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Special Populations in Patient-Centered Management of Dyslipidemia

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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:

Welcome to Lipid Luminations. I am your host, Dr. Alan Brown. We're broadcasting live today from the National Lipid Association meeting in Chicago, Illinois. Joining me today is a close friend of mine and an oracle of wisdom in the field of lipidology, Dr. Peter Jones, Associate Professor of Medicine in Atherosclerosis and Lipidology at Baylor College of Medicine in Houston, Texas. Peter has also been instrumental in helping craft the documents that discuss the National Lipid Association's recommendations for patient-centered management of dyslipidemia.

So, Peter, thank you very much for taking the time out of a busy meeting to come here.

Dr. Jones:

My pleasure, Alan.

Dr. Brown:

So, I know that we're about to launch the labor of love you guys have been working on, which is the second part of the recommendations for lipid management, and probably our listeners hopefully have seen the first section of recommendations, pretty deep science, an in-depth basis of atherosclerosis and why we feel that we should manage atherogenic lipoproteins even ahead of the evidence. Tell us what the difference has been for Part 2. What does that cover?

Dr. Jones:

Well, I think you get to the point where you identify risk and you intensify your treatment based on what your risk of your patient is, and so I think in Part 1 we were helping the practitioner come to a point where they could identify appropriate risk and use some characteristics which are very useful in that risk identification; above and beyond risk calculators, there are clinical situations that help identify risk. That was in a broad sense. We realized that in individual patient-centered care, there are other situations where risk is

maybe more difficult to assess, and that's mostly in primary prevention situations and in children and adolescents, women across their lifespan. Certain special disease states, we call them chronic inflammatory disease states, may be at higher risk at any age than you can identify with usual traditional risk factors or risk calculators. And then, finally, the most difficult I think is older individuals, where age always drives their risk, but that doesn't necessarily mean you have to be as intense or not as intense with your decisions on preventative treatments. So, we thought we'd get into more special populations in Part 2 to help the practitioner apply this to individual patients that they see in their practice, not as general population-based recommendations.

Dr. Brown:

I think that will be intriguing to a lot of our listeners, because with the drift in the Institute of Medicine's suggestion of how guidelines should be written and the emphasis on minimizing expert opinion, it gives you a little leeway to look at populations you know could be in trouble, but there hasn't been a good clinical trial, so I think the audience will be interested in hearing about some expert opinion on these recommendations.

Dr. Jones:

Yes, most of these special populations that we talk about in Part 2 are excluded from randomized clinical trials, so almost all of these really didn't get looked at for the benefits of either lipid treatment to reduce cardiovascular risk or maybe even general cardiovascular risk reduction strategies. So, we tried to put our expert opinion with a broader base of scientific evidence outside of randomized clinical trials to help inform the practitioner's clinical judgement, which is what they're told to do. Everybody punts and says, “What am I supposed to do with this person?” “Well, use your clinical judgment.” Then they go, “Well, I need some help with that clinical judgment.” Well, I think the NLA has tried to do that with our recommendations, in particular this Part 2 recommendation.

Dr. Brown:

Okay, well let's get down to the nitty-gritty a little bit, because when we present the new calculator and some of the recommendations of the ACCHA guidelines, which cover a broad population of people, one recurrent theme that I hear all the time is what about the South Asians who might have 3 or 4 times the risk at any level of body mass index and any lipid level. So, can you tell us a little bit? I'm particularly interested in South Asians. And then another group that I notice that you covered was patients with HIV that we sometimes deal with and we struggle with medication interactions and other things. Let's start just as an example, give some information on those 2 groups.

Dr. Jones:

To start with South Asians, those we tried to broaden it a little bit. Most call South Asians, but you can get down from India and Pakistan and Burma, and so forth, they tend to have higher risks of cardiovascular disease at any age, at any BMI, and particularly at any waist circumference. And if you look at the definitions of obesity and metabolic syndrome, the waist circumference is a lot less for South Asians in defining it than it is in African-Americans and Caucasians. So, they tend to have a higher risk for diabetes, insulin resistance, fatty liver, mixed lipid problems, high triglycerides. Their cholesterol and LDL doesn't tend to be the primary driver of what their risk of heart disease is, and they're not obese by the traditional US characteristics. So, I think that they tend to get overlooked, rarely enrolled enough in randomized clinical trials to know whether statins reduce their risk of heart disease compared to other ethnic groups, but we wanted to point out that just be especially aware of evaluating them for high risk of cardiovascular disease, the tendency for insulin resistance and the propensity for diabetes. There does tend to be a general higher level of LP(a) in South Asians than you see in Caucasians and Hispanics. We see the same thing in African-Americans. Their baseline LP(a)'s are a little higher. Is that part of the contribution to the risk of heart disease? It may be, although we don't have directed treatments towards that, but it maybe one of the characteristics that helps a practitioner put together a package that may be considered as their risk.

Dr. Brown:

And I've been struck working in a community where we have a lot of South Asians that the youth is present when they present with an acute event, a lot of them in their 30s, 20s, and I think that traditionally when we assess patients at that age with even chest pain, we

tend to think that the prevalence of the disease is pretty low.

Dr. Jones:

You would think it would be pretty low. And I think part of the issue too with South Asians is the ones we see here in the United States, many of them are first born and they all tell us family history, “Well, you know, there's not really much family history. All my family lives in India.” Well, they come here and adopt an American lifestyle and they do get more obese, they do get insulin resistance earlier and fatty liver and dyslipidemias, so the trajectory of earlier cardiovascular disease may be present in those first born South Asians as opposed to what their family history may be from their original parents, grandparents, etc. who are still in India or Pakistan.

Dr. Brown:

So, the other topic, one of the many that was covered in the document, was how to look at patients with HIV.

Dr. Jones:

Right.

Dr. Brown:

And I don't think there's a general understanding about how much increased risk they have for atherosclerotic disease. We had done another interview with Dr. Myerson, that's her specialty, but I was pleased to see that was in the document for a lot of reasons, not the least of which they get sent to us on their medications for dyslipidemia.

Dr. Jones:

Correct.

Dr. Brown:

So, I wonder if you can comment a little bit on the summary of your recommendations?

Dr. Jones:

Well, in the summary of recommendations, we agree with the experts in the field of human immunodeficiency virus groups. They do tend to have a higher risk of cardiovascular disease earlier in life. They're now living longer because of the wonderful medications, the antiretrovirals that we have available. They're living longer, so now they're not getting problems with infections and cancer-specific issues; they're now getting cardiovascular disease. They do have insulin resistance. Some of the medications that they're given, the highly active antiretrovirals increase the risk of progression to diabetes, so they do need to be treated for their lipid risk contribution. The issue is that many of medications they use, the retrovirals do have drug-drug interactions through the cytochrome P450 system, specifically, lovastatin and simvastatin. And I think in our document we specifically say if you are going to use a moderate- to high-intensity statin, it not be lovastatin and simvastatin. We suggest that you consider some, and if it's high intensity, we recommend more rosuvastatin as being the high-intensity statin. And then when you get to moderate intensity, it widens a little bit more where you can include atorvastatin at a lower dose, fluvastatin and pravastatin and pitavastatin as options in the moderate-intensity statin group.

Dr. Brown:

If you're just joining us, you're listening to Lipid Luminations on ReachMD. I'm your host, Dr. Alan Brown, and I have the pleasure of speaking with Dr. Peter Jones today.

So, Peter, you know the stuff inside and out and you were intimately involved in the development of the recommendations. If I were to ask you what piece of Part 2 are you most proud of, what do you think is the piece of it that you really feel fills the greatest gap?

Dr. Jones:

I believe that we have firmly come out in the stance that women are at high risk for heart disease and they need to be considered across their lifespan for the risk of heart disease, particularly noticing and recognizing familial hypercholesterolemia in women and not being afraid in their childbearing years to move towards a treatment strategy that can prevent their lifetime risk of coronary disease; but we also, with some of the controversy about the fact that primary prevention with statins in women is not substantiated and there's not really

good evidence to suggest they benefit, I think we made a pretty good stance that women do benefit in primary prevention with statin use, with appropriate risk assessment. We tell you how to do that, that it is safe and that it probably is more benefit than harm to do primary prevention in women. So, I think since that's half of the population, regardless of their ethnicity, I think we made a firm stance that women are important. And as opposed to some people out there that are suggesting we're overtreating women by putting them on statins, I think we've put our opinion that that is not the case with appropriate assessment.

Dr. Brown:

Let's shift gears a little bit. Let's go back to the assessment of the primary prevention patient where the data for reduction in mortality is hard to come by, probably because theiroverall mortality, greater impact from other things, not just atherosclerosis, right?

Dr. Jones:

Correct.

Dr. Brown:

In the absence of other risk factors. There's been a lot of discussion lately about combination therapy with the disappointing results in AIM-HIGH, (**HBS through Thrive* 11:08)** ACCORD. Give us your opinion, particularly in primary prevention, what types of patients we should be thinking about combination therapy as opposed to just intensive LDL lowering, which is pretty much what the literature suggests and why the guideline groups said this is all the science that we have.

Dr. Jones:

Well, I agree. I mean, there's no question that the randomized clinical trials and the evidence would support as high an intensity statin to match the risk of the patient, and that should be their monotherapy. I mean, statins are the go-to, and we completely agree with that. The issues of combination drug treatment depend on several factors, one of which is whether the patient can adequately tolerate that intensity of statin treatment, and then we get into this issue of statin-intolerant patients. I'm not going to go into how we define them, and it's a very difficult process sometimes, but we all clinically have seen patients who have trouble tolerating statins and won't take them. We recommend that you try as any dose of a statin that they can take and then assess where they are with LDL cholesterol and non-HDL cholesterol. And if they're still even in primary prevention not at that level because of polygenic cholesterol elevations or combination lipid problems, then you may need to consider additional LDL-lowering drugs that we have, that we know are safe, that have been looked at in their own randomized clinical trials in decades past, and that involves now ezetimibe, bile acid resins. Fibrates may be necessary in some situations, and there still is a role in some patients for niacin, but it's not a routine medication.

Overall, familial hypercholesterolemia patients need more than one drug. Even if they can take a high intensity statin, they will probably need additional medications to achieve LDL and non-HDLs into optimal levels. We recommend that that be an evidence-based approach of adding those drugs on to FH, and that would be ezetimibe first, then a bile acid resin second, and then, up to now, it was a third add-on to a high-intensity statin would be a niacin at that point. I think fortunately we now have as of this past week other options for familial hypercholesterolemia that will be add-ons to high-intensity statin that may minimize some of that other older drug use, but they are a population that does need combination almost all the time.

Then, of course, there are the odd patients that we all get that are very clear; they're significant mixed dyslipidemia, high cholesterol, very high triglycerides, and their severe hypertriglyceridemia. Many of those patients need combination drug treatments, and they're complex, and lipid specialists are probably the ones who need to be in charge of that. But we address those as well and talk about the drugs that we feel are effective and safe to be used with statins to deal with those more genetically determined significant dyslipidemias.

Dr. Brown:

As a final discussion, I just want to bring up a philosophy that I'd like your comments on. Obviously, we traditionally grew up with targets, and what we take from trials that showed progressively lower and lower numbers on sometimes fixed doses of treatment, the benefit is that maybe we should be lowering our target numbers. I was intrigued to hear that one of the authors of the IMPROVE-IT trial, who is a big believer in maintaining targets, his institution is excited to add ezetimibe to everybody with high-dose statin because it looked like that gave clinical benefit across the spectrum of people with acute coronary syndrome.

Dr. Jones:

Right.

Dr. Brown:

So it wasn't based on an LDL target. It was, okay, this is the way we did this study, put them on max dose statin, and randomize them to placebo or adding ezetimibe, and the ezetimibe group did better, so everybody should go on ezetimibe.

Dr. Jones:

Right.

Dr. Brown:

And I'm only asking that question because that's the way some people interpreted using 80 mg of atorvastatin alone after an acute coronary event going back to the IMPROVE-IT trial.

Dr. Jones:

Right.

Dr. Brown:

So, is that right? Should we be shooting for targets? Should we be shooting for just adding drugs that have been proven to work in clinical trials? Or, should we have a hybrid approach where if the numbers are still high we go crazy and try and get them way down no matter how many drugs, and for those that the numbers are low, we have to pick some appropriate treatment option?

Dr. Jones:

It is a hybrid approach. I mean, there's no question that high-intensity statins in the right patient should be given. The caveat is that not everybody responds to that high-intensity statin the same way. Some can get a 35% reduction. Some will get a 60% reduction. Well, you'd love the 60% reduction to the high-intensity statin because you're probably going to get that lower is better LDL and atherogenic cholesterol level. Well, what about the guy or the woman who got 35%? They don't have the benefit of lower is better for them. So, while I do think atherogenic cholesterol is directly and causally related to atherosclerosis and the lower the better, it does matter how you get there. And if you can't get there with evidence-based treatment because of variability in response, then I do believe we have evidence with ezetimibe that a non-statin way of lowering LDL does help, so other non-statin methods of safely lowering LDL should be additive. So, it's an individual patient-centered approach. Yes, you can put everybody on the same thing and assume they all respond the same way. My feeling would be it's fine to do that but make sure you understand how their response has been with the ultimate goal being I want the lowest LDL non-HDL in the safest way because I believe that will give the best outcome over the long haul.

Dr. Brown:

It's very interesting how the trials get interpreted. It's almost like looking at the Bible and deciding are we going to take it literally or are we going to use it as a guide in modern day life, and I wouldn't dare to say which of those I think is right, but that's kind of the approach.

Dr. Jones:

Agreed.

Dr. Brown:

So, some people would say, “Okay, they're on 80 of atorva(statin) after an acute event. Their LDL is 50. I'm fine with that.”

Dr. Jones:

Right.

Dr. Brown:

And others would say, “Well, wait a minute. We looked at a bunch of those in a clinical trial and they overall got more benefit by adding ezetimibe. We should add ezetimibe.” Which is the right approach?

Dr. Jones:

I don't think there's any right approach. I think if you get a patient with high-intensity statin, their LDL is 50, for instance, your example, if they can take that high-intensity statin and will for the rest of their life and stay there with good lifestyle changes, I think nobody would

quarrel with that at all. If you wanted to add ezetimibe and get them to 38 instead of 50, I have no problem with that either if the patient will take both, continue lifestyle and do that for the rest of their life. I think both patients will do very well. We hopefully will get the lower end of LDL figured out in the not too distant future, but I think if you get most people on a high-intensity statin down to 50, I think you've done a fantastic job. And if they will take the drug for the rest of their life and tolerate it, you've done a fabulous job.

Dr. Brown:

Well, thank you very much, Peter. I'm disappointed we are out of time. I'm your host, Dr. Alan Brown. Thank you very much for joining us from the National Lipid Association Meeting in Chicago. This is Lipid Luminations on ReachMD.

Narrator:

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