Today’s roadmap is I’m going to give you a case presentation of a patient I saw several years ago. I’m also going to give you definition about what we are talking about, the proper evaluation of patients with hypertensive emergencies and then how to manage them. I’m going to restrict my comments today primarily to the adult population and I’m not going to talk about preeclamptic hypertensive emergencies or pediatric hypertensive emergencies.

Our case presentation is a 51 year old gentleman who was admitted to an outside hospital, his chief complaint at that time was the sudden onset of left sided weakness. He had a severe headache andslurred speech and left facial droop. His blood pressure at the time of admission was 260/172 at theoutside hospital, and head CT scan was obtained that showed a right basal ganglia hemorrhage with shift. The remainder of the history of present illness became pertinent for us when he was transported by ambulance to Presbyterian University Hospital here at UPMC and because of declining mental status he was intubated en route.

He did have a past medical history of hypertension according to his wife who was supplying thehistory, but as frequently happens he was not adherent with his prescribed medications. And forthose of you that follow this literature know that this is quite common with any type of medicationthat’s prescribed by physicians. We – she did not know what his medications were, she was notaware of any drug allergies that the patient had and his family history was also pertinent forhypertension and cerebral vascular accident.
When he came to UPMC his blood pressure was 196/130 and at that particular time he exam was positive for a left dense hemiparesis.

On the second hospital day he had a dilated right pupil, he had to be taken emergently for a right frontal temporal craniotomy and the clot was evacuated. His subsequent hospital course was pertinent for difficult to control blood pressure, it was also complicated by pneumonia. As one of the interesting sidelights of his evaluation he had a renal MRI done which showed a right kidney that was 8.1 centimeters in length with 3 renal arteries and a left kidney that was 12.2 centimeters with 2 renal arteries. Eventually the patient’s blood pressure came under control, his pneumonia came under control, his neurologic status stabilized and he was transferred to UPMC South Side Hospital on the 19th of July, almost 3 years ago to the day.

So your first question is, especially since I’ve thrown you a little bit of a red herring in the history, is actually I threw you 2 red herrings in the history, is what is the main cause of hypertensive emergency in the United States today: renovascular disease, pheochromocytoma, nonadherence to antihypertensive drugs, hyperaldosteronism and chronic renal disease? And I can tell that this is a sophisticated audience because you all got that it was nonadherence to antihypertensive drugs. Renal vascular disease is quite common and also tends not to be that much of a cause of hypertensive emergencies, a relatively small component. The red herring here was that the guy had a big disproportion between his kidney sizes, so you’d have to think about that and he would probably need renal vessel studies.
Hyperaldosteronism tends not to present with hypertensive emergency because the change in volume is slow over time. Chronic kidney disease also because of the slow change in volume over time tends not to cause hypertensive emergency, but it can. And pheochromocytoma doesn’t present like this, it’s much more episodic. And we get to see quite a few pheos here because we have a very active endocrinologic surgery department and so quite familiar with pheos, they usually don’t present this way.

So just a little bit more history is that you have to always remember that when you hear hoofbeats you don’t think of the multicolored zebra but rather you think of the most common thing. And we do get a lot of zebras here, but this, this particular case it wasn’t a zebra.

According to the Joint National Commission Version 7 and we keep waiting for Version 8 to come out, hypertensive emergency is a severely elevated blood pressure, generally greater than 180/120 with signs and symptoms of acute end organ damage. It is absolutely a disorder that requires the patient to be hospitalized and it’s absolutely a disorder that requires intravenous correction of the problem, and your timeframe for correcting this particular abnormality is minutes to hours.

I want you to contrast that with hypertensive urgency. This is a severely elevated blood pressure without signs of target organ or end organ damage. This can be managed as an outpatient and this is something that can be managed with oral medications. You really don’t need to take care of these
patients in hospital, you just have to make sure that you are seeing them back in your office within 24 to 48 hours in order to monitor them. After some of you with gray hair like me might remember when this was called malignant hypertension. That term isn’t used anymore, the nomenclature became obsolete about 1993, so I can now say in the last century it’s not used anymore, and it is the sort of illness, or the disease modification has been made because it really doesn’t reflect the difference between hypertensive emergency and hypertensive urgency. So we are going to really spend most of our time today on hypertensive emergency.

The end organs that are affected by hypertensive emergency are the cerebral nervous system, the central nervous system, patients can present with encephalopathy, they can have intracranial bleeds, although intracranial bleeds tend to be uncommon with this disorder; grade 3 to grade 4 retinopathy, heart disease with congestive heart failure, myocardial infarction, angina; I can also see kidney injury and microscopic hematuria and the vasculature can be affected. We have quite a plethora of patients with aortic dissection on the service right now, and many of them present in crisis and with very elevated blood pressures. And the vascular component in pregnancy would be preeclampsia.

The epidemiology is that hypertensive emergencies are common but when I tell you that they only affect 1 or 2% of the hypertensive population well you say well how common is that? Well, last year this slide said that there were 45 million American adults with hypertension, this year you’ll notice it says there are 50 million American adults with hypertension, and this will continue to grow because if we have the good fortune to live to be 80 or 90, 90% of us will have hypertension and be
on medication. It’s something that came out of the Framingham study. The incidence of who is affected by hypertensive emergencies reflects the people that are affected with primary hypertension, so this is a disease that is more common in the elderly, it’s more common in the African-American population, and the incidence is twice as high in men as it is in women.

The other common associations that have been noted and this is where I finally get to the answer to the question is that a previous history of hypertension is important, also the lack of a primary care physician. In a study that was done in New York City where they evaluated hypertensive emergencies coming into the emergency room, the single largest association was the lack of a primary care physician to renew the drug for the patient for financial reasons and what have you. In a study that was done in Georgia at Emory what was found was that the largest cause in their particular study was nonadherence to the antihypertensive drugs. And finally, as the drug pattern of use of illicit drugs has increased in the United States, there are more people that are doing methamphetamine and they are doing cocaine and things like that, so illicit drug use is common as well. And we have several of those on service right now in addition to our aortic aneurisms.

It’s interesting when you do the background reading on the research in this is that when it comes to etiology and pathophysiology they all say the same thing, the pathophysiology of hypertensive emergencies is unclear. One of the common things that you see is as a common factor is a sudden increase in systemic vascular resistance with an increase in blood pressure. So it would make sense that if someone is taking blood pressure medication and then they abruptly stop it you are going to
get this change very quickly in vascular resistance. You’ll get hypertension and then the next thing that happens is because of increased blood flow rates and increased stretch on the vasculature you get increased mechanical stress, it injures the endothelium, you get increased permeability of the blood vessels, you start to get coagulation abnormalities, increased platelet activation and fibrin deposition. And for those of you that are familiar with thrombotic thrombocytopenic purpura and the hypertension that you get with that, or hemolytic uremic syndrome this is very much almost a classic example of the same thing that happens in hypertensive emergencies. You end up with fibrinoid necrosis in the blood vessels, ischemia to downstream organs, activation of the renin adjutants in the aldosterone system and the release of a lot of proinflammatory cytokines.

This is shown schematically in an article by Vaughan et all from the Lancet in 2000, and what you see on this slide is the nitric oxide, Prostacyclin, which maintain the balance on the vascular endothelium as far as vasodilators and when you get this sudden vasoconstriction what happens is that you have far more of the vasoconstrictive enzymes present, so Angiotensin II, Catecholamine known as CAT, Endothelin, ADH, which is a vasopressor as well and you get changes in the cellular adhesion molecules which are released. If this continues and you get further damage, you get more release of other vasoactive substances, thromboxane, cytokines and so forth, you start to form platelet clot, increased permeability and you destroy the blood vessel.

Now there are an active role right now for genetics that’s being investigated for this. If you take a rat model and you double the number of renin genes, the REN II genes, just having the one REN
gene in there increases your chance of having systemic hypertension, if you put two of these genes in, the REN II genes, you are much more at risk for getting systemic or hypertensive emergencies. There is also a murine gene that has been identified that when translocated into rat models causes hypertensive emergencies as well.

The pathologic changes that you see are fairly nonspecific, they just represent the changes of a very elevated blood pressure. Again, this is a glomerulus, it’s for the nephrologist’s eye, it’s an underperfused glomerulus because the capillary loops aren’t very large, and what you see in this particular photomicrograph is the afrin arterial which has hylan deposition, which is due to the change in permeability, and this is becoming a nonfunctional glomerulus as the lumen becomes occluded. Again, another glomerulus and here you see a larger artery, maybe an intralobular artery, and you see the characteristic onion skinning changes of the fibrin building up in layers and so forth. And you can do immunofluorescent studies as well, which will light up the protein deposits. So it really is a disease of blood vessels and destruction of blood vessels that is the underpinning for hypertensive emergencies.

As a nod and a wink to Dr. Shapiro, I always put in this slide about candidate genes and hypertension, there are roughly 30 now that have been identified and this is – continues to be a very vigorous area of research in the hypertension field. The ones that are the best so far are the angiotensinogens, angiotensin 2 receptor type 1, the renin gene which I mentioned, renin binding protein, alpha adducin, the beta 2-adrenergic receptor and the angiotensin 1 converting enzyme
itself, and the changes in their activity can cause this. One gene that has been extensively studied in humans is the angiotensin converting enzyme VD genotype which is associated with malignant hypertension. Also, something near and dear to my boss’s heart the epithelial sodium channel, the absence of the beta and gamma subunits of the epithelial sodium channel are associated with ________ hypertension and there are some other modulators which are elevated. We don’t know whether they are causal or whether they are reactive, but adrenal medullin, natriuretic peptide levels and abnormalities in oxidative obstructs markers and endothelial dysfunction. All of those are seen in malignant hypertension, and all of them correct whenever you correct the underlying disorder. So causal or reactive is still not known.

So the next question is that since we are seeing about 500,000 of these cases a year in the United States what is the most common complaint in hypertensive emergencies? And I changed the answers, folks, so you can’t depend on last year’s knowledge, aphasia, gross hematuria, chest pain, headache or epistaxis? And headache was what most people reported. And the right answer is chest pain. And really it’s sort of a not a very fair question to ask you because the true answer is that it’s variable. Depending on the series and depending on where you look you are going to get different answers about how people present.

The largest single study that has been done was a European study done by Zampaglione and reported in Hypertension in 1996 where they looked at close to 14,000 emergency room visits, they got the 1% incidence of hypertensive emergency with 108, and these folks had a systolic blood pressure of
210/130 and you can see the standard deviations there. And this was the breakdown of the chief complaints at the time, and you can see that they are not much different. Chest pain in 27%, dyspnea in 22%, neuro deficit in 21% and interestingly in this study, which is one of the reasons I put this study up, headache was only seen in 3% of the presenting population, and 0% in this study. So the take home point from this question is you’ve got to consider everything. You can’t go and say well headache is going to be the most common thing because frequently it isn’t, there is other sort of symptoms. Look how close chest pain, dyspnea and neuro deficit are in this study. In my mind those numbers are the same, and so you have to really do a thorough investigation of all systems.

The next question is, and I actually gave you the answer to this already, is hypertensive emergency is associated with essential blood pressure of systolic of 225, diastolic of greater than 110, systolic of greater than 250, diastolic of greater than 120, and all of the above. And some said the diastolic of 120, but the majority of you did well, and got all of the above. And it’s an interesting phenomenon with hypertensive emergency is that there is no specific blood pressure at which hypertensive emergencies occur. It really depends on where the patients starts with their blood pressure.

One thing that we will say is that organ dysfunction is low if diastolic blood pressure is less than 130, but that the rate of increase from the patient’s blood pressure where they live at normally up to where they are at the time of presentation is probably much more important than the absolute blood pressure measurement. And that may be one of the reasons why in the pediatric population and in the pregnant population where they’ve been living at very low blood pressures, if they come in with
an elevation that we would consider to be a normal essential poorly treated hypertension that they actually have encephalopathy and end organ damage, it’s because the delta has affected them and has also affected the area where they autoregulate their perfusion to other organ systems.

So the initial evaluation involves what is near and dear to an internist’s heart, which is a focused history. One of the first things to establish is the most common problem that these patients have, is do they have a history of hypertension. The next thing is to ask the patient how well is their hypertension controlled. What antihypertensives are used, because withdrawal of say beta blockers or the clonidine group of drugs are much more associated with rebound phenomenon than other medications. How adherent is the patient to the antihypertensive regimen? I usually go into this when I ask my patients, I say wow, you are on a lot of medication, how is it that you take all these medications? Do you get every dose? If you open the door to the patient that they can be nonadherent to their – and they will be much more truthful to you whenever they give you the history. And the other thing to ask them is their last dose of antihypertension, or antihypertensive medication.

So yesterday when I saw a dialysis patient with a blood pressure of 220/130 my first question to him was when was your last antihypertensive dose? And sure enough, he had ran out of his medications two days before and hadn’t had anything for two days. So he was relatively easy to treat, he didn’t have any neurologic findings, we restarted his medications, gave him a little bit of labetalol and he did much better.
Social history, we live in interesting times, we have people that like to experience different realities and basically one of the things you have to be very, very cognizant of is that people use recreational drugs. So ask them about amphetamines, methamphetamine, ask them about cocaine. The young doctors in the room don’t remember Phencyclidine, angel dust, but the more mature doctors in the room do remember Phencyclidine and angel dust, so called angel dust because patients believed they could fly whenever they took it and frequently were found at the bottom of a building after they had jumped and found out they couldn’t fly. But Phencyclidine is one of the drugs that causes this as well.

So the initial evaluation is to confirm the blood pressure in both arms. You are going to be looking for co-arced and things like that, so there might be a difference in blood pressure. Usually the dominant arm will have the highest blood pressure, that’s the blood pressure you are going to treat. Use an appropriately sized blood pressure cuff, this is a very common error clinically, especially with an ever increasing population in terms of their weight. Frequently the blood pressure cuffs that are available are too small and you can get as much as 10 to 20 millimeters of elevation by using too small of a blood pressure cuff.

This is a picture that I borrowed from Normal Kaplan’s book, the 8th edition of Hypertension and published in 2002. This is really a wonderfully practical book clinically and it shows an interesting gentleman with very short legs having his blood pressure drawn or done. But it points out a couple
of things and I was actually complaining a little bit to one of my colleagues prior to the talk about I even disagree with this slide. The arm is not elevated enough, okay, so that there is still a column of blood here that can contribute to the blood pressure, and they also say place the stethoscope diaphragm over the brachial artery, you should use the bell, these are low frequency sounds that you are looking for so you have to use the bell whenever you take the blood pressure.

I usually go through a long description about the right way to take a blood pressure, but what I have done is I have found a video on the New England Journal of Medicine which is absolutely wonderful. These slides will be made available to you and this is the website for the short video that’s there and they go through, it takes about 3 to 5 minutes to go through, and they really show you a nice way of taking the blood pressure. Failure to elevate the arm, use the right size cuff, that in and of itself can throw you off by about 20 millimeters of mercury, and you need those blood pressure measurements in order to do this properly. Again, this is a very good book by one of the experts in hypertension in our field, Norman Kaplan, and for those of you that want to find out a lot more about the basics of blood pressure treatment and so forth it’s really a very approachable and good reference.

So the – continuing the initial evaluation, you are going to evaluate for end organ damage in the areas that we mentioned, so brain, heart, vasculature and kidneys. You are going to assess the pulses in all the extremities, looking for discrepancies which might tell if there is a dissecting aneurism, you are going to auscultate over the renal arteries looking for bruits, you’ll be limited in heavier
people because of the pannus will interfere with hearing renal bruits. I tend to also look for the renal bruits from the back as well, which tends to be less distorted by abdominal fat pads and such.

For the cardiopulmonary exam you are going to listen for signs of congestive heart failure, murmurs and gallops, signs of cardiac dysfunction. The neurologic exam is going to be looking for mental status changes, orientation, signs of increased intracranial pressure and pressure on the area of postrema which is responsible for nausea and vomiting. If there is increased intracranial pressure the patient will have nausea, vomiting, they might have seizures, they’ll have changes in vision. Four weeks ago the primary diagnosis of hypertensive emergencies was made by the ophthalmologist because the guy presented to the ophthalmologist with blurred vision. And we’ll go over the next part of this, which is the retinal exam. Lateralizing signs are uncommon, which is why the case I presented to you is a little bit unusual for malignant hypertension. Lateralizing signs usually suggests there is a vascular accident, but you still have to consider that it might be an association with hypertensive emergency.

Retinal exam literally is becoming a lost art. There are a number of us, usually the endocrinologists and the kidney doctors, that carry around little pocket ophthalmoscopes, and we’re all taught how to do this, but it’s very, very important because the retina is the only place in your body where you can actually see a nerve without sending the patient to radiology to see the optic disk. It’s also the only place in the body where you can see blood vessels easily, and it’s where the history of the patient’s hypertension is ______ large. Keith Wagener and Barker in 1939 came up with the first
classification and please indulge me because I’m going to review this because I think this is important. Grade 1 hypertensive changes are narrowing of the arterials, the so called copper-wire changes as the diameter of the blood vessel changes it reflects light differently. It becomes more coppery in tone. Grade 2 are moderate narrowing copper-wire changes, and when the arterial lies on top of the vein it pushed down and causes nicking. These changes are associated with long standing essential hypertension, in and of themselves they are not worrisome in someone that comes in with elevated blood pressure. And too, my medical students always tell me I have to show them normal, and I think that I should show everybody normal. So there is nothing wrong with this particular retina exam, you have a very nice sharp optic disk, you have the proper ratio between the blood vessels and the arterial – could we dim the lights a little bit if we can? Or do we have to leave the lights up? Okay. I’m sorry, so we’ll just go ahead. The changes are not so subtle so they’ll show up.

This is Grade 1 hypertensive retinopathy and the primary thing that you can see here is that when the arterial goes across the vein it pushes down and causes some nicking in that particular area. Grade 2 shows changes that are a little bit more prominent with regards to the nicking. The blood vessel has a sort of whitish characteristic to it, but really isn’t narrowed very much, you can still see a nice sharp optic disk.

The next changes which are quite important are Grade 3 changes with severe narrowing, silver-wire changes and you start to get bleeding from the blood vessels, so you get hemorrhage, you get signs
of old bleeding from the blood vessels with hard exudates and cotton wool spots which represent extravasation of protein into the retina and then clearing of the blood and the protein and leaving these behind.

And then finally the Grade 4 change which you see, all the changes you see in Grade 3 but you see an association with papilledema. And for those of you in the emergency room, if you do a retinal exam on someone and they have Grade 4 hypertensive retinopathy you put the ophthalmoscope down and you start writing admission orders. This is target organ damage, this patient has to be admitted. And a number of years ago, 30 years ago when the article was presented folks that present with Grade 4 and 3 changes are highly associated with going on to end stage renal disease and have decreased survival. So these are very important prognostic signs and very easy to find.

These are your Grade 3 changes, again you can see a nice sharp optic disk, you can see what’s a cotton wool exudate and hard exudate. Not seen so well because of the lighting, this slide shows a lot of hemorrhaging and so forth. And then finally Grade 4 hypertensive changes where the thing that I want to point out is you no longer have the optic disk visible, and the mechanism behind this is that cerebral pressure has gotten so high that it’s pushing the nerve out beyond the focal plane of the retina, so you can’t focus on it in the same plane. And then again, this patient needs to be admitted and treated.
The cardiogram, you are going to look for evidence of long standing hypertension, so you look for ischemia, injury, infarct, left ventricular hypertrophy. I always get nervous when I talk about cardiograms with Dr. Follansbee here, he’ll probably ask me a question.

Renal function tests, maybe I’ll defer the question to him. The renal function tests that we see are elevated BUN, creatinine, proteinuria and hematuria. You should check the CBC. Why? Because of associated diseases, thrombotic thrombocytopenic purpura, you’ll get anemia, you’ll get low platelet count, the same with HUS, you’ll get anemia with chronic kidney disease so these can be clues that something else is going on. The chest x-ray is remarkable for pulmonary edema, you get what’s called an ectatic aorta the sorts of unwinds to lead to cardiac enlargement on the chest x-ray as well.

Aortic dissection is relatively easy, it’s given away by the quality of the pain that the patients complain about, usually it’s severe tearing chest pain, a discrepancy in the pulses depending on where the aneurism is, chest x-ray will show widened mediastinum and these folks are usually addressed with a contrast CT scan or an MRI, and even in the face of renal insufficiency you need these studies in order to characterize what you need to do for the patient.

With pulmonary edema and congestive heart failure they need an echocardiogram in order to evaluate systolic and diastolic function, and also to look for different types of valvular abnormalities that may have resulted in the elevation of blood pressure or being a cause of the underlying condition.
Again, an elevated blood pressure without any of the end organ damage that I’ve just reviewed is not hypertensive emergency, it’s hypertensive urgency. We usually treat these patients with any of the oral medications that are available and the goal is the gradual reduction of the blood pressure over 24 to 48 hours. The management for those with hypertensive emergency with target organ damage again is parenteral medications and here is an important teaching point is not to reduce the blood pressure too quickly. The goals that are given in the literature are a reduction of blood pressure by 15 to 25%, or to get the diastolic down to about 110. Going further than that can result in failure of auto regulation in downstream organs and you can cause further ischemia. It should be done relatively quickly, but don’t aim to correct these people to normality very quickly.

Cerebral blood flow in a normal individual is relatively constant over a large range of blood pressures, mean arterial pressures of 60 to 120, in someone that’s chronically hypertensive they reset that, they go up to higher mean arterial pressures and their range can be as much as 100 to 120, up to 150 to 160. And you have impaired auto regulation in people that have stiff blood vessels and those that have underlying cerebral vascular disease. So the elderly will have a great deal more difficulty in auto regulating simply because of the dynamics of their blood vessels.

This shows the auto regulatory phenomenon. One of the things is that when you are hypertensive you go up and you are maintaining renal blood flow at normal, but you can see that if you fall below this level and over-correct you can end up with stroke, extension of stroke, you can end up with
mental status changes and cerebral ischemia. And you can also – the kidneys are especially sensitive to this as well because they auto regulate and pretty much auto regulation is a phenomenon found in any capillary bed so that you know the possibility of effect on any of the systems that are affected in this disease.

So again the general rule of thumb, and I’m going to give you the middle of the recommendations is 20% within the first hour, these patients should be in the intensive care unit and watched extremely closely for further damage. They require intraarterial blood pressure monitoring for the most part, although reading the more recent literature is that this is not as required with some of the slower acting medications, but for me I would want the patient in an ICU setting with an arterial line in place so that I can monitor them.

Which parenteral med? As a truism from this, I will tell you that Fenoldopam and Nicardipine are becoming choice drugs. Nitroprusside, Sodium Nitroprusside is becoming less frequently used but it still has a lot of usefulness. Which specific drugs you use will depend on the situation, but those 3 should always be on your list upfront.

So which of the following drugs should not be used to treat hypertensive emergencies? Sublingual Nifedipine, Labetalol, an ace inhibitor, Nicardipine, or question number 5, 1 and 3. And we’ve got sublingual Nifedipine, ace inhibitors and both. And for those of you that picked any of those 3 answers you are either partly right or all right. The one thing that you see in the recommendations
that have been made is that ace inhibitors are really restricted to the specific condition of hypertensive emergency associated with cardiac problems. That one of the reasons why is that hypertensive emergency is frequently associated with volume depletion and that if you give the ace inhibitors you can really decrease glomerular filtration rate and you can cause acute kidney failure by using it.

The sublingual Nifedipine is also something that is old timing. In 1992 to 1996 sublingual Nifedipine came out, we loved it. You put a little pinhole in the Nifedipine capsule, you squirt it onto the patient’s tongue and their blood pressure came right down. And then one of the things that I noticed was in my diabetic patients they were all becoming tachycardic and short of breath, and then at the cardiology meetings I think in Arizona in that year there was an abstract that was presented that showed that there was an increased incidence of myocardial infarction with using sublingual Nifedipine. And the FDA came out soon after that and said this is not a situation where you supposed to use short acting Nifedipine. It really has no role at all in treating hypertension emergencies and should be avoided at all cost. Ace inhibitors do have a small role but you should make sure that your patient is not volume depleted whenever you use it.

Your preferred agents, the ones that will get you through the day tend to be the beta blockers, Labetalol and Esmolol, calcium entry blockers as I mentioned, Nicardipine is used, the dopamine-1 receptor agonists, Fenoldopam is frequently used, is well acting, can be used parenterally. And then
vasodilators such as Sodium Nitroprusside and Nitroglycerine, the Nitroglycerine is more reserved for patients that come in with chest pain.

In our case with an acute ischemic stroke and cerebral vascular bleed it’s a little bit of a different situation, again you don’t want to lower the blood pressure too much because of a chance of extending the infarct area of bleeding. The agents that would be recommended in this particular case would be Fenoldopam, Labetalol and Nicardipine. We did start those in this particular individual and later on switched him to oral meds. I’m blanking on which oral meds we used at that particular time.

Blood pressure elevation can be reactive, the so-called reflex that’s necessary to retain blood flow into an affected area so you should not really aggressively treat these folks unless you are going to use thrombolytic therapy and you want to decrease the chance of a bleed, or if the blood pressure is really excessively high. The diastolic blood pressure should be the goal, try to get it down to about 110 and a systolic pressure of about 185 and so forth.

Acute pulmonary edema with systolic dysfunction, and again I’ll apologize because these are going to be laundry lists over the next few slides, Nicardipine, Fenoldopam, Sodium Nitroprusside are recommended. Nitroglycerine can be used if there is a chest pain component and usually a loop diuretic. You want to start off with a loop rather than a thiazide because you want something that’s going to be relatively uniformly effective and will help diurese the patient.
If they have diastolic dysfunction use your beta blockers with caution. Verapamil is a good choice, again Nitroglycerine is a good choice and a loop diuretic is a good choice, but all these have to be done cautiously in a monitored setting.

With an acute myocardial ischemia, chest pain, I recommend Esmolol, Labetalol, Nitroglycerine as a good way of going. If you rule out the patient and they no longer have chest pain and they don’t have any evidence of myocardial infarction, there is really no need to consider to use Nitroglycerine, there are other drugs that can be used. It works, but there are better drugs for controlling the blood pressure than Nitroglycerine.

Sympathetic crisis is generally an association with the recreation drugs that I mentioned previously. And the other place that it can happen is with sudden cessation of Clonidine and Beta-adrenergic antagonists. Clonidine is interesting, the incidence of sympathetic crisis with Clonidine is about 30%. It usually is reserved for patients that are taking more than .6 milligrams of Clonidine per day. And the abrupt cessation of that will cause this basic outflow from the central nervous system, there is increased receptor density because of the Clonidine inhibition and that causes the blood pressure to go up. It’s very easy to treat, you give them the Clonidine back.
Beta-adrenergic antagonists nearly always in common and conjunction with tachycardia and elevated blood pressure; the most common scenario I see that is someone preop and then postop is where the beta blocker is stopped, or where a patient stops taking their beta blocker.

Pheochromocytoma is rare, we do a lot of evaluations for pheochromocytoma but it is a very rare occurrence. It should be considered if you’ve ruled out everything else.

Now the next question, actually I had a nice question about this the last time I gave this lecture and I want to comment on the two articles that were forwarded to me. Which of the following drugs should be avoided in sympathetic crisis with hypertensive emergency: Phentolamine, Benzodiazepine, Labetalol, Nicardipine or Fenoldopam?

And Phentolamine – Phentolamine can be used for pheochromocytoma. So if you’ve got someone that’s got a pheo crisis it’s good for that. Interestingly enough, Benzodiazepine is a wonderful adjunct because there’s usually a big component of anxiety associated with cocaine. Labetalol is definitely the right answer, even though it’s a non-selective beta blocker you can still get unopposed alpha adrenergic stimulation secondary to the cocaine. And you can end up with accelerated hypertension, seizures and encephalopathy. It’s temping because of the myocardial infarction syndrome where beta blockers have quite a bit of a role. Nicardipine probably - is probably a good choice and Fenoldopam is probably a good choice. So for those of you that answered Labetalol you got it right.
The beta-adrenergic antagonists generally even with a non-selected agent like Labetalol you still don’t have very much alpha adrenergic activity and as I mentioned beta blockers can increase the blood pressure, they can actually cause more angina and they can decrease survival. So it’s recommended that we avoid beta blockade. The article that was given to me last year from the Annals of Internal Medicine I believe about 2007 and what they looked at was a population coming into the emergency room that had chest pain. And what they showed was a decrease in myocardial infarction by using Labetalol in that particular hypertensive emergency situation. The editorial that accompanied that was, to be polite, scathing. They really said that the study size was too small, that the selection of patients was inappropriate and that they felt that it was really not prime time to start using beta blocker in cocaine overdoses or methamphetamine use even if they did have chest pain.

They also mentioned that the incidence of myocardial infarction in this particular population tends to be about 5%, and therefore the gain versus the risk with beta blocker in this population was relatively small. So the editorial that accompanied this article pretty much said nope, we’re going to continue to avoid beta blockade in this population.

So that the recommended drugs for sympathetic crisis are Nicardipine, Fenoldopam, Verapamil, a benzodiazepine for the anxiety and if pheo is suspected to use Phentolamine, the presentation for pheochromocytoma, every single one that I have seen, which is not many, I mean you can count on 2 hands the number of pheos that I’ve seen, but they all had episodic blood pressure elevations, they
all had sweats, they all had pallor, they all had tachycardia, their blood pressure goes up and it
doesn’t remain the same, it comes down relatively quickly on its own. So they sort of tell them what
is happening.

The other thing that is very much fun to do is when you are vigorously palpating the abdomen on
somebody with a pheo you can induce a pheo crisis by compressing the pheochromocytoma, which
I’ve also had the misfortune of having happen to me. And let me tell you that there are several of
the gray hairs up there are because of that.

In aortic dissection this is one of the places where you really want to get the blood pressure down
quickly. 75% of patients with ascending aortic aneurisms will die in 2 weeks without successful
therapy. And we have made very, very good progress in this particular area. We’ve increased 5 year
survival dramatically. Two articles, one from Chest, one from the New England Journal of Medicine
have shown that the 5 year survival with aortic dissection is now 75%. And this is one of the
diseases over my career I’ve been very happy to see this sort of change where we really are doing a
much better job at treating blood pressure and treating this problem.

A vasodilator alone, you really don’t want to do that. It creates a reflex tachycardia, the more
rapidly the heart beats the more rapid the stroke, the more velocity you have and the more shear
stretch you have. And for those of you that want to, you know, experience shear stress firsthand, you
can take a drink out of your garden hose as it’s very bubbly, you know coming out at a low speed or
you can go up and try to take a sip out of a fire hydrant and see how that feels to your lips. That’s shear stress. Shear stress activates the endothelium, you can get dissection increasing, a lot of vasoactive substances are released in response to shear stress and you can make the hypertension worse and extend the dissection. So your standard therapy is to slow the heart rate down with a beta blocker, to use the vasodilator and Esmolol and Nicardipine or Fenoldopam are good choices with that. And you can use Nitroprusside as well in conjunction with beta blockade as a good choice.

Postoperative hypertension, and I have to tell you that usually when I see this it’s not because of the things I’m going to talk about, it’s because of the medications they didn’t stop. It’s thought that there might be hyperresponsiveness to surgical trauma, that there might be epinephrine release, you might have activation of the renin angiotensin aldosterone system. Cold, hypothermia causes stress and can increase blood pressure and hypoxia, carbon dioxide retention, bladder distention. I think all of you know what the effects of bladder distension is on your blood pressure.

Prevention is it’s safe to give antihypertensives preop, you should be very cautious about not stopping beta blockade before, you might want to avoid diuretic before the surgery because of decreasing intravascular volume and increasing the chance of renal damage. The treatment really depends on the blood pressure. I can honestly tell you that I have not had a postop hypertensive emergency. I’ve had postop hypertensive urgencies, but not emergencies. And really it makes sense, you control the pain, sedate the patient a little bit, if they are NPO you can use IV Nicardipine, Esmolol, Labetalol, and you resume their oral medications as quickly as you can.
So what happened to Sodium Nitroprusside, which was the mainstay of therapy whenever I was an intern, resident and fellow? And Mansoor and Friedman recommended it as the drug of choice in all hypertensive emergencies except eclampsia in 2002, and then a mere 4 years later, 5 years later Marik and Varon are saying that it’s only recommended for acute aortic dissection and pulmonary edema with systolic dysfunction. Well, there’s some disadvantages of riding the pride. One of which is that there are changes in coronary regional blood flow, there’s also changes in cerebral blood flow as well, which can cause deleterious effects. There is the risk of cyanide toxicity especially when patients have liver disease and whenever they have kidney disease. You need the liver for cyanide breakdown and you need the kidney to get rid of the byproducts. You can accumulate thiocyanate levels, so it’s use should be avoided in hepatic and liver disease, or in kidney disease, and if you have anybody that has these particular problems with their hypertensive emergency you should be measuring the thiocyanate levels daily.

Have we made progress? The first description of hypertension was not too many years after we started measuring blood pressure. Mohammed in Great Britain invented the blood pressure cuff about 1895, the actual blood pressure cuff that we use these days. And Volhard and Fahr, Fahr is a hero in the renal field and Die Brightsche Nierenkrankenheit Klinik Patholgie Und Atlas, which is Brightsche disease of the kidney clinical atlas or clinical pathology atlas, that was the first description of it. These patients all uniformly died of kidney failure.
Keith Wagener and Barker in the American Journal of Science came up with our classification system and based on the retina, and what they found is in people with advanced retinal damage that their survival on average was about 10.5 months, and none lived beyond 5 years and they all died of renal disease. So we have made progress, and the progress is that there’s a number of drugs that we have to choose from is monumental. We are much better at diagnosing hypertension now, we have a lot more intensive care units. And for those of you that work here at Presby, at UPMC, you know how many intensive care units that we have. The survival now with people that present with hypertensive emergency and urgency is almost the same as someone with uncomplicated hypertension, 18 to 25 years versus 21 years.

So on that note, I’d like to thank all my colleagues for attending. I’ll be happy to entertain any questions.

Thank you Dr. Johnson, another outstanding lecture. So I won’t bother you too much with the genetics ____________, since you’ve gotten to my question which I believe was if you took all of the hypertensive patients off their medicines would they all develop hypertensive emergency or just a subset? You’ve shown us that there certainly are subsets, beings that are predisposed both to hypertension as well as hypertensive emergency.

That’s correct.
So now I’ll bother you with the environmental piece, if you – you’ve shown us that if you take patients off their medicines abruptly they may be predisposed, and recreational drugs may predispose it. Any other predisposing factors to hypertensive emergency?

There’s an association, so did all of you hear the question, of a predisposing environmental component? Stress increases the incidence of hypertension overall. There was a really interesting study that was done in Bosnia during the Bosnian Slovenia conflict, and it was – the study was quite simple. What they did was look at the incidence of hypertension before the conflict, and then look at the incidence of hypertension after the conflict. And the percentage of patients with hypertension increased significantly in the 6 to 9 months following the conflict, even after the conflict was resolved. It is definitely a stress component to this. There are the group at Columbia, Lara’s group will tell you that rapid volume loading, which would cause increases vascular resistance and increased vascular stress may also be associated with it. So when you guys go to the Original Hot Dog Shop and have this small order of fries, which you know covers an entire dinner plate and it’s about 2 feet high, the salt load there might be enough to induce a hypertensive emergency. So I’d say salt loading and stress are your 2 environmental factors.

Other questions for Dr. Johnson?

One more question. This isn’t necessarily related to hypertensive emergencies, but I would have to think with the excessive cost of healthcare that patients being nonadherent to medications or not
being diagnosed with hypertension have to be perhaps the leading extra unnecessary cost that we have. You mentioned the primary care physician is important. How would you change our medical delivery system to improve this?

That’s an excellent question and I think Dr. Shapiro knows my politics. My – I’ll give you a little base ground for this, which was the best long term study looking at hypertensive control, estimates that we control hypertension effectively in about 30% of our patients. And that about 30% of our patients are undiagnosed with hypertension. In order to increase adherence to medication regimens I think the best thing to do is, number one empower the patient. So all of my patients when we talk about hypertension get a blood pressure cuff and they get a blood pressure notebook, and they have to record their blood pressures for me twice a week. And then we handle a lot of it by the phone. And so that they are aware that I’m going to be asking about this, so that’s one way of doing it is empowering the patient to take their own blood pressure and to keep the doctor informed.

One of the other ways of doing it that has been very effective is to have a nurse practitioner call center follow-up with patients on a regular basis. How are you doing with the medications? Are you having any side effects? And the last aspect of Big Brother is the pill counter on top of the bottle, and the pharmacy following how rapidly the prescriptions are being filled, which is sort of a Big Brother aspect. But there are places where this is done and it has increased adherence. But until you get everybody coming into the doctor’s office, we have a gentleman on service right now that presented with pericardial friction rub, end stage liver disease and end stage kidney disease, who
hadn’t seen a doctor in 30 years. And you know until we get people with regular care that’s just not going to happen. That’s the end of the editorial comments I promise.

Which was basically the description of patient centered continuous care.

Exactly right.

Other questions? If not, thank you and I appreciate it.

Thank you.