DR. DOMINIC DEKERATRY: Going forward I want to start with a clinical vignette. And this is a really nice article that was published in a journal last year, looking at a historical perspective of patients with asthma. So this is in 1828. This is a woman who is 35 years old. She has a husband, four children, a cook, two maids, a stable boy and a footman.

And she has intermittent fits of dyspnea, musical noise in her chest. She labors to draw and expel a full breath. And her cook keep a steaming kettle always at the ready for her to inhale. Her symptoms are worse in the spring. And during periods of confinement for childbearing-- I don't want to go any further on that-- her fits were less severe.

The prescription at the time, almost 20 years ago, was for her to smoke the leaf of a*Datura stramonium,* which is a thorn apple leaf. And this was controversial even at that time. And I'm going to elaborate on that in a little bit. Because it seemed to help people's symptoms with asthma.

But there seem to be some increased incidence of death reported in patients who smoked this thorn apple. And this is an example of some of the asthma cigarettes that had been offered for therapeutic relief of symptoms over the years. For those of you that are interested, there's an inhalatorium.com website.

So in terms of definition, the major societies, particularly the National Asthma Education prevention program and NIH program has defined asthma as a chronic inflammatory disease of the airways. And you're going to hear the word information over and over again through my talk. Basically, a variety of different inflammatory cells play a role, particularly mast cells, eosinophils, and lymphocytes. In susceptible individuals, the inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, cough, and particularly prominent symptoms at night or early in the morning. And most often these symptoms are associated with variable airflow limitation that is at least partially reversible.

So the pathophysiology is actually quite broad. I'm going to go through a couple things here, because much of the talk has to deal with airway smooth muscle, as you'll see. There's hypertrophy and hyperplasia. There's microvascular leakage, activation of airway neurons stimulating the muscarinic cascade. There's stimulation of mucus-secreting cells, disrupted ciliated epithelium. And ultimately there's laying down of bad collagen.

This is CDC data, in terms of the incidence and prevalence. And basically whether you're an adult or you're a child, whether you're a man or a woman, whether you're black, white, or Hispanic, the incidence and prevalence runs around 7% to 8%, up to 11% across the United States. And this is data from the CDC for Texas across various age groups.

And you can see that adults with current asthma, the incidence runs around 8%, whether you're 18 or you're 80. So we have patients all the time that come. And they're 65 years old. I diagnose them with asthma. And they say, well, I can't believe that you're diagnosing me with asthma. I never had it as a child.

But it's very commonplace. It's not an uncommon disease. Over 22 million people in the United States have been diagnosed with asthma.

This is Texas compared to the United States, in terms of historical trends. This is from the Texas Department of Health. And basically the bottom graph is incidence. And the top graph is prevalence. So again, incidence is around 7% or 8%. The answer is always eight in medicine.

So in terms of components of asthma care, we're going to skip over a lot of things, and go to medicines, and then non lessons. But certainly I don't ever want to lose sight of the importance of assessing and monitoring asthma severity and asthma control. There are guidelines out there from the global initiative of asthma care and also the National Asthma Education Program. I'll show you some charts in a moment that really stress how important it is to get a good handle on asthma severity, so you know what to do, so that you can develop a plan. It's always important to titrate up and titrate down, and escalate and deescalate depending on how the patient is responding to your therapy.

In terms of education, really important to help patients and providers understand the difference between controller medicines and symptom medicines. There's a big difference. And certainly, have an asthma plan.

And also, control of environmental factors. And remember that there are many comorbidities that affect asthma. Not all that wheezes is asthma.

Sometimes we have asthmatic patients that come to us that have airway obstructions for a variety of different reasons. Certainly, there are aggravating factors. There's allergic bronchopulmonary aspergillosis. There are bronchiostrictures, obesity with diastolic heart disease. For that matter, if you were back in the 1828 time frame, as our 35-year-old woman was with asthma, you have to think about mitral stenosis. You have to think about tuberculosis, that sort of thing.

I think one of the often under appreciated aggravating comorbidities is reflux disease. And the statistics vary quite a bit, from 20 to 90% incidence of reflux in a severe asthmatic. But probably it averages at least a third of patients. So don't forget to treat reflux disease.

Then we have the medications. And then something new, which we'll talk about. And these are the types.

The most prevalent one that we deal with this extrinsic asthma or allergic asthma. And that's really what we're going to focus on today. So this is one of the charts that I was commenting on, from the NIH and the Asthma Education. And it's a complicated chart. But it's really available on the internet. And so you hone down on it.

But this helps you divide asthma severity by two different groups. There is intermittent asthma. And there is persistent asthma.

And the patients who have persistent asthma are divided into mild, moderate, or severe, depending on what their symptoms are. Are they having daily symptoms, weekly symptoms? Do they wake up in the middle of the night? Does it interfere with their quality of life, with their work, with their school?

And what is their lung function? And how many exacerbations do they have? And based on where their patient falls in the severity category, then that ties to the treatment algorithm.

So step one treatment is for an intermittent asthmatic. And somebody might get by with just a typical short-acting beta agonist. And then step two and above, the persistent asthmatics, typically benefit most from inhaled corticosteroids.

So I want to talk about inhaled corticosteroids, remembering that asthma is an inflammatory disease. And it needs an anti-inflammatory medicine to treat-- not an epinephrine bong, or Primatene Mist, or Afrin. And it is not uncommon still for patients to come in and say, all I use is Primatene Mist, because that's the only thing that works. It's getting a little hard to find nowadays. But people can still come up with it somehow.

These are the symptom medications. These are the short-acting beta agonists. And also, I added Combivent in here.

Because ipratroprium is not an unreasonable choice for symptom control. You just have to be prepared to counsel the patient that it doesn't kick in quite as quickly as the albuterol or Xopenex. But these are symptom medicines. These are not controller medicines.

It's not uncommon for us to get a consult in a pulmonary clinic-- in mine or any other pulmonologist-- and say, what brings you here today, Mrs. Smith? And the answer is, well my asthma is acting up. I'm so short of breath, I can't walk from the bathroom to the kitchen. And so I'm gaining all this weight, because I can't exercise.

And I'll say, well, what is your asthma medicine? Albuterol. Yes, ma'am. But that's your system medicine. What is your asthma medicine? Albuterol.

Well, how many times do you use your albuterol a day? 27 times. So you're drinking your albuterol.

But it says here that Dr. Smith puts you on Advair. Oh, that's got a steroid in it. I can't use that.

And it's like, you have to do a lot of education. Because people think that steroids are bad. And I'm going to hopefully convince you that, not only are they not bad, but they are beneficial.

Also want to break for just a second, and show you a YouTube video. It's really quick. But it's kind of cute. Probably a lot of you have seen it.

[VIDEO PLAYBACK]

-Well, sometimes doctors make mistakes, Anna, and we have to try twice as hard to fix them. Are you using your inhaler?

-All the time. Go through one a week.

-You sure you're using it right?

-Do I look like an idiot?

-No. Why don't you show me how your inhaler works?

[MUSIC PLAYING]

-Jerk.

[END VIDEO PLAYBACK]

DR. DOMINIC DEKERATRY: There's data out there that suggests that 70-plus percent of people who use inhaled medications use them incorrectly. So when people have for poor asthma control, don't forget that. And certainly don't forget to spend time educating them on the proper use of the medication.

ICS, Inhaled Corticosteroid, this is the treatment for extrinsic asthma. These are the controller medicines. This is Asthmanex, and Pulmicort, and QVAR, and Flovent, and Alvesco. So these are inhaled steroids. And inhaled steroids do not have any significant systemic effects.

If you are 90 years old and weighs 70 pounds, and you're on high dose Advair, probably you're going to get some osteoporosis. But generally speaking, it doesn't affect diabetes. And it doesn't cause weight gain and fluid retention, and anything else.

And in fact this is 13-plus-year-old data that was published in the*New England Journal of Medicine* that says for patients with persistent asthma, low dose inhaled steroids prevention of death-- so this is the number of canisters of inhaled corticosteroid per year-- i.e. they went through one-- if you were at 12, you used your medicine critically. And if you were less than 12, you died. So the relative risk of dying goes way down in a very nice curve, the more you use your inhaled corticosteroids. So it has morbidity and mortality benefit.

A comment about ICS LABA combinations. Long-acting beta agonists like Serevent and Foradil and a couple of others are also not wrong to use in asthma. There's a black box warning-- [INAUDIBLE], which is the Salmeterol Multicenter Asthma Research Trial that was published predominantly out of a hospital in Denver five or six years ago.

Basically took patients who had asthma, and put them in their normal treatment, versus their normal treatment plus salmeterol. And sure enough, in that trial, patients who in the salmeterol group, there were eight deaths more per 10,000 patients. So not a huge difference. But enough that it raised a lot of red flags.

And people said, gosh, we better be careful with LABAs. Can't use them in kids. Shouldn't use them in adults.

But if you-- admittedly, that was a randomized trial. But if you do the post hoc analysis, only 38% of those patients were on inhaled corticosteroids. So to me it's like somebody doing an acute coronary syndrome trial on Tylenol versus aspirin. There's no anti-inflammatory meds in the salmeterol group.

And in fact, if you looked at the patients who were on inhaled corticosteroids in that study, there's no difference in the endpoints, which were death and respiratory failure were the endpoint for that study. So long-acting beta agonists can be helpful. But you should never use them without an inhaled corticosteroid.

OK, systemic steroids, we all know they are a blessing and curse. They are a multiplier. They can help you with your breathing. But then they can cause everything else-- cataracts, and obesity, renal dysfunction, osteoporosis for sure, psychosis, lots and lots of problems with diabetes.

And so whenever you get to the level of five and six on the step up therapy for asthma, you're running out of gas in terms of complementary medicines. And the systemic steroids are often the only thing we have to go to. Alternatively, we can use Omalizumab in some patients.

And this is a drug that, for those of you who don't know, it merits discussion. I think it was FDA approved in around 2000, 2001. And it's an injectable. It is a IGE and inhibitor.

And basically, for people who have severe persistent asthma, and have a specific allergen, as documented by an allergist immunologist, those folks can really benefit from Omalizumab injections. In fact, just recently in 2013, *Chest* published that in a study where add-on Omalizumab to and inhaled corticosteroid LABA combination really does reduce the risk of hospitalizations and ED visits. It's expensive.

And it requires a lot of work, in terms of getting the injections. Any nurses in the audience who sit there and rolled those vials for 45 minutes because you can't put them in a centrifuge in preparation for injections, it's a pain in the rear. But if you can get it done, it can really help a lot of patients.

So we went from basically a SABA to Xolair. I didn't mention, and I should, that along the way there is plenty of room to use other add-on agents. Leukotriene modifiers are perfectly appropriate to use. In a persistent mild asthmatic, they can sometimes be the primary controller medicine, which is great. But in the moderate to severe persistent asthmatic, they're typically not potent enough to control symptoms. So they would be add-on to the inhaled corticosteroid.

Other things like theophylline are also possible. Theophylline is a weak bronchodilator. It can help improve diaphragmatic function, muscle function the chest. It's not used as much as it used to be. But in some patients we just need to add it on, but never in lieu of the inhaled steroid.

This is a study that I think merits some discussion as well. So this is tiotropium, or Spiriva. And this study was published in *New England Journal* in 2010. Basically, it was three way double blind triple dummy crossover trial in about 200 patients. And what they did was compare tiotropium with an ICS to doubling your ICS to ICS plus LABA.

And this was a non inferiority study. So you really have to be careful about extrapolating too much data from it. In comparison with a LABA, tiotropium was a non inferior in all assessed outcomes, but increased the pre bronchodilator FEV1 more than salmeterol, for what it's worth. So it's perfectly appropriate to use as an add-on therapy to an inhaled corticosteroid.

What is interesting to me is, getting back to the cigarettes, this thorn apple plant, as it's been studied, it turns out that the active ingredient was an antimuscarinic agent. So this is like smoking Spiriva cigarettes. And if you think about it, it was controversial 200 years ago. Yes, it helped your symptoms, but there's an increased risk of death.

And I think it's just basically helps remind people that you still need a controller medicine for asthma. And while you can drink albuterol all you want, and take it 27 times a day, that is not going to be the controller medicine for your disease, nor is a LABA or tiotropium.

OK, I want to comment a little bit about asthma in relation to pregnancy. Because this comes up quite a bit. There's a significant impact, potentially, with an uncontrolled asthmatic mom.

There's preterm labor, potentially. There's preeclampsia, congenital abnormalities, growth retardation, et cetera. And, guess what? In terms of statistics, 7% of women have asthma, just like anybody else.

Classic teaching in the medical literature is that it's a disease of thirds. A third get worse. A third stay the same. And a third improve during pregnancy.

It does tend to be a little bit worse in the middle of pregnancy. The standard teaching is, if somebody was controlled with controller meds before, they should be controlled with controller meds during pregnancy. In terms of the medications, SABAs-- albuterol and Xopenex-- those are pregnancy category C agents. Inhaled corticosteroids, for example budesonide, is category B.

It has been around since 1963. It's as old as Pepto Bismol. It is an old, well established preferred agent for the control of asthma, particularly in pregnant ladies.

All the other inhaled corticosteroids are still category C, but not an unreasonable choices in a persistent asthmatic. Leukotriene receptor antagonists can be used, except for not Zileuton. This is a Zyflo. Because there's some hepatic toxicity, and some potential ill effects on the infant. Theophylline can be used, but it's category C as well.

Other drugs in pregnancy, you can add a LABA to ICS. It's not a problem. And you can increase the dose of ICS.

And actually, Omalizumab or Xolair is a category B, if you need it. Kind of scary to do that. But it's category B.

All right. So let's get back to this chart again. You've worked your way up.

You have controller medicines. You have LABAs. You have add on therapy. And as you get up worse and worse, to step five and step six, about five to 10% of asthmatics-- 8%-- have severe persistent asthma, despite maximum medical therapy.

In Texas, 1.3 million asthmatics are out there. And the severe aesthetics number over 100,000 in Texas alone. So it's quite a prevalent problem.

But up here there's not a lot of options other than chronic systemic steroids, et cetera. Other medicines have been tried over the years. The ones I have asterisks by have been looked at in randomized prospective trials, although they're very small. And the outcomes are not very good. Because there was a high dropout rate.

Everything from methotrexate to IVIG infusions to the inhaled heparin have been looked at. But nothing on this list has definitely been helpful without significant side effects. And most of them have been a wash at best. So not particularly advocated. So we're still looking for another therapy for these patients with severe asthma.

So now enter this other concept. This is airway smooth muscle. This is a cross section of a bronchus. This is a normal airway. And this is an asthmatic airway.

The airway smooth muscle is a vestigial organ. It's like an appendix. As an adult, nobody knows why we need it.

Probably, it had some benefit in infancy to help expel meconium ileus. But other than that, it's just an appendix. It doesn't seem to be helpful, and certainly can be harmful. And it's a maladaptive hypertrophy that occurs in an asthmatic patient.

And certainly, whenever you have an asthma attack, you have constriction, and mucous plugs, and wheezing. So there is a need for patients at step five and six to have additional options. And this is where we have now the only non pharmacologic treatment for asthma that's available.

Bronchial thermoplasty basically reduces airway smooth muscle, thus reducing broncho constriction, reducing asthma exacerbations, and improves quality of life. So let me teach you a little bit about BT. This is a technique that was FDA a approved in April of 2010. It delivers thermal energy to the airways, via bronchoscope, typically under moderate sedation, and sometimes under total IV anesthesia with jet ventilation. Depends on the situation.

And the idea is to perform the procedure in stages. We do one part of the lung one time. Let the patient recover. Do another part of the lung another time. And then the third time.

It is a complementary treatment to inhaler corticosteroids. Is not a replacement to current asthma medications that are controller medicines. It is very important as everybody starts to learn about BT. You don't get BT, and then your asthma goes away.

Asthma is an inflammatory disease. You need an anti-inflammatory medicine. But the treatment with bronchial thermoplasty has been shown to increase asthma control, and improve quality of life in patients with severe disease.

So this is the setup. This is called the Alair catheter. This is a radial array catheter with four different electrodes.

This is the generator. And it generates a monopolar energy that is delivered at about 65 degrees Celsius.

So this is a little cooler than a hot cup of coffee. So every morning when you put a cup of coffee to your lips, it's hotter than bronchial thermoplasty. And I say that because, as orient you into BT, there are still many people that send patients to us for ablations, and for laser surgery for their asthma, and stuff. And this is not what BT is. And that's not what we do.

It is the radio frequency energy. It's a cool heat. And the idea is that some smart person realized that when you ablate in the bronchial region, or you apply the energy, I should say, that the airway smooth muscle is inherently heat sensitive. And over time what happens is that there is apoptosis, an atrophy of the smooth muscle. Somewhere between 30 and 50% of the smooth muscle shrinks down over time.

So I'm going to go ahead and, Steve, can you hit that so we can show this video? This is a long video. I'm going to cut it short.

But we'll get it started here. This is just a cartoon of the way BT works. The patient is under spontaneous respirations, typically.

And most of the times it's done in an endoscopy suite. This is a similar cartoon to what you saw a moment ago. This is the airway smooth muscle. It constricts.

And the idea is that this is a maladaptive process. And so we're trying to treat the airway smooth muscle to reduce the symptoms, and improve control. And the bronchoscope is introduced typically through the nose.

It goes down into the airways. We start with the right lower lobe first. Then a few weeks later we do the left lower lobe. And then a few weeks later we do both uppers.

And the catheter is deployed through the working channel of the bronchoscope. And it comes out. It is marked in five millimeter increments.

We open up the catheter. We step on the pedal. It administers the energy for 10 seconds.

We come down, back up five millimeters, go up. Hit it again. It's a rather tedious process.

But the typical person gets about 60 to 65 or maybe 70 treatments per session. So we go throughout the whole right lower lobe, including the superior segment. And then let the patient recover, and come back three weeks later and do the left side, et cetera.

OK, so this is a canine model. When BT was first being investigated, this was interesting data. This was canine models that were treated, and then examined serially over a several year period. This is thee year data, post-treatment.

So this was the same animal model. This is untreated segment. And this is treated segment of airway epithelium. You can see the ciliated epithelium on both slides is preserved.

This is cartilage. The pulmonary parenchyma is down here, and it's normal. What's the most obvious thing is that this airway smooth muscle will basically void here. And it's important to remember that there's no evidence of residual scar tissue or residual acute or chronic inflammation in the histological tissues that we have available.

This is a cartoon, again, of a canine model. The left bronchus this has been treated with bronchial thermoplasty. And the right side has not. And these folks instilled methacholine directly into both with this catheter. And there's your prevention of vasoconstriction.

So as you think about how BT can compliment therapy, it does not predictably change FEV1s. It is not a bronchodilator. It is to help prevent broncho constriction, which is a very different concept.

This is the typical Netter diagram that we used to map our way when we're doing the cases. For those of you who are interested we spare the middle lobe on the right. But we do the lingula.

OK, so bronchial thermoplasty, again, has been FDA approved now for almost three years. And there were several trials that led to the FDA approval. And first there was a feasibility study.

Then there was an air trial, which is a randomized trial. RISA is the Research In Severe Asthma. There's a small cohort. But it was also randomized.

And then the pivotal study, which is the AIR2 trial. There were 190 treated patients at 30 different sites. And I'm going to show you some of the data from that.

So this is an investigational device exemption study. This is not a drug study. Remember, this is a pacemaker, or hip joint. This is a prosthetic, or something other than a medication.

And the studies are designed with an intention to prove worthiness in the sick population. It's not like you give it to healthy volunteers. So the study population was severe asthmatics. They were symptomatic, despite high dose ICS and LABA. And the primary endpoints were the Asthma Quality of Life Questionnaire score, or AQLQ.

This is a self administered, 32-questions questionnaire that has four different sections in it. It's one to seven. And you just basically add them up.

And in a meaningful, important difference on the scale, which is a very well validate scale is 0.5 on that scale. And of the patients were treated with BT, 79% of patients had a 0.5 or greater increase. And the effect persisted across six, nine, and 12 months.

So the secondary endpoints were pretty interesting as well. Improved clinical compared to control-- 32% decreased in severe asthma exacerbations in a 12 month period. And the authors defined a priori the definition of severe asthma exacerbation as somebody requiring a burst of systemic steroids. So 32% reduction in prednisone, for example, or IV steroids.

And 84% reduction ER visits. 73% reduction hospitalization. And 66% less days lost from work, school, and other activities due to asthma.

Moreover, there was no unanticipated [INAUDIBLE] adverse events or deaths. And therefore it's been deemed to have an acceptable safety profile. This is a sham study, two to one. So everybody went to bronchoscopy.

And for the uninitiated, historically, bronchoscopy in a severe asthmatic has been relative contraindication. Because everybody's worried about inducing bronchospasm and causing trouble in an asthmatic. So it's the only study of it's kind. We took-- they took-- I was not a participant. Excuse me.

They took everybody to anesthesia, to sedation. Got the catheters out. Ran them down there.

And then they opened the envelope and said, this person gets it. This person doesn't. And even when the person didn't get it, when they stepped on the pedal it made the sound, as if it did.

And the patient, and also the providers who saw patients in follow up were blinded to the technique. And they did follow the patients for three, six, nine, and 12 months. And now there's long term data follow up as well.

So this was another way of looking at the data. I told you a minute ago, this is a statistically significant difference. 32% decrease in severe exacerbations. Emergency room visits went down by 84%. And hospitalizations went down by 73%.

This is the effectiveness of BT, published after two years. Showed that the patients who were treated-- this is the year prior to the study, in terms of severe exacerbation percentage, ED visits, hospitalizations. Everything went down year one. But also, everything stayed down at year two.

850 bronchoscopies were performed in patients with severe asthma. No device related deaths. And whenever you're, again, doing a bronchoscopy, the average person who gets a transbronchial lung biopsy, the risk of pneumothorax is around 4%. So compared to standard agnostic bronchoscopy, it's a relatively safe procedure.

And then several of these patients have been followed out with serial CAT scans over a five year period, once a year. There's no evidence of bronchiostrictures or bronchiectasis, or anything else, for that matter. This merits some discussion. And I think I may have some questions about this, or I hope I do.

Respiratory related hospitalizations during the treatment period-- when you do bronchoscopy on a patient, and you administer thermal energy, radio frequency energy, 75 times to their right lower lobe, very often, people have an asthma exacerbation. The chances of having a hospitalization due to a respiratory related issue is about 10% across all three procedures. So a little over 3% per procedure, patients need to come in.

Often we bring them in just for observation overnight, give them some Solu Medrol overnight, maybe a Z-Pak. And then typically they can go home the next day, sometimes two days later. But you have to counsel your patients that 10% of you guys, over the treatment period, are going to be hospitalized.

Safety data has been published for two years from the AIR2 trial. No deaths. Absence of complications. And then the CT scans showed no structural changes. These were reviewed by independent radiologists.

This is published data from five year safety bronchial thermoplasty in the AIR1 trial that basically said, again, no adverse events had come up. Pulmonary functions stayed stable. No instances of pneumothorax intubation, mechanical ventilation, et cetera, felt due to BT.

All right. So I'm actually a little ahead of schedule. And I hope this generates a little bit of discussion. But I wanted to give you our clinical vignette, face forward 200 years.

This is our first patient we did a couple years ago. She was 30-year-old woman with lifelong asthma, mother of two employed by a large regional computer company. Nonsmoker, although she had been a smoker in the past. And her meds were Advair 500, Singulair, Duo-nebs, Albuterol, Claritin, and Fluticasone. And she had been hospitalized twice in the last year, and two or three times every year for a number of years.

And very often, she was on prednisone. Probably six months out of 12, she was on prednisone. Her FEV1 pre-procedure was 77%. She had a 14% bronchodilator response.

And after BT she's not been hospitalized for asthma. Now, she's required prednisone as an outpatient. But generally, her hospitalization rate has gone to zero.

This is important because, even though we counsel people that BT is not anything but a complimentary therapy to existing therapy, if you get BT and you still have asthma, people seem to be surprised. It is a complementary therapy. And it is intended to reduce your prednisone, and improve quality of life. There is data that suggests it decreases the need for rescue inhalers over time. But it doesn't cure asthma.

OK, so remember that inhaled corticosteroids are the controller medicines for asthma. ICSs are the mainstay of therapy. They do not cause diabetes.

They do not cause osteoporosis or psychosis, or whatever your patients are afflicted with. Going to [INAUDIBLE] does. But if you take your medicine, you'll have a better chance of symptom control.

Add-on therapies include the long-acting beta agonists, which are perfectly fine to use-- tiotropium, leukotriene modifiers, theophylline, Omalizumabs, systemic steroids. And for patients who have severe asthma on maximum medical therapy with persistent symptoms, consider BT.

A couple of resources that I put in here that I think are very valuable is the Global Initiative for Asthma, which is www.ginasthma.com, and then the National Asthma Education prevention program. These are two great websites that are full of information. They can talk about everything from control of environmental triggers, all the way up to Omalizumab, for example.

And this is room for questions. And I put this up here because my wife, who hopefully is listening in Georgetown, is my partner. And she's expecting a baby.

And we weren't sure if were going to make it today. But we made it. So we're good. Congratulations.

[APPLAUSE]