Kendal Williams, MD (Host): Welcome to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams.

In this podcast, we seek to bring together members of the Penn Medicine community and have collegial discussions about different topics that are of concern to all of us. The purpose is to spread the knowledge and expertise that is at Penn to all of us within the community, and also to the greater world.

We're still doing our introductory series. And so in this series, we've chosen topics that are of interest to all of us, conditions that clinicians at Penn and other places manage every day. No condition fits that category more than hypertension.

Today we're going to talk about some of the nuts and bolts of blood pressure management.

We've brought in two experts really on this topic, from the Penn community. Dr. Jordana Cohen is a Nephrologist and Hypertension Specialist in the Renal and Electrolyte Division at Penn. She also maintains an appointment in the Center for Clinical Epidemiology and Biostatistics. Thanks so much, Jordy, for joining us.

Jordana Cohen, MD, MSCE: Thank you so much for having me to talk about my favorite topic.

Dr. Williams: I'm also joined and she's in the cohost chair today, my colleague Alison Purcell.

Alison is a Family Nurse Practitioner at Penn Family Care which is the Department of Family Medicine and Community Health. And she runs the Hypertension Program which includes running the Hypertension Clinic as well.

Allie, thank you for coming.

Alison Purcell, MSN, CRNP: Thanks so much for having me.

Dr. Williams: So hypertension is something we manage all the time. But even for those of us who do it all the time, subtle questions and challenges come up. And for this podcast, we wanted to start with the fundamentals, talk about the major classes of drugs, some of the subtleties of using them and get a little bit into the more challenging scenarios that are common.

One of the goals of this podcast generally, is to get beyond the textbooks and really have collegial discussions that become practical advice as we care for our patients. So, you know, these are kind of the water cooler conversations that we have about, well, how would you manage this? That's what we want to capture in this podcast.

Let's start with a typical case, a 58 year old woman comes to your office for the first time, she is in good health overall, but is noted to have a blood pressure of 156/88. You look back at the various encounters she's had. And note that she's been high in the same range before. She admits no knowledge of high blood pressure, and nobody's ever mentioned to it, to her previously.

This is a fairly common experience for me and I'm sure it is for others. And now I'm faced with a patient who feels fine. And I have to now move them through a process of understanding that they likely have elevated blood pressure. They're going to need to address it, and they're probably going to need to take a medication possibly the rest of their lives.

So, there's a little bit of convincing. And one of the first things that patients ask is, is the blood pressure real and a lot of people feel that they have white coat hypertension probably more than actually do. So Jordie, I'm going to punt this to you first. What are some of the ways you approach proving to yourself and others that the blood pressure elevation is actually real?

Dr. Cohen: Yeah so this is a big challenge, especially as you mentioned that many people are convinced that they have white coat hypertension and don't necessarily have it. And we really have to prove that.

So if they were seen in my clinic, luxury of having 24-hour ambulatory blood pressure monitors about 10 feet from my office. So, that's always my immediate go-to.

And of course, everyone in the primary care practices is welcomed to refer their patients, to us, to use our ambulatory blood pressure monitor devices. This is the gold standard way to diagnose whether or not somebody has white coat hypertension, masked hypertension, meaning the normal office blood pressure and elevated out of office blood pressure or they have true, genuine uncontrolled hypertension.

And so this is recommended by the USPSTF, it's recommended by the AHACC guidelines. And we really stand by that. It's the most phenomenal tool we have to do it, but it's not always accessible to everybody. And it's not very convenient for patients. Because it means wearing that ambulatory blood pressure monitor for 24 hours.

It goes off about every half hour during the day and every hour at night, so it can disturb sleep and it can disturb people's jobs. It's an amazing tool and I still push it in as many people as I can convince to do it. But obviously the much more accessible option is doing home blood pressure monitoring, which is an outstanding tool, also.

But of course it has to be handled with care. Not every patient can afford a monitor. We know that several of our practices have obtained grants and other ways to lend out monitors to patients when that's the case. And even once they're able to get one it's the matter of, is it an accurate monitor and are they checking their blood pressure correctly?

And that's something that takes time and a lot of caution to make sure that people are doing things correctly so we can trust the numbers. It means sitting a patient down and showing them this is exactly how you should check your blood pressure.

I usually refer patients to my favorite infographic on targetbp.org, which has just a beautiful one pager that was created by the American Medical Association and American Heart Association that walks patients through in a very visual way, exactly how to check their blood pressure with the feet flat on the ground, with their back supported with their arm of, at the level of their heart, to in front of them, checking more than one reading in a sitting, making sure they've sat for five minutes, making sure they're in a quiet room.

If you can communicate all of this to a patient in a very simple and straightforward way, it can go an incredibly long way in making sure that we actually can trust the readings we get. But I wouldn't diagnose somebody with diagnosis of hypertension in this day and age, just with office readings alone, given how much evidence we have of how true it is that hite coat hypertension is real that treating it can cause harm and can make our patients lose trust in us because we can cause hypotension, we can cause adverse effects that aren't necessary.

And I really am a firm believer in confirming with out of office readings in most patients, unless their blood pressures are running greater than the 160/100s.

Dr. Williams: And Jordy, I've just want to highlight that's targetbp.org.

Dr. Cohen: Yeah. That's the website target, so T-A-R-G-E-T bp.org. And it's sponsored by the American Heart Association and American Medical Association.

Dr. Williams: So Allie for you in a primary care environment, is this similar to your experience as well?

Ms. Purcell: We are trying to get patients to do self-monitoring of blood pressures at home, as much as we can for the past few years. We've been as a group closely with leadership from Cory Rhodes and Penn Partners in Care, to also try to have a nurse care manager a nurse run model across some of the practices to follow patients home blood pressure monitoring, and of course using American Heart Association guidelines for getting the patient the right sized cuff, getting them a validated cuff, having a plan for how they're going to get us their numbers.

And trying to push patients to do this, you know, very intensive seven day, twice a day. But in really just encouraging them to do it when they can.

We certainly have barriers of cuff coverage. We have barriers of patients having the time to come and learn how to use it. We have resource barriers just in terms of being able to teach the patients and the technology, but we do try to prove that and make sure that the cuffs are validated.

Dr. Williams: Yeah, I would say that a lot of my patients get home BP cuffs and get serious about it. I do have difficulty getting ambulatory blood pressure monitoring. So, I'm usually fairly selective about who I order that for. Think I probably do it in young people. Most people who I'm not really sure they are maybe less than 40 and I'm trying to sort out, do they really have high blood pressure, especially given some of the low prevalence in that community. And the fact that they'll be on a blood pressure medicine, the rest of their life. If I document that it's real.

So, let's talk about the issue of the revised blood pressure targets.

You know, moving down to 130/80 has made a lot more people hypertensive, and I think that's a challenge in primary care. Jordi, can you speak to the reasoning behind changing the targets?

Dr. Cohen: Yeah, so it's driven by meta-analyses of several trials. But mostly to off course driven by the SPRINT trial, which was our famous really landmark randomized control trial that randomized patients who were at risk for adverse cardiac events to either a blood pressure of less than 140, which was the standard arm or a blood pressure of less than 120 which was the intensive arm.

The people in the 120 arm achieved blood pressures that were in the 120s. So, not less than 120 on average, their blood pressure was about 122. And they had the study as many folks will know, the study was stopped early because they had such an impressive reduction in cardiovascular events compared to people in the standard group.

And this is now more recently been corroborated by another study in older patients in Europe. And so we're seeing that this is really consistent across many studies that, that more intensive blood pressure control really seems to be incredibly beneficial and there's evidence to support doing it. And it really threw a lot of people for a loop. These guidelines came out not long after JNC8, which had gone in the reverse direction and had recommended looser blood pressure control in older patients. But I think it's important to really think about that change in the context of why those guidelines came out the way they did.

They were based off of specifically that group being tasked by the National Institutes of Health to only provide level 1A evidence. And there hadn't been any trials yet that had looked at intensive blood pressure control in non-diabetics in the way that SPRINT had. And so they weren't allowed to use pool data from trials that, where that wasn't the primary endpoint.

They had to just use data from trials where that was the goal. And there was very limited evidence. And so a lot of what JNC8 was a lot of expert opinion or discussing what evidence we had and admitting to an absence of evidence.

And so I, I think that folks really lost a lot of trust in these 130/80 thresholds because of that timing, that unfortunate timing of how all of this information came out. But more and more, we're seeing a lot of data to really support these more intensive blood pressure goals for reduction of cardiac events and for reduction of dementia.

Dr. Williams: That's great. It's been a challenge. I mean, I think definitely in primary care getting from 130 to 140 to 130 may often involve the addition of another medication or other issue. So, it is a challenge and it's nice to know there's good evidence behind it.

Dr. Cohen: Yeah though to your point though, in people who are very difficult to control that's one group that we're not a hundred percent sure. People who need like that fourth or fifth medication to get them to that blood pressure of less than 130, instead of less than 140, we may be causing more harm than good.

So it's always important to think about it in the context of the patient. Am I potentially introducing an adverse event that could cause this person harm? Always check orthostatics and make sure that you're not making somebody have worse orthostatic hypotension, of course or increasing the risk of falls. And of course, think about potential risk of electrolyte abnormalities.

Dr. Williams: So the next thing I like to do is to use the opportunity of the discussion of hypertension with patients and the targets to talk about lifestyle factors with them, because there often are lifestyle factors that can be adjusted to make a difference. So I, recently recertified for the boards and in the process of studying for that, I was really struck by the data that suggested you get up to 20% reduction with lifestyle factors alone, including alcohol reduction.

So, I just want to throw it out to both of you in terms of those types of discussions, what is your expectation that you can achieve with weight loss and some of the other things that we do? And how do you go about talking to patients about that?

Ms. Purcell: At Penn Family Care, I where, we're serving many of our patients in west Philadelphia. I try to drive home the sodium aspect and pushing a low sodium diet, discussing their snacking habits, discussing what access to food they have, trying to understand if they're in food desert area or a place where they are limited, or if it's just a matter of meal planning and snack planning ahead of time.

I think patients are really excited to have those conversations. I think having those conversations versus the hesitancy of adding a second or third medication is something they're very interested in and they want more information. So, I think they will be more and more interested in getting more sodium reduction.

Dr. Cohen: Yeah, I completely agree. And I have a smart phrase. If anybody wants to steal it from me, that is dot Jordy lifestyle modifications, which is actually a chart of all of the randomized control trials. And what they've shown on average people's reduction in blood pressure is based of each lifestyle modification.

So for my more savvy patients, I print out this chart to give it to them so that they can see a concrete number of what on average we expect. But I always give them the caveat of every person is different. And if you exercise more, it may or may not help to reduce your blood pressure, but I can guarantee it'll very likely reduce you risk of serious cardiac issues in the future, even if it doesn't improve your blood pressure. So, that's usually how I, pose it.

One other thing that it's in, that's included on there that I think folks don't always know about that not just sodium reduction, but actually the addition of potassium has a huge impact on blood pressure.

There was just a very exciting cluster randomized control trial that was done in China that was just presented at the European Society of Cardiology conference, which demonstrated that when you randomize people to a, potassium based salt substitute that people's blood pressure on average really does lower quite remarkably on a population level.

This can really mean a great deal in terms of long-term cardiac risk. And there have been smaller trials of potassium supplements that have demonstrated similar, very impressive reductions, even more so than the reduction in blood pressure you get from restricting salt with regard to your blood pressure control.

And so, we really do you think this is an incredible potential intervention when appropriate. Obviously not in my patients with more advanced chronic kidney disease who can't excrete their potassium well but in most people it's a really great thing that you can suggest to them. And it means adding something rather than taking away, because there are so many tasty foods that are high in potassium, like citrus fruits, for example. It seems like it's a really, it's a win-win.

Dr. Williams: And so you recommend that potassium increase mostly through foods?

Dr. Cohen: Yeah. Mostly through food, especially because most high potassium foods are quite healthy as well. And even potatoes are fantastic. I just say it's just not in the fried form.

Dr. Williams: I'm not familiar with potassium based salt substitutes. Are they common?

Dr. Cohen: Yeah. No Salt is an example of it in the that's available in most supermarkets. So, most salt substitutes are potassium based.

Dr. Williams: Oh, that's terrific news. That's going to have some personal ramifications on my own life, looking for those salts substitutes. So, you know, I think that global perspective is, and, Allie had said this is that, you know, you can almost use this as a carrot because the lifestyle factors, other than maybe the potassium issue, but you know, reducing alcohol, reducing weight and so forth, have benefits that are beyond that, the reduced risk of diabetes and cholesterol and so forth.

So, they target those other risk factors. I often kind of use this as the carrot to try and get people to move towards those kinds of behaviors. Once you get to the phase where you now need to start a medication, it now becomes an issue of which one. And you know, there are probably dozens of options. But I think in the modern day it really comes down and you can correct me, but it really comes down to four main classes, thiazide diuretics, ACE inhibitors, angiotensin receptor blockers, or ARBs, and calcium channel blockers.

When I was in training and this is going back into the late nineties, early two thousands, we used to use beta blockers quite a bit. And I want to discuss those later but now I think that's those four main categories.

Jordy, would you agree?

Dr. Cohen: I completely agree and very glad to hear that you're no longer using beta blockers as first-line agents.

It's something that we discovered as being done more often than it really should be, especially in the community. And some of the research we've done and it's really a dangerous agent to consider for first-line antihypertensive treatment until you've gone through these other four classes that you mentioned.

Dr. Williams: Can you expand on that a little bit, because, I personally had gone through this period where I trained and I trained in primary care. I trained, I practiced primary care. And then I actually went to hospitalist medicine for a period of time and then came back to primary care. And I sort of missed this period where that switch occurred.

Can you elucidate a little bit of the data that led to that switch?

Dr. Cohen: Yeah, with pleasure.

The ALLHAT trial was of course our main enormous randomized control trial of tens of thousands of patients in the US that really identified our optimal first-line antihypertensive therapies, and ALLHAT

trial patients received, they were randomized to either receiving chlorthalidone and lisinopril, amlodipine or doxazosin.

And the doxazosin arm was actually ended early because of elevated risk. But that's where we get those original three classes of the ACE inhibitor, the calcium channel blocker and the thiazide diuretic or thiazide like diuretic, really being our optimal first-line agents.

Then more additional trials that have come out over the last couple of decades have really clarified it. And observational studies have clarified that beta blockers are associated with an elevated risk of heart failure and some cardiac events when used for first-line antihypertensive therapy. And they also have higher risk of adverse side effects as well.

And so we do try to avoid these for first-line anti-hypertensives. Of course, if someone has an indication to be on a beta blocker, it's another story. If they're being used for prophylaxis for migraines, if they're being used, of course, for atrial fibrillation or for post myocardial infarction reduction of cardiac remodeling or for some, sorry for appropriate use with cardiac remodeling. Then of course they're the appropriate agent but not just for run of the mill hypertension.

Dr. Williams: So let's go through each category and I want to tease out some of the features of each of them. I'm going to sort of ask you to sort of almost free associate, both of you about these various classes. So let's start with thiazides. So we've got hydroclorothiazide and chlorthalidone. Primarily hydroclorothiazide also comes complex with triamterene as Maxide and Dyazide and so forth. So, Allie, maybe I'll punt it to you. What do you think of when you think of thiazide diuretics? How do you think about this class of medications?

Ms. Purcell: I think of it as a first-line. In recent months and years, I've also been thinking about it in combination therapy which is where I'm using it more and more. I do worry, I see so much hypokalemia on rechecks these days. So, you know, monitoring that really closely, I was really excited about chlorthalidone for a while in studies that said use that first rather than HCTZ, but I have seen so much hypokalemia on repeat labs that I've kind of gotten away with it and moved towards the dual agents.

I'm interested to hear from Jordy where her take is, and then also, you know, what kind of patient that you would just want to start a thiazide or a monotherapy agent.

Dr. Cohen: Thanks. Yeah, I agree with you.

I think first-line agents, of course. And I think hydroclorothiazide is best in combination therapy because it is a pretty weak antihypertensive on its own, but it can still be great for the right person, especially people with salt sensitivity and chlorthalidone, I think is superior of course, but unfortunately it's not available in that half dose, we can't, and it's very hard to cut in half. So, the electrolyte problems are real.

But the reason that it is superior is because it's longer acting. And so chlorthalidone really does last for a full 24 hour period. So it helps to reduce some of the issues with urgency that you see with hydroclorothiazide, but also more so you end up with having that better antihypertensive effect for that full 24 hours.

Whereas with hydrochlorothiazide, it tends to wear off after about 12 hours. So, when patients take it in the morning, if they have a very salty meal at dinner, they're not getting protected overnight from it. So it's not quite as optimal except I still obviously use it all of the time.

But it's best when paired with a long acting ACE inhibitor or ARB, because at least they'll get coverage overnight. But like you said, the electrolyte abnormalities are the biggest problem, chlorthalidone is known to have higher risk of hyponatremia and hypokalemia than hydroclorothiazide.

Anytime that I do see hypokalemia in a hypertensive patient, even if it's provoked by thiazide diuretic, I think it's a really great opportunity to check a renin and aldo just to make sure it's not somebody with primary aldosteronism that was triggered that just exposed itself based off of the thiazide.

Dr. Williams: Yeah, it's actually a good way to test for that isn't it?

Dr. Cohen: Yeah, it is a good stress test for it.

Dr. Williams: The diuretic effect of hydroclorothiazide, my impression is that it wears off over time. The drug continues to work, but the people notice less diuretic effect. Is that based on anything?

Dr. Cohen: Yes, it does. It is. It's usually based on the fact that you've gotten that often people are initially quite volume overloaded and then once they've been on it for a longterm, they're less so, so I think that tends to be the reason for it. But yes we observe that as well.

Dr. Williams: So let's talk about ACE inhibitors next.

Most of us are probably most familiar with lisinopril, but of course there's others. So when I think of ACE inhibitors, I get warm feelings.

One part of my career, I was directing the Center for Evidence-Based Practice at Penn, and we would do evidence summaries, systematic reviews on questions of all kinds. So, we got used to looking at a lot of sort of aggregated data and meta analysis formed, a lot of forest plots you know, you look at enough forest plots and you see that, even things that we're pretty confident about in medicine, there's often a couple of studies that are on the other side of the line.

When ACE inhibitors were studied in heart failure, it was just so impressive on how all of them had a reduction in mortality and it was remarkably consistent. So it gave me this impression of ACE inhibitors that had, has never left me, but that was not in hypertension. And you know, Jordy, how do you think about ACE inhibitors for hypertension?

Dr. Cohen: Oh, I think they're a fantastic class. We know that they're associated with very good blood pressure control, they're long acting typically except for ramipril and and enalapril, are a bit shorter acting, but the other ones are long acting. So once a day is sufficient and they're very effective.

They're great in combination with thiazide diuretics and because they have potassium in them, you get, see a bit hypokalemia and those people and of course, as a nephrologist, I think they're remarkable because of the anti partner effects, especially great for patients who are diabetic with microalbuminuria.

So I agree with you. I think that they're just an absolute blessing of a class for anyone except for pregnant women.

Dr. Williams: Allie, what's your experience with ACE inhibitors?

Ms. Purcell: I agree with Jordy. I think they're wonderful overall. They have renal protective effects.

I am concerned about in some patients the cough side effect do get concerned about the, you know, low risk of angioedema with our patients and when in that trust factor so I, I like them. I also liked the ARBs.

Dr. Williams: Yeah, we'll get to the ARBs in a second. You know how often I'm curious do the two of you just go ahead and start a combination agent with hydroclorothiazide rather than just an individual thiazide or an ACE.

Ms. Purcell: I am trying to do that more and more with the morbidity mortality data coming out, supporting, patients who are started on combination, even lower dose products. And so we're trying to do that. I tend to do that better in patients where hypertension is newer diagnosis. Otherwise I find myself kind of building on to what the patient is already had.

So, I am trying to move in that direction. I would love to hear from Jordy about patients who aren't ideal for a dual agent, and also what happens when that monitoring check comes back and that creatanine has bumped and where to think along those lines.

Dr. Cohen: Yeah, these are great points. I completely agree with you. There are several trials that have now demonstrated that low doses of fixed dose combination of medications are associated with better blood pressure control and better toleration of, or better tolerance that the side effects by patients.

And if you can start at a lower dose of these agents in a fixed dose combination, it really can have remarkable benefits for most patients. But per your point, it's about thinking very carefully about whether it's right for your patient.

A little old lady with gout is probably not the right person to start on the thiazide diuretic with an ACE inhibitor combination. Cause she's going to be angry at you about her incontinence potentially and have a gout flare. But I think that in most people, it really can be beneficial because again, you'll get less side effects risk because they'll be on a lower dose of each agent and basically because you're using multiple agents, it targets whatever their cause of hypertension is effectively. And you are more likely to be targeting it with that first shot. So you're more likely to actually get their blood pressure under better control, but it's not likely to cause hypotension necessarily.

Because again, you're not starting at massive doses of these agents. You're starting at a lower dose of the combination.

We're doing it more and more in terms of the example, though, of a patient who starts on a thiazide and ACE inhibitor or ARB combination, and has more than a 30% increase in their creatanine. That's a very specific case. We do see that obviously, usually these are people who the most common reason for that is renal artery stenosis. Especially bilateral renal artery stenosis or people with kidney disease.

And so I think it's a good opportunity to be screening for underlying. I would check a urinalysis and urine protein creatinine ratio, and I would do a renal Doppler ultrasound. It's not an ideal screening test for renal artery stenosis, but at least it's a starting step. And then basically just try just one of the agents, not both and see if it recurs and if it recurs, then I would refer them to us to help with further evaluation.

Dr. Williams: So, similar to ACEs, are the ARBs the ARBs and I think ARBs have always been somewhat of a little brother to ACE inhibitors and we probably haven't given them their due. I've recently become to appreciate them more, mostly because as Allie mentioned, you see the cough with ACEs and more angioedema. They're pretty easy to prescribe. I tend to use losartan myself, although I'm starting to gradually use some of the others as well.

And so, you know, Jordy, how do you think about this drug class?

Dr. Cohen: Yeah, I think it's most research has suggested that they're relatively equivalent to ACE inhibitors, except as you mentioned, lower risk of cough.

I actually trained in the time when these medications had started to just become generic and really that was what I was using for my training. And so it became heuristic to use ARBs rather than ACE inhibitors. I think it's just so interesting because it really just depends on where you train, when you train, potentially which specialty, which one you use. And so I, I definitely am preferential to ARBs. I use a lot of ARB combination medications on my patients. But it really, the only reason for it is heuristic.

There's no rationale for using it over an ACE inhibitor at this point in time, based on the evidence we have. One thing I would say though, that I always like to throw in as a tidbit is that losartan is actually pretty short acting. The duration of action really isn't very long.

So it's ideally should be dosed twice daily, which is why I do prefer using the other ARBs because all of the other ARBs, are very long acting. So, telmisartan, olmesartan, valsartan, any of them are much longer acting and tend to be my preference. Olmesartin, particularly because it's in all the fixed dose combinations.

Dr. Williams: I just prescribed that in my last patient of the day who was having, it was not completely controlled with losartan hydrochlorothiazide combination. So I switched him to olmesartan hydroclorothiazide and I think they're a little more, it's a more potent as well, right? Allie, do you use a fair amount of these?

Ms. Purcell: I do. I have been using more. I would say Jordy's consults early on really got me away from prescribing losartan anymore unless the patient's already on it and comfortable with it. I really have loved the generic, olmesartan and valsartan combination products and I wish they were

available for every patient in every pharmacy. So yes, I'm choosing more olmesartan and valsartan these days.

Dr. Williams: So our last class to discuss are the ubiquitous calcium channel blockers. And as much as I'd like the others, I do find myself still using this class. And it's probably more than I should. Primarily because there's just so easy to use right, there are no lab checks, they're safe. They're generally cheap. And most times that we're reaching, I'm reaching for a dihydropyridines like amlodipine and of course there are others.

So, Allie, I'm curious what your experiences in primary care, are you using these a fair amount as well?

Ms. Purcell: Certainly we're using them a fair amount. And we I agree with the ease of not having to worry about what might happen with that little old lady's creatanine and the fairly well tolerated taking it at bedtime, not having to worry about the urinary frequency. So yes, we were probably using them a little bit more first-line than we should.

Dr. Williams: Now I feel somewhat guilty about this because I have it in the back of my mind that I'm probably not giving the patient maximal benefit from the drug I'm prescribing. Jordy, would you say that's true?

Dr. Cohen: I think the evidence supports that it's as good of a first-line agent as a hydrochlorothiazide and ACE inhibitors or ARBs. So I really think it's absolutely a fine option. And I prefer it actually, per both of your points. Love it in younger patients who I worry that they might not end up getting labs every year.

And I just want to make sure that I'm going to get them on something that they won't have to think too much about. I really am a fan of it. You're ever worried that the potency isn't sufficient then can always switch over to nifedipine, which is a bit more potent than amlodipine, but I, really have had great experiences with amlodipine and much like our other medications. It's sort of the one that we're stuck with in fixed dose combinations. And that's not such a bad thing.

Dr. Williams: Amlodipine is the drug you usually choose?

Dr. Cohen: Yeah, again, because it's available in fixed dose combinations. Cause my goal is to always try to get people on as few pills as possible. Cause I just think that psychologically, it helps so much with adherence. And also with what we talked about with those fixed dose combinations, starting at these lower doses, two medications helps to reduce the risk of side effects. So, if we can keep somebody on less than 10 milligrams of amlodipine by adding a low dose of an ARB, for example, then it really, I think, works wonders because then they don't end up seeing that edema. ARBs also counteract some of the edema as well. And they'll be more likely to take it long term.

Dr. Williams: I've been surprised how much edema I see as a result of amlodipine.

Dr. Cohen: It's a potent vasodilator. Yes. So I think it's rare for me to not to see it than to see it on people who are on 10 milligrams.

Dr. Williams: So I think we're going to have to have you both back to talk about some more detailed discussion on hypertension. Generally, some of the challenges we face, particularly secondary hypertension, so forth, but I, before we leave, I want to address the patient. We start them on a drug, maybe we do a combo and you have them at max dose yet, but you really haven't achieved much. They come back and it's really not any lower. What should we do with those patients? Should we take them off of it and put them on something else? Or should we just keep adding? Jordy, I guess I'll throw that.

Dr. Cohen: Yeah. So I think first of all, I try to really get into the person's head very deeply and understand why might it not have lowered? Have you made any of the lifestyle modifications that we suggested or did you make them earlier and then suddenly reverse on them when we started medications? And just make sure there's not a major confounder, really make sure they're taking it.

We try to call the pharmacies as often as we can in situations like this, just to confirm they've at least been filling it. And if they swear they've been taking it and they still really didn't have a benefit, there are a couple of different approaches you can take. And the older approach was always to just stop the medication and switch to a different one. Think if it's a low dose fixed dose combination and they didn't have any improvement, it might've just been that we underdosed them.

And so I think it is reasonable to just add the third medication at a low dose or to increase the dose. For example, when you do have the fixed dose combination, the dose of hydrochlorothiazide, the 12.5 milligrams is actually lower than the recommended dose to use for hypertension. So it's great because it doesn't cause much adverse effects, but it really has very little antihypertensive effect at 12.5, except in your very small thin people or people who are just extremely volume overloaded, where they just needed something. So I really can just, I do give them a shot of increasing the dose. Seeing if we can get a little bit farther adding another medicine before stopping the ones that they were on, initially.

Dr. Williams: I heard this interesting statistic as I was studying for the boards. I think it might've been out of one of the ACP things that said that 75% of the effect of a blood pressure agent is achieved at 50% of the dose. If you double the dose, you're only going to get about 25% more effect. I don't know the studies from which that comes, but it seemed like a useful rule of thumb.

Dr. Cohen: Yeah. So the median dose is usually where you get the optimal effect for most blood pressure medications, and then going above the median dose is where you tend to see less benefit from a blood pressure standpoint and more adverse effects relative to the blood pressure benefit. So that's why I was mentioning amlodipine.

I love trying to keep it at five in as many people as I can. Obviously we often have to go up to 10 milligrams, but same issue with high dose nifedipine. But with hydroclorothiazide it's a little different, really the optimal dose and the initial dose is 25 milligrams. But most other medications, that's the case. When you have a sort of this wide range of doses available.

Dr. Williams: So this has been a terrific discussion of just really the basics of hypertension management. Before we close out, though, I want to give you each an opportunity to say is, are there any other pearls that you feel the primary care community should know about?

Ms. Purcell: Well, I will say at Penn Family Care and the Department of Family Medicine, what we've been really trying to focus on this year is more of the engagement of the patients and paying

attention to that need to really do the two to four week follow ups after titrations, rather than the standard, see you in three months, hope you're still taking that medicine.

And this year we have focused on instituting access for those patients to come in and see myself or get back in with their PCP more quickly. And we've really focused on engaging that patient for a couple months at a time. And we're really hoping that the initial titrations and getting the patient to goal can last versus the every three to six months discussions.

Dr. Williams: Cause once you get people on that, that their dose, if you will, you could go years without having to change it, if you're lucky.

Ms. Purcell: We hope so.

Dr. Williams: It's worth you know, upfront doing some intense management. Jordy, is there anything you'd want to say to the Penn Primary Care Community?

Dr. Cohen: I really love Alison's point. Allie, that's spot on. I completely agree. Especially cause most medications reach their peak effect about one to two weeks after starting them. Since these are all long acting medications. And so by a month you're going to have the best you're going to get from it. So I think it's just such a wonderful approach.

In terms of the other plug that I'd like to make, I think everybody should be aware of the American Medical Association's Validated Device Listing. I will. Disclosure admit that I'm one, the co-chair of it. But I really think it's just such an incredible effort by the American Medical Association.

And I'm so proud of the work being done with it. So, this is listing of all of the validated blood pressure devices that have been carefully peer reviewed, for really truly being valid devices based off of very rigorous standards. The website is www.validatebp.org. I can't encourage people enough to check it out and to encourage their patients to as well.

Dr. Williams: That's fantastic. I really appreciate both of you coming on. This has been a great discussion. I've learned a lot. I'm sure others will as well. And we're going to definitely have to do this again.

Thank you everyone for listening to the Penn Primary Care Podcast. We look forward to having you back. We're doing these every two weeks, so we should be coming out every twice a month with new content.

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