FACT SHEET

NATIONAL INSTITUTES OF HEALTH

Autosomal Dominant Polycystic Kidney Disease

Yesterday

- Autosomal Dominant Polycystic Kidney Disease (ADPKD) resulted in end-stage renal disease (ESRD) by age 53, on average, and was responsible for 6 percent of ESRD cases in the U.S.
- The details of the genetics of ADPKD were unknown other than the observation that 50 percent of children born to an affected parent would develop the disease.
- Diagnosis of well-established ADPKD in adults was relatively straightforward with available imaging techniques (ultrasound and computerized tomography). Diagnosis of earlier stages of disease in children and young adults was much more difficult.
- Few treatments were available for chronic kidney disease in general, and there was no specific therapy for ADPKD. The importance of controlling blood pressure and dietary protein intake in patients with chronic kidney disease was not recognized.
- Two lifesaving kidney function replacement therapies—hemodialysis and kidney transplantation, developed through fundamental NIH research in the 1960s—were increasingly available for ADPKD patients; however, neither was ideal. Because the genetics of ADPKD were not understood, some transplant centers were unwilling to perform transplants from family members who wished to donate a kidney.

Today

- Through NIH-supported research, mutations in one of two genes—PKD1 and PKD2—have been identified in eighty five percent of patients with ADPKD. NIH funded studies are searching for additional genetic changes that might explain person to person variation in kidney growth and disease severity.
- Development of age-specific diagnostic criteria and genetic testing has facilitated early diagnosis of ADPKD. Newer imaging methods, specifically magnetic resonance imaging, provide better kidney cyst imaging.
- The ability to detect mutations in either PKD1 or PKD2 provides important prognostic information. NIH-supported clinical studies have shown that patients with mutations in PKD2 tend to develop kidney cysts, high blood pressure, and ESRD at a later age than do patients with mutations in PKD1.
- Although the molecular mechanisms by which PKD1 and PKD2 mutations cause ADPKD are not known, NIH-supported researchers have studied how these genes are involved in basic biological processes within kidney cells, and are exploring new avenues of investigation to understand how mutations might cause kidney cysts.
- The NIH funded two large clinical studies of ADPKD. The Consortium for Radiologic Imaging of PKD (CRISP) provided new and useful information regarding the reliability of non-invasive magnetic resonance imaging for monitoring disease progression in patients with ADPKD. The HALT-PKD study is using these imaging methods to test whether newer classes of blood pressure medications can prevent or delay progression of kidney size functional decline in ADPKD.
- Basic research supported by NIH facilitates testing of other potential drug therapies for ADPKD , and other clinical trials of ADPKD are implementing new imaging methods for assessing progression of ADPKD.
- The average age for development of ESRD for patients with ADPKD has increased from 53 to 57 years of age. ADPKD is currently responsible for 4.5 percent of overall ESRD cases and 2.2 percent of new ESRD cases each year in the U.S.
- The high cardiovascular death rate in dialysis patients with ADPKD remains a problem.
- Kidney transplantation is widely available, and nearly 13 percent of ADPKD patients who develop ESRD receive a transplant before beginning dialysis therapy. Limited organ availability has resulted in longer waiting times.
- Transplant failure due to acute organ rejection is much less common, with one-year success rates exceeding 90 percent.

Tomorrow

- The continued development and testing of new potential therapies for chronic kidney disease in general—and ADPKD in particular—will result in fewer people developing advanced kidney disease and kidney failure. This in turn will result in less need for dialysis and transplantation.
- As our understanding of the genetics and progression of ADPKD increases, we hope that there will be a decrease in the number of ADPKD patients that progress to ESRD.
- Because ADPKD can affect patients very differently, even within the same family, the NIH is assembling a large genetic sample collection for future investigations that would identify genetic markers that might predict who will develop more rapidly progressive kidney disease. These genetic studies could also provide new information on identifying key disease pathways and help design new drug treatment strategies. The studies also may yield clues about how to intervene earlier, more precisely, and more effectively in ADPKD.
- The results of the HALT-PKD trials should help NIH extend the success of therapies for other forms of kidney injury to ADPKD, by testing interventions that can control the accelerated development of cardiovascular disease, the main cause of death in kidney patients. Other ongoing studies supported by NIH will determine new risk factors for accelerated cardiovascular disease, and permit individualized prevention strategies.
- If detected sufficiently early, it may be possible to restore lost kidney function. More aggressive management of diabetes and high blood pressure, as well as drugs that target kidney fibrosis, may give patients additional years of life without dialysis.
- For those patients who need dialysis, NIH is studying whether more frequent dialysis improves physical function and cardiovascular health. Studies are also underway to examine the factors that influence the functioning of fistulas—a surgically-created site used to access blood—in patients undergoing hemodialysis.
- Despite our best immunosuppressant therapies, a number of patients with kidney transplants still lose their transplanted kidney due to chronic rejection. Better strategies to maintain the function of transplanted kidneys and prevent chronic scarring are likely to emerge from on-going basic research and improved imaging methods.

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