

ADPKD

Autosomal dominant polycystic kidney disease • Theory and bedside practice

01 GENETICS & PATHOPHYSIOLOGY

Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disorder characterised by progressive cyst formation in both kidneys and manifestations outside the kidneys. Most cases are caused by pathogenic variants in PKD1 or PKD2, which encode polycystin-1 and polycystin-2. Abnormal polycystin signalling disrupts tubular cell function and promotes cell proliferation and fluid secretion into cysts. Each child of an affected parent has a 50% chance of inheriting the pathogenic variant. A negative family history does not exclude ADPKD because new variants and previously unrecognised disease can occur. PKD1-related disease generally progresses more rapidly than PKD2-related disease, although individual outcomes vary. Cysts enlarge over time, increasing kidney size and gradually damaging functioning kidney tissue.

02 CLINICAL MANIFESTATIONS

Hypertension is common and may develop before kidney function becomes abnormal. Typical clinical features include flank pain, visible haematuria, urinary tract infections and kidney stones. Fever with flank or abdominal pain should raise suspicion of cyst infection, while sudden pain may indicate cyst haemorrhage or a stone. Liver cysts are the most common extrarenal manifestation and may cause abdominal enlargement, discomfort or early satiety. Other associated abnormalities include intracranial aneurysms, abdominal wall hernias and cardiac valve abnormalities. A thunderclap headache requires immediate assessment for possible subarachnoid haemorrhage.

03 DIAGNOSIS, PROGRESSION & TREATMENT

Diagnosis usually relies on imaging, with ultrasound criteria interpreted according to age and family history. Genetic testing is useful when imaging is inconclusive, the presentation is atypical or a related living kidney donor is being evaluated. Progression is assessed using the eGFR trend, kidney volume, age and clinical and genetic information. Management includes blood pressure control, usually with an ACE inhibitor or ARB, cardiovascular risk reduction and avoidance of chronic NSAID use. Tolvaptan blocks vasopressin V2 receptors and can slow kidney-function decline in selected adults at risk of rapid progression, but causes aquaresis and requires liver monitoring. Intracranial aneurysm screening is recommended in selected patients, particularly those with previous subarachnoid haemorrhage or a family history of aneurysm, subarachnoid haemorrhage or unexplained sudden death. Patients with progressive kidney disease need early preparation for kidney replacement therapy, including consideration of pre-emptive kidney transplantation.

04 PRACTICAL APPROACH TO THE PATIENT

- **Assess kidney function over time:** review previous creatinine and eGFR results to determine whether the disease is stable or progressing.
- **Check blood pressure:** measure it during the visit, review home readings and ask about medication adherence.
- **Ask about typical complications:** haematuria, urinary infections, kidney stones, flank pain and abdominal fullness.
- **Fever with flank pain:** suspect cyst infection and arrange prompt clinical assessment.
- **Sudden flank pain:** consider cyst haemorrhage or a kidney stone and assess the need for imaging.
- **Persistent or recurrent haematuria:** investigate other causes rather than automatically attributing it to cysts.
- **Take a focused family history:** ask about ADPKD, the age at kidney failure, brain aneurysms and unexplained sudden death.
- **Examine the abdomen:** assess kidney or liver enlargement, tenderness and hernias.
- **Monitor urine and CKD complications:** check albuminuria or proteinuria, potassium, bicarbonate and, when appropriate, haemoglobin and mineral metabolism.
- **Explain neurological red flags:** a sudden, extremely severe headache requires immediate emergency assessment.
- **Consider aneurysm screening:** discuss it particularly when the personal or family history suggests increased risk.
- **Protect kidney function:** control hypertension, discourage smoking, avoid chronic NSAID use and individualise hydration advice.
- **Assess eligibility for tolvaptan:** identify patients at risk of rapid progression and discuss polyuria, thirst and liver monitoring.
- **Address the family:** offer genetic counselling and discuss appropriate assessment of relatives.
- **Plan kidney replacement therapy early:** consider pre-emptive transplantation and carefully exclude ADPKD in any biologically related potential donor.

REFERENCES

KDIGO. Clinical Practice Guideline for the Evaluation, Management, and Treatment of ADPKD. *Kidney Int.* 2025;107(Suppl 2S):S1–S239.

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