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Dyslipidemia in Children and Adolescents

Narrator:

Welcome to ReachMD. You are listening to Lipid Luminations, produced in partnership with the National Lipid Association and supported by an educational grant from AstraZeneca. Your host is Dr. Alan Brown, Director of the Division of Cardiology at Advocate Lutheran General Hospital and Director of Midwest Heart Disease Prevention Center at Midwest Heart Specialists at Advocate Health Care.

Dr. Brown:

I'm your host, Dr. Alan Brown, and with me today is Dr. Don Wilson, endocrinologist at Cook Children's Health Care System in Fort Worth, Texas. I've had the privilege of speaking on a program with Dr. Wilson, and he's a fantastic expert in prevention of cardiovascular disease as it relates to our children. So, I'm really thrilled that you were able to join us today, Don. Thank you very much.

Dr. Wilson:

Thank you, Dr. Brown.

Dr. Brown:

So, Don, tell me a little bit about lipids, children and risk factors. Obviously, we've focused a lot over the years on 10-year risk, whether we did it with Framingham scoring or even the ASCVD risk, and the new guidelines have kind of said we don't have any lifetime studies, so you could think about it, but it was kind of a secondary consideration. So, for children all of that kind of goes out the window, doesn't it?

Dr. Wilson:

Exactly. And I think the children are a new opportunity for us to relook at true prevention. We've talked about primordial prevention, but that's kind of an odd term for most people. True primary prevention simply means we keep them from having any kind of risk factors, and, ultimately, keep them from having any kind of cardiovascular event.

Dr. Brown:

It sure seems like people who have low lipids over a long period of time have a much lower risk than even the patients that we treat

aggressively later in life.

Dr. Wilson:

Well, the recommendations for screening children actually started in 1992 but hasn't gotten much traction. I think two things have changed. We'll talk a little bit about the 2011 recommendations and, more recently, the National Lipid Association recommendations, but I think the thing that has really brought this to the forefront are the genetic mutations. Historically, we looked at mutations that actually increase risk by increasing LDL cholesterol, lowering HDL, whatever; but at the end of the day, there are also a group of polymorphisms that are equally, if not more, interesting and actually lower risk by lowering LDL cholesterol genetically. The key to it is that you can either have significant or modest reduction in LDL cholesterol, but it's played out over the entire lifespan of the individual, so that means from birth all the way to the end of life.

Dr. Brown:

So, you get almost an exponential reduction in risk then, right, when you do it over...

Dr. Wilson:

Exactly, and this is also borne out when you look at a head-to-head comparison between genetic polymorphisms and the use of statins in middle age or older individuals. So, it actually takes 3 times the amount of LDL lowering to be comparable to what you see in a genetic polymorphism. Now, that's not to say that medications necessarily can replicate that, but there's optimism that low level of LDL cholesterol over a long period of time, even a modest reduction, say levels of 100 mg/dL, will be cardioprotective.

Dr. Brown:

So, as a clinician -- I think a lot of our audience, they span multiple specialties, but they don't have a real firm idea of what the numbers ought to look like in kids. I'd like to ask you two questions. Number one, what do the current recommendations say about which children should be screened and at what age? And then secondly, over the course of time from very young children to, say, adolescents, what should be considered a normal lipid profile?

Dr. Wilson:

Okay, so let's start with that. Typically, if you have a newborn, the levels of a newborn is less than 40 mg/dL. That level rises within the first 2 years of life to about 100 mg/dL.

Dr. Brown:

And we're talking about LDL here, right?

Dr. Wilson:

LDL, yes, thank you for the clarification. And it will stay that way until about age 9 or 10. Then interesting, and here is something people need to pay attention to, is that LDL levels actually go down during adolescence. So, if you sort of have a fixed endpoint looking at screening, you may actually miss some kids because they are physiologically going down during adolescence, and that number will rise as they become a young adult.

The recommendations in 1992 actually focused on a targeted audience, so it made sense. We wanted to improve everybody's eating habits and have children have a much healthier lifestyle. Well, unfortunately, much of that hasn't happened, as much as we have tried to counsel families about the importance of healthy lifestyles. But, it basically said if you have a biologic parent that has an elevated cholesterol level or you've had a first-degree or extended second-degree family member who's had a cardiovascular event, then those are children who really need to have screening. The problem with that approach is it misses about 30-60% of kids who actually have significant elevations of LDL cholesterol that need to be addressed, so that approach didn't work very well.

Number two, many of our children come from single-parent families, so you're missing one of the biologic parents, and that might be

the parent of interest. And then we have children who are adopted and so forth. So, that strategy, even though it's still reasonable, I mean, if you have biologic parents and you can get a good history, that's great. But starting in 2011, the current recommendations are that between the ages of 9 to 11, so age around 10, we just screen the kids no matter what. No matter what their family history is, no matter what their health history is, you just need a single screen. Good news is that can actually be done with a nonfasting sample because we're looking at total cholesterol. If it needs to be followed up, you can actually arrange for a follow-up fasting sample, but the good news is you don't have to fast the kids, which makes it practical. Number two, you can actually do it on a finger stick, which is helpful in pediatric practice. And for people who have point-of-care testing in their office, it's equally valid as sending them to a laboratory. So, by whatever method, by whatever means, recommendations say once between the ages of 9 and 11, around age 10, and then repeat that if it's normal somewhere between the ages of 17 and 21. So, by the age of 21, ideally everyone would have had at least 2 screens.

Now, as far as the numbers are concerned, we currently describe the pediatric population by looking at percentiles. That doesn't necessarily mean that the total cholesterol or LDL cholesterol we describe is a healthy cholesterol. It simply means that's currently what the population norms are. So, we defined the upper limit of normal as being the 95th percentile for gender and for age, but those numbers typically are for 95th percentile for children is around 200 and above for total cholesterol, 130 mg/dL and above for LDL cholesterol.

Dr. Brown:

So, you'd like to see less than 130 LDL in those kids, and when it's higher, that's a red flag.

Dr. Wilson:

That's correct.

Dr. Brown:

I know the guidelines say around 10 years old to screen everybody, but there's a particular recommendation if a parent has familial hypercholesterolemia, right? So, I think we've been on a mission at the NLA to help the practitioner understand when LDL is over 190 in an adult, they probably have FH and they should be screening the children. But the screening recommendations if you have a parent with FH is slightly more aggressive, is it not?

Dr. Wilson:

Yes, age 2 and above, so it's very aggressive, but I think rightfully so, because this is the target population, as you and I have discussed several times before, this is a population we really want to focus on. Where this kind of gets a little bit murky is that we've expanded the definition of at-risk children now, and I mean, we're all faced with children who are overweight and obese, so those kids primarily have high triglycerides, low HDL, and it is a significant cardiovascular risk factor. But that's really not the target for most of our screening efforts. Most of our screening efforts are looking at asymptomatic children who may have wonderful health habits, they may be very slender and trim, but they may have LDL cholesterols that are 250 and 300, which puts them in significant lifetime risk.

Dr. Brown:

So, I often get asked, okay, you've screened one of these kids and at 2 years old you find their LDL is 210 and they have a parent with FH, so you've identified them. They have FH. The current recommendations are to start statin therapy somewhere around age 7. So, in your practice as an expert, what do you do between age 2 and age 7 when you identify one of these children? What are the recommendations?

Dr. Wilson:

Well, first of all, I think it's important that the child later on -- obviously, a 2-year-old is not going to understand this -- but the parents

for now understand what the child has and why they have it. Number two, you can start educating that child about the importance of lifestyle, because even though that child is going to require medications to lower cholesterol to a safe level, the reality is you can make a bad situation worse by allowing a child to become overweight or obese, to start smoking, to become sedentary, all those behaviors that we fight every day in the office. So, there are a few exceptions, but most of the time we've chosen the age of 8, or in Europe it's 6, to start drug therapy because we think it's probably better, but those are arbitrary based on current studies. We don't go below the age of 2 because we really don't understand the biology of lipids and there's a concern, obviously, a legitimate concern, under age 2. But, beyond that, I mean, (inaudible 9:09) questions have been around forever. So, aside from interfering with absorption of multivitamins and so forth, they're perfectly safe, and you can actually start some of those medications early on. So, I think there are some things you can do even before.

Dr. Brown:

If you're just joining us, you're listening to Lipid Luminations on ReachMD. I'm your host,

Dr. Alan Brown. With me today is Dr. Don Wilson, endocrinologist at Cook Children's Health Care System in Fort Worth, Texas.

I don't know if it's been your experience, but when you do have to start medication on children, there seems to be a lot of barriers. So, even my FH kids that come in that I want to start statin therapy on at age 6, 7 years old, the parents frequently feel that the medicine might be more dangerous than the disease. Their pediatrician many times is not comfortable with starting them on medication. What types of strategies do you use to stress the importance of starting treatment early, and tell us a little bit what the safety studies show in children with statin therapy?

Dr. Wilson:

So, a couple thoughts. One is that it's important that we all remember that this is a marathon, not a sprint, so these people have lifelong elevations of cholesterol which will result in significant morbidity and mortality, unfortunately, but potentially very reversible if you start early enough. The good news is we don't have to use high potency statins in these kids necessarily because they may respond to less potent statins in a lower dose, because again, we're trying to achieve lowering dose over a long period of time. Number two is, there is a whole class of emerging drugs, so statins may not be the answer for FH for anybody, or certainly for this population long-term. So, those are the kind of conversations we have with parents. But back to my comment about this being a marathon, I don't think the first day that you see the patient, and you don't really have an established relationship with them, certainly, as a subspecialist, that that's the time necessarily to put children on medication. So, I think it's important that you establish a relationship. You examine, as you said very nicely, you examine the parents' history and what their history had been on medications, what their response had been to their own medications, and then try to understand what their fears and concerns are. I mean, ultimately, the problem is going to be that you have to then educate the child as they become older, and then you have to encourage them to continue taking medication. And they, particularly as an adolescent, may not see any benefit, right? It may cost a little money. You have to take it every day. You have to remember to take it every day. And if you're a teenager, that's not going to be real high on your priority list. And, by the way, we're preventing disease here, so it's not like you've had an MI and all the sudden you're fearful of dying, and so you're going to take a medication to prevent that. These are perfectly healthy kids, and if we start early enough, always will be.

As far as any major side effects, I mean, we're always very cognizant of those, but the studies that have been done for a reasonably long period of time. We haven't studied a lot of high potency statin therapy in kids, but the ones that we have studied have looked at sexual maturation and growth development, cognitive function and all those things to be intact. I don't think we see nearly the complaints of myalgias and myopathies that you see in adults, maybe for a variety of reasons. We're using lower potency drugs, and most of our kids are not taking any other medications or have any other health conditions. So, I think as far as the safety profiles, the statin drugs have actually performed pretty well.

Dr. Brown:

So, that brings us to the last few minutes. I could talk to you for hours on this topic. So, you have a unique perspective as a pediatrician and as someone who is really interested in prevention. When we know that the lifetime risk for males in the United States is about 50/50 for a major cardiovascular event. Do you think what we've learned in the studies on FH children and then the genetic evidence that if you're lucky enough to have a mutation that causes your LDL just a modest decrease translates into a huge 401(k) plan for your health in the future? Do you have any thoughts on whether we should consider population-based therapy on a broader scale and at a younger age?

Dr. Wilson:

Yes, I mean, I think this is an emerging field, so I think the job of primary care physicians and family physicians is to try to help us identify these populations at risk. And then, in most areas, now you have someone who's interested in lipid disorders in children. Since this is an emerging field, I think probably my advice is if you're uncomfortable with that, or even if you're not, maybe allowing those individuals in your community to try to help lead the charge in terms of therapies and stuff like that, because I think ultimately we'll all know the answer 20 or 30 years from now. I mean, the things that are still unknown is, that we don't know what effects long-term medications over an individual's lifetime starting at age 6 or 7 would be. I mean, that's a legitimate concern. That being said, again, the choices of drugs today and next year are going to be different. But I think we have a tremendous opportunity to reduce or eliminate cardiovascular disease in the future in a huge segment of our population and increase productivity of individuals, their lifespan, and hopefully their happiness over their lifespan. You know, the future is ours to define, I think.

What we really need is the primary care physicians to get involved and not be surprised when you have a thin, 8-year-old child who's got an LDL cholesterol of 250. It's a genetic disorder. We know it's going to be high in that population. By the way, this is something that's very frequent. The other thing we think is these are all rare diseases, but this is like 1 in 200 to 1 in 500. So, if anyone in the audience actually has someone in their practice or they know a child with type 1 diabetes, it's the same frequency. Actually, it's more common than type 1, perhaps even double the number of people with type 1 diabetes.

So, still a lot of work to be done, but I'm excited about the opportunity and the emergence of new knowledge and new technology.

Dr. Brown:

Well, Don, thank you very much. I'm disappointed we're out of time. I think all of us who treat adults with familial hypercholesterolemia have had terrible stories where the patient in our hands had very high cholesterol. They were adults so they had been tested at some point, identified, and people were treating them, but they forgot to screen the children. They forgot that this is an autosomal dominant disease. They forgot to make the diagnosis or didn't know how to, and then you see children dying in their 20s and sometimes even in their teens.

I applaud your work, and I hope that our pediatric colleagues and our adult colleagues in primary care will heed the guidelines, screen these patients, and that our audience will not forget that when you have a patient with LDL cholesterol that's over 190, you want to screen all the children. And if the siblings of that patient also have the same phenotype, you want to screen their children. So, cascade screening is critical to save the lives of our young people.

Dr. Wilson:

Absolutely. And I can't say enough about the primary care physicians because they do yeoman's work here, and I also appreciate them actually voicing concerns and caution because that makes us all cautious, not that we're not otherwise. But at the end of the day, I think these people have a tremendous rapport. And I try to use the primary care physician as a resource. I invite people to go back and talk to their primary care physicians or their pediatricians about their fears and concerns. But ultimately, I think we have to embrace this as a healthcare profession. It's all about trying to help people stay healthy.

Dr. Brown:

Thank you very much, Don. It was a pleasure, and I know our audience will appreciate your insights on children and dyslipidemia.

I'd like to thank the audience for joining us, and I'm your host, Dr. Alan Brown. You've been listening to Lipid Luminations on ReachMD. Thanks a lot.

Narrator:

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