

# AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE (ARPKD)

Linkage Analysis - **Tests 4 & 5**

- updated 08-10-09 -

Mendelian Inheritance in Man number: [\\*606702](#)

Click here for [Gene Reviews](#) Clinical Summary.

Autosomal Recessive Polycystic Kidney Disease (ARPKD) is characterized by enlarged cystic kidneys and hepatic fibrosis. The diagnosis is often made pre- or neonatally, but some patients are still diagnosed later in life. The severity varies widely, with a high mortality rate in the first months of life. ARPKD is one of the more common hereditary childhood nephropathies with an estimated incidence of 1:20,000-1:40,000. The carrier frequency in the general population is estimated to be 1 in 70 to 1 in 100. Mutations in *PKHD1* are scattered throughout the gene. Most families carry their own "private" mutations. For more information on the condition please refer to the review on the [GeneTests](#) website and [Online Mendelian Inheritance in Man](#).

## Genetics of ARPKD

The gene for ARPKD, *PKHD1* (*Polycystic Kidney and Hepatic Disease 1*), resides on chromosome 6p21-p12, spans 470 kb of genomic DNA and is the only gene known to be associated with the wide clinical spectrum of autosomal recessive polycystic kidney disease. 86 exons have been identified and multiple alternative transcripts are known. Over 300 mutations have been reported. Missense, nonsense, frameshift, splicing and multi-exon deletions can occur and the mutations are located throughout the length of the gene, with no major mutational hotspots known, as shown in the [PKHD1 mutation database](#).

## INDICATIONS FOR DIRECT TESTING

- Informativity testing (**test 4**) and prenatal analysis (**test 5**) by haplotype analysis in families with an accurate clinical diagnosis of ARPKD *and/or* in families in whom only 1 unequivocal pathogenic *PKHD1* mutation could be identified after bidirectional sequencing of the longest open reading frames.

## TESTING METHODOLOGY

Haplotype studies are based upon and rely on the accurate clinical diagnosis of ARPKD in the affected family member and accurate delineation of the biological relationships in the family. Haplotype studies also depend on the availability and/or willingness to be tested of at least the proband and both parents. Haplotype analysis is performed by amplifying 6 highly informative microsatellite markers residing intragenically and closely flanking the *PKHD1* gene.

Paraffin-embedded tissue as well as a cell line, tissue biopsy, or blood sample can be used as the starting material from the affected proband for testing. In cases where only 1 pathogenic mutation was identified by direct sequencing of the entire longest open reading frame, haplotype studies can be applied for future prenatal diagnosis, if clinical diagnosis in the proband was accurate. Prenatal haplotype based testing is available

starting from direct or cultured CVS, fresh or cultured amniocytes. All prenatal samples are performed in duplicate independently by two technicians.

## **SPECIMEN REQUIREMENTS**

Please send samples from the parents and their children for informativity testing.

**(1)** 10ml of whole blood in EDTA (purple topped) tubes. (2 ml minimum for pediatric patients)

**(2)** Paraffin-embedded tissue blocks or whole tissue from affected individual

**(3)** For prenatal samples (**Test 5**),

**(1)** minimum of 15 mg of chorionic villus specimen. Send specimen in transport media in 15-mL centrifuge tube.

**(2)** 20 mL of amniotic fluid. Send specimen refrigerated, but not frozen.

**(3)** 2-T25 flasks of cultured CVS (>70% confluent), sent at ambient temperature.

**(4)** 2-T25 flasks of cultured amniocytes. (>70% confluent), sent at ambient temperature.

## **TRANSPORT**

If the specimen is from clinics within UAB or Kirklin Clinic, please call 934-5562 for pickup. If specimens are being sent from some other location, please ship via UPS or Federal Express.

1. Be sure that the shipping air bill is marked “**Priority**”, either Domestic or International.

2. Specimens must be packaged to prevent breakage and absorbent material must be included in the package to absorb liquids in the event that breakage occurs. Also, the package must be shipped in double watertight containers (e.g. a specimen pouch + the shipping companies Diagnostic Envelope). **You can use our collection kits, which we will send to physicians directly upon request.**

3. Please contact us (Email – [mgl@genetics.uab.edu](mailto:mgl@genetics.uab.edu), Phone – 205-934-5562) prior to sample shipment and provide us with the **date of shipment** and the **tracking number** of the package, so that we can better ensure receipt of the samples

## **TURN AROUND TIME**

**Test 4:**

4 weeks

**Test 5:**

6 working days after sample is received

## **CPT CODES AND PRICES**

**Please note that prices listed correspond to institutional rates; please contact the lab for insurance rates.**

**Test 4:**

\$400, -USD per individual ([currency converter](#))

83891 (x1), 83909 (x3), 83896 (x7), 83898 (x7), 83912 (x1)

**Test 5:**

\$500, -USD per individual ([currency converter](#))

83891 (x2), 83909 (x6), 83896 (x14), 83898 (x14), 83912 (x1)

**REQUIRED FORMS**

[ARPKD Test Requisition](#)

\*Phenotypic checklist does not need to be filled out for prenatal tests.

**Note:** Requests for Molecular Genetic testing for ARPKD will **not** be accepted for the following reasons:

- No label (patients full name and date of collection) on the specimens
- No referring physician's or genetic counselor's names and addresses
- No billing information
- No informed consent
- No phenotypic information

**For more information, test requisition forms, or sample collection and mailing kits, please call: 205-934-5562.**

**REFERENCES**

Bergmann C, Senderek J, Kupper F, Schneider F, Dornia C, Windelen E, Eggermann T, Rudnik-Schoneborn S, Kirfel J, Furu L, Onuchic LF, Rossetti S, Harris PC, Somlo S, Guay-Woodford L, Germino GG, Moser M, Buttner R, Zerres K. (2004) PKHD1 mutations in autosomal recessive polycystic kidney disease (ARPKD). *Hum Mutat.* 2004 May;23(5):453-63. ([pubmed](#))

Sharp AM, Messiaen LM, Page G, Antignac C, Gubler MC, Onuchic LF, Somlo S, Germino GG, Guay-Woodford LM. (2005). Comprehensive genomic analysis of PKHD1 mutations in ARPKD cohorts. *J. Med. Genet.* Apr; 42(4): 336-49. ([pubmed](#))

Zerres K, Rudnik-Schoneborn S, Senderek J, Eggermann T, Bergmann C. (2003) Autosomal recessive polycystic kidney disease (ARPKD). *J Nephrol.* 2003 May-Jun;16(3):453-8. ([pubmed](#))

Zerres K, Senderek J, Rudnik-Schoneborn S, Eggermann T, Kunze J, Mononen T, Kaariainen H, Kirfel J, Moser M, Buettner R, Bergmann C. (2004) New options for prenatal diagnosis in autosomal recessive polycystic kidney disease by mutation analysis of the PKHD1 gene. *Clin Genet.* 2004 Jul;66(1):53-7. ([pubmed](#))