



Managing Progressive CKD in People with Diabetes

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Introduction

I have been involved in Indian Health for a long time. I worked for Indian Health until about seven years ago, when I came to the NIH to direct the National Kidney Disease Education Program. But much of what we do in this program is based on what I learned from my colleagues and patients in Indian Health Service.

What we're going to talk about is some basic stuff about kidney disease including how to utilize a lab test for identifying and monitoring CKD, and I'm trying to assess the risks of progression based on those laboratory tests to formulate some kind of strategy for improving outcomes for CKD in the primary care setting, to integrate evidence based care for patients with CKD into clinical practice, then talk about some patient education tools, and also talk about referral to nephrology which is a big issue in Indian healthcare.

Just to be sure we all understand what CKD is, CKD, the diagnosis is based on one of two criteria. The first is a functional definition which is a decrease in kidney function to a GFR less than 60 milliliters per minute, which is about half of normal. And the second criterion is an indication of kidney damage, and that can be almost anything. It can be an x-ray that shows that there's a missing kidney. It can be hematuria. It can be a history of biopsy as a child showing minimal change disease.

But in almost all cases, the evidence of kidney damage is albuminuria. And the upper limit of normal for the purposes of diagnosis is generally considered 30 milligrams per gram. I'll go over that in detail what that really means. By using those criteria, either a GFR less than 60 milliliters per minute per 1.73 meters squared, or urine albumin greater than 30 milligrams per gram or 30 milligrams per day, about 10% of the U.S. adults may have Chronic Kidney Disease. And if you look at materials from advocacy groups, they usually say, "Do have Chronic Kidney Disease?". Well, that's not entirely clear. If you look at this middle column here, for people over 65, a very high percentage of those people meet those criteria. However, we don't really know what a normal GFR is for an elderly person and we really don't have a lot of data yet on the rate at which GFR normally declines.

So meeting these criterion and making estimates simply based on projecting them on the NHANES population, which is the way this is done, probably over-states, the CKD population in the United States. There are lots of people with CKD and it is a fairly common problem, especially in Indian communities, but it's not probably quite as high as what some advocacy groups promote. What we do know quite firmly is over the last three decades; the number of people on dialysis has increased by a factor of four. And almost over 400,000 people now are on dialysis or have a transplant. Now, the ESRD means that (patients are) on dialysis or with a transplant. It is not synonymous with kidney failure which is simply a GFR of less than 15.

What we're seeing in the United States as a whole is what we've seen in Indian communities since World War II which is an increase in changing lifestyle, followed by an increase in obesity, followed by an increase in diabetes, followed by an increase in diabetic complications.

So, what happened with the sort of natural history that we saw in Indian communities beginning after the war and which led to real peak in ESRD at the turn of the century, that's 2000, is now occurring in the population as a whole.

And you can see that nationally, this term here is diabetes is the predominant cause of kidney failure in United States. And that's true in all ethnic groups including African-Americans and Hispanics.

The other cause is hypertension, which is major but has leveled off. And the other two significant causes are glomerulonephritis and polycystic kidney diseases are pretty flat. So what's happening in

the U.S. population as a whole is an increase in CKD, which is almost -- mostly due to diabetes. And in most cases, that's type 2 diabetes.

In Indian communities in particular, the rates are quite significant. And in the Southwest, where data is collected by End Stage Renal Disease Network 15, there are a large number of Indian people on dialysis. This is mostly Arizona and New Mexico.

In Arizona alone, there are about 1,366 patients on dialysis at the end of 2011, and there are about 300 new patients. The largest number of patients on dialysis who are identified as American Indian is in Arizona. Arizona and New Mexico together comprised about 40% of all the people identified as Indian by their dialysis units, and probably around 60% to 70% of the Indian people on dialysis who are in the user population for Indian healthcare.

So, I think one of the reasons why the Diabetes Program has devoted an hour to this topic is that there are interventions, which will slow the progression of kidney disease. And slowing the progression in one patient for one year produces significant savings in addition to reducing suffering and social dislocations.

So, on average it costs about \$77,000 to have a patient on dialysis. If you figure that the costs of someone who has advanced kidney disease but isn't on dialysis is about \$25,000 per year, there's probably a saving of \$50,000 a year. So, what does that mean? That means if you identify a patient who is at risk of rapid progression and you do something to slow that progression by one year, you've not only saved that person significant morbidity but you've actually saved the healthcare system about \$50,000. So, this is a very, very cost-effective intervention.

Identifying and Monitoring CKD

So, just to talk in detail about the two tests that we use to identify people with kidney disease, eGFR and urine albumin.

eGFR

So, Chronic Kidney Disease (CKD) essentially means fewer functioning nephrons. Each kidney has about one million nephrons, which are the filtering units, and they tend to be lost one by one. So, we have a lot of extra kidney capacity. And losing even a significant number of nephrons is often not associated with any symptoms.

You know that you can donate a kidney, which is 50% of your nephrons without any significant adverse effect. If there were an adverse effect, people wouldn't be allowed to donate kidneys. So we have this large physiologic reserve and most people remain asymptomatic often until more than three quarters of kidney function is lost. And that's very significant, because if you're trying to educate patients, you're often talking to them about something that's very scary, although they have no symptoms. They may not be happy about that.

So we assess kidney function by glomerular filtration rate (GFR). So the way I explain these patients is that the kidney is a filter, like the filter you put in a truck, but it is not one big filter. Each kidney is made up of a million filtering units, a million nephrons and they tend to get damaged one by one. If we can estimate how well the kidney is filtering, we can get a rough idea of the number of functioning nephrons. If the GFR is 50% of normal that suggests about 50% of the nephrons are still functioning.

So, how do you get an intuitive sense of what the glomerular filtration rate is? Well, the cardiac output is approximately six liters per minute. So, your heart pumps six liters through the aorta every minute. About 10% of that goes to each kidney. About 20% of all the cardiac output goes to the kidneys, so that's about 1.2 liters per minute. That means the kidneys are very vascular.

Now, what gets filtered is not the total blood, it's the plasma which is about 50% of the blood volume. So 50% of 1.2 is 600, so there's 600 milliliters of plasma flowing to the kidneys every minute.

Now, not all the plasma can be filtered. If that happened, then you would have 100% cells left in the small blood vessels in the kidney and they wouldn't flow. So, only about 20% of the plasma gets filtered, leaving 80% still in the small blood vessels maintaining blood flow. So, 20% of 600 is about 120 milliliters per minute. That's where you get sort of a sense of what normal kidney function is.

Now, we don't measure GFR except in research settings. It's very difficult. So, what we do is we estimate GFR and we use an equation. And the most widely used one is still what's called the Modification of Diet in Renal Disease or MDRD, and this is the equation right here. Looking at that, it doesn't do much for most people except remind them how much math they've forgotten since high school.

But the key thing here is to look -- the equation has four variables, so that's important. eGFR is equal to the serum creatinine, times the age -- these exponents are, I obviously modified that -- using gender, and then race. Now, there is a newer equation which is a little bit better which is called the CKD-EPI equation but it doesn't fundamentally change anything but it uses the same variables.

So, it's important to remember that this is an estimate of GFR. This is not the measured GFR. And we've been very successful in promoting the routine reporting of estimated GFR along with the serum creatinine throughout the U.S. And in fact, Indian Health Service was the first major provider of healthcare, national provider of healthcare, to routinely report estimated GFR with creatinine and that was 10 years ago.

But eGFR, the estimated GFR, is not the measured GFR. It's based on formula that's derived from population-based studies and you should really think of it as a good estimate of a patient's risk for having actually decreased kidney function. So, the way these are developed is they have a study population, which for some reason is getting a measured GFR, which is a laborious, difficult process, and then, the results of that are analyzed along with clinical characteristics or demographic characteristics of the patient and through regression analysis.

An equation is developed using variables that are commonly available and they develop the equation, which gives the closest match to the measured GFR. So, what that means is the estimated GFR that you get on your lab sheet is probably a pretty good estimate of the actual GFR in maybe a hundred people who have the same age, gender, race, and serum creatinine. But the individual who is sitting in front of you probably has a GFR that's somewhat different. And the operating characteristics with these equations are not very narrow so you should really think of this as -- remember, it's an estimate and it can be affected by other factors. It's much better than looking just at the creatinine but it's still not perfect. And that's why it's important to be careful about labeling people with kidney disease simply based on one GFR that might be a little bit low.

Okay. So, the way we explain GFR to the patients is to say that this green area above 60 is normal. Well, that's not really true, normal is 120. But the equations don't function very well up in this range, so you can't distinguish GFRs above 60 from normal though, so we say normal. 15 to 60 is considered chronic kidney disease, and below 15 is called kidney failure. Some people with GFRs below 15 need dialysis and some are able to continue to function without it.

So, the other thing that's quite important is to remember that there are certain circumstances where creatinine-based estimates of kidney function whether you're looking at just creatinine or these estimating equations will give you very distorted results. So, you can't use anything based on creatinine in people who are generally acutely ill, particularly people who have changing levels of creatinine.

For example, if you have someone who has normal kidney function and something tragic happens and they lose all kidney function, if the creatinine today was one, tomorrow it will be two. If they show up at the hospital tomorrow and they draw the blood and it's two, they'll plug that into equation and they'll get back some number, you know GFR is 45. Well, actually the GFR is zero but creatinine is rising and so it doesn't give you an accurate indication.

And also, because creatinine is affected by muscle mass, it's a metabolite of muscle tissue, people who have extreme amounts of muscle, body builders, or people who are very cachectic will have creatinines that don't necessarily reflect their GFR. So, you need to be quite cautious about using creatinine-based estimates in patients who meet any of these criteria, including almost all hospitalized patients. There are medications as well that interfere with the secretion of serum creatinine by the tubules and Septra is one of them.

So, I'm going to encourage you to think about distinguishing decreased kidney function versus kidney disease. Because estimate equations are less reliable at higher GFRs, and because kidney function declines with age, there may be older people who have decreased GFRs, who don't have anything else to suggest an active disease process, they have no albuminuria, they have no hypertension, they might not even be diabetic.

Those patients, you need to be quite cautious, because in some settings, if they ask to look at their lab results, they'll see GFR 55, patient has stage three kidney disease, that's alarming news for them to receive and it may actually be unnecessary. They may or may not have something that is a progressive disease.

Urine Albumin

Okay. I want to move on to urine albumin. Urine albumin is a marker for kidney damage and particularly for glomerular damage. In addition to being a marker for kidney disease, increased urine albumin is a marker for cardiovascular disease and thought to be a reflection of generalized endothelial damage. Urine albumin results can be used in many ways. It's obviously a way to identify diabetic kidney disease, and you all do that.

And in the general public, about 40% of the people identified with chronic kidney disease is on the basis - it's not a decrease GFR but on the presence of elevated urine albumin. It's very important to understand that increased urine albumin is a marker for progression, especially in diabetic nephropathy.

So, if you see someone who has 1,500 milligrams of albumin per day, even if their GFR appears to be normal or close to normal, they're probably in big trouble and likely to progress fairly rapidly.

The final use for urine albumin which you may not be taking advantage of is that it's an excellent tool for educating patients because as I can show you later that everything that we do to lower urine albumin slows progression of kidney disease. And if you can report to patients that the amount of albumin in their urine is less, and that everything we know suggests that their kidneys are likely to function better for a longer period of time, they will find that helpful. It's no harder to explain than hemoglobin A1c or estimated average glucose or estimated GFR.

So, it's important. Albuminuria is associated with increased mortality in all people; male, female, black, and white. There's no data from this report on American-Indians but it's true.

Now, how do we assess urine albumin? Now first of all, you notice I'm saying urine albumin because -- and I may use it indistinctly with proteinuria. I'm not going to talk about proteinuria because protein-creatinine ratio and proteinuria is kind of going to go away. And the reason is because it's such a heterogeneous collection of materials; it's not a test that can be standardized. And we're moving more and more towards laboratory tests that we can standardize which mean you get the same results at every lab across the country. That will never be true for total protein or urine protein/creatinine ratios.

So, what we're all moving towards is the measurement of urine albumin and it's the urine albumin to creatinine ratio that we use for assessing kidney disease. And this is a collection that's based on a spot urine specimen. And what we look at is the ratio of urine albumin to urine creatinine in that spot specimen.

So, why is that useful? Well, we know that the ratio in a spot specimen is equivalent to the ratio or similar to the ratio in 24 hours. So, if you have twice as much albumin as creatinine in a spot specimen, you'll have twice as much in 24 hours.

Why does that help you? Well, it helps you because on average, most people put out about one gram of creatinine in 24 hours. So as a result, the ratio on that spot specimen is equivalent to the excretion in 24 hours. And the way it's usually reported is milligrams albumin per gram creatinine, which is the same as milligrams of albumin per day. Now historically, the upper limit of normal is 30 milligrams per gram or 30 milligrams per day. And that will probably change but I'm not going to go into that right now.

So the thing is, is that this is a continuous variable. So, 30 is worse than 20, 200 is worse than 100, 350 is worse than 250 milligrams per day. There is nothing magic about going to 300 or over 300. Traditionally, what we've done is describe 30 milligrams to 300 milligrams as microalbuminuria. So 30 to 300 is the range between what's the upper limit of normal and what is picked up with one plus on the dipstick which approximately equivalent to 300 milligrams per gram and that's where the term microalbuminuria came, and above that was macroalbuminuria. This is sort of confusing to most people and unnecessary because there's nothing that happens at 300 that's physiologic.

So, what we're moving towards is to test the urine albumin base on an albumin/creatinine ratio and it will be reported as a continuous variable. And I think IHS is moving in that direction which is a good thing.

Now, the way to explain urine albumin -- this is a form that we developed that I will discuss briefly at the end of the talk but it's basically meant to explain the urine albumin at a level between the fourth and sixth grade and it uses these diagrams here which we developed at tremendous taxpayer expense.

But the ability to explain this to patients is quite important and most patients find it very helpful. You know, you say, "Look, we put you on the lisinopril, your blood pressure came down and in the amount of albumin and urine went down by half. Now you can't feel that, but that's a sign that your kidneys are much happier."

Okay. So, what happens to people with diabetes and why do they get kidney damage? Well, people with elevated blood sugars filter more sugar in their urine and the kidney attempts to reabsorb sugar. And when that happens, it reabsorbs water and salt as well. That leads to some volume expansion. There's a hormonal response, which results where the kidney tries to respond to that volume by increased blood pressure and flows in the kidney and that is called "hyperfiltration". And that's one of the ways in which the kidney gets injured.

So, what happens in the natural history of diabetic kidney disease is that this red line here is GFR. So initially, when someone develops hyperglycemia, their GFR goes up. And then overtime, as kidney damage begins to occur, it starts to decline on a steady path, around the time that it passes back down through the normal level, right around here, urine albumin starts to go up.

So at this point when kidney disease is really being manifest, GFR appears normal but urine albumin is elevated. That's why urine albumin excretion -- what we used to call microalbuminuria and some people still do, is the first sign of diabetic kidney disease.

So over time, the albuminuria goes up, sometimes to extremely high levels. And here, this is this grey line and this is the scale while GFR declines. And the albumin doesn't really begin declining until GFR gets so low that there's just very little albumin being filtered.

So on average, it takes about 10 years to develop clinical signs of kidney disease in diabetes and another 10 to 15 years to lose kidney function in those people who developed progressive kidney disease.

Key Issues in Managing CKD- Part 1

So what are the key issues in managing people with diabetes and CKD? One is to make sure that their diagnosis is correct. Just because someone has diabetes and kidney disease, doesn't mean their kidney disease is from diabetes and that's particularly true in populations with high rates of diabetes. If 50% of your patient population has diabetes, that means 50% of the people with lupus will also have diabetes. So, you need to do a -- there's a screening evaluation which I'll talk about briefly.

It's important to monitor progression with eGFR and urine albumin. It's important to implement the appropriate interventions to slow progression, I'm going to talk about that, screen for complications, educate the patient, and then help prepare them for kidney failure and its treatment.

I'm not going to talk about staging. We don't use staging in the educational materials that we produce for a number of reasons but mostly because by itself, eGFR is probably too narrow a basis on which to talk about diagnosis and prognosis. I can answer questions about that if you'd like later. But I think, eventually, we'll probably evolve to a multifactor prediction score that includes eGFR, UACR, age, diabetes status, blood pressure control, maybe some other biomarkers.

So, what can we do to slow progression of chronic kidney disease? I'm going to talk briefly about hypertension, diabetes, reducing urine albumin, and addressing cardiovascular risk factors.

So, the complications and the risk for cardiovascular disease increase as kidney function declines. The fewer functioning nephrons means blood pressure is harder to control because it's harder for the kidney to get rid of salt and water. You may see more frequent low blood sugars for people with diabetes because insulin is metabolized by the kidney.

The kidney produces erythropoietin, and anemia may appear, and there are fairly complex derangements of vitamin D and parathyroid hormone, which result in significant morbidity. How we treat that is still up in the air since it's mostly based on observational data.

And then there's uremia where waste products build up in the blood. Some of that includes acid-base disturbance where the kidney actually has trouble excreting acid. Phosphorous increases as well as potassium.

Now, the first issue we want to address is blood pressure. And in general, blood pressure is not well treated in people with kidney disease. And the worse the kidney function, the higher the blood pressure. Actually, the Indian Health Service does a better job than most settings, with I think close to 75% of people with blood pressures less than 140/90.

Blood pressure goals have traditionally been, or at least in the last 10 years since JNC 7, 130/80. This was really not based on very good evidence. The consensus now is that the evidence really supports 140/90. Regardless, the major issue is people with really uncontrolled high blood pressure.

Lifestyle modifications work and you're familiar with these; I just want to reiterate them. You can look at this later. The DASH Diet probably is one of the best public health interventions that have gotten out there that works. It lowers blood pressure and is very effective. It is not widely used or tested in people with CKD because it may be a little bit higher in protein, and potassium, and phosphorus. But if you have a patient who has resistant hypertension and you can't -- and this is a diet that works for them. You know, it's probably best to go with what works than what's perfect.

Again, diabetes is the leading cause of kidney disease in the United States. And the natural history as I outlined earlier shows damage beginning early; well before it becomes clinically apparent. It doesn't become clinically apparent until out here. And what we know is that, tight glycemic control makes a difference early, probably for the development of kidney disease, and that's been validated. The control of even newly diagnosed type 2 diabetes may lower the risk of albuminuria. It's not clear if it really changes the progression over time.

A lot of the studies of type control were done in Scandinavia 30 years ago and they showed an effect, the slowing or regression of kidney disease prior to the development of clinically apparent kidney disease. So the problem is that -- we're talking about the difference between very good control and very tight control. And for many of our patients, we're not talking about the difference in A1C of 7.5 versus 6.5. We're talking about A1C of 9.5 versus 7.5. And that's a study that won't be done because it's simply not ethical to have a control group with blood sugars that are really, really out of control.

And the other issue why glucose control is important, even if it doesn't slow the progression of kidney disease once kidney disease is established, is that most people with kidneys show up in clinics with eyes, legs, hearts, and diabetes control for those complications clearly is beneficial.

The goal for patients with kidney disease needs to be individualized because there's not a huge advantage in slowing the progression of kidney disease that's established. Very, very, tight control is not necessarily beneficial and particularly in older people who have limited life expectancy and multiple other complications, and at more risk of hypoglycemia. The risks may exceed the benefit.

In terms of losing weight, many of our patients are interested in high protein diets. And these are generally not recommended for diabetic kidney disease or any other kind of kidney disease because excessive protein intake is also associated with hyperfiltration. And theoretically, at least, it is likely to adversely affect the kidneys. In addition, it's a much higher burden of waste that needs to be excreted by the kidney. And simply by itself, high protein intake is associated with increased urine albumin excretion.

And the fact that these high protein diets, after in the long-term aren't any more effective than just changing to a more appropriate diet, we tend to discourage patients from eating high protein diets.

The recommendation for people with diabetes and kidney disease really is not as complicated as it might seem. We don't have very good evidence that very low protein diets make a difference. We know that excessive protein intake is not beneficial to anybody. So if we aim for the RDA of .8 grams of

protein per kilo per day, we will provide the maximum benefit to the most people, which is fortunate because trying to go below that really results in a diet that people have a very hard time living with.

Also, this is a level of protein that the whole family, even the people without kidney disease can live with, and is appropriate for them. There have been a lot of questions over the past about protein intake. And getting below .8 is very, very difficult and may not be beneficial, and the main issue is getting people to not eat excessive protein.

The one thing about diabetes and kidney disease is that, because insulin is metabolized in the kidney, there may be an increased frequency of hypoglycemia as CKD is progressing even if it looks like the eGFR stable. So, if you're seeing a patient and they suddenly say, "I'm having more hypoglycemia." that might be nice for them because they can be on less insulin and less medication but it may not be good because it's a reflection of decreased kidney function.

Key Issues in Managing CKD – Part 2

Now, the second goal in addition to lowering blood pressure, or the third, in treating diabetes is to make interventions to decrease albuminuria. In addition to the known risk factors over here, there are other risk factors that are associated with increased protein and albumin excretion.

Now, why is it important? These are sort of schematic diagrams from two different studies. This study, which is the Chronic Renal Insufficiency Cohort study, which is sort of the kidney Framingham study, shows that the risk of a bad outcome in kidney disease is associated with the albumin/creatinine ratio at the time of diagnosis.

So, the higher the albumin excretion at the time of diagnosis, the more likely that someone is going to lose their kidney function. Prognostically, it's very important. It's also true that if you can show a decrease in urine albumin, things get better. This is from the RENAL study, which looked at losartan and diabetes, and this is along the horizontal axis. It's the reduction in urine albumin/creatinine ratio after starting losartan and the vertical axis is the risk of something bad happening kidney-wise, which is dialysis, loss of half of kidney function, or death. And you can see that the greater the decrease in urine albumin after starting losartan, the lower the risk of badness happening. So, you can tell your patients that if the amount of albumin in the urine has decreased, then everything that we know points to a better outcome for them.

So, we know that ACE inhibitors and ARBs are renal protective beyond just their control of blood pressure, they'll reduce albumin in the urine or protein, you can use those interchangeably. You can use them as the same there.

And in fact, with people who have lots of protein in the urine, they may be used even if they're not hypertensive. There is some risk of hyperkalemia but less than what we may anticipate.

I would not recommend restricting potassium in patients unless they're hyperkalemic. And we do see this quite a bit is that people put an ACE inhibitor and even though they're K is 3.8, they're told to eat less potassium which often means eating less fruits and vegetables. So, we don't want to iatrogenically make their diet worse.

Weight loss is associated with decreased proteinuria. Obesity by itself is associated with increased proteinuria and over time kidney injury even without diabetes.

And the other thing that you need to keep in mind is that the effect of ACEs and ARBs is maximized by reducing sodium intake. And in fact, you may not see much of any effect if someone continues to take a very high sodium intake despite the fact that they are on an ACE and ARB, or an ARB.

You can reduce your urine albumin by controlling blood pressure, reducing sodium intake, good diabetes control, weight loss, stop smoking, and reduce excessive protein intake.

The third thing you need to address in these patients is their cardiovascular risk because this is what people die from. People with progressive kidney disease are much more likely to die from heart disease than to die -- than to go on dialysis.

So in addition to the traditional risk factors, which you are all aware of, there are some others that are associated with the increased cardiovascular risk. And probably, the main factor among the non-traditional risk is the abnormal calcium and phosphorus metabolism.

Lipid abnormalities increase as GFR declines. Your lipid abnormality increases, rather, and it's appropriate to treat hyperlipidemia in people with CKD. It may not slow the progression of their kidney disease, but it reduces mortality because of their cardiovascular risk. If people are on dialysis, there is not evidence that starting a statin in the most patients that changes their outcome. You do need to use statins cautiously in people with CKD because of higher risk of rhabdomyolysis.

Now there are complications of chronic kidney disease that you may be familiar with. There is anemia, due to increased erythropoietin production. Hyperkalemia occurs particularly in diabetics, particularly in diabetics who are on ACEs and ARBs. There is malnutrition; there is metabolic acidosis which is basically serum bicarb of less than 22. This reflects the kidney's difficulty in excreting hydrogen ion so they're acidemic. This can be treated with sodium bicarbonate.

And then there's bone disease. And you'll notice, of all these complications, the only one I mentioned the therapy for is acidosis because the treatments for anemia, as well as bone disease are largely based on observational data. And although there are lots of algorithms which you may cringe at when look about treating vitamin D and using calcium phosphorus binders and so on, we don't have compelling data that that actually changes morbidity or mortality.

So, I'm not going to include a lot of discussion of what you should do in terms of monitoring vitamin D and PTH because those are not based on very strong data. The nephrologist that you work with may have strong feelings about that and you'll need to work in collaboration with them.

Okay. Finally, the transition from chronic kidney disease to kidney failure is something that needs to be addressed in the primary care setting. Kidney failure is a GFR of less than 15. And by that time, the kidneys have a tough time maintaining homeostasis. There are fluid, electrolyte, hormonal imbalances, and metabolic abnormalities. End-stage renal disease means the patient is on dialysis or has a kidney transplant. ESRD is not really a diagnosis. It's an administrative status.

Now, Medicare will pay for kidney disease education for people with GFRs less than 30, and if it's provided by a limited group of providers. Now, this does not include all the people that I think should be able to provide this, but this is what they decided, and it does not include dietitians in particular. And Medicare will pay for six sessions. I don't know if any of you are doing this.

This is CMS' poster on this and it talks about what is covered. What you need to know is that we have developed; my program has developed a tool to be used in collaboration within the Indian Health Service to educate patients if you want to get involved in this. I'm not going to go into detail.

Challenges to Improving CKD Care

So, what are the challenges in improving CKD care? It's under-diagnosed, implementation of recommended care is poor because people often don't understand even the lab tests, urine albumin/creatinine ratios are widely misunderstood. People use the term microalbumin test in a way that is confusing.

Clinical recommendations are very unclear. The Kidney Foundation and others have produced guidelines that are the size of phone books and rarely read and difficult to use if you're not a nephrologist. They're sort of predicated on the idea that everyone you see has kidney disease and that's not the way it is.

And the third problem is that most providers spend their careers in recovery from the renal block in professional school and they never want to see kidney disease again. And that's made worse because over time the relationship between primary providers and nephrologists is not good. Communication is poor. It's not clear who to send for referral.

But the major issue is that the patients aren't even aware that they have kidney disease. This is from NHANES and it just shows that even among people who've lost between half and three quarters of their kidney function, only 20% knew they had kidney disease in NHANES. Most people are unaware.

If you look though at patients were actually followed by nephrologists, in this study this included a large number of patients, almost a half had no knowledge of treatment options and little knowledge of their diagnosis. And in this group of patients, this is another study, again about a third of patients really were in the dark. And these are patients who were actually followed by a nephrologist.

So, the recommendation of the renal community in large part is you want to make things better, send him to a nephrologist early. It's not clear that that's the answer. If you look at how we're doing -- and Indian Health Service does better than this data that I'm showing here nationally, but you can see that knowledge levels are low. This is for Healthy People 2020. The baseline is about 2010. Only a quarter of people are getting routine evaluation. And you know, only about a quarter of patients in general have blood pressure control. Indian Health Service does better but we can all still improve, and that's why you guys do the diabetes audit.

I'm going to skip this. And you know, one of the most surprising things is for people starting dialysis, only about four percent -- only one out of 25 has ever seen a dietitian more than a year prior to when they started dialysis. And dietary interventions make a huge difference in kidney disease. I don't know if it's better in IHS, we don't keep track of this. But dietary interventions make a huge difference. Indian Health Services is fortunate in that most settings to have access to a dietitian. And we have developed -- we used to do workshops and we have materials now to help general practice dietitians understand and feel confident talking to people with CKD.

So, defining the optimal care is not really the primary barrier though. The primary barrier in kidney diseases is getting it to people who need it, and that's your job. And what you can do is not focus on which vitamin D analogue is most important. Just simply recognize and test people at-risk which means a yearly eGFR and albumin/creatinine ratio. Screen for complications, which basically means in addition to the routine biochemical panel, get a phosphorous, and a CBC, and you'll have everything you need.

How you treat that is still controversial, how you treat the calcium and the phosphorous and hemoglobin. But things have changed. Treat cardiovascular risk. Refer to a dietitian for nutritional guidance. Almost all of this is routine good diabetes care so it's not a huge step. The most radical

thing you can do is to talk to your patients about CKD. And that is hard because telling people they have CKD is kind of like telling them they have cancer. It's not something you can do as they're walking out the door.

Lessons Learned

So my program that I came here to work on in the NIH really has the goal of improving outcomes by improving detection. But not just everybody, but trying to help providers identify the small number of patients in their practice who are at greatest risk in progression because everyone is overwhelmed. So you can't tell people, providers, to spend more time with 50% of their patients but you can say, "Look, here's how to identify the dozen or two patients in your practice that really are at risk." And most people can fit in the time to focus a little bit more on them.

Promoting evidence-based interventions is important. There aren't very many in kidney disease, and then, trying to get the different federal agencies involved in kidney disease including IHS and CMS to talk to each other. We use the Chronic Care Model which if you're in IHS you're familiar with. And then we've also developed materials that are really meant to be used and developed within the Indian healthcare setting. And these are Indian healthcare specific.

This is a sheet for providing patients the results of their eGFR up here and the urine albumin/creatinine ratio. And it's written at a fourth to sixth grade level. And on the back of the sheet is some basic information on things they can do to protect their kidneys.

Also, a one-page sheet on one side of eGFR for providers, the other side is urine albumin. And on the back of the care sheet for patients is four basic points to get across to people with CKD.

Now, I can't tell you that you need to spend 20 minutes with each patient to tell him about CKD, you'll laugh me out of the room. But if I say, "If you cover one of these points in 60 seconds, that's something you can do. You can extend the visit that long." And so, we've actually given two or three sentences that you can say that get the point across. And this one is -- you can see on this slide. This one is -- What kidney disease is, what the tests are. This is the idea that it's progressive; that it's not going to get better but you can slow how fast it gets worse. And this is a little bit about dialysis and transplant.

Now if you go through these in four visits, each in a minute or two, the patient won't have encyclopedic knowledge of kidney disease but they'll do a lot better than that data I showed earlier where they don't even know they have kidney disease.

This is a lesson builder that we developed. This is on our website. If you want to educate your patients, this gives all the materials including pre and posttests and a curriculum that you can use, and it also meets the CMS criteria so you could bill for this. Finally, I have a form for sending patients to a dietitian. The dietitian needs a referral. And this form includes very basic information. It's one page that you can fill out and sign. This is the bottom half.

And then, finally, I want to talk about referral to a nephrologist. I don't believe in referring people simply based on what their GFR is. I think there are important reasons to send a patient to a nephrologist. If they have primary kidney diseases like glomerulonephritis they're going to need remittive drugs, you should send them, regardless of what their eGFR is, soon as you diagnose them.

Preparing for renal replacement therapy, especially if the GFR is less than 30, it may be appropriate, people who have a rapid decline in eGFR which is not typical for their disease or any disease, if it's difficult managing them, or if they have acute kidney injury. But simply sending everybody with a certain level of GFR, I don't think makes any sense.

This is a referral form, and that dietitian referral form is based on this. This is the fillable PDF, one page, which includes some history if they have diabetes, how long, and whether albumin is present and how much, history of what their GFR has done over the past couple of years, and additional work up. And this has some very basic screening tests, which are worthwhile doing especially if you're spending contract health money to send the patient out. The patient shows up with some basic screening tests which you can get done, that patient may be able to be told by a nephrologist, "Look, I think you have diabetic kidney disease, there are a few other tests I want. The results will go to your primary doctor. If they're negative, I don't need to see you again for a while."

But if they show up with no background screening test, the nephrologist will say, "I really don't know what you have, probably diabetes. When you get these tests, I want you to come back again." which is inconvenient for the patient and also more expensive.

Down here, it asks you to let the nephrologist know whether the patient knows that they have kidney disease, how serious is it, or if they'll need dialysis. Many patients will show up -- and I can tell you this, it happened to me all the time. They say, "I don't know. I have kidney disease? I need dialysis?" And the useful conversation ends there and usually nothing happens until the next visit.

So just so you know that I'm not blowing smoke, I continue to see patients within the Indian Health Service. I do it by Telemedicine. This is my office at the NIH. This is in Zuni. We have over 1,100 visits over the past few years including people with very advanced kidney disease.

So, what have I learned actually in Indian Health Service, which I'm trying to bring to the program that I direct now? Well, CKD needs to be part of primary care, that to do a better job you have to improve the system. That usually means involving the non-physician health professionals. They are the ones you often really make the changes and implement them.

The best way to improve kidney care is not to have a lot of kidney clinics. The best way to do it is to tweak and improve the way you address kidney disease within the context of diabetes care. And that's very much consistent with how IHS does it.

And then focus -- when it comes to referral, focus on making sure the patient gets what they need from somebody who is competent to deliver it, not with referring. If you simply think about referring at a GFR of 30, that means you almost have permission not to do anything until the GFR is 30 and you say, "Well, I'm referring my patients at 30, I'm a good person, I'm a good provider." You've actually missed the opportunities.

And in some places, people feel quite comfortable with a GFR less than 30 if they've managed lots of patients like this, like at Zuni. In other places, they don't, and so it's an individual threshold.

So, what does all this mean and does any of this make a difference? If you look at the rates of ESRD caused by diabetes among different racial groups over the last 30 years, you'll see that it's going up in all groups. This is American Indians, African Americans, and the bottom two lines are Asians and Caucasians.

The one group that went up and now has come down significantly is American Indians. And the risk of an American Indian with diabetes developing end-stage renal disease has decreased by about 30% in the last 10 years, which is a remarkable accomplishment. I can't prove to you that's due to the IHS Diabetes program but I believe that -- and a lot of people who've looked at this very carefully, including skeptical people at the CDC, also believe that.

So all of the work you're doing, even though it has its frustrations, is making a huge difference. And by effectively implementing the Diabetes Standards of Care, it's been a huge benefit to the people that we all serve.

So improving the care of people with CKD means a change in clinical practice especially where the high-risk populations are served, like Indian Health Service. You need to improve the care before the point of referral. Indian healthcare is really the model that I use and that's looked to widely for improving care for people with diabetes and kidney disease. And the program that I work at now really benefits from what we continue to learn from the effective implementation of change in the delivery of care to people with diabetes.

Here's my email address and we have a website. All of the materials I have referred to and plus lots more are on this website. And if you have questions or you think there's something that needs to be developed to help you do a better job understanding what's going on, or even to educate the patients, please contact me. The best ideas come from people who are right at the front lines trying to make things better every day and that are what I think most of the people in this call are doing. So I really appreciate your attention.