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Guidelines for Diagnosis and Management of Dyslipidemia in Patients with HIV

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:

Good morning. I'm your host, Dr. Alan Brown, and with me today is Dr. Merle Myerson. Dr. Myerson is a cardiologist and Board Certified Lipidologist. She holds a Doctorate in Exercise Physiology and is an expert in sports cardiology. She's the Founder and Director of the Cardiology Section in the Institute of Advanced Medicine and HIV Program at Mount Sinai Health System. She's a professor at Columbia University Teachers College Division of Applied Exercise Physiology where she teaches and conducts research. And we have the privilege today of broadcasting live from the National Lipid Association Meeting in Chicago. So, thank you very much, Dr. Myerson, for taking time to talk with us today.

I know that you have a particular expertise in HIV, and it's something that my perception is a lot of people consider the self preventionalists don't have a strong background in, so I'm very excited to hear your thoughts. Can you tell us a little bit about the changing face of HIV? Obviously, when I was young it was almost a uniformly lethal diagnosis. So, tell us about the current state of the art in terms of the prognosis and treatment.

Dr. Myerson:

Yeah, exactly. I remember when I was treating it was, you know, you'd see a patient one week and then in a couple weeks you would not see them because most did not survive. With the advent of antiretrovirals, it's really changed the face of HIV, and patients now are living longer lives, healthier lives, as long as they maintain their regimen of medication. So, now with that come the side effects of medication and also diseases of aging, so this has become more of a chronic disease. And some of the side effects of the medication are producing a dyslipidemia, a metabolic syndrome. Patients, as I said, **we're living*** (inaudible noise 2:09) where cardiovascular disease and some of the cancers are becoming more prevalent.

Dr. Brown:

So, let me ask you, as someone who is like us, a lipidologist and a prevention geek, what got you interested in treating patients with HIV?

Dr. Myerson:

In 2008 I was at St. Luke's Roosevelt Hospital, where I'm still at -- it's now part of Mount Sinai -- and I read the reports from the American Heart Association that had convened an expert's panel and multidisciplinary meeting headed by Steve Grinspoon**,** and it was very interesting, because prior to this, I didn't really think that prevention in HIV went together; and after I read that, I went to the head of our very large HIV clinic and I prepared a little presentation. I said I was a prevention specialist, cardiologist, lipid specialist, and, "I think your patients need my care." And they said, "That's great, but we don't like to send out. We bring people in. We're going to bring you

in. This has never been done in the United States. And we'd like to probably go forward with this." And after that the flood gates opened. Not only was I doing prevention, but there were people with coronary artery disease, valve disease, fainting, you know, the whole breadth of cardiology. And then we began knowing more and more about it, and I started doing research and trying to develop models of care.

Dr. Brown:

So, let me ask you, I think a lot of people don't realize that HIV is really a chronic disease and people live much, much longer, and we have the successful therapeutic agents. There is such an increased risk for cardiovascular disease in these patients. Can you tell us a little bit about what is the magnitude of increased risk, and what do you think the pathophysiology is?

Dr. Myerson:

Some estimates say that they are twice as likely to get cardiovascular disease, but it's very hard to sort out the other things. For example, many more patients smoke than in the general population. Many don't have access to good care. We also think that the HIV in and of itself produces metabolic changes that increase the risk. Then you have the antiretrovirals. Now, some of the newer antiretrovirals are less cardiotoxic or less likely to produce the metabolic changes. However, we're still looking at those medicines as probably exacerbating the problem. So, added to that we have inflammation, and HIV is an inflammatory disease. Now, the exact way that inflammation is different or unique in these patients is unclear. There's an ongoing NIH study called the REPRIEVE study which is looking at the use of pitavastatin in these patients, patients who are otherwise at lower risk for cardiovascular disease, to see, to look at inflammation, the effect of statins. So, we have a lot to learn, and there are a lot of reasons and possible reasons why they are at increased risk.

Dr. Brown:

So, actually, I'm going to approach you with three different questions. I want to ask you a little bit about when you first encounter a patient with HIV, what kind of vascular workup do you do, how do you assess them since their risk is higher; and then what the effects of the treatment are, and the thing most dear to our heart, the dyslipidemia, and whatever else you think is relevant to the development of atherosclerosis; and then finally, what the best options for treating those metabolic abnormalities are?

So, let's start with, do you have sort of a protocol when you see a new patient with HIV for a workup for vascular disease?

Dr. Myerson:

Yes, I do, and a lot of this does follow the National Lipid Association and the NCEP ATPIII risk stratification. However, I do modify it, and there will be a paper out in *Journal of Clinical Pharmac*ology where I go step-by-step to take the clinician through this. So, I add some different things to the history, for example, I really look at substance abuse. We all know that cocaine can cause an acute heart attack and over time may increase risk for atherosclerotic disease. I also ask about who cooks for them? Many patients do not live in a place where they have access to a kitchen, where they can buy good food, exercise, things like that. I also look at all their medications, because certainly using some of the lipid medicines, which also work in the liver, but many have hepatitis, are on lots of medications that work in the liver. So, I think in some I follow the traditional risk stratification and history and physical, but I add something to that, the relevant aspects of care for patients living with HIV.

Dr. Brown:

Okay, so then once therapy gets started and you put patients on antiretroviral agents, what are the changes that people could attribute to metabolic effects of the medication? And then we'll get to how you deal with that.

Dr. Myerson:

So, the HIV, not including the antiretrovirals, probably produces a metabolic syndrome, not so much the hypertension but the high triglycerides, low HDL, the increased waist circumference, also the insulin resistance; so added on that some of the medications, especially the protease inhibitors, which are being used less often these days, would exacerbate that. So, I do look at the medications, but remember that the primary importance is that they are virally suppressed; so, if they're already on a regimen that they tolerate, that they're adhering to and is working, I'm not going to so much look at that and say, well, we should change the antiretrovirals. I'll work around it. Then I get a fasting lipid panel as well. I try to get the waist circumference but a little difficult because I can't get the nurses to do that yet, which I understand. And I speak to them about their risk. I also try to work with lifestyle modification, if I can get them to stop smoking or even reduce, if I can get them to move, if not, adopt a regular exercise program. So, I get my fasting lipid panel. I do like apolipoprotein B, because it's important to remember in these patients they tend to have more of a discordance between LDL cholesterol and LDL particle or apo B. And we're actually putting out a paper looking at that. I presented that at NLA a couple years

ago.

Dr. Brown:

Do you think that's primarily because of the metabolic syndrome so that they have increased particle numbers, low HDL, high triglycerides?

Dr. Myerson:

Yes.

Dr. Brown:

And is there any idea mechanistically how the HIV leads to metabolic syndrome in itself?

Dr. Myerson:

Yes, I do, I believe that part of this is the metabolic syndrome, and we're seeing that reflected in that discordance between LDL cholesterol, LDL particle and apo B much the same way we see in diabetics and metabolic syndrome. So, why this is true, probably because of the inflammatory state, the insulin resistance is all contributing to that.

You know, we're just beginning to delve into that, and my paper that hopefully will be out in the next 6 months is just going to be more descriptive, and after that we'll start looking into reasons use. But I do think it's important to know that LDL cholesterol may not reflect their total atherosclerotic particle burden.

Dr. Brown:

If you're just tuning in, you're listening to Lipid Luminations on ReachMD. I'm your host, Dr. Alan Brown, and I'm speaking with Dr. Merle Myerson about HIV and atherosclerotic disease.

So, Dr. Myerson, can you tell us then once you add antiretrovirals, do you see the exacerbation of the metabolic syndrome type dyslipidemia, or does the LDL go up?

Dr. Myerson:

There are some very good tables. Actually, Ken Kellick has excellent tables that I've used in some of my papers looking at the changes and interactions but, in general, we most often see that the triglycerides are up and the HDL down, and the LDL less affected by the antiretrovirals. But going forward, there are different classes of antiretrovirals that probably are going to be a lot less effective, a lot less damaging to their cardiovascular risk and won't alter the lipid profile as much.

Dr. Brown:

Okay, so that brings us to the million dollar question, which is, when you have a patient who's on treatment, obviously, many of the treatments share a common metabolic pathway with our statin therapies. And secondly, so obviously, as lipid geeks we're anxious to treat those numbers. Is there any evidence, first of all, that certain drugs are more appropriate in patients who are on therapy for HIV? And then secondly, is there any evidence that treating the numbers improves the outcome in these patients?

Dr. Myerson:

In terms of using medications, yes, the statins still for all the reasons we use statins for the general population are very good. With HIV we tend not to use certain ones. Some are contraindicated with certain antiretrovirals, and those are lovastatin, simvastatin. The ones that we do use are atorvastatin. We do sometimes monitor the dose and not go above 40. Pravastatin, a great medicine, but it's not as potent as the other statins, and rosuvastatin can be used, and pitavastatin. Pitavastatin is the medication that has probably the most research for these patients, and also some research showing that it does not seem to affect the insulin resistance. So, that being said, I am a big fan of non-statin drugs when appropriate, and certainly, many of these patients have very high triglycerides, and I'll reach for my fibrates and fish oil. One thing to remember with the fish oil, it's 4 large pills, and these patients are already on many pills. I don't blame them for having a hard time taking all the pills, you know, if I give them 4 of, say, prescription fish oil. Zetia I've used in patients with HIV. I tend to avoid the bile acid sequestrants, and the reason for that is they interfere with absorption of other medications and they can raise triglycerides. Niacin can be used, although whether it worsens their insulin resistance, also the side effects, and it's another medication that does work in the liver. So, certainly, there are more limitations, and on top of that we have lack of insurance coverage. Many of these patients do not have good insurance plans, very, very hard to get the optimal medications for them.

Dr. Brown:

So, that's fascinating. The final piece is outcome data in patients who have dyslipidemia due to either their HIV or their therapy for HIV. Do we have data that treating the lipids improves their cardiovascular outcome?

Dr. Myerson:

We don't have very good outcome studies. We hopefully will get information from the REPRIEVE study, although, these are at low-risk patients. And I should say here that my feeling is that when you have HIV, you may not be at low risk. We do not have HIV-specific risk stratification, but as we are writing in these Part 2 guidelines -- our chair is Judith Aberg on this and I'm on the committee -- we feel that if someone has HIV, you should consider raising one risk group. In other words, if someone has maybe one or two risk factors and they may be considered lower risk, bump it up a bit.

So, I think that in terms of treating and outcomes, we extrapolate from the general population, and from decades of research we know that lowering LDL is good no matter how you lower it. So, my feeling is that, yes, aggressive risk factor treatment, especially dyslipidemia, will lower their risk for heart events. And I hope in the future we'll have better information, better outcome studies.

Dr. Brown:

Well, thank you very much for a really illuminating interview with regard to HIV patients. I think they are a group of patients that many of us need to learn more about, and we certainly appreciate your experience. Thank you, Dr. Myerson, for being with us today. Unfortunately, we've run out of time. For our audience, I'm your...(end of audio)