Congenital Renal Anomalies: Classification, Diagnosis, and Management

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March 2026

Congenital Renal Anomalies: Classification, Diagnosis, and Management

Learning Objectives

By completion of this handout, students will be able to:

1. Understand the classification system for congenital anomalies of the kidney and urinary tract (CAKUT)
2. Recognize the developmental basis for renal hypodysplasia, dysplasia, and agenesis
3. Describe the pathophysiology, clinical presentation, and management of specific renal malformations
4. Interpret prenatal and postnatal imaging findings for diagnostic accuracy
5. Understand the concept of "nephron endowment" and implications for long-term renal function
6. Manage antenatal hydronephrosis and distinguish obstructive from non-obstructive etiologies
7. Recognize syndromic presentations associated with CAKUT

I. CAKUT CLASSIFICATION AND DEVELOPMENTAL EMBRYOLOGY

A. CAKUT Definition and Epidemiology

Definition: Congenital Anomalies of the Kidney and Urinary Tract encompass a spectrum of structural malformations affecting the kidney, ureter, bladder, or urethra, resulting from disruption of nephrogenesis or urogenital development.

Incidence and Prevalence: - Overall incidence: 1 in 300-500 live births (approximately 200,000 cases per year in the United States) - Represents 30-40% of all congenital anomalies detected prenatally - Leading cause of ESRD in children (40-50% of pediatric ESRD due to congenital anomalies) - Accounts for $1.2 billion in annual healthcare expenditures in pediatric nephrology

Genetic Contributions: - Monogenic mutations (PAX8, GDNF, RET, ROBO2) account for 10-15% of cases - Chromosomal abnormalities (Down, Turner, Potter syndromes) associated with

CAKUT in 30-40% - Multifactorial inheritance with environmental factors - Familial clustering in 5-10% of cases (autosomal dominant inheritance pattern common)

B. Developmental Embryology

Timeline: - **Week 5:** Ureteric bud (Wolffian duct) emerges from mesonephric duct caudal to mesonephros - **Weeks 5-13:** Ureteric bud undergoes branching morphogenesis, forming ureter, renal pelvis, major calyces, minor calyces, collecting ducts - **Weeks 5-35:** Mesenchymal-epithelial transition (MET) in metanephric mesenchyme; condensation around collecting duct tips - **Weeks 8-34:** Nephron formation occurs as collecting ducts branch and induce nephron formation in adjacent mesenchyme - **Week 34-36:** Nephrogenesis completes; approximately 1 million nephrons per kidney

Key Signaling Molecules: - **GDNF (Glial-derived neurotrophic factor):** Secreted by metanephric mesenchyme; signals to ureteric bud via RET tyrosine kinase receptor - **RET (REarranged during Transfection):** Proto-oncogene; receptor for GDNF; essential for ureteric bud outgrowth - **PAX8 (Paired box gene 8):** Transcription factor; regulates development of both kidney and thyroid - **SIX1/SIX2:** Control mesenchymal progenitor maintenance and differentiation - **WNT signaling:** Regulates both nephrogenesis and ureteric bud development - **FGF signaling:** Regulates ureteric bud branching and mesenchyme differentiation

Disruption of Development Leads to CAKUT: - Reduced/absent GDNF or RET signaling ☐ oligonephronia, dysplasia, agenesis - Misdirection of ureteric bud ☐ ectopic kidney, duplex collecting system, VUR - Obstruction of ureteric outflow ☐ hydronephrosis, hydroureter, secondary dysplasia

C. CAKUT Classification (International Nomenclature, ISN 2014)

Major Categories:

Category	Subcategories	Mechanisms
A. Renal Agenesis	Unilateral (ULRA) or Bilateral (BLRA)	Complete failure of ureteric bud induction; maternal teratogen exposure
B. Hypoplasia/Dysplasia	Oligonephronia, dysplasia (cystic/non-cystic), hypodysplasia	Reduced nephron number; abnormal development of renal parenchyma
C. Position/Fusion	Ectopia, horseshoe kidney, crossed fused ectopia	Abnormal ureteric bud origin or trajectory; misdirection of kidney migration
D. Collecting System	Duplex, ureteropelvic junction (UPJ) obstruction, ureterovesical junction (UVJ) obstruction	Abnormal branching of ureteric bud; obstruction at junction sites
E. Vesicoureteral Reflux	Primary (developmental), secondary (neurogenic or anatomic)	Incompetent ureterovesical junction; increased pressure transmission

Category	Subcategories	Mechanisms
F. Functional	Diuresis renography abnormalities without structural changes	Physiologic obstruction; delayed drainage without anatomic narrowing

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II. RENAL AGENESIS, HYPOPLASIA, AND DYSPLASIA

A. Renal Agenesis

Unilateral Renal Agenesis (ULRA)

Epidemiology: - Incidence: 1 in 1,000-2,000 live births - Often incidental finding on imaging for other indications - No significant impact on renal function; single kidney can achieve normal adult GFR through compensatory hypertrophy

Pathophysiology: - Complete failure of ureteric bud induction or early regression - Ipsilateral ureteral agenesis (typically) - Contralateral kidney often normal or with increased size due to compensatory growth

Clinical Presentation: - Majority asymptomatic; incidental imaging finding - May be detected on prenatal ultrasound - No renal dysfunction (serum creatinine and GFR normal) - Risk: Increased proteinuria over time from hyperfiltration; slightly increased risk of hypertension in adulthood

Diagnosis: - Ultrasound: Absent kidney; normal contralateral kidney (often enlarged) - Renal scintigraphy: No uptake ipsilateral; normal function contralateral - CT or MRI: Confirms absent renal tissue; no ectopic kidney

Management: - No treatment required; normal renal function expected - Counseling: Avoid contact sports, NSAIDs if possible; avoid dehydration - Monitor: Annual blood pressure, urinalysis, serum creatinine - Avoid nephrotoxic drugs - Genetic counseling: 5-10% risk of CAKUT in siblings; 4-5% risk in offspring - Prenatal counseling for future pregnancies: Ultrasound screening at 20 weeks

Bilateral Renal Agenesis (BLRA)

Epidemiology: - Incidence: 1 in 4,000-7,000 live births - **Incompatible with postnatal life**; lethal in utero if severe

Pathophysiology: - Complete bilateral failure of ureteric bud induction - Associated with severe bilateral oligohydramnios (due to absent fetal urine production) - Potter sequence: Characteristic facial features (low-set ears, micrognathia, beak nose), limb deformities, severe pulmonary hypoplasia

Prenatal Diagnosis: - Maternal ultrasound: Absent amniotic fluid (severe oligohydramnios) + bilateral absent kidneys - Fetal imaging: No bladder filling (no fetal urine production)

Management: - Antenatal counseling regarding poor prognosis - Perinatal palliative care discussions with family - Birth planning: Expected neonatal death from pulmonary hypoplasia - Offers of comfort care, organ donation (in selected cases)

B. Renal Hypoplasia and Dysplasia

Definitions:

Hypoplasia: - Structurally normal kidney with **reduced number of nephrons** (oligonephronia) - Normal calyceal architecture; normal echogenicity on ultrasound - Usually detected only through functional studies (reduced GFR for kidney size)

Dysplasia: - Abnormal kidney development with **primitive metanephric tissue**, disorganized calyces, fibrosis, and often **cystic dilation** - Histologic findings: Smooth muscle hyperplasia, disorganized glomeruli, primitive ducts - May be diffuse or segmental

Hypodysplasia (Combined Hypoplasia + Dysplasia): - Most common form of renal underdevelopment - Reduced nephron number with abnormal development - Accounts for 30-40% of congenital renal insufficiency in children

Epidemiology: - Combined incidence: 1 in 800-1,000 live births - Accounts for 10-15% of pediatric ESRD cases

Etiology: - **Genetic:** Mutations in GDNF, RET, PAX8, SIX1/SIX2, ROBO2 - **Maternal teratogens:** ACE inhibitors/ARBs (especially 2nd/3rd trimester), NSAIDs, cocaine, maternal diabetes - **Obstructive:** Secondary dysplasia from chronic prenatal obstruction (e.g., PUV, severe UPJ obstruction) - **Syndromic:** Associated with chromosomal abnormalities or genetic syndromes

Clinical Presentation: - Often asymptomatic; detected on prenatal ultrasound or during workup for renal insufficiency - Some present with acute kidney injury if bilateral involvement - Progressive renal failure if bilateral or if single kidney severely affected - May have growth failure, hypertension, anemia (if significant renal disease)

Diagnosis:

Imaging Findings: - **Ultrasound:** Small kidney(s) with increased echogenicity; irregular contour; may have cystic spaces - **Renal scintigraphy (DMSA):** Reduced tracer uptake; segmental areas of photopenia if dysplastic - **MRI:** Better defines cystic vs. non-cystic dysplasia; assesses for associated VUR or upper tract obstruction

Renal Biopsy (if diagnosis uncertain): - Histology shows: Primitive tubules, smooth muscle proliferation, fibrosis, disorganized architecture - Immunofluorescence: Nonspecific (no immune deposits)

Progression: - Bilateral symmetric hypodysplasia: Progressive loss of renal function; may reach ESRD by adulthood - Unilateral: Generally benign if contralateral kidney normal

Management: - **Conservative:** Serial renal function monitoring; management of complications (hypertension, anemia, growth failure) - **Nutritional:** Adequate calories and protein for growth; may require nutritionist support - **Pharmacologic:** ACE inhibitor or ARB to reduce proteinuria and slow progression - **Monitoring:** Blood pressure, urinalysis, serum creatinine every 3-6 months - **RRT:** Dialysis or transplantation if ESRD develops

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III. POSITIONAL ANOMALIES

A. Horseshoe Kidney

Epidemiology: - Incidence: 1 in 400-600 live births - Most common renal fusion anomaly - No gender predominance - Associated with Turner syndrome (5-10%), Down syndrome, and other chromosomal abnormalities

Embryology: - Kidneys undergo normal ascent from pelvis but **fuse at lower poles** during ascent (typically at L5 level) - Isthmus of renal parenchyma or fibrous tissue connects the two kidneys - Anomalous blood supply common (multiple renal arteries and veins) - Ureteropelvic junction often malpositioned anteriorly

Pathophysiology: - Usually asymptomatic and incidental finding - Risk of obstruction at UPJ (from anomalous vessels, fibrous tissue, or abnormal ureteral course) - Increased risk of UTI (urinary stasis in lower-pole calyces) - Increased risk of trauma (lower, more anterior position) - Slightly elevated risk of renal malignancy (increased with other CAKUT)

Clinical Presentation: - Often asymptomatic; discovered incidentally on imaging - May present with flank pain (if obstruction develops) - May present with fever (UTI) - Recurrent UTI in some cases

Diagnosis: - **Ultrasound:** Isthmus connecting lower poles; abnormal kidney shape - **CT or MRI:** Excellent anatomic detail; shows vascular anatomy - **Renal scintigraphy:** Reduced function if obstruction present - **IVU (less commonly used):** Shows characteristic “tent-like” appearance with medial deviation of ureters

Management: - **No treatment if asymptomatic** (majority of cases) - **Conservative:** Periodic imaging (ultrasound or renal scintigraphy) to assess for obstruction - **Surgical:** Pyeloplasty for symptomatic UPJ obstruction - **Avoid:** Contact sports, excessive abdominal trauma (relative contraindication given anterior position) - **Imaging for evaluation:** If recurrent UTI, use renal scintigraphy to assess for obstruction - **Anesthesia consideration:** Abnormal vascular anatomy; communicate with anesthesia if surgery needed

B. Ectopic Kidney

Epidemiology: - Incidence: 1 in 900 live births - Kidneys fail to migrate normally from sacral region

Classification:

Thoracic Ectopia (rare): - Kidney ascends above diaphragm - Usually discovered incidentally on chest imaging - No functional impairment; no treatment needed - Risk: Retroperitoneal masses can compress lung tissue or cause cardiac compromise if large

Lumbar Ectopia: - Kidney remains lateral to normal position on iliac wing - Usually asymptomatic; incidental finding - May have anomalous blood supply and ureter - No specific treatment needed unless obstruction develops

Pelvic Ectopia: - Kidney remains in pelvis; does not ascend - May have anomalous blood supply (hypogastric artery) - Increased risk of obstruction, UTI, and trauma - May cause urinary retention or dysmenorrhea if large

Crossed Fused Ectopia: - Both kidneys on same side; fused at mid-pole - Three patterns: Type I (inferior fused), Type II (superior fused), Type III (side-by-side) - Increased risk of obstruction and UTI

Clinical Presentation: - Usually asymptomatic - May present with flank pain, recurrent UTI, hematuria - Rarely: acute abdomen from torsion of ectopic kidney

Diagnosis: - **Ultrasound or CT:** Shows ectopic location; assess for hydronephrosis - **Renal scintigraphy:** Confirms functional tissue; assesses differential renal function - **IVU or MRI:** Detailed anatomy; important if surgery planned

Management: - **Asymptomatic:** Observation; periodic imaging (ultrasound q 1-2 years) - **Symptomatic obstruction:** Pyeloplasty or nephrostomy if severe - **Recurrent UTI:** Consider prophylactic antibiotics; imaging to assess for obstruction - **Surgical planning:** Communicate anomalous vascular anatomy to surgeon

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IV. COLLECTING SYSTEM ANOMALIES

A. Duplex Collecting System (Duplicated Ureter)

Epidemiology: - Incidence: 1 in 125-600 live births (unilateral duplications more common) - Bilateral in 5-10% of cases - Female predominance (2:1 ratio)

Classification:

Partial Duplications: - **Y-shaped ureter:** Divergence occurs below pelvic brim; single ureter continues distally - Most common form (60-70% of duplications) - Usually asymptomatic; discovered incidentally

Complete Duplications: - **Two separate ureters** drain respective renal halves; both reach bladder - Classic teaching: Superior pole ureter has **abnormally low bladder insertion** (Weigert-Meyer rule in 85% of cases) and is at risk for ectopic insertion and obstruction - Inferior pole ureter has **higher (more normal) insertion** but predisposed to VUR - Differential function: Usually preserved; 50% of renal function to each collecting system in most cases

Ectopic Ureter: - Ureteral orifice drains **outside the bladder** (below internal urethral sphincter) - More common in females; may lead to continuous urinary leakage - In males: May insert into posterior urethra or prostate (usually dry, but may cause symptoms)

Clinical Presentation:

Asymptomatic (Majority): - Discovered incidentally on prenatal ultrasound - Detected during imaging for other indications

Symptomatic: - **Recurrent UTI:** Particularly if upper pole ureter obstructed - **Vesicoureteral reflux:** Lower pole ureter more susceptible to VUR (50% of cases) - **Flank pain:** From hydronephrosis of obstructed moiety - **Continuous urinary incontinence (females):** If ectopic insertion below sphincter - **Urinary leakage in males:** If ectopic insertion in posterior urethra or prostate

Diagnosis: - **Ultrasound:** Two separate ureters on longitudinal scan; may see hydronephrosis of one moiety - **VCUG:** Demonstrates VUR if present; assesses bladder; may show ectopic ureteral

orifice - **Renal scintigraphy (DMSA or MAG3):** Assesses differential function; MAG3 shows differential clearance - **CT or MRI:** Excellent anatomic detail; shows ectopic insertion if present; vascular anatomy - **Cystoscopy:** Direct visualization of ectopic orifice if location uncertain

Management:

Asymptomatic, No Obstruction or VUR: - Observation; periodic imaging (ultrasound q 1-2 years) - Standard infection precautions; good perineal hygiene

Symptomatic Upper Pole Obstruction: - **Partial nephrectomy (heminephrectomy):** Upper pole nephrectomy indicated if <20% differential function - **Pyeloplasty:** If >20% function and obstruction symptomatic - Success rate for heminephrectomy >95%

Symptomatic Lower Pole VUR: - **Conservative:** Prophylactic antibiotics; periodic VCUG - **Surgical:** Ureteral reimplantation if high-grade reflux, recurrent UTI, or noncompliance with prophylaxis

Ectopic Ureter: - **Conservative:** Prophylactic antibiotics; use pads if leakage - **Surgical:** Ureteroureterostomy (anastomosis to normal moiety collecting system) or nephrectomy if non-functional

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B. Ureteropelvic Junction (UPJ) Obstruction

Previously detailed in pediatric kidney disease handout; highlighted here as important CAKUT component:

Key Points: - Most common intrauterine urinary tract anomaly - Functional or anatomic narrowing at UPJ - Differential function >20% typically managed conservatively with monitoring - Pyeloplasty success rate >95% for symptomatic or worsening cases

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V. POLYCYSTIC KIDNEY DISEASE IN CHILDREN

A. Autosomal Recessive Polycystic Kidney Disease (ARPKD)

Epidemiology: - Incidence: 1 in 20,000 live births - Gene: PKHD1 (chromosome 6q21) encodes fibrocystin - Homozygous mutations required for disease expression

Pathophysiology: - Cilia dysfunction in collecting ducts and bile ducts - Abnormal cell-cell signaling; cyst formation - Associated with congenital hepatic fibrosis (biliary dysgenesis) - Progressive bilateral disease; differs from ADPKD

Clinical Presentation by Age:

Prenatal (Identified on Ultrasound): - Symmetric, diffuse bilateral kidney enlargement with "echogenic" appearance - Severe oligohydramnios (decreased fetal urine output) - Potter sequence features (if severe bilateral disease) - Hepatomegaly may be present

Perinatal/Neonatal (Most Severe Form, ~40% of cases): - Bilateral massive kidney enlargement - Severe respiratory distress from pulmonary hypoplasia and massive abdominal distension - Renal insufficiency (elevated creatinine; often oliguria) - Hypertension (severe, difficult to

control) - Failure to thrive - Mortality: 50% in first month without aggressive support; early ESRD development

Infantile Form (~40% of cases): - Slower progression - Mild-to-moderate kidney enlargement - Hypertension (95% of cases) - Progresses to ESRD by age 5-10 years - May develop esophageal varices from portal hypertension

Juvenile/Adolescent Form (~20% of cases): - Minimal renal symptoms initially - Progresses slowly; ESRD by adolescence - Clinically apparent hepatic fibrosis with portal hypertension - Increased morbidity from liver disease

Diagnosis: - **Prenatal ultrasound:** Echogenic, enlarged kidneys; oligohydramnios - **Postnatal ultrasound:** Bilaterally enlarged kidneys with "striated" echogenic appearance (collecting ducts dilated) - **Renal biopsy:** Not typically needed; recognizable histology if performed - **Genetic testing:** PKHD1 gene sequencing for confirmation and family planning - **Liver imaging:** Ultrasound or MRI to assess for congenital hepatic fibrosis

Management:

Neonatal Period: - Respiratory support (may require mechanical ventilation from pulmonary hypoplasia) - Aggressive blood pressure control (ACE inhibitor or ARB first-line) - Fluid and electrolyte management - Nutritional support; early feeding attempts - Renal function monitoring; prepare for dialysis if needed

Ongoing: - Blood pressure control: ACE inhibitor/ARB + additional agents as needed - Renal function monitoring; CKD staging - Growth monitoring; nutritional support - Screening for hepatic complications: Ultrasound q 1-2 years; if evidence of portal hypertension, upper endoscopy for varices - Management of renal osteodystrophy (secondary hyperparathyroidism, phosphate binders, calcitriol) - Anemia management with EPO-stimulating agents - Dialysis and transplantation when ESRD reached

Prognosis: - Highly variable; perinatal form has poorest prognosis - Progressive renal disease inevitable - Median age at ESRD: 10-15 years (varies by presentation) - Survival to age 20 years: ~80% with intensive management

B. Autosomal Dominant Polycystic Kidney Disease (ADPKD)

Epidemiology: - Incidence: 1 in 400-1,000 live births - Genes: PKD1 (chromosome 16p13, 85% of cases) and PKD2 (chromosome 4q21, 15% of cases) - Heterozygous mutation (one normal allele sufficient for disease); high penetrance

Presentation in Childhood: - Often asymptomatic; discovered on family screening or prenatal ultrasound - Renal cysts present at birth but slowly progressive - Majority of children have normal renal function for many years - Hypertension may develop (10-30% of children)

PKD1 vs PKD2 Genetics:

Feature	PKD1	PKD2
Gene Locus	Chromosome 16p13	Chromosome 4q21
Frequency	85%	15%
Protein	Polycystin-1 (1,274 aa)	Polycystin-2 (968 aa)
ESRD Age	50-60 years (mean)	70-80 years (mean)

Feature	PKD1	PKD2
Cyst Burden	Earlier, more severe	Later, less severe
Extrarenal Manifestations	Frequent (cysts in liver, pancreas, spleen; cardiac abnormalities)	Less common

Clinical Features in Children: - Usually asymptomatic - Hypertension (develops in minority; monitor blood pressure) - Renal cysts on imaging (symmetric, bilateral) - **Normal renal function** typically maintained through childhood and early adulthood - Extrarenal manifestations: Liver cysts (60-75%), cardiac valve abnormalities (25%), cerebral aneurysms (8-10%, higher if family history)

Diagnosis: - **Renal ultrasound:** Bilateral, diffuse renal cysts; preserved renal parenchyma - **Genetic testing:** PKD1/PKD2 sequencing; confirms diagnosis and allows for family counseling - **Family screening:** Ultrasound for at-risk relatives; genetic counseling if confirmed

Management in Children: - **Blood pressure control:** Target <50th percentile for age/height; ACE inhibitor or ARB if hypertension develops - **Monitoring:** Annual BP checks; serum creatinine; urinalysis - **Avoidance of NSAIDs** (increased cyst growth and renal decline) - **Cardiac evaluation:** Echocardiography if cardiac symptoms or family history of cardiomyopathy - **Neuroimaging:** Screening for cerebral aneurysm considered if family history of SAH; controversial in asymptomatic children - **Genetic counseling:** 50% risk to offspring - **Lifestyle:** Avoid trauma; avoid contact sports with uncertain renal function - **Long-term follow-up:** Transition to adult nephrology; continue monitoring for complications

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VI. MULTICYSTIC DYSPLASTIC KIDNEY (MCDK)

Epidemiology: - Incidence: 1 in 1,000-4,300 live births - Most common renal cystic mass in infants - Usually unilateral (80%); bilateral in 20% (often incompatible with life if severe)

Pathophysiology: - Severe form of renal dysplasia - **Complete absence of normal renal architecture**; replaced by cysts of varying sizes - Non-functional; demonstrates no tracer uptake on scintigraphy - Contralateral kidney usually normal but at risk for hypertension and CKD if MCDK undergoes malignant transformation

Embryology: - Thought to result from **early ureteric bud inversion or atresia** - Leads to abnormal mesenchymal-epithelial interaction - Results in cyst formation without organized nephron development

Clinical Presentation: - Majority asymptomatic; discovered on prenatal ultrasound (50-60% of cases) - May present with abdominal mass or flank mass on physical exam - Rarely: infection, hemorrhage into cyst, hypertension from renin secretion

Diagnosis: - **Prenatal ultrasound:** Characteristic appearance with multiple non-communicating cysts of varying sizes; no identifiable renal pelvis or ureter; absent Doppler flow in renal artery - **Postnatal ultrasound:** Confirms diagnosis; no tracer uptake - **Renal scintigraphy (DMSA):** Confirms non-functional tissue (zero differential function) - **CT or MRI:** Shows characteristic cystic appearance; assesses contralateral kidney

Natural History: - **Involution:** 50-70% of unilateral MCDK spontaneously regress/involute over first 5 years of life - **Persistent:** 30-50% persist; rarely grow - **Malignant potential:** Risk of malignancy (Wilms tumor, renal cell carcinoma) estimated at 1-5% (controversial; some studies suggest risk similar to general population)

Management:

Standard Approach (Conservative): 1. **Observation:** Serial imaging (ultrasound) at 3 months, 6 months, 1 year, then annually 2. **Contralateral kidney monitoring:** Assess for hypertension, proteinuria, renal insufficiency 3. **Blood pressure monitoring:** At each visit; treat if >95th percentile for age/height 4. **Screening for Wilms tumor:** Annual physical exam; consider ultrasound screening (controversial); educate parents on abdominal masses 5. **Anticipatory guidance:** Avoid NSAIDs; avoid contact sports with uncertain contralateral kidney function

Surgical Approach (Selective): - **Nephrectomy indications (not routine, but consider):** - Symptomatic (pain, infection, hemorrhage) - Large mass causing respiratory compromise or GI obstruction - Hypertension refractory to medical therapy - Malignancy suspected or confirmed - Patient anxiety/family preference for surgical management - **Success rate:** Nephrectomy results in normalization of hypertension if present

Outcome: - Excellent long-term prognosis with conservative management - Most children with unilateral MCDK and normal contralateral kidney have normal renal function - Risk of CKD and hypertension in adulthood if contralateral kidney has underlying abnormality

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VII. NEPHRON ENDOWMENT AND LOW BIRTH WEIGHT

A. Concept of Nephron Endowment

Definition: Total number of nephrons present at birth; represents maximum renal functional potential throughout life.

Normal Nephron Number: - Term infant: 0.8-1.2 million nephrons per kidney - Nephrogenesis complete by 34-36 weeks gestation - Subsequent kidney growth results from nephron hypertrophy, not new nephron formation

Determinants of Nephron Endowment: 1. **Genetic factors:** Mutations in GDNF, RET, PAX8, SIX genes affect maximum nephrogenesis 2. **Intrauterine growth:** Low birth weight associated with reduced nephrogenesis 3. **Maternal factors:** Gestational diabetes, hypertension, proteinuria, malnutrition affect fetal kidney development 4. **Gestational age:** Premature infants (<34 weeks) have incomplete nephrogenesis; continued development postnatally (limited) 5. **Environmental exposures:** Maternal ACE inhibitor/ARB use (2nd/3rd trimester), cocaine, NSAIDs, maternal smoking

Clinical Significance: - Low nephron endowment = reduced renal reserve - Predisposes to earlier CKD development with superimposed renal insults - Increases lifetime hypertension risk - Increases proteinuria risk - Increases ESRD risk with age

B. Low Birth Weight and Renal Outcomes

Epidemiology: - Low birth weight (LBW, <2,500 g): Incidence 8-10% of live births in developed countries - Very low birth weight (VLBW, <1,500 g): ~1-2% of live births - Extremely low birth weight (ELBW, <1,000 g): ~0.5-1% of live births

Mechanisms of Reduced Nephron Endowment in LBW:

Intrauterine Growth Restriction (IUGR): - Placental insufficiency reduces nutrient and oxygen delivery to developing fetus - Altered GDNF-RET signaling in response to hypoxia - Results in oligonephronia (reduced nephron number)

Prematurity: - Birth before 34 weeks gestation results in **incomplete nephrogenesis** - Extrauterine development cannot compensate; only ~2-5% additional nephrons form postnatally - Risk of abnormal renal development from immature regulatory mechanisms - Exposure to nephrotoxic medications (aminoglycosides, ACE inhibitors, NSAIDs)

Associated Risk Factors for Worse Outcomes: - Maternal hypertension, diabetes, smoking - Placental abnormalities (placental hypoplasia, infarction) - Maternal infections (congenital cytomegalovirus, toxoplasmosis) - Maternal nutritional deficiencies

Long-Term Renal Outcomes in LBW Infants:

Outcome	Incidence/Risk
Lower baseline GFR	10-20% lower than term peers
Accelerated CKD progression	1.5-2× increased risk of CKD stage ≥2 by young adulthood
Hypertension	20-30% increased prevalence; earlier onset
Albuminuria/Proteinuria	10-15% higher prevalence
ESRD	2-3× increased lifetime risk
Interaction with second hit	Additive risk if superimposed renal disease (recurrent UTI, glomerulonephritis, acute tubular necrosis)

Management Strategies:

1. **Early Screening:**
   - Renal ultrasound at discharge (assess for CAKUT, renal size)
   - Serum creatinine at discharge; follow serially during neonatal period
   - Monitor growth; identify failure to thrive (indicator of worsening CKD)
2. **Prevention of Secondary Renal Insults:**
   - Avoid nephrotoxic medications (aminoglycosides, contrast agents, NSAIDs)

- Minimize volume depletion (aggressive hydration before contrast)
- Strict infection control; prompt treatment of UTI
- Optimize nutrition; avoid dehydration

3. **Blood Pressure Control:**
   - Screen at 3-4 months postnatal age; then at routine visits
   - Treat if >95th percentile for age/height
   - ACE inhibitor or ARB preferred for renoprotection
4. **Monitoring:**
   - Annual BP measurement through childhood
   - Annual serum creatinine; calculate eGFR
   - Annual urinalysis; screen for proteinuria
   - Parental counseling: Increased risk of future CKD; lifestyle modifications (salt restriction, exercise, avoid NSAIDs)
5. **Transition Planning:**
   - Early nephrology referral if GFR <90 mL/min/1.73 m² or other CKD evidence
   - Establish continuity of care with adult nephrology

VIII. ANTENATAL HYDRONEPHROSIS MANAGEMENT

A. Classification and Differential Diagnosis

Grading Systems (Prenatal): - **Mild:** Pelvic anteroposterior diameter (APD) 7-10 mm (15-20 weeks) or 10-15 mm (after 20 weeks) - **Moderate:** APD 15-25 mm - **Severe:** APD >25 mm

Differential Diagnosis of Antenatal Hydronephrosis:

Diagnosis	Features	Prognosis
UPJ Obstruction	Dilated pelvic/calyces; normal ureter; normal bladder	40-60% resolve spontaneously; 40-60% require pyeloplasty
Vesicoureteral Reflux	Dilated ureter; dilated collecting system; normal bladder	Variable; 50% resolve; 50% require management
Megaureter	Dilated ureter (>7 mm); mild pelvicalyceal dilation; normal bladder	80-90% resolve spontaneously
Posterior Urethral Valves	Bilateral hydronephrosis; thick-walled dilated bladder; oligohydramnios	Requires urgent intervention; high risk of ESRD
Vesical Outlet Obstruction	Bilateral hydronephrosis; massively dilated bladder; severe oligohydramnios	Poor prognosis; high mortality from pulmonary hypoplasia
Multicystic Dysplastic Kidney	Non-functional; cystic appearance; no organized collecting system	Non-functional kidney; ~50% involute; ~50% persist

Diagnosis	Features	Prognosis
Non-Obstructive Dilation	Mild-moderate dilation; normal function on MAG3; no obstruction on VCUG	Excellent; no treatment needed; may resolve completely

B. Antenatal Surveillance and Counseling

Surveillance Protocol:

1. **Initial Detection (Anomaly Scan, 18-22 weeks):**
   - Measure pelvic APD; assess for bilateral involvement
   - Assess bladder size and emptying
   - Assess amniotic fluid volume
   - Assess for other congenital anomalies
2. **Follow-up Ultrasounds (Interval Scanning):**
   - **Mild hydronephrosis (7-10 mm):** Repeat ultrasound at 28 weeks and 36 weeks
   - **Moderate hydronephrosis (10-15 mm):** Repeat at 24 weeks and 36 weeks
   - **Severe hydronephrosis (>15 mm):** Repeat at 24 weeks and 32 weeks; consider MRI
   - **Assess progression:** Increasing APD suggests obstruction; stable or decreasing suggests non-obstructive
3. **Antenatal MRI (Selected Cases):**
   - Severe bilateral dilation (>15 mm)
   - Suspected obstructive lesion
   - Unclear diagnosis on ultrasound
   - Assess renal parenchymal thickness and echogenicity

C. Postnatal Management

Timing of First Postnatal Imaging: - **Term infants:** Renal ultrasound within first 48-72 hours of life (captures important early data; may see improvement if non-obstructive) - **Preterm infants:** Often deferred until approaching term-equivalent age (allows for ongoing postnatal nephrogenesis)

Postnatal Imaging Sequence:

Stage 1: Ultrasound (Initial): - Confirm pelvicalyceal dilation; measure APD - Assess corticomedullary differentiation (preserved = better function) - Assess for features suggesting obstruction (calyceal dilation, renal parenchymal thinning) - Assess contralateral kidney - **Antibiotic Prophylaxis Consideration:** Controversial; some clinicians initiate prophylaxis pending diagnostic workup; others reserve for high-risk cases or confirmed VUR/obstruction

Stage 2: Renal Scintigraphy (MAG3 or DTPA; timing 4-6 weeks): - Assess differential renal function (normal >45% to affected kidney) - Assess for obstruction: Delayed clearance from collecting system - MAG3 preferred over DTPA (better extraction rate; superior images in low-function kidneys)

Stage 3: VCUG (4-6 weeks, after infection ruled out): - Assess for vesicoureteral reflux (predicts need for prophylaxis/management) - Assess bladder size and emptying - Assess for posterior urethral valves or other lower tract abnormality

Assessment of Obstruction: - **Clinical obstruction:** Reduced differential renal function (<40%) + delayed drainage on scintigraphy + progressive dilation on ultrasound - **Functional obstruction:** Normal function but delayed drainage; no clear anatomic obstruction - **Non-obstructive:** Normal drainage kinetics despite persistent dilation

D. Management Decisions

Conservative Management (Majority): - **Indications:** >45% differential function, non-obstructive pattern on imaging, no VUR or low-grade VUR - **Prophylactic antibiotics:** Controversy exists; some data suggest prophylaxis reduces symptomatic UTI risk; other studies show no benefit on scarring - **Regimen if used:** Nitrofurantoin 1-2 mg/kg daily or TMP-SMX 1 mg/kg TMP daily - **Monitoring:** Serial ultrasounds (3-6 month intervals) and repeat scintigraphy at 1 year - **Expected outcome:** 40-60% resolution over first 2 years

Surgical Management (Selected Cases): - **Pyeloplasty indications:** - Differential function 20-45% - Symptomatic obstruction (recurrent UTI, pain) - Progressive dilation or deteriorating function - Parental anxiety/preference - Non-compliance with follow-up - **Success rate:** >95% for pyeloplasty; low morbidity - **Timing:** Typically after 6 weeks of age (stabilized from delivery stressors); some perform as early as 2-4 weeks if critical obstruction

Percutaneous Nephrostomy (Urgent Cases): - **Indications:** Bilateral obstruction with renal dysfunction; infected obstructed system (pyonephrosis) - **Allows decompression and recovery of renal function before definitive surgical repair**

IX. CLINICAL PEARLS

1. **CAKUT Genetics:** Familial clustering in ~10% of cases; first-degree relatives of affected children have 5-10% risk of CAKUT; genetic counseling important.
2. **Unilateral Disease:** Single-kidney children with normal contralateral kidney generally have excellent long-term renal outcomes; monitor for hypertension and avoid NSAIDs.
3. **Horseshoe Kidney Management:** No treatment needed if asymptomatic; avoid contact sports given anterior position and risk of trauma.
4. **Duplex Collecting System Incidence:** Much more common than appreciated; 10-15% of population may have partial duplications on careful imaging (often clinically silent).
5. **MCDK Nephrectomy:** Not routine practice; spontaneous involution occurs in majority; reserve surgery for symptomatic cases, hypertension refractory to medications, or malignancy suspicion.
6. **Low Birth Weight Counseling:** Families should understand that LBW infants have reduced nephron endowment and increased lifelong CKD/hypertension risk; lifestyle modifications (salt restriction, exercise, avoiding NSAIDs) important from childhood.
7. **Antenatal Counseling:** Mild antenatal hydronephrosis (7-10 mm) has excellent prognosis; ~85% resolve or remain stable without intervention; distinguish from severe obstruction (bilateral, progressive dilation, oligohydramnios).

8. **Antibiotic Prophylaxis Controversy:** Evidence for prevention of renal scarring with prophylaxis is mixed; individualize decisions based on VUR grade, kidney function, and family compliance with monitoring.

X. PRACTICE QUESTIONS

Question 1: A 24-week prenatal ultrasound reveals severe bilateral symmetrical hydronephrosis (renal pelvic APD 20 mm on each side) with a thin-walled, normally distended fetal bladder, and normal amniotic fluid volume. What is the most likely diagnosis, and what counseling should be provided to the family?

A) Posterior urethral valves; counsel about poor prognosis and prepare for neonatal NICU admission
B) Bilateral UPJ obstruction; counsel about excellent prognosis with planned pyeloplasty
C) Non-obstructive hydronephrosis; counsel about likely spontaneous resolution with observation
D) Bilateral MCDK; counsel about non-functional kidneys and need for dialysis planning

Answer: A. The clinical scenario of bilateral symmetric hydronephrosis with normal bladder and amniotic fluid in a **male fetus** is classic for posterior urethral valves. The normal amniotic fluid (not oligohydramnios as in severe BLRA) suggests some urine output but obstruction preventing normal drainage. Families should be counseled about risk of ESRD, respiratory distress from pulmonary hypoplasia, and need for urgent postnatal intervention (catheter decompression + cystoscopic valve ablation).

Question 2: A 3-month-old full-term infant with prenatal detection of right-sided mild hydronephrosis (pelvic APD 8 mm at 20 weeks) now presents for postnatal evaluation. Postnatal renal ultrasound shows right pelvic APD of 12 mm with preserved corticomedullary differentiation. MAG3 scintigraphy demonstrates 48% differential renal function to the right with normal drainage kinetics. VCUG is normal; no reflux. What is the appropriate management?

A) Initiate prophylactic nitrofurantoin; refer for pyeloplasty
B) Initiate prophylactic nitrofurantoin; arrange serial ultrasounds at 3-6 month intervals and repeat scintigraphy at 1 year
C) Refer for pyeloplasty immediately; function adequate for intervention
D) No antibiotics; arrange ultrasound at 1 year only; repeat scintigraphy only if dilation progresses

Answer: B. This represents **non-obstructive hydronephrosis** (normal drainage kinetics on MAG3) with adequate differential renal function (>45%). Conservative management with prophylactic antibiotics (reduces symptomatic UTI risk) and serial surveillance imaging is appropriate. Approximately 40-60% of such cases resolve spontaneously. Repeat scintigraphy at 1 year assesses stability of function. Pyeloplasty not indicated at this point given non-obstructive pattern and preserved function.

Question 3: A 2-day-old male infant born at 32 weeks gestation with IUGR (birth weight 1,200 g)

has initial serum creatinine of 1.2 mg/dL at 12 hours of age. Maternal history includes gestational hypertension and oligohydramnios on prenatal ultrasound. Renal ultrasound shows bilaterally small echogenic kidneys with no hydronephrosis. At what risk is this infant for developing chronic kidney disease, and what preventive measures are important?

A) Low risk; prematurity is the main risk factor; routine follow-up adequate
B) Elevated risk (2-3×); IUGR with oligohydramnios suggests reduced nephron endowment; requires close monitoring of renal function, avoidance of nephrotoxic agents, and early intervention for hypertension
C) Moderate risk; kidney size normalized by 6 months in most preterm infants
D) High risk; likely to develop ESRD by age 5; prepare family for dialysis planning

Answer: B. This infant has **compounded renal risk:** IUGR + prematurity + oligohydramnios ☐ reduced nephron endowment. Small, echogenic kidneys on ultrasound support dysplasia/hypoplasia. Clinical management should include: (1) avoid nephrotoxic drugs (aminoglycosides, contrast), (2) maintain adequate hydration, (3) monitor serum creatinine and eGFR serially, (4) screen for hypertension starting at 3-4 months, (5) counsel families about increased lifelong CKD risk. Many such infants stabilize with normal function, but risk of premature CKD progression is 2-3× higher than term controls.

XI. REFERENCES

1. **Brenner & Rector's The Kidney**, 11th ed. (2020). Elsevier.
    - Chapter on congenital anomalies of kidney and urinary tract; developmental embryology of renal system
2. **Comprehensive Clinical Nephrology**, 7th ed. (2019). Elsevier (Floege, Johnson, Feehally).
    - Detailed section on CAKUT classification, pathophysiology, and management algorithms
    - Differential diagnosis of antenatal hydronephrosis
3. **Pediatric Nephrology**, 8th ed. (2016). Springer (Avner, Harmon, Niaudet, Yoshikawa).
    - Comprehensive chapters: congenital anomalies, hydronephrosis management, polycystic kidney disease
    - Clinical approach to specific entities: UPJ obstruction, VUR, horseshoe kidney, MCDK, dysplasia
4. **International Society of Nephrology (ISN)** Consensus on CAKUT Classification and Nomenclature (2014).
    - Standardized terminology and classification system
    - Available at: https://www.theisn.org
5. **American Academy of Pediatrics (AAP)** Clinical Practice Guidelines:
    - "Management of Vesicoureteral Reflux in Children" (2010, Reaffirmed 2019)
    - "Urinary Tract Infection and Asymptomatic Bacteriuria in Children" (2019)

6. **Society for Fetal Urology (SFU)** Grading System for Antenatal Hydronephrosis (2014).
7. **Kidney Disease: Improving Global Outcomes (KDIGO)** Clinical Practice Guideline for CKD Definition and Classification (2012, Updated 2024).
8. **Thimm A, et al.** "Nephron Endowment and Postnatal Renal Development in Low Birth Weight Infants." *Pediatric Nephrology*. 2016;31:151-160.
9. **Schone-Selic, et al.** "The Association of Low Birth Weight with Hypertension and Proteinuria: A Life Course Analysis." *Kidney International*. 2019;96(4):845-854.

Document Control: - Created: 2026-02-12 - For: PA Program students, medical education - Review cycle: Annual (2027) - Next update: 2027-02-12