Feline Polycystic Kidney Disease

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Profile

Definition

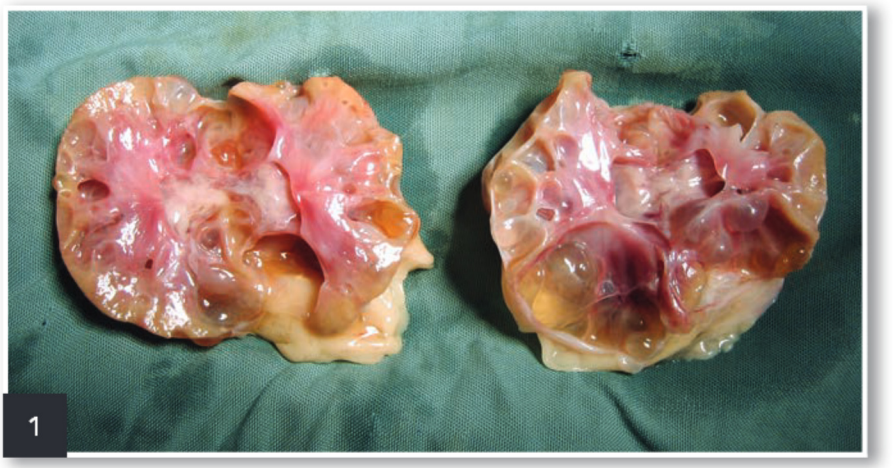
- Polycystic kidney disease (PKD) is the most common inherited renal disease of cats.[1]
- PKD is one of the leading causes of chronic kidney disease (CKD) in Persians and related breeds.[2]
- PKD progresses slowly as portions of the cortex and medulla are replaced by cysts (**Figure 1**).
  - Cysts compress functional parenchyma as they enlarge, thus decreasing kidney function.
- Cyst number and rate of growth are highly variable.[2]

Systems

- Kidneys ± liver and/or pancreas[1,3-6]

Genetic Implications

- Autosomal dominant (AD) mode of inheritance with variable penetrance
- Affected cats are heterozygotes; homozygous expression is embryonic lethal.[7,8]
- Mutation in *PKD1* gene leads to a C>A transversion in exon 29, leading to a stop codon.
  - This is the basis for genetic testing.[7-9]
- Variable expression is seen in related and unrelated individuals.
  - Cyst size and number varies from cat to cat and parent to offspring.
  - Mildly affected queens can produce offspring with severe disease and vice versa.[2]



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Necropsy of both sectioned kidneys from a cat with PKD; note fluid-filled cysts of varying sizes and obliteration of large portions of both the cortex and medulla. Only scant amount of renal parenchyma (pink) remains. Image courtesy of Dr. Susan Little

Incidence & Prevalence

- Affects approximately 6% of cats.
- May affect up to 37%–50% within Persians and related breeds.[10-13]
- In other breeds, prevalence may be as high as 16%.[14]

Geographic Distribution

- Worldwide

Signalment

Breed Predilection[15]

- High risk: Persian, Himalayan, exotic shorthair breeds, British shorthair breeds
- Moderate risk: Asian, Birman, Bombay, Burmilla, Cornish rex, Devon rex, ragdoll, Snowshoe, Tiffanie

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Screening to identify PKD carriers is essential for a breeding program, regardless of whether the cat is clinically affected.

AD = autosomal dominant, CKD = chronic kidney disease, PKD = polycystic kidney disease

- Low risk: Abyssinian, Angora, Balinese, Bengal, Burmese, Chartreux, Egyptian Mau, Korat, Maine coon, Norwegian forest cat, Ocicat, Oriental longhair, Oriental shorthair, Russian blue, Siamese, Singapura, Somali, Tonkinese, Turkish van
- Cystic renal disease occurs with a low prevalence in the Maine coon and is unrelated to the *PKD1* mutation observed in Persians and related breeds.[16]
- Despite conscientious warnings and screenings by breeders, the ragdoll has a low prevalence of PKD (<3%).[17,18]

Age & Range

- Affected cats usually develop CKD signs between 3–10 years of age (mean, 7 years).

Sex

- No sex predilection

Absence of cysts at youth does not guarantee the cat will not develop them later; also, a cat with cysts may never show clinical disease.

Pathophysiology

- Polycystin-1, encoded by the *PKD1* gene, is a renal tubule membrane glycoprotein needed for epithelial cell proliferation and differentiation.
  - Substitution of a cytosine base for an adenine base results in insufficient polycystin-1 production.
  - Insufficient polycystin-1 results in tubule remodeling and cyst formation.
- Cysts may develop in the embryo.*
  - This is under investigation.
- Stress may cause CKD manifestation in predisposed individuals.[19]
- One study showed increased mean arterial pressures and aldosterone: renin ratios[20]; one therapeutic case series showed no resolution of hypertension after surgical drainage.[21]
  - However, PKD does not result in hypertension in cats as it does in humans and dogs.[22]
  - Cats that develop CKD secondary to PKD may be at risk for hypertension.

History & Clinical Signs

- Many cats remain subclinical for an extended time.
- History and clinical signs are those typical of CKD:
  - Polyuria, polydipsia, dehydration, lethargy, inappetence/anorexia, nausea/vomiting, constipation, weight loss, muscle wasting, and oral ulceration
- Cysts may also result in hematuria and increased risk for urinary tract infections.[23]

Table **PKD Differential Diagnosis**

	Cause	*Imaging Findings*	*Prognosis*
PKD	AD mutation of *PKD1* gene	Multiple, variably sized cysts in both kidneys ± hepatic, pancreatic cysts	Because of variable progression, some cats remain asymptomatic while others develop CKD rapidly
Perinephric pseudocysts	Numerous causes (eg, trauma, perirenal fat necrosis, neoplasia, idiopathic)	Fluid-filled sac surrounding one or both kidneys; fluid accumulates between renal capsule and parenchyma	Reduction of pressure by ultrasound-guided drainage or surgical resection or fenestration ± omentalization has good outcome depending on degree or age of compression-induced CKD
Acquired cysts	Intraluminal tubular obstruction by inflammatory debris; extraluminal compression of tubules by parenchymal inflammation or fibrosis	Unilateral or bilateral, variably sized and located cysts	Compression-induced CKD progresses with rate depending on severity of lesion

AD = autosomal dominant, CKD = chronic kidney disease, PCR = polymerase chain reaction, PKD = polycystic kidney disease

*Personal correspondence with Leslie Lyons, MS, PhD; August 2014

- Cats with large cysts have irregular, large kidneys.
  - Cysts are often bilateral.
- Patients may present with signs associated with liver disease, albeit rarely.
  - 6%–68% of affected cats have hepatic cysts.[4,24]
- Rarely, hepatic encephalopathy may be present with hepatic cysts and fibrosis.[25,26]

Dx Diagnosis

Definitive Diagnosis

- CBC, serum chemistry, and urinalysis are required for CKD diagnosis.
- Ultrasonography and genetic testing are required to definitively diagnose PKD.
  - Cats may not have the same genetic mutation.[27]
  - Cysts may not be visible in very young cats.[27]
- Genetic testing identifies only the AD form of PKD, not other forms of cystic kidney disease.
- Ultrasonography is sensitive for PKD detection, assesses severity, is repeatable, and is useful for monitoring disease progression.[28]

Differential Diagnosis

- Renomegaly: Lymphoma, feline infectious peritonitis granulomatous nephritis, perinephric pseudocysts, acquired renal cysts, hydronephrosis, acromegaly
- See **PKD Differential Diagnosis**

Laboratory Findings

- Depending on CKD stage, increases in BUN and creatinine, low urine-specific gravity secondary to decreased concentrating ability, alterations in electrolytes, and anemia may be present.

Imaging

- Radiography is not useful in early stages.
  - Once large cysts are present, renomegaly and asymmetry of renal size will be apparent ± dystrophic calcification.
- Ultrasonography can typically identify renal cysts >2 mm in diameter (**Figure 2**).
  - Diagnostic sensitivity of ultrasound is 91% in cats >9 months of age.[27]
  - Phenotypic variation in cyst size and number is considerable.
  - Cysts are smooth, round, or irregular anechoic structures of variable size located throughout the renal cortex and medulla and grow over sequential assessment.[2,29]
  - Affected kidneys have indistinct corticomedullary junctions and foci of mineralization.[3,29]
  - Absence of cysts at youth does not guarantee the cat will not develop them later.
  - Cysts may be found as early as 6–8 weeks of age.
  - False negatives at this age are a result of small cysts or operator inexperience.
  - Kittens from affected lines should be screened at ~10 months of age.[3]

Genetic Testing (PCR)

- Detects *PKD1* gene
  - Useful for early diagnosis in potential breeding stock
  - Buccal swab can be used in very young kittens.
  - Care must be taken if the kitten is not weaned; milk may contaminate the sample.
  - In preweaned or older cats, blood sample may be used in lieu of buccal swab.
  - Several tests are available.[7,8]

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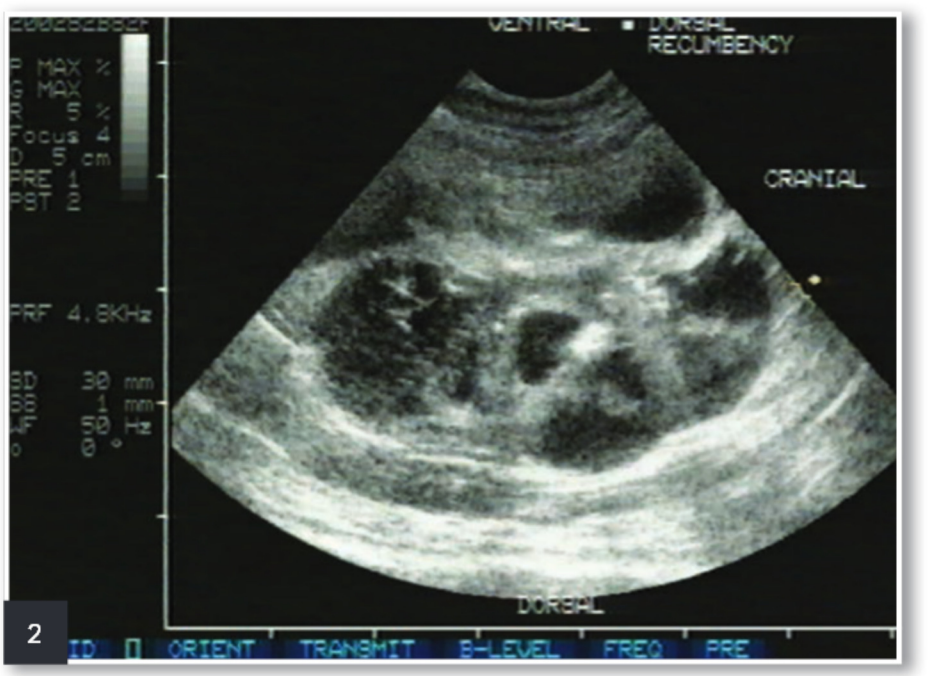

Ultrasound image of a polycystic kidney in a young Himalayan cat with multiple hypoechoic cysts. Image courtesy of Dr. Susan Little

Postmortem Findings & Histopathology

- Cysts are focal dilations of the renal tubules.
  - Varying amounts of normal renal parenchyma remain surrounded by fibrous tissue.

Tx Treatment

Medical

- No definitive cure; condition is inherited, irreversible, and progressive.
- Therapy reflects IRIS stage (iris-kidney.com) with in-hospital or home fluid therapy, potassium supplementation, phosphate binders, H_2-receptor antagonists, antiemetics, appetite stimulants, and erythropoietin as needed.
- When present, CKD hypertension should be managed with amlodipine.
- When present, proteinuria should be managed with benazepril or telmisartan (eg, an angiotensin receptor blocker).
- Urinary tract infection must be treated with appropriately sensitive antimicrobials to prevent secondary cyst infection and sepsis.
- Analgesics may be warranted.

Surgical

- Cyst drainage fails to slow progression but may reduce discomfort.
- Ultrasound-assisted drainage and alcoholization has been evaluated.[21]

Nutritional

- If muscle wasting is not present, a renal diet may be considered after IRIS Stage 3.
- Appetite stimulants may be beneficial; caloric and protein requirements should be calculated.
- Short-term feeding tubes may ensure adequate nutrition is received.

Client Education

- Knowing which cats are affected allows for planned mating to reduce PKD.
- All Persians and related cats and cats with known familial risk should be screened.
- Combining ultrasound with genetic testing improves diagnostic yield.
  - Some cats with cystic kidney disease are not *PKD1* positive and do not have PKD.
- Complete elimination of all affected Persians from breeding programs would reduce the diversity of the breed and may lead to other undesirable characteristics.
  - Mating an affected progenitor with a healthy individual results in 50% of descendants being disease free; this type of crossing helps avoid losing a genetic line while conserving genetic diversity.

Follow-Up

Patient Monitoring

- Cats with PKD should be monitored q6–12mo via ultrasound to evaluate cyst progression and detect changes indicating supportive care for emerging CKD.
- Once CKD is present, cats should be monitored as often as is indicated.

Both ultrasound and genetic testing should be used to screen for disease.

In General

Relative Cost

- Diagnostics:
  - Ultrasound: $$
  - Genetic testing (PCR): $
- CKD treatment: $$–$$$$$

Cost Key
$ = up to $100
$$ = $101–$250
$$$ = $251–$500
$$$$ = $501–$1000
$$$$$ = more than $1000

Prognosis

- If minimally affected: Good
- If rapidly progressive: Poor

Prevention

- Affected individuals should be identified to enable planned breeding.

General Comments

- Breeders are encouraged to use the International Cat Care PKD Negative Register (icatcare.org/breeders/registers/PKD) to select breeding stock and register negative cats (noting whether negative result is based on ultrasound or genetic screening). ■ cb

See **Aids & Resources**, back page, for references & suggested reading.

CKD = chronic kidney disease, PKD = polycystic kidney disease