Exploring the Laragh method of treating hypertension: transcript

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Introduction

Eric Welcome to OslerCast, I'm Eric LaMotte. This episode is about how to pick the best medication regimen for each hypertensive patient. In order to do that, we're going to explore Dr. John Laragh's approach to treating hypertension. My guest, Dr. Armando Lindner, is a nephrologist with an interest in hypertension, and a lot of experience with using the Laragh method of treating hypertension. Now, neither of us recommend that you use this method as it was originally described, but still, it will teach you so many clinical pearls. It's definitely worth knowing about.

So let me outline this episode for you. Dr. Lindner and I are first going to talk about the two groups of hypertension that Laragh proposes: volume mediated hypertension, and vasoconstriction mediated hypertension. We'll discuss which drugs are best for which type, and how to figure out if your patient has one type of hypertension or the other. Then we'll also discuss some of the major hypertension trials and their implications on which drug classes to use.Without further ado, let's get to the interview.

Part I
The Laragh method of treating hypertension

Eric Dr. Lindner, Thanks for joining me.

Dr. Lindner Yeah, my pleasure

Eric Can you tell me a little bit about your background in treating hypertension, what your practice has been like?

Dr. Lindner Yes, well I used to be, and I still am, a faculty at University of Washington. In the last few years, since I retired, I'm clinical faculty. But before my retirement, I was at the VA at the time, there were very few nephrologists left in the team, and I ended up being the only one for the last two years. So for about five years or so, I was running the hypertension clinic in an informal way, but singlehandedly taking care of all the cases. Before that, I have done quite a few pharmacologic studies that help me understand the response to medication much better, in a practical way. But I was never funded to do this type of work, in terms of which medications I would use, so I have no conflicts of interest whatsoever. And so, whatever I do is based on mostly scientific fact, that I try to handle in the best possible way.

Eric And today we're going to be talking about the Laragh method of treating hypertension. Can you tell me how you came into contact with that, or how you first learned about it?

Dr. Lindner Yes, many years ago, of course, Dr. Laragh was already quite important in the field, he was the chief of hypertension at Cornell at the New York hospital, he was the president of the society of hypertension for a number of years, and he and his wife, Jean Sealey, who is a biochemist, developed a number of methods for measuring plasma renin activity, and studied that physiologically in patients, in terms of analyzing what stimulates renin, and what does not, and definitely most of what we know about the renin angiotensin system, was published by the Laragh and Sealey team. I think the contributions he made to the field are enormous.

Eric To elaborate on this, Dr. Laragh was actually on the cover of Time magazine in the 1970s for his research in hypertension. He founded and served as president of the American Society of Hypertension, and was the founding editor of the American Journal of Hypertension. And he also treated patients and taught other clinicians about his approach to treating patients. Dr. Laragh passed away in 2015, after I recorded my interview with Dr. Lindner, but before this episode was posted online.
Let's imagine you were talking with a general internist who is kind of following the JNC 8 guidelines, but has never heard of this method, how would you explain to them, the underpinnings or the understanding that you need to treat hypertension?

Dr. Lindner The concept is a hemodynamic concept, and it has to do with the elements that determine the blood pressure. And they are two. On one side you have the cardiac output, and on the other side, on the right side of the equation if you will, you have the peripheral resistance. If you are on the left side, its mostly volume and sodium. The vasoconstriction depends really for the most part, if you are on the right side of the equation, depends on angiotensin II. So really what I tell a clinician is, you have volume and you have vasoconstriction. The vasoconstriction is mostly angiotensin II.

Eric So a person with hypertension has either too much volume or too much vasoconstriction. There are a number of different pairs of terms which can be used to describe these two types.
Laragh liked to call volume-mediated hypertension V hypertension, V for volume. A patient who's only problem is volume excess has an appropriately suppressed renin level causing a vasodilated state, so another term for V hypertension is low renin hypertension. Vasoconstriction-mediated hypertension is abbreviated as R-type hypertension, with R standing for resistance, as in resistance to flow, not resistance to treatment. In these patients, there is an absolute or relative renin excess, so it is called medium or high renin hypertension. Patients with V hypertension are sensitive to changes in the sodium content of their diet, so they are often called salt sensitive patients. Patients with R hypertension remain vasoconstricted and hypertensive even without excess salt in their diets, so they are called salt resistant.

Dr. Lindner The idea is, how do you tell if somebody has a high volume type of high blood pressure, or vasoconstriction due to angiotensin II. That is, are you angiotensin dependent? Or not.

Eric Dr. Lindner, why is medium renin grouped in with high renin, as opposed to low renin?

Dr. Lindner What we call normal is what 100 people without hypertension have, what is their renin level, in relation to sodium excretion, that's the normal. But, um, for a hypertensive, relatively speaking, you would expect that the high blood pressure has a negative feedback, and actually lowers the renin. If it doesn't go down, below the normal, it's already sort of abnromal. Even a normal level he would consider, is slightly abnormal, because you would expect it to be lower than that, but it's not.

Eric We're used to thinking of secondary causes of hypertension versus primary or essential hypertension. Can you use this framework for both of those?

Dr. Lindner There are some times of hypertension that are typical of one kind or the other. For example, on the left side, the volume type, you have to definitely say low renin essential hypertension is there, and secondly, um, primary aldosteronism would be considered that one. Some forms of endocrine hypertension may fit there too, in children for example. In the vasoconstriction or angiotensin dependent side, you have high renin essential hypertension, and then you have things like secondary forms, for example renal artery stenosis.

Eric So why does this matter, why is it important for us as clinicians to have a guess about which pathway is driving a patient's hypertension?

Dr. Lindner I think the main value of this system, is that if you have an angiotensin dependent state, that means you are going to be very sensitive, exquisitely sensitive to even low doses of angiotensin blockers. ACE inhibitors, ARBs, even the direct renin inhibitor, aliskiren. Whichiever you use, you will find that these people respond to low doses, and they respond so well, that they ... sometimes remarkable. So, if they don't respond at all, what that would say is, either the angiotensin is less important in a case, or else there is also an important volume component. You can unmask that, giving the patient a very low salt diet, and/or diuretics. If now, you see a significant fall, a measured fall back to normal, then you can say one is possibly more volume than anything else. But only if you see a drop in blood pressure that is moderate, certainly better than before, but you are using just ACE inhibitors, then you can say maybe there

is a combination, where I have an angiotensin excess and then I also have a volume condition, so there may be more than one factor involved in hypertension. both sides of the problem can be high. You can have a vasoconstriction due to angiotensin II, and you can have a high cardiac output due to too much sodium and volume.

Eric So, so if a patient has a high renin hypertension and an ace inhibitor would work particularly well for that patient, what if someone has a low renin hypertension, what would be a good antihypertensive for that person?

Dr. Lindner A diuretic, or a calcium blocker. Either one of those. Again, um, when you start people on diuretics, you may improve the situation in some. Diuretics unfortunately don't work for everybody. In the ALLHAT study, they were able to lower the blood pressure back to normal in less than 50% of the patients. So it's not that effective. So if it doesnt work, it may be that you have an angiotensin situation.

Eric So why would calcium blockers be considered volume drugs, if they cause lower extremity edema? That side effect suggests an increase in volume.

Dr. Lindner I did a study in renal physiology in conscious dogs in which I looked at the renal effects of calcium blockers. That was published a nyumber of years ago, quite a few, but it was a classic physiology of the whole body p hysiology, not cellular, and I showed very very clearly that calcium blockers actually are diuretics, and surprisingly, they are one of the most powerful diuretics that we know of, because they work in the proxiaml tubule. They inhibit sodium reabsorption in the proximal tubule. Unfortunately, all of that sodium going down that tubule finds the distal tubule, and some of that gets reabsorbed again. But again, there is some net losses of sodium, that are equivalent to what you will find with a diuretic like say chlorthalidone or maybe any of the thiazides. So they are weak diuretics. So why do the people have edema sometimes with these agents? It so happens that the edema is due to local hemodynamics in the leg. Well you have venodilation too, and decreased venous return, and therefore you have some trouble in returning all that fluid from your legs up to the circulation.

Eric It's clear that knowing the patient's type of hypertension is going to help us find the best drug to treat them. But how can we tell what type of hypertension a patient has? There are three ways, and we'll discuss them in the same order they can be used clinically.

Dr. Lindner One of them is to simply look at, is the patient African-American or white? Is the patient, obese, older, diabetic, or not? And if you have somebody who is, and this is done by a good study by I think this is matherson at the VA, one of the VA studies, in which they looked at this and they found that if you are older than 60, obese, especialy if you are h the, and/or diabetic, all of those make you very likely to be volume dependent. But if you are white, skinny, never failed a resistance drug like lisinopril, and you are not diabetic, chances are you will have an angiotensin dependence. So when somebody opens the door into my office, and comes in and says OK, I have high blood pressure, and I look at the man, or the woman, and I immediately make an estimate that this is most likely (although it's never 100%), it definitely is a guide that will allow me to choose some of the first medications for that patient, you know which one I'm gonna use.

Eric Ok , which is more common, volume or vasoconstriction.

Dr. Lindner I believe that probably high renin is the more common form. Dr Lindner, can you tell me about the first way to get a sense of what type of hypertension a patient has?

Eric OK so to summarize that, overall medium/high renin hypertension is more common, but factors that make low renin hypertension more likely are an age over 60, African american race, obesity, and diabetes. So this gives us a first guess of a patient's renin status. This guess might be right about 60% of the time. It's not that much better than a coin flip, but it's still a little better. Now if you look at the JNC 8 guidelines in light of this, the lighbulb over your head is going to light up. Notice that if you just use this first approximation alone, you will end prescribing the antihypertensives that are recommended by the JNC 8 guidelines and other recent guidelines. They recommend giving calcium channel blockers or diuretics to older patients, and African-American patients, and lisinopril to younger, Caucasian patients, and this difference in the prevalence of the different types of hypertension explains why.
So Dr. Lindner, what did Dr. Laragh teach as the next way to refine our guess of what type of hypertension a patient has?

Dr. Lindner When the patient comes in, we also look at the effect of every medication. Is it helping or not? And depending on the response, he [Lindner] can tell if he was right or wrong. By choosing for example an ACE inhibitor, if it didnt do anything, he was wrong, The point is, the proof is in the pudding. That's in his own words. If something works with ace inhibitors, its angiotensin dependent. If it doesn't, its not. In the end, he simply looks at the response to medication as a probe. And this is what we do, and this is what we did at the VA.

Eric Dr. Laragh used the Latin term, "diagnosis ex juvantibus," for this process, which means inferring the diagnosis from the effective treatment. So assess whether a medication is helping, and if it's not helping at all, you can stop it and try a medication from the opposite class. But keep in mind that a patient may need to be on a combination of anti-V and anti-R drugs. So we've now talked about two strategies to guess a patient's renin status: using demographic information, and using response to treatment. Let's discuss the third strategy, the most controversial strategy, which is checking the plasma renin activity level.

Eric If you're using a plasma renin activity, what are the cutoffs that you would use. Just looking at the renin activity, what determines low, medium, high?

Dr. Lindner I use Laragh's method, he says that if you have anything more than 0.65 ng(/mL). Below 0.65 he calls it low. So thats his cutoff, is 0.65.

Eric There are a few subtleties to interpreting the PRA when patients are already on medications.
Diuretics and calcium channel blockers will cause the body to lose salt, so the renin activity will be driven up to compensate. Beta blockers should lower the plasma renin activity because they're preventing activation of renin by endogenous catecholamines. The toughest effect to understand is that of ACE inhibitors or ARBs. These meds block the effects of the renin angiotensin system downstream of the production of angiotensin I by renin, so negative feedback mechanisms will ramp up the production of renin and angiotensin I. So the plasma renin activity will actually go up, by about a factor of 10, but the angiotensin I that's getting produced is not going to have a downstream effect on blood pressure. Therefore for ACE inhibitors and ARBs, Dr. Laragh recommended dividing the renin activity by 10 and cosnidering the result to be the effective plasma renin activity, which you can compare to the 0.65 ng/mL cutoff.
Renin testing is controversial because theres's a wide range of ideas about when it should be used. The hypertension guidelines don't discuss checking renin levels at all in the management of plain old primary hypertension. Dr. Laragh's recommendation was to check the PRA early and often. He even recommended using it at the first visit where a patient had an elevated blood pressure, even before hypertension was confirmed at a second outpatient visit. That way, he could use the level to determine which drug to start at the next clinic visit. He developed an algorithm that recommends which drug class to add next, based on the patient's current medication regimen and their PRA level. For example, If a patient still had a low renin when treated with a V drug, he would recommend adding another V drug. Otherwise, most patients would be put on a VR combination.
He and others published an RCT in 2009, comparing this algorithmic method against clinical care provided by hypertension specialists without the benefit of renin testing. They found that blood pressure was controlled in 74% in the renin testing group, versus 59% in the hypertension specialist group, despite having similar final numbers of antihypertensive prescriptions. I thought this study was pretty cool, especially because the algorithm could be followed by any primary care doctor. But this studied the algorithm in resistant patients already on multiple drugs and referred to a hypertension clinic, so the initial part of the algorithm still really hasn't been studied with an RCT.

Dr. Lindner That introduces a cost element that not everybody wants to pay.

Eric And the PRA doesn't have perfect test charactersitics either. If you started with a 40 year old caucasian patient with a 70% prior probability of having high renin hypertension, and you checked plasma renin activity and it was actually low, you'd go from a 70% chance of high renin hypertension, to somewhere around a 50% chance. And if the plasma renin were high, you'd be confirming what you pretty much already knew. So testing wouldn't really be helpful in the cast. To get the most bang for your renin-testing buck, from a Bayesian perspective you'd want to test the patients whose demographics leave you with a 50/50 chance of having high or low renin hypertension. That would be black patients younger than 60, or white patients older than 60. This is what Gary Schwartz and others recommended in 2013 based on a retrospective analysis, which is linked to in the show notes. Dr. Lindner, When would you recommend checking a plasma renin level?

Dr. Lindner Well when there are problems. For example somebody who is very resistant, and is not responding to the usual medication, I think it makes sense. Also, like we used to do in the early days, looking for renal artery stenosis, you are looking for the very young, and the very old. The very young, because they may have something like an endocrine problem or renal artery fibrosis. Fibromuscular dysplasia. In the aged, you have renal artery stenosis. Someone who had a normal, uh who had a good blood pressure and then suddenly becomes hypertensive, there too I would look for renin activity.

Eric Would you say that Dr. laraghs method is considered controversial among nephrologists or hypertension specialists?

Dr. Lindner Yes, yes it is. But i cannot tell you if this is because his analysis is suspect, which I don't think so, I think the analysis was excellent, and was based on a lot of good information at the time, I think there may be other reasons why it hasn't become popular. One of them is that the cost of doing plasma renins in a lot of people, and if you can handle the patient without, you are saving money. So that's one reason. there may be others that have to do more with the politics of the treatment of hypertension, and the tendencies that you support. If you ahve preconceived ideas that diuretics are fantastic for hypertension, because your company sells them, then you're going to color all of your results by that idea.

Eric So to summarize this discussion on when to check a PRA in treating hypertension, there's really no clear consensus. This is a cheap test, it costs about $30, although in the US, the patient may be billed up to $70. So we shouldn't be afraid of using this test to help decide on the next agent to use in a patient who has been really difficult to treat.

I'd like to switch topics to another focus of controversy, which is when to discontinue seemingly ineffective medications. One of the differences between Laragh's method and JNC 8 is the idea of discontinuing drugs that don't seem to be helping. The previous JNC 7 guideline suggested that if someone isn't well controlled on a drug, you can try switching to monotherapy with another drug class. That's also what Dr. Laragh recommended. That language is gone in JNC 8, and the approach that they advocate is to keep adding more and more drugs until the patient is controlled. Dr. Laragh felt that every patient should have the opportunity to be on the appropriate monotherapy for their type of hypertension, and that opportunity would be lost with the new recommendations. He would say, just because you faled monotherapy with chlorthalidone doesn't mean that you would fail monotherapy with lisinopril.

Dr. Lindner He was looking for economy of thought, and economy of treatment, and there is something to be said for that. I still try to stay economical, we spend too much money on treatments of these patients. And with very little results sometimes. In JNC 8, they always add a second drug. JNC 7 was nicer in my opinion, because it allowed you to switch. And that's my basic approach. If something doesn't work, don't use it. My example would be, if I take a bus to go from here to downtown, from university to downtown, and all of a sudden, I'm going north to Vancouver, I realize I'm on the wrong bus. So I have a choice, do I stay on the bus til I'm in Vancouver and then come back, or do I get off, cross the street, and get on a bus that will really take me to where I want to go. And that's my approach. I get rid of things that don't work. Because if they don't work, they're not going to work, no matter what.

Eric That completes our discussion of the Laragh method. In the second part of this episode, Dr. Lindner and I will discuss a few hypertension trials, some of which Dr. Lindner feels have been over- or under-rated. It's interesting to think about these landmark trials in hypertension using Dr. Laragh's framework.

Part II
Antihypertensive medications and trials

Eric Let's talk about some of the antihypertensives, starting with diuretics. ALLHAT was the major trial in the early 2000s that established diuretics as the go-to antihypertensive. But Dr. Laragh published some significant criticisms of ALLHAT, the major one being that it didn't really study monotherapies, because most subjects in each group were uncontrolled on the monotherapies that they got started on, and then beta blockers were the universal second agent that got added. So it really compared a lot of patients on a diuretic plus a beta blocker, versus people on an ACE inhibitor plus a beta blocker. Most patients are going

to do better with a VR combo than two R drugs. So his biggest criticsm of ALLHAT was that the design favored diuretics from the start.

Dr. Lindner Mine too, I agree with that wholeheartedly. I think that the ALLHAT study was done by people who had a preconceived idea, in which they wanted to defend the diuretics at all costs, because they were in the so-called diuretic lobby, and therefore they did everything they could to demonstrate, and in their conclusions they say, that the diuretics are equal to or better than all the other drugs, the newer drugs, like calcium blockers and ace inhibitors. In terms of cardiovascular outcomes. They are as good as. The way I read the conclusions, is all the other drugs are as good or better than the diuretics. Because the diuretics are not all that effective in that study. They use chlorthalidone, their results were less than 50% of the people improved their blood pressure, and more importantly, there was a tremendous amount of metabolic side effects**.** If you are lowering somebody's blood pressure with that drug, but you make him a diabetic, you're not doing that patient any favors. And those that have diabetes in the first place, worsened. And they require either more insulin, or more metformin, or whatever.

Eric Diuretics can cause hypokalemia, which is not totally harmless.

Dr. Lindner Hypokalemia on diuretics is fairly common and it's one of the reasons that diuretics are not as good as they are claimed to be. Its very hard to treat hypokalemia orally with potassium chloride. Because, if you have a urinary leak, its going to continue leaking. And no matter how much you put from the top, the tank will leak at the bottom, and its better to put the bubble gum and plug the hole in your car if its leaking gasoline, the same with potassium. It works better to stop the leak, and so once you know more or less why the leak is there, or if you measure potassium in the urine and its high, at the time he's hypokalemic, you know for sure he's, you know losing it in the urine. So the answer is to block that, and we have very efficient methods. I have used, for many years, amiloride for that, and amiloride will help in many cases, improve the potassium, and at the same time lower the blood pressure too.

Eric Let's talk beta blockers. These aren't firstline for hypertension, so why is that? Dr Laragh believed there was a paradoxical pressor response that can occur in patients on beta blockers.

Dr. Lindner Oh yes, that happens, and it happens specifically with beta blockers. Which is one of the reasons not to use them. When I studied them at the VA, in a study of benazepril, one of the ACE inhibitors, we had to remove the beta blocker in hypertensives, wait for a washout period, up to three to four weeks, and if the blood pressure went up, off the beta blocker, then they could be started on a calcium blocker, or the benazepril that we were studying then. The great surprise is that in elderly people older than 65, when they came in, and they were on beta blockers at the time, and you remove that, after a week of time, the blood pressure fell, and it fell down to normal. And I had as much as 35% of the volunteers for that study improve their blood pressure off the beta blocker, and so the question was, after a month, six weeks, they continued to be normotensive, when they were hypertensive on beta blockers, definitely there is a group of people or a subgroup of patients, that has a paradoxical hypertension with beta blockers.
There is also the fact that if you look at central blood pressures, compared with peripheral blood pressures, and that can be done very easily today with non-invasive methods, like pulse wave analysis on your radial artery, if you look at, derive the formulas for central pressures from peripheral pressures, you will find that the most important pressure is the central pressure, its what happens in your aorta, because it correlates better with any kind of cardiovascular outcomes, so there are many reasons to measure central pressures instead of peripheral. If you look at central pressures, beta blockers may lower the peripheral a little bit but increases central pressure, which is a pseudoantihypertensive effect. There is no real antihypertensive. And in fact its raising your central pressures. And I was an example of that myself. I had it checked with pulse wave analysis on beta blockers, and later on, on calcium blockers. The results were amazing. Beta blockers increased my central pressure and did not do much for my periphery, but calcium blockers like amlodopine at low dose, lower everything, the peripheral back to normal, and the central down to 115, at the low dose, of only 2.5 of amlodopine.

Eric Are you sure that you don't sell amlodopine, Dr. Lindner?

Dr. Lindner No, no I'm just referring to real measurements. There is a very good analysis of all this, done by Frank Messerli, in Circulation, 2008, its a very very well studied, uh analysis of all of the evidence on beta blockers, and his conclusion was they have no role in the treatment of hypertension. They may be used for cardiac disease, for arrhythmias or tachycardias, for angina, yes, but not for the treatment of hypertension.

Eric No discussion of treating hypertension in the US in 2015 would be complete without discussing JNC 8. You mentioend earlier that you prefer JNC 7 in some ways?

Dr. Lindner Well, as you know, when the JNC 8 report came out about a year ago, it was not an official report. It was published by a number of people, that were in the panel studying the JNC 8, but the NIH withdrew from that study and did not allow the publication of the report, so the members of the panel took it upon themselves, to come with a paper anyway that was not the official decision of the NIH or the [American] Heart Association. At the same time, within days, the Annals [of Internal Medicine], published the minority view of the JNC 8 panel, and these are the people who believe that lowering the blood pressure goals, the targets, of blood pressure treatment, that is, raising the blood pressure at which you start treatment, or stop treatment, it can be detrimental to society. And in fact knowing what we know today, about the effect of the high blood pressure on cardiovascular disease, it's really risky to relax those goals. And I happen to go more with the minority view, than with the majority in this case.

Eric It seems like they were being kind of conservative, they didn't want to recommend more than what the evidence had strictly shown, (yes) but there wasnt any evidence that its bad.

Dr. Lindner Yes, but, but, being conservative is not always good for you, or for society, what is conservative in this, they only use randomized trials, of which there are few, but they ignore many that are just as good, although smaller or not randomized necessarily, which is the highest levels of evidence, but because there are so few studies, their report is based on so few studies too, and they excluded a number of impressive studies, like the ACCOMPLISH stuff, for example ACCOMPLISH was not included in the original report. They had to come back in 2009, and they decided oh come on, we have to include ACCOMPLISH, because its a landmark in the study of the treatment of hypertension, its something that changed the field entirely, and they did not include it. Only later on they came in to look at it. Also, its based on some studies that in themselves, have a lot of question. ACCORD, for example, looking at hypertension in diabetics, is totally flawed by the use of an increased amount of medication, they used in the ACCORD trial that is one of the bases for this report in diabetics, they increase the treatment by adding more and more of the most toxic drugs. By adding more alpha blockers, diuretics, and beta blockers, and at high doses, so they also increase all of the possible metabolic side effects, so if it didn't do any good to the poor diabetics that took all that combination, its not surprising, I reanalyzed, I got into the study, to look at these figures, the increase in the use of alpha blockers was 1000%. Now, since ALLHAT, we are not using alpha blockers anymore, because it was one of the original groups that was eliminated from the study, when they found that alpha blockers had a higher cardiovascular mortality and congestive heart failure than all of the other groups, so ten thousand patients were eliminated from ALLHAT, and when they demonstrated that alpha blockers are bad for you. And we cannot ethically continue this group, so they removed it. So we don't use alpha blockers, except for prostate. You know, if you have a problem with your prostate, you may have to take alpha blockers, but don't take them for hypertension because you increase mortality.

Eric So it seems like, its a question of not jsut what blood pressure should we treat to, but what should we use to get there.

Dr. Lindner What should you use, or how do you get there. And the way they got there, was by using everything that was the old treatments, alpha blockers, diuretics, and beta blockers. As opposite to the new treatment, all of the angiotensin blockers, and the calcium blockers. And one of the early studies that demonstrated the beauty of treating with the newer agents, was the ASCOT-BPLA study, that was one in England and Scandanavia. If you look at the ASCOT study, it showed that the effects of treating with the new agents, was much superior to the old ones, diuretics and beta blockers, and they had to stop the study prematurely, because ethically it was impossible to continue, once it was shown how much better the new agents were. Cardiovascular effects, I'm talking about. Not just treating high blood pressure, we're talking about cardiovascular outcomes. So I recommend to everybody, to read the ASCOT trial, and definitely the ACCOMPLISH trial.

Eric That brings us to the end of our discussion on drugs and hypertension trials. To summarize, Dr. Lindner favors the use of ACE inhibitors and calcium channel blockers over diuretics, and all of these drugs are favored over beta blockers and alpha blockers. The ACCORD trial studied strict vs. liberalized blood pressure control in diabetic patients, andit found no improvement in cardiovascular outcomes with strict control, but more medication related events. But it did it using some pretty toxic antihypertensives that we no longer consider firstline. So maybe that question needs to be asked again, using the current first

line drugs. How do we know that current drugs are less toxic? Well, the ASCOT-BPLA looked in a different population of hypertensive patients with or without diabetes, but it compared a calcium channel blocker/ACEi regimen against a diuretic/beta blocker regimen, and was stopped early due to a decrease in many of cardiovascular complications used as secondary endpoints. And the ACCOMPLISH trial found that amlodipine performed better than hydrochlorothiazide at reducing cardiovascular events when each was combined with an ACE inhibitor.
I want to thank you so much for joining me with this interview!

Dr. Lindner Well, thank you for inviting me, my pleasure.