

# Autosomal dominant polycystic kidney disease in childhood

**Author: Professor Patrick Niaudet, MD<sup>1</sup>**

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<sup>1</sup>member of the European editorial committee of Orphanet encyclopedia

<sup>2</sup>Service de néphrologie pédiatrique, Hôpital Necker - Enfants Malades, 149 Rue de Sèvres, 75743 Paris Cedex 15, France. [niaudet@necker.fr](mailto:niaudet@necker.fr)

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## Abstract

*The term polycystic kidney disease should be reserved for two hereditary diseases: [autosomal recessive polycystic kidney disease](#) (ARPKD) and, most commonly, autosomal dominant polycystic kidney disease (ADPKD). ADPKD is characterized by the presence of cysts any part of the nephron, including Bowman's space, it is quite common, since it occurs in one in every 400 to 1000 live births. Affected children can have macro or microscopic hematuria, hypertension, cyst infection and/or renal insufficiency. Hypertension and renal insufficiency should be treated. Renal cyst infection represents a difficult problem and requires aggressive antibiotic therapy. Most families have a defect on chromosome 16 (the PKD1 abnormality), while the abnormal gene is on chromosome 4 in at least some other families. Ultrasonography can be used for antenatal diagnosis, with enlarged, hyperechogenic kidneys as the primary finding, but cysts may already be visible.*

## Keywords

Enlarged hyperechogenic kidneys, cysts in the nephron, renal failure, hematuria, hypertension

## Disease name and synonyms

Autosomal dominant polycystic kidney disease (ADPKD)

and, less commonly, autosomal dominant polycystic kidney disease (ADPKD).

ADPKD is characterized by the presence of cysts in any part of the nephron.

## Definition/Diagnosis criteria

The term polycystic kidney disease should be reserved for two hereditary diseases: autosomal recessive polycystic kidney disease (ARPKD)

## Incidence

ADPKD is quite common, as it occurs in one in every 400 to 1000 live births.

**Clinical description**

Renal manifestations - Although unusual, ADPKD can become clinically apparent in young children, even though the affected parent has adult-onset disease. In rare cases, the presence of cysts is discovered by antenatal ultrasonography or, because of enlarged kidneys, during the neonatal period or the first year of life [1-4]. Both kidneys are usually involved, but a unilateral abdominal mass in some children has been reported [4]. Why the disease is of such early onset is not known. Two possibilities are instability of DNA [5] or inheritance of a modifier gene that markedly increases the severity of the defect caused by the *PKD* gene. In addition, some patients have a "contiguous gene" syndrome in which there is a large deletion in both *PKD1* and the adjacent gene for tuberous sclerosis. Some of these children will develop the characteristic manifestations of tuberous sclerosis during early adolescence.

**Course**

Affected children can develop any of the renal symptoms associated with ADPKD [2]. These include macro or microscopic hematuria, hypertension, cyst infection and/or renal insufficiency.

Most affected children have few or no symptoms during childhood and present as adults. Two studies have enhanced our understanding of the course of the disease during childhood by prospectively following over 80 children who were identified by the radiologic screening of offspring of parents with ADPKD [1,6]. In one of the studies, at least one cyst was found in 44% of the offspring at a mean age of 8.7 years [6]. Some affected children already had more than 10 cysts and, during follow-up, almost all showed signs of progressive disease such as increasing cyst size or number. The frequencies of flank or back pain and hypertension are directly related to the severity of the structural involvement. However, the glomerular filtration rate in these children was generally stable [1,6,7]. Authors of a recent study were able to identify children at risk of rapid progression who benefit from future therapeutic intervention. This is consistent with the natural history of ADPKD in which renal insufficiency develops after the age of 30.

Children presenting symptoms during the first year of life usually do not progress rapidly to end stage renal failure. In one study on 11 children diagnosed *in utero* or during the first year of life, it was found that, during follow-up over 3 to 15 years (mean 6.8 years), two children had end-

stage renal failure and eight had normal or nearly normal creatinine clearance rates [8].

**Pathology**

Renal involvement is characterized by cystic dilatations in all parts of the nephron including Bowman's space. During the early stages, there may be only a few macrocysts irregularly distributed. Later, both kidneys are enlarged and large cysts are present in the cortex and the medulla. Cysts in the liver, pancreas, and other organs are common in ADPKD, but congenital hepatic fibrosis is rare [9,10]. Cerebral vessel malformations have also been described in pediatric patients [11].

**Management and treatment**

Hypertension and renal insufficiency should be treated as for patients with ARPKD. Renal cyst infection represents a difficult problem and requires aggressive antibiotic therapy. New therapies may become available. [12].

**Etiology**

Most families have a defect on chromosome 16 (the *PKD1* abnormality), while the abnormal gene is on chromosome 4 in at least some other families. Why some cases present in childhood is unclear, since there is no evidence for genetic heterogeneity when compared to the more classic cases of ADPKD that present in adulthood [13]. There is a familial incidence of childhood presentation, as offspring of affected parents have a greater risk of early disease. However, this relationship within families is not absolute, since some infants with severe disease have a parent with stable renal function [1].

**Diagnostic methods**

The diagnosis of polycystic kidney disease is usually established by ultrasonography, which reveals diffuse hyperechogenicity, enlarged kidneys, and, in most children, cysts; these changes are usually but not always bilateral [4,14,15]. Intravenous urography is less sensitive, since distortion of the calyces is seen only with larger macrocysts [4].

**Differential diagnosis**

The ultrasonographic appearance may not distinguish autosomal recessive from autosomal dominant disease [16]. In this setting, a careful family history and analysis of the parents is often helpful. Ultrasonography of parents of children with ARPKD will not show cysts while ADPKD is often first discovered in a parent at the time of diagnosis in the child. However, parents with ADPKD under the age of 25 to 30 may not yet have cysts detectable by ultrasonography and

establishing the diagnosis may require evaluation of the grandparents. In addition, extrarenal (hepatic, pancreatic) cysts also favor the presence of autosomal dominant disease, while portal fibrosis or signs of portal hypertension, cholangitis, or biliary dysgenesis favor the diagnosis of autosomal recessive disease.

### Antenatal diagnosis

Ultrasonography can be used for antenatal diagnosis [15,17,18]. Most antenatal studies have been performed between 31 and 36 weeks of gestation, often at the request of the parents. Enlarged, hyperechogenic kidneys are the primary finding, but cysts may already be visible [19,20].

It should also be recognized that the ultrasonographic finding of enlarged, echogenic kidneys in the fetus is not diagnostic of polycystic kidney disease. Other disorders that can produce these changes include malformation syndromes, such as the Meckel syndrome, renal dysplasia, the congenital nephrotic syndrome, and transient nephromegaly in which the ultrasonographic abnormalities return to normal after birth [21].

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