

Division of Diabetes Treatment and Prevention

Childhood Diabetes: Treatment and Prevention

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We want to thank everyone else here with the Division of Diabetes Treatment and Prevention including Dr. Wendy Sandoval. I appreciate this opportunity to speak with you today about childhood diabetes prevention and treatment. I'm a Creek Indian originally from Oklahoma, trained as a general pediatrician, currently on faculty at the Colorado School of Public Health, Centers for American-Indian and Alaska Native Health located in Aurora, Colorado.

I worked for 20 years for the Indian Health Service and my last 10 years we're working specifically with diabetes. I formerly was the Area Diabetes Consultant for Billings Area, IHS and actually started doing that at the advent of the Special Diabetes Program for Indians. After five years of working in Billings Area, I transferred to the National Diabetes Program Office and worked here for five years under Dr. Acton as the former director - she was working as the former director for the Division of Diabetes Treatment and Prevention. And following retirement from the Commissioned Corp, I joined the Colorado School of Public Health.

Currently at the Colorado School of Public Health, I am working under a CDC grant. We call it the Center of Excellence in Eliminating Health Disparities that is focused on reducing cardiovascular and diabetes risk among American Indian and Alaska Native adults. But certainly as a pediatrician and working for 20 years in the Indian Health Service, I am familiar of working on the front lines with the problems of childhood obesity and Type 2 diabetes that we're seeing in our American Indian and Alaska Native communities and have been a part of a number of other committees and activities related nationally to addressing this problem and important public health concern.

Today, what I'm going to be talking with you about specifically, is going over the diagnosis of prediabetes and Type 2 diabetes in children and adolescents, including some current controversies related to the use of hemoglobin A1C, particularly in the diagnosis of Type 2 diabetes. But I'll cover Type 2 diabetes management and go over some of the key recommendations from a new clinical guideline that was just released yesterday by the American Academy of Pediatrics. In addition, I'll talk about screening, not only for Type 2 diabetes but also for overweight and obesity, as well as, prevention and mainly covering that from a primary prevention perspective in terms of obesity prevention. Because that certainly is the major public health concern other than Type 2 diabetes among our children and youth.

I wanted to start off with some background information and forgive me if this is an overview that many of you heard in the past, but I think it's important to remember sort of where this started especially for the Indian Health Service and our diabetes programs. You may not know this, but some of you may, but Type 2 diabetes was first described almost 35 years ago in Diabetes and it was described in Pima Indians where the NIH longitudinal epidemiologic study was being conducted.

Almost 20 years later, CDC conducted an analysis, a six case series, almost 600 cases of American Indian and First Nations' children and at diagnosis they showed that it was a problem, primarily for minority groups, occurring in 94%. That more than half presented with acanthosis nigricans,



anywhere from the 56% to 92% depending upon which case series was being reviewed. The mean age was again early adolescence, 12 to 14 years of age and unfortunately, most of the children at diagnosis had an elevated hemoglobin A1C with a range of 10% to 13%.

Also at the same time, in December of 1998, at the 50th anniversary of Diabetes Forecast, the Stewart family from the Gila River Indian community were featured and there was an article again talking about embracing traditions in terms of combating the epidemic of diabetes, but certainly, everyone was worried about why kids were getting Type 2 diabetes and there was much worry and concern over the devastating burden of Type 2 diabetes among children that was thought to shortly come.

If we look at some current prevalence data of Type 2 diabetes, in Pima and American-Indian children, again, this is a data from the Centers for Disease Control and some of it is from their SEARCH data, but we see that in Pima, they have almost 51 cases per 1000 among 15 to 19-year-olds. If we look at all American Indian adolescents, it's about 4.5 per 1000 cases, and if you compare that to the Type 1 diabetes prevalence for all American children, zero to 19 years of age, it's only 1.7. So, it is a significant problem, but we're still seeing very low numbers of actual cases of Type 2 diabetes among our youth. Of course, many of you know that this epidemic if you will, has occurred in parallel with the childhood obesity epidemic that we're seeing in our country and throughout the world. And certainly, the problem of Type 2 diabetes among children and adolescents has become a global concern. I'll share more data about the problems of obesity and some more specific data about prevalence later in my talk.

I first wanted to go into the diagnosis of diabetes. Since 2000, a statement that was endorsed by the American Diabetes Association and the American Academy of Pediatrics has suggested that diabetes basically should be diagnosed the same way as it is in adults in terms of cutoff, and certainly Hemoglobin A1C has been added to that as well. These are the criteria from the American Diabetes Association that I'm sure all of you are familiar with. We certainly know that the first three criteria for diabetes should be confirmed by repeat testing on another day if there is not unequivocal hyperglycemia. Having said that we know that there are issues, and sometimes difficulty differentiating between childhood Type 1 and Type 2 diabetes. This has certainly been associated with the childhood obesity epidemic and that we are seeing children who are obese and overweight who have Type 1 diabetes.

The statement that I referred to earlier that was just released, the new clinical guideline from the American Academy of Pediatrics goes over these descriptions of what is commonly associated with childhood Type 2 diabetes. Typically, these children or adolescents are overweight or obese; they have a strong family history of Type 2 diabetes; they have substantial residual influence secretory capacity at diagnosis, whether these are normal or elevated insulin and C-peptide levels; they have an insidious onset of their disease; they demonstrate insulin resistance including clinical evidence of polycystic ovarian syndrome or acanthosis nigricans, but they lack evidence for diabetic autoimmunity.

There certainly can be difficulties in differentiation between Type 1 and Type 2 diabetes at diagnosis and the 2009 Clinical Practice Consensus Guidelines on Type 2 Diabetes in Children and Adolescents from ISPAD, the International Society for Pediatric and Adolescent Diabetes, provides more information on the classification of diabetes in children and adolescents with new diagnosis. That reference is available in Pediatric Diabetes 2009 Supplement 12, pages 17 to 32 and I can provide that to the Division of Diabetes if you would like more information on this diagnostic quandary that sometimes occurs. Certainly, if there are questions on whether or not an individual has Type 1 or Type 2, and is a child or adolescent, it makes sense to talk with a pediatric endocrinologist or someone who is familiar with making this difficult diagnosis at times.

There has been much controversy recently with the addition of A1C, and some of you may have been reading some of the debate that has been ongoing in the medical literature. There have been several articles in the past few years in Diabetes Care that discuss some of the issues with A1C in terms of it has a lower sensitivity than fasting plasma glucose or the Oral Glucose Tolerance Test. It's a poor predictor of diabetes and prediabetes for adolescents compared with adults. Many of you are probably also aware that there are certain medical conditions that can alter A1C, results including iron deficiency anemia, cystic fibrosis, sickle cell and other hemoglobinopathies. It can also miss Type 1 since they have a more dramatic onset and they may not have had elevated blood sugars for as long as an individual with Type 2 diabetes.

Interestingly, the debate continues with a recent study published by a group from the University of Pittsburgh in Diabetes Care 2012 that shows that A1C prediabetes criteria actually do correspond to decrease beta cell function in overweight and obese youth.

Yesterday, a new statement, new clinical guideline was released by the American Academy of Pediatrics in their e-pages on the management on newly diagnosed Type 2 diabetes mellitus in children and adolescents. I happen to be a member of the Committee that wrote this along with Dr. Terry Ramer who some of you may know. He is a former ADC for California area and also for Alaska area. It was a very long and complicated process. There is an additional document that was also released that includes screening schedules and management tools and goes over in more detail some of the methodology related to producing these evidence-based practice guidelines. It's an accompanying technical report. I will provide the link to that document in a later slide. But it's important to know that this doesn't really cover prediabetes management. It doesn't cover isolated insulin resistance nor is there anything really on diabetes and pregnant adolescents in this document.

It was a unique experience, being a part of this because there was a rigorous methodology applied to the use of articles and studies that were included in the development of this clinical practice guideline and it was really quite different from other sorts of clinical statements that I've been involved with, which relied more on expert and consensus opinion.

I'm going to go through the key action statements that are actually recommended and the grading of each recommendation is noted in the full document. This first recommendation is that clinicians must ensure that insulin therapy is initiated for children and adolescents with Type 2 diabetes who are ketotic or in DKA, and in whom the distinction between Type 1 and Type 2 is unclear. And in usual cases, should initiate insulin therapy for those who have plasma or random venous blood glucose levels that are the greater than 250 or whose HA1C is greater than 9%.

This is a strong recommendation even though validating studies can't be performed. But we know that even these children or adolescents who have the elevated A1C or who have levels of glucose greater than 250, could benefit from initial treatment with insulin at least on a short-term basis. This could allow for a quicker restoration of glycemic control and theoretically, could also allow islet beta cells to reset and recover. There have also been some studies that have shown that it could also enhance the patient's perception of the seriousness of the diagnosis of the disease and may increase actual long term adherence.

The next key action statement relates to initiating a lifestyle modification program in all other instances. Because of the low success rate of diet and exercise alone in pediatric patients with Type 2 diabetes, metformin should be initiated along with promotion of lifestyle changes. We also know that in pediatric patients, lifestyle change – I guess some people are still having trouble hearing me. But in pediatric patients – so, I'm going to try and speak a little bit louder. Lifestyle change is most

likely to be successful when a multi-disciplinary approach is used and the entire family are involved. We also know unfortunately, that efforts at lifestyle change often fail for a variety of reasons including high rates of lost to follow-up, a high rate of depression in teenagers which affects adherence, and peer pressure to participate in activities that often center on unhealthy eating.

Two prospective observational studies reveal that treatment with lifestyle modification alone is associated with a higher rate of lost to follow-up than that found in patients who received medication. And certainly, there are a number of things that should be addressed before initiating treatment with metformin. The first being making sure that you know that the child has indeed Type 2 diabetes.

The third key action statement talks about clinicians monitoring A1C levels every three months and intensifying treatment if treatments goals for finger-stick blood glucose and A1C levels are not being met. No randomized control trials have actually evaluated the relationship between glycemic control and the risk of developing microvascular and/or macrovascular complications in children and adolescents with Type 2 diabetes. But certainly, there have been a number of studies in children with Type 1 as well as adults with Type 2 that have shown a significant relationship between glycemic control as measured by A1C and the risk of microvascular complication such as retinopathy, nephropathy and neuropathy.

In terms of a target goal for A1C, there are several review articles that suggest a level of less than 7% for children and adolescents with Type 2 diabetes. However, while we agree that perhaps the ideal target goal should be less than 7%, it's certainly important that specific goals be individualized for each patient.

Key action statement four suggest that clinicians advise patients to monitor finger-stick blood glucose levels and particularly, those who are taking insulin or other medications with the risk of hypoglycemia, who are initiating or changing their diabetes treatment regimen, who've not met current treatment goals or who have intercurrent illness.

Again, although such studies evaluating the efficacy of frequent blood glucose monitoring have not been conducted in children and adolescents with Type 2 diabetes, benefits have been described in insulin treated adults with Type 2 diabetes who check their blood glucose four times per day compared with adults who followed a less frequent monitoring regimen. And, although normal glycemia may be difficult to achieve in adolescents with Type 2 diabetes, a fasting blood glucose concentration of 70 to 130 remains a reasonable target for most. Postprandial blood glucose testing may be valuable in patients whose fasting plasma glucose is normal but whose A1C is not quite yet at target.

The Committee also suggests that clinicians incorporate the American Dietetic Association's Pediatric Weight Management Evidence-Based Nutrition Practice Guidelines in their dietary or nutrition counseling of patients with Type 2 diabetes at the time of diagnosis and as part of ongoing management. We don't really have conclusive evidence about the best meal plan for patients with diabetes. However, studies specifically addressing the diet of children and adolescents with Type 2 diabetes are also limited. However, we have a lot of studies that have been conducted in overweight children and adolescents. So, the Committee does recommend that clinicians refer patients to a Registered Dietitian who have expertise in the nutritional needs of youth with Type 2 diabetes and incorporate the Academy of Nutrition and Dietetics Pediatric Weight Management Evidence-Based Nutrition Practice Guidelines which describe effective evidence-based treatment options for weight management and those are actually summarized in the document.

The last key action statement relates to a recommendation for physical activity and for nonacademic screen time. Certainly, we know this has been a cornerstone of diabetes therapy for quite some

time. We believe that adherence may be improved if clinicians actually provide the patient with a written prescription to engage in physical activity including a dose describing the ideal duration, intensity, and frequency. It's important to know that the recommended 60 minutes of exercise do not have to be accomplished in one session but can be completed through several shorter increments for example 10 to 15 minutes.

Pending new data in terms of screen time and sedentary activity, the Committee is recommending that clinicians follow the AAP Committee on Nutrition's Guideline: Prevention of Pediatric Overweight and Obesity, which includes several recommendations but certainly, the recommendation to restrict nonacademic screen time to a maximum of two hours per day as well as discouraging the presence of video screens and television sets in children's bedrooms.

There are other resources that are available and certainly, the guidelines, that clinical report that was specific to Native American children that was published by Pediatrics in 2003 by Sheil Gahagan and Dr. Janet Silverstein who is also an author of this guideline remains an important document for those working with American Indian and Alaska Native children as most of you are. The technical report that I mentioned earlier, that was released yesterday as well, that provides recommendations on monitoring and screening for comorbidities of Type 2 diabetes in children and adolescents is available, and the Global IDF/ISPAD Guideline is available on through this link, through the second link on the slide. I also included recommendations for transition of care. While this may not necessarily be an issue for your sites since IHS is more of a family-based primary care setting for the care of chronic disease. I think it is a good statement and something includes items that would be important for many of you to consider as your adolescents transition to adult diabetes care. I know for some sites within the Indian Health System, for example Phoenix, children may be cared for by adults even sooner than what most of us would traditionally expect that transition to take place.

I now want to turn to some issues related to screening. As I mentioned, I was going to provide some data on the increase of diagnosed diabetes among children and young people that we've seen in the Indian Health Service. This is data from 1990 through 2001. And among 15 to 19-year-olds we'd actually seen a 106% increase, but please note that the number of cases per 1000 is still reasonably low, particularly when we compare it to 25 to 34-year-olds during the same time period. There was close to 35 cases per 1000 for that age group. If we look at more recent data from 2009, we can also see kind of a leveling off actually of the increase in diagnosed diabetes among adolescents 15 to 19 years of age.

As I said earlier, many experts certainly point to the obesity epidemic as being a strong causal factor for the increase in the epidemic of Type 2 diabetes that we've been seeing. If you'll note, the line for American Indians and Alaska Native is actually, the slope continues to rise and it's at the highest point in 2008 as compared to total which appears to have leveled off and other groups where it's declining. It's even shown here to be leveling off among Hispanic children as well.

We look at adolescents and high school students, again, data from the Youth Risk Behavior Survey from 2001 through 2009. We see that American Indians and Alaska Natives, the purple bars again – the highest in terms of overweight and certainly very high for obese adolescents as well.

Fortunately, the most recent Cochrane review of interventions preventing childhood obesity which is from 2011, the authors tried to work out whether or not there was any potential harm associated with children being involved in overweight and obesity interventions. Although only a few studies actually looked at whether programs were harmful, the results suggest that those obesity prevention strategies did not increase body image concerns, unhealthy dieting practices, level of underweight, or unhealthy attitudes to weight and that all children could benefit.

These recommendations of screening for overweight and obesity in all youth and testing for prediabetes and diabetes and at risk youth are certainly taken from the Indian Health Service Youth Diabetes Best Practice. But I think it's important before any programs considering screening for childhood obesity or for prediabetes and diabetes, that you identify and clarify your current resources for intervention.

I think in terms of childhood obesity, we also need more studies in the very young as well as adolescents to find out more about obesity prevention in these age groups and we also need to assess how long the effect of these interventions actually last. I think it's also important in terms of obesity prevention that we look to see how all children can benefit by making sure that we embed all those successful activities into everyday practices in homes, schools, child care settings, the health system, and the wider community as well.

These are the recommendations from the American Diabetes Association and American Academy of Pediatrics on who should be tested for diabetes. In terms of testing for diabetes, do we know that it will actually help? Are we ignoring the cost of screening and potential costs or harms that might be associated with screening for Type 2 diabetes? The testing methods, there's no real recommended screening test and a finger-stick isn't really included in the recommended testing methods from experts with the American Diabetes Association and the American Academy of Pediatrics. Certainly, you do need to think about how easily these tests can be done in your clinics and hospitals and certainly obtaining these tests in children and teenagers.

When we think about primary diabetes prevention, it's important to think back to the literature and these are risk factors that have been identified in the Pima from their longitudinal NIH study. The first few are certainly more specific to children, but we need to look at this in terms of what we think is modifiable in terms of what we can change.

If you look at this listing, I think it points to why we have Indian Health Service Best Practice recommendations related to one on breastfeeding support, addressing the problem with bottle-feeding that's associated with the development of later Type 2 diabetes as well as one on diabetes in pregnancy. We know that research has shown that infants born in hospitals that practice the Baby Friendly 10 steps are more likely to breast-feed longer and more exclusively than those who are not.

But, the in-utero exposure has certainly been shown to be the strongest association for Pima children in terms of the later development of Type 2 diabetes. I think programs that prevent and/or treat obesity as well as programs that target young women of childbearing age to reduce their risk for developing diabetes before they become pregnant and while they are pregnant are certainly activities that diabetes programs should be addressing in their communities.

I wanted to mention one other pilot study that was actually included in this last Cochrane review. It was actually home visitation study and using home visitation to prevent obesity. Many of you are probably aware that home visitation has been used, certainly the David Olds model, to prevent a lot of other adverse issues associated with children and adolescents, but this study was actually conducted in an American-Indian community. The intervention was an adaptation of the Active Parenting Curriculum where 11 parenting topics were covered in 16 weeks. Results showed a significant decreased intake was noted among children in the intervention group and mothers in the intervention group showed less restrictive feeding styles over time as well. I believe that this study actually shows another promising practice. With many tribes now using and being trained on home visitation, this might be another avenue to consider for the prevention of obesity as a primary prevention strategy for the prevention of Type 2 diabetes.

An ecological approach has been recommended by the Institute of Medicine for the prevention of obesity. This ecological model focuses not only on the behavior of individuals but also on the social and environmental context in which people live. The model includes characteristics of the individual and interpersonal level, changes that could occur on institutional or organizational level. Certainly for children, we might be thinking of schools but Day Care Centers might be another factor here -- community factors and public policy.

This is one schematic for the social ecological models for levels of influence. Again, further describing the characteristics of each one of these levels of influence.

This schematic has been developed and I think provides more descriptions that pertain to American Indian and Alaska Native youth. It was developed for the use in First Nation's communities. In Canada, they are also looking at the social ecological model in terms of policy systems and environmental approaches or public health approaches to the problem of obesity and the lack of physical activity opportunities and access to fresh and healthy food choices that happens, in many communities that are poor. I think this schematic looks and speaks to and would resonate with many of our community members in terms of changes that they'd like to see within their communities that could make healthy choices available and easier for everyone in the community.

This model has been recognized by a number of funding agencies, the Robert Wood Johnson Foundation, Centers for Disease Control, Kellogg Foundation and others are looking at some of these policy systems and environmental approaches. The Association of American Indian Physicians has developed a policy brief that is available on their website, which is actually a call to action for advocacy for childhood obesity prevention. It's an educational tool for physicians and other healthcare professionals who are interested in implementing policy systems and environmental change to impact childhood obesity in their communities. It includes a number of resources that are helpful and speaks to different ways for approaching the problem of childhood obesity in this manner.

There have been a number of lessons though that have been learned in terms of using this type of public health approach and it's an approach that we are also using at the Center of Excellence in Eliminating Disparities. We're working with Urban Indian health organizations throughout the country out to see how these policies and changes can be implemented in a way that's culturally relevant for Urban Indians and in a way that can reduce their risk for the development of cardiovascular disease and diabetes.

It's important to know that a cookie-cutter approach isn't going to work for everyone and you have to be willing to adapt from other successful communities that have used this type of approach. It does take a lot of time and legwork and you need a foundation before implementing it and in the many cases, it's impossible to conduct this kind of activity without having a coalition in place and involving leaders in the community and other partners that we wouldn't traditionally consider health partners such as Department of Parks and Recreation, businesses such as grocery stores, certainly schools, the faith organizations and the others who could be used to leverage their resources in terms of getting this through in their communities.

It's important to be realistic. We know that this takes time. It's not traditional. A lot of people think they need to throw out everything else that they're doing in the community related to educating the community in traditional health promotion approaches and events, but that's not true. Those are still needed. This is just to augment it and move the process along but there's a lot of value in using a National American Indian/Alaska Native Organization such as the Association of American Indian Physicians. It's also important to remember tribal customs and traditions and trying to incorporate those into some of the changes that are made such as including more traditional foods, more traditional activities in school curricula.

Type 2 diabetes prevention itself though is certainly difficult to address. We know that prevalence figures for impaired glucose tolerance, it's about 3% for all US adolescents, 12 to 19 years of age, certainly higher among obese adolescents. And then, a study that was published in 2010 in the New England Journal of Medicine, the prevalence of IGT was determined to be about 4% among Pima, five to 19 years of age. But I do know that due to better screening, better clinical acumen among providers within the Indian Health System that Type 2 diabetes and prediabetes are certainly being seen at younger ages in our patient population and in the communities that you serve.

I think we really have to think about what is our best strategy in terms of approaching those kids with prediabetes. Think about what it means in terms of the Evidence-Based Guidelines that were just released even though they don't actually address prediabetes but do summarize many of the randomized control trials that have been done and many of the evidence related to obesity prevention.

So, I leave you with the question of what is our best strategy in terms of Type 2 diabetes prevention. Obviously, I think we need to focus on primary prevention activities, that I mentioned earlier related to obesity prevention. This public systems and environmental approach, policy approach to increasing physical activity opportunities and increasing access to healthy foods and addressing problems such as food insecurity as well as breastfeeding promotion, as well as working with women of childbearing age.

Do we need to think about a diabetes prevention program strategy for our adolescents with impaired glucose tolerance? It is certainly something to consider and I think a conversation that should continue with the National Diabetes Program Office.