NOTES
CONGENITAL KIDNEY CONDITIONS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Kidney abnormalities present at birth
- Polycystic kidney disease, multicystic dysplastic kidney, horseshoe kidney, renal agenesis

Developmental phases

- Pronephros → mesonephros → migrate upwards into abdomen → separate into two kidneys

COMPLICATIONS

- Progressive renal damage, renal failure

RISK FACTORS

- More common in individuals who are biologically male
- *Pregnancy:* high BMI, alcohol abuse, smoking, teratogenic medication
- Genetics

SIGNS & SYMPTOMS

- Potter sequence (epicanthal folds, low-set ears, flat nose, recessed chin)

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound, CT scan, intravenous urethrogram, MRI

LAB RESULTS

- Evaluate renal function; blood urea nitrogen (BUN), creatinine, estimated glomerular filtration rate (eGFR), serum electrolytes

OTHER DIAGNOSTICS

- *Visible at birth:* bladder exstrophy, hypospadias, epispadias

TREATMENT

MEDICATIONS

- Support renal function
  - Diuretics, erythropoietin (EPO), medication for electrolyte imbalances, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers

SURGERY

- Kidney transplant

OTHER INTERVENTIONS

Dialysis

- If kidney(s) no longer functional, machine performs kidney function; filtering, purifying blood by removing waste, excess fluid

HORSESHOE KIDNEY

osms.it/horseshoe-kidney

PATHOLOGY & CAUSES

- AKA renal fusion, congenital disorder; two kidneys fuse during fetal development → one large, horseshoe-shaped kidney
- Week 7–8
  - Horseshoe-shaped kidney tries to migrate from pelvis up into abdomen → gets hooked around inferior mesenteric artery → remains low in abdomen

CAUSES

Mechanical fusion

- Metanephros stage (gestation week 5)
- Flexion/growth of developing spine, pelvic organs → pushes kidneys together → lower poles of kidneys fuse → fibrous isthmus forms
  - Isthmus made of connective tissue

Teratogenic event

- Posterior nephrogenic cells (help form part of kidney) migrate to wrong spot → parenchymal isthmus forms → connects kidneys
  - Isthmus made of kidney cells

RISK FACTORS

- More common in individuals who are biologically male
- Chromosomal disorders (e.g. Turner syndrome, trisomy 13, 18, 21)
- Neural tube defects

COMPLICATIONS

- Hydronephrosis, kidney stones, infection, kidney cancer (especially Wilms' tumor, carcinoid tumor), obstruction, vesicoureteral reflux, infection, polycystic kidney disease

SIGNS & SYMPTOMS

- Mostly asymptomatic, sweating, nausea, vomiting; hematuria; fever, chills; cloudy urine

DIAGNOSIS

- Usually incidental

DIAGNOSTIC IMAGING

Ultrasound

- Periodic monitoring for early Wilms' tumor detection

CT scan

- *3D scanning:* evaluate anatomy, collecting system

MRI

- Provide anatomical information
- Evaluate arterial anatomy before surgery
- Check renal artery stenosis in hypertensive people

LAB RESULTS

- BUN, creatinine, glomerular filtration rate (GFR), serum studies, 24-hour kidney stone risk assessment

TREATMENT

MEDICATIONS

- For renal disease (e.g. erythropoietin, ACE inhibitors)

SURGERY

- Possibly corrective surgery

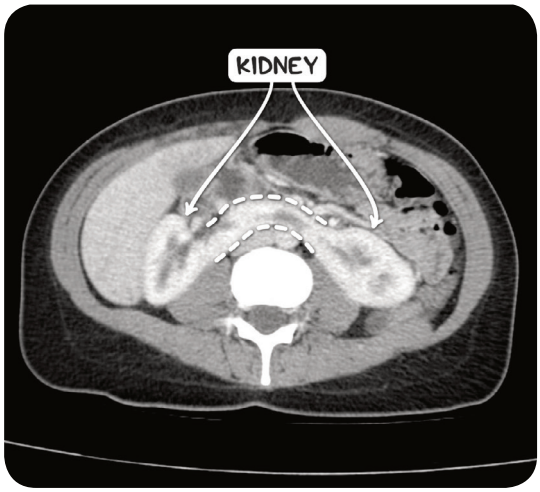

Figure 110.1 An abdominal CT scan in the axial plane demonstrating a horseshoe kidney. There is renal tissue connecting the right and left kidneys.

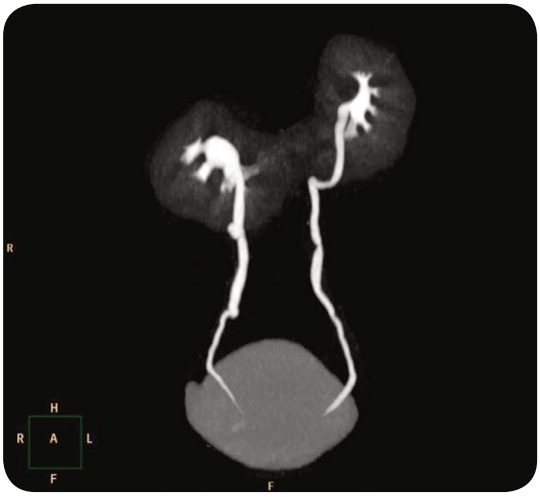

Figure 110.2 A 3D-reconstruction MRI in an anterior view in an individual with a horseshoe kidney.

MEDULLARY CYSTIC KIDNEY DISEASE (MCKD)

osms.it/mdullary-cystic-kidney-disease

PATHOLOGY & CAUSES

- A group of autosomal dominant kidney diseases that cause progressive renal failure
- AKA autosomal dominant tubulointerstitial kidney disease (ADTKD)

TYPES

Uromodulin kidney disease (UKD)

- Caused by UMOD gene mutations
- Encodes uromodulin (Tamm–Horsfall protein), a non-ciliary protein
  - Maintains integrity of the thick ascending limb of the loop of Henle
- Intracellular abnormal uromodulin accumulation → tubular cell atrophy → progressive renal failure + ↓ urate excretion → hyperuricemia, gout

ADTKD due to REN mutations: REN (ADTKD-REN)

- Caused by *REN* gene mutations
- Encodes renin, a key hormone in the RAAS pathway
- Intracellular pre-prorenin accumulation → structural damage, apoptosis of renin-producing cells → progressive renal failure + ↓ renin production → ↓ blood pressure, anemia

Mucin-1 kidney disease (MKD)

- Caused by *MUC1* gene mutations
- Encodes mucin-1
- Pathophysiology not completely understood; results in progressive renal failure

COMPLICATIONS

- Gout, chronic kidney disease, end-stage renal disease (ESRD), low blood pressure, anemia

SIGNS & SYMPTOMS

- Clinical manifestations of chronic kidney disease

UKD

- Gout occurs at early age

ADTKD-REN

- Low/low-normal blood pressures, anemia (occurs in childhood; resolves in adolescence from the influence of sex hormones), mild hyperkalemia

MKD

- ↑ serum creatinine, hyperuricemia and gout occurring later in life

DIAGNOSIS

DIAGNOSTIC IMAGING

Ultrasound

- Small to normal kidneys with occasional cysts

LAB RESULTS

Urinalysis

- See presumptive diagnosis factors for each subtype

Biopsy

- Interstitial fibrosis

OTHER DIAGNOSTICS

- Confirmed through genetic testing

UKD (presumptive diagnosis factors)

- All three of the following
  - Strong family history of kidney disease
  - Family history of gout
  - *Urinalysis:* bland urinary sediment; absence of proteinuria or hematuria

ADKTD-REN (presumptive diagnosis factors)

- Family history of chronic kidney disease, plus one of the following
- Unexplained anemia out of proportion to ↓ glomerular filtration rate
- Evidence of acute kidney injury; bland urinary sediment
- Chronic kidney disease + hyperkalemia, low or low-normal blood pressure, and hyperuricemia

MKD (presumptive diagnosis factors)

- Presentation chronic kidney disease plus each of the following findings
  - *Urinalysis:* bland urinary sediment; little or no proteinuria
  - Absence of symptoms associated with UKD (precocious gout) or ADKTD-REN (childhood anemia, hyperkalemia, and hyperuricemia)

TREATMENT

MEDICATIONS

UKD

- *Gout:* allopurinol

ADTKD-REN

- *Symptomatic anemia:* erythropoietin
- *Low blood pressure, hyperkalemia:* fludrocortisone
- Avoid NSAIDs

SURGERY

- Treat progressive renal failure; kidney transplantation

MEDULLARY SPONGE KIDNEY (MSK)

osms.it/medullary-sponge-kidney

PATHOLOGY & CAUSES

- Rare congenital disorder characterized by ectasia (dilation) of the renal collecting ducts
- Genetic basis for developmental abnormality is incompletely understood; may involve embryonic disruption of the ureteral-bud and the metanephric blastema
- Renal collecting duct dilation, distension → urinary stasis → medullary cyst formation → impaired acidification in the terminal collecting duct → ↑ urine pH → nephrocalcinosis

RISK FACTORS

- Associated conditions include hemihypertrophy, Beckwith–Wiedemann syndrome

COMPLICATIONS

- Urinary tract infections
- Nephrocalcinosis
- Renal calculi (calcium phosphate, calcium oxalate)
- Chronic kidney disease

SIGNS & SYMPTOMS

- Often asymptomatic, flank pain, renal colic, hematuria, dysuria, nocturia

DIAGNOSIS

- Often discovered incidentally during investigations for another indication

DIAGNOSTIC IMAGING

Intravenous pyelography

- Cystic dilatations have brushlike appearance; enlarged pyramids; clusters of stones

CT scan

- Medullary nephrocalcinosis

LAB RESULTS

- Hypercalciuria, hyperuricosuria, hypocitraturia, and hyperoxaluria

TREATMENT

MEDICATIONS

Treat complications

- *Urinary tract infection:* antibiotics
- *Recurrent stone formation:* potassium citrate, thiazide diuretics, ↑ fluid intake, ↓ sodium in diet

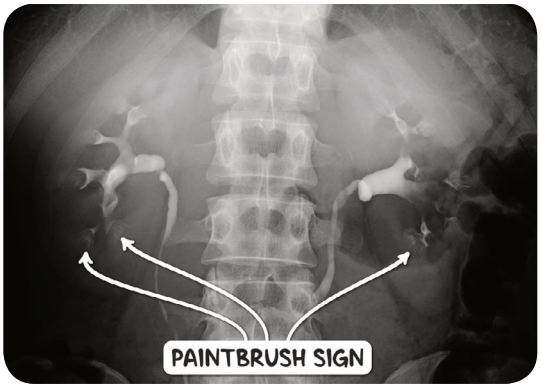

Figure 110.3 An X-ray image of the kidney, ureters and bladder. The dilated collecting ducts of the nephron give a paintbrush effect to each renal calyx.

MULTICYSTIC DYSPLASTIC KIDNEY (MCDK)

osms.it/dysplastic-kidney

PATHOLOGY & CAUSES

- Congenital disease, one/both kidneys do not form correctly → urine does not drain properly, builds up in kidneys, forms multiple fluid-filled sacs (cysts)
- Result of abnormal induction of metanephric blastema by ureteric bud
  - Possibly due to malformation of mesonephric duct/ureteric bud/both
- Ureteric bud fails to produce ureters, renal calyces, collecting ducts, collecting tubules
  - Urine cannot exit kidney, builds up → forms fluid-filled cysts
  - Fluid-filled cysts composed of abnormal connective tissue replace normal kidney tissue → kidney function decreases

CAUSES

- Mostly sporadic
- Potential link to medication during pregnancy
  - ACE inhibitors, illicit drugs (e.g. cocaine)
- Without treatment → kidney involutes (shrinks due to inactivity)

RISK FACTORS

- More common in individuals who are biologically male, genetic syndromes (papillorenal syndrome; error in genes *EYA1*, *SIX1*, *PAX2*)

COMPLICATIONS

Bilateral MCDK

- Potter sequence

Unilateral MCDK

- Uncommon, risk of chronic kidney disease

SIGNS & SYMPTOMS

Unilateral MCDK

- Asymptomatic/palpable flank mass

Bilateral MCDK

- Potter sequence

DIAGNOSIS

- May go undiagnosed if unilateral, no palpable flank mass, remaining kidney compensating fully

DIAGNOSTIC IMAGING

Antenatal ultrasound

- Most common
- Visualize kidney containing multiple large, peripheral cysts

Ultrasound

- Performed on neonate if health professionals detect palpable flank mass

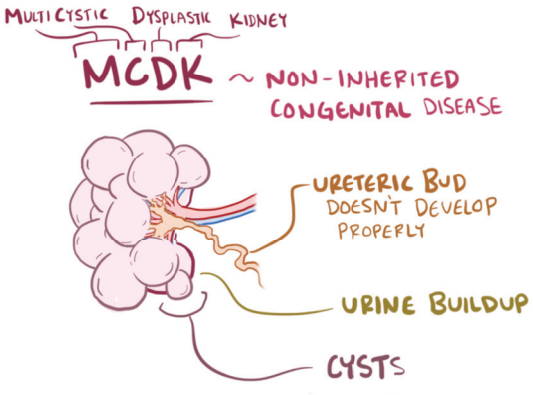

Figure 110.4 Pathological features of multicystic dysplastic kidney.

TREATMENT

SURGERY

Mild bilateral MCDK

- Dialysis, kidney transplant
- Newborn requires dialysis/kidney transplant

OTHER INTERVENTIONS

Unilateral MCDK

- Observation
  - Affected kidney involutes
- Follow-up
  - Serial ultrasound evaluation at birth, four weeks, two years, five years, 10 years of age; blood pressure, urinalysis (for proteinuria), renal function studies

Severe bilateral MCDK

- Provide support for Potter sequence
- Newborns generally don't survive

POLYCYSTIC KIDNEY DISEASE (PKD)

osms.it/polycystic-kidney

PATHOLOGY & CAUSES

- Genetic disease, kidneys fill with hundreds of cysts → become larger, unable to function
- Cysts in outer layer (cortex), inner layer (medulla) of kidneys
- Cysts lined with renal tubular epithelium, become larger
- Cysts make kidneys larger over time → compress blood vessels of neighboring healthy nephrons → starve neighboring nephrons of oxygen → poor perfusion of kidneys activates renin-angiotensin-aldosterone system → retain fluid → hypertension
- Large cysts → compress collecting system → urinary stasis → kidney stones

TYPES

Autosomal dominant

- AKA adult PKD; usually manifests in adulthood
- Polycystin 1 (PKD1), polycystin 2 (PKD2)
  - Necessary for inhibition of cell proliferation; if absent, cells proliferate abnormally, water moves to cyst lumen
- *PKD1* gene mutation → more severe, earlier onset
- *PKD2* gene mutation → less severe, later onset

Autosomal recessive

- AKA infantile PKD; usually manifests in infancy
  - Possible renal failure before birth → trouble producing urine → low amniotic fluid (oligohydramnios)
- Inherited mutation on both copies of polycystic kidney hepatic disease 1 (*PKHD1*) gene, fibrocystin protein
  - Fibrocystin co-localizes with PKD2 regulation pathway, calcium signaling similar to autosomal dominant

RISK FACTORS

Autosomal dominant

- One parent passes along PKD1/PKD2 mutation

Autosomal recessive

- Both parents pass along *PKHD1* mutation

COMPLICATIONS

- Renal insufficiency → renal failure
- Kidney stones

Autosomal dominant

- Cerebral artery berry aneurysms
- Mitral valve prolapse
- Benign hepatic cysts
- Heart failure (due to aortic root dilation)

Autosomal recessive

- Congenital hepatic fibrosis → portal hypertension
- Ascending cholangitis (due to obstructed biliary tree)

SIGNS & SYMPTOMS

- Flank pain, high blood pressure, hematuria (blood in urine), renal insufficiency, renal failure, fetal oligohydramnios in autosomal recessive PKD

DIAGNOSIS

DIAGNOSTIC IMAGING

Prenatal ultrasound

- For autosomal recessive polycystic kidney disease
- Bilaterally large kidneys with cysts, oligohydramnios

LAB RESULTS

- Complete blood count (CBC), urinalysis, urine culture

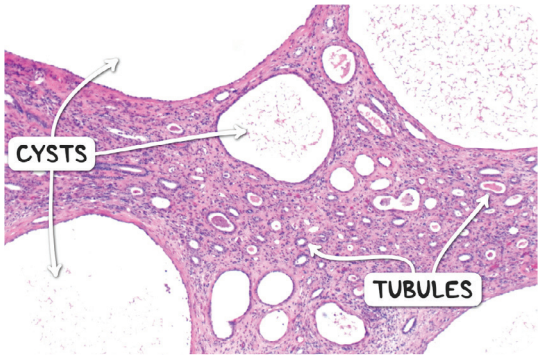

Figure 110.5 Histological appearance of renal parenchyma in a case of polycystic kidney disease.

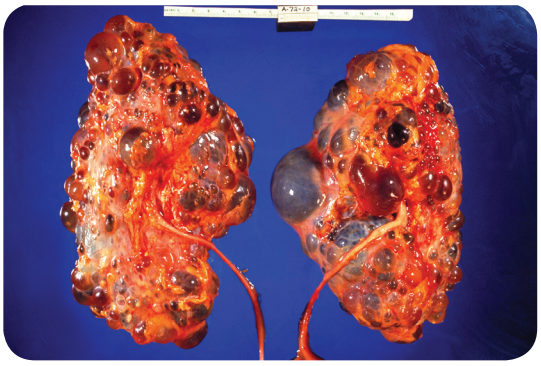

Figure 110.7 The gross pathological appearance of polycystic kidneys.

TREATMENT

MEDICATIONS

- *Hypertension:* ACE inhibitors, angiotensin receptor blockers
- *Cholestasis:* ursodiol (slows down rate of cholesterol absorption by intestines)

SURGERY

- Kidney transplant

Portal hypertension

- Portocaval shunt → bypasses liver, connects portal vein to inferior vena cava; liver transplant

OTHER INTERVENTIONS

- Dialysis

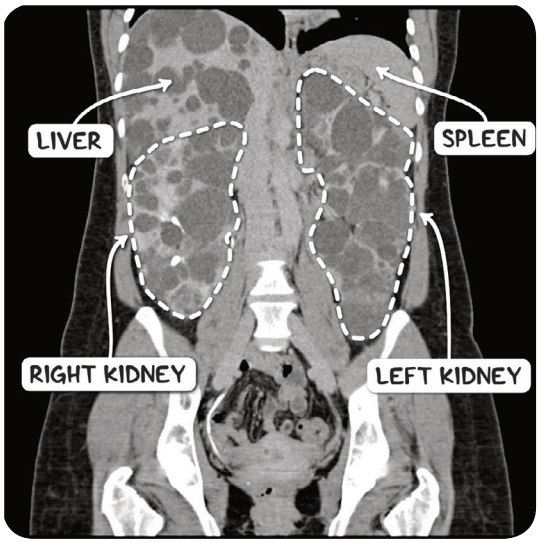

Figure 110.6 A CT scan in the coronal plane demonstrating innumerable cysts in the kidneys and liver in autosomal dominant polycystic kidney disease.

RENAL AGENESIS

osms.it/renal-agenesis

PATHOLOGY & CAUSES

- Ureteric bud fails to induce metanephric blastema to develop → one/both kidneys don't form

TYPES

Unilateral renal agenesis (URA)

- One kidney does not develop
  - Usually asymptomatic if other kidney healthy, able to compensate
  - Predisposes individuals to more serious renal problems

Bilateral renal agenesis (BRA)

- Neither kidney develops
  - Incompatible with life outside womb
  - Usually fatal within first few days after birth; no treatment

CAUSES

- Combination of genetic/*in utero* environmental factors (toxins, infections)

RISK FACTORS

- More common in individuals who are biologically male

COMPLICATIONS

URA

- Hypertrophy of remaining kidney, infections, kidney stones, hypertension, renal failure

BRA

- Oligohydramnios, pulmonary hypoplasia, Potter sequence

SIGNS & SYMPTOMS

- Oligohydramnios/anhydramnios (no amniotic fluid)
- Symptoms at birth include high blood pressure, protein/blood in urine, swelling of face/extremities

URA

- Bsually asymptomatic if other kidney healthy

BRA

- Babies ill at birth, usually do not live
  - Widely separated eyes with epicanthal folds
  - Low set ears
  - Flat, broad nose
  - Small chin
  - Underdeveloped lungs

DIAGNOSIS

DIAGNOSTIC IMAGING

Prenatal ultrasound/MRI

- Confirm diagnosis

OTHER DIAGNOSTICS

- Oligohydramnios/anhydramnios

TREATMENT

SURGERY

- Kidney transplant

OTHER INTERVENTIONS

- Routine monitoring
- Dialysis

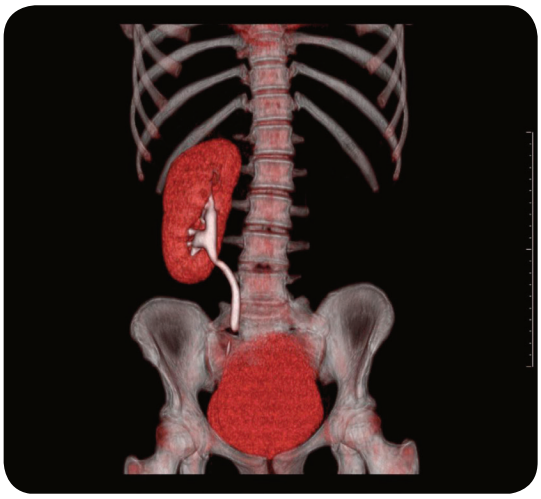

Figure 110.8 A 3D reconstruction of a CT scan demonstrating left-sided renal agenesis.

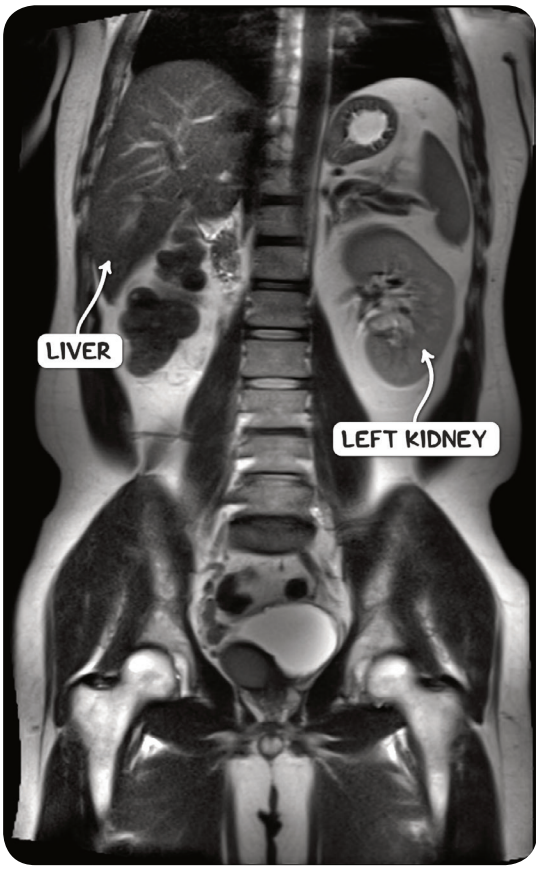

Figure 110.9 An MRI scan in the coronal plane demonstrating right-sided renal agenesis.