Cystic kidney disease

Classification (Committee on Classification, Nomenclature, and Terminology of the American Academy of Pediatrics, Urology Section)

- **Hereditary cysts:**
  - *Infantile or autosomal recessive polycystic kidney disease*: bilateral cystic kidney disease with dilatation of the collecting tubules and hepatic involvement. Rare (1/40,000).
  - *Adult or autosomal dominant polycystic kidney disease*: common multisystem cystic disease (1/500-1/1000 newborns) with 100% penetrance; responsible for 10% of CRF dialysis cases (most common cause of end-stage CRF).
  - *Juvenile nephronophthisis-medullary cystic disease complex*: juvenile nephronophthisis is Au recessive whereas medullary cystic disease is Au dominant. Both present with dilatation and progressive atrophy of the renal tubules along with interstitial and periglomerular fibrosis.
  - *Congenital nephrosis*: cystic disease involving dilatation of the proximal convoluted tubules.
  - *Familial hypoplastic glomerulocystic disease (cortical microcystic disease)*: Au dominant disease with progressive CRF and small or normal-sized kidneys with irregular calyces and papillary abnormalities.
  - *Cystic disease associated with multiple malformations*: the cysts are part of a series of multiple malformation syndromes, some of which are Au dominant (e.g. tuberous sclerosis and Von Hippel-Lindau disease), while others are Au recessive, including Meckel syndrome, Jeune syndrome (asphyxiating thoracic dystrophy), and Zellweger (cerebrohepatorenal) syndrome.

- **Nonhereditary cysts:**
  - *Simple cysts*: benign, fluid-filled, cortical or medullary cavities; can be single or multiple.
  - *Multilocular benign cysts (cystic nephroma)*: cystic lesions appearing in childhood with variable sizes, a polar location, a thick capsule, and internal septa; the adjacent parenchyma is normal.
  - *Multicystic dysplastic kidney*: severe non-genetic dysplasia, usually unilateral, in which the non-functioning kidney takes on the appearance of a grape cluster.
  - *Medullary sponge kidney (Cacchi-Ricci disease)*: dilatation of the distal end of the collecting tubules in the renal pyramid with associated cysts and diverticula.
  - *Sporadic glomerulocystic disease*: nonhereditary disorder that presents with enlarged kidneys full of small cysts located in Bowman’s space.
  - *Acquired cystic kidney disease*: progressive replacement of the atrophic renal parenchyma with bilateral corticomedullary cysts in patients with CRF.
  - *Calyceal diverticula and pyelogenic cysts*: small intrarenal dilatations communicating through a narrow neck with a calyx or infundibulum, usually in the upper pole (calyceal diverticula) or the renal pelvis (pyelogenic cysts).
  - *Parapyelic and renal sinus cysts*: cysts located near the sinus, from which they derive. These non-parenchymal cysts appear to have a lymphatic etiology.
  - *Hydatid cysts*: parasitic cysts caused by *Echinococcus granulosus*. 
**Infantile or autosomal recessive polycystic kidney disease**

- **Definition:** bilateral, Au recessive renal cystic disease with fusiform dilatation of the renal collecting tubules and liver fibrosis. Rare (1/40,000). Presents at birth or later, but before the 13th year of life. The earlier the manifestation, the more severe the disease.
- **Genetics:** mutation of the PKHD1 gene on chromosome 6 (encoding fibrocystin or polyductin). Siblings have a 1 in 4 chance of being affected.
- **Symptoms:** severe forms manifest themselves before delivery with oligohydramnios. After delivery they present with oliguria, an abdominal mass, respiratory distress, and Potter facies. 50% die within the first month and of those who survive, only 50% reach the age of 10. Milder forms present with slow onset of renal failure and more severe liver fibrosis.
- **Ultrasound:** can be detected in utero; the kidneys are bilaterally enlarged with homogeneous medullary hyperechogenicity.
- **IVP:** functioning kidney shows striation with persistent, radiating, opaque streaks in delayed images (“sunburst” nephrogram). These are caused by the collecting tubules as they fill with contrast medium. Pyelocalyceal structures are not visible.
- **Treatment:** of hypertension, portal hypertension, and esophageal varicosities; dialysis and kidney transplantation.

**Adult or autosomal dominant polycystic kidney disease**

- **Definition:** multisystem autosomal dominant cystic disease (with kidney, liver, pancreas, spleen, and lung cysts along with brain aneurysms) that appears in 1/500-1/1000 newborns and is responsible for 10% of hemodialysis cases.
- **Genetics:** 90% mutation of the PKD1 gene (chromosome 16) that encodes fibrocystin 1; 10% mutation of the PKD2 gene (chromosome 4) encoding fibrocystin 2; PKD3 gene is rarely affected. Has a penetrance of 100%. Because it is Au dominant, 50% of siblings are affected.
- **Symptoms:** typically appears between the ages of 30-50.
  - **In children:** abdominal mass, proteinuria, hematuria, and hypertension.
  - **In adults:** CRF (rare in patients <40 years of age), hypertension, colic, hematuria, compressive symptoms, renal lithiasis, UTI, cerebral hemorrhage. No ↓ of erythropoietin. In PKD2 mutations, CRF appears later (between 60-70 years) and complications are rarer.
- **IVP:** enlarged kidneys with sharp, distorted calyces, and a “swiss cheese” nephrogram.
- **CT:** multiple location cysts with enlarged, lobulated kidneys. CT is useful for diagnosing hemorrhagic cysts, differentiating old hemorrhages from new ones (50-90 Hounsfield units).
- **Treatment:** of complications. Dialysis and renal transplantation.

**Juvenile nephronophthisis-medullary cystic disease complex**

- **Definition:** both diseases share anatomical features with nephritis, tubulointerstitial and periglomerular fibrosis, and cysts in the corticomedullary junction, but differ in their form of transmission and clinical presentation.
  - **Juvenile nephronophthisis:** NPH1, NPH2, or NPH3 gene mutation (juvenile/adolescent variant with sterility). Au recessive. On average, CRF appears at age 13.
  - **Medullary cystic disease:** MCKD1 or MCKD2 gene mutation. Au dominant. CRF appears at 20-40 years old.
- **Symptoms:**
  - **Juvenile nephronophthisis:** polyuria/polydipsia due to Na+ loss and absence of hypertension. CRF and ↓ erythropoietin. In 20% there is extrarenal involvement with retinitis pigmentosa, skeletal abnormalities, liver fibrosis, or Bardet-Biedl syndrome.
  - **Medullary cystic disease:** hypodensification, but no Na+ loss; ↓ erythropoietin and CRF.
- **Ultrasound:** kidneys somewhat diminished in size with small cysts and a hyperechogenic parenchyma due to tubulointerstitial fibrosis.
- **CT:** cysts that are sometimes not visible in the ultrasound can be seen. CT is recommended over ultrasound to examine family members; in cases of CRF, MRI is better.
- **Treatment:** Na+ replacement if there are losses. Dialysis and renal transplantation.
Congenital nephrosis

- **Definition:** cystic disease caused by dilatation of the proximal convoluted tubules and interstitial fibrosis. There are two clinical presentations:
  - Finnish type: mutation on chromosome 19 with Au recessive transmission.
  - Diffuse mesangial sclerosis: most cases are sporadic; some are familial.
- **Symptoms:** proteinuria, edema, CRF (from birth in the Finnish type and before the age of 3 in diffuse mesangial sclerosis), and potentially fatal sepsis.
- **Ultrasound:** enlarged kidneys with an absence of corticomedullary differentiation.
- **Treatment:** dialysis and renal transplantation.

Familial hypoplastic glomerulocystic disease

- **Definition:** also called cortical microcystic disease. It is associated with **prognathism**. Au dominant transmission. Four elements are necessary for a positive diagnosis:
  - Stable or progressive CRF.
  - Small or normal sized kidneys with irregular calyces and papillary abnormalities.
  - Appearance in at least two generations of one family.
  - Histological evidence of thin-walled, subcapsular renal cysts.

Cystic disease associated with multiple malformations

- **Tuberous sclerosis:** Au dominant or sporadic disease characterized by epilepsy, mental retardation, and adenoma sebaceum. Renal cysts and angiomylipomas appear in 50% of cases. The cysts have a hyperplastic coating of eosinophilic cells. CRF appears in patients >40 years of age. 2% develop renal cell carcinoma.
- **Von Hippel-Lindau disease:** Au dominant disease due to mutation of the VHL gene on chromosome 3. Presents with cerebellar and retinal hemangioblastomas, renal cysts (76% of cases), pancreatic and epididymal cysts, renal carcinoma (50% of cases), epididymal cystoadenoma, and pheochromocytoma. Cysts tend to be asymptomatic, bilateral, and multiple.
- **Meckel syndrome:** Au recessive disease characterized by microcephaly, polydactyly, posterior or encephalocele, and renal cysts in (usually) nonfunctioning kidneys.
- **Jeune syndrome (asphyxiating thoracic dystrophy):** Au recessive disease characterized by thoracic chondrodysplasia and diffuse cystic dysplasia.
- **Zellweger (cerebrohepatorenal) syndrome:** Au recessive disease with hypotonia, high forehead, hepatomegaly, and glomerular and cortical cysts with no impact on renal function.

Simple cysts

- **Definition:** fluid-filled, benign, single or multiple, cortical or medullary cavities that often go unnoticed and are found incidentally after an ultrasound. 0.1% of newborns have cysts, but their frequency increases with age (50% of adults >50 years of age).
- **Symptoms:** almost always nonexistent, but sometimes calyceal obstruction, abdominal mass, compressive signs, or hypertension.
- **Ultrasound:** anechoic oval or spherical image with posterior hyperechoic reinforcement, absence of internal echoes, and a thin wall that is smooth and well-defined.
- **CT:** spheroid masses with fine, well-defined walls and a homogenous liquid content with a density similar to that of water, between −10 and +20 Hounsfield units. They are not enhanced with injection of contrast medium. If the liquid is hyperdense (20–90 HU), it should not be enhanced with intravenous contrast injections. MRI may be useful in cases of hyperdense cysts of doubtful nature.
- **Differential diagnosis:** when ultrasound or CT results are inconclusive, other pathologies must be considered, including infected, hemorrhagic, or malignant cysts. To determine when to explore or remove a complex cyst, Bosniak’s tomographic classification can be used.
### Bosniak classification for evaluation of renal cysts (2003)

<table>
<thead>
<tr>
<th>Bosniak Classification</th>
<th>Malignant risk, follow-up required, characteristics</th>
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</thead>
<tbody>
<tr>
<td>Bosniak I</td>
<td>Less than 1%; no follow-up required:</td>
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<tr>
<td></td>
<td>1) uncomplicated, simple benign cyst.</td>
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<td></td>
<td>2) anechoic, posterior enhancement, round or oval shape, thin, smooth wall.</td>
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<td></td>
<td>3) homogeneous water content, sharp delineation with the renal parenchyma, no calcification, enhancement or wall-thickening.</td>
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<tr>
<td>Bosniak II</td>
<td>Less than 3%; no follow-up required:</td>
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<tr>
<td></td>
<td>1) &lt;1 mm septations (hairline thin)</td>
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<td></td>
<td>2) fine calcifications within the septum or wall.</td>
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<td></td>
<td>3) &lt;3 cm in diameter</td>
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<td></td>
<td>4) hyperdense cysts (&gt;20 Hounsfield units)</td>
</tr>
<tr>
<td>Bosniak IIF</td>
<td>5-10%; follow-up recommended:</td>
</tr>
<tr>
<td></td>
<td>1) multiple thin septa</td>
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<tr>
<td></td>
<td>2) septa thicker than hairline or slightly thick wall</td>
</tr>
<tr>
<td></td>
<td>3) calcification, sometimes thick</td>
</tr>
<tr>
<td></td>
<td>4) intrarenal cyst, &gt;3 cm, NO contrast enhancement</td>
</tr>
<tr>
<td>Bosniak III</td>
<td>40-60%; surgical excision recommended:</td>
</tr>
<tr>
<td></td>
<td>1) uniform wall thickening/nodularity</td>
</tr>
<tr>
<td></td>
<td>2) thick/irregular calcification</td>
</tr>
<tr>
<td></td>
<td>3) thick septa</td>
</tr>
<tr>
<td></td>
<td>4) enhances with contrast</td>
</tr>
<tr>
<td>Bosniak IV</td>
<td>Greater than 80%; surgical excision recommended:</td>
</tr>
<tr>
<td></td>
<td>1) large cystic components</td>
</tr>
<tr>
<td></td>
<td>2) irregular margins/prominent nodules</td>
</tr>
<tr>
<td></td>
<td>3) solid enhancing elements independent of septa</td>
</tr>
</tbody>
</table>

#### Treatment:
- only for symptomatic cysts.
  - Percutaneous puncture + sclerosis with Povidone-iodine (BETADINE®) or Ethanol. Povidone is instilled every day in an amount equal to 50% of the aspirate until the deficit is minimized. If Ethanol is used, instill 70% of the aspirated amount in a single dose.
  - Open or laparoscopic surgical deroofing.

### Multilocular benign cyst (cystic nephroma)

- **Definition:** benign cystic neoplastic lesion that appears in childhood before the age of 4 or in adulthood after the age of 30 and which has a variable size, polar location, and thick capsule. The adjacent parenchyma is normal. It is on the benign end of a pathological spectrum that includes at its most malignant end the cystic Wilms tumor in children and cystic renal cell carcinoma in adults. The contralateral kidney and ipsilateral ureter are generally normal.
- **Symptoms:** flank mass, asymptomatic in children; pain, hematuria, hypertension in adults.
- **Ultrasound:** spherical anechoic image with an echogenic wall and interior echoes.
- **CT:** wall mass less dense than the normal parenchyma, although it may take on a solid appearance when filled with myxomatous material.
- **Differential diagnosis:** with partially differentiated nephroblastomas or Wilms tumors.
- **Treatment:** tumorectomy, partial nephrectomy, or simple nephrectomy in cases of doubt.

### Multicystic dysplastic kidney

- **Definition:** severe, non-genetic, usually unilateral dysplasia occurring predominantly in children and in which the nonfunctioning kidney (small or highly enlarged) takes on a grape cluster appearance with no drainage system (ipsilateral ureteral atresia). Variants:
  - **Solid cystic dysplasia:** small cysts with a predominance of stroma.
  - **Hydronephrotic dysplasia:** multicystic dysplasia associated with a dilated renal pelvis.
  - **Bilateral dysplasia:** associated with other malformations; incompatible with life.
- **Symptoms:** the most common cause of cystic disease in infants and one of the most common causes of abdominal mass. Can be diagnosed prenatally and may be asymptomatic. The contralateral system may be abnormal (3-12% UPJ stenosis, 18-43% VUR). May be associated with cystic dysplasia of the ipsilateral testis.

- **Ultrasound:** small or highly enlarged kidney with multiple cysts distributed irregularly with separation between them and with no identification of the renal sinus. It is difficult to distinguish from congenital hydronephrosis. Involution of the dysplastic kidney usually occurs pre- or postnatally and may not be identified in an ultrasound.

- **VCUG:** rules out contralateral VUR in patients with contralateral ureterectasis or UTI.

- **DMSA:** unlike congenital hydronephrosis, in which the kidney is functional, renal function in the multicystic kidney is minimal or totally absent.

- **Treatment:**
  - Conservative: annual ultrasound and monitoring of the contralateral tract.
  - Nephrectomy if there are symptoms (hypertension), if US findings lead to suspicion of associated malignancy, or if a significant volume persists in children >5 years of age.

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**Suspicion of neonatal multicystic dysplastic kidney**

- **US on the first day after delivery**
  - **signs of hydronephrosis**
    - Neonatal hydronephrosis protocol
  - **signs of multicystic kidney**
    - **DMSA scan in the first month**
      - **Preserved renal function**
      - **Lack of renal function**
        - **Multicystic dysplastic**
Medullary sponge kidney (Cacchi-Ricci disease)

- **Definition:** dilatation of the distal end of the collecting tubules in the renal pyramid (precalyceal tubular ectasia) with numerous associated cysts and diverticula. The cysts contain a yellowish-brown fluid, desquamated cells, and often calcifications. Sometimes associated with congenital hemihypertrophy, Beckwith-Wiedemann syndrome, Ehlers-Danlos syndrome, anodontia, and Caroli’s disease.

- **Symptoms:** sometimes asymptomatic, in which case it may never be diagnosed. Other times it presents with repetitive renal colic (50-60%) due to phosphocalcic or oxalocalcic lithiasis, urinary infections (20-33%), hematuria (10-18%), and hypercalcemia/hypercalciuria (33%).

- **IVP:** enlarged kidneys with papillary calcifications and dilated tubules that fill with contrast medium (“brushlike” pattern).

- **Treatment:** Hydrochlorothiazide/Amlorilide (MODURETIC®) 1 tab of 50 mg/day and Potassium citrate (ACALKA®) 1 tab of 1.08 g/8 h prevent hypercalciuria and hypocitraturia, limiting the formation of stones. See chapter on Medullary Sponge Kidney.

Sporadic glomerulocystic disease

- **Definition:** nonhereditary disorder that presents with enlarged kidneys full of small cysts in the Bowman space. Unlike familial hypoplastic glomerulocystic disease, this pathology is not hereditary and the kidneys are larger.

Acquired cystic kidney disease

- **Definition:** progressive replacement of the atrophic renal parenchyma by bilateral corticomedullary cysts in patients with CRF. Its incidence increases with the number of years on dialysis (hemodialysis or peritoneal dialysis).

- **Symptoms:** usually asymptomatic. Sometimes presents with back pain, UTI, or hematuria. 20-25% of patients develop benign or malignant renal tumors in the first 10 years of dialysis. Tumors measuring <1 cm are adenomas, those >3 cm are carcinomas, and those between 1-3 cm need further study. After transplantation, the cysts may subside, but not the incidence of renal carcinoma.

- **CT:** small kidneys with multiple cysts. 3-5 cysts in an ultrasound, CT, or MRI are required for a correct diagnosis (with ultrasound being the least sensitive).

- **Treatment:** in cases of infection, percutaneous drainage or nephrectomy. In cases of malignant degeneration, nephrectomy.

Calyceal diverticula and pyelogenic cysts

- **Definition:** small intrarenal dilatations communicating through a narrow neck with a calyx or infundibulum, usually in the upper pole (calyceal or type I diverticula) or the renal pelvis (pyelogenic cysts or type II diverticula). The latter tend to be larger and are more often symptomatic.

- **Symptoms:** almost always asymptomatic. Sometimes present with flank pain, infection, or lithiasis (39%).

- **IVP/CT:** cavity in contact with a calyx or with the renal pelvis and which fills with contrast medium.

- **Treatment:** not usually necessary since they are asymptomatic. When needed:
  - ESWL of diverticular stones: only 50% of the stones can be eliminated.
  - Percutaneous or ureterosopic access: elimination of the stone and infundibular dilatation or mucosal ablation.
  - Open or laparoscopic surgery:
    - Polar nephrectomy.
    - Diverticulectomy.
    - Marsupialization of the diverticulum.
Parapyelic and renal sinus cysts

- **Definition:** the term *parapyelic cyst* refers to their location near the sinus, but they may be parenchymal or true *renal sinus cysts* derived from arteries, fatty tissue, or lymph vessels (the most common). They are usually multiple and bilateral and appear in patients >50.
- **Symptoms:** usually asymptomatic. Rarely cause *obstruction, infection, or lithiasis.*
- **IVP:** displacement and even obstruction. “*Trumpet*” image of the renal pelvis, with elongated infundibula.
- **CT:** show the presence and exact location of the cysts.
- **Differential diagnosis:** with sinus lipomatosis and infundibular diverticula.
- **Treatment:** usually unnecessary since they are asymptomatic. If needed, an evacuatory percutaneous puncture with sclerosis can be performed, as in simple cysts.

Hydatid cyst

- **Definition:** parasitic cyst caused by *Echinococcus granulosus.*
- **Symptoms:** *flank pain, renal mass, hematuria,* or *anaphylactic shock* due to rupture of the cyst.
- **Ultrasound:** multi-walled cystic mass with a thickened wall and internal echoes.
- **CT:** spherical mass with a thick wall that captures contrast medium.
- **Treatment:**
  - *Albendazole* (ESKAZOLE®) 400 mg/12 h 28 d, 3 cycles with a 14-day rest between them.
  - *Surgical:* cystectomy, marsupialization, or nephrectomy.