

This Week in Virology

with Vincent Racaniello, Ph.D.

Special Episode

Interview with Dr. Peter Palese

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Vincent Racaniello

This Week in Virology. The podcast about viruses—the kind that make you sick.

This Week in Virology Special Episode for May 6, 2009. From New York City, I'm Vincent Racaniello and I'm talking with Dr. Peter Palese. He's Chairman and Professor of Microbiology at the Mt. Sinai School of Medicine here in New York City. Dr. Palese is an expert on Influenza viruses and has agreed to chat with us today about the influenza H1N1 virus that is currently circulating globally.

Thanks for agreeing to talk to me today, Peter. I really appreciate it.

Dr Peter Palese

Thank you.

Vincent Racaniello

I wanted to talk about the new influenza virus, H1N1, and the listeners of This Week in Virology, my podcast, are pretty knowledgeable about viruses, so I want to really focus on the virus and its biology and the science, if you will.

Dr Peter Palese

Sure.

Vincent Racaniello

One of the questions that is always arising is—this is called an H1N1 influenza virus and, you know, there've been previous H1N1 strains as well, so how does this relate to them?

Dr Peter Palese

So we have currently a regular influenza virus season. We have actually three different influenza viruses: we have the H1N1, the H3N2—both of them are influenza A viruses—and then we have an influenza B virus. So these three different strains make up the three flavors which are circulating during the winter period from about November to March over the last at least ten years. Two influenza A viruses, one influenza B virus.

And the new thing was at about maybe fourteen days ago—two weeks ago—another H1N1 virus was reported in patients, particularly in Mexico and also in California. So this H1N1 virus—this new H1N1 virus—has one component, the hemagglutinin, which is very similar to the hemagglutinin of swine virus, and that's why it's called the "swine virus". And I'd like to use this name as we discuss this virus because it is actually distinct from the current H1N1 virus which is circulating also in the human population.

Vincent Racaniello

So is the fact that they're both H1, does that imply any antigenic cross-reactivity between the two?

Dr Peter Palese

There is clearly an H1N1 similarity. In other words, the hemagglutinin of all H1 strains is much more similar than the hemagglutinin—the H1 hemagglutinin—to an H2 or an H3, a different subtype. So, yes, the swine virus, the H1N1 swine virus, has similarities with the current seasonal H1N1 virus and we all have been exposed to the regular seasonal H1N1 virus, and there is some herd immunity in the population against seasonal influenza viruses, and we can be certain that there is some cross-protection, some cross-reactive immunity in the human population against this H1N1 virus which is also the hallmark or a sort of the characteristic of the swine virus. So, yes, there is some cross-protection. How much? Yes, is a little bit of a question. In other words, it's certainly not full protection because people do get infected, but I think it will result in a dampening of the virulence and pathogenicity of this new swine virus.

Vincent Racaniello

Because the CDC has said they wouldn't expect to see any protection in people who were infected with the previous season H1N1 against this, but it seems to me that remains to be seen, right?

Dr Peter Palese

I have heard about this and I think what one can—okay, depends how much protection one wants to see. I think what the CDC is saying in order to really have good protection, we have to make a vaccine. So they are really concerned that people are saying, “Okay, this is just an H1N1 virus and we don't have to worry.” Clearly, this new H1N1 viruses are causing disease and I would sort of see as a cautionary statement by the CDC that they really would like to make people aware that in order to be fully protected, we need a specific vaccine made against that swine virus, not rely on the partial cross-reactivity with the current vaccine.

Vincent Racaniello

I see. So, I got an email from someone who said they were a recruit in 1976 and they had gotten infected with swine influenza virus in that episode, would that confer some partial protection as well?

Dr Peter Palese

The 1976 swine virus was another example of a swine virus jumping into humans and, as you mentioned, there were 40 million people vaccinated. However, this is now more than 30 years, so the immunity which was afforded by this vaccination would certainly have gone down by now. And also we looked at the sequence of the New Jersey swine virus, which is again different. It almost forms a triangle in terms of relatedness. So the current swine virus has many difference to the New Jersey swine virus as it has to regular H1N1 strain circulating, so it's really a sort of almost a triangle in terms of genetic distances among those three viruses.

Vincent Racaniello

So I presume that the 1918 would be even further antigenically from this one?

Dr Peter Palese

Correct, the 1918 is even more distantly related. But the precursor to all of these H1N1 viruses: the swine virus from 2009, our current H1N1 viruses, and the New Jersey H1N1 virus from 1976, they are all derived from the 1918 virus.

Vincent Racaniello

Right. Now, I understand that this virus, although it's a swine virus and resembles viruses that are in pigs, actually has some RNA segments from avian and human strains which went to the pigs, I think, in the 1990's, is that correct?

Dr Peter Palese

That's correct, yes. So this is really a triple reassortant, meaning the swine virus from 2009 has actually sequences, which were derived from three different influenza viruses: avian influenza virus, human influenza virus, and the swine influenza viruses.

Vincent Racaniello

Now, I remember in 1976, that H1 used to be called "H1Sw", is that correct?

Dr Peter Palese

Yes.

Vincent Racaniello

So, is that what we call the "classical swine H1N1"?

Dr Peter Palese

Yes, I mean, the 1976 swine virus was actually a true classical swine virus which jumped directly from swine into humans. So that virus was actually shown to circulate several years before that in the swine population, that is in 1976, several years before that and it is also known that in 1918 the human influenza virus jumped into pigs during that period of time, and then was propagated for several decades in the swine population, and this antigenically-drifted human 1918 virus then was jumping into humans in 1976.

Vincent Racaniello

So is it fair to say that the H1 of this 2009 swine virus is more similar to the avian H1's than to the 1976 swine H1?

Dr Peter Palese

Can you repeat the question, please?

Vincent Racaniello

So is it fair to say that the hemagglutinin, the H1, of the 2009 swine flu is more similar to avian H1's from that went into pigs in the 90's rather than the H1 from 1976, say?

Dr Peter Palese

That will be correct, yes. But it is a little bit confusing when you then call the swine HA of the swine virus an avian one.

Vincent Racaniello

Sure, sure. Yes, yes.

Dr Peter Palese

In a way, you're absolutely right. I mean this just highlights what's going on with influenza viruses is that there is a jumping of, if not complete viruses, but certainly of genes of influenza viruses from one species to the other.

Vincent Racaniello

Right. So, from my reading of the literature, it seems that from about 1918 till somewhere in the '90's I think, this classical swine viruses were constant in pigs. But then in the '90's or earlier perhaps, bird and human influenza viruses began to infect pigs, and do we have any understanding of why that began to occur at that time?

Dr Peter Palese

Not really. I think this is a very good question. It may have to do that there was an increase in the number of pigs and swine worldwide. This was a time when the economies in Asia really took off, and it is known for example that the poultry industry and the number of chicken in the world, I mean, is probably ten times higher now than it was only 25 years ago. So it might be that there were more animals, there was a bigger substrate for influenza viruses, and that may have contributed to this sort of increased mixing of influenza viruses in the pig population.

Vincent Racaniello

So the unique aspect of this virus, from what I understand and you tell me if this is wrong, is that it has sequences from Eurasian and North American swine flu viruses, is that right?

Dr Peter Palese

Correct, yes.

Vincent Racaniello

Do you have any idea how this mixture occurred and where?

Dr Peter Palese

When genes get shuffled, this is always a result of a co-infection of a single cell with, let's assume a Eurasian pig virus with an avian virus, and this can happen either in a pig, it could have happened in a bird, or even in a human cell. So even though pigs have been postulated to be a good mixing vessel because they have receptors—pigs, that is—in the respiratory tract, they have receptors which allow the growth of both avian and mammalian influenza viruses, the actual site or the actual species where this mixing and co-infection of influenza viruses from different species occurs is not completely clear. But I think assuming that it happened in a pig is probably not out of the question.

Vincent Racaniello

So I understand there's going to be increased surveillance of pigs, and virus isolations, and sequencing. So maybe we'll be able to find something related to this, from that work.

Dr Peter Palese

Absolutely. I think it is important to really do the surveillance and the NIH is actually funding a lot of groups worldwide, not only in the US, looking at different influenza viruses in different species. Obviously the pig, the swine, is getting more attention but the surveillance covers many other avian species as well as pigs, horses, dogs, and there is quite a lot of work going on worldwide in terms of trying to understand where the reservoir of these viruses is—and where, as we discussed before, such reassortment may take place.

Vincent Racaniello

Yes, it's a good time to be going into virology for all of the post-docs and graduate students out there. There's plenty of work to do it sounds.

Dr Peter Palese

I think it's a very good time for young people there are many jobs, whether in industry, vaccine manufacturing, surveillance. Center for Disease Control has very interesting positions. The FDA is expanding. Also regional and state laboratories are very interested in these viruses, in virology, per se. So I think this is a very good time for people with this training.

Vincent Racaniello

One more thing about the pigs, I heard that in Canada this virus has been reintroduced into a pig herd and so that's a concerning issue I'm sure. It brings up the question of whether this virus would get back into pigs and somehow recombine, with say, avian H5 viruses and produce something different. Is that possible?

Dr Peter Palese

Right now, the swine virus really looks as very similar to other H1N1 viruses, clearly, having received genes or acquired genes from viruses from different species. So, in a way, the answer to your question: could this virus—the swine virus—acquire either new mutations or could it acquire a different gene or several genes from influenza virus from a different species and thereby acquire new and higher virulence, cannot be excluded. So, yes, influenza viruses always have the possibility via mutation or reassortment, that is shuffling of genes from different influenza viruses, to change their virulence. But that is not limited or is not possible not only with the current new swine virus, but it's also possible with the other H1N1, H3N2, as well as influenza B viruses to a certain extent. We should be always cautious and be aware that influenza may have some surprises in store for us, but I'm not sure that there is an increased possibility that the present swine virus would undergo those changes leading to a, let's say, killer virus.

Vincent Racaniello

Now, so far, I see there are less than two thousand lab-confirmed cases globally, I think. This virus is different from other swine viruses in that it has been able to spread from person to person. So by looking at the sequences, do we have any clue as to why that might be?

Dr Peter Palese

Okay, so clearly what is important for an influenza virus is that: one, it is transmissible from one person to the other, but the second also is that it has virulence characteristics. And in the case of the H1N1 swine virus, there is obvious evidence that the virus can be transmitted from one person to the other. However, this swine virus lacks certain virulence characteristics and virulence genes which have been shown to be present in highly virulent influenza viruses, and one major gene which confers high virulence is a gene coding for about 80 amino acids and this is referred to as PB1-F2, this is a sort of lab jargon. PB1 is the one component of the polymerase, and the F2 stands for frame 2, open reading frame 2. So there's a protein which is expressed in highly-virulent viruses that is, for example, the 1918 virus; the pandemic strain from 1957, the H2N2 Asian flu; and is also present in the 1968 Hong Kong flu which also caused a worldwide epidemic/pandemic. So in all of these pandemic influenza virus strains from the last century, they all have PB1-F2. The new swine virus is lacking this PB1-F2. So that I think is another sort of important difference to the previous pandemic viruses which caused a lot of disease and death. That this current one, even though it is transmitting very well, is lacking a virulence characteristic namely is not expressing the PB1-F2 and that I think makes this a much more mellow virus than it could be than other highly pathogenic influenza viruses were.

Vincent Racaniello

So how many mutations would it take to have these viruses make a PB1-F2?

Dr Peter Palese

It would be at least three to four point mutations.

Vincent Racaniello

Do viruses want to evolve to become more virulent, do you think? Is this something that you expect might happen for these viruses?

Dr Peter Palese

I think we can't exclude it, but there are many of the H1N1 viruses which are currently circulating in the human population. The other seasonal H1 also do not contain the PB1-F2. I believe, and I think we all believe in Darwinian selection, increased fitness, that this is sort of a biological principle. But on the other hand, it is not necessarily true that a higher virulence may be associated, for example, with better transmissibility. There may be other complex characteristics as a result of this PB1-F2 which make it difficult for the swine virus to actually continuously express such a PB1-F2.

Vincent Racaniello

Yes, it's an interesting question whether—for example, you can imagine that increased virulence would make you sneeze or cough more. In that case, it could help transmit the virus better. But if it kills you too quickly, that's not good. So there has to be some kind of a balance.

Dr Peter Palese

Correct.

Vincent Racaniello

How about NS1? Now you've shown that this is an interferon antagonist, is this NS1 look—like it has any unusual properties?

Dr Peter Palese

So far, by just looking at the sequence, we were not able to see anything staring into our eyes. But, you pointed out, that the NS1 is a virulence gene because it can overcome the interferon response of the host and thereby can counteract the defense mechanism of an infected cell. So clearly that would be another protein we should look at in terms of comparing the swine H1N1 NS1 protein or NS1 gene with other NS1 genes which we have studied in the past.

Vincent Racaniello

And there are probably other genes as well that have virulence determinants, I think. I think the P...

Dr Peter Palese

Absolutely, and for example, the hemagglutinin in the H5N1 in the famous chicken influenza virus—an influenza virus which caused a lot of disease and deaths in the poultry population—so these viruses all have a basic peptide in the hemagglutinin and the result of such a basic peptide is that the cleavage between HA1 and HA2 is rapidly occurring in these chicken viruses and this actually leads to a more effective replication in many host cells and such a virus is more virulent than one which doesn't contain this basic peptide. And, again, the swine virus does not have a basic peptide in the hemagglutinin.

Vincent Racaniello

Right. Great. Now, as you know, there are sequences of many, many isolates already available which to me is amazing. I think back to 1968 where we couldn't sequence anything and now we have sequences within a day, so there are hundreds. But looking at these, they all look very similar, and to my eye there's no reason to think that the viruses from Mexico are any different from viruses that are anywhere else in the world which brings up the question: why have there been twenty-nine deaths in Mexico and very few elsewhere? Do you have any idea about that?

Dr Peter Palese

So this was certainly disturbing to hear that so many people died of this new swine virus, but what we don't know is how many people in Mexico have been infected acutely or subclinically. So that the denominator may be large. If it's a million people, for example—I don't know if this number is correct—but then if you have hundred deaths, for example, then that number would not be so unusual as compared to regular H1N1 influenza. We have about 30,000 deaths in the United States in a regular influenza virus season caused by infection with regular H1N1, regular H3N2, and regular influenza B viruses. So the question of: Is the Mexican swine virus more virulent than other currently circulating influenza viruses? I think it's an important question, but the answer to that question has to wait until we really know how widely spread that virus was. And also, the numbers are still small that one has to find out whether they were superinfection with bacterial strains in those patients who died, and whether there was any other exacerbating situations like malnutrition, et cetera.

Vincent Racaniello

Yes, I think it's unfortunate that this happened initially because it has scared a lot of people, and if we had taken Mexico out of the equation then it would be much less panic and hype I think globally about this virus.

Dr Peter Palese

Absolutely, you are right. And there is I think somewhat of a hype going on and somewhat of a panic in looking at this virus. Certainly, I was travelling last week and went into a supermarket and there were—all the pork products were on sale. You could get pork cutlets for a third of the price, sausages, anything having swine products were on sale suggesting that people don't buy pork. There is absolutely no reason why one should not—if one eats pork—one should not continue to do so.

Vincent Racaniello

Yes, and I think there are similar issues with chicken when there were outbreaks of avian viruses in chicken farms. People tend not to want to buy chicken for a while, right?

Dr Peter Palese

Correct, that is certainly not justified.

Vincent Racaniello

One thing I heard the other day from WHO is that a spokesman said that there's an unusual amount of diarrhea and gastrointestinal symptoms associated with this influenza, and this really disturbs me because I know in humans that this is not an enteric virus, so what's that a consequence of?

Dr Peter Palese

I think these reports have to be confirmed. That they are not really only anecdotal reports but that they are real numbers in terms of how many people have been checked, whether they are really hospitalized and whether there are any samples available. There are some reports that, for example, H5N1 viruses in Vietnamese patients were isolated from feces. So these are very rare examples where virus is found outside the respiratory tract. And clearly, if that is true, if that can be confirmed, it would be something disturbing and unusual, but I think the jury is still out on that question.

Vincent Racaniello

So the avian viruses have a broader tropism, right? Because of the cleavage site.

Dr Peter Palese

Yes, and they are infecting a completely different animal, other than humans, yes.

Vincent Racaniello

But the H1N1, the H3N2 viruses don't have the ability to grow in the intestine, right?

Dr Peter Palese

They have...

Vincent Racaniello

In the human intestine.

Dr Peter Palese

In the human intestine they do not and the only recent report is associated with these very few cases of H5N1 infections in very sick patients in Vietnam.

Vincent Racaniello

Right. So in kids who get diarrhea, it may be a bacterial infection or perhaps even a cytokine that causes the diarrhea but not viral replication, right?

Dr Peter Palese

Absolutely, yes. There is no evidence that regular influenza viruses can be isolated either from serum, from blood, or from feces, and there is no evidence that they replicate in the gastrointestinal tract.

Vincent Racaniello

Now I notice that these H1N1 swine viruses—the 2009 variety—are resistant to amantadines which was interesting to me. Is that because the amantadines are used in pigs or is there another reason?

Dr Peter Palese

The M gene is derived from swine viruses, from influenza viruses in swine, so that could be one of the explanations. There are, however, other human influenza viruses which carry a human M gene, namely the H3N2 viruses, and they are also—most of them in the 2009 series—were also amantadine-resistant. And there's no evidence that the H3N2 viruses, the regular ones, had any pig connection, and even in those viruses, we found that the majority of them is amantadine-resistant.

Vincent Racaniello

Is the drug used in pig farms, do you know?

Dr Peter Palese

Not in the US, but there are rumors that in Asia, amantadine, because it is so cheap, is widely used in agriculture including chicken farms as well as pig farms.

Vincent Racaniello

I saw some papers from quite some time ago where they surveyed pig influenza isolates, I think from the '70s or '80s, and they randomly found amantadine resistance, and they suggested that it may be a random event; that, if by chance, you have the right mutation in the M2 and that does it.

Dr Peter Palese

I think that cannot be excluded.

Vincent Racaniello

Yes. Now, the neuraminidase inhibitors will inhibit this new virus, correct?

Dr Peter Palese

It's correct. The new swine viruses, in contrast to the regular H1N1 viruses of the seasonal influenza, the swine viruses are sensitive to the neuraminidase inhibitor, Tamiflu.

Vincent Racaniello

And so that is going to be used in certain situations I presume to ameliorate infections?

Dr Peter Palese

Absolutely, yes.

Vincent Racaniello

Do you think that will lead to rapid resistance or is that something that will take longer?

Dr Peter Palese

I think the reason the H1N1 viruses carry Tamiflu resistance right now has nothing to do with the usage of this drug. It has to do with a mutation which got fixed because the hemagglutinin also changed. So there was a balancing between the hemagglutinin change and the neuraminidase so that this was really not induced by the use of medication. In the case of the swine H1N1 viruses, the future will tell whether a neuraminidase resistant to Tamiflu, whether that is a viable virus one or a virus which has a lesser fitness. So this is not clear yet. And I think that will be important to find out experimentally also and it may very well be that Tamiflu resistance with the new swine virus results in a lower transmissibility and a lesser fitness of the virus.

Vincent Racaniello

Yes, in fact you have shown in your guinea pigs that the human H1N1s, that are resistant to Tamiflu, don't transmit very well, right?

Dr Peter Palese

So we actually demonstrated this with H3N2 viruses and that really led to a major loss in fitness of the virus which had gained resistance to a drug but it also lost a lot of its "pizzazz", so to speak.

Vincent Racaniello

So that could be a silver lining in the resistance then?

Dr Peter Palese

Correct. So, in a way, yes, it takes away the advantages we have using an antiviral but, on the other hand, if the virus becomes so attenuated, so weakened, that it's actually not a real danger anymore in terms of causing a lot of disease.

Vincent Racaniello

The last thing I want to talk to you about is vaccine. I understand that a vaccine is already being produced against this new H1N1 virus. Now from my old days in influenza, I remember that to produce vaccines in eggs you have to make a high-yielding recombinant. Is that still done? Is that going to be done with this virus?

Dr Peter Palese

There are efforts underway to make influenza virus vaccines which are based upon the new swine H1 and N1 surface glycoproteins and the manufacturing—depending whether it's a killed influenza virus vaccine or a live influenza virus vaccine—involves making either high-yielding reassortant viruses and that can be done in several ways by making reassortants in the laboratory. In terms of the live influenza viruses vaccines, these new swine hemagglutinin and swine neuraminidase genes have to be grafted on to a cold-adapted backbone and vaccines are being made as we speak in companies which are geared

up to make either killed influenza virus vaccines or live influenza virus vaccines. It's important that we are prepared. Whether these vaccines will ever be used in the future is still a question. It might very well be that the swine virus in the Northern hemisphere sort of just declines so that we won't have many more cases next week or two weeks from now, and that also no new cases occur and emerge in the Southern hemisphere. And so it could very well be that the swine influenza virus is dying out both in the Northern hemisphere and in the Southern hemisphere, and then any kind of vaccine which has been produced would probably not be administered to the population. I think stockpiling and watchful waiting I think is a better strategy in this case rather than vaccinating a portion of the population just in case such a virus might take.

Vincent Racaniello

So if this virus declines in the Northern hemisphere which we would expect because it's the end of the flu season, and then takes off in the Southern hemisphere, that would be evidence to use the vaccine in the Northern Hemisphere back in the fall again, right?

Dr Peter Palese

Absolutely. I think this would be the sign and the signal which will persuade us to really get a fourth vaccine strain for the upcoming season.

Vincent Racaniello

So you think the existing strain, the trivalent vaccine which is now being prepared for use here in the fall that would also be used in conjunction with new one?

Dr Peter Palese

I think, I mean, predictions are always difficult to make, especially about the future, there is no reason to believe that these regular three influenza viruses—regular H1N1, H3N2, and B—would die out suddenly in the next season, and so those three I think are given, more or less, for the upcoming 2009/2010 influenza season. The question is really whether a monovalent fourth influenza virus vaccine should be given which is made against the swine H1N1 virus.

Vincent Racaniello

So isn't it true that when you have a new pandemic strain, that it replaces the previous circulating one?

Dr Peter Palese

This happened in 1957 when an H2N2 strain replaced the H1N1; however, we have two different subtypes circulating since 1977. So I think it's, again, very difficult to predict whether we will enter an era of four different influenza virus strains or whether the swine virus will replace either the H1N1 or H3N2 as well. So I think it's an interesting question, and we really have to wait what the winter season in the Southern hemisphere shows whether there will be four strains circulating or whether three or only one or two. I think all of the above is possible. But I think the more likely event is that we'll have the three regular ones and I think there's a fifty-fifty chance that this swine virus may actually persist.

Vincent Racaniello

That would be unprecedented from my meager knowledge of influenza, it's very unusual. There are many possible reasons and, you know, the farming business is possibly part of it. But could it also be that our surveillance is so much better than it was in 1968 that we can pick up other strains circulating that we would not have before?

Dr Peter Palese

At this point, you're absolutely right. I think it's not clear whether 20 or 30 years ago one would have even realized an event such as the swine virus. However, the swine virus may really become more prevalent than it is right now, and then I think surveillance was not that bad 30 or 40 years ago.

Vincent Racaniello

Yes.

Dr Peter Palese

So if one would really have, let's say like ten or twenty percent of all the influenza virus strains would be the swine virus, I think one would have seen that also several decades ago. But at this point, I'm not sure that we would have picked that up with methodologies which were available several decades ago.

Vincent Racaniello

So it sounds to me like that you're not convinced that this is the next pandemic strain, is that right?

Dr Peter Palese

Yes, I think this is still an open question. I think it's really a fifty-fifty chance that the swine virus will actually die out and not become a prevalent strain in the next season.

Vincent Racaniello

And we'll know that in the next few months I suppose in the Southern hemisphere?

Dr Peter Palese

I think we probably—I think the first sort of event to watch is what happens in the next week, a week or two, in our Northern hemisphere, and then certainly what will happen in a month or two in the Southern hemisphere. And that I think will more or less define the probability whether that virus will be prevalent in the winter time in 2009/2010.

Vincent Racaniello

I think this is a very exciting time to be in virology. Here we can watch a new virus, whether it spreads or not, and we have great scientific tools to study it. And I think more people need to go into virology because you can see all the exciting things that we have to do.

Dr Peter Palese

Absolutely, this is really a very important time and that we have tools available that allow us, one, to watch this carefully but also to intervene with the outbreak of the new pandemic strain.

Vincent Racaniello

So, I know you're all wrapped up with all the media and the hype here, but scientifically you must find this very exciting, right?

Dr Peter Palese

It is very, very interesting and full of surprises, yes.

Vincent Racaniello

And I can't wait for the journal articles to start coming out.

Dr Peter Palese

Yes, there's a lot going on.

Vincent Racaniello

Peter, thanks so much for talking with me. I've heard your phone ringing. I know a lot of people want to talk to you so I appreciate the time.

Dr Peter Palese

Thank you very much, Dr. Racaniello.

Vincent Racaniello

Dr. Palese, bye!

Dr Peter Palese

Bye-bye.

Another TWiV is viral.

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