

### Transcript Details

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### Assessing Atypical Diabetes: Detection & Diagnosis

Dr. Wysham:

When a patient presents to our offices with a diagnosis of diabetes, we often make the diagnosis of type 1 or type 2 diabetes based upon symptoms, age and body habitus. However, we are now aware that there are people with diabetes who do not fit into our stereotypes for type 1 or type 2 diabetes. Recognizing them is key to understanding how to optimally treat them. Welcome to *Diabetes Discourse* on ReachMD. I'm Dr. Carol Wysham and joining me, today, to discuss atypical diabetes is Dr. Janet McGill, Professor of Medicine at the Washington School of Medicine in St. Louis, Missouri. Dr. McGill, welcome to the program.

Dr. McGill:

Thank you, Dr. Wysham. Pleasure to be here.

Dr. Wysham:

Well great, I'm so, I'm so glad you accepted our invitation to speak. So, to start out with, can you give our listeners some background on what is meant by atypical diabetes?

Dr. McGill:

Sure. Atypical diabetes is diabetes that does not fit into the classic auto-immune type of diabetes, but it also doesn't fit into the classic type 2 diabetes phenotype. The type 2 diabetes phenotype would be older age of onset, generally accompanied by, excess weight, slow onset, variable family history, that sort of thing. Type 1 diabetes can occur at any age, but should be antibody-positive and proceed to low or undetectable C-peptide. There are many, many other forms of diabetes, some we call monogenic diabetes, and some are attributable to, say, pancreatic, dysfunction of various types.

Dr. Wysham:

So, why is it important for us to recognize, if our patients may have atypical diabetes?

Dr. McGill:

It's absolutely critical to recognize atypical diabetes. First, the treatment might change, so the common forms of monogenic diabetes, the MODY 2 and 3 are very important to recognize. MODY 2, does not respond to treatment, so, efforts, elaborates efforts, sometimes to use insulin, insulin pumps, other therapies simply don't work. So, recognizing that the treatments are not going to work is key to understanding these patients and this form of diabetes there are many, many other forms of diabetes in addition to these particular forms of monogenic diabetes.

Dr. Wysham:

I think that's all very important, background, can you list some important clues on how what we as practitioners should be looking for in terms of clues, for patients with atypical diabetes?

Dr. McGill:

In the atypical diabetes study that's happening, RADIANT, offers some clues to this. First of all, when in doubt, check the type 1 diabetes antibodies. In adults, the anti-GAD is most likely to be positive and the most likely to be persistent. However, if you're able to check antibodies within 5 years of diagnosis, I would get the whole panel. If the antibodies are positive, there's a good chance that the patient very likely has autoimmune form of type 1 diabetes, even though C-peptide is not absent at that point, but you have some notion that it may progress, they may become more insulin-deficient and it really helps you treat that patient, earlier insulin start, for example. So, the first thing to do is antibodies and C-peptide. Once you have those in hand, you'd want a family history. Do you see dominant

inheritance? Do other family members have diabetes that occurred in young adults with a phenotype that you would not expect for type 2 diabetes? So, history, family history, antibodies, and C-peptides are the first things you want to check.

Dr. Wysham:

Thank you. And I think you made a really good point. For those of you just tuning in, you're listening to *Diabetes Discourse* on ReachMD. I'm Dr. Carol Wysham and I'm speaking with Dr. Janet McGill about atypical diabetes. So, Dr. McGill, you mentioned earlier the RADIANT study. Can you tell us what the RADIANT study is and what the study protocols are and what you're looking for?

Dr. McGill:

Absolutely. The RADIANT study is an NIH-funded study that is designed to look for genetic causes of diabetes. So, how are we going to do this? Patients sign up online, they can go to [atypicaldiabetesnetwork.org](http://atypicaldiabetesnetwork.org) or search search for the RADIANT study online, they can, see the details, get more information and if they think they have an atypical form of diabetes, they can click the button that says, "Join RADIANT". They will be asked for some health information, family history, their personal history of diabetes, then they will be sent to a laboratory to get antibodies tested. If the antibodies are positive, we will let them know that they have positive antibodies, and it appears if they have type 1 diabetes or latent autoimmune diabetes in adults. If the antibodies are negative, their case will proceed to an adjudication committee and people on these committees will look at information, look at anything a physician might've sent in, their provider, endocrinologist and make a determination whether their type, their case of diabetes appears to be atypical. If they're adjudicated and pass the adjudication, they'll proceed to the second step. In step 2 or stage 2, they'll actually visit a study center, have basic exams and some other basic tests that also have blood drawn for whole genome sequencing. So, we move fairly quickly to whole genome sequencing and then depending on what the whole genome sequencing shows us, we may recommend additional tests. So, the stage 3 test will depend on what's found in the whole genome sequencing. So, we're hopeful to uncover new types of atypical diabetes beyond the known monogenic varieties.

Dr. Wysham:

So, in terms of referring to this study how would you suggest that physicians or practitioners identify appropriate patients to refer to look further into this study? Is there any, you know, 1 or 2 or 3 things that you could let the listeners know are important to consider when thinking about this study?

Dr. McGill:

So, there are many, many factors. We have adjudicated patients with other, what appears to be other genetic defects. So, patients who appear to have congenital abnormalities that are completely aside from their diabetes that have not been worked up or identified. We've had a couple of those. So, other abnormalities, let's say the patient has a congenital heart defect and then has diabetes that has an atypical presentation, perhaps at too young of an age or a type 2 presentation in a thinner patient or something like that. We would accept that patient to see if there is a unifying genetic problem. There are also cases that would best be, fall into a lipodystrophy category, where the patient has extreme insulin-resistance and a marked type of body habitus. Patients who have ketosis-prone diabetes is another category that's of interest. They go into decay but that have reasonable C-peptide and may or may not need insulin after their decay episode, we're interested in those patients. So, there are a number of different, buckets or groups of patients that would be interesting to the RADIANT study.

Dr. Wysham:

So, you know, very, very good clues for the practitioners. And again, the family history is something, I guess, we can't, emphasize enough. So, are there any other final messages you'd like to leave with our listeners as it relates to the diagnosis of atypical diabetes or suspicion of atypical diabetes?

Dr. McGill:

Yes. Another category of diabetes that we miss is pancreatic diabetes. If you don't ask the patient, "Have you ever had pancreatitis or any other pancreatic, gallstone episode or, abdominal surgery, pancreatic surgery?", it may be missed and I have patients who I've asked about pancreatic disease after treating them for a few years and the answer is, "Yes, I had an episode of pancreatitis in 2011," and it was before our current EMR, so it's not listed anywhere. So, those patients I do a little extra workup. I do amylase and lipase to see if it's low normal or below normal. I found a patient who I knew had a partial pancreatectomy in the past. I did fat soluble vitamins and found it isolated low vitamin A, for example. So, these patients mostly need insulin, which is why we see them. Some progress to insulin over a period of time, but some have other problems and other deficiencies and I think we need to pay closer attention to pancreatic diabetes in addition to genetic forms of diabetes and understand who has autoimmune diabetes at any age.

Dr. Wysham:

That's right. That's right. Well thank you. That's a great way to round out our discussion on atypical diabetes and I wanna thank my guest, Dr. Janet McGill for joining me to discuss atypical diabetes. Dr. McGill, it was great having you on the program.

Dr. McGill:

Thank you. Thank you. It was a pleasure.

Dr. Wysham:

I'm Dr. Carol Wysham. To access this and other episodes in our series, visit [ReachMD.com/DiabetesDiscourse](https://ReachMD.com/DiabetesDiscourse), where you can Be Part of the Knowledge. Thanks for listening.