**BroadcastMed | The Acute Ischemic Stroke Patient**

SPEAKER 1: My presentation is going to be about the acute ischemic stroke patient. What I want to cover in about the 45 minutes I'm going to be speaking is an introduction to what stroke and TIA are, a little bit about the acute stroke patient and why time is important. I want to review the IV-tPA data, talk about anatomy and collateral systems of the brain, and then go over the imaging of acute stroke, and then management points about the acute stroke patient. So what is a stroke? It's defined by a loss of brain function due to lack of blood flow. And it's going to occur either in an ischemic situation or hemorrhagic. If you have an ischemic situation, that suggests that there's a clot there sitting to block blood flow. So you don't get blood flow to a certain focal area of the brain. And that causes focal neurologic symptoms. In the contrary situation, we have hemorrhagic stroke where the blood vessel ruptures. And that causes damage to an area, which consequently will usually cause focal symptoms as well. About 87% of stroke is going to be ischemic. And so that's really what I want to talk about today. So just some statistics is that about every 40 seconds in the US, somebody is suffering from a stroke. That's a lot. And every year, there's about 795,000, which is rising every year. And about 600,000 of those are first time events. And the other plus minus little under 200,000 are recurrent events. It's the leading cause of long term adult disability. As most of these strokes are actually happening in patients over age 65, about 3/4 of them. And it's responsible for 1 in every 17 deaths. 80% of strokes are preventable. And that just blows my mind, because all these patients are coming in and it's such a huge problem. But just to think about the hands of primary care physicians and how much you can do in trying to prevent this disease. There's a huge disparity that exists within both women and minorities. Women are twice as likely to die of stroke. And African Americans also have a higher death rate, in addition to Hispanics. There's also Hispanics that speak Spanish, that don't speak English, are much less able to talk about stroke symptoms and recognize that they're actually happening. It's a really interesting disparity. African American, Hispanics, they also have higher incidences, or risk factors, like hypertension and diabetes. And so they're also more likely to have stroke. The direct and indirect cost of having a stroke in the US estimated 2010 was about $73 billion. And the mean lifetime cost of somebody having a stroke is about $150,000, which is pretty significant. This is the graph on all the cardiovascular disease, where stroke stands. And I think it's still pretty impressive, even though it's fourth on all the lists. So what is a TIA? A TIA means that it's a transient ischemic attack. So the symptoms should be transient. And what the classic definition suggests is that the symptoms go away within 24 hours. But more commonly what happens is they're hours to minutes. And it really should be less than an hour. And because it's ischemic attack, it should suggest that there's symptoms going on that are related to focal ischemia versus a seizure. It also suggests that you should have a negative MRI. What that means is that a long time ago, we had this term called CITS, cerebral infarc with transient symptoms. And so could still have a hyperdensity on CT or you could have an MRI that showed a positive infarc, but the symptoms would be transient. So they'd go away. So they considered it TIA. But now, we consider that stroke. Anybody who has positive imaging finding should be considered stroke, not TIA. So what are some of the percentages about TIA? About 0.3% of all ED visits, which equals about 240,000 per year. And this is actually a lower number than we expect, because a lot of people have TIAs and don't report it to their providers. This is probably a lot higher. And the main reason we care about TIA in a lot of circumstances is because these patients are at risk for going on to have stroke and permanent neurologic deficits. And 10% to 15% of patients are at risk within the first 90 days, with additional risks of having even more vascular events like sudden cardiac death or acute coronary syndrome within those 90 days. So we care about our TIAs because you want to modify those risk factors and potentially prevent a full blown stroke, instead of just the transient ischemic attack. So now I just want to talk a little bit about what to do with the acute ischemic stroke patient and really how to approach it. And the way that I see it is that everything is time-based for stroke right now. And a long time ago, we didn't have therapy. But now we do. And so it's important to think that if anybody's having symptoms, it doesn't matter if those symptoms are going to go away in an hour. You don't know. If they're coming in with symptoms, they should be treated the same. And you should consider them for our interventions and our therapy, which are very narrow according to the time windows that we have. So acute care for stroke should always be focused on getting them therapy as soon as possible. And all stroke patients, in addition to what some people would argue all TIA patients, should be hospitalized. So we can modify those risk factors and find out why this happened and to prevent that again from happening. So acute stroke care is really, again, very time dependent. And it's based on a last known NORMAL. And I want to emphasize that, because a lot of people think that the acute stroke happens when symptoms happen. But that's not accurate. Sometimes the last known NORMAL can be the same as symptom onset, but oftentimes they're different. So when you're asking families or trying to establish a last known NORMAL patient, make sure it's when they're normal and not when they're symptomatic. That allows us to see where they are in being able to receive their thrombotic therapy. We also have time windows for when we want to get tPA in the door. And so a lot of acute care hospitals, including St. David's, what our goal is to get IV-tPA into the patient by 60 minutes once they've hit the door. And that requires a lot of care coordination between multiple members of the team. It starts in the community when a patient has to recognize that they're having symptoms or somebody in their family has to recognize that they're having acute stroke symptoms, somebody has to call 911. EMS has to come. EMS has to do an evaluation that says, this looks like an acute stroke. And they have to deliver them to the hospital and alert the ER that this is an acute stroke or they think that this could be. Then the ED has to see them, alert the neurology team. They need to get a CT scan. And all these things need to happen very, very quickly. And so our goal, and our national goal, is less than 60 minutes from them hitting the actual door and getting the IV-tPA administered to them. So time matters. And later on, I'm going to talk a little bit more about this. But the earlier that people get tPA, the better that they have in regards to functional recovery. So I really want to suggest that time is very important. So this is cerebral ischemia. And this is my least favorite slide because it's so busy and it's kind of blurry. And it's a lot going on here. But when there's an acute clot in the blood vessel, it basically activates platelets. It causes cellular activation. There's an increase in inflammation. It causes then lots of blood flow to the cell. The sodium pumps fail or cytotoxicity. You just go on and on. It's a lot of jargon. But what happens is that the cell dies. And so that's what happened when the clot sits there. So our goal is to resolve clots so that you can restore blood flow. And hopefully, the cell won't die. And that's what tPA tries to do. As you can see in the circled area in red, it basically is a serine protease, which works on plasminogen to convert it to plasmin. And plasmin works to cut down fibrin. And clots are made of fibrin. So that's what tPA does. And if we can resolve the clot, then we can restore the blood flow and hopefully help out the patient. So that's the goal of what tPA does. So this is actually-- I stole a slide from my mentor who passed away who was an excellent stroke physician. But I loved it. I thought it was really funny. And we have a few different recombinant tPAs available. But alteplase is actually the only approved for acute ischemic stroke, while the others are approved for-- Like tencteplase and reteplase are approved for MI and PE. So alteplase is the only one for acute stroke. And if you're administering it, it needs to be at a 0.9 mg per kg does with a 90 milligram max. So patients over 100 kilos, they'll get the same dose. You don't increase the dose above that. 10% of the bolus is given over the first minute and the remainder is given over for the hour after that. So now I just want to go over, how did IV-tPA actually get approved? And I think this is revolutionary, because stroke care back before the NINDS trial of 1995 was, the patient came in with a stroke. OK, let's admit him in the hospital. We're going to watch him, give him aspirin. But once the NINDS came out with their published data, it shifted stroke care to an acute emergent condition. And I think that's pretty revolutionary. So here's the data that was published in The New England Journal back in 1996 after the study was done. It took about 700 patients. And they divided them between getting tPA and placebo. And what they wanted to do was they wanted to look at the independent functional outcome at 90 days. And they used a bunch of different scales, which you can see on the right. The modified Rankin scale, which looked at disabilities. So you had a stroke. And did you have symptoms that interfered with your daily activities of living? All these scaled pretty much to the same, except for the NIH stroke scale, which just looks at plegia, sensory loss, and vision. But what they found is it didn't matter which index you used. You could use a Barthel Index, the modified Rankin, the Glasgow, or the NIH stroke scale. And there was still a significant benefit in receiving tPA over placebo. So that means that more people are able to return to their normal daily life, be able to go back and function without a lot of disability in about 13% increase in all of those scales. So what that translates to, the number needed to treat at eight. So that means if you treat eight patients with tPA within three hours, that means that for every eight you treat, one of those patients is going to gain functional independence over naught. So that's actually a really good number. Because if you compare number needed to treat for aspirin, it's about 340 to 350 patients you have to treat to prevent one stroke in one year. So eight is a very low number. And after the NINDS trial, they had ECASS, the MAST. They had a bunch of trials that happened. And what they did is there's a Cochrane meta-analysis that took all these. And they looked at all of the death and dependency again at 90 days. And they found that there was an absolute reduction in about 13% in just death and dependency

alone. So even despite that data, there's a lot of patients that were still being excluded. And so in 2008, the European Collaborative Acute Stroke study went on to ECASS-3 study. And what that did is they wanted to extend that window from three to four a half hours so we could have more patients that we could give therapy to. And what they found was that, over here on the way bottom, -- this was published in Lancet-- that per protocol, a population of the patients that met all of their, what they wanted for inclusion and exclusion criteria. And what they found is that patients at 90 days had a modified Rankin of 0 to 1. So 0 is, I have no symptoms at all and exactly the same as I was. 1 is, I have a little bit of disability, but I can still do everything that I used to do. So that's incredible. And that shifted the people who didn't get anything to the people that had tPA by about 7%. So that's huge. And I drew the red line to show you. But if you include it all the way to modified Rankin of 2, which a lot of studies will do where you have, maybe some are having plegia but you don't require assistance from other people. And you can still perform your activities of daily living. That increases it all the way up to about 15%. So I think that's pretty significant, if you're treating patients all the way up to four a half hours. And so the guidelines were actually revised based on that data to include tPA to be given to four a half hours in 2009. And the number needed, they found, was 14, which is still a really, really good number. So I just want to review these guidelines, because everybody asks, well who can get tPA? Who can't? Patients greater than 18 years old. So all the studies that were done are basically looked in adults. There hasn't been really any evidence to suggest-- Or there really hasn't been any studies to look at whether or not pediatric patients would benefit in this. Symptoms should be suggestive of acute stroke. So sometimes we get confounded by things like seizure. This is a very interesting and debated topic about should there be a lower level of NIH stroke scale that a patient should have to have in order to receive tPA. And a lot of people would say, no. And the reason for that is there's actually a study done where they took few hundred to almost 1,000 patients. And they looked at them and they said, well, which of these patients didn't receive tPA? And there was about 37% of them. And so why didn't they receive tPA? The number one answer was because, well they looked too good. The stroke scale was low. Or they were improving. And 30% of that group of patients actually wound up in the hospital dead or dependent. So a terrible outcome. And so what that suggests is that even if somebody has a lower stroke scale, it shouldn't be the defining point for when we're getting therapy. And stroke scale is not just ubiquitous. Somebody of a stroke scale of 3 could have hemiplegia, could have numbness, or could have aphasia. And to say that's going to be a deficit that's going to be easy to recover from or that's going to lead to some independent, functional outcome is just kind of a fallacy. You can't treat all strokes the same. So I suggest that this is what we call a relative contraindication, meaning you should still think about giving tPA to somebody who may be improving or have a low stroke scale. Blood pressure, very well defined. The reason that we want blood pressure restrictions like this is because we don't want ischemic strokes turning into hemorrhagic strokes or bleeding. Glucose level, as they say, greater than 50 or less than 400 mainly because at those levels or under, you can have focal neurologic deficits that can be confounding. This is another debated topic a little bit in the literature. There's a guideline that says if that if you've had an MI in the last three months, then you shouldn't receive IV-tPA because it could destabilize the wall. You could wind up with hemopericardium. You could risk cardiac rupture. And so there was a recent article in Neurology that said, well, we should really narrow that down to seven weeks, because this isn't really based on any data. Most of these are just the exclusion criteria from the NINDS trial. So there is some suggestion that maybe we don't need to say, well it's three months out, maybe just seven weeks. But that hasn't been quite clarified. And then these are what I consider as the intuitive guidelines, meaning tPA is a clot buster and it's going to cause bleeding. If you give it to somebody that's actively bleeding. That's going to be a bad situation. So when patients hit the door, we check their INR. We check their platelets just to make sure that they have a stable coagulation system. The rest of it, obviously, nobody with a bleed inside their head, who's actively bleeding, who has a noncompressible site, who's recently had an intracranial surgery, who has head trauma, anything like that that would increase that risk of bleeding. Those are patients we don't really want to give tPA to. SPEAKER 2: What's the data behind it? SPEAKER 1: Behind what? SPEAKER 2: Well, for me when I get phone calls about someone who had a little bit of traumatic sub-arachnoid hemorrhage two months prior, oh they're not going to get IV-tPA. SPEAKER 1: It's weak data. SPEAKER 2: I don't necessarily agree. SPEAKER 1: It's week data. Some of the things are a little weak. Somebody who has a history of cerebral hemorrhage, what does that mean? Does that mean they had a small sub-arachnoid? Does that mean they had a large intercerebral hemmorhage? It's not well defined. These are just things that they used, again, for exclusion criteria. So I think it's important if you can really get a good history to say, how much did they have? And is this really going to put them at risk for bleeding? And sometimes, I think you can do a better assessment of that. So then the other guidelines that are introduced for the three to the four and half window were taken from the past ECASS-3. So similarly, those exclusion criteria exist. Any patient who is on oral anticoagulants is actually excluded from that three to four and a half hour window. Anybody can't be over the age of 80. You can see that it's even limited based on all of these guidelines that are set up. So again, I want a little bit more about why time's important and what the data has shown in regards to how fast you can get tPA. But the earlier the administration of tPA after system onset, the greater patient functional recovery. So this was a huge Cochrane meta-analysis where they pooled all the data from the ECASS and NEA. And they look at the odds ratio for good functional outcome, which is mainly this modified Rankin 0 to 1. And what they showed was that there was a huge favorable odds in earlier times. So you can see the odds ratio on the left and then onset to treatment time on the right. And then that curve that comes down is what the odds are that they're going to have a favorable outcome or independent functional recovery. And it's significant and it kind of drops off. But what's important is that there's definitely a time treatment effect, meaning the earlier the better. But also, there are patients that are still benefiting all the way out to four hours. So we're talking about patients that still get benefit way out. So based on all that pooled data, these were the numbers needed to treat. And to me that says two things, the earlier the better. And number needed to treat of two, I don't even know any other data that exists in-- well, plus, minus-- that could actually give you a number needed to treat of two. So I thought that was very impressive. And there are still patients that are benefiting later time windows. So who and why benefits at later time windows? And I think the answer lies in the collateral circulation of the brain. I think that's the main reason. And the collateral circulation, to give you three of the main circulations, circle of Willis, leptomeningeal arteries, and the extracranial arteries, which I'm going to talk a little bit about. The diagram on the bottom shows what's going one when you have an acute clot that lodges in the arteries. The tissue dies and it's not getting enough blood flow. But surrounding that tissue or that core infarc is an area that's had very low blood flow, that's at risk for going on to be dead. But it's holding on somehow. And some of that is based on the collateral circulation that's applying it from other territory. But that's the stuff we want to see. That's why we give IV-tPA and we do intervention so that that doesn't convert to completely dead tissue. So on the left is the circle of Willis. And for those who aren't familiar, the bottom shows the back vertebral arteries going into the basal artery. And the front shows the internal carotid coming up to split off to the interior and middle cerebral arteries. And then in between those, we have these little skinny guys called the posterior communicating and anterior communicating arteries. And you can see in the back and the front there. And that forms the quote unquote circle. And so the circle's important because it allows redundancy in the circulation system. So you could have blood flow transfer from one hemisphere to the other and from anterior to posterior, which is a great system to have set up. Unfortunately, only about 30% of the population actually has a full circle of Willis. But it provides that anatomic advantage and potentially the setting of an acute ischemic stroke. So that's one way that patients can benefit. If you have a clot in one of the major arteries and you have flow that can circumvent it, then you could be in an advantageous situation where you're setting up tissue to stay alive longer. And then on the right is an example of what we call the leptomeningeal collaterals. And this is showing internal carotid coming up. It gives off an MCA branch to the right, an ACA to the left. And at the very, very ends of the MCA and ACA, there's an area where they are almost sharing the territory. That's kind of the watershed territory. But the leptomeningeal collaterals are giving flow to each other. So if you shut off that MCA, potentially, you can have some flow coming from the ACA to help out it's buddy over there. And then this is just a diagram of the external carotid artery. It shows the facial branch. And I'm sorry I didn't mark them. The facial lit shows the occipital branch coming backward. It's just very difficult to see. What I want you to understand from it is that the external carotid artery can supply the internal carotid artery in addition to the intracranial artery's supply of blood flow if potentially the internal carotid was to get blocked or potentially the intracranial artery. So it's just another system set up to try to aid at blood flow, potentially in that acute situation. And people who have really well developed collateral system, maybe those patients who are getting out to those later time windows. So imaging acute stroke. So what do we want to do for patients when they come into the ER? The first thing we want to do get is get a CAT scanner. Every patient should get this kind of CAT scan. And on the top, it shows on the left, I want you to focus on the left top one. And that is a non-contrasted head CT and an axial cut. And what it's showing is

this is a patient who is probably having a stroke in less than four hours. And what we would expect is that we don't see anything, right? You don't see anything. It should look normal. Within a day, the patient's going to have a large hyperdensity. Within two days, it's going to be even a more significant hyperdensity. So that's an MCA infarc that's evolved over time. But head CTs shouldn't show changes in under four hours, typically. So we're not looking to see changes there. But that also suggests that it's not going to be very sensitive for acute ischemia until we get to that four hour period. On the bottom where we call the acute stroke signs. So maybe close to that four hour period, we want to see, is there a suggestion that there could be a large infarc going on? And what that little arrow is point to, the yellow arrow, is to the gray and white that you usually see on the other side, where you can see the cortex nicely and you can see the gray matter, is now blurred. So you can't see the difference. It suggests that there is edema going on there. And then the black arrows are pointing to the insula-- it's an area of the temporal lobes-- showing the same thing. What we call that is a loss of the insular ribbon, where the gray and the white start to blur together. And then finally, sometimes on non-contrasting CT you can see the clot is so dense, it's sitting in the artery. And even if you don't give contrast, you can still see that the vessel is dense and lighting up because there's a large clot sitting there. So we like to supplement acute stroke imaging with CT Angiography or some sort of vessel imaging. It's important to get an idea about the vessel because that could change your management, whether the patient needs further than tPA, further stroke treatment. And so what this shows is you inject the patient with iodine contrast dye. And at the same time you're going to the head CT done, you can get the CT angiogram done in about five minutes. So it's really fast and it's really convenient. Mose centers have a CT scanner, in general. And the only contraindications are renal failure, if you have an iodine contrast allergy, pregnant, or metformin use. So it's a pretty accessible study. What this is showing is the different sides. The non-contrasted head CT that we see on the left with the MCA clot. And then on the right side, you see the CT angiogram, which basically just confirms the same thing, is that there's a clot sitting in the MCA there. So this is helpful for us. And again, it's really towards directing management. Here at St. David's, we do some CT perfusion imaging. And I think that perfusion imaging, whether it's with CT or MRI, is the way of the future. It allows us to image acutely what's considered penumbral and what's considered core. So I want to focus on the bottom slices and images. If you look all the way to the left, that's the head CT of a patient presenting within four hours, four and a half, somewhere around then. We don't see that there's any changes there. We don't see any gray areas of differentiation. Then we image them with what's called a mean transit time sequence. And what that means is, what's the mean transmit time for the as the dye passes through for it to get to an artery and vein of choice? And based on that, the mean transit time is an indirect measurement of collateral situation or in addition, a little bit of the penumbral tissue. If you compare that with the cerebral blood volume on the right, which is the CBV, what that shows is that the CBV should really be the representation for core. So if you compare CBV and MTT, what you get is penumbra. That's basically what it is. The difference between those two is the penumbra. The CBF is the calculation of the two. So penumbral tissue, if it's not salvaged by giving IV-tPA or some sort of thrombectomy or restoring flow will eventually convert to ischemia . And that's what happened to this patient. They didn't get therapy. And then this is their head CT follow up is that that whole area on the MCT plane is converted to ischemia. So MRI is the other option. And MRI is a little bit more difficult and not as readily accessible in a lot of centers, but it is more sensitive for acute ischemia. So it can pick up ischemia within about 40 minutes is the typical, instead of all the way to four hours. And so what you see up on the top is you have a head scan, which doesn't show any changes. And then next to it, you have a DWI sequence which shows that there's an acute stroke going on. On the bottom, I just want to demonstrate that diffusion sequences on MRI look for the random diffusion of water molecules. And if you have restriction of that , which happens in cytotoxic edema and acute stroke, then you're going to see brightness. And then we correlate it with what is called an apparent diffusion coefficient. That's dark. And that suggests acute ischemia. So that's the kind of sequence that we're looking for. MRI has the same ability as CT to do perfusion. So again, what you see on the left is that the patient has some acute ischemia going on, which is represented by a bright signal on DWI. And then the middle sequence is the mean of transit time sequence. And what you see this is that there's huge area that's at risk, but it doesn't correlate. So there's a quote unquote mismatch between the A and B sequences. And if that tissue is not salvaged, then at the 24 hour follow up on the MRI, that's the stroke that you're left with. Because all of that mean transit time, which was tissue at risk, which is penumbra, which collaterals are just trying to hold onto, has gone to necrotic ichemic tissue. So it really allows, with acute stroke imaging, especially the advanced acute stroke imaging how much tissue is damaged and how much is potentially salvageable. And that allows us to direct towards therapy, such as the IV-tPA to IA and the thrombectomy. And I just wanted to give this one slide example of tPA doesn't always work. It'd be nice to think that every patient that had got tPA into would make them better and things would do well. But based on clot location, it's actually more or less likely to do well. So that 66% is when you have a clot that's lodged, what we call distally, all the way in the MCA. 35% if it's in the proximal, the top of the internal carotid. And only 9% of cases of IV-tPA assist in the clot that's including the internal carotid artery. And this is why we have other interventions, like thrombectomy and IA-tPA. So I just want to mention the bleeding with IV-tPA was actually-- This data is that from the SITS-MOST registry, which is about 14 different countries keep tabs on the bleeding side effects from IV-tPA. And the quoted percentage is about 6.4% versus placebo at 0.6%. So I want to bring this up because a lot of physicians are reluctant to give tPA because of the bleeding risks. Obviously, there's a bleeding risk. But also, I want you to notice that the mortality is actually lower with tPA. And that's because the people that were not tPAing are dying in a hospital and they're having dependency. And so even though the patients bleed on tPA, they actually do better in the long run. And I want to point out some of the risk factors to the people who have hemorrhagic conversion or wind bleeding intracranially with IV-tPA. And those are patients who have longer time of treatment, older age groups. They're hypertensive in presentation, hyperglycemia, higher stroke scales, early CT changes, or severe white matter. All of these have been identified as risk factors. So finally, I just want to talk about acute management points. And one of the first things is that I feel like every patient she should be considered by tPA, but the important things need to be addressed first. So is this patient protecting their air way? Oftentimes, they're not. And so do they need intubation? That needs to be addressed. Are they in athea with RVR, need to be treated and need to be addressed first before anything else is considered. Hypoxemia worsens in cerebral ischemia. It increases the rate of neuronal death. They like to keep their sats at least above 94%. Temperature regulation in the brain's a little bit hotter than the core body temperature, but it definitely doesn't tolerate in a hyperthermia situation. And these patients have worse outcomes if you leave them febrile. I would just suggest that you be aggressive about fever work up and keeping them in the normal thermic. And then finally, glucose regulation. A lot of stroke patients will come in actually hyperglycemic. That's often times a cortisol response in response to the acute stroke. But we need to be really aggressive with their glucose regulation, because that also affects how fast their neuronal death will happen. And this is a great graph that was taken from a study back in 1980. And I know the acute blood glucose is a millimolar per liter. But that 10 right there is about 180 on the glucose, which is like 270 on our milligrams per deciliter scale. So when you look at penumbral salvage, which means how long is that tissue staying viable? How well is it doing when we salvage it? Well, at lower glucose, it's doing great. But the minute that you're going up 120s, 150s, even up towards-- That's not that much. We're seeing a lot worse outcome. And I'm sorry about the black. I know it doesn't come out that well. In regards to blood pressure management and what you want to do for their blood pressure, it's really all based on what's happening with the brain in the acute stroke situation in regards to hemodynamics. So on the left, you see that there's cerebral blood flow over there. You see that right? Cerebral blood flow. And that little line across on blue, that's a normal patient. And the line that comes right across is 50, because everybody likes to live right at that 50. That's how much blood flow that the brain wants to get. And the blood flow is equivalent to how much perfusion it's getting over the vascular resistance of the brain. And your perfusion is really mainly dependent on your blood pressure minus ICP, which is typically negligible. So in general, you're perfusion is providing cerebral blood flow. And the reason that it's able to stay constant like that is because you have little arterioles that are dilating and constricting and keeping everything stable across that, keeping it right at 50. Now, the pinker, whitest line in the middle there, that's the ischemic stroke patient. They completely lose that autoregulation ability. So they can't constrict and dilate, like you and I could, to keep that nice 50. So what happens is that their blood flow becomes completely dependent on their blood pressure or their mean arterial pressure. So that means that they are already trying to perfuse a higher pressure. So they've typically come in to higher blood pressures in the ER. But also, what that means is that you shouldn't be lowering them either. Because the minute you're lowering them, you're putting them down into an ischemic range. And ischemia is about down there near about 10 or 12 once you hit the bottom of the curve. And that's complete ischemia. So you drop them down there, their brain's not going to like it. And then just to bring up that not every patient's going to be the same, especially patients who live chronically hypertensive. So the green curve is

somebody who's curve has been shifted to the right, because they live at higher blood pressures. And so they may need even higher pressure in order for their brain to steady. So you can sometimes spot those people, because they fluctuate a lot even with little blood pressure decreases. SPEAKER 3: How long post-stroke do you want to keep their blood pressure up? SPEAKER 1: So usually, it depends. But 24 hours is usually is what is permissive, quote unquote. But it can really depend. It can depend on, number one, did it have a clot that's sitting in their internal carotid or something else that's not going to allow them that perfusion? How they've done with even with little blood pressure fluctuations. The recommendation is that after 24 hours, you could start to consider blood pressure lowering, but I think it's very individual dependent. And then also knowing, are there already blocks that are going to impair flow? So our goal is that our permissive levels are about 220 over 120. And then we're a little bit aggressive about pre- and post-tPA just because we don't want that bleeding risk for hemorrhagic convergence. So the agents that we recommend are either nicardipine or Alocril. And the reason we like those is because they're IV. They're easy onset, two to five minutes. Nicardipine's on here because it's easily titratable. You hook them up to an IV and you can monitor a lot easier. Things we don't recommend are nitroprusside or hydrolazine because those actually increase the intercranial pressure, in addition to vasodilating. It's a bad situation to put an ischemic stroke patient in. The other way to increase perfusion outside of just allowing their blood pressure to be permissive is they studied a bunch of patients with MCA clots. And when they took them from 30 degrees down to 0 degrees and laid them flat, it increases perfusion by 20%. So it's a really easy measure to do. Just use gravity. And we like all our patients to be flat, as long as they can tolerate aspirating or are having other respiratory problems. IV fluids are also really important. What they thought, initially, was that you shouldn't give patients IV fluid. It's going to worsen cerebral edema. But it's actually the opposite. A lot of patients are dehydrated because they've been sitting at home. They can't swallow. They've been on the ground, something like that. So it's actually recommended that all patients receive IV fluid or resuscitation with normal saline. If they don't have impaired kidney or heart function, they can receive about 100 cc an hour. If you're really awesome, you can calculate their fluid balance to try to put them to-- If you believe me, I'm not that great. But patients with impaired heat function or kidney can go down to about 50 cc per hour. And then finally, I just want to say that if the patient's not going to get tPA, they should at least get aspirin when they hit the door. And there's actually been only this study to tell you with acute stroke trial to look at patients who didn't get tPA what to give them when they hit the hospital, they all got within 48 hours, this is 21,000 patients. And they found that mortality occurrence, ischemic stroke or death and dependence, in six months all showed benefit with getting aspirin. So just conclusions is that every patient with any full neurologic deficit, so look like they're going to be having acute stroke should be considered for tPA. And every person involved with patient care plays an important role in getting us that time clot and getting those patients in that window that we can give therapy and potentially improve their outcome. And then, these are just some select references. And that's it.