Chronic Kidney Disease:

Screening and Monitoring

Indian Health Service
Division of Diabetes Treatment and Prevention
5300 Homestead Road NE
Albuquerque, New Mexico 87110
http://www.diabetes.ihs.gov/

Table of Contents

CKD SCREENING, DIAGNOSIS AND MONITORING ..... - 3 -

TESTING ISSUES – PART I ..... - 7 -

TESTING ISSUES - PART II ..... - 9 -

NEPHROLOGY REFERRALS ..... - 10 -

CKD TOOLS ..... - 12 -

CASE STUDIES ..... - 13 -

Chronic Kidney Disease: Definitions and Data

Hello and welcome. My name is Dr. Ann Bullock. I am the clinical consultant for the Indian Health Service's Division of Diabetes Treatment and Prevention. This training is on the screening and monitoring of chronic kidney disease in our patients with diabetes. I'd like to start by thanking our colleague, Dr. Andy Narva, the chief clinical consultant for nephrology for Indian Health Service. He provided a few of these slides as well as his ongoing support of chronic kidney disease issues in our native patients.

This presentation will cover several areas, first is some definitions, chronic kidney disease and diabetic nephropathy. Then we'll talk about some CKD data in our population and luckily we have some good news to discuss here. Then we'll talk about CKD screening, diagnosis and monitoring, and particularly the two tests that help us to do that: the eGFR and UACR. Then we'll talk about CKD tools and where you can get them to help you take good care of your patients with diabetes and chronic kidney disease. And finally we'll talk about a few case studies that hopefully will illustrate the concepts that we'll talk about in the presentation.

So first of all, why are kidney function issues so important in our patients with diabetes? Well, diabetic nephropathy does occur in 20 to 40 percent of our patients who have diabetes, making it the single leading cause of end stage renal disease in the United States. So it's important that we're screening for and monitoring for CKD in our patients with diabetes and even more importantly, trying to intervene, to prevent or at least slow their progress toward end stage renal disease.

So then what's the difference between the terms chronic kidney disease and diabetic nephropathy? Well we often use the terms interchangeably and there is a lot of overlap. There's a few differences that are worth noting. Diabetic nephropathy indicates the damage to the kidneys caused by diabetes. Chronic kidney disease has a clinical definition that I'll talk about in a minute and may be caused by diabetes but it can be caused by other diseases or by a combination. Both of these terms reflect processes in the body that reflect damage to the systemic vasculature, as well as, to the kidneys. Meaning that patients who have CKD, diabetic nephropathy, whatever you choose to call it, they also have cardiovascular and other kinds of problems because of the same process happening throughout the body.

The chart on the next slide shows data on national, United States data, on end stage renal disease in people with diabetes, by race going way back into the 1980s up through the mid 2000s. And as you can see, despite the sharp increase in the early years of this chart for our Native American patients, that in the last year since about the late 90s, around 2000, our rates have actually been decreasing. You'll note that of all the groups on this chart, it's the only group that is showing a decrease. The others are either relatively flat or actually still gradually increasing.

This is a great accomplishment and undoubtedly it's at least in part explained by the improved clinical care that clinicians throughout the Indian Health System have been providing to patients with diabetes. We've been among the first to really make a concerted effort to improve blood pressure control, to use ACE inhibitors or ARBs as appropriate for patients with diabetes to help slow down chronic kidney disease. So we need to first of all,

acknowledge that we are already doing a good job. We just want to make sure that we are continuing this downward trend so that our patients can be free of kidney disease, or at least its main complications for their lives.

The next slide shows data from our IHS Diabetes Audit which indicates that we are, just as we said, using more ACE inhibitors as the years have gone by. And that the rates of proteinuria are decreasing as we'd expect, given the decrease in end stage renal disease, since proteinuria is certainly a good predictor of who's going to progress on to end stage renal disease.

So what is chronic kidney disease? Well, by definition, it's got to be chronic so that means at least three months of either decreased kidney function defined basically as the ability to filter the blood of waste products, or evidence of kidney damage such as finding protein in the urine. And in fact, this is usually the earliest indicator of kidney damage especially the kind that's done by diabetes to the kidneys. And it's important that we monitor both of these together, both kidney function and evidence of kidney damage, because over time they tell us a lot about what diabetes and high blood pressure are doing to our patients' kidneys, including how fast those kidneys may be headed into trouble and when they might be getting there.

So no surprise there then, the National Kidney Foundation's definition of CKD relates to this kidney function and kidney damage definition. Kidney function is defined as the glomerular filtration rate, or GFR, as being less than 60 milliliters per minute per 1.73 meters squares for at least three months. I will note that through the rest of the presentation we will generally not use those large, that long units for GFR, we'll just simply refer to the number. But those are the units that are appropriate for GFR. And we may or may not see evidence of kidney damage when we see decreased GFR. Or, CKD can be kidney damage for at least three months again with or without a decrease in GFR, manifested by either pathologic abnormalities such as abnormalities on blood tests or kidney biopsy or kidney imaging or markers of kidney damage such as proteinuria.

The next slide shows the current definition of the staging of chronic kidney disease and as you can see, all of those stages are defined by the GFR. Stages one and two are actually not distinguishable from a clinical standpoint because as you probably know, the equation that we use to define GFR in our patients, or to estimate GFR actually, is not accurate above 60. So stages one and two are somewhat merged so to speak in clinical practice. Stages three, four and five, we are able to distinguish based on GFR. As we'll be talking about later in the presentation, however, since proteinuria is becoming seen as just as important as GFR in telling us how the kidneys are doing, you could expect in the next few years to be seeing the national organizations who make up these types of definitions to be modifying the staging criteria to include proteinuria.

CKD Screening, Diagnosis and Monitoring

Glomerular Filtration Rate (GFR)

So what is GFR? GFR is equal roughly to the sum of the filtration rates in all of the functioning kidney cells or nephrons. Estimation of the GFR gives us a pretty good idea of

the number of functioning nephrons that actually are still working. GFR cannot be measured directly, especially in clinical practice.

And we, on the next slide, it actually, we can look at what GFR actually is made up of. This isn't necessary for taking good care of your patients but sometimes is nice to kind of understand how this works. So, cardiac output in a normally functioning heart is about six liters per minute. Of that six liters per minute, about 20 percent of that cardiac output goes to the kidneys which is therefore about 1.2 liters per minute. The plasma is about 50 percent of the blood volume, other half being cells, and that's about therefore 600 milliliters per minute. And it is the plasma that is filtered by the kidney and about only 20 percent of that at any given pass through the kidney is filtered or the filtration fraction making that a theoretical GFR of 120 milliliters per minute. So normally functioning heart and kidneys should be able to achieve 120 milliliters per minute.

But since we can't measure that directly, we have to use an estimate, which then often is termed the eGFR. It's based on an equation, usually the MDRD, which stands for the Modified Diet in Renal Disease study equation. It came from a study protocol and it was found to be a better equation than the Cockroft-Gault equation that many of us are more familiar with. And in fact the American Diabetes Association recommends the MDRD for estimating GFR in our patients with diabetes. The MDRD is the equation that is usually the one programmed into our RPMS lab packages so luckily we as providers don't have to think about this too much.

And as we mentioned a minute ago, we need to remember that since it is not accurate for eGFRs above 60, our laboratory should be reporting any GFR above 60, as simply above 60 and not give a numeric value for that GFR. And as we mentioned stages one and two CKD therefore are not distinguishable clinically, at least by the current definitions. Once the national organizations undertake incorporating proteinuria in the staging criteria, it will probably be easier for us to distinguish the earlier stages of CKD.

And like all estimates of kidney function, eGFR is based on the serum creatinine. And that means that to get a good idea of how GFR is really working the creatinine has to be stable and not varying incredibly from moment to moment, as can happen in hospitalized patients especially in an acute situation such as in an emergency room or an ICU. That means that we should not be screening for CKD based on GFRs obtained during these acute settings even if the laboratory provides an automatic calculation of GFR on the lab report.

We also know that creatinine is affected by the amount of muscle mass present in a person's body. So that people who have a tremendous amount of muscle such as body builders versus those who have very little muscle like little old thin ladies can definitely affect serum creatinine. Therefore the eGFR needs to be considered as we're looking at these values.

So the loss of kidney function in chronic kidney disease, it's important for us to assess how fast this is happening so we can predict the time until the onset of kidney failure, until someone's going to need dialysis or a transplant. So we can work backwards to initiate the proper steps for either obtaining a referral for evaluation for transplantation, for placing of the fistula, so it is in place and mature enough to use by the time dialysis is necessary, and also to help the patient, the family, to prepare themselves for this huge change in their

lives which will be coming. We also need to figure out the rate of GFR decline so that we can see if the affect of our interventions we're trying, to slow the GFR are actually working. So we need to be checking GFR before and after we do things that should be helping.

So just like this guy on the next slide, a lot of us usually feel like we have a pretty good understanding of GFR, feel pretty confident about that. The part of kidney screening we sometimes feel a little less comfortable with is what all those kidney protein tests are about and which one we should be using.

Urine Albumin-to-Creatinine Ratio (UACR)

So what about proteinuria? Albumin, first of all, is the primary protein excreted by kidneys that are damaged by diabetic nephropathy. Therefore, in the diabetes world, you often hear the terms, "Proteinuria" and "Albuminuria" used interchangeably because in our patients, they are more or less the same. And we want to clarify this term, we often use in clinical practice, which is microalbumin, but in fact there really is no such thing. The term might imply that we're talking about smaller than usual albumin proteins and that of course is not the case. The correct term is microalbuminuria, which we'll be talking about in a few minutes. And we want to mention that it matters a lot, how much albumin is being excreted, how fast that albumin in the urine is rising and it's important if an intervention manages to reduce it. Sounds a lot like GFR in that respect, that it matters what the value is, how fast it's changing, and if anything we're doing or the patient is doing manages to help slow that down.

This next slide shows a study out of Canada which helps us again to understand that proteinuria is as important as eGFR in figuring out what's going on with our patients with diabetes and their kidneys. This is based on a cohort study of an entire Canadian province so therefore, a very large number of patients: 920,000. And the study authors looked at the risks of mortality, myocardial infarction, progression to kidney failure, that are associated with each level of GFR. And then looked to see what the proteinuria was in those patients and found that the proteinuria also independently predicted increased risk of those bad outcomes in patients.

So, perhaps an example will help us to clarify that most quickly. So, who is at higher risk of these patients that they gave as examples of in the paper? First of all, a patient with a GFR of greater than 60 and a UACR of 400 milligrams per gram. By current staging definitions, that would make this patient in stage one CKD. Then how about a second patient with a GFR of 50 and a UACR of less than 30 milligrams per gram which would, by current staging criteria, would make this patient in stage three CKD? You might think based on that, that the second patient actually is at higher risk than the first but because of that high proteinuria, the truth is when we look to see how these patients fare over the long term, the first patient, the one with the GFR that still looks pretty good, but the high UACR, that patient has two to ten times higher risk for all those bad outcomes listed above than does the second. That really gives us a clue that proteinuria is indeed as important as GFR in telling us how the kidneys are doing.

So, proteinuria then is important in screening, diagnosing, and treating CKD. First of all we know that the diagnosis CKD is very often based on urine albumin alone because it is indeed the earliest for many patients, marker of kidney damage, especially that kind that is

due to diabetes and hypertension. Then for prognosis, where things are headed for the kidneys, urine albumin is an important prognostic marker, again, especially in our diabetic patients and can and should be used to monitor and guide our therapy choices. It's a marker for coronary heart disease, as mentioned earlier, having CKD is a marker not only of problems with the endothelial dysfunction in the kidneys, but of that throughout the body including in the cardiovascular system. And proteinuria is also a tool for patient education and self-management. Just as our patients have come to know what eGFR is, and A1C as we tell them about it, they will come to know what UACR means and how we can work with our patients to influence those values.

The next slide is taken from a wonderful review paper on diabetes and nephropathy in our American Indian population. And from studies in our Native American population, we know that patients with albuminuria, if you have normal glucose tolerance, only about 8 percent in our population have albuminuria, no surprise. Those with impaired glucose tolerance, about twice that, or about 15 percent have albuminuria. And those with frank diabetes, about half of those patients have albuminuria, which is what you would expect but it is also important to realize that there are other causes of albuminuria in our patients with diabetes, as we'll talk about in a minute. Eighteen percent of our patients with diabetes develop albuminuria within four years of the onset of diabetes and as we just saw, some of them actually come to the diagnosis of diabetes already with albuminuria, which is why it's so important to check a urine albumin at the time of diabetes diagnosis, if the patient has type 2 diabetes. Patients with type 1 diabetes can wait for five years after the onset before starting to screen for albuminuria. In our Native patients who are older adults, the prevalence of albuminuria, no surprise, is quite high. Thirty five to 65 percent of those patients have albuminuria.

And perhaps the most important point here is that if you want to get a good idea of what the need for dialysis chairs or contract health dollars for kidney transplants is going to be within the next ten years - a good way to estimate that is to look at your patients with macroalbuminuria now because 50 percent of them are unfortunately going to progress to end stage renal disease within ten years. We hope, of course that as we become more aware and work even harder on the things we can affect to slow that down, that we can make a difference in that number but nonetheless it's important to know that many of those patients who already have more than 300 milligrams per gram of albuminuria will be progressing to end stage renal disease within about ten years.

The next slide show a very important study, the Strong Heart Study, which looked at diabetes and related issues in our Native American patients, because it showed in this study, as others have shown, that albuminuria is a proven risk factor for heart disease in our population. In this study, they looked at how to predict the risk of who would develop heart disease within ten years. And they found that the following were all good predictors: albuminuria, the patient's age and gender, their total cholesterol, their LDL, their HDL, whether they smoked, whether they had diabetes and hypertension. All of those of course, were risk factors for getting heart disease within ten years. And in fact, looking at each of those individually, they found that for macroalbuminuria, for men it was almost twice as likely that they would get heart disease and for women, close to three times as likely. So you can see again that albuminuria is a predictor, a good predictor not only of kidney problems, but of heart disease as well.

And in fact, they created a calculator for our Native American patients for what their ten-year risk for developing heart disease would be. And that calculator absolutely does include whether the patient has micro- or macroalbuminuria. If you would like to use the Strong Heart Study calculator in your clinic, the web address for that calculator is on the slide.

Testing Issues – Part I

So for something so important then, as we're seeing albuminuria assessment to be, we need a really good tests to measure it, but there are a lot of tests out there, which one do we choose? Well urine protein tests are indeed a recipe for confusion currently. There are a lot of tests out there. Some are based on urine albumin; some are based on urine protein. Some are quantitative and give quite precise and reproducible results. Others are semi-quantitative and based on test strip results. Some require timed urine collections such as 24 hour, 4 hour, overnight collections. Some are done on spot or random urine samples. Some account for the concentration of the urine while others don't. Some screening protocols call for one test for screening patients for CKD and then another test or tests to diagnose and monitor it. And the truth is, that many of these tests are not standardized nationally. The laboratory results are not standardized and therefore are not reproducible or interchangeable with results from other laboratories. And on top of all that confusion, the same site might actually use many different names for a single test.

So what are we to do? This is just an example of the LOINC Codes, or laboratory codes that are used for some Urine Albumin Tests. And a test by any other name is indeed quite confusing. So even if our laboratory colleagues have a lot of names for similar tests, we need to be able to sort that out as clinicians to know what test to use. So which tests do the experts say we should be using to screen and monitor our patients with diabetic CKD?

The National Kidney Foundation, the American Diabetes Association, the National Kidney Disease Educational Program, which is part of the NIH, all recommend a spot or random Urine Albumin-to-Creatinine Ratio, which is abbreviated UACR. Well why would all those experts say that? Well first of all the UACR, is by definition the ratio of albumin to creatinine and its done on a spot urine specimen, and it turns out that that ratio actually very closely correlates to the total albumin in excretion that the patient will put out in a full 24 hours as you can see by this equation. This is a very reassuring thing because it has been very hard on our patients to do those full 24-hour urine collections to get us a number on their protein excretion. This is a wonderful convenience for our patients. We don't usually talk about converting the UACR, that ratio, to what it would be in terms of albumin excretion in a 24-hour period. We talk about the milligrams of albumin per gram of creatinine in that particular spot urine. And the current definitions are that normal albuminuria is less than 30 milligrams per gram. Microalbuminuria is 30 to 300 milligrams per gram and macroalbuminuria is greater than 300.

As time goes by and the definitions start to change for CKD, we may find these terms going away, as we'll talk about in a minute they're somewhat arbitrary. And albuminuria is what is called a continuous risk variable. What that means is that there is no one value such as 300, below which risk is much less and right above which risk is much greater. It's a continuous risk variable, meaning that for every little bit of increase in it, the risk for progressing to kidney disease goes up and up. Likely down the road, these terms of

normal, micro and macro will be replaced with other terms and for the abnormal values probably a single term called urine albumin.

So why again is the UACR the recommended test? Well albumin is the primary protein excreted in diabetes patients as we talked about, so therefore measuring urine albumin makes sense. It is the most accurate and reproducible test available. It is quantitative. It is not a semi-quantitative or test strip test. The urine albumin assay itself is being standardized nationally so that laboratories will be able to standardize what they do in the lab and give us results that are reproducible and that are comparable to laboratories across the nation. The urine protein test will never be standardizable because there are too many urine proteins and their assays that would have to be standardized and that is just never really going to be possible. So urine albumin is a more standardizeable value.

UACR allows for early detection and monitoring of CKD. Very small amounts of urine albumin are detectible on this quantitative test. There are still some tests that are available that actually can't even distinguish normal values of urine albumin from the smallest microalbumin values which means that it will be later in the patient's CKD experience that it will be diagnosed and therefore intervened in. We need to intervene at the earliest detectible moment of CKD. UACR can be done on a spot specimen any time of day. It's not necessary for the patient to provide a first morning urine. We don't need to time the specimens, to get a 24-hour specimen or some labs do 4-hour specimen, some, an overnight. All those variations are no longer necessary. And what makes that possible, is that this test accounts for urine concentration using that ratio to creatinine. It does matter whether our patients had just stopped off at the convenience store and had a large soda on the way to the clinic versus if they provide us the most concentrated urine of the day, usually the first morning sample. Because of that ratio to creatinine, this test accounts for this type of variations. There are some albumin only tests available that do not do this, accounting for concentration and therefore that decreases their ability to be accurate.

Well what about those point of care albumin to creatinine ratio test strips? Those are awfully convenient; we sure like to use them in our clinics. Well, Clinitek is the brand most often used and from their own product information, it says that this product provides semi-quantitative results and can be used for screening sample for microalbuminuria. Positive results should be confirmed with quantitative methods for albumin. So even these test strips themselves are telling us what we already know to be true, which is that if you're going to use them at all, you should be using them for screening samples. Once a patient comes up with a positive result for at least microalbuminuria, now these test strips should no longer be used. First of all, the diagnosis should be confirmed with a quantitative method for urine albumin, such as UACR, and then ongoing monitoring and testing should therefore always be done with a quantitative method thereafter for that patient. Whether we should use these Clinitek type strips at all remains sort of to be seen. Certainly they're often used in screening scenarios, particularly community based screenings. And there's some reason for that, but once we are to the point where the patient already has a CKD diagnosis, they're no longer appropriate.

Sometimes the question of cost comes up because those tests are seen to be relatively inexpensive but they often, even the Clinitek type strips, are not real cheap either. But a UACR test does not have to be expensive. To get the right test, we don't have to spend a lot of money. First of all, we can use several different laboratory machines, some of which

are listed on this slide, to do an in-house UACR. And all of our CLIA certified laboratories across Indian Country can do this and you can see that if we do, the mean cost for a UACR is quite reasonable considering how important this test is. And considering the cost of other important tests we use routinely to monitor aspects of diabetes care.

Is there a point of care option for doing UACR? Well there is actually. There's one type of machine, which can be done in a point of care manner right there in the clinic. However, it is not currently a CLIA-waived test procedure. As such, if you elect to do a UACR, as a point of care test, you would have to be doing it, obeying CLIA certifications and regulations. If you'd want to do a send-out UACR, which our laboratories that are not CLIA-certified would need to do, even those can be relatively reasonable in cost. And it definitely helps if you develop a contract with your reference laboratory and often that helps if you can go in with several other Indian Health sites or other local sites or maybe even as an Area to negotiate a contract to get affordable prices for send-out UACRs.

Testing Issues - Part II

UACR results are prognostic. They are accurate and reproducible and therefore they should guide our therapy. As we've been saying, it's important not only how much albumin is in the urine, but also how fast that's going up. And it is indeed a continuous variable, and that as we mentioned a minute ago, the micro- and macroalbuminuria terms are pretty arbitrary. Well where did that 300-milligram cutoff come from between micro and macro? It came from the standard urinalysis dipstick, the UA dipstick that we have used in our clinics for many years. And it is able to detect more than 300 milligrams of protein in the urine. Hence, anything above that came to be called macro. Anything below that, which it could not detect, ended being called micro. As you can see, those terms have nothing to do clinically with something that changes for the patient at that 300-milligram level. It simply comes from the ability of a different test to detect it. As such, we will probably see those terms start to go away within the next few years as urine albumin becomes more and more standardized.

Well if we intervene and decrease urine albumin, this study from the American Journal of Kidney Disease gives us a wonderful indication that we have really truly reduced that patient's risk of progressing in their kidney disease. In fact, the most recent UACR result is the prognostic one, even if previous test results were higher, meaning that if we intervene in a patient who has micro- or macroalbuminuria, and we can show a decrease in the UACR of any type, we have improved that patient's prognosis.

Does UACR work in diabetic kids? Well this study in our population from the Pima population shows that indeed it does. In this long-standing study of the Pima in Arizona it's found that elevated urine albumin in non-diabetic youth is a pretty much an infrequent and pretty much transient phenomenon, not indicative of any truly bad underlying disease. However in our diabetic youth, just as in diabetic adults, the study confirmed that albuminuria is frequent and largely persistent. And more than that, it actually predicts progression to macroalbuminuria. As such, this study in the Journal of Pediatrics tell us that this study supports annual screening for albuminuria in kids with diabetes, just as we do for adults with diabetes.

Well, if we can use UACR in kids just as adults, is it also true that we can use the same thing for GFR for kids as we do for adults? Turns out, we need a little different equation to do that. In adults, the MDRD equation we discussed earlier, the one that's usually programmed into our RPMS lab packages, with the equation shown there, that works just fine for adults. However for our patients less than 18 years of age, we should use a different equation, currently recommended is called the Bedside Schwartz equation. And as you can see, it takes into account height of our patients, which gives us an idea of how growing children, how their GFRs are changing. This equation is generally not programmed into our lab packages but both the National Kidney Disease Educational Program and the Nation Kidney Foundation have online calculators you can use to calculate the GFR in your youth with diabetes.

When should we not screen for CKD? As we talked about with GFR, anytime the serum creatinine is not stable, we should not be looking at the GFR to determine if a chronic condition occurs, meaning that we should not be screening or using the GFR that may be calculated during any acute medical condition. UACR is also affected by many things. In a sense, we're looking for very small amounts of protein in the urine. It's important to not have any of the following which can elevate urine albumin and excretion even a little bit, to be present. So the patient should not have a current infection, certainly not a current urinary tract infection of course, should not be febrile, should not have a CHF exacerbation, should not be dealing with marked hyperglycemia or marked hypertension, and should not have done any significant exercise in the last 24 hours. Significant exercise here does not include a stroll or a walk but certainly would include more vigorous exercise such as running a marathon or doing anything that requires significant exertion.

So how do we make sure that we do urine albumin testing at our sites and that it's done properly? First of all, we should sit down with our lab manager, our clinical applications coordinator or whoever helps us with the computer aspects of our electronic records. We should figure out which urine protein tests are being done and how they're named. Remember that there are often many names for the very same test. Be sure that our lab is performing, or if necessary, sending out the UACR test. We need to be sure that this test is clearly named in the electronic record we're using and that those results are in the correct units; standard units are milligrams per gram. We need to educate our clinical staff about the UACR. Make sure that it is becoming the standard test at our facility for urine protein testing in our patients with diabetes.

Nephrology Referrals

A question often asked is, when should we refer to a Nephrologist? Well first of all, there is no predefined threshold. It really depends on the primary care provider's knowledge and comfort level with CKD and how to manage it. And it depends on our setting. It depends on how rural or urban we are and how easy it is to access nephrology consultation. Situations we really should consider referring or getting that help from our nephrology colleagues, the most important one to be aware of is when we are unsure as to the etiology of the CKD. In other words, anything that's going to require a biopsy or other advanced test to help us sort out the cause of CKD. We need to remember that not all CKD in diabetes is from diabetic nephropathy. And many times, CKD is from multiple causes and it's important that if there is a different and treatable cause of CKD, that that is determined. It's also important to consider a referral to a nephrologist if the patient's CKD is progressing more

rapidly than you would expect and/or if there is significant elevation of the urine albumin. Need to refer if there is difficulty controlling complications of CKD of any kind that we're not comfortable monitoring and managing ourselves.

And if none of the above have led us to a referral to a nephrologist, generally by the time the patient is in stage 4 CKD, when their GFR is less than 30, is a good time to refer the nephrologist. Because during stage 4 is when it is important to teach patients and families about renal replacement options, help them to make the decision as to which renal replacement option they are going to elect including, perhaps transplantation. It's good if this can all be done well in advance of the time when end stage renal disease onset begins. And we need to have the goal to have dialysis begin with a mature fistula or graft or having the patient ready for peritoneal dialysis, if that's what they have chosen, and/or ready for a transplant. And it's best if these things are done calmly and in the light of day with CKD complications controlled, instead of the middle of the night in the emergency room with a fluid overload crisis in process, as unfortunately still happens all too often. This is actually a quality of care indicator, to have dialysis start with a mature fistula or graft in place. So on top of how important it is for our patients for them to have it happen this way, it's also something that we as providers are going to be judged on.

So the bottom line on screening and monitoring is that eGFR and UACR are important tests for screening, diagnosing, and monitoring CKD in our patients with diabetes. We should be ordering these two tests at the time of type 2 diabetes diagnosis, then yearly. As mentioned earlier, for type 1 diabetes, you can start ordering these tests 5 years after diabetes onset and then annually after that. We should be ordering these tests more often than annually if they are changing rapidly. If we are intervening in some way to hopefully slow this down, we need to order the tests again to assess whether we have been successful. And then certainly once CKD is advanced, we should be ordering these tests as frequently as necessary to assess how our patients are progressing. Again the CKD diagnosis is either a GFR of less than 60 or a UACR of at least 30 milligrams per gram. And again, it must be chronic. We have to have this going on for at least three months, which means that the test has to be done once and then confirmed again several months later. Because of the variability in urine albumin excretion, the American Diabetes Association recommends that you can use two out of three UACR specimens with greater than 30 milligrams per gram within a three to six month period to diagnose CKD. And the current definitions and terms, as mentioned earlier, these will likely be changing but the current ones are microalbuminuria is 30 to 300 milligrams per gram and macroalbuminuria as greater than 300 milligrams per gram on a UACR.

Just as important as testing for CKD, of course is treating and intervening. We should be extra diligent with patients with CKD to get their blood pressures to goal. For most patients who are able to tolerate it, the blood pressure goal is less than 130/80. We should certainly be maximizing the ACE inhibitor or ARB we are using, even if blood pressure is well controlled but if the patient has albuminuria. We should of course redouble our efforts to achieve glucose control. And realizing that just as diabetes increases the risk for cardiovascular disease, having CKD and diabetes further increases the risk. As such, we have to be extra careful about achieving lipid targets, to use aspirin when it is indicated in these patients, and to encourage smoking and oral tobacco use cessation. And of course, nephrology referral at least by stage 4 CKD or sooner if we're not quite sure what the CKD

etiology is, if we're seeing a rapid decline in the GFR and/or fairly rapid increase in the UACR, or if we're having difficulty managing any CKD issue.

CKD Tools

Well sometimes all of this sort of feels overwhelming and we can feel kind of like we're tired and don't quite know how to proceed. So, what kind of tools are there available to help us and to sort all of this out and to communicate with our patients about CKD. So in this next section, I want to tell you about two great places to get tools to help you in your clinical practice around CKD.

The first is the National Kidney Disease Education Program website. This is part of the NIH, part of the National Institute of Diabetes and Digestive and Kidney Disease. NKDEP, its director is Dr. Andy Narva, who has been and continues to be our chief clinical consultant in Indian Health Service for nephrology. Dr. Narva certainly knows a lot about what it takes to take care of CKD in our patients. The NKDEP website has many excellent tools, videos, handouts, referral forms to help you communicate with your nephrology consultants. Please do avail yourself of this wonderful, treasure trove of resources at the NKDEP website which is listed on that slide.

One of the many wonderful tools there is this 2-page tool for communicating with your patients about urine albumin to creatinine ratio, the UACR, and the eGFR, what the normal ranges are and what the abnormal ranges are and what they mean. Explaining this to patients can be difficult. Tools like this help to give you a visual tool to help in talking with your patients.

The other website of course, is our own IHS Division of Diabetes website. By definition, you've found that website or you wouldn't be listening to this training. But I want to tell you about some other tools for CKD that are available on our website. As I'll show you in a minute, we have CKD, what we call Quick Guide Cards, can give you some summaries, some fast references, online, available anytime around CKD. We have other CKD online trainings, some done by Dr. Narva and some by Theresa Kuracina on CKD nutrition. These are available on our website where you can get CME and CE credits for doing them and of course they are available any time you can access the web. Our "Advancements in Diabetes" monthly web seminars often have topics related to CKD and several of those sessions that were on CKD are recorded and available for you to listen to at any time. We also have algorithm cards to help you in treating your patients with diabetes. On CKD, we have 2 cards: one is the Urine Protein Testing and the other is on How to Monitor and Treat CKD complications. I'll show you both of those in just a minute. We also have other diabetes algorithm treatment cards including one on Glucose Control, another on Hypertension, one on Lipids, one on Foot Care, particularly around screening for neuropathy and other problems of the feet, How to Use Insulin, and How to Treat Neuropathic Pain.

Finally, our Advances in Indian Health Conference, which occurs each spring, always includes a diabetes track, which also includes several sessions on CKD.

The next slide shows the Urine Protein Testing card, which I just mentioned. Most people use the algorithm cards including this one by printing these out and then folding them in

half down the middle between the two columns, making a front and back card that fits into a white coat pocket. Some people laminate these; other people just post them on the walls of their clinic. But many people have found these algorithm cards to be useful in helping them with many aspects of their diabetes care. As you can see, this one talks about the UACR, and what the definitions are of micro- and macroalbuminuria. It also talks about the other tests that are commonly used out there for urine protein testing and little about why they are not the optimum tests for our patients with diabetes.

The next card is the CKD Complications card in our patients with type 2 diabetes. As you can see, it lists the staging criteria that exist currently, when to refer to a nephrologist, to a dietitian and then the different types of complications that are related to CKD and how to monitor them. And then finally it also shows some medication dosing, particularly around phosphate binders and vitamin D analogs.

The next slide shows the Quick Guide Cards. As you can see, it looks like a drawer full of file folders and there are a number of these file folders, which now have a lot of clinical information available. As you can see, one of them is on chronic kidney disease. So, if you click on that file folder, you'll come up to the CKD Overview card, which will give you a quick overview of issues in CKD that providers need to be aware of, as well as, links to algorithm cards that refer to this topic, to the CKD best practice and to the diabetes standards of care for Indian Health Service which include discussion of CKD issues. If you click on the next tab, the How To tab, you will come to another summary with a little more detail on How to Screen, Monitor and Treat CKD. And again, links to tools that are helpful as you do this.

Case Studies

So let's look at a couple of case studies around CKD to hopefully bring home some of the ideas we've been talking about. First of all, let's start off with a 38-year-old woman who was diagnosed with type 2 diabetes five years ago. Other than her diabetes, she's otherwise healthy and she is a non-smoker. Her A1C is 8.2%, blood pressure 138/82 and her lipids are at target. Her medications include a low-dose ACE inhibitor. On routine annual testing for her, because of her diabetes, you find that her UACR is 127 milligrams per gram, and had never been greater than 30 in the past, and her GFR is greater than 60.

So what do you do? First of all, remember that we need to confirm the diagnosis of microalbuminuria. So we should repeat the UACR in 3 months to confirm that diagnosis. If indeed it is confirmed, then we can diagnosis CKD in this patient. But again, just as important as testing, is intervening and treating. So we should be increasing her ACE inhibitor, getting her blood pressure down to target, she's otherwise healthy, she should be able to tolerate a blood pressure less than 138/80. We need to redouble our efforts to get her A1C down to target, and again, a young healthy person should be able to tolerate an A1C of less than 7 or even down to 6.5%. And of course we need to be extra careful to make sure we are addressing all her cardiovascular disease risk factors. Doing all of these things, you found that six months later when you've rechecked her UACR to see whether your interventions have been successful, her UACR is still on the microalbuminuria range but it is now down to 79 milligrams per gram, which does indeed reflect a real decrease in her risk for progression to end stage renal disease down the road.

Let's look at another case study on CKD. This is a 42-year-old man who was diagnosed with diabetes 6 months ago. His A1C is 7.2%, his blood pressure 146/90, and his medications include the maximum dose of an ACE inhibitor. His GFR is greater than 60, but his UACR is 527 milligrams per gram, which you correctly check again a short time later, two months later and find that it's already 617 milligrams per gram. So this is a fairly high amount of urine albumin, which is rapidly increasing. His retinal exam, importantly, is negative for retinopathy.

So what do you do with this patient? Is this diabetic nephropathy? That should be the first question you ask yourself here. What would make you think that it might not be? Well first of all, the short duration of his diabetes. Even though we know that diabetes can go undiagnosed for several years, he was only diagnosed a short time ago and with his retinal exam being negative for retinopathy, we have to wonder if the retinal exam is negative, if indeed the vascular issues that CKD represents, if they're not happening in the eye, they may not be happening in the kidney yet either from diabetes. We have to rule out another cause for this patient's CKD. That means we need a nephrology referral, as this patient will need to be considered for a kidney biopsy. In the mean time, we should be redoubling our efforts to control his blood pressure and of course to control his cardiovascular disease risk factors. This is a patient that definitely should be considered for referral, to let the nephrologist sort out what the etiology of the CKD is.

And finally a third case study. This is a 76-year-old man who has had diabetes for 24 years. His GFR is 58, putting him by definition in stage 3 CKD. His UACR is 178 milligrams per gram but it's important that you note that in his chart you can see that this has been stable, both of these two values for the last several years. And his other kidney related labs are also normal. His A1C is well controlled at 6.6% and his lipids are also at target. His blood pressure is 138/82 which you might think is slightly above goal, but then you note that 6 months ago, he had some orthostatic symptoms that required reduction in his blood pressure medicines. His retinal exam shows just some minimal non-proliferative retinopathy. He has no peripheral edema, no known cardiovascular disease and he's a non-smoker. His medications include a statin, aspirin, an ARB, gabapentin and insulin.

What is this type of CKD and what do you do with this? Well he has stage 3 CKD, we said by definition given his GFR with microalbuminuria. But both of these have been quite stable for some time. This is what we often see in patients that do have some diabetic nephropathy but also have age related kidney function reductions. As we age, our GFR goes down normally such that when we see patients like this where their GFR is slightly reduced but stable, we are not seeing a progressive CKD kind of situation. We can monitor this patient regularly for GFR and UACR. We of course need to be sure we're addressing his blood pressure issues but given his recent orthostatic symptoms, we need to be very careful what our blood pressure targets are for patients like this. First of all, do no harm. Simply achieving the blood pressure goal of 130/80 and making this patient dizzy is not in his best interest, especially at this age. Does his CKD require a nephrology referral? Most people would not refer this patient. He is stable, he is not having any CKD complications manifesting, and you are able to monitor him should any of this change.

Thank you for participating in this CKD training. I hope it's been of use to you. If you have any questions about the training or any of the content or anything about CKD, please feel

free to email us at the IHS Division of Diabetes Treatment and Prevention at diabetesprogram@ihs.gov We'll be happy to respond to you and answer anything we can.

Thank you for all you do to take care of our American Indian and Alaskan Native patients with diabetes and CKD. And thank you for the difference you are making in how many of our patients are progressing on to end stage renal disease. Together we can indeed make a difference for our patients to benefit their lives. Thank you very much.