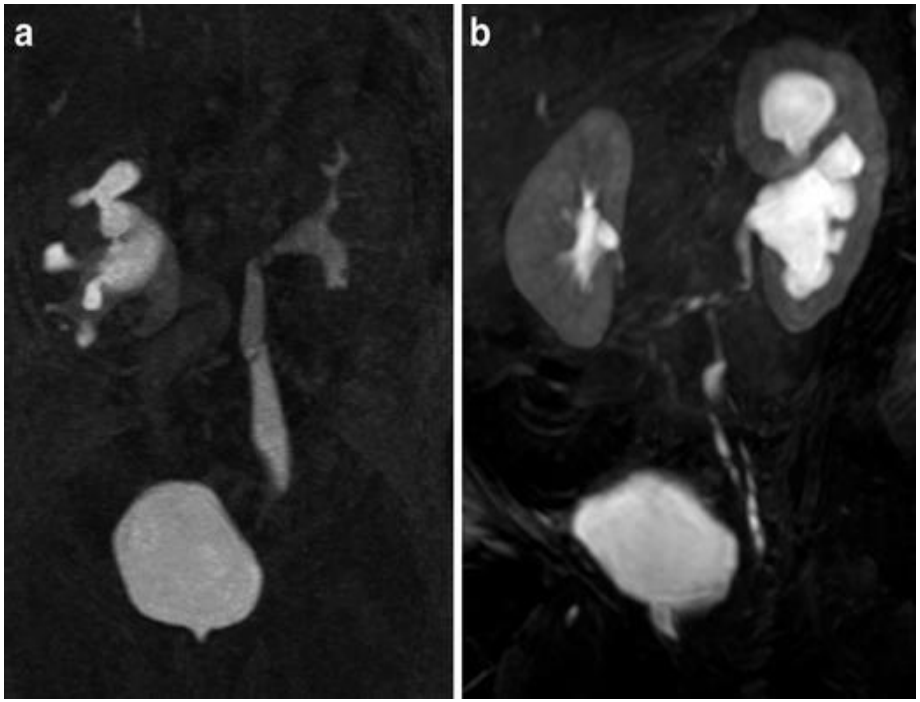




Other imaging studies

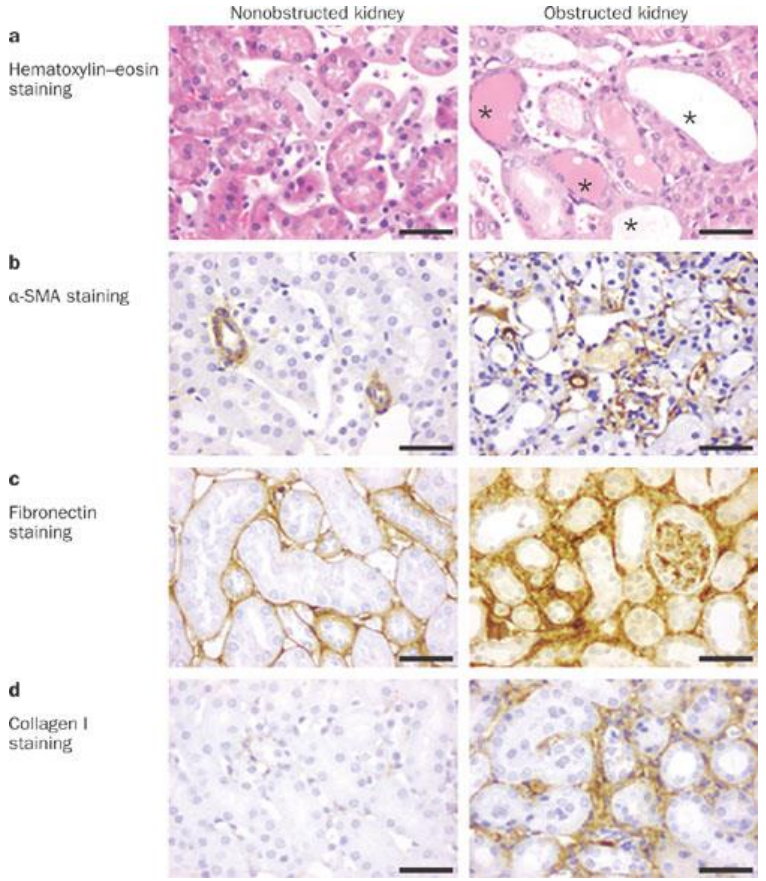
- Computed Tomography:
  - Suspected ureteral calculus
  - Location of calculus and presence of proximal hydronephrosis

- MR urography
  - complicated anatomy (duplicated systems)



Pathophysiology of obstructive nephropathy

- Progressive destruction of tubular epithelial cells by atrophy
- Expression of epidermal growth factor reduced and TGF-β (pro-apoptotic factor) increased
- Infiltration of interstitium by macrophages and fibroblasts
- Activated macrophages induce apoptosis and interstitial fibrosis
- Mechanical stretching of tubular cells and release of cytokines lead to transformation of renal tubular epithelial cells to myofibroblasts leading to interstitial fibrosis
- Tubular atrophy and interstitial fibrosis- result in impaired renal growth



Grande M T and López-Novoa J M (2009) *Nat Rev Nephrol*

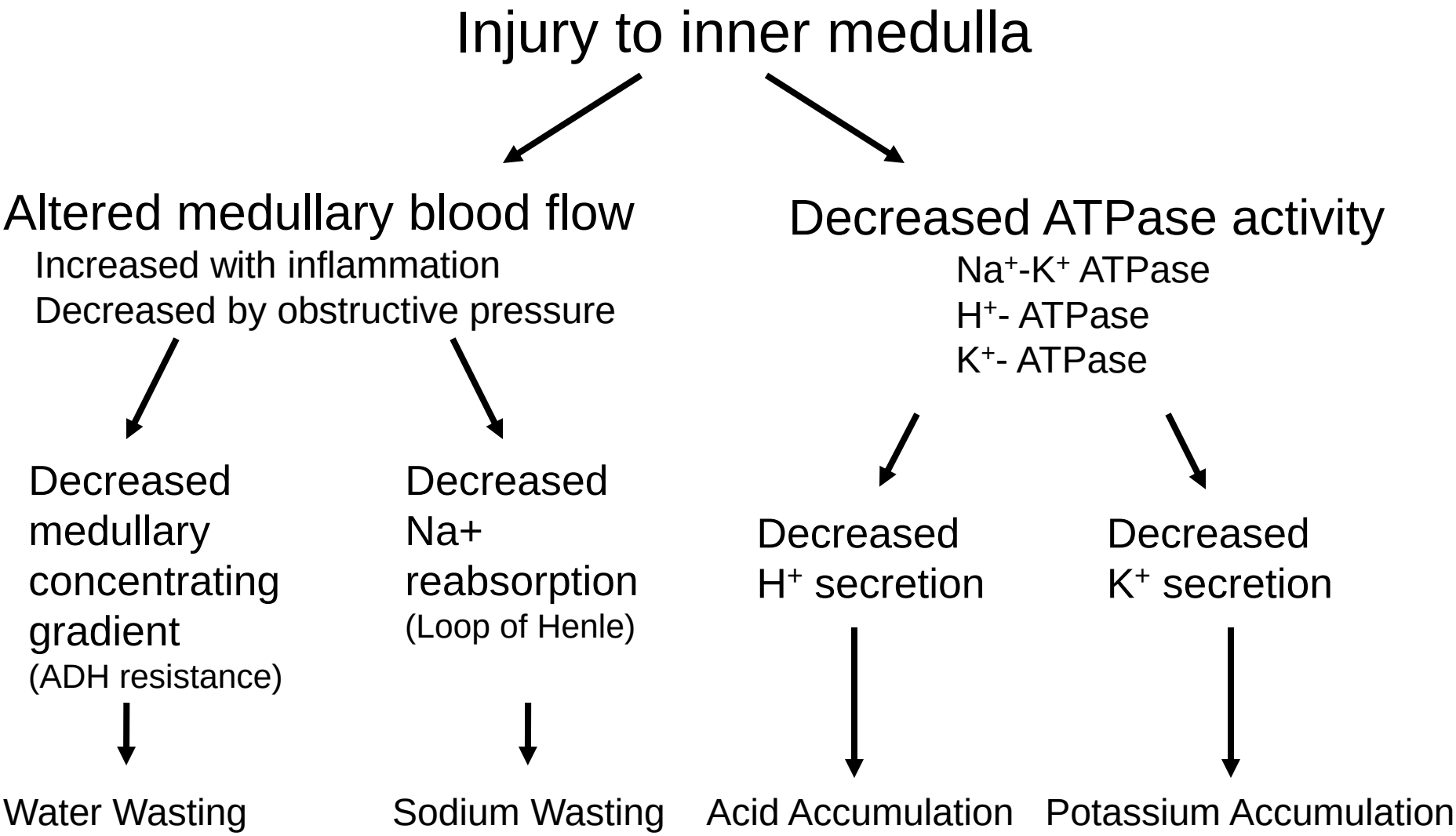
Pathophysiology of obstructive nephropathy

- Loss of nephrons
- Temporary complete obstruction during nephrogenesis can permanently reduce nephron number
- Adaptive growth by remaining nephrons
- Opposite kidney shows compensatory hypertrophy

Impact on tubular function

- Downregulation of sodium transporters, aquaporins, and distortion of medullary architecture lead to reduced concentrating ability
- “postobstructive diuresis”- follows relief of urinary tract obstruction
- Since positive sodium balance required for normal somatic growth in infancy, impaired growth may occur with reduced renal sodium concentration
- Infants may need sodium supplementation to prevent volume contraction and to optimize somatic growth
- Abnormal distal tubular potassium and hydrogen ion secretion from type 4 renal tubular acidosis can limit growth (hyperkalemia and metabolic acidosis)

Summary of pathophysiology



Prenatal management

- Fetuses with unilateral hydronephrosis should have serial US; not candidates for prenatal surgical intervention
- Fetuses with PUV are at risk for pulmonary hypoplasia
- Prenatal intervention by inserting a catheter that diverts urine into amniotic space: results are largely poor, with high incidence of displacement of catheter, amnionitis and fetal loss

Postnatal management

- Unilateral obstruction:

- mild obstruction: in many cases spontaneously resolves with time, so serial US obtained

- moderate to severe: controversy regarding indications for early operative correction vs long-term observation

- Difficulty of repeated US and MAG3 scans- noncompliance with imaging studies may lead to irreversible kidney damage

- Surgical correction of UPJ obstruction: pyeloplasty

Postnatal management

- Bilateral hydronephrosis: VCUG should be done
- Once PUV diagnosed, No.5 or 8 French feeding tube should be inserted for decompression
- Transurethral ablation of valve leaflets endoscopically
- If urethra too small for ablation, temporary vesicostomy done; when child is older, valves are ablated and vesicostomy closed
- Many cases of bladder outlet obstruction associated with reflux, so treat with prophylactic antibiotics

Postnatal management

- Annual renal US
- Blood pressure measurement, urinalysis, electrolytes, BUN, Cr
- Adequate hydration for patients with polyuria
- Oral bicarbonate therapy for patients with renal tubular acidosis

Long-term outcome

- Most patients with PUV diagnosed in the perinatal period develop renal insufficiency by 10 years of age despite correction of the obstruction
- Obstruction leads to bladder detrusor muscle hypertrophy resulting in a thick-walled, trabeculated bladder
- Eventually, an imbalance of muscle and blood vessel growth, as well as pressure damage to nerves cause bladder to become progressively atonic with increasing residual urine
- This bladder structure and function impairment leads to urinary stasis and therefore recurrent infection and back pressure to kidneys
- Polyuria due to concentrating defect
- Incontinence: results from uninhibited bladder contractions, poor bladder compliance, bladder atonia, bladder neck dyssynergia, polyuria
- Hypertension can develop with progressive interstitial fibrosis and glomerular sclerosis

Case

Chief complaint: lethargy, pale-appearance

- HPI: Pt is 1 year old male who has had failure to thrive since infancy. He has also had recurrent episodes of vomiting. Born at 36 weeks gestation. Mother had oligohydramnios.

- Physical exam: Wt 8kg. T 36.4^0C, BP 95/67, PR 110

- Abdominal mass palpable below the umbilicus

Case

- Labs:
  - Na 125, K 6.0, Cl 110, HCO_3 13, Ca 7.2
  - BUN 48, Creat 4.6
  - Urinalysis: S.G. 1.005, pH 7.5, glucose (-), protein (tr), and heme (-).

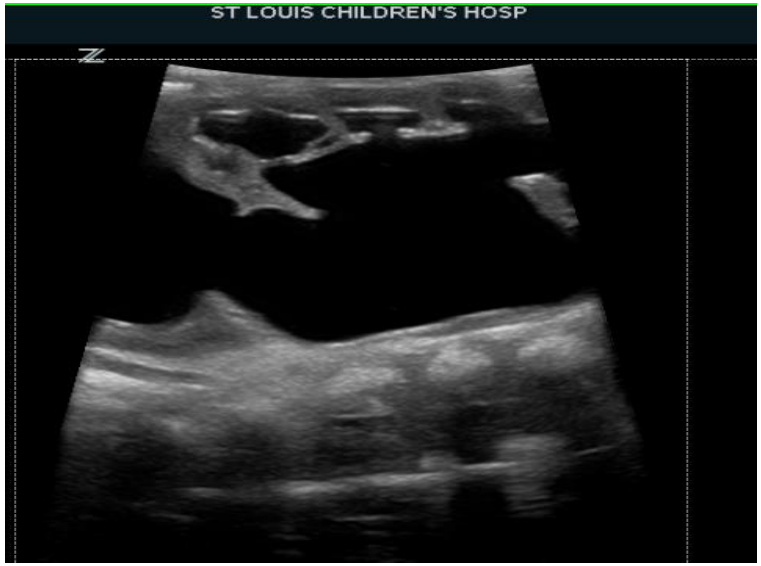
Case

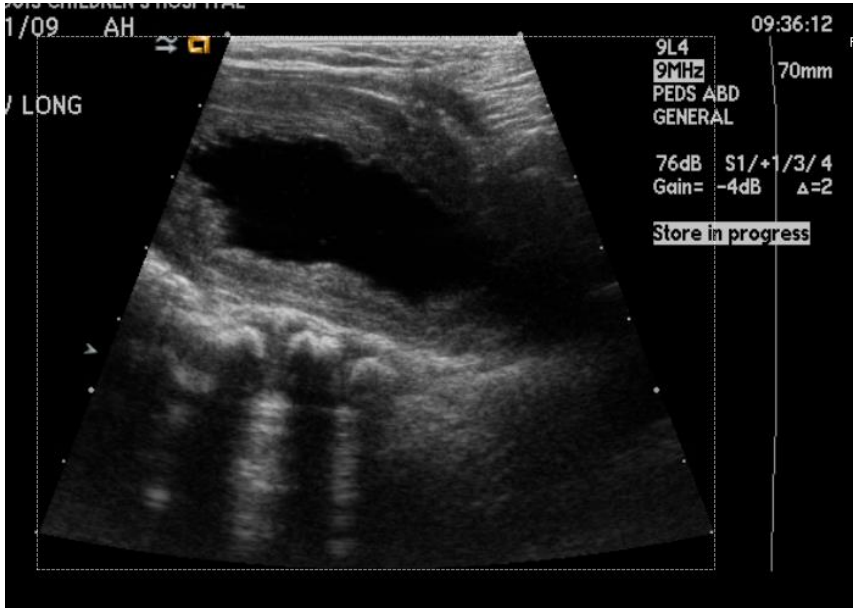
- Abdominal ultrasound:

- Bilateral severe hydronephrosis

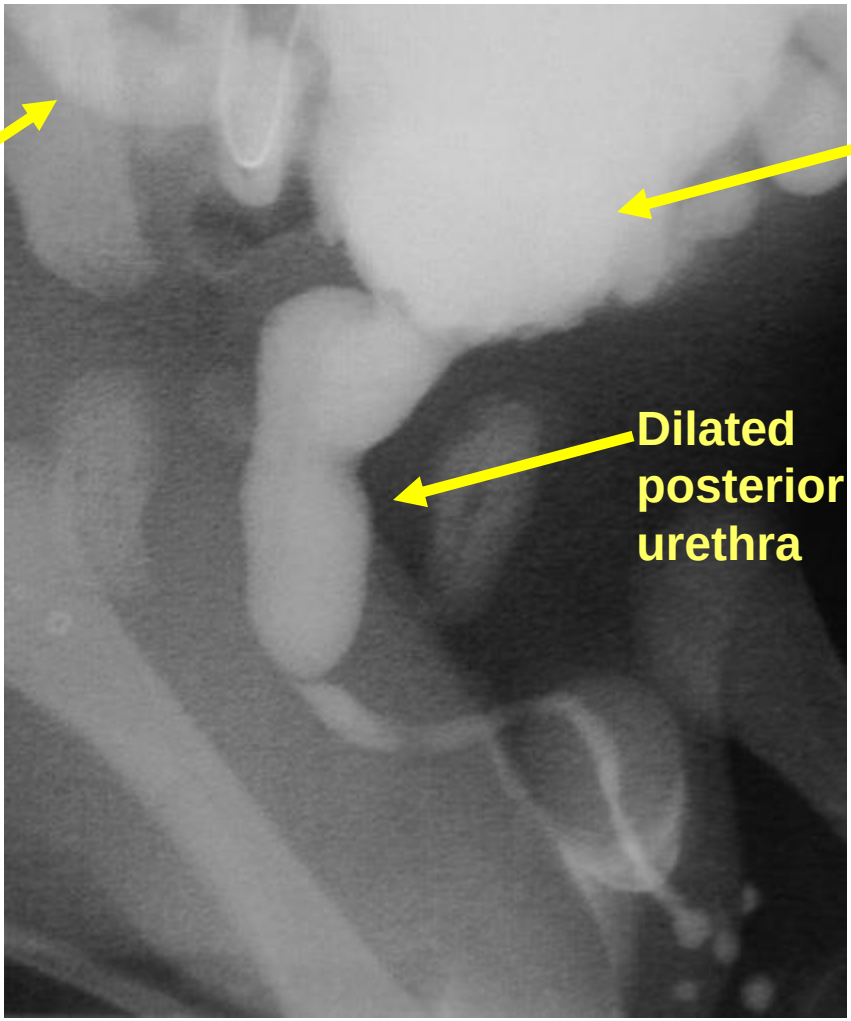
- Dilated ureters

- Thickened and irregular bladder wall





VCUG-Voiding cystourethrogram
Posterior urethral valves



Treatment

- Treatment:

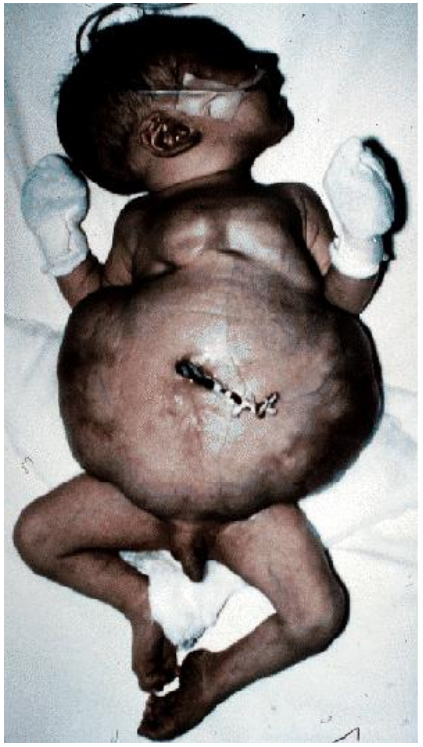
  - Catheter placement

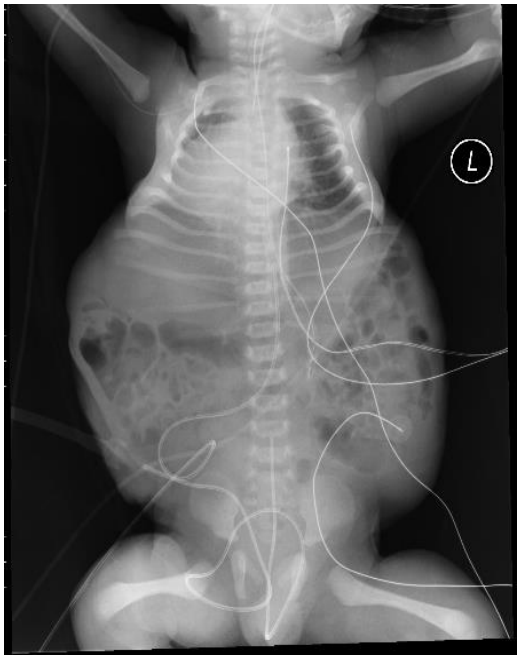
  - Bladder decompression

  - Potassium binding resin (kayexalate) to correct hyperkalemia

Prune-belly syndrome

- Also known as Eagle-Barrett SD
- Prevalence: 1/40,000 births
- 95% Males
- Deficient abdominal muscles, undescended testes, urethral obstruction
- Hydronephrosis, massive dilatation of ureters, large bladder, VUR
- Oligohydramnios and pulmonary hypoplasia
- 1/3 of children are still-born or die within the first few months of life due to pulmonary hypoplasia
- Malrotation of the bowel, cardiac abnormalities (10%), musculoskeletal defects including limb and vertebral anomalies (more than 50%)



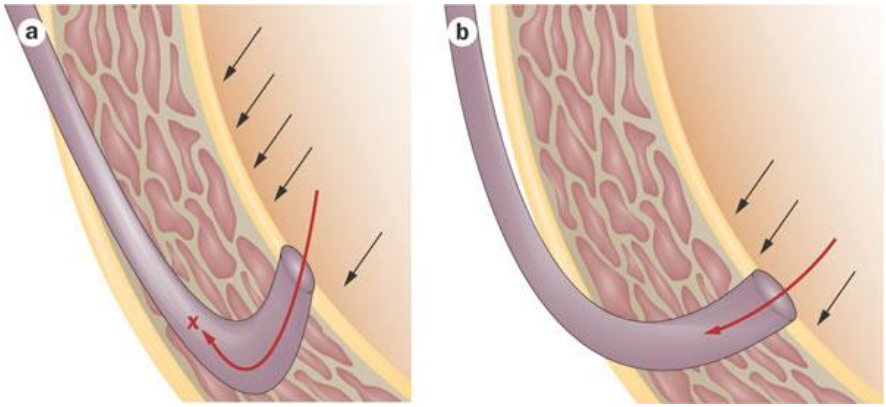


Vesicoureteral reflux: Overview

- Retrograde flow of urine from bladder to ureter
- 1-3% of children affected
- cause of 7-17% of end-stage renal disease in children worldwide
- 30-40% of children under age of 5 years who develop a UTI have VUR
- More than 50% of children younger than 1 year of age who develop a UTI have VUR
- Offspring of individuals with VUR have 27-51% increased risk of having reflux; chance of sibling of child with VUR having reflux is 25%

Causes of vesicoureteral reflux

- Primary VUR: abnormally short intravesical tunnel at the ureterovesical joint

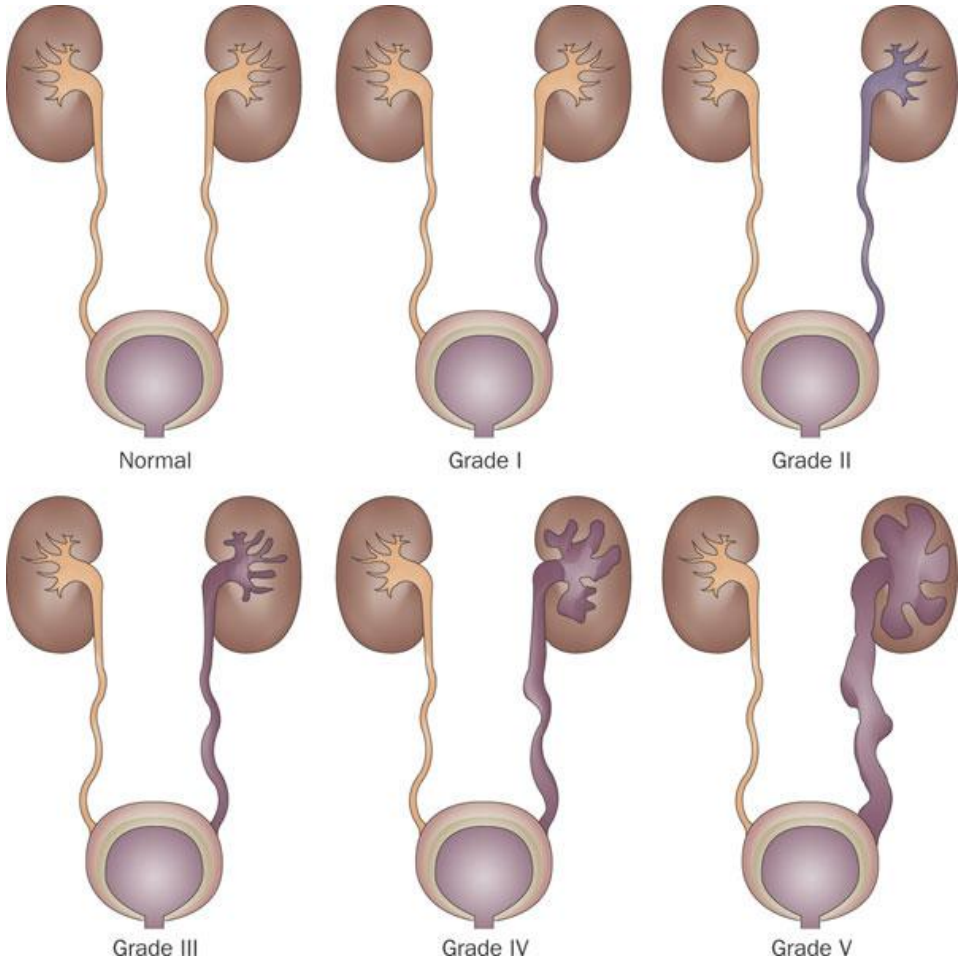


Cooper, C. S. (2009) *Nat. Rev. Urol*

- Secondary VUR: reflux caused by abnormally increased bladder pressures (urethral obstruction, neurogenic bladder)

International Reflux Grading System

- Grade I: reflux into the ureter
- Grade II: reflux into non-dilated pyelocalyceal system
- Grade III: dilatation of the collecting system
- Grade IV: blunting of calyces and tortuosity of the ureter
- Grade V: massive dilation of the collecting system and severe tortuosity of ureter



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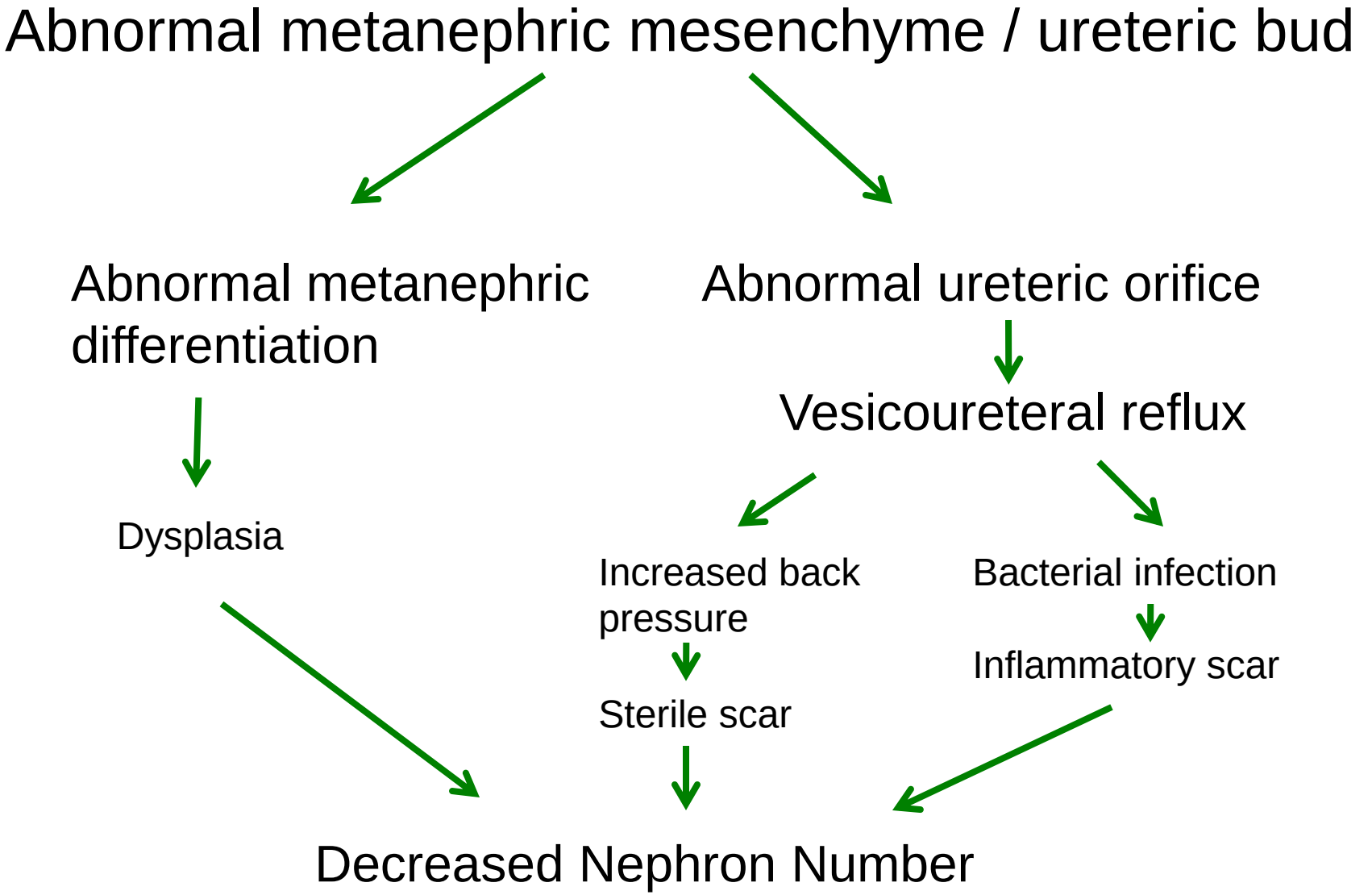
Risk factors for renal injury

- Grade of reflux
- Age
- Laterality
- Bladder volume and pressure
- Presence of renal scars
- Presence of voiding dysfunction: higher incidence of breakthrough infection, renal scarring, higher failure rate following anti-reflux surgery
- History of UTI

Mechanisms of Reflux Nephropathy



Reflux nephropathy outcome

- Spontaneous resolution of reflux in 50-60% of children within 2 years, especially in children with grade III or less VUR
- 1/3 of patients with VUR have renal scars
- Children with unilateral scars have 11% chance of developing HTN, and 18.5% chance if they had bilateral scars
- Children with bilateral renal scars are more likely to develop proteinuria, chronic kidney disease and failure

Clinical management

- Controversial
- Reduction in the occurrence of febrile UTIs in patients who had surgical intervention
- No significant differences in progression or development of new scars, renal function or growth between antibiotic prophylaxis and operative intervention

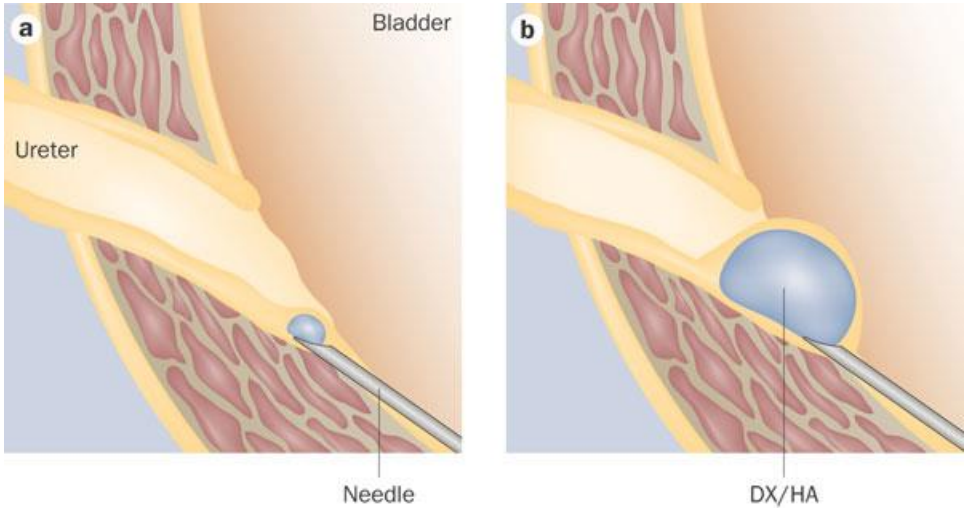
Prophylactic antibiotics

- One-half to one-quarter of the treatment dose is given once daily at bedtime
- Trimethoprim-sulfamethoxazole
- Nitrofurantoin
- Amoxicillin (for infants less than 2 months old: Sulfonamides displace bilirubin from albumin placing the neonate at risk for kernicterus.)

Operative management

- Endoscopic injection of dextranomer/hyaluronic acid copolymer (deflux) at ureteral orifice

- Ureteral reimplantation
  - Indications:
    - patients with grade V VUR
    - progression of renal scarring while on antibiotic prophylaxis (recurrent pyelonephritis)
    - progression of VUR grade (indications may vary by center)



Physiology of micturition

- During infancy, bladder emptying occurs as stretch receptors in the bladder wall reach a critical threshold and initiate a sacral spinal reflex
- As child grows, brain inhibits these reflex bladder contractions through the spino- bulbospinal reflex pathway
- Around 2 yrs of age: child develops conscious sensation of bladder fullness and has urge incontinence
- Child is eventually able to consciously tighten external sphincter to prevent incontinence
- Bladder capacity also increases with age and reaches adult voiding pattern
- Between 2-4 yrs of age, child acquires voluntary control in following order:
  nocturnal bowel control -> daytime bowel control-> daytime bladder control-> nighttime bladder control
- Girls acquire bladder control before boys
- Bowel control achieved before bladder control
- 90-95% continent during day by 5 yrs of age
- 80-85% continent at night

Dysfunctional voiding

- Daytime frequency syndrome: primarily affects boys 4-8yrs of age; acute onset of urinary urgency and frequency; self-limiting
- Postvoid dribbling: prepubertal girls have vaginal trapping of urine; after voiding, pooled urine drains shortly after assuming upright posture
- Giggle incontinence: bladder emptying with giggling
- Stress urinary incontinence: voiding with coughing or sneezing; adolescent females usually affected
- Nocturnal enuresis
- Overactive bladder: most common voiding dysfunction of childhood; occurs between 5-7 years of age (more common in females)

Overactive bladder

- abnormal bladder contraction during the filling phase
- child learns to contract external urinary sphincter to suppress bladder contraction and delay voiding
- results in incontinence before reaching toilet, wet at play
- child displays holding maneuvers to suppress bladder contraction by exerting pressure on external urinary sphincter
- holding maneuvers can cause increased bladder stretch and therefore VUR
- recurrent UTIs may occur
- Treatment:
  - timed voiding
  - anticholinergics (inhibit unopposed detrusor contractions and allow normalization of bladder emptying)
  - treatment of constipation
  - prophylactic antibiotics if recurrent UTIs occur

Posturing in children with dysfunctional voiding

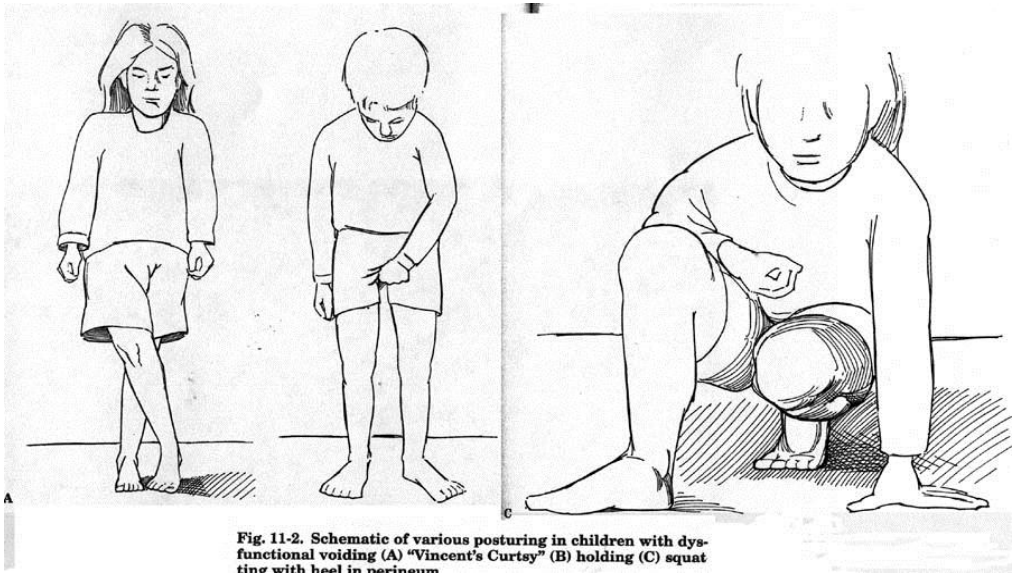


Fig. 11-2. Schematic of various posturing in children with dysfunctional voiding (A) "Vincent's Curtsy" (B) holding (C) squat ting with heel in perineum

Nocturnal enuresis

- Involuntary voiding at night after 5 yrs of age
- Primary (75%): nocturnal urinary control never achieved
- Secondary (25%): dry at night for at least few months, then enuresis occurs
- 60% of patients male
- Family history positive in 50%
- Spontaneous remission in 15% of affected children annually – prevalence decreases to 3% in adolescents

Pathogenesis of primary enuresis

- Reduced bladder capacity and overactivity
- Reduced anti-diuretic hormone production at night
- Delayed maturation of the cortical mechanisms that allow voluntary control of micturition reflex
- Sleep disorder: deep sleepers, however siblings of such patients have also been found to be deep sleepers
- Possible genetic factors

Causes of secondary enuresis

- psychological factors
- diabetes insipidus
- abnormalities in sacral nerves (e.g. tethered spinal cord)
- PUV

Treatment-behavioral

- Restrict fluid intake in the evening
- Void before bedtime
- Wake children a few hours after they go to sleep
- Enuresis alarm: auditory alarm attached to electrodes in underwear. Awakens child to wake up and void. Success rate of 30-60%

Treatment- pharmacologic

- Desmopressin acetate: synthetic analog of anti-diuretic hormone (ADH)

  -effective in 40-70% of patients

  Used for 3-6 months then tapered

- Imipramine (tricyclic antidepressant): mild anticholinergic (relax bladder muscle) and alpha-adrenergic effect (increased sphincter activity) (30-60% effective)

- Oxybutinin: anticholinergic effect (10-50% effective)

Conclusion

- Important to detect structural abnormalities (obstruction, reflux) as soon as possible and initiate treatment when necessary to preserve renal function

- Voiding dysfunction can cause significant renal pathology and may also have social consequences – must be recognized early and treated through behavioral and pharmacologic measures