MARTIN L. FREEMAN: Well thanks very much for the invitation. And I appreciate the opportunity to speak with all of you, and the support from Boston Scientific to make this possible. So we're going to talk about necrotizing pancreatitis, focus on latest terminology, management, modalities, outcomes, and complications.

Acute pancreatitis is the most common gastrointestinal cause for inpatient admissions now in the United States. Over a quarter of a million admissions, resulting in $2.5 billion annually just in the US. You can see that at the University of Minnesota we have a very large experience with acute pancreatitis. These are quarterly admissions.

And compared to all these other major academic transplant centers, we're actually the highest in the country. So we have a service dedicated just to taking care of these patients with four faculty who specialize in pancreas disease. Just some background.

It is very important to understand the lingo and terminology of acute pancreatitis because it has changed. 85% to 90% of pancreatitis is interstitial. And the remaining 10% to 15% is necrotizing. Very important to differentiate the two.

Organ failure is very rare in interstitial pancreatitis. And it's quite common, about 1/2 of patients with necrotizing pancreatitis. Mortality is much higher in necrotizing pancreatitis. Without organ failure, it's very low. With single organ failure about 3%, but with multi-organ failure it's up to 50% traditionally.

We're going to show you that that has been modulated quite a bit with current intervention strategies and supportive care. Probably the single most important thing now is to understand severe acute pancreatitis is to review the classifications of acute pancreatitis from the 2012 revision of the Atlanta criteria. This is an international panel of experts worked on this for a number of years, and it's actually very simple. It's not like memorizing porphyrias, or even segments of liver.

There's four kinds of collections now in acute pancreatitis. Think of it this way, in the first four weeks it's either acute peripancreatic collection in interstitial pancreatitis, or it's an acute necrotic collection if it's necrotizing. After four weeks-- and this is an arbitrary number-- acute peripancreatic fluid collections evolve into pancreatic pseudo cysts-- which a note mind you, are extra pancreatic. And they're rather rare after severe acute pancreatitis.

In necrotizing pancreatitis, the acute necrotic collections evolved to walled off necrosis. And so there's really only four collections that you need to know. Terms like phlegmon, infected pseudocyst, hemorrhagic pancreatitis are all obsolete. And we'll cover that more later.

A pseudocyst, just to differentiate, has a well-defined wall, homogeneous fluid density, no solid component, but most importantly, it's extra pancreatic. So when you see something in the pancreas, part of the pancreas is gone, even if it's liquefied, that's walled off necrosis, not a pseudo cyst. And they're really very rare. We now have 300 necrotizing pancreatitis patients in our database in the last six years at university, and a grand total of 25 pseudocysts.

So it's more than 10 to 1, granted we have something of a referral bias. But you will find that the majority of collections after pancreatitis are actually post necrotic. Now walled off necrosis, has a well-defined wall, heterogeneous, mix density, solid component usually. And they can be intra or extra pancreatic. And we'll cover that.

Here what happens is with pancreatic necrosis, the pancreas itself becomes devitalized. There's a lack of IV contrast enhancement. But in extra pancreatic necrosis, such as this patient, has a perfectly preserved pancreas with perfusion, has massive extra pancreatic necrosis here involving mesenteric fat. And notice this is an obese patient. That's quite typical.

So the term walled off pancreatic necrosis is also obsolete, because walled off necrosis can equally involve pancreatic tissues, extra pancreatic tissues, or both. Extra pancreatic necrosis typically dissects down the left retroperitoneal space into the left pelvis, or it can extend anteriorly into the peritoneal cavity. It's very important to keep those in mind.

I just want to also show that there are some very important consensus meetings recently. I had the privilege of leading a group of international experts, mostly surgeons, radiologists, and GI specialists. And this was the first consensus that really emphasized the role of minimally invasive management.

I think the single best paper for you all to refer to that really covers diagnosis, management, and interventions for pancreatitis is this IAP/APA evidence based guidelines. It was published in 2013 in *Pancreatology.* And it's absolutely spot on, and it's evidence based.

Indications for intervention, when do you need to intervene? And this is true whether it's percutaneous, surgical, or the endoscopic. There are all the same.

And this is per two international consensuses. Suspected or documented infected necrosis with deterioration, and that's important, because just because somebody has infected necrosis, if they're rock stable, and it's premature to intervene because of the evolution of the collection, they don't need urgent intervention. But they do probably eventually need it.

Ongoing organ failure several weeks after the onset of acute pancreatitis, that's a more controversial but important indication. And then in sterile necrosis, once it's walled off-- typically four to eight weeks, but it can be sooner-- if they have gastric outlet intestinal or biliary obstruction, if they have persistent symptoms. And it is quite common.

They just don't feel well. They can't eat. They have pain, or disconnected pancreatic duct.

Now what's key in all of this is that multi-disciplinary management is critical. You cannot do this with just primary care and GI. You need to have sophisticated surgery, diagnostic interventional radiology, and critical care.

If you try to do it solo, it's a little like this guy, probably taking on a bit too much by himself. It takes more than one or two. Timing of intervention should be delayed wherever possible till at least after four weeks. But if patient is deteriorating and infected, you have to pull the trigger sooner, and it's not a good idea to allow somebody to deteriorate too far.

We do know that early interventions are associated with poor outcomes. Now traditionally surgery was the management by any route. Percutaneous catheter drainage, and endoscopic or your other options. They've evolved a lot in the last 10 years at a dramatic pace.

The gold standard was open necrosectomy, but had very high complication rate, mortality, with fistula, diabetes, pancreatic insufficiency, and hernias. And you can see here a very large incision necrosectomy. One of the problems being, this patient's been on a trach for a month with multiple debridements, has an open abdomen, will never put that abdomen back to the normal state.

So there are ways of doing this minimally invasively which we'll just touch on as these details will be subjective of later webcasts. But the brilliant taxonomy by the New Zealand Surgery Group-- Doctor Windsor-- per oral, it's either transluminal, transpapillary in the duct. And these are endoscopic routes. Whether it's surgical, percutaneous, laparoscopic, there's three routes through intervention.

Transperitoneally through the stomach, transperitoneally missing the GI tract, and then most importantly, retroperitoneally. And we always strive for a retroperitoneal approach with catheter based drainage, because the pancreas is a retroperitoneal organ. And the spread of the necrosis is usually retroperitoneal. And if you go transperitoneal, you're risking dissemination of infection throughout the abdomen, which is peritonitis.

It's sometimes necessary, but we try to avoid it. Percutaneous catheter drainage is widely established. Retroperitoneal route here, draining large amounts of infected necrosis. Systematic review shows it's quite effective. But these are selected cases.

Ideal patient for retroperitoneal percutaneous catheter drains, just acutely ill, three week into the course, dying of sepsis on five processors, poorly demarcated, not a good-- no good window for endoscopic management, perfect for retroperitoneal, and in this case intraperitoneal catheter drainage, which you can see here and here. The problem with catheter drainage is external fistulas. Here for whatever reason somebody did a anterior transperitoneal drainage of walled off necrosis that could have been treated through the stomach. Led to six months of an external fistula. You also can't debrief large amounts of solid necrosis through percutaneous catheters such as this.

Video assisted retroperitoneal debridement was developed by Dr. Horvath and colleagues in Seattle, University of Washington, and is now widely used by some surgical centers. A small incision through the retroperitoneal PERT track and debridement. And this classic paper in the New England Journal by the Dutch Pancreatitis Study Group, showed that a step up approach using percutaneous catheter drainage, and video assisted retroperitoneal debridement as needed was superior to open necrosectomy with morbidity, and short and long term morbidity. And a trend in other later studies, a definite improvement in mortality, that's just coming out now.

Now finally, wrap up on endoscopic interventions, because that's really what we're all about. Here, this is a comprehensive systematic review we published in the American Journal of Gastroenterology 2014. It goes through all of the aspects of endoscopic and multi-disciplinary drainage. Remember that there's transluminal drainage, which should be EUS guided. And then there's transluminal necrosectomy, where you actually put a scope through the fistula into the retroperitoneum, and debride the necrosis directly. And this is sort of a summary of EUS guided puncture dilation, and placement of stents, then subsequent necrosectomy.

There is one randomized trial of endoscopic transgastric versus surgical necrosectomy in infected necrotizing pancreatitis. It's a very small study again by the Dutch Pancreatitis Study Group. But it does show that a significantly better outcomes with endoscopic versus surgical necrosectomy trend towards mortality difference. What's interesting is they've now done, and it's in press, a huge multi-national study comparing open, minimally invasive, and endoscopic necrosectomy. And it looks like the mortality difference in endoscopic is dramatically better than open surgery. And it's also better for minimally invasive surgery, than open surgery, but not by nearly as much.

So I just want to show you what necrosectomy looks like. This is video here. I don't know if it projects well. I'll try to use my shadow here.

This is going through a AXIOS stent that has been placed at a previous session a few days earlier to drain infected necrosis, and using a variety of devices-- snares, baskets, we use suction cap. And a lot of time this is under general anesthesia. This is about a two hour procedure.

Using great care to not snare off the portal vein, the splenic artery, other vital structures back there. So multiple gateway involves when you have a very large infected collection like this, walled off necrosis. A single cystogastrostomy won't do it. This is a cystoduodenostomy and a cystogastrostomy.

You can also use that retroperitoneal, but again not transperitoneal. But retroperitoneal percutaneous catheter approach to do sinus tract endoscopy and get at places in the abdomen you just can't reach through the mouth-- such as this patient with pancreatic and huge extra pancreatic necrosis going retroperitoneally down into the pelvis. The only way to get from there to there is multi-modal. And I'll just show you this quickly.

And then this is a very ill patient, three weeks into necrotizing pancreatitis with fevers, sepsis, organ failure. Very poor candidate for surgery. In this you can see how extensive the pancreatic and extra pancreatic necrosis is all infected.

Again the cystoduodenostomy, cystogastrostomy, draining pus, but that will not be adequate, a nasoduodenal tube, and then simultaneously left and right retroperitoneal percutaneous catheter placements, so that we have retroperitoneal, retroperitoneal, internal, internal, and a nasoduodenal tube. And then followed by, not only per oral necrosectomy, but very limited what you can do through the mouth here. So just this is some of the necrosis.

But then sinus tract endoscopy, where we take out the percutaneous drain in the operating room, put a scope through the back-- this patient is prone-- through the percutaneous tract, and you can explore the deep pelvis, go back to cystogastrostomy, you can go through left and right. And the idea is to clean out the cavity. And its the only way you are going to get to a good result. There is a chance of fistulas.

And then just to end on complications, this is really subject for another talk. But just an example of massive bleeding from cystogastrostomy that failed clipping. Patients developed pseudoaneurysmal bleeding in these sometimes dramatic, needs coil embolization. And you can have perforation during necrosectomy, especially with intraperitoneal dissemination of the necrosis, or root of the mesentery.

Air embolism is dreaded. Should be able to be avoided. You must use carbon dioxide.

And then no matter what you do, these approaches fail sometimes. And this is a patient who had unbelievably aggressive six percutaneous drains, two cystogastrostomy, sinus tract endoscopy, developed a colonic fistula, multi-organ failure, had to go to surgery, have all these resections and wash outs. And then there's many short and long term issues we won't touch on.

GJ tubes are often necessary if an NJ can't be tolerated long term. And well these are all subjects for later discussions, disconnected pancreatic duct. And what I want to end on, is an algorithm that we've published in the American Journal of Gastroenterology. If intervention is indicated, try to wait four weeks. But if you can't, don't, if they're infected and deteriorating.

Encapsulated, we do primarily endoscopic. If it's encapsulated near the stomach, endoscopic. If it's distant from the stomach, or it's nonencapsulated, you can't do endoscopic. You need percutaneous catheter management, and we only do surgery for failures.

Using this approach in 221 interventions, you can see that only about 2/3 could be treated purely endoscopically. The rest needed some other modality. 17% didn't need any intervention. But the rest needed other modalities.

We operated on 6%. And mortality in only 3%, which is pretty good. Most of these were infected necrosis.

Many other issues to cover. I just want to say, this is our team that meets-- believe it or not-- weekly for an hour, just to go over necrosis cases in the hospital, and complex patients out of the hospital with follow up issues, general critical care surgery, interventional endoscopy, and interventional radiology. And this is our wonderful OR team, that make these endoscopic interventions possible, and our clinics and coordinating staffs.

So I'm going to thank you very much for your time. I'll stop there. Only 12 minutes over.

[LAUGHING]

OK, questions? Comments?

SPEAKER: So Dr. Freeman, we have a few questions. So the first one is how do you determine infected versus uninfected patients?

MARTIN L. FREEMAN: Very good. That's an excellent question. The classic way of doing that was to define needle aspiration under CT guidance. So it was described about 25 years ago, and it seemed like a reasonable idea, but it's basically completely obsolete now. And if you read the IAP APA guidelines, and look at the evidence, here's why.

If it's positive for bacteria, and the patient isn't ready for intervention, it won't matter. You treat them with antibiotics. If it's-- in your false positives too. If it's negative, it can be a-- for bacteria, it can be a false negative, and especially if patients already been on multiple antibiotics. Most of all, though, the decision for intervention now of necrosis is made clinically. So suspicion of infection is first of all, gas bubbles in the collection.

Almost all the ones I showed you had obvious gas in the collection. That is, by definition, infected. If they don't have gas bubbles in them, then it's spiking fevers, clinical deterioration, and a suitable collection. And rather than ponder whether it's infected or not, that patient needs intervention. So you intervene, usually endoscopically, percutaneously, culture the material while you're doing that, and not so much as a diagnostic, but as to help guide anti-microbial therapy.

But the real intervention is going in there, and draining it, and debriding it. So to summarize, it's a clinical diagnosis, and what drives intervention is not the results of a fine needle aspiration culture. So in the last 300 patients, we have not done one single fine needle aspiration to determine presence or absence of infection. OK?

SPEAKER: Are there any patients where a collection may mask, or a-- it says where a collection is masking as a [INAUDIBLE].

MARTIN L. FREEMAN: Sure. That's always an issue. Is it really an neoplasm? Now, honestly, the appearance of these is so different than neoplasm. For example, mucinous cystic neoplasm typically in a patient without pancreatic disease, who has a nice round collection-- a nice round-- not collection, but a nice round encapsulated lesion in the tail of the pancreas.

So it's pretty rare. These collections result from severe pancreatitis, and that's usually obvious by clinical course. Very rare for a patient to walk in with vague discomfort, no history of pancreatitis, and then have something that looks like an infected necrosis.

SPEAKER: Of the patient after endoscopic intervention?

MARTIN L. FREEMAN: Most of these patients are quite ill. I'll be honest, most of the conversations are with the family, and we have coined the term, "post pancreatitis stress disorder" or PPSD for the syndrome the patients go through, and the families. And we typically have five to 10 patients in-house at any one time with necrotizing pancreatitis, and one of our main issues is to reassure the patients, and the family that this is an incredibly drawn out course.

That it's normal to be discouraged because there's two steps forward, one step back, or sometimes one step forward, two steps back. And it's have faith that in six to 12 months they may well be back to a more normal life, and they're very likely to survive. That's one of the big challenges. Usually, patients feel better right away after the drainage, and then the initial drainage. But they have no idea what an ordeal they're in for, which can be three, four, five six interventions.

They get portal vein thrombosis. There's so many issues-- nutritional issues. This is part of the support that you need to undertake treating this disease. It's why you need a multi-disciplinary team, and really, a dedicated service because it is not just like even repetitive removal of bile duct stones, for example.