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Anemia in CKD: Understanding and Managing the Multisystem Impacts

### Announcer:

You're listening to *Clinician's Roundtable* on ReachMD, and this episode is sponsored by Akebia Therapeutics Medical Affairs. Here's your host, Dr. Jennifer Caudle.

### Dr. Caudle:

This is *Clinician's Roundtable* on ReachMD, and I'm your host, Dr. Jennifer Caudle. Here with me today to discuss the multisystem impacts of anemia in the progression of chronic kidney disease, or CKD for short, is Dr. Gates Colbert. He's an Assistant Clinical Professor at Texas A&M College of Medicine and a practicing physician with the Kidney and Hypertension Associates of Dallas, located at Baylor University Medical Center. Dr. Colbert, welcome to the program.

### Dr. Colbert:

Yes, it's great to be here with you, Dr. Caudle, today.

### Dr. Caudle:

So to start us off, Dr. Colbert, can you give us a brief overview of the connection between anemia and CKD progression?

### Dr. Colbert:

Sure. So a lot of people don't fully realize that anemia can be both a cause and an effect of chronic kidney disease. While we initially think of the liver or the bone marrow as being a primary area for red blood cell production, one of the main components is also produced in the kidney with erythropoietin, one of the most important hormones produced by the kidney. And as we have chronic kidney disease and we develop fibrosis over time, with the kidney losing its GFR and losing its capability to get rid of toxins and, unfortunately, uremia can build up, we also have a decrease in erythropoietin production. And EPO levels can be almost 100 times lower in patients with CKD as those who have normal kidney function. So we have that issue with the lack of production of erythropoietin, but then also as we have chronic kidney disease progression, increased fibrosis, increased secondary downstream effects on end organs, such as the lungs and the heart, we also have an increase in inflammatory production, specifically, a hormone that's produced in the liver called hepcidin. And hepcidin is a gait-regulating hormone that keeps us from absorbing too much iron in our GI system. But unfortunately, in chronic kidney disease, hepcidin can get up-regulated inappropriately, and this prevents us from being able to absorb the oral iron and utilize this iron once it's in our body appropriately. So the kidney is intricately connected with anemia, and it's something we definitely need to be focusing on in patients with chronic kidney disease.

### Dr. Caudle:

So with that being said, how does anemia actually impact CKD progression and increase the risk of cardiovascular events in these patients?

### Dr. Colbert:

So as the kidney has a decrease in function, a loss of GFR, and a decrease in erythropoietin function and production, we start to have a decrease in our hemoglobin and hematocrit. And this loss of hemoglobin and oxygen-carrying capacity throughout the entire body leads to end-organ problems. One of the most common is in the heart, unfortunately, and as the heart does not get enough oxygen, the heart

has to work harder to try to pump more blood to the rest of the body and to the rest of our organs to deliver enough oxygen for the other organs to function adequately. And as this heart is working harder, it's developing fibrosis over time. This is leading to left ventricular hypertrophy, and as this occurs for months and years and decades, it eventually, unfortunately, can lead to heart failure. Additionally, when you are having decreased hemoglobin production, you have an increase in your sympathetic nervous system. This is going to raise your blood pressure, raise your systemic vascular resistance, and further damage both the heart, brain, and the kidneys as our blood pressure is elevated, creating a lot of secondary effects.

**Dr. Caudle:**

And based on your experience, how do patient journeys most often play out? For instance, how common is hospitalization, reduced quality of life, or even mortality among CKD patients with anemia?

**Dr. Colbert:**

When patients have anemia as a primary problem of their chronic kidney disease and as their hemoglobin and hematocrit start to fall, unfortunately, there is going to be a higher risk for increased healthcare utilization. They may need to be changed on medications, there may be an increase in medications, and unfortunately, they're going to be seeking healthcare much more often with both clinic visits, potentially needs for infusions, and even potential for hospitalization if their anemia is severe or if their end-organ damage from that anemia starts to progress and become severe. So all of this leads to a reduced quality of life for our patients with their symptoms; they have increased fatigue, shortness of breath, and they may have decreased exercise tolerance. They may just not be able to do the things that they normally do in terms of activities of daily living, such as climbing stairs or taking care of small children in the way that they want to.

And so all of this leads to an impact on how a patient feels and how they view their basic quality of life and basically have a decrease in what they're able to really accomplish compared to what they've done in the past. And as these decreases in quality of life and decrease in capabilities build up overtime, this could lead to a result of increased mortality.

**Dr. Caudle:**

If we continue focusing on the patient journey for just another moment, Dr. Colbert, are there any particular cases that stand out to you or made a lasting impact on how you approach managing these patients?

**Dr. Colbert:**

When I see patients in clinic, a lot of them are never going to come straight out and say, "I think that I have anemia," or "I think my hemoglobin level is low." They usually say more generalized complaints: "Oh, I'm feeling more fatigued," or "I'm sleeping more now," or "I just don't have the energy that I used to. I'm not able to take the stairs; I'm taking the elevator, or I'm looking for the escalator when I'm out and about doing my shopping." And so really, it's an astute clinician and a history-taking capability that we need to look into are the labs. First, we need to ask these patients about these impacts or problems that they have. And so I have had several patients who will say that they're fatigued, say that something feels off and that they've changed, and I've really tried to look at their hemoglobin levels and then look at their iron levels. And it's very easy that we can see that their iron levels are below our standards and chronic kidney disease guidelines, such as an iron saturation below 20 percent, and we can really make an impact by just repleting those iron levels up to a full capacity and monitoring their ferritin during that process. And we can really see those hemoglobin levels rise. And I've had several patients where I've picked up on these subtle complaints, signs, and symptoms that a patient may have, and if I can correct that hemoglobin up to a higher level first with iron and then second with maybe erythropoietin-stimulating agent as well, you can really have a major impact on how a patient feels.

**Dr. Caudle:**

For those of you who are just tuning in, you're listening to *Clinician's Roundtable* on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Gates Colbert about the various ways anemia can affect patients with chronic kidney disease.

So, Dr. Colbert, if we continue examining the multisystem impacts of anemia in CKD progression, what priorities should we keep top of mind so we can better serve our patients?

**Dr. Colbert:**

So I think you always want to start out your clinic exam or when you're talking to a patient in the hospital by asking, how are they feeling? Has anything changed since you last saw them, whether it be the morning before or maybe 6 months earlier? How are they feeling? How are they doing with their daily activities? Has anything changed with their health? And that's where we're going to pick up on these subtle complaints: fatigue, shortness of breath, decreased activity, or maybe a change in their skin color if they're getting more

pale and pallor. So I really think taking that history and talking to your patients is extremely important. And then we need to look at their lab work, which is not hard for a nephrologist because that's what we love doing: checking on labs. But really paying attention to that hemoglobin level. You know, I think that we forget a lot in our patients that hemoglobin level of 11 in a man or hemoglobin 10.2 in a woman is abnormal; that's a problem. You know, a lot of men have hemoglobin levels of 16, and women may have hemoglobin of 14. So if you've had a pretty significant drop in that hemoglobin over the last treatment time or the time since you've seen them in clinic, that could really have an impact on their health. And so we want to be looking into that hemoglobin and hematocrit level, looking at their iron levels, and then potentially looking at EPO levels, which they do in some clinics, and we want to treat those levels that are less than they should be because that's a really easy way to have a big impact on how a patient feels and how their overall health can improve. Because we know that if we just ignore those hemoglobin levels that have dropped, it's a very likely chance that if their CKD is progressing or if their heart failure is progressing, those hemoglobin levels are just going to continue to drop and drop. And therefore, we're going to have secondary impacts of worsening chronic kidney disease, worsening heart failure, and increasing mortality over time. So really, we want to be the drivers of trying to treat that anemia and helping our patients feel better and do better over time.

**Dr. Caudle:**

And are there any successful interventions or management strategies you've implemented in your practice that our audience might find helpful or surprising?

**Dr. Colbert:**

We always want to make sure in a patient who has anemia that there's not some secondary problem going on. So you always want to ask them about cancer screenings and make sure there's no active bleeding that maybe is hiding. And then we want to check their iron stores and then we want to replace the iron. And there's a couple ways to get iron at adequate levels. They can do oral iron supplementation, or they can do IV iron supplementation. Oral iron can be very effective and is very low-cost and simple for a patient to take once a day. But they also have some side effects. Sometimes there can be constipation or dark stools that patients don't really like, and if that's the case, you may want to choose to do IV iron. I usually give a patient the choice to do oral iron or IV iron. I present the pros and cons of both, and I tell them that we could try oral iron if they wish, but if they fail it and we don't see improvement, we then need to move to IV iron because we know that IV iron is going to be effective and going to have a quick impact. And then once we've done that, we may want to consider erythropoietin stimulating agent, or an ESA, because that really can produce the hormone in the body that a patient can't produce once they have advanced chronic kidney disease.

And then we always want to stress that we're doing all these things because we're trying to avoid a blood transfusion, which can only be done in the hospital, which increases the potential risk of infection and increases healthcare costs. So always try to go along that sort of algorithm with patients and tell them what we're doing along the way so they understand that we have an end goal of helping their health and trying to decrease hospitalization utilization over time.

**Dr. Caudle:**

And now as we wrap up our conversation for today, Dr. Colbert, let's look ahead for just a moment. Are there any novel therapies on the horizon, and if so, how might they impact the way we manage anemia and CKD patients?

**Dr. Colbert:**

In terms of looking at the future, we have a new class of medications in the anemia space for chronic kidney disease. It's a class of medicine called the HIF stabilizers, and HIF stabilizers are an oral pill, so you wouldn't need any sort of injection or shot that a patient can take once a day or maybe twice a day, and this can directly stimulate a patient's own hemoglobin production. And we have one medication that's already been approved by the FDA for patients with dialysis. This is going to be daprodustat. And so that's available here in 2024 as an exciting option for patients who are on dialysis. But then there's also some other medications that are being evaluated by the FDA currently under study, such as the vadadustat, which may be one of the next exciting medicines to be approved depending on the data. And then I know that roxadustat, another medication in the HIF stabilizer class, is also being evaluated and under study. So really, there's some exciting options, it's exciting to have a new pathway of treatment, and we'll have to see what findings come out in the data and what the FDA will approve and for which patient types.

**Dr. Caudle:**

Well, given the profound impact anemia has on patients with chronic kidney disease, I'd like to thank my guest, Dr. Gates Colbert, for joining me to share his insights. Dr. Colbert, it was great having you on the program today.

**Dr. Colbert:**

Yes, thank you so much.

**Announcer:**

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