DAVID LEVINTHAL: Welcome. Good morning. I'm going to be talking about the diagnosis and treatment of esophageal motility disorders. My name is David Levinthal, I'm the director of neurogastroenterology and Motility Center here in the Division of Gastroenterology, Hepatology and Nutrition at UPMC.

So I want to give a little bit of an overview of the talk today that I'm going to give about esophageal issues. I first want to preface things by saying that motility does not imply functional GI disorders. Those terms often are used interchangeably.

In terms of dysphasia and esophageal issues, there are some functional disorders which may not have an actual correlate on dysfunction of motility of the esophagus. So for example, this feeling of globus or functional chest pain or functional heartburn.

So those are functional disorders, some of which ultimately may have some subtle motility issue. But those are not motility disorders, per se. So what we're focusing on today are purely motility-driven issues. OK.

So the goal of my talk is to go over a bit of the principles of esophageal motility testing. To talk about patterns of dysphasia and how that may guide what kind of tests are chosen to do in patients that describe dysphasia.

To go over some of the spectrum of normal findings that one would see in some of the basic tests that are ordered, specifically focusing on some of the high resolution esophageal motility testing, which has been devised over the last perhaps 10 years or so.

Go briefly over the Chicago classification of esophageal motility disorders. And then I want to focus on three clinical disorders, achalasia, scleroderma, which often is accompanied by motility issues of the esophagus, and diffuse esophageal spasm.

We won't have time to be comprehensive this morning about every disorder that involves the esophagus. But I think this will give a good sense of how to think through these issues.

So the first challenge is to really define the problem. When you have a patient that describes dysphasia or difficulty swallowing, what are some of the key historical features that one needs to get to be able to direct some of the testing?

And the first thing that's really important to do is to ask patients, where do you feel that food is getting stuck? And what kind of food is being stuck?

So if patients say that, oh, my gosh, the second I swallow, I feel things stuck in the back of my throat. Or I actually start regurgitating even through my nose, practically. Nasal regurgitation.

Or I have frequent aspiration events, even the sense of choking, that implies that there's an oral pharyngeal source of dysphasia. So dysphasia is not enough. You need to really localizes this a back of the mouth problem or is this actually the esophagus as the issue.

So if it's an immediate issue and it's localized to the back of the throat, sometimes felt in the mid-neck, that implies oral pharyngeal dysphasia. And we're not going to really spend much time on that today.

Now obviously, people can have issues with solids and liquids or solids alone. Solids in general, if that's the sole problem, implies a structural basis rather than a motility basis. And if it's solids and liquids, there is perhaps a suggestion it might be a propulsive problem.

So we're going to focus on the right side of the diagram today. So if people-- patients that you see describe dysphasia, then it takes a few seconds to actually have an impact. So they swallow, they get it down OK.

But then within a few seconds after that, they say it just hangs up. I feel this either sometimes at the base of the neck at the sternal notch or often in the mid-chest. Do they have a history of food inpactions and so on.

That would be big clues that there's an esophageal issue. Then again, asking patients, well, is it only with solids or with solids and liquids? And it's the latter that we're really going to focus on today. OK? So the accompiment of having issues with liquids really implies a motility problem.

Another historical feature is important to ferret out when you talk to patients with dysphasia. That relates to the temporal pattern the onset of the symptom. So is this a new thing?

You know, you've been fine and all of a sudden a week ago, rapid onset issues? Often accompanied by chest pain. So you know, the context matters, especially in immunosuppressed patients or someone on chronic antibiotics. But you think about infectious etiologies, perhaps all of a sudden, becoming symptomatic from GERD, maybe with erosive esophagitis. So this implies some kind of inflammatory pathway, either infectious, or acid reflux.

So if patients say, well, you know, it's kind of been hanging around for a while, that implies that it's probably a motility disorder. And you can have pain with some of these disorders, but it doesn't have to be present. And especially in the case where it's slowly progressive, one gets a little bit more concerned about some other issues that can be going on, such as achalasia, certainly cancer is concerning, other autoimmune processes like scleroderma, which we'll talk about, can have a progressive element.

So we're going to focus on the middle and right-hand side of that divide. So what should you do first, for a patient who describes dysphagia? We've established, perhaps, that it's likely a propulsive problem, if they have solids and liquids. What should you do first? This is actually a source of some controversy and there's a little bit of debate in the literature.

Should one really do a barium esophagram first, or should one go straight to endoscopy? Very few people would advocate for going straight to esophageal manometry. So it's really kind of a debate between these two tests, which is the first one to do? And I think it depends a little bit about the historical features that the patient gives you.

So if it's to solids and liquids, barium esophagram is a really good test. And we'll go into a little detail about what we can learn from using a solid pill, radiopaque 13-millimeter pill, along with the barium esophagram, gives us a sense of structure and function. But for solid dysphagia alone, I think very few people would argue that endoscopy shouldn't be the first test. So someone own presents with solid dysphagia alone, I think that implies there may be some structural basis and endoscopy probably wins out.

So for solids and liquids, this just gives you kind of a sense that if it's really recent or acute onset, this could be Candida esophagitis. It's very painful, patients will have a lot of issues, often, swallowing in that context, not just with pain, but also with motility. But a chronic and progressive issue could be, which we'll talk about, a major issue with achalasia, a well-defined disorder I'm going to spend some time on. So this would be the barium esophagram classic view with a bird's beak point of contraction, at the lower esophageal sphincter. And this would be the endoscopic view of the same anatomical location, where you really have almost a pinpoint GE junction. So that's kind of a classic.

OK, so with a barium esophagram, this is, as I said, a very good test. Not only can one do a double contrast barium esophagram and get actually a very good mucosal resolution. It's not as good as endoscopy, but that's actually quite good degree of sensitivity for esophagitis or ulcerations. But importantly, when they do the barium swallow, where there's a column of liquid going down, that actually has a decent sensitivity for looking at the motility pattern of the esophagus.

And we can infer the contractility pattern based on the timing and the pattern of contrast flow through the esophagus. When you do the pill swallow, this is really an important test because this pill, it's pretty big, 13-millimeter pill is like a big vitamin. So it's a bit of a stress test for the esophagus. It's a dissolvable pill, so even if it gets lodged, it will dissolve and pass.

But this really localizes functionally relevant positions of the transit impairment. So is it hanging up in the midchest? Is a hanging up at the GE junction? Those things are really important to know, because it would guide next steps, and potentially imply that dilation could be offered. And this is obviously testing solids.

So how should we think about the motility that-- pattern seen on the barium esophagram? So this is a schematic, obviously, of what one would see, but it also gives a sense of the timing of what when to see. So that is a cine esophagram, meaning a movie of serial images that are obtained after a patient swallows a column of-- a bolus of liquid.

So it's radiopaque, so that's implied here with the black. So you have to think a little bit in negative space. So essentially if the esophageal lumen is contracted, it will not show up in the barium esophagram exam at that moment. So the second that you swallow, or a few seconds after, and the UES opens and a column of fluid is then the proximal esophagus, the distal esophagus is contracted, and you can see-- you can infer that the esophageal lumen is relaxed, at this moment.

And it's progressively higher tone, to the point where there's enough contraction to hold that bolus in place, at that moment. And as the esophageal contractions propagate distally, that bolus is being forced downward, and there's progressive relaxation in the segments distal. So everywhere where you see a black column, it implies that there's a lower contractility in that segment of the esophagus, and wherever there's luminal obliteration, because of a contraction, that excludes contrasts.

So essentially, you're watching the wave of contraction push that fluid distally. The lower esophageal sphincter would be right here, and it should normally open to allow contrast to flow into the stomach, which it indeed does-- sometimes you see some tertiary contractions right in that location. But this would be a normal progression, in terms of the timing and the morphology of how you would capture the column the fluid, as one does a barium esophagram.

OK, so importantly, this would imply full clearance, so there's no residual contrast. So what's not unusual-- that's a normal barium esophagram. what you often see in someone with either GERD, or especially in the elderly, with a progressive, what they might call presbyesophagus, with less vigorous contractions of the esophagus. It takes a little bit longer for contrast to move through, and you see a larger column of fluid at any one time, because the contraction force of the esophagus in any one segment is not sufficient to push fluid more distally.

And often what you can see is a contraction which comes at a time in which there's still residual contrast, and it almost squirts it more proximally. So that's called proximal escape. So when you read a report from a barium esophagram, that's what the radiologist is referencing. That's an incomplete clearance of the bolus, and that would be insufficient swallow, ineffective swallow.

So someone with this barium esophagram could very well describe dysphagia to liquids, and they're feeling this residual contrast. They may have to double swallow, to then create another peristaltic wave, that that then clears that little residual material in the proximal esophagus. OK, so I mentioned esophageal manometry. We might do a barium esophagram and get a pattern like this, or maybe even a pattern that shows even worse contractility.

So we want to be able to document, what is exactly the pattern of contractile patterns, and over time. So the barium esophagram may give us a sense of, is there an issue, yes or no? But the esophageal manometry is the best test to actually precisely diagnose what kind of esophageal motility disorder there may be.

OK, so to do this, manometry implies that we're measuring the actual pressure. And so this is determining the actual contractile patterns. And we do this over time, and I'll show some slides about how this is done. But there's a caveat to these tests. There's no direct measure of transit. The barium esophagram was a direct measure of transit, you swallowed a bolus and you could see it go through, it implied contractility.

So these are kind of mirror image tests, in a way. When you do manometry, you're looking at the contractile pattern, and there is a impedance measure, which allows for some inferences about transit, but it's not a perfect test of transit, per se. So that's one caveat.

So the general principle of manometry is such that there's a catheter placed-- transnasally, into the stomach-- crossing, spanning the entire esophagus. And there are pressure sensors along that catheter. one In the resting state, there's some basal tone in the regions of the esophagus throughout its extent. So I the mid, distal, and at the lower esophageal sphincter, there's a higher tone at rest, to act as a barrier function.

When one swallows, there's a proximal contraction, which can get picked up. But the distal esophagus hasn't yet contracted. That wave propagates distally, so you can pick that up here. As things revert back to their normal state, there's higher contractions here, at the time that the lower esophageal sphincter relaxes.

So it's very important that we document, what does the lower esophageal sphincter do in response to swallowing? This would be a very normal response to a swallow, and it needs to be precisely timed. The lower esophageal sphincter then gets back to baseline, and the basal pressures in the tubular esophagus reset, after a swallow is completed. So in broad strokes, that's the general pattern that one would see in motility.

So this is as time moves on, this is a slightly compressed time scale that maps into the images I just showed, but things get a little bit more fancy than what I just showed. So we're going to spend some time looking at high-resolution manometry pictures, because this is really the modern way of doing esophageal manometry.

And just to kind of give it a view of what it used to look like-- and even in my career, I kind of span both old and new. We used to have water-perfused catheters that only had four channels of output, and we had to really infer a lot about the motility pattern based on less information and presented in a little bit more abstract way. I think the colorimetric views of some of these tests have really made it easier to interpret, and there's a lot of new data about how to interpret these patterns.

So I'll go into some detail about high-resolution manometry. So what essentially has been done is that instead of four or five channels of, data we now have 30 or more. And so with more precision, we're actually looking temporally at every segment of the esophagus, over the entire timing of the swallow, multiple times-- there's a lot of data. And a lot has been made about different subsets of constructs of data points that can be derived from some of the basic wave patterns. And that's more data, but perhaps not more fundamental insight.

So if you look in the literature, there are a lot of papers written about some of these individual submeasures. But, at the end of the day, what we really want to know is, is there effective contractility in the esophagus? And what does the lower esophageal sphincter do when we swallow? And it really comes down to those two major measures. And that's really no different than in the older version of esophageal manometry.

Some of these newer measures include the speed at which a contraction moves through the esophagus, so the contractile front velocity, one can calculate that. An integrated view of the net pressure that the lower esophageal-- I'm sorry, excuse me, the mid to lower esophageal segments contract. A total measure called the distal contractile integral. And those features rarely change the basic interpretation.

I gave you some caveats before, that we're looking at the patterns and the amplitudes of muscle contraction, not specifically transit. Although, all modern high-resolution manometry-- recording equipment has an impedance channel built in, that we can give some indirect measure of bolus transit. And a pretty good measure, I don't want to overplay that. It is it gives us a sense.

So I'm going to spend a little bit of time on this picture, because I want everyone to really have this in their mind, about what is it that we're looking at? What would be a totally normal high-resolution image of a swallow? OK, so what's shown here is from the top of the screen to the bottom of the screen, all of the pressure readings through the entire high-resolution manometer-- so this is now through the nose, into the stomach, through the back of the throat. And we can actually see the pressure at each of these sensors over time.

So time is increasing from the left to the right, and then proximal to distal is top to bottom. So looking at this is actually almost a three-dimensional thing, because it's a time, and space, and pressure reading. One can view the z-axis coming right out of the screen, if you will, in a colorimetric form, that's integrating the amplitude of the contraction at any one of those sensors over time. So I hope everyone can picture that in their mind. You have to do a little bit of mental gymnastics to see this in its totality.

So the upper esophageal sphincter poses a barrier. And you can see that barrier. So at rest, over here, there's some basal tone to the upper esophageal sphincter. When one swallows, there's a brief mini contraction and then a very quick relaxation. And you can actually see here that the pressure, which is colorimetrically linked to the absolute amplitude. So red is a higher amplitude, dark blue is very low. And essentially, you have this patch of dark blue and the middle and that's because the UES has completely relaxed.

And so, that allows the bolus to enter the esophagus. If that didn't happen then one would have oropharyngeal dysphagia, you would choke. Or things would come back, up very quickly, in the back of the throat. This is the pharyngeal contraction coming down, in the back of the throat, forcing material through an open UES, and then it all relaxes. So it's a very coordinated, quick skeletal muscle contraction that happens.

That is under volitional control, we can control when we start to swallow. And indeed, a patient who's undergoing high-resolution manometry is asked to specifically swallow on command, and so this would be the prototype of that. So what you see, in response to an initiated swallow, within half a second, is a very ordered, strong contraction in the proximal esophagus. And remember, it's important to think about what properties of muscle there are throughout the tubular esophagus.

The proximal esophagus is skeletal muscle, and there's a transition from skeletal to smooth muscle, in the distal esophagus. And in-between, there's a bit of a pass off between the types of fibers that make up the muscles of the esophagus. And in this region, it's kind of a half and half of skeletal and smooth muscle. So what a normal pattern of esophageal contraction would be, intact proximal esophagus contractions, often a low-pressure zone, right in what's called the transition zone between the smooth and skeletal muscle.

And then a pattern of smooth muscle contraction that's often slightly higher amplitude in the distal esophagus than in the mid segments, but nonetheless, a propagated order of events such that, over time, things are propagating top to bottom and left to right. And if you can appreciate that there's a kind of a diagonal to this, that is exactly what we saw before with the barium esophagram, where material was moving-- contractions were moving down the esophagus.

OK, now looking at the lower esophageal sphincter, this is an important feature of every swallow. There is a basal esophageal gastric junction tone so the GE junction, or the LES, which spans that anatomical location. And when we swallow, there's a signal that's neurally mediated to the LES to relax. And that makes room for the bolus, so that it can enter the stomach, akin to the way that the UES relaxed to get the bolus from the mouth into the esophagus.

So sphincters are important, because they can pose both a barrier to flow, and also be the gate that needs to open. And so this is really an essential mechanism for allowing normal swallowing. There's usually an after-contraction of the LES that exceeds baseline, and it relaxes back to its baseline. So this would be a completely normal swallow.

So there are a couple of derived measures which are important for understanding the classification scheme of an esophageal manometry test, which is the standard nowadays. So it really comes down to looking at a window here, over this box here, represented, of looking at the residual pressure. Not so much the basal pressure, but really the residual pressure in that LES zone. And that's called the integrated relaxation pressure. Normal for esophageal manometry, high-resolution manometry, is 15 millimeters of mercury of residual pressure.

Anything less than that would be normal, anything above would be abnormal, and imply impaired relaxation. It's also important to note the pattern of contraction. This is a propagated ordered peristaltic wave, and it's the mean-- it doesn't project on the screen here, but the mean amplitudes are in the normal range, this would be completely normal.

OK, so what can we learn about bolus? I mentioned impedance. So in purple here, is actually another channel that's built into the high-resolution manometer. And we can actually send a current through different segments of that catheter, and the resistance to flow of electricity through that segment implies that there's liquid in that region. So it's an indirect electrical measure of liquid flow. And so at baseline, here, there's nothing in the-- there's not as much in the esophagus. This is gated, so it really picks up the swallowed bolus.

Drinking salt water actually makes the signal even better, so we have people sip some saline, which is very salty, but it at least gives you a good signal. And you can see here that someone swallows a bolus, and you see a thin purple, right through the UES, and then you can see that bolus traversing through, and entering the stomach. The LES closes, and there's no reflux here, and there's full clearance.

So this would be completely normal. Whereas somebody that has a proximal defect, you can see that there's very little contraction in the segment, and that's anatomically, at that transition zone, but that's too big a gap, so that would be abnormal. This is often seen, a pattern in the elderly, some people with dysphagia.

This is the version of proximal escape to the esophagram that I showed you before. So you can see how the bolus-- most of it goes into the stomach, but then there's this gap, and because this contraction came, it kind of squirted out whatever was sitting here, proximally. And then the rest of the bolus, it just hung around after the swallow came.

So how can one think about using some of these tools to define specific disorders? I'm not going to go into too much detail about this, but I want to give you a sense of the current version of this Chicago Classification. This is now in its third iteration that just came out a couple of years ago, 2015.

This is the standard definition of esophageal motility disorders. And it really comes into two major concepts. So one is disorders that primarily involve impairments of the LES function, and those that include impairments of the tubular esophagus, and some of them have a little bit of both. But there's a transition from LES dominant issues to tubular issues.

So it's important, like I mentioned, this IRP, integrated relaxation pressure-- that's a key feature. If that is normal, then that excludes these two disorders. It excludes achalasia, and it excludes an outflow obstruction. And essentially, these are two related disorders, one of which has relatively preserved tubular esophageal contractions, and the other which has very abnormal patterns of tubular esophageal motility. So an impaired LES relaxation could be one of these two disorders.

There are issues with the contractile pattern. So diffusive esophageal spasm, I'll mention is a pattern issue, not so much a amplitude issue. And then there are issues defined as hypercontractile esophagus, which is called jackhammer esophagus. A normal pattern, but one in which the amplitudes are very high. That can be associated with pain and dysphagia. One can have actually absent contractility, but have a normal lower esophageal sphincter, and we'll talk about that as a pattern seen in scleroder-- excuse me, scleroderma.

And then there are minor disorders of peristalsis, which may or may not be accompanied by dysphagia. If you have any of these patterns, it's almost a 100% likelihood that someone will feel dysphagia. But if you see these patterns, it's a little bit iffy, if they actually have a symptom. So some of these are seen in people that are asymptomatic.

But there's ineffective esophageal motility, where someone isn't clearing the bolus very well-- that's akin to the proximal escape that I showed you before. And then there's fragmented peristalsis, which is a issue with having large breaks in the peristaltic wave and often associated with ineffective clearance.

OK, so that's essentially all of the disorders. Anything else is normal or nonspecific results. So let's spend some time looking at achalasia. Clinically, this is a really important topic, because there are treatments, and it has a major impact on people's lives. So achalasia is a not common disorder, but one should really be looking out for it, because it's treatable, as I said.

So the clinical features are, typically solid and liquid dysphagia, typically of gradual onset, with perhaps fluctuating severity and maybe a plateau, but there's been some increase over time. Patients almost always report regurgitation and weight loss. And somewhat unappreciated as it is the fact that a lot of patients actually can have chest pain with achalasia. So that's not unusual to see, but isn't the typical presentation. And often frequent as aspects with aspiration.

So what is the issue with achalasia? So in its classic form, which is, it's divided into three types, and I'll show you pictures of that in a moment. But type I would be the classic achalasia. This is an peristalsis in the tubular esophagus, so there's a complete lack of contractility. And an incomplete relaxation of the lower esophageal sphincter, that's the majority of cases, are type I achalasia.

There are two other types. One in which there's an esophageal compression, essentially, a quivering of the esophagus all at the same time, and also in relation to the swallowed bolus just presenting high pressure throughout the esophagus lumen. And then there's one that actually does have some contractility, but it is very similar to diffuse esophageal spasm, and that's called vigorous, or spastic, or type III achalasia.

So how common is a achalasia? Well, it's pretty rare. One in 100,000 patients per year have this disorder. It does affect a wide range of patients. Typically, in the first several decades of life when people present, but it can occur later in life, too. There's no gender skewing of the disorder, it's common in men and women.

So we really don't know exactly why people get achalasia. But, ultimately, what's happening is that there's a loss of ganglion cells in the enteric nervous system, throughout the esophagus and Auerbach's plexus. Both excitatory and inhibitory pathways are lost. And depending on where one is in the loss of excitatory versus inhibitory pathways, that probably dictates the subtypes of achalasia at any one moment.

Why people get this loss of ganglion cells is not clear. The classic, which I talk about, is Chagas disease, but that's pretty rare. If you look at the total population of achalasia patients, there's a high frequency of having some antibodies to HSV-1, herpes simplex virus type 1, that 84% of patients have antibodies. So they've been exposed to that virus. And actual DNA can be isolated in about 2/3 of patients, so it implies that there may be something about herpes exposure in one's life-- perhaps in some kind of autoimmune or molecular mimicry kind of sense, to target the enteric nervous system.

The diagnosis really should be made with a combination of two modes of-- two modes of diagnostic imaging, the barium esophagram, and then manometry. So those two alone are enough to make the diagnosis. So what would be the classic pattern? I think everyone has seen something like this. This would be a barium esophagram static image of someone who had swallowed several seconds before.

You can see a column of fluid that's about up to here. And you can see a very tight lower esophageal sphincter, this will be the classic bird's beak, from a board question key word. But this is a little unusual, to see it that dramatic, but this would be the classic. And aperistaltic, or widely dilated, esophagus would be classic. But early on in the disease, the degree of dilation is usually not as prominent as a textbook would have you believe.

So this is an evolving process. So people can be symptomatic for quite some time, and catching things in the early stages doesn't always look like this. But it's good to have that in your mind because very few things will ever look like that, and that would be nearly diagnostic of achalasia. Importantly, this is not driven by any inflammatory pathway. You might have a superimposed stasis esophagitis, but essentially, it's a smooth contour of the lumen here.

So under esophageal manometry, as I mentioned, there are three subtypes. And while this doesn't necessarily impact what modes of treatment one would offer a patient with achalasia, it gives a little bit of prognostic information beyond the scope of the lecture today. What one can see in the three different subtypes is essentially a normal pattern of UES function-- so someone swallows, and there's an appropriate pharyngeal, and a proximal UES relaxation, and then it recovers to baseline. But that swallow does not trigger any peristalsis, so that would be aperistalsis, by definition. Just a complete flatline through the entire esophagus.

Interestingly, the manometer is, I think you appreciate here, these striations here, this is breathing. So when one inspires and breathes out, there are different changes in the pressure in the chest, and the manometer can pick that up on the order of a few millimeters of mercury. So you can actually see that fluctuation. But in essence, there's no peristalsis.

Now this is the key feature, here. The LES, at baseline, has some tone, but the swallow that one swallowed doesn't trigger any peristalsis here, but it also fails to lead to any relaxation in the LES. So this would be a slam dunk type I achalasia reading. There's just no other disorder-- those have all the features needed to say, yes, indeed it is.

Now not every swallow in someone with type II achalasia shows this, but if you have at least several swallow with what's called a panesophageal pressurization. So see how this is isobaric through the entire tubular esophagus, essentially a light green in amplitude. That is a-- it's almost as if you have just a large space, and there's a quiver of pressure somewhere, but that gets transmitted through an entire closed space, you have a closed LES you have a closed UES, and pressure is pressure, so it gets transmitted through a closed space.

That's the pan pressurization wave. That doesn't always happen in type I, you can see it maybe one of them. But this is the if this is the dominant pattern, indeed it's type II. And then in type III, you can see some peristalsis. And you may sit back and say, well, that doesn't look too bad.

But if you look very carefully, the onset of this wave is almost vertical. Vertical in high-resolution esophageal manometry implies simultaneous contraction. Right, because it's a temporal pattern. So if the pressure here is the same as the pressure there, all of a sudden-- that is, by definition, simultaneous contraction. And it also comes too early in the swallow.

What I didn't mention before is the timing that matters, and we'll get into this a little bit with diffuse esophageal spasm. But this is essentially what one would see with diffuse esophageal spasm, except that you have a lack of lower esophageal contraction. Excuse me, it's a lack of a lower esophageal sphincter relaxation.

OK, so what are some of the treatments for achalasia? There's really five options, and option one is not even really tried it anymore, so really, four options. Nitrates, calcium channel blockers, beta blockers, make some sense to try to relax that lower esophageal sphincter, but it just doesn't really work very well, and that's been abandoned for quite some time.

Botox injection of the lower esophageal sphincter is a good option for perhaps people that are not surgical candidates, for any other-- or have a lot of co-morbid conditions. That tends to lead to relief, but temporarily. I'll show some data about that in a minute.

There's esophageal dilation, not the dilation that's often done for a stricture, but really a wide balloon dilation, 30 millimeter balloon, so I think a lot of people have seen, perhaps, balloons that are 18 millimeter balloon-- this is 30. And so this is actually really causing disruption, when deployed at the LES. You're, by definition, trying to accomplish, not just the mucosal break, but an actual rip in the muscle layer. So that you can have side effects, unfortunately, a perforation.

And the standard for a long time, has been a Heller myotomy with Dor fundoplication. Essentially, a surgical incision longitudinally through the LES, to actually prevent it from contracting forcefully, and then doing a partial fundoplication to at least partially address the reflux that wouldn't necessarily happen.

And the newcomer on the scene as POEM, or peroral endoscopic myotomy, which actually quickly is becoming a standard of care. So let's look at this a little bit. So this is what I would fear, when one does a balloon dilation. This would be a rip in the-- this would be the GE junction somewhere in here, it's a bloody mess that created a huge defect. There's partially a defect here, and then this looks pretty deep there. Perforation rates in balloon dilation can't be ignored, and I'll get to that.

This is a schematic of what a Heller myotomy with Dor fundoplication looks like. So essentially, the LES is spastic, and so this is the key target in cross section-- obviously it's a circle, so we're looking at it from the outside. A surgeon would incise a long-- cut, starting in the distal esophagus and spanning across the LES well into the stomach. So that's cutting the muscle layers, and sewing it partially up, covering the defect with the fundoplication. So that will prevent the LES from contracting ever again.

So what are some treatment outcomes for these different modalities? This is an older paper from JAMA in 1998, so this is an era in which the balloon dilation wasn't as standardized, and some of the surgical procedures were just coming online. For example, laparoscopic procedures were relatively new for this at that time. But you can kind of see the response rates. Botox injections worked a little bit, 30% of people got relief.

It's not amazing, I'd say clinically, probably about half of people get relief. But the average benefit is about-- this is the follow up-- but it's typical that about a year or so of relief. And you have to do this again and again. So it's not a good long-term strategy.

People with pneumatic dilation had better outcomes, but there were side effects of perforation. And the surgical outcome seemed to be better. So surgery quickly became the standard of care. And this became a little bit of a controversy for a while, is pneumatic dilation better than surgery? And this was addressed in *The New England Journal of Medicine* study that came out several years ago. Made a big impact, because it really came to the conclusion that dilation is equivalent to surgery, and I think it caused a little bit of an uproar.

There's a little bit of a European versus American view of this. The European centers tend to be consolidated in just a very few number of places where they truly are experts, their outcomes are pretty good. I think in the United States it tends to be more distributed and our side effects and the perforation rates in the US were higher than in Europe. So, while the outcomes could be equivalent, I think in the US, this comes at a distinct cost, where the risk of perforation with this is much greater than the surgical risks with myotomy.

So that's kind of summarizing what I just stated. So this just remains a little bit of a controversial topic. I think in the US, pneumatic dilation has fallen out of favor for at least the last five years. So other factors to consider. So, do you have an elderly patient? Do they have a lot of comorbid conditions? What is their life expectancy? What are the severity of their symptoms? Would you offer surgery to that person?

So if you have a 25-year-old with achalasia and no other co-morbidities, you're probably going to do the most definitive thing, which would be surgery, because they have their whole life ahead of them. If it's an 85-year-old with heart failure, and other things, maybe Botox may not be a bad choice. But there's a in-between choice.

There's POEM, so this just summarizes what I just stated. But this is the new alternative to surgery. And this is actually endoscopically delivered therapy and actually is quite effective. So now patients with co-morbid conditions actually can have their achalasia fixed pretty well. This is a schematic of what POEM looks like. I've certainly never done this, but these are pretty nice pictures. Creating a large submucosal cushion, using basically a needle knife to open up a defect. You can actually get the scope to tunnel under the mucosa and through the tubular esophagus.

And so this is a view that none of us probably want to ever really see, but this would be now under the mucosa. And what you would actually see-- and if you can appreciate, in the back here, little stations here. So this is actually the muscle. This is under the mucosa and within the lamina propria. Or there's a little bit in the esophagus, but really under the squamous lining and into the muscle layers.

And if you tunnel into that space, you can actually see sequentially circular muscle. And this is hence the name circular, you can actually see in-- we're looking down the distal aspect of this tunnel we've made, and these are the layers that are going to be incised. The POEM procedure leaves intact the longitudinal muscles, but cuts the inner circular muscle layers. So that's actually kind of interesting. So there's a needle knife device, and you can actually drag that and break through those layers of muscle, leaving this longitudinal muscle, and you can see little fibrils-- fibers of tissue.

So that's what POEM is. And then basically, this is accomplished distally until you get into the stomach, and there are a couple of landmarks that can be-- you're in the stomach, it's a little bit thicker-- and they go a few centimeters into the stomach. So then you can come back out of that tunnel, and sew up the original defect with, basically, clips. And this would be a view of what it looks like and those clips will heal the defect and the clips will fall out and then someone actually recovers quite nicely. It's a same day surgery procedure. So that's the POEM procedure.

So I just wanted to go over, very briefly, before we move on to a few other disorders in the last remaining time of the talk, a couple of classic associations with achalasia that are really important to recognize. So first of all, is the classic association with Chagas disease. Trypanosoma cruzi, a protozoa illness that's endemic in South America and Central America.

If one hasn't traveled to those places, it's unlikely that you have Chagas disease. It's often not subtle, the esophagus issues are prominent for gastroenterologists, but you have to view that Chagas disease is more of a systemic illness, that often effects the heart and other autonomic sites. So, and really, multiple organs with this disorder. But achalasia, in the context of Chagas, is a well-known phenomenon.

There's an increased risk of esophageal squamous cell carcinoma, which is often under appreciated. And there's really no clinical guideline about screening someone lifetime with serial upper endoscopies, or other tests, for squamous cell carcinoma, but there's a almost upwards of 30-fold increase risk 5% lifetime incidence of squamous cell carcinoma in those that have achalasia. And it's independent of having had treatment or not, so it's just the presence of having had achalasia, there's something about that that is related to the risk.

Is it because of a longstanding statis esophagitis in some kind of inflammatory state? It's not really well-known, but that's a very important association. There's also an important thought that achalasia could be due to a secondary issues, so pseudoachalasia. So radiographically and manometrically, look exactly-- and clinically-- indistinguishable, meet all the criteria I just mentioned to you. But about up to 5% of cases are thought to be secondary.

Well, secondary to what? Well, secondary to some kind of infiltrative disorder, where in the LES there's something compressing, either extrinsically or intrinsically, and so there can be GE junction cancers that could be quite subtle. So a GE junction adenocarcinoma is seen in about 50% of cases that are secondary achalasia. So this would be maybe 2% or so, of all achalasia, in the right setting. Pancreatic cancer is a classic, but it can be a variety of other types of cancers.

There are infiltrated processes like amyloidosis or eosinophillic esophagitis, has been described, sarcoid. And it's unclear, really, how paraneoplastic achalasia is. It used to be thought that it was, but no one's really made a great study of what associations there are, so I think that's kind of fallen out of favor.

OK, so, in the remaining time we're going to go quickly over two esophageal manometry patterns, and clinical context, which are important. So changing gears, scleroderma it's obviously a autoimmune disorder characterized by excessive collagen that's deposited within the gut and other areas of the body. Because it's deposited in the gut, that collagen interferes with the contractility of the smooth muscle. The nerves may be intact, and the muscle is there, but the biophysical properties of the tube of the gut is impacted.

So that has a consequence for esophageal motility, and often patients will have dysphagia, reflux. Esophagus is the most common site to have issues, because we're probably so sensitive to bolus transit that comes to awareness more than other areas of the body. So the classic pattern is a hypotensive lower esophageal sphincter, at baseline, and absent tubular contractility. So notice, if I said a poorly relaxing LES and absent tubular, contractility that would have been achalasia. But it all comes down to what is the LES doing?

So, scleroderma, that would be the classic finding. And it was thought to be classic, until people with a little bit more closely in recent years. And interestingly, only about a third of patients with systemic sclerosis-- diffuse type-- have the classic pattern. And there's a wide heterogeneity of patterns one could see in that population. There's a very recent study that came out in a journal called *Clinical Gastroenterology and Hepatology,* which looked at the 100 or so, or more, systemic sclerosis patients. And about a third had the classic pattern, with a variety of other issues. But we'll focus on the classic.

So in a barium esophagram, what would one see? You would see a dilated esophagus, because there's poor contractility. You'd see a column of fluid, just like we did with achalasia. But importantly, there's a wide open LES. So this is just a quiver of no contractility, that is-- couldn't be more clear. So it's the opposite of bird's beak. It is, floodgates are open.

Yet, there's a column of fluid. So you can still have a slowly moving drain, it's just it's not an obstructed LES. What would this look like on esophageal manometry? Well, the UES is intact. So you have some basal tone, it relaxes when you swallow, and it recovers to baseline. There may be some proximal skeletal muscle, which is usually a higher amplitude, so that's left detectable. But in the tubular esophagus, in the smooth muscle compartments, there's nothing left.

And this is a very low basal LES tone. Actually, the blips you see here even, are likely due to the crural diaphragm being transmitted through that area, you can actually see that on each breath. So there's probably a zero LES tone, in this case.

What can you do for someone with scleroderma? Well, it's really supportive therapy. You can eat slowly, eat upright, elevating the head of the bed at night because of-- lifestyle changes for reflux. These patients often need continual acid suppression, it's important to acid suppress patients, because they're going to have free reflux. You saw how open that LES was, so there's basically no barrier function.

So there are possible prokinetic agents one could use. So essentially, using cholinergic targets, muscarinic agonists like bethanechol. Or boosting cholinergic signaling, using pyridostigmine has been used. Could be effective, buspirone has been looked at recently as a serotonergic target that boosts motility. And actually has some evidence that can help even in scleroderma.

All right, so let's just close out with talking about spastic esophageal motility disorders. And one of the classic is diffuse esophageal spasm, or DES, OK. So this is definitely a disorder of peristalsis. It is a manometrically defined disorder. It's unclear if there is a mild form, and it's unclear if every time that you see this pattern, if someone is truly symptomatic on that swallow. Studies haven't really done that well that. It has an unclear epidemiology. But the classic presentation is acute substernal chest pain, dysphagia with severe forms, and potentially even regurgitating secretions, if it's a really severe socked-in spasm.

Pathophysiology is characterized by premature contractions in the mid and distal esophagus. I think a lot of people often think that this is defined by an amplitude, or a high amplitude contraction. That certainly can be seen, but not by definition-- it's the timing that matters.

It's thought to be due to loss of inhibitory neurons, and it can hang in there for even minutes in some patients. So there's the classic definition here, in the third version of the Chicago Classification. Having more than two out of 10 swallows, with a distal latency-- meaning the onset of contraction less than 4.5 seconds after the initiation of the swallow. By definition, they have lower esophageal sphincter relaxation, which is normal.

You guys have seen a corkscrew esophagus, which is the classic pattern. Essentially, there's normal esophageal motility in the proximal and mid, but in the lower portions of the esophagus there's simultaneous contraction. So you see segmental contractions, this hourglass pattern. OK, so that would imply that, at that spot, there is a segment of the muscle that's contracting simultaneously.

So this just another view of that. OK, so what does the esophageal motility look like? They could have an intact proximal, perhaps higher amplitude distal, but it's really the onset. So if I were to draw a straight line down from the onset of the swallow, you get to this point. And the onset of this wave, which is essentially a vertical wall, simultaneous contractions, is 3.7 seconds, that's too early. Anything after 4.5 seconds is normal.

So it's the simultaneous nature of what's happening, rather than having prolonged contractions. And the lower self-heal sphincter relaxes. So that excludes type III achalasia. So that's the key feature of this. Sorry to make it hard to hear me, but-- you can see exactly this, with a band across here, that never relaxes. That would be type III achalasia. This is DES.

OK, so what can we do for patients? There's really no proven therapies. Smooth muscle relaxants are the mainstay. They intuitively should work, but often don't. Calcium channel blockers are the favored approach, just because patients don't tolerate high doses of nitrates very well. Anticholinergics could work as well.

Trazodone, has been looked at, for whatever reason, that seems to work. There's some studies with biofeedback. There's one study with empiric dilation, which patients got relief, but could be a placebo effect, because even the wimpy little 8-millimeter dilator, also was effective, as well. So the take home points from what I've showed you today, and unfortunately, was interrupted, but the esophageal motility disorders presents with dysphagia.

There are several complementary diagnostic approaches. We talked about barium esophagram, endoscopy in some cases, and importantly, esophageal manometry. There are multiple therapeutic modalities available to treat specific esophageal motility disorders, so it's important to know what the disorder is, in order to offer the best most targeted treatment to patients. So thank you, well, let's end the torture there. OK, thanks. Sorry, guys, that was really frustrating.