[MUSIC PLAYING]

KENNETH FASANELLA: This is an area that's kind of near and dear to my heart. When Jared asked me to give grand rounds, he was looking at I think more ICU-related things, like gastrointestinal bleeding. And I said, there's really been nothing new in GI bleeding for about 10 years, probably, as long as I've been practicing.

And this is an area that's I think constantly having some updates and, kind of as an aside, has been a big clinical interest of mine over the decade that I've been practicing, as well, because in addition to being mentored by Kevin McGrath when I was going through my endoscopic ultrasound and Barrett's training, I did three years with Klaus Bielefeld as my clinic attending. And he's departed us at this point for University of Utah, but he was very much more of a motility guy.

And so my practices kind of span the motility and the reflux manifestations of the esophagus. And in addition, due to a personal relationship I had with Robyn Domsic for a decade, I took care of a lot of scleroderma patients, and continue to do that to this day. So ultimately, that's why I think this was more of an interesting subject to talk to the pulmonary group about.

So moving on, as I was asked to do, I broke my talk into three parts, though I can't say they're exactly equal parts. But to begin with, I'm going to give a little bit of a background of GERD, esophageal dysmotility so that you understand some of the terms I'm talking about, and also some of the diagnostic tools we use to evaluate these patients. Then I'm going to discuss some of the literature behind GERD and pulmonary overlay, as well as esophageal dysmotility overlay, and then talk a little bit about how this works in the lung transplant population.

So just a little bit of a background epidemiology, obviously it's very common, or the PPIs wouldn't be the multi-billion dollar industry that they are. Looking at all of Americans who have heartburn daily, it's about 5% to 10% of us. About a quarter to more than a third have monthly symptoms, and lifetime prevalence is between a quarter and a third. As far as patients that have advanced lung disease, it's much, much higher. So if you look at the IPF population, looking at actual distal esophageal acid exposure on pH testing, it's more than 3/4 of these patients have positive testing for reflux. And in the COPD population, it's similar.

So what are the typical symptoms that I never see? Heartburn, regurgitation, and water brash. So those are some of the things you can ask your patients about. What I often see is more people who are being referred from the swallowing center, people being referred by you guys, have chronic cough, laryngitis, globus sensation, throat clearing, and so forth. I had a lady come to me two weeks ago that was showing me how her plastic surgery keeps getting ruined because of the horrible faces she has to contort herself into every time she gags. So that's getting back to the Klaus Bielefeld patient population.

So looking at this pyramid, you can see that, among these atypical symptoms, we get an attenuated response to their treatment the further they go up towards the top of this pyramid, meaning the more atypical their symptoms are, the less responsive they are to medical treatment for acid suppression. What are our typical barriers to GERD? Just because we're going to talk about some of the things that may compromise them.

Ultimately, starting from the top down, the salivary glands. So you're going to have normal salivary function that's going to be compromised, especially in certain connective tissue diseases, [INAUDIBLE] conjunctivitis sicca. That normally has a nice buffer and lubrication function in the esophagus. You're going to have normally a directly opposed diaphragmatic crus to the lower esophageal sphincter down there at the bottom. I don't seem to be able to-- ah, there we go. Down here at the bottom. And that's going to get disrupted in certain situations.

You're going to have normal peristalsis to help you clear the esophagus of whatever does reflux, because we have to know that reflux is a normal thing, and in general the upper limit of normal is 4% acid contact time six centimeters above your lower esophageal sphincter. So certainly, all of us have reflux if we're getting recorded on a 24-hour basis. It's just pathologic if it's associated with symptoms, damage, or other problems.

Certainly, epithelial resistance can be compromised by things like chronic smoking. Delayed gastric emptying can have a significant contributing factor to this. If you have more food in the stomach for a longer period of time, that's going to increase the pressure of reflux contents. And then ultimately, if you have any dysmotility downstream of the stomach, that can also play in. If you have central obesity, that's going to put pressure on the stomach and increase the reflux gradient into the chest.

As far as the mechanisms with most people's normal reflux, most normal people who have reflux and don't have significant anatomic derangements, their main contributing mechanism is going to be increased transient lower esophageal sphincter relaxations. And I just made a list of meds, many of which you guys will be very familiar with because you use them more than I do, and their effects on the esophagus.

And you can see that there is a reason, potentially-- and the reason why I say chicken or egg, there's a reason why a lot of the interventions that we give our pulmonary patients may be contributing to their reflux. Xanthenes, caffeine, nicotine, they all increase transient lower esophageal reflux. LES tone is compromised by the xanthenes, as well, the inhaled sympathomimetics, the anticholinergics.

Now you guys are using sildenafil and other acetylcholinesterase inhibitors in your pulmonary hypertension patients. Those are all going to have significant esophageal compromise associated with them. And as far as peristalsis, I treat a lot of my patients with tricyclics for various irritable bowel type issues or neuropathy. Those can have significant effects on both peristalsis and the LES tone, as well as sildenafil and calcium channel blockers.

So as far as testing strategies go, empiric therapy is what we probably most often do. We put people on a proton pump inhibitor and see what kind of response they have. And this has been advocated as a fairly cost-effective initial strategy for these patients, and ultimately has a sensitivity specificity somewhere between 60% and 80% for association with pH testing formally. Barium swallow can be useful. We'll talk a little bit about each of these. Endoscopy, formal pH testing, manometry and impedance monitoring.

So here's a picture of a fairly useful esophagram. As you can see, this is the diaphragm. And I think most of you guys know how to read a chest x-ray, but this shouldn't be here. This is an intrathoracic stomach. So that's certainly somebody that this would shed some light on why they might be having significant symptoms. This gives you a basic anatomical evaluation, but it also gives you some reasonable physiology evaluations. So if I'm looking for a patient that I'm concerned has significant dysmotility, I think a barium swallow can really shed some light on that. It's not necessarily going to be the most sensitive, but if you see it, it's very specific.

Certainly, if I see something like this, then I'm not so concerned that I'm going to be helping my patient with acid inhibitors. This looks like achalasia. You're going to see a dilated aperistaltic esophagus with a classic bird's beak. And importantly, you're going to see stasis of fluid in the esophagus. And so if these people are complaining of heartburn, it's typically going to be stasis esophagitis, pill esophagitis. If they're complaining of regurgitation, it's not going to be reduced by acid inhibitors. Their LES tone is plenty high.

Endoscopy is going to be somewhat helpful in certain cases. As we'll discuss, it's not going to be helpful in probably a majority of patients who have pulmonary manifestations, interestingly enough. But here's a couple of pictures where you'll see some of the endoscopic findings that we sometimes see. This one demonstrates esophagitis LA grade B. There's several mucosal breaks here. Down here, that might be a tongue of Barrett's. Here, you see an annular stricture. So anytime that we see something like that, we know that this patient has a tendency to have significant acid reflux.

If I see something like this, this is saliva sitting there in the esophagus. Another picture shows the classic esophageal rosette sign. These are epiphrenic diverticula. This is an esophagus that's full of food and saliva. This is an esophagus similar to the last one after I've cleaned it out. Looks like a sharp a. If you see something like that, that's a severe motility disorder, typically achalasia. So that's where endoscopy can be helpful.

Ambulatory pH testing, traditionally done with a transnasal catheter. That's been around since the '70s. Traditionally only checked with a distal probe typically five to six centimeters above the LES. And dual probes have also been advocated, particularly in the ENT community, for diagnosis of LPR. And we'll talk a little bit about the performance characteristics of that.

The Bravo pH system is something that I'm sure most of you who practice clinical medicine are familiar with. This is a wireless pH detector that we put six centimeters above the GE junction. And that's a 48-hour test. So it gives us a little bit more data. Doesn't impede the natural swallowing process quite as much, and so patients certainly prefer it. But it has no ability to give you any proximal information. This is a couple of pictures of what that system looks like.

Impedance combined with pH testing is something that's been around now for about 15 years, and has really been advocated more recently as the gold standard for these patients because, not only does it test for acidic reflux, it can tell you a little bit about non-acid reflux, or quite a bit about non-acid reflux, because not only does it measure pH, it measures electrical inductance of any electrolyte-containing solution.

And this just gives you basically a schematic of how it works, impedance over time. And if you remember back to your physics, impedance goes down with electrical conductance. So when you have a fluid bolus going through the esophagus, you have a nadir in the impedance. And then it will come back up.

So when you have several electrodes that are placed at various levels above the GE junction, normally, if you have propagation of a swallow or electrolyte solution, it's going to go to the right with time, propagating downwards through the esophagus. If it does this backwards, then that's a concern for reflux.

Now this right here, this lead is showing us pH information, that being six, this being four, which is what we consider to be the threshold for normal. And when it dips below four, we consider that acidic. And this is actually going straight up, not propagating with time. So that's a reflux episode that contains acid. So when we're talking about multichannel intraluminal pH, impedance and pH testing, this is what we're looking at. And that records generally for 24 hours.

Manometry is done whenever we have suspicion of somebody having a hypertensive lower sphincter muscle, whenever there's suspicion of poor peristalsis, suspicion of scleroderma. Sometimes, they can have mixed connective tissue disease, and they're wondering if they're going to have a scleroderma phenotype. Pre-surgical evaluation for anti-reflux surgery, it's often helpful to make sure people have relatively normal peristalsis before they tighten up the outlet with [INAUDIBLE].

This is what a traditional manometry looks like. You can see pressure waves propagating with time from top down towards the bottom. This is the lower esophageal sphincter, which at baseline has tone, and then relaxes after this bolus wave pushes the food down to this level. At least, that's what it's supposed to do.

And conditions like achalasia, you can see, in this particular case-- this is a traditional manometry, not high res-- really pretty much absence of any peristaltic waves. And then you have an LES that's not relaxing. This gray zone is what it is above gastric pressures. So it's never relaxing down to gastric baseline, which is what it should do in order to allow for bolus transit. This is a scleroderma esophagus. Classic scleroderma, where they have an aperistaltic esophagus and zero LES tone.

Looking at more recent developments, high-resolution manometry that's been around now for about seven years, this is what we get, is a color-coded demographic, essentially, of-- or graphic interface of the esophagus, where you can see color-coded pressure at various levels in the esophagus. And typically, you're going to have your highest pressure in the lower third. And this is LES tone, which should go away as the bolus transmits towards the LES. This is what you're going to see on the opposite extreme, such as in achalasias. Pan pressurization of the esophagus, because it's got a column of fluid sitting in it that's creating pressure, and lack of LES relaxation.

So looking at manometry results, I reviewed with you what the extremes are, but what do we see most often? Most often, we see ineffective esophageal motility. And I'm going to come back to this a little bit later, several times, because it's really the most common thing that we see. It's the most common thing that you guys see, whether you know it or not, in your pulmonary patients.

This was previously defined by at least 30% failed as follows. The Chicago classification for high-res manometry changed it slightly to make it a little bit more sensitive. But ultimately, it basically means that the esophagus is not contracting strongly or consistently every time. And when they are looked at and compared to other populations, they actually have fairly similar supine reflux patterns to scleroderma patients.

Comparing them to normals, to view spasms, nutcracker esophagus, and hypertensive LES, this is what they had as the percent recumbent time where the esophageal pH was acidic. And this is what they had as the recumbent esophageal acid clearance, meaning how many minutes it takes typically after a reflux episode for them to clear it. And so as you can see, what they're essentially having is poor esophageal clearance. That's the take-home point for IEM.

This is what a barium swallow might show in somebody with middling ground motility abnormality. You can see multiple levels of contraction. You're not really seeing a nice bolus wave that's lumen obliterating. You'll see a lot of different things in these reports. And a lot of it may or may not have any insight.

When the radiologist says proximal escape, for example, that means that the esophagus is contracting backwards, causing a fluid bolus to go up towards the pharynx instead of down towards the stomach. If you see tertiary waves-- these are essentially tertiary waves. Normally, you're only going to have a primary bolus wave and a secondary clearance wave. Tertiary waves are this kind of fibrillation of the esophagus that shouldn't be there.

So this is the most common motility disorder found in patients with GERD-associated respiratory symptoms. And looking-- in people who have manometries done in the setting of pulmonary disease, we find it 41% of the time in chronic cough, and about 50% of the time in asthma.