Hereditary Kidney Disease: All Family Members Are Affected

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In families with hereditary kidney disease, it is common to refer to "affected" and "unaffected" family members, but in reality, all family members are affected. All face uncertainty about whether they have the disease or can pass it on, and whether to be tested. Those with the disease face a lifetime of hardship, and those without the disease must decide whether to become caretakers, kidney donors, or both. The effects on the family depend on many clinical factors, such as the pattern of heredity, the nature of the disease and its treatments, the age at onset of kidney failure, and the ease of detection. Autosomal dominant polycystic kidney disease (ADPKD) has a penetrance of almost 100%, but the onset of kidney failure is generally not until age 50–70 years old, creating some unique issues that, in our view, may not have received sufficient attention. We are uniquely positioned to offer this perspective as physicians who have been personally affected by the disease. R.M.F. is a patient with ADPKD, a retired practicing hematologist-oncologist, and a kidney transplant recipient. A.S.L. is a family member without the disease (husband), an academic nephrologist, and a kidney transplant donor.

ADPKD has an enormous effect on families, including our own. Nearly one half of all first degree relatives in all generations live with the disease for many years. There is ample time for family members to witness the hardship that it imposes, feel helpless as succeeding generations become ill, and ask whether more might have been done. Polycystic kidney disease can be detected reliably in most young adults before the onset of symptoms, creating an obligation for individuals with the disease to decide whether to inform family members at risk and an obligation for family members not known to have the disease to decide whether to be tested. With the emergence of new therapies, guidelines are rapidly evolving.[1] How can physicians best care for these patients and their families?

Before the development of kidney failure, ADPKD is commonly complicated by hypertension, infection, hemorrhage, pain, and changes in body image due to kidney cysts, and less commonly, it is complicated by hepatic cysts and intracranial aneurysms. Individuals known to have the disease are generally counseled to seek medical attention for symptoms of these conditions, enabling more efficient care. Diagnosis of ADPKD before the onset of complications can facilitate appropriate care and avoid distress of diagnosis in the setting of a complication. In families with a history of ruptured intracranial aneurysm, detection of ADPKD may lead to screening for unruptured aneurysms. A recent Kidney Disease Improving Global Outcomes[1] conference gave the following recommendations: "Presymptomatic screening of ADPKD is not currently recommended for at-risk children. For at-risk adults the potential benefits of presymptomatic diagnosis usually out-weigh the risks, and it is most commonly performed by ultrasonography, which is inexpensive and widely available. The implications of a positive diagnosis vary from country to county and should be discussed beforehand." In our experience, this discussion is likely to be far ranging and requires expertise in multiple disciplines.

Young adults may wish to determine their risk of transmitting the disease to their children. In individuals known to have ADPKD, the mutation can be detected in the embryo using amniocentesis or preimplantation screening after *in vitro* fertilization. Because many mutations in the PKD1 and PKD2 genes give rise to ADPKD, it may be necessary to test many family members to identify the mutation with certainty. We have informed our children and our nieces and nephews about these options. It is poignant that the decision about the future of the next generation may be the first decision facing young adults with a family history of ADPKD.

As in other kidney diseases, living donor kidney transplantation is the preferred modality for treatment of kidney failure in ADPKD. Because of the large number of family members with disease, there may not be enough family members without the disease to be kidney donors for all of the family members in need. Creating a family plan for kidney donation and transplantation in advance of the onset of kidney failure requires a concerted effort to evaluate all family members known to have the disease and not known to have the disease, but it may maximize the opportunity for all in

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need to receive a living donor transplant. In our experience, issues of privacy and individual preferences make it challenging to create a family plan, but the participation of one or more physicians caring for individuals with the disease can be helpful.

Advances in diagnosis and treatment of ADPKD have been made possible by participation in clinical research of people with ADPKD and their families. Every patient with ADPKD and their family members should have the opportunity to be informed about participation in clinical research. As more is learned through research, there will be more need for counseling in clinical practice.

Each of these issues requires counseling of individuals with ADPKD and their family members. Ideally, this could be accomplished by a series of family meetings that take place over years with a multidisciplinary team of experts. We have observed many obstacles to counseling patients with ADPKD and their family members. Nephrologists may be too busy meeting the needs of patients with more immediate problems. Primary care physicians and genetic counselors may not have sufficient knowledge about ADPKD. Reimbursement for counseling, ultrasound examinations, genetic testing, and donor and recipient evaluation for transplantation may be restricted. Individuals with the disease may wish to shield other family members from the knowledge of risk. Family members may fear loss of insurability after the diagnosis. Finally, some patients with polycystic kidney disease and their family members may not ask for counseling; but without being offered the opportunity, how can they make an informed decision?

ADPKD affects all members of the family. Knowledge about the disease and its treatments can empower patients and family members to make decisions that affect them and the next generation. We would call on our doctors and our colleagues to further improve the care and empower patients with ADPKD and their families by providing ongoing guidance about the full range of opportunities to care for themselves.

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DISCLOSURES

None.

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In-Center Hemodialysis: Time for a Paradigm Shift

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Chronic hemodialysis (HD) in the United States is almost universally conducted on a thrice-weekly schedule, which means sessions are spaced 2 or 3 days apart. Kjellstrand *et al.*[1] have described the "unphysiology" of dialysis, given that solutes and extracellular volume gradually increase between HD sessions and peak at the end of the 3-day interval. Not surprisingly, extracellular volume overload, right atrial and right ventricle dilation, cardiovascular hospitalizations, and mortality are highest on the day after the 3-day interval.[2] Accordingly, the first dialysis of the week is often characterized by high ultrafiltration rates and rapid shifts in electrolyte and acid-base balance, which provide a mechanistic explanation for why patients are at higher risk of mortality and hospitalization at that time.

Almost 20 years ago, to address this heightened risk, Scribner and Twardowski[3] proposed every-other-day dialysis (EODD). These pioneers in dialysis recognized the obstacles to putting this approach into practice but argued that improved health-related quality of life (HRQoL) would lead to increasing acceptance by patients, medical staff, and dialysis organizations.

Implementing EODD poses challenges to patients, providers, and payers. However, the likelihood of improved clinical outcomes should motivate all stakeholders to develop innovative approaches. Optimal planning of an EODD pilot study would use a process similar to that advocated by the

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