TIMOTHY R. PETERS: We get to talk about pertussis this afternoon, an update on pertussis. And an update on pertussis is a really good idea because pertussis is really a confusing topic. In fact, when I go to national meetings, I try to attend some of the talks on pertussis. And they are so confusing, honestly. In fact, when I go to those talks, most of the time it feels as though knowledge has actually been sucked out of my head. I actually leave dumber about pertussis. Right? Because they start off with some general comments on the epidemic. We talk about the epidemiology. We're all sort of on the same page. And then the immunologists and vaccinologists all talk about correlates of protection. The wheels completely come off. So by question and answer time, there's almost fist fights over pertussis because no one's really on the same page. It's a very confusing topic of great, immediate, national importance.

It's really important to all of your practices. And those of you who have clinical practice, right off the bat, I'm just very curious. How many of you, from the course of your personal, clinical practice, have the sense that pertussis is coming back? Yeah. Yeah. Yeah. So I just wondered. So we're going to launch right into that. But first, yeah. There we go. Good. It's always nice to start these talks with a case. Right? So here's a patient I saw, really, it was eight or nine years ago. But it's illustrative of some of the problems. It'll really feel like the case that's familiar to many of you.

So let's talk about Varqueise. He's a two-month-old boy that we saw in pediatric infectious diseases for the chief complaint of cough. He was well until about one week before he was admitted. He had some cough and no fever. He was seen at a community hospital and diagnosed with oral thrush, started on Nystatin. And his cough persisted, no fever, doing OK.

Diagnosed at another institution with otitis media and started on a amoxicillin. But his cough remained persistent and nonproductive, had some post-tussive emesis. In the review of systems, really, no rhinorrhea, no nasal congestion, no rash, no ill contacts whatsoever. A full-term baby, unremarkable prenatal course, had not yet received his two-month's immunizations, but pretty unremarkable. No family history of note. And he lives at home with his parents and two-year-old siblings. And all have been healthy. There are some smokers around.

And so in the emergency department there, he had a temperature of 100.1. And he was awake but he had some paroxysms of cough. And during his stay in the emergency center, he was noted to have some formula in his oropharynx at the time of his cough. So, from the emergency department, they whisked him off to get an upper GI study, which showed reflux to the oropharynx. Hardly shocking in a 2-month-old, right?

But they found that and admitted him for observation. And in the hospital, a CBC was done, and the results showed a white count that was pretty high, and a lot of lymphocytes. So 21.1 thousand. And that tipped everybody off that this was a baby with pertussis. And as those of you who practice for a long time before, our newer generation pertussis diagnostics will appreciate that this was often how we figured as stumbled across cases of pertussis.

He had a nasopharyngeal direct fluorescent antigen test and cultures were done. And the DFA was negative but the culture was positive for pertussis. So it's-- that wasn't Varqueise. It was another web CDC image of a child with pertussis. But it can be very striking to see these patients in the hospital. Now there's a practical pediatrics I know, so it would be most appropriate for a science type geek head like me not to start talking about gram stains and all that. I tried to leave a couple of these slides out. But woke up the next morning and they had appeared in my talk. I think I did in my sleep. So it feels compulsory. Right? We can't help ourselves.

Just to remind everyone briefly of stuff you already know, especially if you take care of kids for any length of time, pertussis is a gram negative bacteria. Vaccination confers immunity for five to 10 years, but maybe less. Who knows? Right? Incubation period of the disease is 7 to 10 days, and the clinical case definition from the CDC is cough paroxysms, inspiratory whoop, and post-tussive emesis, as long as you don't have anything else. So not a really helpful case definition. But there you go. So, oh, not a gram stain. He put a gram stain up there. I can't explain it. Right? It's a compulsion. Horrible, horrible. And this slide has to be on every pertussis talk given. Its absolute mandatory. Right?

The pertussis phases. We live for this stuff. Phase 1, the catarrhal phase. Right? 0 to 2 weeks, nonspecific URI symptoms, afebrile or a low-grade fever. Here's really helpful, excessive lacrimation. How handy is that in the clinical setting. Right? Wow. I know what this is. And conjunctival injection. Right? OK. So there we go. So phase two is the paroxysmal phase, which is the phase whenever we end up figuring them out, clinically. Right? They have coughing, minimal symptoms between paroxysm of the coughs. Sometimes you might hear a whoop. But usually not. And they have emesis when they cough a lot. And then convalescent phase, that's a whole phase for that where they're getting better. So the 100-day cough.

The point that everybody is compelled to make when they talk about pertussis is that you give antibiotics for treating this bacterial infection, but without any expectation that they will help the patient at all after phase two, which is almost all the time. The only time there is any demonstrated clinical benefit to the patient is when antimicrobials are given in the catarrhal phase, first couple of weeks of illness. And that's usually when we don't catch them. Now this is a point that I tend not to over emphasize when I'm taking care of patients. Right? So this is really given to your child because we don't want them to pass pertussis on to somebody else. Treatment in any phase prevents transmission to other patients. And that's why we give the-- well, you know all this. There we go.

Pertussis diagnosis is not easy. Wow. This is an audience that knows that. Right? This is really a difficult diagnosis. Things have changed and gotten better. There's the update that many of you are familiar with. Well, part of the update is not really an update, it's that our diagnostics have gotten much better for pertussis disease. We take a swab that's made out of polyester or Dacron, the same substance. We swab their nose and we send it off for a PCR assay. And now, unlike in years past, it's my impression that really our commercial labs that make this test available to us do a very good job. And so we send that off for PCR assay and they can give us a pretty quick result that has a much higher sensitivity and specificity than either the culture or the DFA.

The DFA that many of us endured for years is so bad. So nobody really does it anymore. We just have sort of given up on that. But there may be labs that offer it. And if they do, don't use it because it's just awful. Now I put this awful cartoon on there just because, boy, to get a deep nasopharyngeal swab, that sure is a long way. Right?

So part of my job is we do surveillance of respiratory pathogens in kids and adults. And so when we have a new person working in our group I have to train them in how to give a deep nasopharyngeal swab. And so the only person I can really get to do that is me. So I have them swab me. And that goes in a long way if you're really doing it right. So I will say that, as a practical matter, you just keep it coming. And they're like, uh. So it can be very emotional for people who are just learning that there's not that much room. However, I will say that, as a practical matter, in your office or a practice setting, most people aren't really putting that thing way back in there that far. Right? Let's just face it. Really.

Well it turns out that the PCR test is pretty good in just your standard clinical setting where you're pretty sure your team is not putting that swab that far back into the nose of their patients. However, I will say that we should strive to getting good samples because you spend a lot on this test. And there's no reason not to get a good sample to get maximum sensitivity and specificity. And if you've had it done to you a lot of times, you realize it doesn't really hurt that much. It just freaks people out. Right? So if you can get them past that, you realize it's a very satisfactory thing to do.

OK. Let's move on. Treatment. Well, as you all know, we treat with Azithromycin now. It's not much of an update to talk about hypertrophic pyloric stenosis as a risk for treatment with arythromycin. So that's been discussed at great length. But now the macrolide treatment of choice is azithromycin. And really, if they're allergic to the azithromycin, we use bactrim to treat pertussis. Those are the two recommended anitmicrobials. And I made the point about treating during the later phases of disease doesn't really shorten the course of illness.

OK. So let's get into it, the real update stuff, the stuff that's really fun to talk about. And that has to do with why, really, you all raised your hands. We have a vaccine for this illness. Why is it your strong impression, shared with me, that we're seeing a lot more pertussis, really, a lot more? So we have a vaccine. Let's talk about that vaccine a little bit more, because there's been a lot of changes in recommendations and use of this vaccine in our community. So just a little teeny bit of history here.

Whole-cell pertussis vaccine has been available since the 40s and a very effective vaccine. And so in the 1990s was introduced an acellular pertussis vaccine, as you all know, with a better side effect profile. It's that simple. So we have the old vaccine and the new vaccine, which I may use that terminology for clarity here. When I say old vaccine, I'm talking about the whole sale pertussis vaccine. It's used in many parts of the world as the only pertussis vaccine available. But that's what we used to use.

And then those of us who were practicing, taking care of kids in the 1990s, remember that period of time when the new acellular pertussis vaccine was introduced. And there was a time when we gave the whole-cell vaccine to the really young kids. Then we give boosts for the preschool patients. And then we move to toddlers that we gave the acellular pertussis vaccine. Then, finally, we had enough acellular vaccine for everybody. And that's all we use now. Right? There's really no whole-cell vaccine available in this country for use.

So that's how it went. And then in 2005 this Tdap came along with different amounts of antigen in it. But, again, acellular pertussis vaccine for use in adolescents and adults. So the DTaP, you can only use it in persons less than seven, eight years of age. And so we have this Tdap vaccine. And with the recommendation to give it to our adolescent patients, preferably 11 to 12 years, that's all review for you all.

And so this is the current ACIP vaccine schedule, just to get us all on the same page. I know you all know this better than me. 2, 4, and 6 months, 15 months, and 4 to 6 years of age, we recommend the DTaP. The ACIP recommends that. A single Tdap dose for adolescents preferred for 11 to 12 years. We'll go over to some epidemic curves as to why that recommendation has been made.

And here's the deal. Now,-- and it's been such a moving target-- if adults have never had a Tdap, they should get one, but only one, ever, pretty much. Except if they're pregnant women, and then they should get it every single time they're pregnant. And we'll talk more about that. But that's a current recommendation as of this year. And the Tdap adolescent adult dose is especially important for health care workers and persons with infant contact.

That makes some logical sense. But many of you in this room probably have never had a Tdap. So you should go get one sometime so you don't get pertussis, which is pretty miserable if someone manages to diagnose it in you, which would be hard anyway. But if you haven't had it, there's a vaccine out there that you can get. And you should. So if you realize you need a Tdap and didn't get one as an adolescent, which you probably didn't, then you can get one. That's probably worthwhile.

OK. So let's start to look at the kind of data that the CDC is reviewing each year with incredibly great interest to figure out what the heck to do about the pertussis. So first question, we just talked about vaccines. How are we doing? How are we doing nationally at giving our vaccine? Vaccination rates. That's what this slides about. Actually, it turns out, we're doing super well. Pretty darn well, not bad.

So as you see, our national rates between 2004 and 2011 for the three childhood Tdaps is 95%. It's nearly 90% for four doses. And then, as you see in 2005, we talked about this Tdap recommendation to be given to adolescent patients, and up climbs our rates. In 2011, over 80% of our patients are getting that adolescent dose, preferably between 11 and 12 years of age. Fantastic. Now, adults, us in the room, that's not so good. Right? But it's starting to become increased awareness that we ought to be getting that dose. So that's important. As we think about the epidemic it's that it's not a failure of our vaccine to be given. We're doing pretty well. It's going OK. All right. So here's some of the most recent vaccination recommendations, just to review. And, again, these aren't brand new or anything, but just to remind you of what's been going on.

In 2005, the ACIP really started to recommend approaches that surround cocooning to protect young infants from severe disease. And so, in 2005, they said, OK. Moms, after they have their baby, let's vaccinate them really, really quick. As quick as you can. Right? Quick, give them a DTaP. And all the other people who are in the household, those adolescents or adults who haven't had a single dose yet, go ahead and give them, quick.

So you may remember trying to pull that off. It turns out that there's a lot of studies about cocooning that shows it's very hard to accomplish. Right? It doesn't actually happen that much. It's hard to get dads and adolescents to their doctors. Right? But it is a potentially effective way to protect young infants from transmission from household contact with pertussis.

Well then, in 2011, the recommendation came along, this is a safe vaccine, we're just going to give it to unvaccinated pregnant women. And they ought to get a dose at some point when they're pregnant. Just give them a dose. Then 2012 rolled around. They said, woah, woah, woah, woah, woah. OK. Let's give it to all women, every pregnancy, everyone. Let's give it to everyone. Let's give it to every single pregnancy. Between 27 and 36 weeks, for each pregnancy, let's go ahead and give the Tdap vaccine. Well there seems to be a lot more pertussis around, and so hence my first pole. Right?

So we all raised our hand. You all have that feeling, too. So let's really talk about that, because that's what this update is all about. There sure seems to be. Well, is there more pertussis or are there just more reported cases of pertussis? And we, in this room, have to decide where we are on that before we can really understand and appreciate how the recommendations are changing. So if you read prominent IV specialists who write editorials in the *New England Journal* and other journals, there's always a couple of different issues.

More awareness. So if all of a sudden everybody became very aware that they have to look for pertussis a lot more, than you're going to see a whole lot more pertussis. And that's not really a resurgence of disease, that's just a lot more people saying, hey, these kids have pertussis. That's not a resurgent in pertussis. But it's an important thing can greatly impact the epidemiologic curve of reported illness. The second thing is increased test sensitivity. Man, that PCR test is way better than that the DFA test. It really is. So I'm sure many of you have had patients where you have made that discovery.

Now, in particular, in our hospital now, we have the respiratory virus panel, and many of you are practicing in settings where you're using that as well. And within the last year or so, pertussis has been added to that list of organisms that we routinely test when we swab a kid's nose and send it to the respiratory virus panel. And within even weeks of the introduction of this new test in our hospital, we had kids who, bing, popped up with pertussis that wasn't particularly suspected. I mean, on the list, but no one had asked for a specific pertussis test. But all of a sudden, bing, out comes a positive pertussis.

And that's a very exciting time, when that thing happens and our diagnostics significantly improve. Then that's very gratifying, to start to identify cases of kids with pertussis where we hadn't suspected it before. And that's happened in our hospital for sure. So increased test sensitivity, though, is not resurgence of an epidemic. That's just we're recognizing the pertussis that was already there. So those two, in particular, are important issues as we interpret epidemiologic data.

OK. So there are some other things. Could it be that Bordetella pertussis is actually changing, that the bacteria is changing its genetic composition, that the antigens that we use in our vaccine no longer match what's circulating? That's a possibility. And then, lastly, this is the big one that we're going to talk about. Is DTaP flat out inferior to the older vaccine of the DT whole-cell pertussis? Are we using a vaccine that just doesn't work as well? So one of these things is making the ACIP members a little bit crazy about pertussis, and we're getting all this flood of new recommendations every year, well, I guess the point I would like to make is that pertussis is resurgent.

Epidemiologists have argued over this for some years, but, really, there is a strong consensus now that it's not just that we're just more aware or better at making the diagnosis. Pertussis is back and gaining. So let me show you that data. And this is really interesting. This is the data that was presented most recently to the ACIP members from epidemic health service, CDC, that sort of thing. So here we go. Well, this is a very broad epidemic curve. Let's see. How am I doing this? All right. There we go.

Over time, so as you can see, since the 1950s or 60s, the epidemic curve has drop. Here was the introduction of DT whole-cell pertussis in the United States with a very gratifying drop in cases of pertussis. And there we go. Uh-oh. OK. So DTaP was introduced along with some new diagnostics and the rest. And we start to see this thing really climb this epidemic curve. It's pretty significant. I guess, to be fair, over here-- well, you get the idea. It's not that complicated.

So if you look in the last couple of years, especially as 2005 and then 2010 and then 2012, we now have rates of disease in the United States that really exceed anything we've seen since the 1950s. This is a much bigger and more rapid blip than we could possibly ascribe to improved diagnostic testing, which has been introduced over a longer period of time. It just doesn't make sense. So we're seeing a bunch more. So that's an alarming number. So let's look a little more.

So if you have the maps-- In 2010, you all will remember from the newspaper that California had a very big outbreak of pertussis. So from 2011 to 2012, we look at all the states that had an increase. The only state-- oops, sorry-- that actually didn't have an increase between 2011 and 2012 is California, but that's because they were just finishing up a big California outbreak in 2010. So 2011 to 2012, that was a banner year for pertussis, 2012. Every single state had some increase. And some, like North Carolina, had a more than three-fold increase in disease over that period of time.

Then we're still back in red of an increase from 2012 to 2013. Overall, the epidemic peak dropped off in the past year. But not as much as you'd like. So many of these states actually had a decrease in total reported pertussis. Not us, but some states did have a modest drop. So, really, this is the most recent epidemiological data. Who's getting it, though? Who's getting pertussis? And it's our patients. It's pediatric. Oops. Man, I'm a mess So here we go. It's the technology thing. It's no good. One of those old slide projectors, click.

OK. So who's getting this? It's our patients that are getting pertussis. If you look at reported cases of pertussis, it's, of course, very young infants, less than a year old. That will surprise no one. And there's this big surge in adolescent patients and young adults who have pertussis. That's where the burden of disease is. So let's look at what I think is the most interesting slide that I have for you of data. And let's really talk this over a little bit. I'm going to wander a bit, a little bit. But there are three slides, basically, encapsulated in this piece of works.

I want you all to look first at just the 2004 blue line and the blue shaded area. So I'll explain this to both screens here. So in 2004, this was the epidemic curve, this blue line. And, at that time, in 2004, persons who were six years and younger only had acellular pertussis vaccine. But people who were older than six years old had at least one dose of whole-cell pertussis vaccine.

That's the age cohort with the new vaccine. So the epidemic curve looks like this and shows this boost of a bunch of adolescent patients who have pertussis. Just to reiterate what I was saying there, we have this blue line of 2004 epidemic curve in persons' cases of pertussis in persons of different ages. And this blue area, age six and younger, those patients all had all a acellular pertussis vaccine. So here we go. So there we go. There's our curve.

OK. So that's 2004. Well, it doesn't take a rocket scientist to understand why, in 2005, we got all pretty excited about recommending that adolescent dose of the Tdap. Right? And why everybody would say, boy, we really prefer that you give it between 11 and 12 years of age. Right? Because that's right before we're seeing this boost. Well, let's look again at the next phase of the slide.

Now we're going to look at 2010. Here's our curve, big boost here. Right? And here's the age cohort of kids who've only gotten a acellular pertussis. They've never gotten any whole-cell pertussis vaccine. Up here, these older patients, have at least one dose of whole-cell pertussis vaccine. Now we have a pretty darn, big peak here. That's not too good. So there, our peak now, we have higher rates in those kids who have never had a whole-cell vaccine. They've only acellular. OK. So you all get that over here. We're talking about this line here, and then this group of patients who are 12 and under who 've only had acellular pertussis. That's the curve.

Along comes 2012. We have a big, national epidemic of pertussis, highest rates of overall pertussis that we've seen in the country since the 50s. And here's our curve. So all these patients, younger than 14 years of age, none of them ever got whole-cell pertussis, even a single dose. They're all just are acellular pertussis, new vaccine kids.

And look at this curve. I mean, we have increases in younger patients that are significant. We have these big, large numbers of patients who have increases in pertussis disease in adolescent patients. So that's where things are going to give us a one-slide snapshot. But just to remind you now, we have all of these increases in the context between 2004, 2005, when Tdap that was recommended. 2011 and 2012 are way out here.

Our adolescent doses, we're doing a great job of getting that vaccine into the kids, and still we're getting these very large increases in pertussis in our adolescent patients. So this is the kind of data when you're really asked the question, is pertussis resurgent or not? Is your impression that you're seeing more pertussis because we actually have more pertussis? True.

That is the reason we are seeing a lot more pertussis. So that's not so great. Well, pertussis is increasing. Resurgence of disease is really occurring in our older school age children despite very high vaccination coverage. And the increasing incidence of adolescent disease is occurring despite our new recommendations for a lot more vaccine in adolescent patients. So it's pretty unsettling. So you see why the talks at national meetings get pretty lively. Why? OK. Why?

Now we're getting to the update stuff, and that's more fun. Why is it resurgent? OK. This is really very interesting. So basically there's been a series of recently published papers that really provide you with support for what you're probably thinking right now, common sense conclusion. The hypothesis is that the new vaccine, the acellular vaccine, just doesn't work that well on a population scale than the old whole-cell pertussis vaccine that they replaced.

And here's what they looked at. They just looked at those kids who were primed with acellular pertussis vaccine and compared those to kids who had at least one dose of whole-cell pertussis, at least a little. And they just compared those two groups. And what they find is a two-fold to five-fold greater risk of getting pertussis if you never had a whole-cell dose. That's really interesting. And it's published by a number of different groups and very well-done retrospective studies.

That's a new update. Now this is a practical pediatrics. So there's no way-- It would be completely inappropriate for me to talk to you about animal data from baboons and things like that. So I'm committed. I'm not going to do that. Except for this one. Right? Yeah. This is great. You got to love it.

This was just published last month in the proceeding's in the National Academy of Science. It's really interesting. And I just have to adopt this. So what they did was they looked at an animal model using baboons. And they vaccinated these baboons with either old vaccine or a new vaccine. Right? They used the whole-cell vaccine and then they got some new vaccine, just pertussis. And then they gave them their 2-, 4-, 6-moth vaccines and then challenged them with pertussis at seven months of age. And they used unvaccinated controls, too. And what they found was really fascinating.

So all the groups that were vaccinated were protected from pertussis. They were protected from disease. But vaccination with acellular, new vaccine, did not change at all how long they shed the bacteria. So it had no difference in their capacity to shed. Clearance of the bacteria from their nasopharynx was no faster than unvaccinated baboons. And when they put those baboons in a cage with uninfected baboons, they transmitted the disease just fine, just as well as unvaccinated. So whole-cell pertussis vaccinated baboons had a much shorter duration of shedding, about half as long. And so unvaccinated baboons that were previously infected, they didn't have any shedding at all.

So if you get wild-type disease before and recover from it, then you really don't have any colonization on rechallenge. So this is an incredibly interesting study that really highlights the difference of these two vaccines. And so it supports the hypothesis that our new vaccine is not preventing pertussis from circulating in the population. So there's lots of pertussis around that our new vaccine is not preventing. OK.

OK. What do we do now? OK. What can we do about this? OK. What about a second Tdap dose for adults? We've been talking about that for a while. We were recommending the one that you get when you're an adolescent or some other time, but just one dose. Is there any point in actually doing that, in giving more? Could we just start to give a whole bunch more Tdap to adults to see if we can try to reduce the amount of disease in the adult population?

Turns out that if you do a lot of math modeling,-- and those papers are really hard to read. It's a lot of sigmas and stuff. It's no good-- the bottom line is, when they model it out, they find that that's not going to have much of an impact on the overall-- it's just not going to work. It looks like, when you get a Tdap, that immunity wanes too quickly for that to have an impact on the overall population.

Now, as a practical matter, that doesn't mean the vaccine wouldn't protect that particular person for some period of time from getting pertussis. That's not what it means. It means that, on a population level, Tdap for an adult isn't recommended as part of our vaccination program. But what it doesn't mean is that if you have a family who wants to find ways to protect their infant from pertussis, vaccinating dad, a young dad who maybe had a Tdap when they were 12, would not help reduce the risk of pertussis in that infant. That doesn't mean that. It just has not reached the level of national recommendation. But still something that you can do if you want to.

This is NASCAR champion, Jeff Gordon, he's on the left, and Perri Tussis congratulating him for getting his adult Tdap vaccine. So trying to get some patient awareness, some website, where you can send your patients to have some wonderful resources and talk about how to protect themselves from pertussis. Really interesting. Just, very briefly, to talk about a couple things that we did.

This is my kid, Bobby. And I'm a high-strung ID guy. No, no, it's true. So when I had my kid, I'm like, man, I will feel so much better once we get some vaccines in this kid. Right? Get older, faster. Right? Let's go. I'm ready. And so I was anxious about that because I'm just high-strung anyway. Then Jenny came along. And I was feeling the same way. Can we get some vaccines into this kid, for heaven's sakes? And it turns out that we read a little more, and it was like, well, actually, why can't we?

The pertussis vaccination, all of our two-month vaccines, you can give at six weeks of age. You give them all at six weeks of age and still be on the reservation. You're not doing experimental work. So if you did that, if you just decided that you were going to give all your vaccines in six weeks, how much benefit could you expect from pertussis disease? And we did a paper that we published because of Jenny and Bobby, but mostly Jenny, on just a mathematical modeling, to look how many cases you could prevent doing that. So that's an option for practitioners. You can just decide to give your two-month vaccines earlier. That's one thing.

Cocooning. So what's the idea? We did a paper on cocooning as well with Gretchen Banks. Gretchen is one of the pediatricians that many of you know. She did wonderful work with us on this mathematical study to look, to say if you really use that Tdap in adults and kids,-- I'm sorry. If you really made an effort to vaccinate dads and moms before an infant was born, how much could you actually reduce the incidence of infant pertussis, if you just went ahead and vaccinated them? It turns out you can make a pretty significant impact even in your individual practice if you can figure out a way to do it. And that's just to vaccinate them it.

I made the point earlier that you all can recommend or offer or find or encourage your dads of new infants to your practice to get vaccinated with Tdap. And you don't have to tell them not to get it if they got it as a 12- or 13- or 18-year-old. They can get another vaccine. There's nothing unsafe about giving them that shot. And it will offer some protection to the infant. It's just not a national recommendation. That's a practical pediatric bit. That's Jenny now after I got a hold of her again with vaccines.

So thank you all for your kind attention. And I think I'm supposed to stop. Three minutes and then I'm going to get the beatdown.