

Host: This is the podcast from the journal *Clinical Chemistry*. I am Bob Barrett. After cholesterol, LDL cholesterol, and HDL cholesterol, there seem to be a bewildering number of apolipoproteins, oxidized particles, and particle subclasses that have each been implicated in cardiovascular disease.

The March issue of the journal *Clinical Chemistry* published a paper from a group led by Dr. Paul Durrington in England that suggests following serum concentrations of the apolipoprotein apo B provides a more consistent goal for statin treatment than LDL cholesterol. The same issue contains a companion editorial on that study by Allan Sniderman and Amirreza Solhpour.

Dr. Allan Sniderman is the Edwards Professor of Cardiology at McGill University in Montreal. Working with his colleagues, he has developed evidence that measuring the lipoprotein component, apo B, and thus the number of atherogenic cholesterol particles is a more accurate measure of the risk for vascular disease than LDL cholesterol.

So, Dr. Sniderman, why do you believe that apo B is better at gauging the risk of LDL than just measuring LDL cholesterol?

Dr. Allan Sniderman: The LDL cholesterol measurement quantitates the amount of cholesterol that's carried in LDL particle, and it turns out that it's the LDL particle that enters the artery wall and causes the damage. The cholesterol is one of the constituent, one of the most important constituents of that particle, but it's not the only poison in the particle.

LDL particles can differ in size, some of them are larger and they have more cholesterol within them, and some of them are smaller, and they have less cholesterol. And many people we know to be at high risk of vascular disease, such as people with diabetes, people whose triglyceride levels are high, people with abdominal obesity, men in general versus women, all tend to have the smaller LDL particles that contain less cholesterol.

So, when you measure the cholesterol, you get a false idea, an inaccurate estimation of the number of these particles that can enter and damage the wall. On the other hand, each of these particles has one molecule of a protein called apo B, and that relationship is invariant, it's biologically totally fixed.

So if you measure the apo B, you know accurately the number of these particles, and this difference in the information between apo B and LDL cholesterol can be critical in selecting out who should be treated and making

sure that those who are treated are completely treated and having the levels reduced of LDL to where they should be.

Host: How strong is the evidence that apo B is a better measure than LDL cholesterol?

Dr. Allan Sniderman: I think the evidence is extremely substantial, and there are a number of groups that they have come out with that view. For example, last year the American Diabetes Association and the American College of Cardiology issued a joint report in which they recommended that patients who are being treated with the statin drugs, the drugs that lower cholesterol, which also lower the particle, the apo B, that they have their apo B measured to ensure that they actually get the right amount of treatment to get the maximum benefit from the therapies that have been proven to reduce the risk of heart attack.

Very recently, the American Association of Clinical Chemistry also came out with a very extensive report, in which they reviewed all of the evidence that has been accumulated over the last 20 years or so, including the question of measurement itself. The apo B offers advantages to the patient in the laboratory because the patient actually doesn't have to be fasting, whereas when you go to get your LDL cholesterol measured, you do have to be fasting. Well that's a little thing; it turns out to be a big thing because it complicates peoples' lives.

But beyond that, the methodology to measure apo B is actually available in virtually every hospital, and it would require only ordering some new chemical reagents to be able to make that test available to people, whereas it isn't generally available to people today.

Host: Well, talking just from a laboratory perspective, is apo B a more difficult thing to measure than LDL cholesterol?

Dr. Allan Sniderman: No, it's actually in many regards easier to measure than LDL cholesterol. It was one of the first parameters that was standardized by committee from the International Federation of Clinical Chemistry in the World Health Organization, a group led by Santica Marcovina and John Albers from the University of Washington in United States.

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Apo B can be measured on automated machines using standardized reagents. In the modern medical world, all tests have to be monitored to make sure that you are doing a good job, but this is a very simple test to do.

Host: Well, you are not the lone crusader in this effort so to speak. There are some other people agreeing with you, some other people going that way. If the evidence that apo B could save lives, if it is as strong as you suggest then why do you think some experts oppose introducing it into clinical practice?

Dr. Allan Sniderman: It's hard to read other peoples' minds. Part of it I have been told by people is that so much effort has been spent on the word "cholesterol." Cholesterol is a word that exists in every language in the world, I am sure that how can we at this stage of the game, turn around and bring in another measurement.

My answer to that is that all of medical progress involves change. You don't get ahead without moving ahead. And what the people who depend on us, our patients depend on us is they don't really care what we measure. They care about how well we can do the job of identifying what risk they are at, and preventing them from having—if they have already had an episode, of having further damage. There is no question that it would require a considerable educational effort.

There is also no question that it would require causes of cost involved for measuring apo B. Now, I am not associated with any company that measures apo B, I have never been associated with any company that makes apo B, I don't have any stock, I don't make any money from apo B. So I have no conflict of interest in apo B, and I can say that actually I am astounded that in the medical care system of the huge difference between cost and charges, there are lots of things that are in your medical system and mine where the charge of something is far greater than the actual cost of doing it.

So, I think that in your country I know that your new President, President Obama, is trying to lead an effort to healthcare reform, and one of the reforms that's going to have to come in is that charge is more realistically approximate cost. In my hospital, the cost of doing this test is about two Canadian dollars. That doesn't mean that's what it's going to be charged for in an American hospital; it's certainly going to be higher, but it shouldn't be excessive, this is not a costly technology.

There is also a human element. People perceive that science is independent of human passion and human conflict, and science is like all of the human activity. It's chock-a-block full of human passion and conceit, and I am as human as the next.

We have to take positions if we are going to try and discover things. You have to become committed to a point of view before you actually have the evidence to support it. You don't know how it works for other people, but for me and most of the people. I know you actually have to getting your head and understanding of how the world works before you really test it.

So all of this has to protect against the built-in emotional commitments we make to positions. That's why you have this peer review and testing of your knowledge in science. But we can develop positions that are fixed, and if we have too much power in the decision-making process then that can lead to obstruction of change. A colleague, Curt Furberg, recently wrote an editorial, a commentary in the *Journal of the American Medical Association*, "Why Guideline-Making Needs Reform."

A lot of medical practice now is determined by expert opinion, and it's critical that all of the points of view come to bear on these decisions, because only when debate is opened, do you really have true scientific exchange, with all of our human practices. Science can, unfortunately, fall into the same weaknesses where people become accustomed to being both opinion holders and decision makers, and they can be reluctant to see change that they didn't initiate take place.

So my hope is there are a lot of extremely independent-minded and open-minded people and that the benefits of this technology will be realized by the people that we have developed it for the patients in your country, my country, and indeed across the world.

(09:58:00)

Host: Well, I asked you to read minds a minute ago, how about I ask you to look into the future now? Do you see this change coming about?

Dr. Allan Sniderman: I don't know. I am worried that it won't. I am worried that some of your opinion leaders are too powerful, I am worried that the pharmaceutical industry in your country is too committed to a certain form of communication that they have become extremely comfortable with.

I think there will be great loss of life that could have been saved, if it doesn't come up about. We are just generating sort of calculations what the impact could be and the impact goes far beyond the United States or Canada. Countries like India, most of the deaths from heart disease now occur in the developing world. India is the diabetic poster country for

the world, and vascular disease, it is just an epidemic in India.

They don't have a medical infrastructure as developed as ours, and this kind of technology leads itself to application in countries with much less developed infrastructures, and if they go on a pathway of repeating our practice step-by-step, then the consequences for us are real, and the consequences for them are just enormous.

So, I am not optimistic, and I am not totally pessimistic because we are trying to, in a civil and responsible way, debate the advantages and the disadvantages of different approaches to saving peoples' lives. Good people can differ, but if you want to reform your healthcare system, if you want to be able to do more for less, you got to do better technology and better biology.

So if you fight this off, then you are condemning yourself to using more old-fashion technology that's weaker, and that we'll pay the price for it.

Host: Dr. Sniderman, thank you so much. This has been great.

Dr. Allan Sniderman: Hey! Thank you so much.

Host: Dr. Allan Sniderman is Professor of Cardiology at McGill University in Montreal, and he has been our guest in this podcast from the journal *Clinical Chemistry*. Thanks for listening. I am Bob Barrett.

Total Duration: 12 Minutes