LEWIS LIPSITZ: Well thanks, Doug. It's really a pleasure to be here. It's nice to bring some geriatrics to cardiology because it's coming down the pipe. Lots of older people have cardiovascular problems. So I'd like to share with you some observations I've made over the years and try to introduce maybe a novel way of thinking about blood pressure. I do not have any disclosures. So why don't we go forward.

Let's start with a common scenario. This is a scenario particularly common to those of us who care for people over the age of 80. But I am certain that you folks see this as well. Mrs. T is an 80-year-old woman with hypertension and coronary artery disease. She is slowing down in her memory and gait over the years, now having some difficulty preparing meals.

After an overnight rest one day, she arose from bed, took her usual medications, which included atenolol, hydrochlorothiazide, and isosorbide. She ate breakfast. She read the paper. She then went to the toilet. And as many of our patients unfortunately do, she strained to defecate. Upon standing up, she suddenly fell to the floor unconscious. Medics of course were called. The ambulance arrived. And they recorded a blood pressure of 90 over 50 and took her to the hospital.

There her systolic blood pressure ranged from 160 to 185. Her cardiac exam was normal. She ruled out for myocardial infarction. And she had left ventricular hypertrophy in a normal ejection fraction on her cardiac echo. So I'd like you to keep this scenario in mind, particularly the sequence of events that this particular patient had. And we'll go through that during the rest of the talk.

So this particular patient and so many of our patients had hypertension. Hypertension as you can see increases in prevalence with age, very nicely demonstrated in this work from the Honolulu Heart Study. But here nearly over 3/4 of females and 2/3 of men have hypertension by the time they reach 75. So this is almost ubiquitous, a very, very common problem among older patients.

Here is the prevalence of orthostatic hypotension, so the opposite side of the coin. And you can see here that this also increases with age. Here in the Honolulu Heart Study blood pressure was measured supine and standing at three minutes. And you can see that with increasing age from 71 to 74 all the way up to 85 plus, there's an increase in the prevalence of orthostatic hypotension such that 10% to 12% of people over the age of 85 have this particular problem.

So there is a very important relationship between aging, hypertension, and abnormalities in blood pressure regulation. And that's illustrated here. This slide really indicates the thesis of my presentation this morning. As I've shown you, aging is associated with blood pressure elevation. Aging is also associated with impairments in blood pressure regulation, which I will demonstrate in a few minutes. But so is blood pressure elevation associated with impairments and blood pressure regulation. If you cannot regulate blood pressure properly, you can experience periods of hypotension, which can lead to cerebral hypoperfusion and a number of important consequences.

Now there's not much we can or really want to do about aging per se. I think we all want to achieve that. But there's a lot we can do about hypertension. So if we knocked out this limb of this particular triangle here, we might actually be able to improve blood pressure regulation and prevent some of the adverse consequences. So I will show you some evidence that this might, in fact, be the case.

So what are the consequences of impaired blood pressure regulation in older people? Well, they include orthostatic, postprandial, and drug-induced hypotension. Now if people are experiencing declines in blood pressure during the day, they may have decreases in cerebral profusion. This can lead to syncope, falls, fractures. And I think one other area that's particularly important and perhaps overlooked is cerebral microangiopathy or small vessel disease we commonly see in our older patients. And this can lead to cognitive dysfunction and gait disorders, which are particularly common among older patients.

So yes. You in cardiology, who deal with blood pressure, are also going to have to deal with cognitive dysfunction and gait disorders. So this really is the merger of many organ systems as well as many different fields.

This is the blood pressure equation that we all learn in medical school. As you know, blood pressure is the product of heart rate times vascular resistance times stroke volume. So let's look what happens to these different parameters as a function of aging. First there's a decrease in baroreflex sensitivity. This is perhaps one of the most profound and earliest observations about the effect of aging. As you know, the baroreflex is intended to maintain a relatively stable blood pressure. When blood pressure falls, carotid baroreceptors sense decrease in stretch, send signals to the brain stem, which results in cardio acceleration and increase in vascular resistance.

You can stand an older person up. And you don't see much cardio acceleration because of the impairment in baroreflex control. So think of the older person as already being somewhat beta blocked. We know that this is due to a receptor defect in the heart in the beta receptor. But I think it's easiest to just think that your older patient is not going to cardio accelerate when exposed to hypotension.

We also know that the older kidney has impairments in renal salt and water excretion. There's actually an increase in the excretion of salt water, particularly overnight in an older patient, which is why they're getting up to go to the bathroom and why they're relatively dehydrated in the morning. And this is due to declines of renin angiotensin and increases in atrial natriuretic peptide with age.

And finally I'm sure it's well known in this audience that aging is associated with impairments in diastolic ventricular filling, which makes older people particularly preload dependent. And with any reduction in preload, there could be a reduction in cardiac output. So each of these effects of aging conspire against normal blood pressure regulation.

Here's just an example. Decreased blood baroreflex sensitivity impairs the heart rate response to hypotensive stress and the vascular resistance response. The increase in renal salt water excretion leads to decrease in stroke volume and dehydration in older patients, as does impaired diastolic ventricular filling can also reduce stroke volume. So if these parameters are reduced, so will blood pressure be impacted, particularly the ability to regulate blood pressure.

Now aging has a profound effect as I've just shown you. But hypertension superimposed on aging is a double whammy. So hypertension further impairs many of these regulatory mechanisms. And here's just a couple of examples. We know that higher blood pressure is required for cerebral profusion in hypertensive patients. I'll show you that in a minute.

Hypertension impairs cerebral blood flow regulation. So if you drop your blood pressure, your perfusion pressure, and you're hypertensive, you're going to have less ability to improve cerebral blood flow. Hypertension further impairs baroreflex sensitivity. Hypertension further decreases vascular compliance. And therefore the vascular response is impaired. And hypertension further impairs diastolic ventricular filling. So now we've got aging and hypertension. It's no wonder that older people might have problems regulating blood pressure.

So let's look for a moment at the effect of hypertension on cerebral autoregulation. regulation. This is the classic cerebral autoregulation curve that has certainly been in textbooks for about 100 years and just to take you through this for a minute, what it looks at is the response of cerebral blood flow here on the y-axis in response to variations in cerebral perfusion pressure. And the normal curve looks something like this, that there's a period right in the middle here in which there's a relative plateau.

Changes in cerebral perfusion pressure over this particular range do not result in much change in cerebral blood flow. And that's because the brain vessels are autoregulating flow. Down below a certain threshold, which is a mean pressure of about 70 or 80, there's a drop off in cerebral blood flow. And above a certain pressure, 180, 190 systolic, there is now a increase in cerebral blood flow with increases in cerebral perfusion pressure.

So now let's look at what hypertension does to this curve. Hypertension shifts it to the right. So now imagine first of all, that you're supine and then standing in the normal curve. You'll see that if your cerebral perfusion pressure supine is here, and then standing, it reduces, there's really no change in cerebral blood flow under normal circumstances.

But now if you're hypertensive, when you go from supine to standing, you've exceeded that threshold. And now when you stand up, your cerebral blood flow may fall. So this is what I mean by hypertension increasing the threshold for cerebral autoregulation. And hypertensive people might in fact come in this range and reduce their blood flow to the brain when they do something so simple as standing up.

The good news is that if we treat hypertension, we can begin to shift that curve back toward normal. So this finely dotted line represents the treatment of hypertension. And you can see here that we're coming back toward normal so that the person, when they stand up, now might be able to maintain cerebral profusion. So hypertension impairs cerebral blood flow and its autoregulation. But the treatment of hypertension is a good thing and could restore this particular regulatory process to normal.

So let's go back to our patient. As you recall, she had done a number of things that morning. She'd gotten up out of bed. She had taken her usual medications. She had stood up from her breakfast table She ate breakfast. She went to the bathroom. What happens to blood pressure during these common daily activities in older patients?

Well, a number of years ago we asked this question and actually examined blood pressure during a standardized series of activities in a group of older people living in a nursing facility. These were people average age of 82 and young employees, fellows, residents who were also there. We measured systolic blood pressure shown here on the y-axis from 7:00 AM to 1:00 PM.

During these standardized activities, they were first supine after an overnight rest. Everybody slept in the facility overnight including the young people. They then stood to do their daily hygiene. They then sat down for breakfast. They then stood and ambulated about an hour after breakfast. We later gave them a nitroglycerin tablet, something to replicate the isosorbide that this patient had taken and something that was very common in our older patients. We then had them stand up, ambulate, take their usual medications, eat lunch, and then lie down again.

And look what happened. Look at the blood pressure responses. First of all, the older people started relatively hypertensive first thing in the morning, about 160 on average systolic blood pressure. And there was tremendous variability in blood pressure during the course of these daily activities with declines initially on standing up.

Look at this. After breakfast, marked decline in blood pressure. Nitroglycerin, blood pressure plummeted. Ambulating and standing up again, eating medications, and eating lunch. Now the young had some blood pressure variability. First of all, they started lower, some blood pressure variability. But by no means did they have the same hypotensive responses to these daily activities.

So what do standing up, eating a meal, and taking nitroglycerin all have in common? I think I heard it, drop in preload. That's exactly right. So what should the cardiovascular system due to compensate for that decrease in preload or decrease in venous return? Increase heart rate is one thing and increase vascular resistance.

So let's look at the heart rate response. Here the slide is set up the exact same way, only now we're looking at heart rate on the y-axis in response to these common activities. And the curves are reversed. Now it's the young people in yellow that have tremendous variability in heart rate with marked increases after standing up first thing in the morning, after breakfast, after standing and ambulating, after nitroglycerin, and after lunch and medications. And it's the old folks that have the reduction in heart rate response.

This is the baroreflex impairment that I was talking about. And this of course predisposes those older individuals to hypotension during activities that reduce preload. So keep this in mind. This is happening every day in your older patients. We've done this a number of times. We've shown this to be true. And this variability is characteristic of many of our 80-year-olds and above.

So let's shift gears a little bit to orthostatic hypotension, which is one of the hypotensive syndromes that you're probably most familiar with. We looked at this also a number of years ago just to do some epidemiology and determine the prevalence of orthostatic hypotension with age. There have been a number of studies that have looked at this as I showed you. The Honolulu Heart Study was one of them.

But in this particular study, we looked at the NHANES, the National Health and Nutrition Survey. And in that particular study, subjects were studied sitting and standing. And the prevalence of orthostatic hypotension is plotted here as a function of the age of the subjects in five year increments so from 55 to 59, 60-64, 65 to 69, and 70 to 74.

And here you can see what I mentioned earlier. The prevalence of orthostatic hypotension increases with age from about 12% in the middle age group up to about 16% in the older group. So story over. Looks like orthostatic hypotension is a function of age. But not so quick.

Now let's look at the prevalence of or orthostatic hypotension in the exact same data set, same people, but stratified by the level of supine blood pressure, systolic blood pressure. Here we've divided the subjects into those with systolic pressures less than 120, 120 to 139, 140-159, and over 160. And we've looked at the percent of those with 20 millimeter or greater drops in blood pressure and standing up. Here the prevalence increases dramatically with hypertension from about 3% in those less than 120 all the way up to 27% in those with the highest blood pressures. So now it looks like orthostatic hypotension is a function of hypertension.

Let's do one last thing. Now let's just extract from this population all those people whose supine systolic blood pressure is greater than 160. If we do that and again look at the different age groups we find a very, very high prevalence of orthostatic hypotension, 25% to 28%. But the age effect went away. So we no longer see an age phenomenon. This looks very much like a blood pressure phenomenon. And indeed that is true that the higher you are, the farther you fall. People with hypertension are at the greatest risk of orthostatic hypotension. Somewhat of a paradox, but one that makes treatment particularly difficult. But we'll get to that.

So the next phenomenon that we've been researching and thinking about is postprandial hypotension. As I've mentioned, a number of years ago we were looking at causes of syncope in older patients and discovered that many of them experience drops in blood pressure after meals. All of us feel a little sleepy after meals. But that's not due to low blood pressure. In older patients it might be however.

So we did a study here in which on the left is a meal study. We gave a 400 kilocalorie meal in a standardized way to three groups of people. We looked at elderly, healthy people, older people who had experienced syncope within an hour of eating a meal, and a group of young controls. Young in the triangles, old in open circles, and old controls in the closed circles. And here we're plotting the mean arterial blood pressure as a function of time. This basal is before the meal. And then we looked up to 90 minutes after the meal.

And you can see here that the older controls did have a small decline in mean arterial pressure just sitting in a chair for an hour and a half after eating. The young subjects had no change in their mean arterial pressure. And those with postprandial syncope had a marked decline, pressures starting in about 100 mean arterial pressure down to almost 70. When we did another study, exactly the same circumstances, but no meal was given. There were small declines but not significantly. And this was just sitting in a chair for an hour.

So this is a real phenomenon. Postprandial hypotension is something you should think about when you have in older patient with syncope. And it's pretty straightforward. You want to measure their pressure before and after they eat. This too can be a cause of falls and fainting. And again, the higher you are, the farther you fall. Here we've plotted the systolic blood pressure change at 60 minutes after a meal as a function of their basal systolic blood pressure. And those with the highest blood pressures were the ones with the greatest decline in blood pressure after eating. So once again it's looking like it's the hypertension of old age that might in fact influence these phenomenon the most.

So what are the consequences of these daily declines in blood pressure? If we're having our patients drop their blood pressures during these common daily activities, what's going on? What's going to happen to vital organs that are expecting a good head of pressure in order to be properly perfused? Well, one of the consequences that has been discovered is cerebral microangiopathy.

Here is an MRI of an older individual who has this white matter hyperintensity shown in the arrows surrounding the large ventricles. This is often reported by your radiologist as white matter hyperintensities consistent with age or some possible small vessel disease of no significance. These really do have significance as I'll show you.

So why here? Why in these periventricular regions do you see this damage? Well, these regions are watershed areas of the brain. So if you look at this cerebral vasculature, the carotid branching out to the middle cerebral artery and then these perforating vessels here, there is an area right next to the ventricles which is a watershed region where there is threatened blood flow. And if we're experiencing hypoperfusion during the day, these are the very areas that are going to experience damage. And that damage is manifest as this white matter hyperintensity.

This is strongly correlated with hypertension and has significant implications. It is associated with slowing of gait, executive dysfunction, and depressive symptoms. In about 17% of our population, these symptoms come together and are probably due to abnormalities in these areas, which are areas representing myelinated nerve fibers coming from the frontal lobes down to the rest of the brain. The frontal lobes are very important in executive function, depressive symptoms, and gait. So this finding is really quite important. Hypertension is strongly associated with white matter lesions. And hypertensive individuals show greater progression of white matter lesions.

So here is one study from Verhaaren in the Netherlands in 2013. And here you can see that the bottom, the baseline white matter lesion volume is shown. Even though it's going down, it's an increase in volume down toward the bottom of the graph. And you can see in persistent normatensives, there's a little bit of white matter lesion. By the control-treated hypertension is a little more. Uncontrolled treated hypertensive is even greater. And uncontrolled, untreated hypertensive is about the same.

So this is associated with hypertension, particularly poor control of hypertension. And progression over several years ahead of time is greatest in those individuals with uncontrolled, untreated hypertension. So this is very important to think about particularly when you get those MRI reports of your older patients.

So a few key points I'd like to leave you with. First elderly patients, especially those with hypertension, are at risk of hypotension and cerebral hypoperfusion during common daily activities. Secondly, hypertension and associated blood pressure variability are also associated with the presence and progression of cerebral white matter lesions. And these white matter lesions are associated with executive dysfunction, slow gait, and falls.

So let's now turn our attention to the question does the treatment of hypertension worsen hypertension and impair cerebral perfusion? Or as I suggested earlier does it actually improve blood pressure regulation and improve cerebral perfusion? Really a key question as we're trying to decide how aggressive to be in treating our older patients.

Well, the first question is what about the acute effects of antihypertensive therapy? And I think we've all seen syncope after the first dose or first few doses of a antihypertensive medication. And indeed that can certainly happen.

This is a study now done many, many years ago by Rick Shannon, who was both a cardiology and a geriatrics fellow at the time. And what Rick and colleagues did is took a group of older individuals shown in the open circles and younger individuals in the closed circles and exposed them to a very quick tilt test. And he looked at the change of systolic blood pressure when people were tilted upright on a tilt table for three minutes.

The solid lines show what happened when they were just in their normal state. You can see not much. Not much happened. The older and younger individuals maintained their blood pressure pretty well when they were tilted upright under their normal, pretty well-hydrated conditions. But then he gave them hydrochlorothiazide for three days. And he dropped their weight by about a half to one kilogram and did the tilt test again.

When he did it again, the young people had no problem regulating their blood pressure. And they maintained a nice, stable blood pressure during that three minute tilt. But look what happened to the old. They dropped their pressure quite profoundly at an average of about 25 millimeters by two minutes. So the acute administration of a diuretic or acute volume contraction in an older patient can be dangerous and can certainly result in hypotension.

But what about the chronic administration of antihypertensives? You know, there have been a number of trials done now in which older individuals are getting antihypertensive treatment for many months or years. And the prevalence of syncope in orthostatic hypertension is almost unreported. So what happens with chronic therapy? Well, there are actually a number of studies showing that orthostatic hypotension is reduced by chronic antihypertensive therapy.

And here's just one summary from a number of years ago. Here is a study that looked at the prevalence of or orthostatic hypotension at baseline in a group of hypertensive people before they were treated. And then two years later after two years of treatment. And you can see the normatensives had a very low prevalence both the baseline and two years later. And on all of these other medication treatments, nifedipine, metoprolol, enalapril, prazosin, and thiazide, the baseline rate was pretty high, 18% to 22% had orthostatic hypotension. But after a period of treatment with some of these, orthostatic hypotension went away.

Now prazosin, an alpha blocker, is particularly problematic, because if people, older people are already beta blocked by virtue of their age or medications we give them, adding an alpha blocker completely wipes out their regulatory capacity. So the alpha blockers are particularly dangerous and here on thiazide as well, if it results in volume contraction, can be a problem. So it looks like antihypertensive therapy in general, particularly ACE inhibitors and calcium blockers, are particularly beneficial.

What about cerebral blood flow? Well, it's a little hard to measure cerebral blood flow. But we've been able to do it with a transcranial Doppler technique that shines an ultrasound beam to the middle cerebral artery. That then bounces off the red cells flowing through the middle cerebral artery and can be detected back at the probe. Using this technique, we can actually measure cerebral blood flow during a variety of activities such as sitting and standing up, something you can't do in an MRI machine.

So this has been very useful. And we did a study a number of years ago now in which we looked at the effect of six months of blood pressure control on cerebral blood flow. And first let me show you what cerebral blood flow looks like in the baseline condition before any treatment for hypertension. And you can see here in the solid circles and dark line that cerebral blood flow is about 35 to 40 cc, centimeters per second. And when people stand up, it drops a little bit. This was the baseline condition.

But then we treated people with a ACE inhibitor therapy for six months. And we expected maybe cerebral blood flow would fall as we brought blood pressure down. Everybody started at systolics above 160. And we treated everybody to get their pressures down to 140 or less. And look what happened. In fact, cerebral blood flow increased after that period of six months of treatment.

So one need not worry too much that the treatment of hypertension is going to impair cerebral blood flow if done slowly, chronically, over a period of time. In fact, it can improve cerebral blood flow.

There's also been quite a concern that antihypertensive medications might precipitate falls, perhaps by reducing blood flow to the brain and causing syncope or falls. And we recently looked at this question as well in a large population-based cohort that we have called the MOBILIZE Boston Study. And here we looked at the effect of ACE inhibitors and calcium blockers and other medications on cerebral blood flow and actually found that ACE inhibitors and calcium blockers increased cerebral blood flow. It was associated with an increase in cerebral blood flow in this population.

And then we look to see whether these medications increase the risk of falls. And those data are shown here. Here we're plotting the odds ratios on the x-axis with three doses of medications. No dose at all for ACE inhibitors on the top and calcium blockers on the bottom. Low or standard doses and then high doses which was the highest tertile of the doses given to this population.

And here instead of seeing an increased odds of falls, we actually saw a decreased odds of falls which was dose-dependent, quite to our surprise. And here the low and the higher doses of ACE inhibitors had a particularly significant effect on injurious falls, and the calcium channel blockers, particularly high dose reduced indoor falls and all falls. Divide our falls into different types and you can see different effects on different types. So once again, it looks like the treatment of hypertension in older age might be beneficial particularly in improving cerebral blood flow and perhaps reducing fall events.

So in the time that remains I'd like to move to some more clinical information about how we can diagnose and treat both orthostatic and postprandial hypotension since these may be topics that you see but may not think about that much.

So orthostatic hypotension. Let's start with that. What is the definition of orthostatic hypotension? Well, you know, that's a really tough question. Because nobody has studied it all that well. Conventionally we say it is a 20 millimeter or greater decline in systolic blood pressure and/or 10 millimeter or greater decline in diastolic blood pressure when changing from a supine to upright position.

Well, all kinds of questions. Should it be at one minute, three minutes, five minutes? Can you go from lying to sitting and then sitting to standing? How do you do this? And why 20 millimeters? Does that mean anything? The gold standard would be what is associated with an adverse event? And I'll show you in a minute that 20 millimeters or greater is associated with adverse events. That's probably a reasonably good criteria.

And I like to do it at one minute and three minutes. Because many people, ourselves included, might show the nadir of blood pressure within 30 seconds to a minute of standing up. But then it should recover by three minutes. And people with autonomic failure do not recover by three minutes. They continue to decline. So it's good to get an immediate value and a delayed value.

And it's best to do the full stress test from supine to standing. But if somebody has injured themselves or can't stand up, we sometimes go supine to sitting. Or in an office practice, sitting to standing. Remember heart rate is not a reliable indicator of orthostatic hypotension in geriatric patients. Because they already have that baroreflex impairment. And heart rate is not going to increase very much.

So is this definition of orthostatic hypotension dangerous if so many people have it? Well, it is. It is an independent predictor of all-cause and cardiovascular mortality. It is associated with recurrent falls in people who live in the nursing home and have previously had falls. And it is a marker of physical frailty.

Here is a one study again, the Honolulu Heart Study, that looked at the systolic blood pressure change sitting to standing and its association with mortality. And here you can see total mortality per 1,000 person years on the y-axis. And the greater the decline in blood pressure, the greatest mortality. Diastolic orthostatic hypotension is also associated with mortality as shown here. Again a 10 millimeter or greater reduction is associated with a largest mortality. So these syndromes do have clinical implications.

And what about falls? This is the study we did a while ago that looked at the frequency of orthostatic hypotension and recurrent falls. And here you can see those people in yellow who had multiple episodes of orthostatic hypotension during the day had the highest risk of subsequent falls when falling over a year's period of time. So this is again important outcome. And the 20 millimeter threshold, regardless of where you started from, seem to be an important predictor of adverse events.

So what are the causes of orthostatic hypotension? Well, I'd like to divide that in this slide to common causes that all of us will see and then to neurologic causes in the next slide. The systemic causes, as I mentioned before, start with hypertension. So you have to think is this a hypertensive patient who has orthostatic hypotension? Or is this some other condition? And the other conditions that are so common, of course, are dehydration, deconditioning, and don't forget adrenocortical insufficiency. Sometimes we see patients with adrenal failure who present with orthostatic hypotension.

Deconditioning is profound. If you send an astronaut up to space for 24 hours, they can barely walk when they get back to Earth. Because their baroreflexes are completely unable to compensate for gravity once they're out of our atmosphere. Drugs of course are on this list. And the common ones are antipsychotic medications, MAO inhibitors, and tricyclic antidepressants, acute doses of antihypertensives as we've mentioned, vasodilators like nitroglycerin and alpha blockers, L-Dopa, and then sometimes beta blockers and calcium channel blockers.

Then there are neurologic conditions. And I like to think of those as the central nervous system disorders and autonomic neuropathies. The most common central nervous system disorders that we see are multiple systems atrophy or the old shy drager syndrome was the name of it, Parkinson's disease, multiple strokes, myelopathy, the brain stem lesions, and Lewy Body Dementia.

And then the autonomic insufficiencies, most commonly diabetes. Many of our diabetic patients have occult orthostatic hypotension until it's too late. And they fall. And they're fainting. But also amyloidosis, syphilis, paraneoplastic syndromes, alcohol, some nutritional myelopathies, particularly B12, and then pure autonomic failure, which is probably a viral syndrome.

So let me present another case that again is quite common and often overlooked. Mr. B, this is a patient of ours about a year or two ago. He was an 83-year-old former butler for some of our wealthy donors who was admitted to the hospital after a fall in his apartment. He had a history of mild dementia, weight loss, and restless leg syndrome. He developed delirium at night in the hospital and was given haloperidol.

He became severely agitated, experienced visual hallucinations, and fell when getting out of bed to go to the toilet. His supine blood pressure was 142 over 75 and a heart rate of 76. Sitting it was 102 over 72 and a heart rate of 80. Standing it dropped to 85 palpable heart rate of 79. Virtually no change in his heart rate. He had marked lower extremity rigidity. No tremor. He was disoriented and unable to recall three objects.

What do you think's going on? Any?

SPEAKER 2: Haloperidol?

LEWIS LIPSITZ: Sorry?

SPEAKER 2: Haloperidol?

LEWIS LIPSITZ: Well, that certainly had an effect on his agitation and confusion. Yeah. That's for sure and could do this. Any other? All right. Any geriatricians in the audience?

SPEAKER 3: Lewy body dementia?

LEWIS LIPSITZ: There you go. There you go. So he had Lewy body dementia. We often forget about this condition when the patient in the hospital is markedly delirious. We give them Haldol unfortunately. And they get worse.

So here's some of the characteristics that he had that are classic for Lewy body dementia. Cognitive impairment, usually more executive disfunction than memory, visual hallucinations, Parkinsonian features, orthostatic hypotension, marked sensitivity to antipsychotic medications, and a history of movement disorders like restless leg syndrome.

So he had the classic Lewy body dementia, which is quite challenging to treat. We treated him with salt and fluids, fludrocortisone, midodrine, thigh-high stockings, and elevating the head of his bed, which can reduce some diuresis that can occur overnight in such patients. So keep this in mind as you see patients in the medical service or perhaps even on your own service.

So how do we evaluate orthostatic hypotension? Well, obviously there are many symptoms, postural dizziness, falls, syncope. We also ask about oral intake. Because many of our older patients lose their sense of thirst and do not replete their volume losses by going to drink fluids. It can also be associated of course with sweating, incontinence, headache, common diarrhea, constipation, impotence, poor night vision are all common characteristics of patients with autonomic problems. We look for histories of hypertension of course, diabetes, cancer, stroke, Parkinson's disease, arrhythmias, medications and alcohol.

The evaluation requires the blood pressure to be measured. And it's amazing how many followers and patients with syncope come into the emergency department and never get orthostatic vital signs. It's probably common here as well as in Boston. But we want to measure the blood pressure and heart rate, both supine and at one and three minutes of standing. Look at their pupils for the ability to respond to light. That's an indicator of autonomic control, the skin for sweating, cardiovascular systems and neurologic systems, of course.

Some laboratory tests are often helpful, hematocrit, electrolytes, glucose. Look for abnormalities in proteins that might indicate amyloidosis or other conditions, B12 and RPR. And then we do some special tests, cortisols to make sure they don't have Addisonian symptoms, brain imaging, sometimes tilt tests, and measures of heart rate variability can often be helpful.

So the first step to treatment is nonpharmacologic treatment. We want to stop unnecessarily hypotensive medication if the patient has autonomic failure. If they, in fact, have hypertension, we may want to very gently treat their hypertension and see what happens. We want to avoid warm environments where their [INAUDIBLE] are dilated. Avoid straining activities such as our first patient had when she went to defecate. Sometimes squatting and crossing the legs is helpful, though older patients have trouble doing that.

Increasing salt intake in their diet, waist-high compression stockings are helpful. Thigh-high stockings and, I'm sorry, knee-high stockings bunch up under the knees and prevent venous return. So they're not particularly good. So we like thigh or waist-high. And sleeping in the head-up position, as I mentioned briefly, can prevent the nocturnal diuresis that occurs in these patients. So we put a block under the head of their bed or a couple of pillows or a wedge or even a bed to allow them to have their head up.

Recently a paper was published showing that supine leg resistance exercises can actually reduce systolic hypertension in older adults. This was a study published in JAGS two years ago now of 42 patients over 65. And they had these patients exercise after 10 minutes of bed rest with 10 extensions of the ankle, knee, and hips against a resistance band. And then they stood up after 10 repetitions and recorded blood pressure and heart rate. Here is just an example of these kinds of exercises that can be done very easily in bed.

And there was also this study showed that under control conditions when no exercises were done, mean systolic blood pressure fell by 27 millimeters of mercury and immediately upon standing. But after the exercise, it only fell by 10 millimeters of mercury, a significant difference. During the next five minutes of standing, the return to baseline occurred more slowly in the control group. And 67% of the control group reported orthostatic hypotension symptoms while only 38% in the exercise group.

So it's not perfect. But it is something that has actually been tested and does seem to work to some extent. And it's a series of exercises that our older patients can probably do with a simple elastic band that they can purchase.

Pharmacologic treatments for orthostatic hypotension are listed here. And I've kept in white those that are most common and that anyone can use. The others in blue are much more research-oriented and need very selective evaluations before we should give them. But fludrocortisone is the mainstay of treatment. It is a steroid that causes the kidneys to retain salt and water, and as a result, can have several adverse effects. You must check the potassium in these patients after a week or two of treatment. I've had patients go into ventricular tachycardia because of very, very low potassium on this. So we have to be very diligent about checking that.

It can also cause supine hypertension. But the treatment of that is don't let your patients be supine. Have them sleep with their head up. Or get them up. And they'll drop their pressure. And the other, of course, is congestive heart failure. In a patient who has heart failure and orthostatic hypotension, this is particularly challenging. Because we can't give them salt. We can't give them fludrocortisone. And we're really balancing a very difficult situation. We can talk some more about that if you wish.

Midodrine is an alpha agonist. It can sustain the blood pressure by increasing vasoconstriction and can also be helpful, particularly in combination with fludrocortisone, and then sometimes non-steroidal anti-inflammatory drugs which cause the kidneys to retain salt in water and can result, as you know, in hypertension. Caffeine has been tested. In some tests, it's been helpful. In others, it hasn't. We generally recommend two cups of strong brewed, caffeinated coffee in the morning but not later in the day. It'll keep patients up. And people develop tachyphylaxis or tolerance to it.

So last let's talk for a minute about postprandial hypotension. This is our former President George Bush fainting after a big meal in the lap of his Japanese host. I'd like to think he had postprandial hypotension. I'm not sure. Nobody checked it. And we define that also as a 20 millimeter or greater decline in systolic blood pressure within two hours of the start of a meal.

It's also associated with hypertension, autonomic failure, Parkinson's disease, diabetes, and renal failure. We found it in a quarter to a third of nursing home residents. And you'll see residents in nursing homes just sitting in their wheelchairs endlessly outside of the nurse's station, often with their heads slumped in their lap. And if you were to actually measure their pressures, you'd probably find it quite low.

We found, in previous literature, found about a quarter of all the patients admitted to geriatric hospitals with syncope or falls had postprandial hypotension. We found 50% of elderly patients with unexplained syncope actually had postprandial hypotension. And it can result in angina, TIA's, lacunar infarcts, and this white matter hyperintensities. It again is an important condition in older patients that should not be overlooked.

How do we evaluate it? Well, we can measure blood pressure before and after meals. You would think that would be easy to do in the hospital. Unfortunately, it's very difficult to get people to do that. But our fellows do it. And in the office, you can actually ask a patient to bring lunch to the office, have a nurse measure their pressure before they eat and then at 30 minute intervals after they eat. And then see you for an office visit an hour or two after eating.

We generally use a high carbohydrate meal of 400 kilocalories to promote this. That's a good sandwich. We use Carnation Instant Breakfast. Because it's easy to give in a standardized fashion. We get a history of the medications they're on. Many people take their medicines before meals, a common practice as our first patient I presented did. And the combination of the meals and medications can sometimes precipitate this.

Alcohol is a big issue. That also is often ingested with meals. And we look for autonomic symptoms, hypertension, and various diseases that can be associated. And of course, we want to make sure that they're not experiencing angina. So we often get EKGs as well. But nonpharmacologic treatment is the first line of treatment. We stop hypotensive medications. Or give them between meals if people have severe postprandial hypotension.

We want to avoid preload reduction from diuretics or prolonged sitting like the nursing home patients I mentioned, and maintain adequate intravascular volume. Avoid alcohol. Studies have shown that multiple small meals of protein and fat are helpful. So instead of having these three big meals a day, have your patients graze. And eat small meals throughout the day off and often composed more of protein and fat than carbohydrate. Walking exercise after meals can actually help. I'll show you that. And cold rather than warm meals has been tested and seems to be helpful as well.

So a number of years ago with a fellow, we did kind of a gutsy study. We took a bunch of nursing home residents with postprandial hypotension and asked, what would happen if we stood them up and walked them after they ate. We do this all the time. So why not actually test it systematically?

So in this slide, you can see the mean arterial pressure on the y-axis and the time after the meal on the x-axis. On the yellow is a day we actually gave them a meal and watch their blood pressure fell from a mean of about 100 down to a mean of about 85 or so. But on another day, and we randomized the sequence of these days, we actually got them up to walk at 35 minutes after the meal when their blood pressure hit its nadir. Look what happened. It improved, probably due to the pumping function of muscle activity as they walked. We were able to restore blood pressure.

The bad news is when they sat down again, their blood pressure came back down to where it was. So this at least informed us that the old German folk wisdom is correct. Nach dem essen sollst du ruhen oder tausand schritte tuen. After the meal, you should rest or take 1,000 steps. Remember that.

So the pharmacologic treatment of postprandial hypertension is similar to that for orthostatic hypotension, again, two cups of brewed coffee in the morning can be helpful. Fludrocortisone but watch for heart failure, supine hypertension, and hypokalemia. Octreotide has been very helpful. Somatostatin analog increases blood pressure. But it has to be given parenterally or sub Q injection before each meal, which is quite difficult and costly.

Midodrine can also be helpful as can acarbose, which as you know, is used for diabetes. It slows the absorption of glucose. And we've had some experience with that that is very positive. It can reduce the absorption of glucose, produce the insulin secretion, and as a result, reduce the vasodilation that occurs when insulin is circulating. The problem is, it causes a lot of gas and stomach irritation sometimes. But it's helpful.

So if I haven't confused you by now, I'll try this slide to try to clarify things. How do we approach this complex issue of blood pressure disregulation? Well, the first and foremost is we need multiple blood pressure values during variety of different activities in our older patients. We should check their pressure standing, before and after meals, before and after medications.

And how do we do this? You can get 24-hour blood pressure monitoring. But it doesn't give you the kind of granularity that I want. I'd like to know exactly what happens in response to given activities. And you can sort of get that from the diary of the 24-hour measures. But I like to actually give them a piece of paper that has on it some columns and rows. It says Monday, Wednesday, Friday, 8:00 AM before breakfast, sitting, standing, 9:00 AM an hour after breakfast, sitting, standing. If I'm interested, 3:00 PM in the afternoon, and before they go to bed, sitting and standing, three days a week for three weeks. And bring it back to me.

And then I can see are they hypertensive first thing in the morning, which many of our patients are. Do they have orthostatic hypotension? Do they have postprandial hypotension. Does it happen after they take their medications? What's the pattern, the diurnal pattern? Because I don't want to aggressively treat their blood pressure first thing in the morning and then have them sit down to a meal and drop their pressure. So maybe I want to give those medicines at night before they go to bed.

So that alone, that diary is extremely helpful. And then they either have persistent hypertension throughout the day with some blood pressure variability. Or I can find orthostatic and postprandial hypotension. If they have persistent hypertension, I want to treat that. And I want to treat it carefully, slowly, judiciously, and watch for orthostatic and postprandial hypotension. If on the other hand, it looks like they may have autonomic failure with orthostatic or postprandial hypotension, I want to support their blood pressure under these conditions and that I might use fludrocortisone and all the nonpharmacologic measures that I mentioned.

So let's revisit Mrs. T and conclude with her story. Why is she slowing down? Well, she possibly has this frontal subcortical cerebral microvascular disease I showed you on the MRI, which affects her executive function and gait. Remember, she couldn't cook anymore, which requires the management of multiple things and planning, organizing, following a recipe. And she lost her ability to do that and slowed down in her gait, another manifestation of frontal lobe disease.

Why did she faint? Well, she probably had a hypotensive response to volume contraction first thing in the morning, posture change, medications, a meal, and Valsalva maneuver during defecation. She had a number of reasons. And what getting a CT scan and MRI, an EEG, a Holter monitor, that's OK. But I think that's not going to tell us the answer to that or these particular causes of syncope.

Is she hypertensive? Yes. She is hypertensive. Remember when she was found, her pressure was 90. But back in the ED, it was up to 160. A highly variable blood pressure is a feature of hypertension in older patients. And should she be treated for hypertension? Yes. But I would monitor her carefully for orthostatic and postprandial hypotension within the first few days and weeks of her treatment. And avoid volume contraction.

So in summary, aging and hypertension impair blood pressure regulation and increase the risk of orthostatic postprandial and drug-induced hypotension. The careful treatment of hypertension may actually improve blood pressure regulation. You should measure blood pressure during usual daily activities in your patients. Evaluate patients for autonomic failure if they seem to have persistent or symptomatic hypotension. And always start with nonpharmacologic therapy. So thank you very much.