Inherited Kidney Diseases and Developmental Abnormalities of the Urogenital Tract

Block 11

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Congenital Abnormalities of Urogenital Tract

- **Congenital abnormalities of the UGT are common**
  - Occurs in up to 10 % of the population
  - Contributes to $^{1}/_{3}$ of all congenital abnormalities
- **Discovered when complications develop**
  - UTI
  - Abdominal mass palpated
  - Investigation for poor weight gain
  - Routine urine test (co-incidental finding)
- **Often detected with routine antenatal u/s**

Embriology

The kidney originates from two main structures

- **Ureteric bud –**

  Abnormal development affects the –

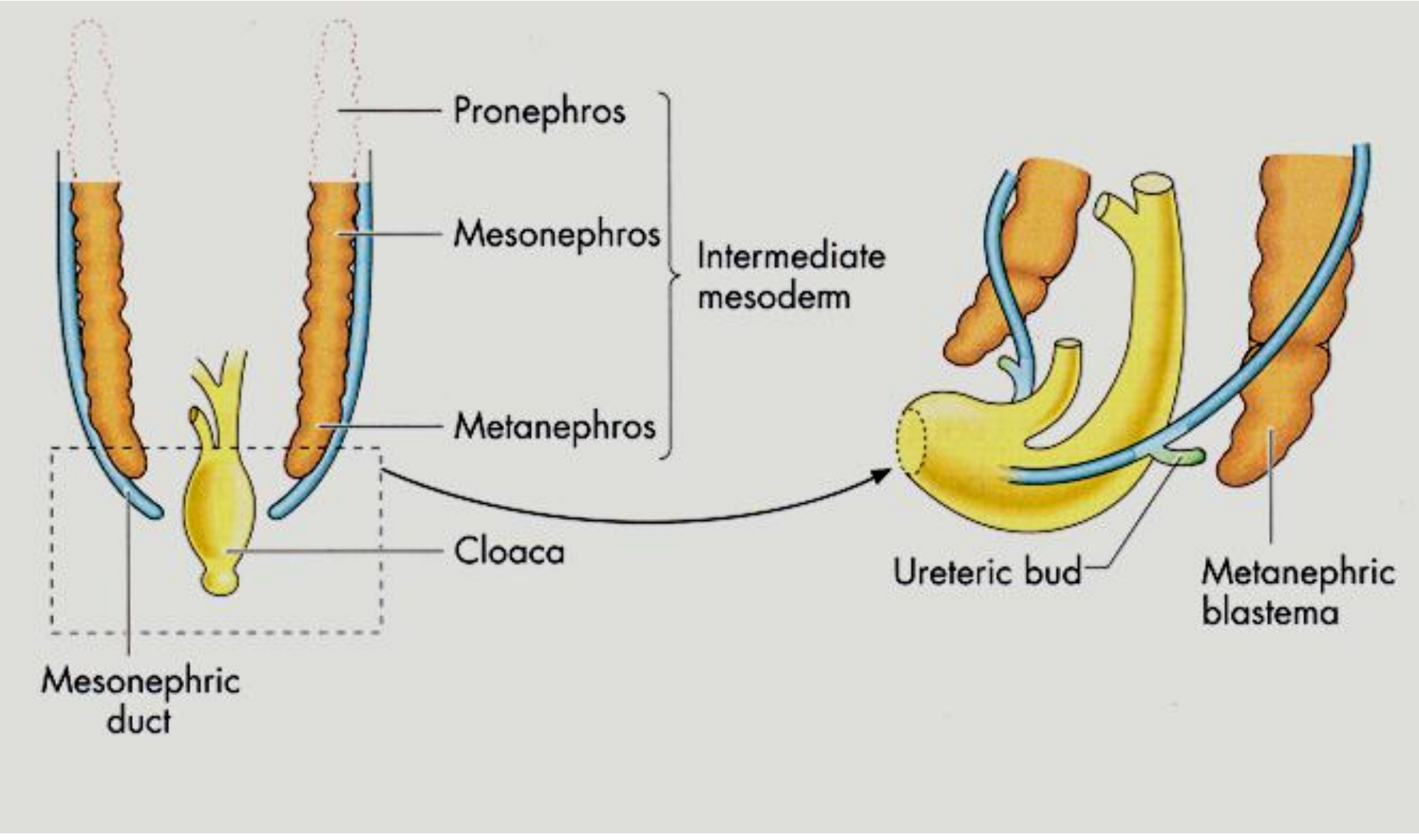
  - Renal collection system
  - Calyces
  - Pelvis & ureter

- **Metanephros (Metanephric blastema)**

  Abnormal development affects the –

  - Nephrons

Genitourinary Tract Embriology



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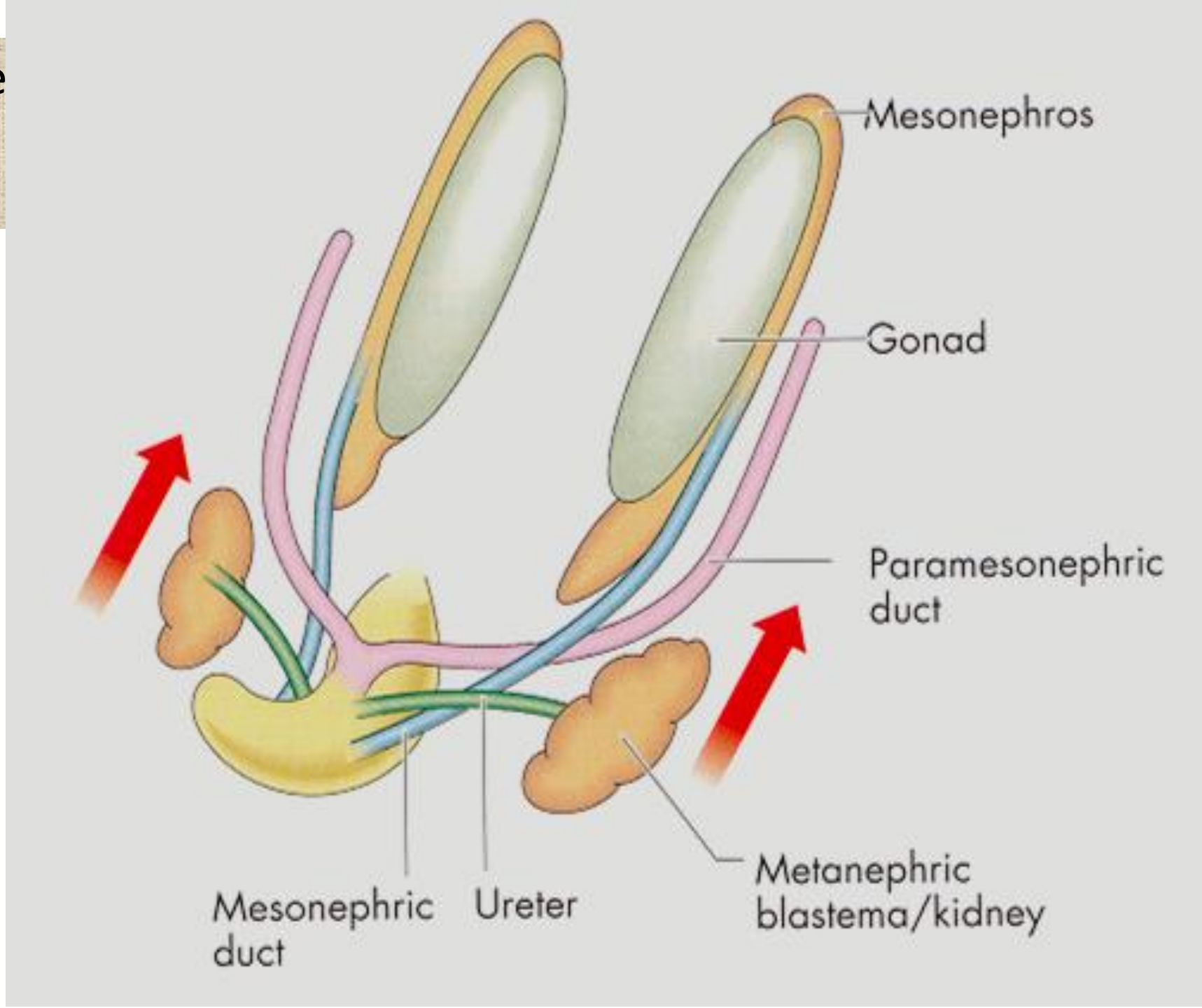

Mesonephros
Gonad
Paramesonephric duct
Metanephric blastema/kidney
Mesonephric duct
Ureter

Renal Parenchymal Abnormalities

- Renal agenesis / renal hypoplasia
  - Result of abnormal induction of nephrogenesis
  - Apoptosis is a programmed form of cell death
  - Due to imbalance of apoptotic and growth factors
  - ↑ apoptosis or
  - Relative deficiency of cellular growth factors

Renal Agenesis and Hypoplasia

- Renal agenesis = absent kidney
- Hypoplasia = kidney $\leq {}^{1}/_{3}$ of normal size
  - May occur uni- or bilaterally
  - 90% is sporadic
  - 10% is familial

Unilateral Renal Hypoplasia

- Patients usually remain asymptomatic
- Contralateral kidney
  - Compensatory hypertrophy
  - Compensatory function
- Renal function is normal
- Occasionally hypertension develops

Renal outcome of children with one functioning kidney from birth

Study of 99 patients and a review of the literature

Does progressive CKD develop in patients with a single functioning kidney from birth within a period of 10 years?

Vu K-Hahn Van Dyck M et al

Pediatr Nephrol 2008;167: 885-89

Literature

- 9 ± comparable studies on fate of solitary kidneys in childhood over past 22 yrs
- All indicate: variable % will develop HT,

  ↓ GFR and proteinuria
- Study that best illustrates the risk of solitary kidney: (Baudoin et al)
  - heterogeneous cohort of 111 patients
  - nehprectomy < 16 years
  - demonstrate that the incidence of
  - ↓ GFR, HT, and proteinuria increases with time to become striking with FU of over 25 years

Conclusion

Individuals with single functioning kidney for whatever reason deserve long-term FU during and after childhood

Bilateral Renal Hypoplasia

- Degree of renal functional impairment varies
- Clinical problems:
  - polyuria
  - polydypsia
  - dehydration
- Tubulopathy: “salt-losing nephropathy”
  - $\rightarrow$ poor growth
- Develop progressive renal functional impairment

Bilateral Renal Agenesis

- Occurs in 1/4000 pregnancies
- Mother has oligohydramnios
- Baby has Potter Sequence
- Baby dies shortly after birth due to respiratory distress / hypoplastic lungs

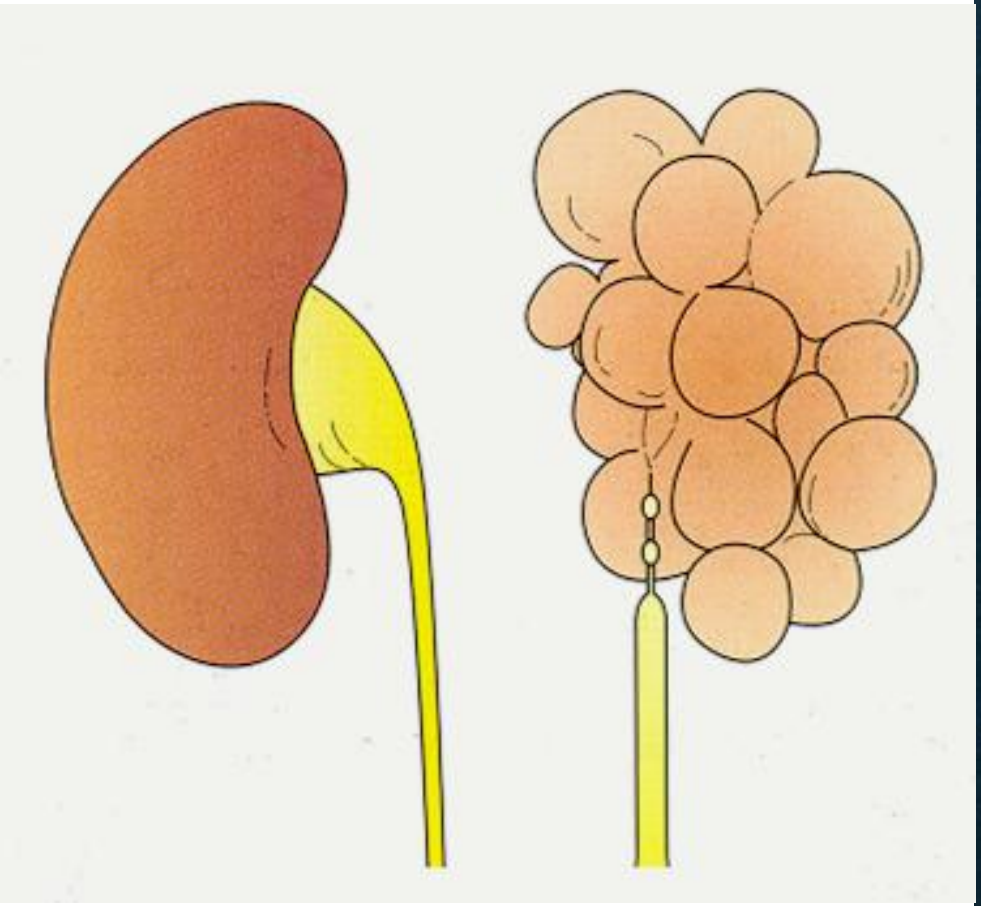
Cystic Renal Diseases

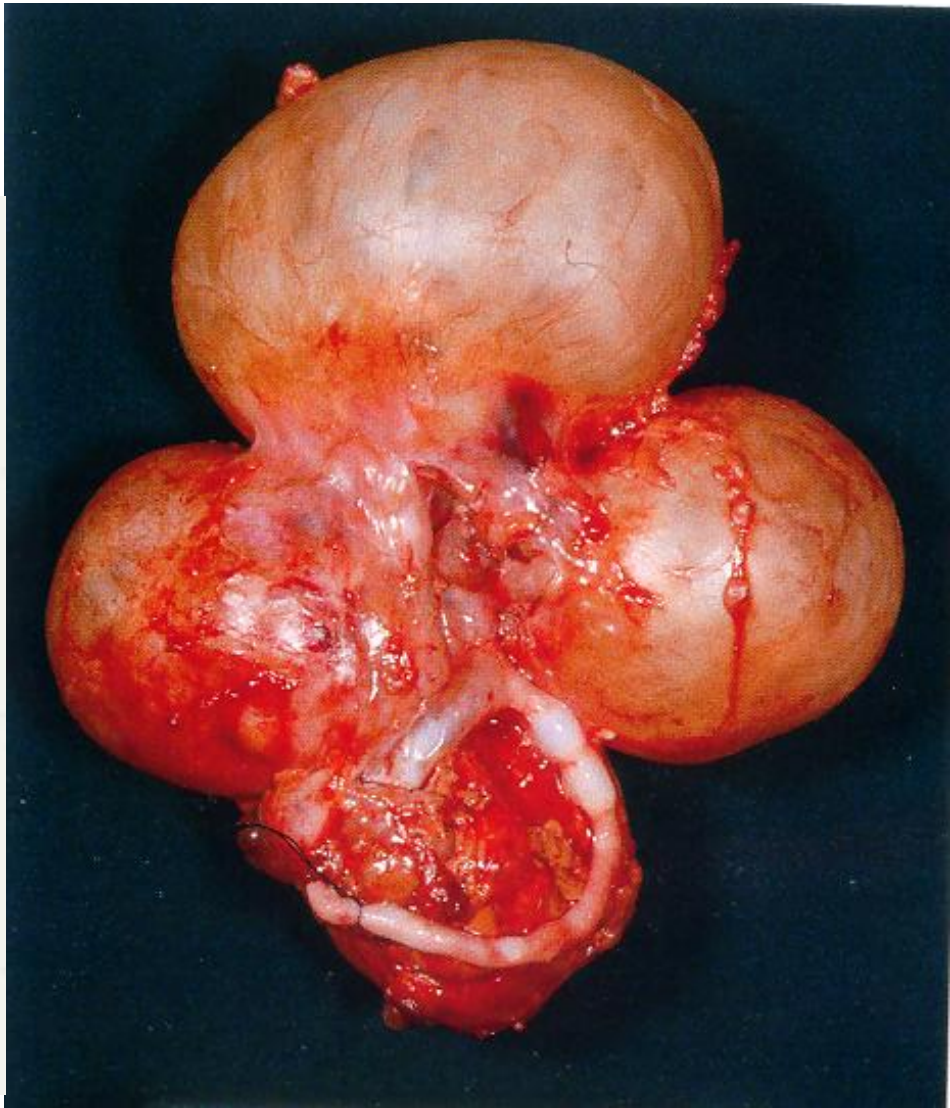
- Multicystic kidney
- Polycystic Kidney Disease
  - Autosomal Recessive PCKD
  - Autosomal Dominant PCKD
  - Medullary Cystic Kidneys

Multicystic Kidney

- Usually unilateral
- Morphology
  - Large irregular mass
  - Consists of undifferentiated dysplastic elements and cysts of different sizes
- Non-functional kidney
- Associated with pelvis/ureter abnormalities on contralateral side
- Because MCDK is usually unilateral, it is
  - Asymptomatic or
  - Discovered when abdominal mass is detected

Multicystic Dysplastic Kidney





Polycystic Kidneys (PCKD)

- Inherited kidney diseases
- Two different forms of inheritence
  - Autosomal Dominant (ADPCKD)
  - Autosomal Recessive (ARPCKD)
- Bilateral enlarged kidneys

ADPCKD ("Adult PCKD")

- Incidence I/1000 of the general population
- Bilateral large kidneys, with normal shape
- Large cysts of varying sizes
    - May have cysts in liver, lungs and pancreas
- Usually symptomatic by 3rd to 4th decade
- Presents with HT, UTI and CRF
- Cerebral aneurisms -↑ risk of intracranial haemorrhage

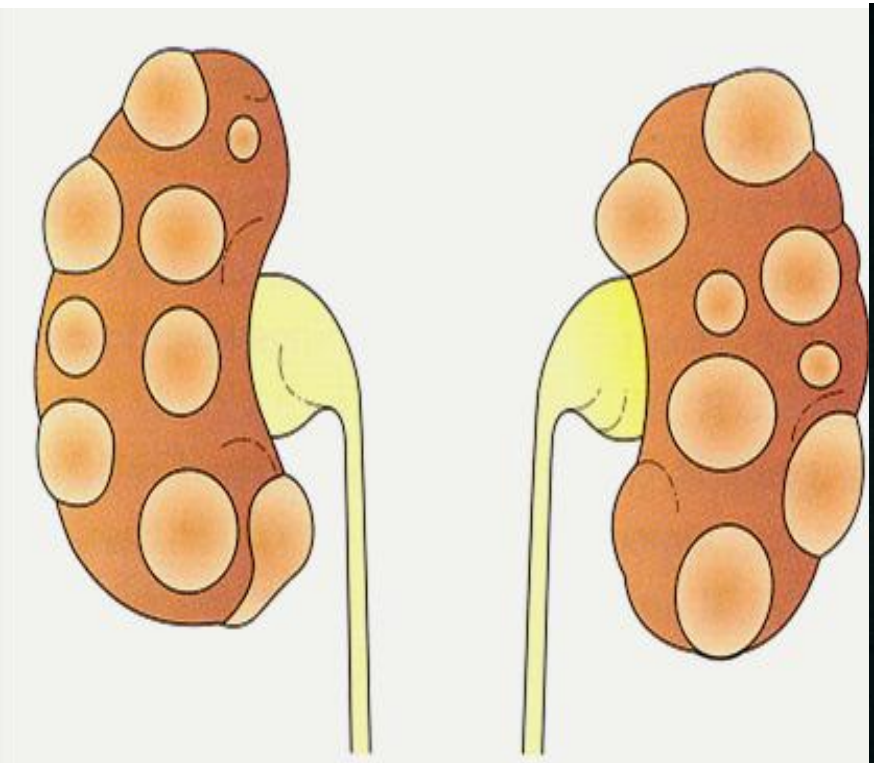
ADPCKD ("Adult PCKD")

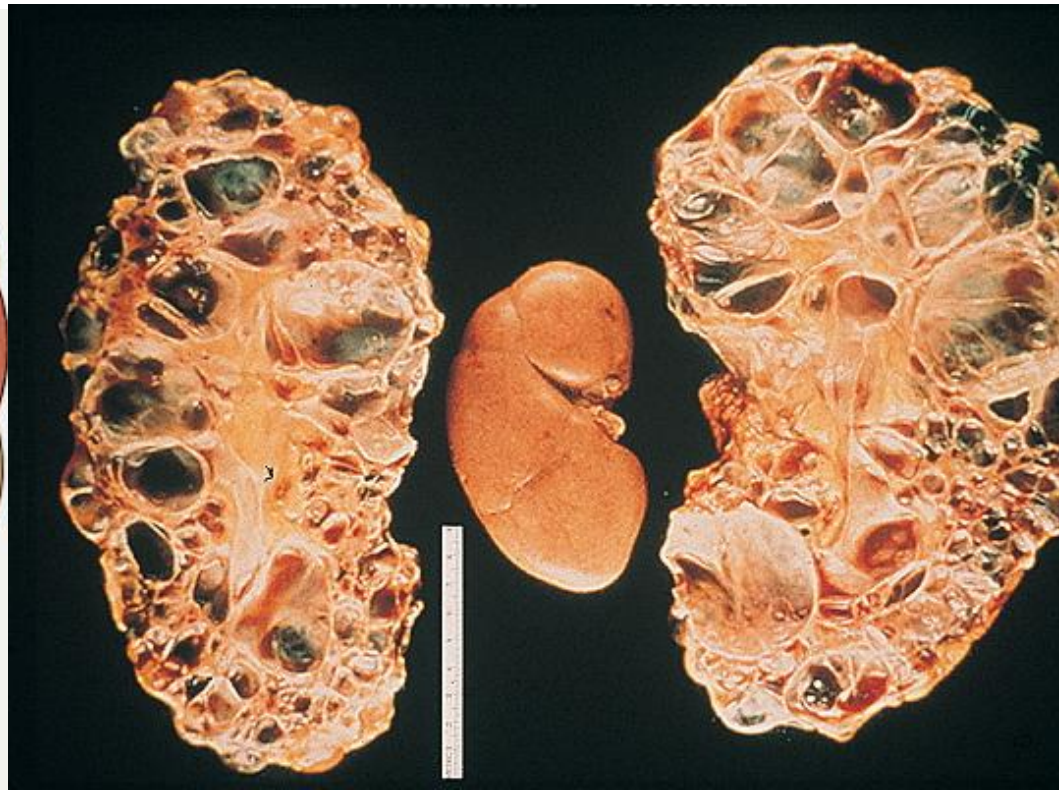
Large kidneys

Discreet cysts

Varying sizes

Areas of normal parenchyma



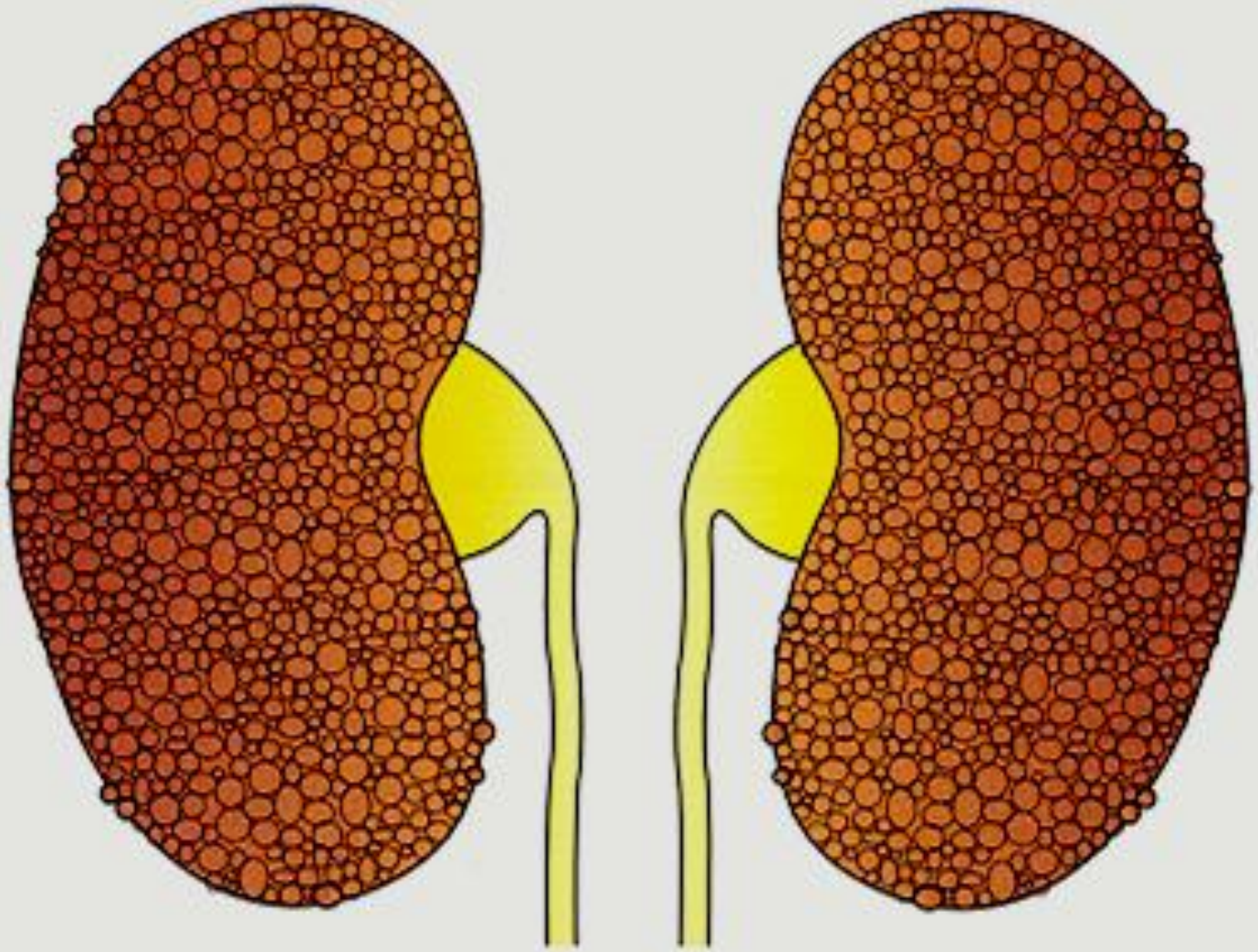


ARPCKD ("Infantile PCKD")

- Bilateral large kidneys, normal shape
- **Small cysts**
- Invariably associated with **hepatic fibrosis**
- Two peak periods of presentation
  - Neonate –
    - Potter sequence due to oligohydramnios
    - RDS due to hypoplastic lungs, respiratory failure
  - Older child –
    - Poor growth
    - Severe hypertension
    - CRF and hepatic fibrosis

ARPCKD

Diffuse small cysts & bilateral renal enlargement



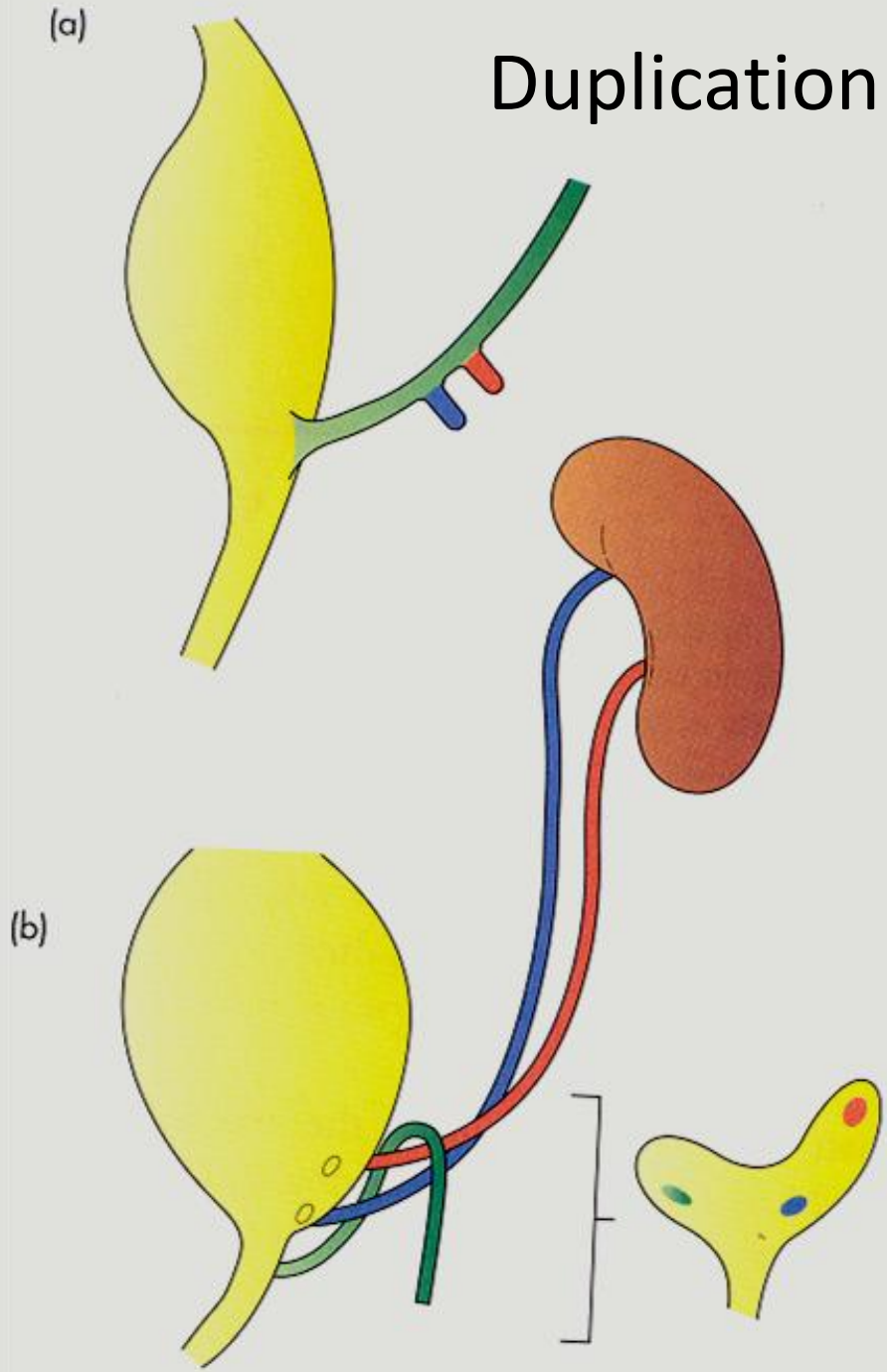
ARPCKD

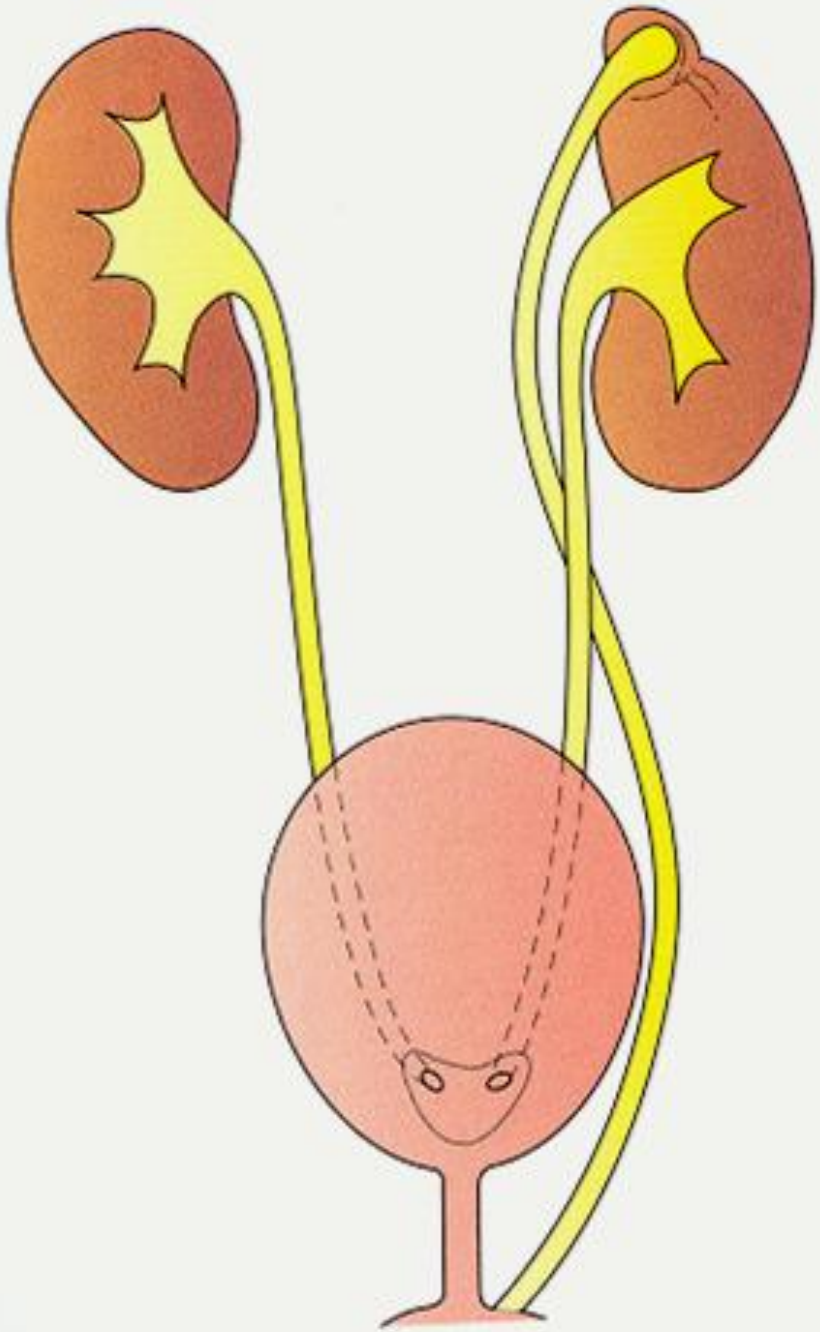
Developmental Abnormalities of the Ureteric Bud & Urinary Drainage System

Pelvo-Ureteric Junctional Obstruction (PUJ)

- Dilated pelvis
- Usually unilateral
- Contralateral kidney may have abnormality -
  - Vesico-ureteric reflux (VUR)
  - Cystic dysplastic kidney

Duplication





Vesico-Ureteric Reflux (VUR)

- More common in Caucasians compared to Blacks
- Genetics play a role
- Occurs in 30-50 % sibs of index case
- Usually presents with recurrent UTI

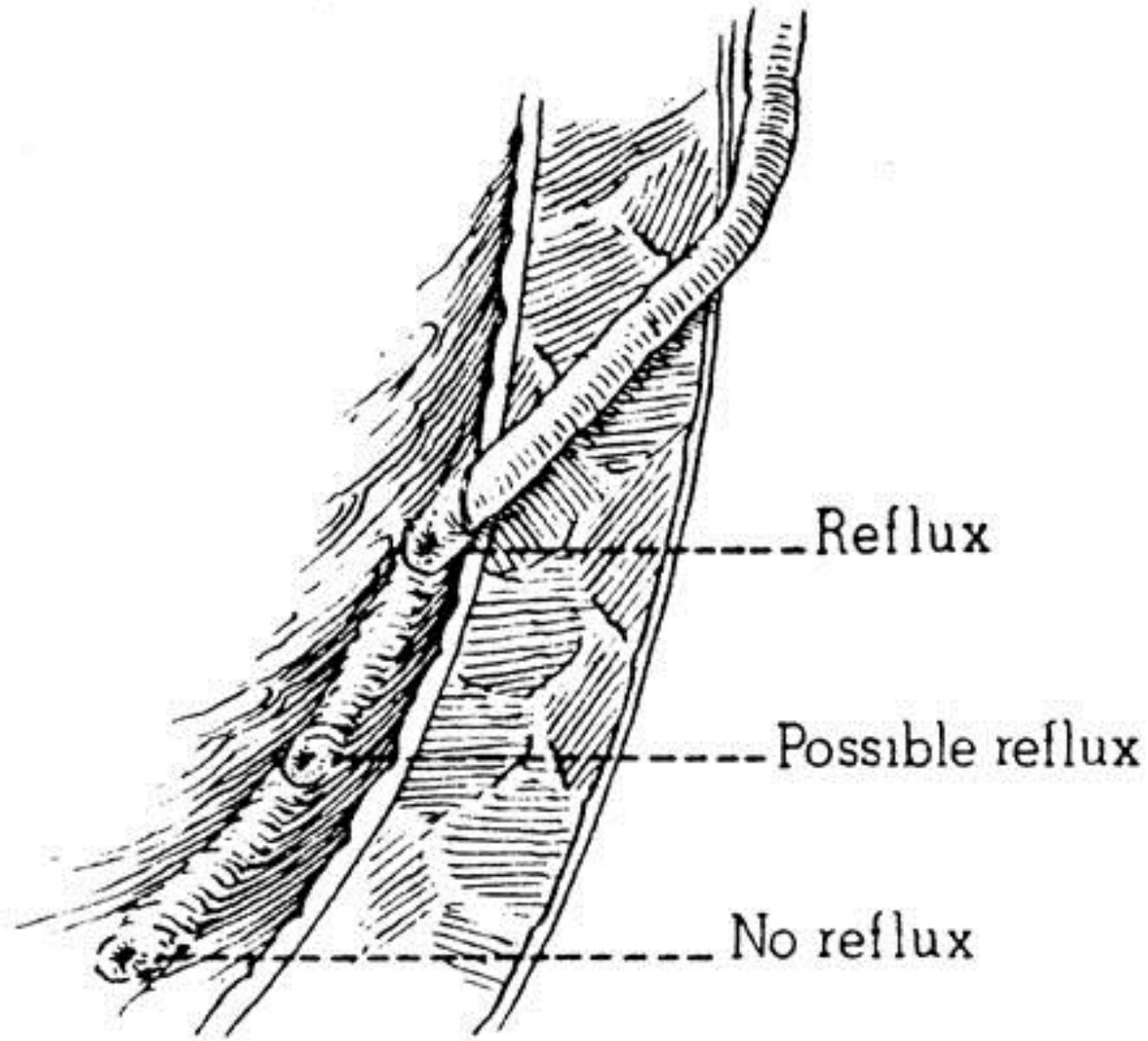
Pathogenesis of VUR

- Abnormal development of the ureteric bud
- VUR more common in young babies
- May outgrow VUR by age 2 years
- In adults the ureters
  - pursue a 1-1.5 cm sub-mucosal oblique course through the bladder wall – longer tunnel
- In infants the ureters
  - have a shorter tunnel and open perpendicular into the bladder wall

Etiology and Pathogenesis of VUR

- Pathologically refluxing ureters
  - Located more lateral and cephalad in the bladder
  - Short submucosal tunnel
  - Perpendicular course through bladder wall
  - Gaping opening in the bladder

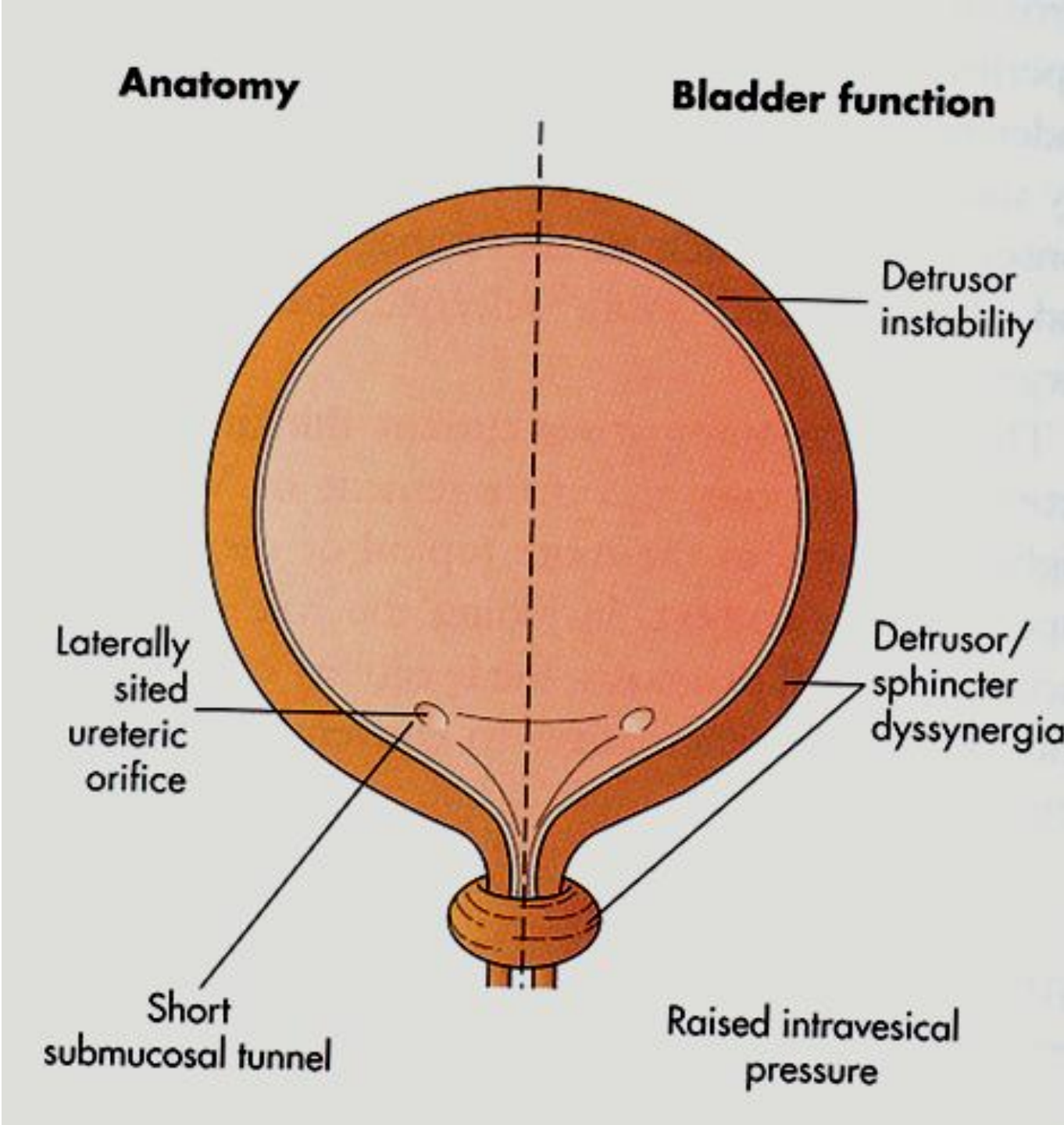
5:1 tunnel length to wall ratio



Paquin (1959)

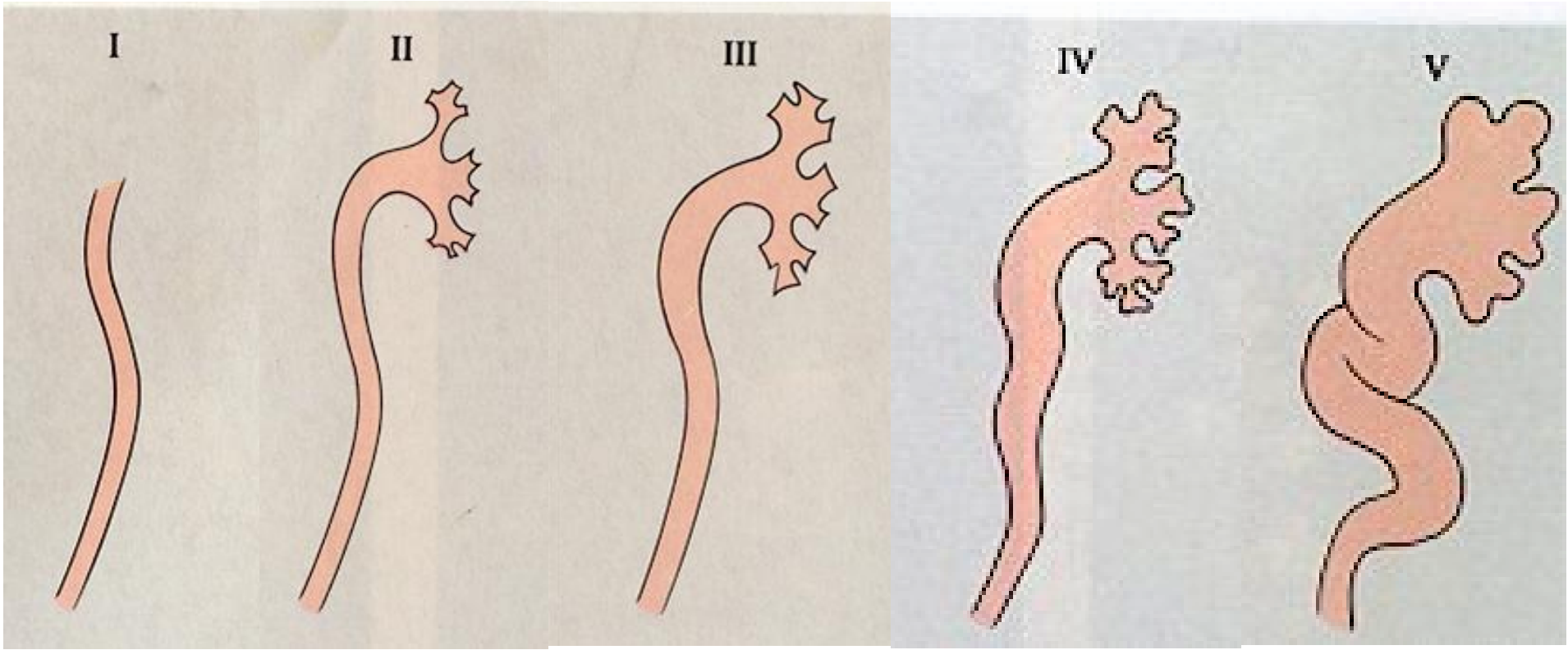
Aetiology of VUR

Balance of functional and anatomical factors



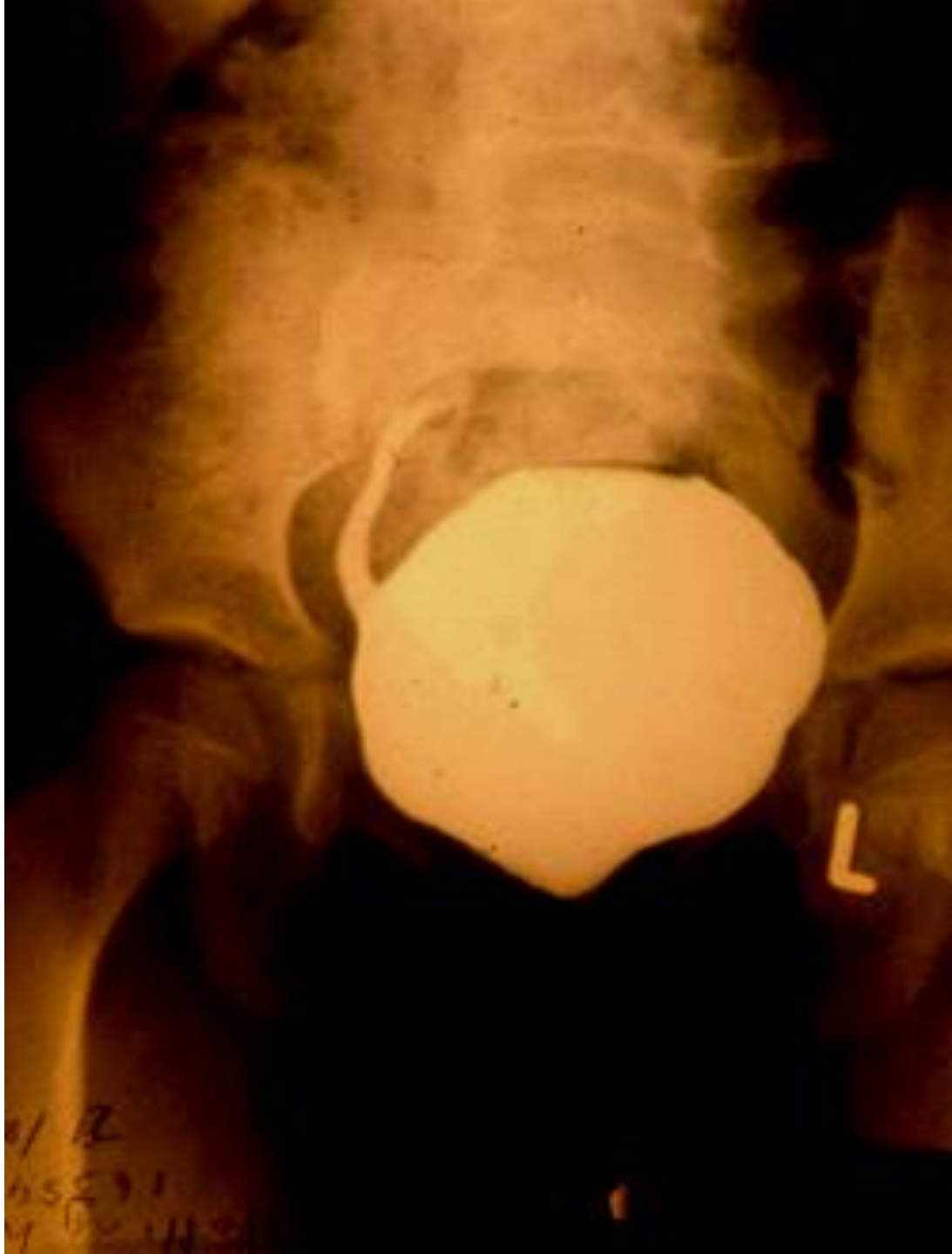
International Classification

Vesico-Ureteric Reflux Grades



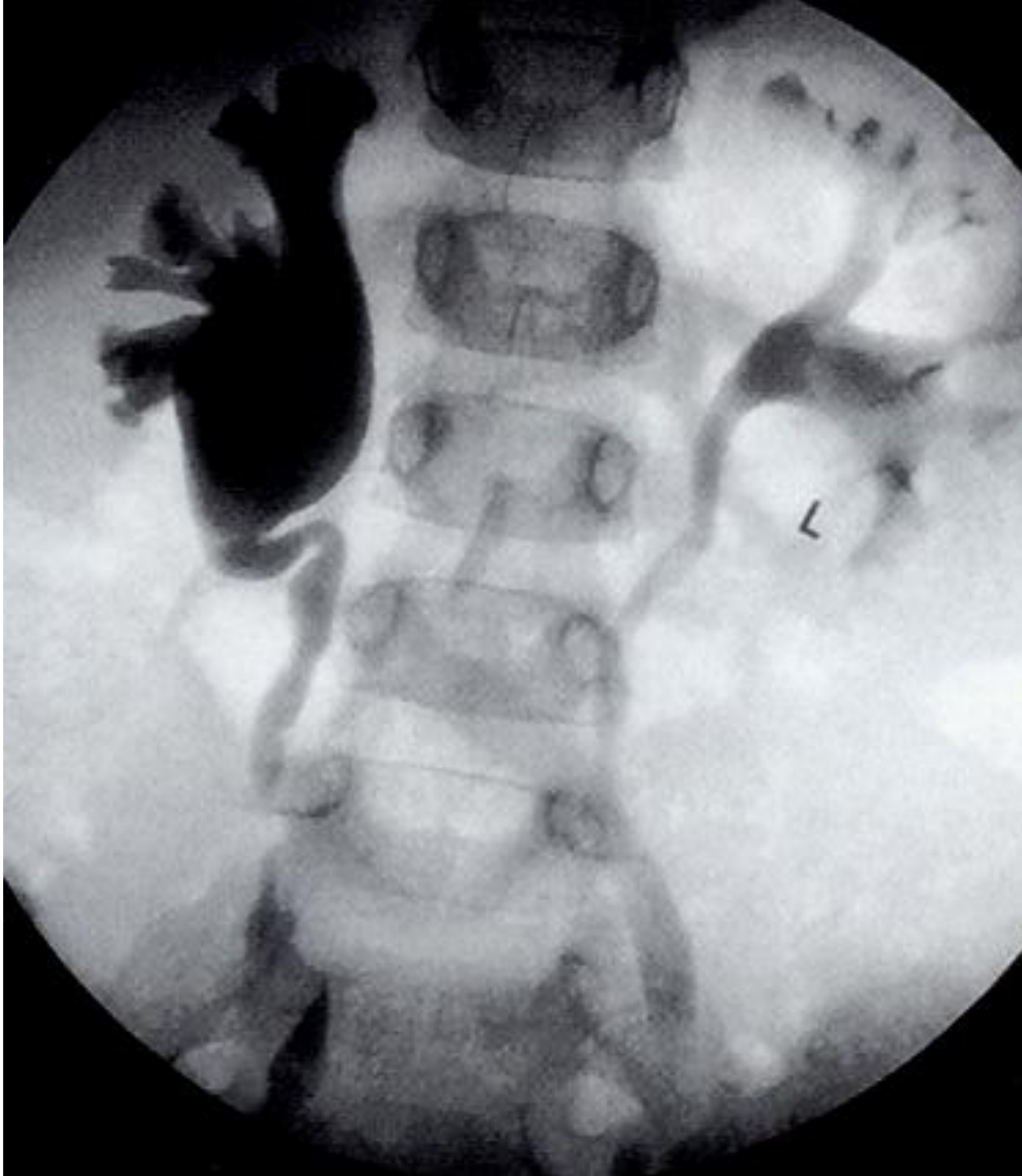
Voiding cystogram

Grade I VUR in the right ureter



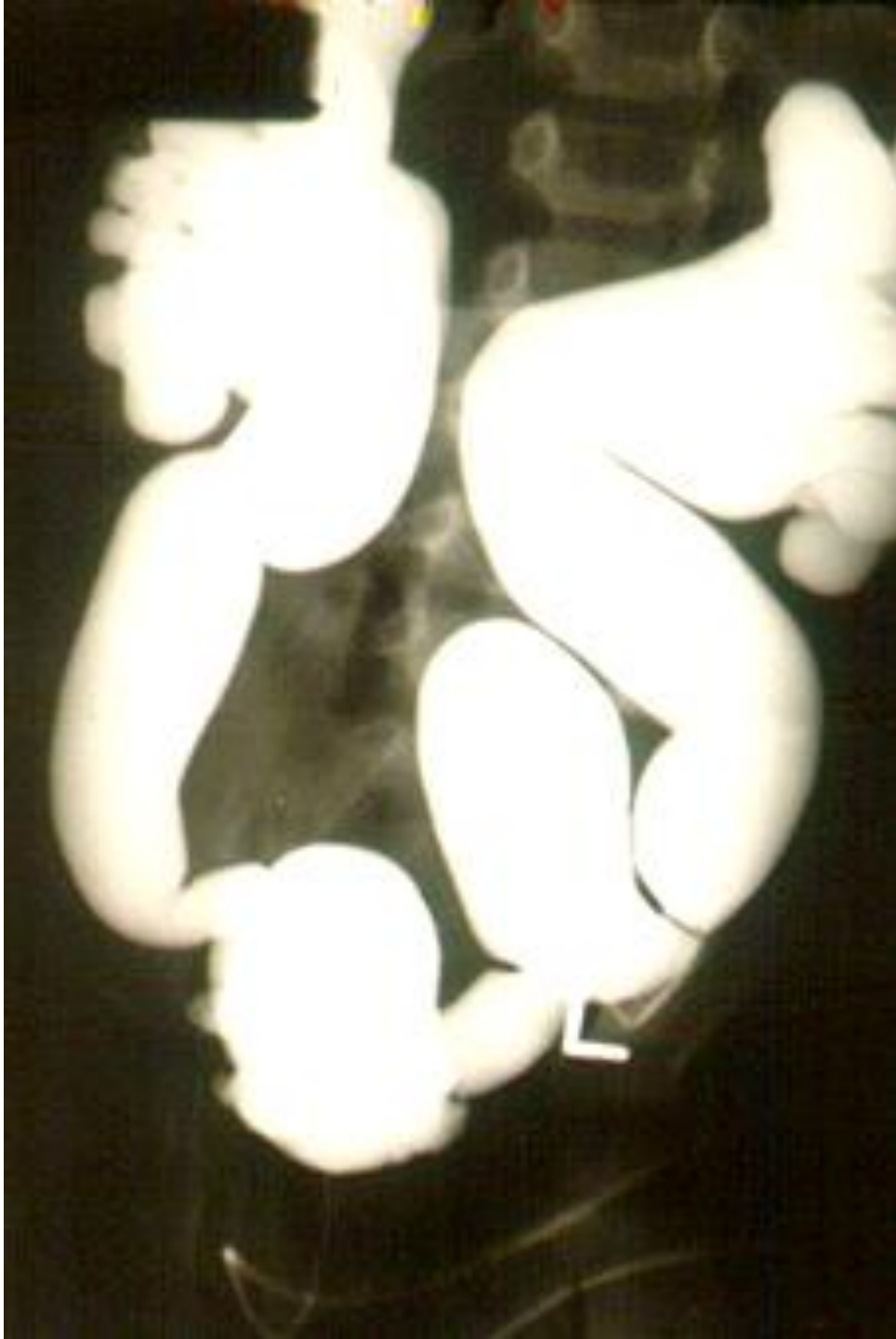
VCUG

Right Grade IV VUR



VCUG

- Grade V VUR
- Severe hydronephrosis
- Blunting of calyces
- Thinning of renal cortex
- Tortuous and wide ureters



Developmental Abnormalities of the Urethra

Congenital Obstructive Posterior Urethral Membrane (COPUM)

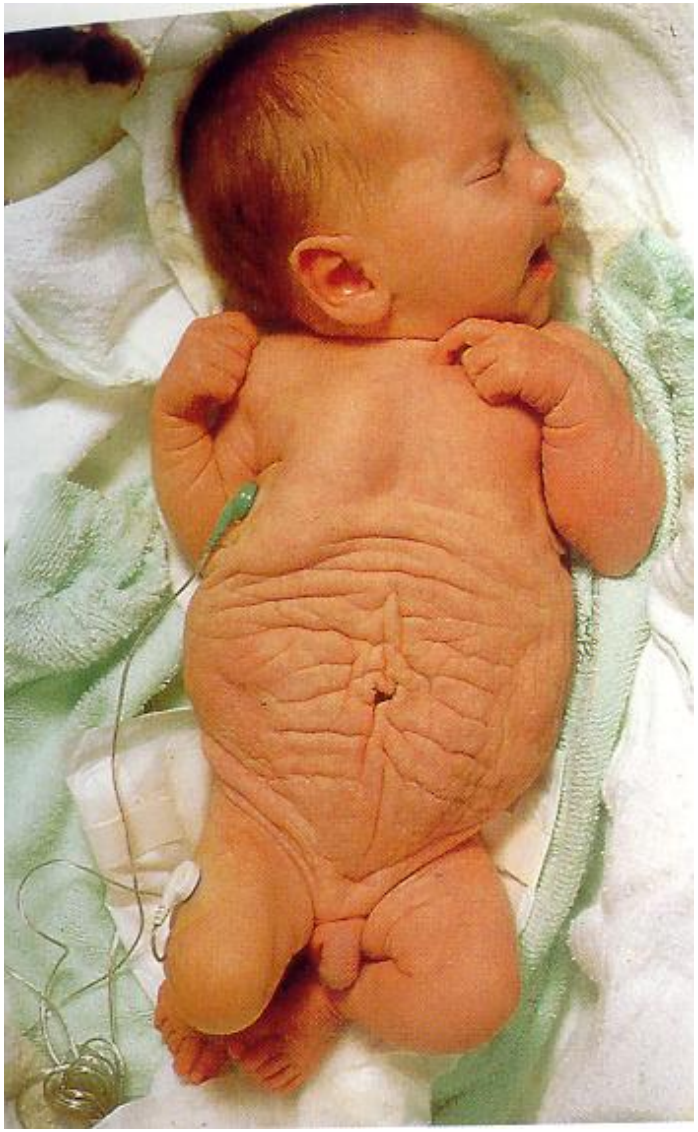
- Usually in boys (95%); rarely in girls
- Developmental abn. of the posterior urethra → outlet obstruction of the bladder
- Associated with
  - oligohydramnios
  - varying degrees of renal dysplasia
- If oligohydramnios develops before 16th week of gestation → very poor prognosis

Clinical Presentation

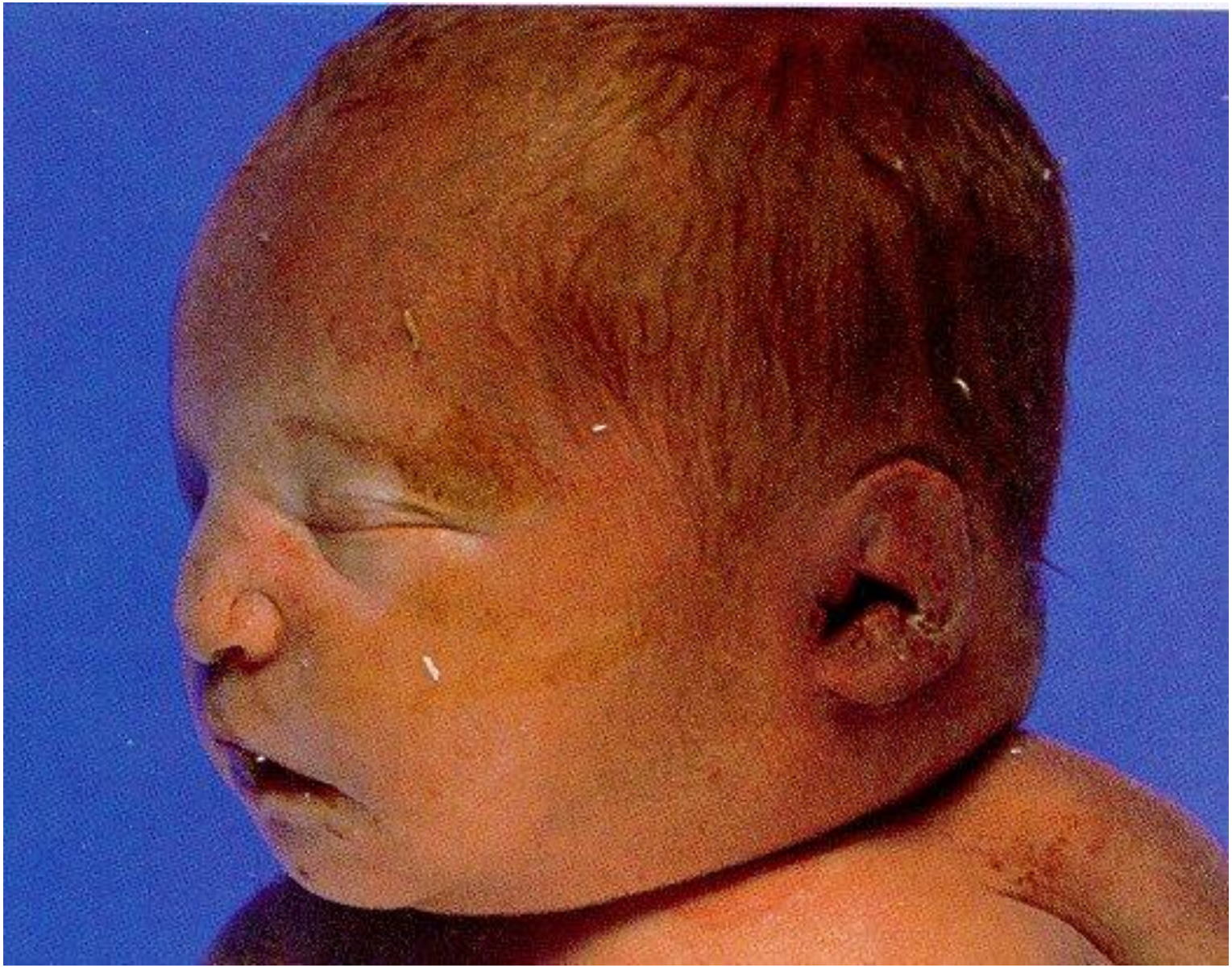
- Potter sequence
- Respiratory distress at birth
- Bilateral palpable kidneys
- Bladder palpable above pubis
- Dribbling of urine or total obstruction
- May present with urinary ascites

Prune Belly Syndrome

- Consists of triad:
- Non obstructive megacystis mega-ureter and hydronephrosis
- Absence of abdominal wall muscles
- Undescended testes (cryptorchidism)



Potter Facies

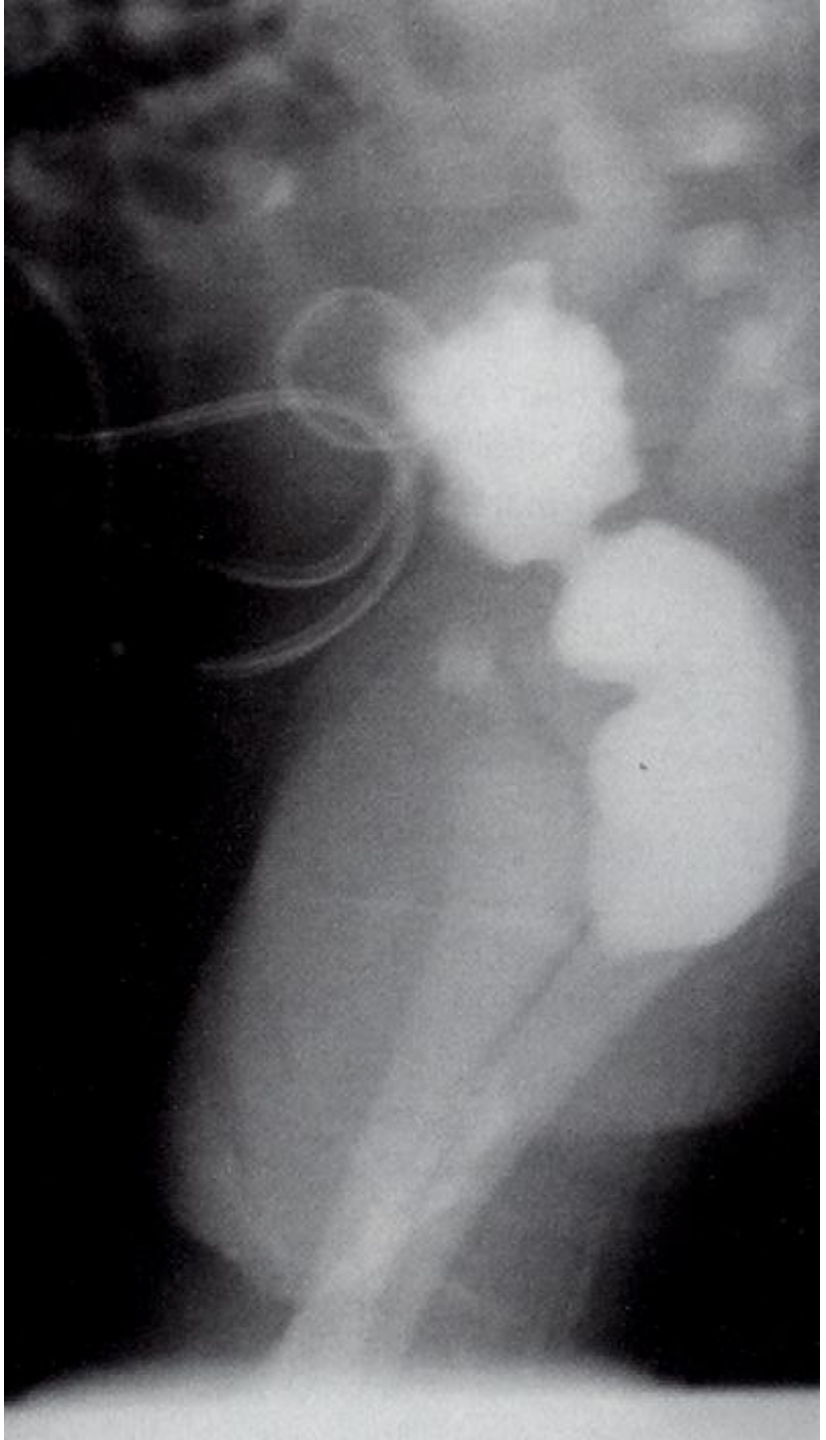


Voiding cysto-urethrogram

Dilated posterior urethra

Indentation by prominent bladder neck

Small trabeculated bladder



Voiding cysto-urethrogram

Dilated posterior urethra

Indentation : Narrowing

Trabeculated bladder

Recommendations

- All patients with congenital abnormalities of kidneys or single functioning kidneys deserve regular FU
- At 2 years kidney function is mature – good time to evaluate kidney function
- At all visits do
  - Growth assessment
  - Blood pressure
  - Urine dipstix
  - Spot u: protein:creat ratio or micro albuminuria (marker of glomerular hypertrophy and hyperfiltration)
  - GFR should be estimated once a year
- If signs of progression are documented, ACEI may be indicated

References

Illustrations, diagrams and photos

- Thomas DFM, Rickwood AMK, Duffy PG. Essentials of Paediatric Urology. London: Martin Dunitz Ltd; 2002
- Johnson RJ, Feehally J. Comprehensive Clinical Nephrology. 2nd ed. London: Mosby; 2003