Renal Cysts and Homoeopathy

Definition

A renal cyst is a fluid-filled sac (Pseudopsora) that grows on the surface of or within the kidney. Its origin is unclear, but is thought to come from a defect in the collecting tubules of the kidney (Syphilis). It has recently been reported that up to 40% of people over age 60 have renal cysts.

Classification of Renal cysts

Broad categories of cystic disease include the following:

- **Developmental** -Multicystic dysplastic kidney (MCDK) (Pseudopsora)
- **Genetic** -Autosomal recessive polycystic kidney disease (ARPKD), autosomal dominant polycystic kidney disease (ADPKD), juvenile nephronophthisis (JNPHP), medullary cystic kidney disease (MCKD), glomerulocystic kidney disease (GCKD) (Syphilis)
- **Cysts associated with systemic disease** -Von Hippel-Lindau syndrome (VHLS), tuberous sclerosis (TS) (Psora/ Syphilis)
- **Acquired** - Simple cysts, acquired cystic renal disease, medullary sponge kidney (MSK) (Psora/ Sycosis)
- **Malignancy** -Cystic renal cell carcinoma (RCC) (Cancerous)

Note -The most common larger cysts include acquired cysts, simple cysts, and cysts associated with ADPKD. Smaller cysts characterize ARPKD, JNPHP, MCKD, and MSK. In adults, renal angiomyolipomas and RCC may also have cystic components.

Pathophysiology

Cysts develop from renal tubule segments and most detach from the parent tubule after they grow to a few millimeters in size (Psora/ Syphilis). Cyst development is generally attributed to increased proliferation (Psora/Sycosis) of tubular epithelium, abnormalities in tubular cilia, and excessive fluid secretion (Psora).

Developmental cystic renal disease

MCDK represents abnormal development or formation of the kidney and may involve part, or all of, one or both kidneys. (Pseudopsora))

Inherited cystic renal disease

ADPKD is due to mutations in the genes PKD1 and PKD2, which encode polycystin proteins (Psora).

ARPKD is due to mutations in PKHD1, a large gene that encodes fibrocystin/polyductin, which plays critical roles in collecting-tubule and biliary development (Psora).

GCKD is often confused with ADPKD, as it is common in individuals with a family history of ADPKD (Psora).

JNPHP and **medullary cystic** disease are two diseases that some consider a disease complex. They share similar pathologic features but are due to different genetic mutations and have different inheritance patterns. (Psora/ Pseudopsora)

Systemic disease with associated renal cysts

Tuberous Sclerosis is caused by mutations in the suppressor genes TSC1 and TSC2 (psora). Renal cysts and angiomyolipomas are part of a syndrome that includes seizures and dermatologic findings (Pseudopsora).

VHLS is due to mutations in the VHL gene (Psora), which increases the risk for malignancy, including RCC. Affected individuals develop cysts in multiple organs, including the kidney, pancreas, liver, and epididymis.(Psora/ Syphilis/ Sycosis)

Acquired cystic renal disease

The exact cause of this disease is not known. It occurs exclusively in patients on dialysis (Causa occasionalis).

History

Developmental cystic renal disease

Multicystic dysplastic kidney (MCDK) is identified during prenatal sonographic examination. The involved kidney partially or completely improves with age in 40-90% of patients. Bilateral renal involvement is not compatible with life. MCDK can exist independently or as part of syndromes such as the vertebral defects, anal atresia, tracheoesophageal fistula with esophageal atresia, and radial and renal anomalies association i.e. Zellweger syndrome; or BOR syndrome.

Inherited cystic renal disease

Autosomal dominant polycystic kidney disease

Patients present in the fourth decade of life with flank pain or intermittent haematuria. Their may also be cyst hemorrhage, renal infection, or nephrolithiasis. Hypertension and chronic renal failure are noted in the fifth decade of life, and patients progress to end-stage renal disease (ESRD) in the sixth decade of life. Hypertension is seen in 50% of patients with ADPKD aged 20-34 years.

The disease course varies considerably among affected individuals. Only 50% of carriers actually progress to renal failure.

Kidney size increases exponentially over time and appears symmetric in a given individual, with an equal growth rate in both kidneys.

Hepatic cysts are the most common extrarenal manifestation of autosomal dominant polycystic kidney disease (ADPKD). Other clinical associations include cardiac valve disease (particularly mitral valve prolapse 25%), diverticulosis, cerebral aneurysms (5-10%), pancreatic cysts, and seminal vesicle cysts.

Autosomal recessive polycystic kidney disease

Autosomal recessive polycystic kidney disease (ARPKD) affects renal and hepatic development (dysgenesis of the portal triad), but the degree of organ involvement varies in relation to the age of onset.

In the neonatal period, pulmonary disease, resulting from nephromegaly and oligohydramnios, dominates the presentation. Typically, the neonate has profound respiratory compromise, often exacerbated by pneumothorax. This presentation may result in neonatal death.

Symptoms in an infant include hypertension (80%), diminished urine concentrating ability, and renal insufficiency. In older children (4-8 y), the kidneys often are less severely affected, while hepatic disease may predominate. Hepatic involvement usually presents with symptoms secondary to portal hypertension, particularly varices and splenomegaly.

Glomerulocystic kidney disease (GCKD)

This occurs in early (neonatal) and late (adult) forms. Neonates present with hypertension, abdominal masses, and variable degrees of renal failure. Adults typically present with flank pain, hematuria, and hypertension. Hepatic cysts may also develop.

Juvenile nephronophthisis (JNPHP)

This has several different phenotypic expressions depending on the gene involved. Infantile (NPHP2), juvenile (NPHP1, NPHP4) and adolescent (NPHP3) forms of the disease exist, but most symptoms appear during the first decade of life. These include growth retardation, urine concentrating defects, skeletal dysplasia, and progressive renal failure. Some degree of hepatic fibrosis and biliary duct enlargement is usually present.

Medullary cystic kidney disease

This is clinically milder than JNPHP, occurs later in life (third to fourth decades), and has limited extrarenal manifestations.

Systemic disease with associated renal cysts

Tuberous sclerosis (TS): Clinical features of TS include facial nevi, cardiac rhabdomyomas, epilepsy, angiofibromas, and mental retardation.

Von Hippel-Lindau syndrome (VHLS): Clinical features of VHLS include retinal and cerebellar hemangioblastomas, pheochromocytomas, and cystic disease of the kidneys, pancreas, and epididymis.

Acquired cystic renal disease

Acquired cystic disease may be found in patients with all etiologies of ESRD, particularly in patients who are dialysis-dependent. Hemorrhagic cysts occur in 50% of patients.

Medullary sponge kidney (MSK)

It is usually detected on radiographic evaluation of adults with nephrolithiasis. Fifteen to 20% of patients with calcium oxalate and calcium phosphate renal calculi have MSK. Patients may also have a history of hematuria or urinary tract infection (UTI).

Simple cysts

These are usually are clinically silent, although they occasionally hemorrhage and cause acute pain.

Physical

Developmental cystic renal disease

MCDK may be palpable as a flank mass in an otherwise healthy infant and is the most common cause of a renal mass and the second most common cause of a palpable abdominal mass in neonates.

Inherited cystic renal disease

ARPKD: Bilateral flank masses are palpable in 30% of neonates and infants with this disease. Older children may demonstrate signs of portal hypertension.

ADPKD: The enlarged kidneys and liver may be palpable.

Acquired cystic renal disease

Simple cysts rarely become large enough to be palpable.

Causes

- **Developmental cystic renal disease:** MCDK is thought to arise from abnormal development of the metanephros.
- **Inherited cystic renal disease:** The vast majority of mutations affect the primary cilia of the tubular epithelium, indicating that disruption of this structure relates to disease development. Additionally, dedifferentiation and increased proliferation of tubular epithelium, along with abnormal fluid secretion, appear to be common elements in cystic disease.
    - **ADPKD:** Inheritance is autosomal dominant, with close to 100% penetrance. PKD1 (chromosome 16) encodes for the transmembrane protein polycystin-1 (PC1), which is responsible for cell-to-cell and cell–to–extracellular matrix binding. Mutations in this gene are responsible for 85-90% of cases. Mutations in polycystin-2 (PKD2, chromosome 4), a calcium channel important for PC1 localization and function, account for the remaining 10-15%. Interestingly, while this is a genetic disease that affects every cell in the kidney, cysts involve only 1-2% of the nephrons or collecting ducts, supporting the hypothesis that a "second hit," or mutation of the abnormal allele, must occur. Five to 8% of cases do not involve a family history and are the result of spontaneous mutations.
    - **ARPKD:** Inheritance is autosomal recessive. All cases are caused by mutations in PKHD1, a large gene that encodes fibrocystin/polyductin, which

appears to be related to the polycystin complex and controls epithelial proliferation, secretion, and structure and development of the renal tubules and biliary ducts. The genetic defect is located on chromosome 6p21.1-p12.
    - In both ADPKD and ARPKD, epidermal growth factor (EGF) has been identified as an important stimulus for proliferation of cystic epithelium.
    - **GCKD** is a rare disease that is transmitted in an autosomal dominant manner. The involved gene has not been identified, and both familial and sporadic forms exist.
    - **JNPHP** is inherited in an autosomal recessive manner and is due to mutations in the NPHP genes (NPHP1-NPHP5) which are located on multiple different chromosomes and encode nephrocystins and inversin. All of the gene products are found in the primary cilium. Ten to 20% of cases are associated with retinal disease and are termed Senior-Loken syndrome.
        - NPHP1 is located on chromosome 2q12-13 and encodes nephrocystin.
        - NPHP2 is found on chromosome 9q22-31 and encodes inversin.
        - NPHP3 is found on chromosome 3q21-22 and encodes nephrocystin-3.
        - NPHP4 is located at chromosome 1q36 and encodes nephrocystin-4.
        - NPHP5 (chromosome 3q13.33-21.2) encodes nephrocystin-5 and is found only in cases associated with Senior-Loken syndrome.
    - **Medullary cystic kidney disease (MCKD)** is due to mutations in the MCKD1 (chromosome 1q21) and MCKD2 (chromosome 16p12) genes and is inherited in an autosomal dominant manner.
- Systemic disease with associated renal cysts
    - **TS:** Inheritance is autosomal dominant, with variable penetrance. Sixty to 70% of cases are due to sporadic mutations. Genetic markers have been identified at chromosome band 9q34 (TSC1, which encodes hamartin) and chromosome band 16p13 (TSC2, which encodes tuberin). TSC2 accounts for two thirds of TS cases. While the functions of these genes are not understood, TSC2 is adjacent to the PKD1 gene, which is involved in the most common form of ADPKD. In some cases, a contiguous gene syndrome has been described, involving large deletions that affect both TSC2 and PKD1.
    - **VHLS:** Inheritance is autosomal dominant, with variable penetrance. The genetic defect has been localized to chromosome band 3p25.
- Biochemical analyses have identified a protein (mTOR) that may be part of a common pathway in several of the genetic forms of cystic disease. mTOR activity is related to cell growth, proliferation, apoptosis, and differentiation. Levels of mTOR have been demonstrated to be increased in cyst epithelium. Under normal conditions, PC1 (mutated in ADPKD) and TSC2 (mutated in TS) suppress or inactivate mTOR. When these genes, as well as others that relate to the primary cilia, mutate, mTOR activity becomes dysregulated, possibly allowing cyst formation.
- **Acquired cystic renal disease:** The exact cause of cyst formation has not been identified. One theory suggests that the development of cysts in acquired renal cystic disease (ARCD) is secondary to obstruction of the tubules by fibrosis or oxalate crystals. Another hypothesis invokes the accumulation of growth factors and stimulatory chemicals (uremia), including EGF, which leads to the development of cysts. The disease occurs in patients on all types of dialysis and appears to regress after transplantation.

Differentials

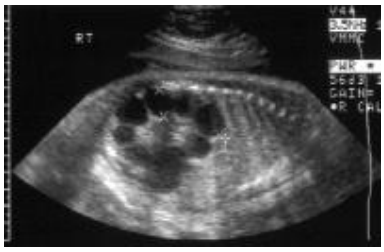
- Neuroblastoma
- Renal Corticomedullary Abscess
- Wilms Tumor

Laboratory Studies

- **Developmental cystic disease (MCDK):** In MCDK, because of the associated ureteral obstruction, the patient may have pyelonephritis in spite of an unremarkable urine specimen. However, blood cultures and clinical examination should readily suggest this diagnosis.
- **Inherited cystic renal disease**
    - **Autosomal dominant polycystic kidney disease (ADPKD):** Diagnosis is primarily clinical, but, in presymptomatic patients with a family history, gene linkage analysis can be used in combination with sonography for screening. The combination of these 2 modalities can achieve a detection sensitivity of 88.5% in patients younger than 30 years and 100% in patients older than 30 years. Some authors suggest that until effective treatments become available, the adverse effects from presymptomatic diagnosis in children (psychological, educational, career, and insurability issues) outweigh the benefits.
    - **Autosomal recessive polycystic kidney disease (ARPKD):** Genetic testing for mutations at PKHD1 is currently available, with 80-85% detection rates. A neonate may have hyponatremia during the first few weeks of life. The infant subsequently may demonstrate diminished urine osmolality (ie, < 500 mOsm/kg) secondary to reduced concentrating ability and metabolic acidosis secondary to decreased urinary acidification capacity. The patient may also have recurrent pyuria. Bilirubin and hepatic enzyme values may also be elevated.
    - **Juvenile nephronophthisis (JNPHP) and medullary cystic kidney disease (MCKD):** The urine has elevated sodium levels and low specific gravity with minimal proteinuria and normal sediment. Renal tubular acidosis may result in alkalotic urine and systemic acidosis. Genetic linkage analysis may be used to establish the diagnosis.
- **Systemic disease with associated renal cysts:** Prenatal screening is available for tuberous sclerosis (TS) if the diseased allele can be identified in an affected family member. In the absence of this, no reliable genetic marker for TS is known. Genetic screening techniques can be used to identify likely disease-causing mutations in 58-68% of cases.

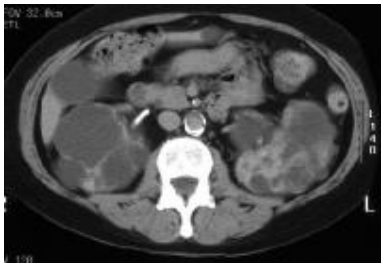
Imaging Studies

- **Developmental cystic renal disease (MCDK)**
    - Prenatal sonography is the diagnostic tool of choice and can be used to identify MCDK as early as 15 menstrual weeks. It demonstrates multiple variably sized, noncommunicating cysts outlined by hyperechoic intervening renal parenchyma. The corresponding ureter and renal pelvis are typically not visualized.



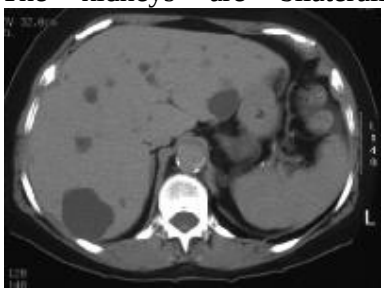
- A prenatal sonogram of a fetus with a multicystic dysplastic kidney. The right kidney is appreciated as a large multicystic paraspinal mass. The left kidney and bladder are normal, and a normal amount of amniotic fluid is present.
- After birth, serial (one within days of life and another one month later) high-quality sonography should be performed to confirm the diagnosis and to evaluate the contralateral kidney and the rest of the urinary tract.
- Intravenous pyelography (IVP) may show a nonfunctioning kidney or a deformed mass with faint specks of contrast corresponding to small areas of functioning renal tissue. No collecting system or ureter is identified. Shell-like calcifications outlining some of the cysts may be noted.
- Ureteral obstruction with collecting system dilatation may be difficult to differentiate from MCDK. In these cases, nuclear medicine functional studies can be helpful and demonstrate a rim of functional tissue in the obstructive cases.
- An association with contralateral ureteropelvic junction obstruction, as well as with renal ectopia, exists. Previously, voiding cystourethrography (VCUG) was routinely performed to rule out reflux into the contralateral kidney. Recent data suggest, however, that VCUG is of little value if serial high-quality ultrasonography findings are consistent with MCDK and demonstrate a normal bladder and contralateral kidney.

- **Inherited cystic renal disease**
  - **Autosomal dominant polycystic kidney disease**
    - Typically, cysts first are observed radiographically in the second to third decades of life. With progression, the kidneys become enlarged with multiple spherical fluid-filled cysts (1-3 cm) that are appreciated readily with CT scanning, ultrasonography, or MRI. Sonographic criteria for ADPKD depend on patient age. Sonographic diagnosis in individuals at 50% risk for the disease involves 2 unilateral or bilateral cysts in patients younger than 30 years, 2 cysts in each kidney in individuals aged 30-59 years, and 4 cysts in each kidney in individuals 60 years or older.



CT examination of the abdomen of a 70-year-old woman with autosomal dominant polycystic kidney disease (ADPKD) is shown.

The kidneys are bilaterally enlarged with multiple cysts.



CT scan of the same patient (70-year-old woman with autosomal dominant polycystic kidney disease [ADPKD]) demonstrating multiple hepatic cysts.

- Debris may produce heterogeneous cyst attenuation, and cysts may have fluid-fluid levels from hemorrhage. Hemorrhagic cysts demonstrate unenhanced CT attenuation values of 40-100 Hounsfield units (HU). Symptomatic episodes of gross hematuria underestimate the true incidence of hemorrhage, as up to 90% of patients with ADPKD have cysts that are hyperdense on CT. Calcification may be observed in the cyst walls or in the parenchyma between cysts, and nephrocalcinosis or nephrolithiasis is observed in as many as 50% of patients. Calcification likelihood increases with age and is fairly common in patients older than 50 years. Contrast enhancement of the renal parenchyma provides an indication of the amount of functioning renal parenchyma that remains. The likelihood of hepatic cysts increases with age; 40% of patients demonstrate liver cysts by the fourth decade of life, and nearly 90% of patients have them by the sixth decade of life.
- When ADPKD presents in childhood, ultrasonography may reveal hyperechoic enlarged cystic kidneys, a pattern that may be difficult to differentiate from ARPKD. In this situation, family history and possible ultrasonography of the parents' or grandparents' kidneys is recommended.
- When malignancy or infected cysts are a concern, a contrast-enhanced CT scan can be performed.
- Patients should be screened for intracranial aneurysms. This can be readily accomplished noninvasively with magnetic resonance angiography (MRA).

o **Autosomal recessive polycystic kidney** disease

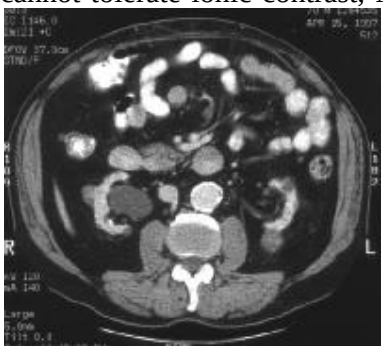
- Severe cases of this disease can be are detected with sonography in utero, with most cases detected in the third trimester of gestation. Features include enlarged kidneys that maintain their reniform shape and have increased echogenicity. With severe renal disease, urine may be absent in the bladder, and oligohydramnios, pulmonary hypoplasia, and a small thorax may be observed. At birth, neonates require assisted ventilation, and pneumothorax is common.
- In children, kidney size is typically at least 2 standard deviations greater than normal and diffusely hyperechogenic. Loss of corticomedullary differentiation may be observed, and small cysts

oriented in a radial pattern in the distribution of the collecting ducts may be evident. The cysts tend to enlarge over time.

- Precontrast CT scan images show enlarged smooth kidneys with low attenuation (likely representing the large volume of fluid in the collecting tubules). Renal calcifications are frequently noted. With contrast, poor opacification of the kidneys may be observed (with severe renal failure), and the physician may appreciate radial streaks of contrast extending from the cortical surface to the inner medulla. The classic radial streak pattern is best appreciated with IVP.
- Liver disease: Ultrasonography demonstrates hepatomegaly with echogenic parenchyma (secondary to fibrosis), hepatic cysts, and dilatation of the peripheral hepatic ducts with fibrous bridging.[4] Magnetic resonance cholangiography is more sensitive in detecting dilated biliary ducts.

- **Glomerulocystic kidney disease**
  - The kidneys appear either hypoplastic or normal in size on sonography and maintain their reniform shape. Cysts are small (< 1 cm) and are observed in an echogenic cortex; the medulla is spared. Corticomedullary differentiation is lost.
  - On CT and MRI, glomerulocystic kidney disease (GCKD) appears as numerous small cortical cysts. These do not enhance with gadolinium during MRI.
- **JNPHP and MCKD:** Sonography and CT scan reveal bilaterally shrunken kidneys. On sonography, cysts are observed at the corticomedullary junction in a background of diffusely echogenic renal parenchyma.

- **Acquired cystic renal disease**
  - **Acquired renal cystic disease (ARCD):** Diagnosis can be made if involvement is bilateral, with at least 4 cysts per kidney. Once cysts are observed sonographically, further evaluation with contrast-enhanced CT scan is indicated to rule out carcinoma. Contrast-enhanced helical CT scanning has 96% sensitivity and 95% specificity in detecting carcinoma. In patients who cannot tolerate ionic contrast, MRI may be useful to evaluate for neoplasms.



This CT scan demonstrates acquired renal cystic disease (ARCD) in a 70-year-old man who is dialysis-dependent. The CT scan demonstrates bilateral atrophic kidneys with multiple renal cysts.

  - **Medullary sponge kidney (MSK):** Findings on plain radiographs may be normal, or they may exhibit medullary nephrocalcinosis (represented by multiple discrete calculi clustered in the renal pyramids). At least one renal

calculus (typically < 5 mm) is often observed. IVP demonstrates a "bouquet of flowers" or "paintbrush" pattern. Ectatic tubules are observed as dense streaks of contrast material radiating from the calyces, while papillary cysts are observed as round opacifications in the papillae. The "brush" pattern of the ectatic tubules must be differentiated from a dense papillary blush, which may be observed in healthy patients; with low-osmolar contrast, papillary blush is observed in as many as 13% of routine IVPs. A greater than 0.3-mm cylinder or streak diameter has been recommended to help differentiate between pathologic tubular ectasia and normal variant physiology. CT scan may show calcifications at the corticomedullary junction.

- **Simple cyst:** The most clinically significant aspect of a simple cyst is differentiating it from carcinoma. Simple-cyst walls occasionally calcify and, thus, radiographically mimic malignancy. Sonographic features that support the diagnosis of simple cyst include an anechoic round mass with a smooth and sharply demarcated wall and through-transmission with strong posterior wall echo. If the ultrasonography findings are suspicious or equivocal, a CT scan is warranted. CT scan criteria for a benign cyst include (1) sharp demarcation cyst with a smooth thin wall, (2) homogenous fluid within the cyst (typically with density < 20 HU, although higher measurements may be found with a benign proteinaceous cyst or if hemorrhage is present in a benign cyst), and (3) no contrast enhancement. Enlargement of the cyst can raise the concern of malignancy, although the natural history of benign renal cysts does show progressive slow enlargement.
- Bosniak classification: Bosniak has described a classification scheme for renal cysts based on CT scan findings.
    - **Category I (simple cyst) -** Thin wall without septa, calcifications, or solid components; measures water density (< 20 HU) and does not enhance (< 2% chance of malignancy)
    - **Category II (minimally complex cyst) -** Thin wall (< 1 mm) and no enhancement; may contain 1 or 2 hairline-thin septa, fine calcification, or short segment of slightly thickened calcification; includes high-attenuation lesions that are smaller than 3 cm (Malignancy rates in series range from 0-14%. Series with higher malignancy rates include IIF lesions.)
    - Category IIF (indeterminate) - Minimal enhancement and/or thickening of a hairline-thin smooth septum or wall; mildly thickened or nodular calcification; no enhancing soft-tissue components; includes nonenhancing high-attenuation lesions that are 3 cm or larger (approximately 20% likelihood of malignancy)
    - Category III (suspicious indeterminate) - Multilocular lesion with multiple enhancing septae, uniform wall thickening, nodularity, or thick or irregular calcification (30-60% likelihood of malignancy)
    - Category IV (malignant) - Contains enhancing (>10 HU) large nodules or clearly solid components (>90% likelihood of malignancy)
- Multiphasic CT in combination with Bosniak class can improve diagnostic accuracy. To predict a renal cell carcinoma, a corticomedullary phase minus precontrast phase value of >42 HU resulted in 97.1% sensitivity and 85.7% specificity. This technique can further help guide treatment options.
- Another option for patients with renal impairment or allergy to iodinated contrast is contrast-enhanced ultrasound (CE-US). CE-US is a technique that

has been shown to be equivalent to CT, and in one experience CE-US was found to be better than CT in the diagnosis of malignancy in Bosniak IIF and III renal cysts.[22]

- MRI may be used to help evaluate renal lesions in patients with either renal impairment or allergy to iodinated contrast material. Contrast-enhanced MRI and CT scan reveal similar findings in most cystic renal lesions. However, MRI suggests a higher classification for some lesions by identifying more septae, areas of wall thickening, or enhancement. Additionally, calcification may not be appreciated with MRI.

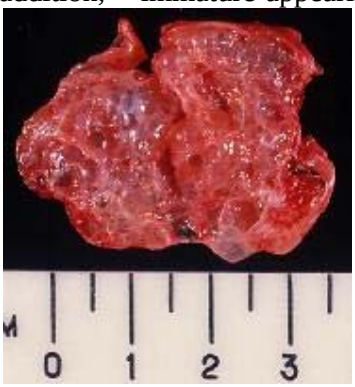
Procedures

Aspiration: In the evaluation of an intermediate renal cyst, fine-needle aspiration has a limited role. Some centers report a sensitivity of more than 70% for core biopsy and cyst aspiration with cytology. The enzyme CA9 is being studied as a new marker for clear cell renal cell carcinoma. One report showed that CA9 can be detected in the fluid of malignant cystic, but not benign, renal tumors. This marker may be useful to help guide decisions of treatment versus observation in select populations.

Histologic Findings

Developmental cystic renal disease

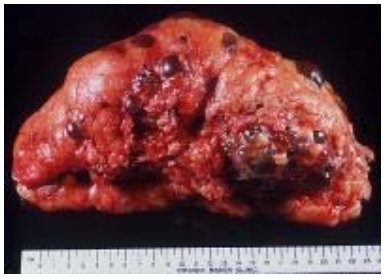
- **Multicystic dysplastic kidney:** Cystic dysplasia is a subset of renal dysplasia. In this form, typical renal configuration is lost. The disease is usually a unilateral process, but it ranges from involving a portion of one kidney to completely involving both kidneys. Grossly, the kidney appears to be an enlarged mass of cysts among immature primitive tissue, often with surrounding fibrosis and an atretic collecting system.[10] The ureter is often stenotic or hypoplastic, and the renal artery is often small or absent.[4] Microscopy reveals small areas of otherwise normal-appearing glomeruli and tubules interspersed with cysts lined with cuboidal epithelium and surrounded by collars of spindle cells. The cysts are filled with proteinaceous or sanguinous fluid. In addition, immature-appearing cartilage is often present in the tissue.



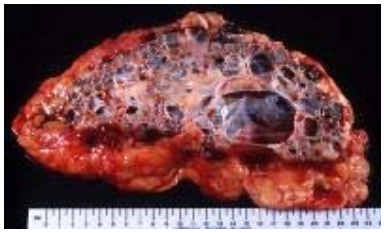
Cut surface of a nephrectomy specimen from a patient with a multicystic dysplastic kidney (MCDK).

Inherited cystic renal disease

- **Autosomal dominant polycystic kidney disease**
  - The kidneys are enlarged and distorted by multiple renal cysts. Cystic kidneys can exceed 40 cm in length and weigh as much as 5 kg. Cysts range in size from a few millimeters to several centimeters and are distributed relatively uniformly through the medulla and cortex. Cyst fluid ranges from clear to hemorrhagic.
  - Microscopic evaluation shows cystic dilatations in all segments of the nephron, with loss of connection to the tubule. While all segments are involved, the cysts derived from the collecting duct are the largest and most numerous. The cysts are lined by a single layer of flattened-to-cuboidal epithelium. The intervening parenchyma demonstrates interstitial fibrosis, tubular atrophy, chronic inflammation, and vascular sclerosis.



External surface of a nephrectomy specimen from a patient with autosomal dominant polycystic kidney disease (ADPKD).



Cut surface of the same nephrectomy specimen from a patient with autosomal dominant polycystic kidney disease (ADPKD).

- **Autosomal recessive polycystic kidney disease**
  - The kidneys are enlarged bilaterally, but a reniform shape is preserved. With neonatal presentation, the kidneys may be 10-20 times normal size. Radial cysts are typically smaller than 3 mm in diameter and extend perpendicularly from the papillary tips to the surface of the cortex. Microscopically, the cysts are lined by flattened (undifferentiated) epithelium and represent fusiform dilation of collecting tubules that retain their connection to the afferent and efferent tubules. The parenchyma adjacent to the cysts progressively develops interstitial fibrosis and glomerulosclerosis.
  - The liver is grossly enlarged, and microscopic evaluation demonstrates bile duct dilatation and periportal fibrosis. This histologic pattern is known as congenital hepatic fibrosis (CHF) and is always present in ARPKD. However, CHF is not specific to this disease.

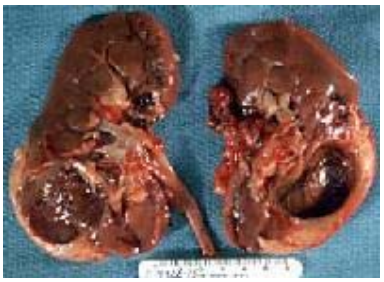
- GCKD is characterized by dilatation of Bowman space without involvement of the related tubule. The dilated Bowman spaces are lined by a flattened epithelium and contain rudimentary glomerular tufts.
- **Juvenile nephronophthisis and medullary cystic kidney disease:** These diseases are characterized by thickening and wrinkling of the tubular basement membrane, tubular atrophy, and interstitial fibrosis, leading to bilaterally small kidneys with a pitted surface.[3] The renal cortex is uniformly thinned, and cysts are located at the corticomedullary junction and are derived from the collecting ducts and distal tubules.[12] The number of cysts varies (5-50), and cysts measure from several millimeters to 1 cm. However, 25% of cases do not involve grossly visible cysts. Microscopic evaluation demonstrates that the cysts are lined by single layers of cuboidal epithelium.

Systemic disease with associated renal cysts

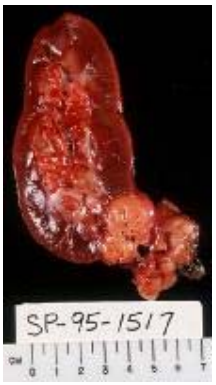
- **TS:** Renal cysts are uncommon and usually not extensive, but diffuse cystic renal disease that involves both the cortex and the medulla is occasionally noted, particularly in children. Cysts vary in size from several millimeters to 3 cm. Diffuse renal cystic disease grossly resembles kidneys affected by ADPKD. Microscopically, the cysts are lined by large eosinophilic cells with enlarged hyperchromatic nuclei.[1]
- **Von Hippel-Lindau syndrome (VHLS):** Multiple renal cysts develop bilaterally. Renal cysts are lined with glycogen-rich, clear-appearing cells (similar to those observed with grade I clear-cell renal cell carcinoma [RCC]). Atypia and epithelial hyperplasia are common in the cysts.

Acquired cystic renal disease

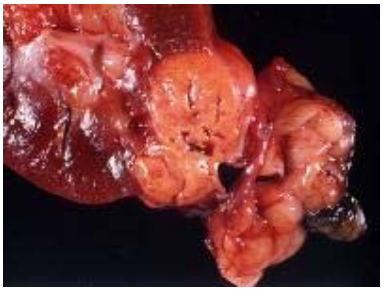
- **Acquired renal cystic disease**
    - Gross evaluation of early disease reveals cortical cysts filled with clear fluid. Cysts are usually smaller than 0.5 cm in diameter but may be as large as 3 cm in diameter. With more advanced disease, medullary cysts are observed. The disease may progress to numerous diffusely distributed cysts and resemble a small kidney affected by ADPKD.
    - Microscopy reveals a flattened, hyperplastic tubular epithelial lining. Foci of epithelial hyperplasia or renal adenomas are common. The remaining renal tissue exhibits sclerotic glomeruli, atrophic tubules, and interstitial fibrosis. Oxalate crystals are common in the walls of cysts.
- **MSK:** Gross evaluation reveals normal-sized kidneys, which may be unremarkable with the exception of at least one enlarged and pale renal pyramid. The disease is bilateral in 70% of cases. Microscopic evaluation reveals dilated collecting ducts lined by cuboidal or flattened epithelium. The cystlike cavities range in size from 1-7.5 mm (usually 1-3 mm) and are present in the papillary portions of the pyramids. Roughly half of the dilated channels contain calcifications. Inflammatory infiltrate is found adjacent to the dilated tubules.
- Simple cysts: Cysts measure 1-5 cm in diameter and are filled with clear fluid. The cysts are usually lined by a flattened layer of epithelium, although they may lack an epithelial lining.



Nephrectomy specimen from a patient with a large benign simple cyst.



Cut section of nephrectomy specimen demonstrating renal cell carcinoma (RCC), with an adjacent simple cyst.



Close-up photograph of the cut surface of the same nephrectomy specimen demonstrating a simple cyst adjacent to a renal cell carcinoma (RCC).

Medical Care

Effective means of prevention or modulation of disease have not yet been identified. Current treatment is aimed at symptom control. In general, therapy is reserved for pain, hypertension, infection, renal salt wasting, and nephrolithiasis.

- **Inherited cystic renal disease**
  - **Autosomal dominant polycystic kidney disease**
    - Patients have decreased ability to concentrate urine and should be encouraged to drink 1-2 L of water daily.
    - Generally, 130/80 is considered the treatment goal for hypertension in this population. Moderate hypertension may be treated with sodium restriction (ie, < 100 mEq/d), exercise, and weight control.

Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are effective in controlling hypertension in autosomal dominant polycystic kidney disease (ADPKD). However, ACE inhibitors have been associated with reversible renal failure in polycystic kidney disease. Calcium channel blockers also are effective in managing hypertension in ADPKD.

- Hypertension appears to correlate with the size of the cyst, and aspiration of renal cysts results in a reduction of blood pressure.[25]
- Prevention of infection with appropriate precautions is important, particularly in women. Avoid urinary tract instrumentation whenever possible.
- Treatment of infection involving cystic kidneys requires a prolonged course of antibiotics. Most cyst walls are permeable to polar antibiotics, including cephalosporins, penicillin derivatives, and aminoglycosides. Occasionally, cysts are relatively impermeable to these agents and require parenteral lipophilic antibiotics, such as ciprofloxacin, erythromycin, chloramphenicol, or a tetracycline. Clinical evaluation findings, including sterile urine, lack of fever, and no renal pain on deep palpation, should guide the route and duration of antibiotic therapy.

  - **Autosomal recessive polycystic kidney disease (ARPKD):** The newborn is provided supportive therapy while the degree of pulmonary insufficiency and the etiology is reviewed. Dialysis may be required for renal failure. With less severe childhood disease, edema often is a problem and is managed with sodium restriction and loop diuretics. Hypertension is controlled with salt restriction and antihypertensives, with particular emphasis on the use of ACE inhibitors and ARBs.
  - **Juvenile nephronophthisis (JNPHP) and medullary cystic kidney disease:** With severe salt wasting, salt supplementation may improve renal function and slow renal demise. End-stage renal insufficiency necessitates dialysis or renal transplantation.

- **Acquired cystic renal disease**
  - **Acquired renal cystic disease (ARCD):** Mild bleeding episodes may be managed with bed rest and analgesics.
  - **Medullary sponge kidney (MSK):** Encourage patients with nephrolithiasis to produce 2 L of urine daily. Patients with hypercalcuria may benefit from oral thiazide diuretics. Patients may develop UTI and should be taught preventative measures.
  - **Simple cyst:** An infected simple cyst usually requires a combination of antimicrobial and surgical management. Pathogens encountered most frequently in infected simple cysts include Enterobacteriaceae, staphylococci, and Proteus species.

Recent research is beginning to identify biochemical targets that may allow disease-modifying therapy.

- Inhibitors of the EGF receptor tyrosine kinase have been shown to slow cyst development and extend the life span in polycystic mice. Clinical trials with these agents are underway.

- Vasopressin receptor activation results in increased levels of cAMP. cAMP has been shown to be cystogenic and provides the rationale for vasopressin receptor blockade. Tolvaptan is a vasopressin receptor antagonist with high affinity in humans and is currently in Phase III clinical trials in patients with ADPCK.
- The identification of mTOR as a possible common pathway to cyst development makes this protein an attractive target for therapy. Rapamycin inhibits mTOR and has been shown to stop kidney growth and even allow regression in kidney size in a mouse model. Additionally, a retrospective comparison of patients treated with rapamycin to those not treated demonstrated a 25% decrease in kidney volume in the treatment group. These animal studies have failed to correlate with human clinical trials. In adults with ADPKD and early chronic kidney disease, 18 months of treatment with sirolimus, an mTOR inhibitor **,** did not halt polycystic kidney growth.[

Surgical Care

- **Multicystic dysplastic kidney (MCDK):** Previously, the involved kidney was routinely removed to prevent the subsequent development of symptoms. Today, however, surgical excision is indicated only if the dysplastic kidney interferes with respiratory or digestive function or if significant hypertension has developed. Additionally, cyst rupture, which can occur spontaneously or secondary to trauma, may require emergent surgical intervention.
- **Inherited cystic renal disease**
    - **ADPKD:** Significant chronic pain may result from expansion of renal cysts. Needle aspiration is usually the first-line approach to symptomatic cysts. Initial resolution and then return of symptoms with reaccumulation of cyst fluid increases the chance that a laparoscopic cyst decortication will eliminate the patient's pain. However, for the management of severe pain, hypertension, hematuria, or infection, surgical excision may be preferred. Complex cysts can be explored laparoscopically and treated appropriately based on intraoperative frozen sections. Laparoscopic techniques have been used with good results. New studies have reported good outcomes of laparoscopic cyst decortication using a retroperitoneal approach especially for posterior or lower pole lesions.
    - Percutaneous endocystolysis is another technique described for treatment of symptomatic cysts. The technique involves obtaining percutaneous access, dilating the tract, and then introducing a resectoscope with rollerball electrode to cauterize the internal surface of the cyst. A 13-year experience with this technique reported clinical improvement in 100% of the patients with minimal complications.
    - Nephrectomy may be performed simultaneously with renal transplantation to create space for the transplanted kidney and to relieve symptoms associated with the native polycystic kidney. The timing of performing the nephrectomy in the transplant patient has been debated. Data suggest that open ipsilateral nephrectomy at the time of transplantation with staged contralateral native nephrectomy has fewer perioperative complications than performing a laparoscopic bilateral nephrectomy. In extreme cases of liver enlargement, severe pain and wasting may result. Partial hepatectomy may alleviate these symptoms.
    - **ARPKD:** In patients with severe portal hypertension, sclerotherapy or portosystemic shunt placement may be necessary to control bleeding.

Splenectomy may be indicated for splenomegaly with significant complications.

- **JNPHP and medullary cystic kidney disease (MCKD):** If transplantation is considered, selecting an older or unrelated donor is advisable to minimize the risk of the transplanted kidney also being affected with these diseases.

- **Acquired cystic renal disease**
  - **ARCD:** Persistent or severe hemorrhage may necessitate nephrectomy or renal embolization. If a 3-cm renal mass suggestive of renal cell carcinoma (RCC) is noted, a partial or radical nephrectomy is indicated.
  - **Simple, intermediate, and suspicious cysts:** Simple renal cysts rarely require surgical management to relieve pain or obstruction. Treatment options include aspiration, sclerosis, open resection, endoscopic marsupialization and fulguration, percutaneous resection, and laparoscopic resection.
  - Bosniak category III and IV renal cysts require surgical exploration. Approximately 50% of Bosniak category III cystic renal lesions are malignant. Management depends on the appearance of the lesion and varies from exploration and biopsy to nephrectomy. The current standard approach is open exploration with anticipated partial nephrectomy. However, as the experience with laparoscopic exploration and nephrectomy grows, this technique may prove equally reasonable.
- **Cystic clear cell renal cell carcinoma:** Whether the patient has known pathologically diagnosed malignancy from biopsy or suspected malignancy based on Bosniak classification, a urologist can anticipate good surgical outcomes after resection. A study evaluating laparoscopic nephrectomy for cystic clear cell renal cell carcinoma revealed that all patients treated were alive after 5 years and that no patient had extrarenal disease at the time of surgery. These data suggest that patients with cystic RCC should expect to be cured after surgical resection, and furthermore should undergo nephron-sparing surgery when possible.

Medication Summary

No specific medical therapies are available for the renal cysts themselves. Complications of cystic renal diseases, such as hypertension, infection, and pain, are treated with standard medical therapy.

Homoeopathic Treatment