

AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE (ARPKD)

Prenatal Detection of Known Mutation(s) - **Test 3**

- updated 08-10-09 -

DESCRIPTION

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

- Prenatal analysis by sequence analysis of 1 or 2 exons in families where both mutations were identified in a previously affected child

TESTING METHODOLOGY

We offer **targeted detection** of the family-specific *PKHD1* mutations if **both** mutations have previously been identified within the family. From direct or cultured chorionic villi sample (CVS), fresh or cultured amniocytes, DNA is extracted, the target regions are amplified and analyzed for either the presence or absence of the family-specific mutations. Maternal cell contamination is verified using microsatellite marker analysis. All prenatal analyses are performed in duplicate and independently by two technicians. A blood sample of the mother needs to accompany the fetal sample for purposes of verification of maternal contamination of fetal tissue.

If only 1 pathological mutation was previously identified in the proband, prenatal testing can be offered using haplotype analysis (see under **Tests 4-5**).

SPECIMEN REQUIREMENTS

(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.

Please also send 1-5 ml of blood or buccal swab sample from the mother for maternal contamination studies.

TRANSPORT

If specimen is from clinics within UAB or Kirklin Clinic, please call 934-7107 for pick-up. 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, Phone – 205-934-5562) prior to sending a sample for prenatal testing 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 within the 60-hour window

TURN AROUND TIME

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.

\$1,000, -USD ([currency converter](#))

83891 (x3), 83909 (x6), 83898 (x20), 83904 (x16), 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

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

REFERENCES

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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](#))

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