Nonadherence in Kidney Care

In this month’s issue, ASN Kidney News editorial board member Edgar Lerma interviewed Thomas Nevins, professor of pediatrics at the University of Minnesota Amplatz Children’s Hospital in Minneapolis, about nonadherence among patients—and care providers—in transplantation, dialysis, and kidney care in general.

What does the term nonadherence mean in nephrology?
In the broadest sense, nonadherence describes the failure to follow specific recommendations concerning a patient’s health care. Nonadherence is usually thought of in a single dimension—that the patient fails to take a medication as prescribed. Upon further reflection, nonadherence is obviously multidimensional and includes a whole range of behaviors in addition to the patient’s medication adherence. It may even be expanded to include the health-care worker’s behavior in terms of following widely accepted guidelines and protocols defining a patient’s care.

In nephrology, therapies are often quite complex and, correspondingly, so is adherence. Patients are regularly asked to take numerous medications, follow a defined diet, and engage in other follow-up activities, such as clinic and laboratory visits or dialysis sessions. A variety of more specific behaviors may also be required based on each patient’s unique clinical status. Nephrology professionals also have a number of guidelines (e.g., JNC7 and KDQOI) and specific protocols they are expected to follow while directing patient care.

Is nonadherence synonymous with noncompliance?
In medical use and in the behavioral literature, several words—compliance, adherence, concordance, and persistence—have all been used interchangeably but with a focus on underlying assumptions implicit with each word. Historically, “noncompliance” was the term first used and remains useful, since even outside health care, everyone generally understands what is meant.

But in the interpersonal environment of patient care, many are concerned that the term “compliance” is too authoritarian, emphasizing the asymmetry of power that exists between physicians and patients.

“Adherence” then is intended to suggest that the recommendations are the result of a dialogue between the health-care professional and the patient. In Great Britain, extending this concept, the synonym “concordance” (or “consensual prescribing”) is meant to describe an agreement between a patient and a health-care professional about whether, when, and how medications will be taken. Finally, “persistence” has been defined as the actual duration of time a patient takes a specific medication or otherwise follows a health recommendation.

What is the Physicians’ Health Study?
The Physicians’ Health Study is a randomized, double-blind, placebo-controlled clinical trial initiated in 1982 by researchers at Harvard University. The research was designed to examine the efficacy of aspirin and beta-carotene in respectively reducing cardiovascular mortality and new malignancies. The study recruited a cohort of U.S. male physicians (n=35,223; age 40–84 years). To be eligible for this study and deemed “compliant,” physicians had to report taking at least two-thirds of their pills over a specified time.

An unintended consequence of the study’s 18-week “run-in” observation period was to highlight the self-reported noncompliance of physician volunteers (25 to 30 percent) with the daily drug regimen prescribed. In December 1987, the aspirin limb of the study was halted early due to the increased frequency of cardiovascular events in physicians receiving placebo. A later analysis of physicians in the aspirin group even demonstrated a further association between regimen noncompliance and an increased rate of cardiovascular events.

Thus, in a volunteer, motivated, and educated population taking a single daily drug dose, the frequency of self-reported noncompliance was more than one in four. The report highlights that we are all human and despite our best intentions we do not always do what we intend or promise. Recognizing this simple fact should help us avoid “blaming” patients and move us closer to working with our patients to minimize this problem.

The theme for this issue is kidney transplantation. What is the impact of nonadherence on renal transplants?
Given today’s effective and potent immunosuppressive drugs, medication adherence is now central to the success of any solid organ transplant. It is profoundly counterintuitive that competent adult transplant recipients would fail to take the very medications needed to preserve their graft function. Despite that simple analysis, many renal transplant patients regularly miss some of their medication doses.

In our studies of azathioprine adherence after renal transplant, nearly 20 percent of patients missed more than 10 percent of their drug doses during the first posttransplant month. This pattern was monotonously repeated during each of the first six months. Not surprisingly, the group missing the most doses of azathioprine also experienced the highest rate of acute rejection episodes. In later follow-up, this group also experienced the highest rate of graft loss. Recently, we demonstrated a similar frequency and pattern of medication nonadherence in current transplant recipients taking either mycophenolate or sirolimus.

In addition, long-term renal transplant survivors often experience hypertension, hyperlipidemia, increased weight gain, and an increased frequency of cardiovascular events. Successful prevention or treatment of these complications requires adherence to lifestyle changes and medical therapy. However, there is no evidence that transplant patients will be any more adherent with these additional prescriptions. Following technically successful renal transplantation, medication adherence is one of the most important factors impacting both near-term and longer-term outcomes.

Wherein lies the problem? Is it the health-care system per se? Is it the provider? Or is it the patient?
Perhaps the most fundamental aspect of the “noncompliance problem” is simply recognizing it! Medication nonadherence is ubiquitous, and it appears early posttransplant. However, except for patients with florid rejection, who admit they have discontinued their medications, physicians are slow to recognize noncompliance. Instead, when the observed clinical response is subpar, we often just increase the prescribed medication dose. So the first step with every patient is to ask, “How often do you miss medication doses?”

Because the etiologies of nonadherence are multifactorial, the underlying causes will be as many and diverse as our individual patients and their associated health-care systems. Again, focusing on renal transplantation, the “system” isn’t usually the central problem. Indeed, nonadherence is found in every culture and health-care delivery system where it has been carefully sought. Certainly, patients can’t take drugs they don’t have. So a lack of insurance, restrictive formularies, or high co-payments may all be significant barriers to medication adherence. However, even in the context of national health insurance (Canada and European countries) medication nonadherence is a significant posttransplant problem regularly impairing outcomes. Even in homogeneous subspecialty clinics, and in cultures acknowledged for their attention to protocol and detail, nonadherence remains a central issue.

Besides recognizing nonadherence, what is the role of health-care providers? Studies in other chronic diseases (e.g.,
Because the issue of medication nonadherence is so complicated, there are no simple “solutions.” However, there are approaches that will reduce medication nonadherence. While recognizing that we really can’t choose our patients or alter their behavior, it is clear that the one behavior we can reliably change is ours. In the end, nonadherence is a simple fact of life, a reflection of our shared humanity. Our task as nephrologists is to recognize nonadherence and then help blunt its impact on our patients and their lives.

Medication regimen
- Prescribe drugs with lower side-effect profiles.
- Early on, simplify the dosing schedule by eliminating unnecessary drugs.
- Document the patient’s adherence with their regimen (drug levels, prescription refill records).

Discussion
- At each clinic visit, proactively review medication adherence.
- Discuss any patient concerns about their medications and any side effects.
- Inquire about the use of nonprescription or herbal therapies.

Solutions
- Encourage the use of medication boxes and other reminder systems.
- Identify and use robust daily habits as cues to remember medications.

Help the patient to “problem-solve,” overcoming adherence barriers.
- Be aware of failed appointments (lab or clinic), and missed prescription refills—these may be markers for declining adherence.

What is your advice on how to solve the problem of nonadherence?

Because the issue of medication nonadherence is so complicated, there are no simple “solutions.” However, there are approaches that will reduce medication nonadherence. While recognizing that we really can’t choose our patients or alter their behavior, it is clear that the one behavior we can reliably change is ours. In that regard, there are several important areas that the nephrologist can address to improve medication adherence:

- Medication regimen
  - Prescribe “forgiving” drugs—those with long half-lives and simpler schedules.
- Education
  - Ensure patients know all of their medications and each drug’s purpose.
  - Document the patient’s adherence with their regimen (drug levels, prescription refill records).
- Help the patient to “problem-solve,” overcoming adherence barriers.

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