Giving Shingles Immunization Your Best Shot: Implementing A Shingles Vaccination Protocol In Your Practice

CMEO Podcast Transcript

William Schaffner:

Hello, everyone. I'm Dr. Bill Schaffner. On behalf of CME Outfitters, I'd like to welcome and thank you for joining us for today's educational activity, which is titled, Giving Shingles Immunization Your Best Shot: Implementing A Shingles Vaccination Protocol In Your Practice. Today's activity is brought to you by CME Outfitters, an accredited provider of continuing education for clinicians worldwide. Today's CME CE activity is also eligible for ABIM MOC points. So make sure you engage in today's event, answering poll questions, and provide your feedback. Once you complete today's program, be sure to provide your ABIM ID and birthdate in the evaluation. CME Outfitters will submit your MOC points.

As I mentioned, I'm Dr. Bill Schaffner, I'm Professor of Preventive Medicine, and Professor of Infectious Diseases at the Vanderbilt University School of Medicine in Nashville, Tennessee. Let me introduce our faculty. Joining me today is my colleague, Dr. Anthony Cunningham. Tony is Director of the Westmead Institute for Virus Research, and Professor of Medicine and Health at the University of Sydney Medical School. Tony is also the Director of the Australian Center for HIV and Hepatitis Virology Research, and the New South Wales Australian Capital Territory state branch Chair of the Australian Academy of health and medical sciences in Westmead, New South Wales Australia. Welcome Tony. And thanks for joining us from Australia.

Anthony Cunningham:

Thank you Bill.

William Schaffner:

I would like to introduce also my colleague, Dr. Iris Gorfinkel. Iris is founder and principal investigator at Prime Health Clinical Research in Toronto, Ontario, Canada. Welcome Iris.

Iris Gorfinkel:

Thank you so much.

William Schaffner:

And thanks for joining in from Canada. Yes, good to have you. So let's review our learning objectives. Our first learning objective is to identify the primary risk factors and the clinical and quality of life complications imposed by shingles. Our second learning objective is to more frequently and effectively educate eligible patients about shingles and shingles vaccination, and to improve their uptake of vaccination, and series completion for shingles vaccine. Our final learning objective is to apply real world strategies to implement shingles immunization that consider safety and efficacy of available therapies, storage, and administration, and pharmacy-based vaccination.

So let's start. I'd like to get you, our audience somewhat involved here. The question is, which of the following is accurate regarding the risk of shingles? So, Tony, let's start with you. What are some of the key risk factors for herpes zoster, of which clinicians should be aware of please?

Anthony Cunningham:

Bill, the most important risk factor for herpes zoster is increasing age. And there's been a lot of discussion about whether this might be less opportunity for boosting, particularly since we've had the chickenpox vaccine in Australia, Canada, and the USA, and less frequent exposure to kids with varicella. But clearly the most important factor here is so-called immunosenescence or declining immunity with age. Of course, we now know that important other factors are involved in risk for herpes zoster, particularly those of us who practice in hospitals, cell-mediated immunosuppressive disorders, hematologic malignancies, immunosuppressive drugs, HIV before anti-retrovirals, about 12 to 17 fold, still about six fold with anti-retrovirals.

Interestingly, there's a greater risk in women men. And surprisingly, risk in African Americans is less than half that of whites. Trauma or surgery in the infected dermatome is of course well known to most of us. And a really interesting factor is that if you get early chicken pox, particularly in utero or early infancy, you'll get sometimes early zoster, and the youngest I've seen is seven. But the literature documents three years old for a case of herpes zoster. Thanks Bill.

William Schaffner:

Very good.

Iris Gorfinkel:

Tony, thank you so much for pointing that out. What's so surprising about that, I want to point out to the audience, is that African American risk is less than half of that of whites. That is a notable exception to the regular social determinants we see of health where generally African Americans suffer way more. Here, it's less than half of whites.

William Schaffner:

Good point. Glad you emphasized that Iris, and we all agree that herpes is more than just a rash. So let's have a look at an animation. Shingles is more than a rash. The impact of shingles can be extensive and include the cerebral vascular system. For example, some research has indicated an increased risk of stroke in individuals who have shingles, with the highest risk within the first month after shingles onset. Shingles can also have a neurologic impact, it can result in meningitis, and or encephalitis, as well as paresis of the extra-ocular muscles. In addition, individuals with shingles can also develop peripheral neuropathies, causing paresis of the gut, as well as paresis of the diaphragm and of the bladder.

The pervasive nature of shingles may also result in damage to the ophthalmic system, such as ocular lesions of the ophthalmic division of the trigeminal nerve, as well as conditions such as glaucoma, tosis, corneal ulcerations, conjunctivitis, and lid retraction. Though shingles is often associated with a rash, it can also lead to secondary skin infections. The gastroneurologic system can also be impacted by shingles. The result can vary from abdominal pain to constipation. Shingles has also been associated with major gastroenterologic conditions, such as inflammatory bowel disease. Overall, the key message is that shingles can be extremely debilitating, and vaccination is critical to reduce the disease burden.

But now talking about the incidence of herpes zoster. And you can see here as I mentioned before, the marked difference if we look going upwards from gray to brown, the marked difference in the incidence of herpes zoster with age, marked at increasing. In fact, almost a three to four fold increase, to 15 per thousand cases on admission, which is really pretty high.

William Schaffner:

And you can see this remarkable increase in the incidence of herpes zoster over time. This has been documented in all high income countries. People at first thought this might relate to chickenpox vaccination and the absence of boosting. That's not the case. It's probably got something to do with the aging of our population, but its still got many of the epidemiologists stumped. Of course, this is now declining with shingles immunization and we'll talk more about that later.

Iris Gorfinkel:

This is an absolutely fascinating slide. I want to point out that this data was collected out of Kaiser Permanente. So what you're seeing is, in fact, a bit of a selection bias. You can see it's biased toward the younger patient population. And what we would normally expect is to see the curve increasing with every passing decade, the incidence of herpes zoster goes up with age. And in fact, our most risk patients are those who are the most immunosenescent, those who are over 60, aggressively over 70, 80, et cetera. What we see here on this slide is a selection of younger patients, because it is a selection of patients from Kaiser Permanente.

So here we can see, I think the main take home message of this slide is one thing, look how common it is in younger individuals. In fact, that does carry a very significant burden of disease, the patient who's over 50 and you can see how it actually peaks and then it goes down a tiny bit. It's a relatively small population, that of the Californians. But the take home message is, it is not just a disease of the elders and super elders. It is a disease that can in fact, infect younger patients. And I think most clinicians have seen it even patients in their 40s.

If we go to the next slide, what's fascinating about this, is this is looking at the cumulative incidence of herpes zoster in an immunocompetent unvaccinated population. Now this is recurrence. So in other words, they've had it once and what happens, can they get it again? So the common thinking is no, people don't get it again. But if you take a look at this graph, in fact, we can see that individuals do get it again. And the likelihood of getting it again depends on how far away they were from the actual infection. This adjusts the actual infection does give some immunity. But it is not long lasting immunity, they can in fact get a second episode.

William Schaffner:

I think we're going to questions now for the audience. Which of the following do you think is accurate regarding the risk of shingles? You're on.

Iris Gorfinkel:

What I find absolutely fascinating about this is, I'm going to focus on answer number C for just a second. There is about a twofold increased risk. It is absolutely striking. The increased risk is not just twofold. Tony, what did you say about the increased risk of HIV individuals?

Anthony Cunningham:

Well, as I said before anti retrovirals, it was as high as 12 to 17 fold. It's dropped with anti retrovirals, but the risk is still there. And we'll talk a little bit more about the role of shingles vaccination later on in patients who have HIV, and obviously an important group. But Iris, clicking back to you, the audience has rightfully discerned that answer number four is the dominant one. And this is what we said before, the surprising risk that whites actually suffer more zoster than African Americans.

Iris Gorfinkel:

It's such a notable exception, because again, not to overly emphasize the effect the disease has on American blacks, but it is absolutely incredible. We see that across the board. It's highly exceptional in disease. And in fact, we know that the burden of COVID-19 deaths was largely fallen on blacks. It's very exceptional. Tony, would you have any idea what why that might be?

Anthony Cunningham:

I think it may relate to... Of course, shingles is a recurrent disease. And it may relate to the prevalence of chickenpox, declining immunity, et cetera. But the answer is, I don't know. I really don't know. Something that needs to be looked at in more detail.

William Schaffner:

Tony, let's shift gears. Why not talk about the clinical manifestations of classical herpes zoster?

Anthony Cunningham:

Right. Thank you. Indeed, Bill. Well, the prodromal phase of acute pain and remembering that the pain of herpes zoster can be worse than that of childbirth, and developing dermatomal pain in the thoracic region or in the abdomen can be mistaken for cardiac disease or for an acute abdomen. So, watch out, for the prodromal doesn't occur in every person. And I'll come back to that in terms of risk for postherpetic neuralgia later on.

The acute phase, which lasts about four weeks, three to four weeks, but can be very mild, is characterized by pain, which can be neuritic, lancinating, or burning, and is characterized by a dermatomal rash anywhere in the body. So, abdominal, thoracic, in the head, in the leg, but characteristically dermatomal. And it goes through a phase like chicken pox of papules, vesicles, and crusting, and often evolves from front to back. So if you have thoracic zoster, you'll see crusting on the back, and on the front you'll see vesicles. But very clearly have a vesicular rash. That's the characteristic. Complications, most commonly skin, and postherpetic neuralgia. The most feared is postherpetic neuralgia, and the eye complications of zoster, Bill.

William Schaffner:

So Iris, let's go back again to that sample of Southern California patients. What did they discover about herpes zoster that you would particularly would like to emphasize and found striking?

Iris Gorfinkel:

I was surprised that it's a cause of death, and a cause of hospitalization. These things occur, but they are rare. The take home message of this slide is cutaneous complications rule. That's what people are experiencing. There are hospitalizations. And another thing this slide demonstrates quite nicely is that we see the biggest burden of disease in the most immunosenescent of patients. So as patients get older, and you can see that in orange, see how high those bars are. That tells you that immunosenescence is in fact playing a very significant role. And the postherpetic neuralgia of pain should not be underestimated. It is a very major problem in individuals lives.

William Schaffner:

And so, Tony, what would you like to add to that regarding herpes zoster associated pain, and actually the risk factors for postherpetic neuralgia?

Anthony Cunningham:

Yes. So the risk factors for postherpetic neuralgia are in particular age, Bill. But let's talk about the pain first. And that is that it can be quite deceptive, it can persist. And this is pain beyond 90 days, as you can see in the last point after rash onset is defined now as postherpetic neuralgia. That's shifted around over the years, but this is a very clear definition. Of course, you can have pain also between the cessation of the rash which is about 30 days, up to 90 days, that's sub-acute pain. But post herpetic neuralgia is defined as that over 90 days, and it can disappear and come back. It can change its character. Neuritic pain, which represents the nerve component, and also it can be burning, and assume other characteristics as well.

The cause of it is not clearly defined, but we do know stuff that we published is that the virus causes inflammation and necrosis in the dorsal root ganglion near the spine. But it affects the whole of the nerve that goes back into the nerve root. And this results in scarring, it results in aberrant nerve conduction, and this can result in really quite severe pain which may be complicated by light touch causing pain itself. And the risk factors for it are age, particularly increasing age. So you rarely see postherpetic neuralgia under the age of 55. There's little inflection over the age of 55. But then it goes up very, very quickly. And in fact, in people over the age of 80, that 25% of people will have postherpetic neuralgia, very age-related. Women more. We used to think it didn't occur in immunosuppression, but it does. And it's exactly the same as occurs in immunosuppression, or immunosenescence with advancing age. And of course, that also relates to an amalgam immunosupressive conditions such as autoimmune diseases, and asthma.

What predicts the occurrence of postherpetic neuralgia? The presence of a prodrome is highly predictive, and severe acute pain. So if you see someone with a prodrome and severe acute pain, watch out for postherpetic neuralgia, particularly if they're over the age of 70. In our shingles vaccine trials, almost all the cases of PHN were seen over the age of 70. But you can get it from 60 upwards.

Iris Gorfinkel:

Tony, I think that is such a big pearl. The presence of prodromal pain predicts postherpetic neuralgia. Can we concentrate on that for just a moment? And I have a question for you as a family doctor, actually, which is, if a patient has horrible pain, should we be giving them a dose of corticosteroids? Is that been shown to be helpful?

Anthony Cunningham:

Well, that's a very interesting question. Corticosteroids has been shown many years ago to assist acute pain along with all of the other pain relief, and we go through in terms of... I don't want to turn this into a pain lecture, but there's a clear hierarchy of pain relief that one goes through right through to the need for opioids. As I said before, this can be incredibly severe. Steroids can be useful for acute pain. They're not useful for PHN. Don't use them. They're clearly shown by controlled trials not to be useful for PHN.

Iris Gorfinkel:

Thank you.

William Schaffner:

So Iris, you know, there's an aspect of herpes that goes beyond pathophysiology. It's one of the things that you emphasize all the time, and I think is often overlooked. So talk a little bit about the quality of life that's impacted by shingles.

Iris Gorfinkel:

I think when approaching patients who have those, there's really one way to approach it, which is optimized. And that is the biopsychosocial model. And I think for any doctor who tries to overlook one of those aspects, we're not doing our patients the best service. So it's not just a physical pain that needs to be addressed. We know that chronic pain holds hands with severe psychological problems potentially.

Of course, it interferes with their sleep, and therefore can cause difficulty in concentration, depression, and potential anxiety. The social aspects should not be overlooked also. If someone is having a lot of pain, that can impact on their socialization, on their willingness to go out, on their willingness to see other people, which in turn can... One just feeds right into the next. That can aggravate their depression. That can actually interfere with their sleep. Just the social losses can.

So I want to point out in this slide, the functional psychological and social losses, actually one thing feeds right into the next. They should not be viewed as separate problems, but as one problem altogether. And just a simple question. Hi, how are you doing? And then for the patient who focuses solely on the pain, asking them specifically about these other areas, is hugely helpful in optimizing the care provided to these patients.

William Schaffner:

Actually, if that were not enough, in addition to the quality of life impact, is an economic impact. Say a few words about that.

Iris Gorfinkel:

Thank you, Bill. If we take a look at the economic impact on this slide, this slide has three different categories. And what you'll see to the far right is the patient who's impacted by postherpetic neuralgia. And this is often the patient who can afford it the least, the older patient. Look at the economic burden. In all categories, it's in the many thousands of dollars. But it's especially acute in the patient who has postherpetic neuralgia. Not surprising, the least economic burden happens in those individuals who have zoster but have no postherpetic neuralgia.

And then here we can see the overall impact of shingles in patients. So the take home message from this is not to memorize how many thousands of dollars it is, but it is a very significant economic burden, both to the patient and to the healthcare system.

William Schaffner:

We've all decided that herpes is not a good thing. So let's change the focus now, on to the rationale for a shingles or a herpes zoster vaccine. Tony, you and Iris have brought up some good points on the impact of the disease itself. So now tell us about the data that support the need for a vaccine.

Anthony Cunningham:

Bill, one of the things that happens to us as we get older, together I think you and me, not Iris, is a decline in T cell immunity and B cells called immunosenescence. And this is a fascinating condition which is not well documented. But it actually involves shrinkage of our lymph nodes and some degree of scarring. And in those lymph nodes, the interaction between the immune cells is important. And so this gives rise to impairment of the function of all branches of the immune system. An eight B cell T cell.

Anthony Cunningham:

But, anybody stays up because we're just little antibody factories, T cells drop off to the chickenpox virus, and so cleverly Mike Oxman and Myron Levine decided to run a trial to boost this T cell immunity, and reported it in 2005 with some preliminary data beforehand showing that they could reboost with a live attenuated concentrated chickenpox vaccine, T cell immunity. And I remember sitting on Mike Oxman's couch, as he described this to me, and thinking, "You'll never get this up." He did. He did the trial in 30000 people and showed the principle, which was wonderful.

Iris Gorfinkel:

This is incredible looking at the slide. And the impact on T cell immunity is profound as we get older, and you can't help but wonder on this day of COVID-19 is the same impact that, is that why we're seeing this chronic patients, and patients over the age of 60, carrying the burden of disease. Here in Canada, the deaths took place almost solely in long term care institutions in which patients do suffer from many chronic diseases.

Anthony Cunningham:

I was going to say it's the same in Australia, and I agree with you entirely. And I think we're using the example of the shingles vaccine to produce a vaccine that's aimed directly at the aging. And that must be involved not only antibodies, but also at T cells.

William Schaffner:

Sure. So now we're going to involve the audience again, I have a couple of questions for them. Let me read the first one. To the audience, how confident are you in implementing shingles immunization programs, protocols that consider safety, efficacy, administration, and storage? All right, thank you. So here's the second question. And Tony, why don't you chat about the results.

Anthony Cunningham:

So we can see here, people have said, the majority say that 81% say there's only one FDA approved vaccine for shingles, 6% said two, and they are correct. In Australia, it would be the people who said one would be correct. But because we don't yet have the recombinant zoster vaccine, but the correct answer is two. And Bill, we'll talk about that in just a moment. But perhaps the reason for this is going to become apparent on the next slide, Bill.

William Schaffner:

Yes, exactly. Exactly. And that's because the CDC's Advisory Committee on Immunization Practices, made some recommendations recently. And the first is they absolutely recommended for immuno-competent adults age 50 and older, immuno-competent, they should all be vaccinated against zoster. Number two, they said, if you've been vaccinated previously with the live virus, you should now be vaccinated again with the recombinant vaccine. Indeed, they made a preferential recommendation, very unusual for the ACIP. They actually made a preferential recommendation for recombinant vaccine.

So, Tony, we know now that in the United States zoster vaccine live, ZVL, is no longer being manufactured as of July 1st this year. Some pharmacies and clinics likely will still have it in stock for a period of time. But you were part of some of the pivotal vaccine clinical trials. So what do we know about the relative effectiveness of RZV, the recombinant vaccine, particularly in comparison to the live attenuated vaccine, ZVL?

Anthony Cunningham:

Yes, and people should know that, you're fortunate. Again, this relates to COVID vaccines and the rollout of the recombinant RZV has been reasonably slow because of bottlenecks with the immunostimulant or adjuvant in it, and so it's available in North America, and in Europe, and soon will be in Japan and China. But Australia is still waiting. So, North America is in a fortunate position of having this new vaccine. The reason for this is well shown on this slide, that if you look at the first column that shows the efficacy against shingles, firstly, the first three rows that it declines from 70 to 38% in the 10-year age cohorts from 50, 60, and 70, whereas the RZV, I'm using Z not Zed, Bill. And I'm learning. It's my old American roots back at Stanford.

So RZV is in fact 97% effective. Now in subsequent trials that appeared to drop, but in fact, the confidence intervals were the same. So let's just say it's more than 90% effective. And it's more than 90% effective in those over 70 and those over 80, which is remarkable. And that's because of the immunostimulant or adjuvant in the vaccine. Now with the live attenuated vaccine, interestingly, there was not the same drop in the efficacy against postherpetic neuralgia. So it actually had an additional benefit in attenuating the disease and people had breakthrough on the vaccine. And that's true for PHN as well. With RZV, it was so effective that you couldn't detect any such effect. So its effect on PHN was due to its effect on zoster, but still much greater than ZVL. And that's why the ACIP made the decision they did.

Iris Gorfinkel:

Tony, I just would like to interject one very small thing just for our audience. It's my family physician brain in action. So I just want to point out that RZV is also called Shingrix, that is the trade name. We are referring to it by RZV. But that is known as Shingrix, and ZVL refers to the older vaccination Zostavax. I just want to clarify that for the audience.

William Schaffner:

Yeah. So while you're up, as it were, Iris, say a little bit about how impressive that efficacy is in people older than 50, and indeed older than 70. That's spectacular. We're talking about immunosenescence in old people. But this vaccine with its adjuvant has overcome that problem.

Iris Gorfinkel:

I have to share with you. I still remember because we were also part of that very exciting trial. And when we heard the efficacy, it was unbelievably exciting. It is highly unusual to see a vaccination which is this effective, and also against a disease which is a common disease. Here we see a vaccination, the RZV, which is taking what is now a common disease, and turning it into a rare event. Extremely exciting. This means saving a tremendous number of people, a tremendous problem.

Anthony Cunningham:

I think, Bill, the other key issue here is, as we discussed with COVID and influenza, the principle of just a single protein, as opposed to all of the proteins which the live attenuated virus has got, and the immunostimulant. The immunostimulant, is it. If you actually look at the phase two trials, if you did not have the immunostimulant there, the efficacy drops below 20%. So it's really created a revolution in thinking about vaccines for the aging, and now we have flu vaccines that differ for those over 65 and under. And I suspect that might happen with other diseases, and may even happen with COVID in the future.

Iris Gorfinkel:

It's absolutely fascinating because you look at... It just goes to show you predicting the mechanism of how a vaccine will work is not what we need to be doing. This vaccination trial, it is probably the best representation of a vaccination trial that we have. There are many, many different areas in which is what basically one in the same. It affects the same age group. We see an increasing amount of disease burden with COVID as we do with shingles with increasing age. This trial, the two trials, ZOE 50, and ZOE 70, which was cited as one of the top trials of the year, arguably the decade. What we found from this trial is that it did provide almost 97% efficacy across the board, extremely exciting, but it also took 30,000 participants over many different countries.

Let's not underemphasize the tremendous effort that this represented. This trial took four years to complete. And moreover, it's going on for an additional six years to better understand the duration of the immunity.

William Schaffner:

Well, I'll go back to the Advisory Committee on Immunization Practices recommendation. Everyone who's immuno-competent, who's 50 years of age or older, they say, should be vaccinated with this vaccine. So back to Tony, patients, and even some providers are concerned about the risk of developing herpes zoster after vaccination despite the vaccine. What's the risk in people who are 70 and older, that high risk group?

Anthony Cunningham:

So this simply shows what Iris was talking about before, Bill, and I'll address your question as we go through. One of the really encouraging things here. And we have mentioned this is, that the efficacy was the same when we looked at prevention of herpes zoster in years one, two, three, and four after the immunization and the immune stimulation or immunogenicity of the vaccine last out to nine years. So, we are involved in following this up over a period of 10 years, in view of the fact that the live attenuated vaccine tails off and loses efficacy at about eight years. And it's something we haven't mentioned. But that's another point for recommending this vaccine over the live attenuated vaccine.

Notice in this slide where the vaccine recipients are in green, and the placebo are in gray, that they're still diverging at four years. And that is an indication of just the ongoing efficacy of the vaccine itself. So, duration is very important. And the chances of breakthrough, of course, are only in that five to 10% of people who don't respond to the vaccine itself. We'd like to know why. We do know that there are genetic factors involved in people who don't respond to vaccines. And this is something that we will need to study in more detail in the future. Probably related to T cell responses, some people simply don't get a good T cell response. So ongoing research, we'll get up to 100% eventually.

William Schaffner:

Oh, I hope that's right. So, we like that graph. But here's another one that looks very much like it, and it has to do with the risk of actually postherpetic neuralgia after receiving recombinant vaccine. Speak to that.

Anthony Cunningham:

Well, you can see the same. Green for the vaccine and gray for placebo. And again, they're continuing to diverge at four years. So the prevention is not slowing down. There is no loss of prevention at year four, and we predict from the immunogenicity that the vaccine, we hope, will last for more than 10 years, and perhaps 15. So, obviously, that needs to be checked. Again, it's a lesson for COVID. Be careful, if you have a vaccine trial only running for a year. You're going to need to follow up on that.

William Schaffner:

You bet. So we've looked at one side of the coin. Very, very important. Effectiveness. How efficacious is this vaccine. Iris, talk a little bit about the safety, because that's also important.

Iris Gorfinkel:

It actually is very important. And especially for those patients who may be vaccine hesitant, which that compromises, apparently some 30 to 40% of individuals. Even without that, patients deserve to have really good information. And looking at those, it's not unexpected, they're going to have redness and soreness at the injection site. I think people generally expect that with an intramuscular vaccination, that will lead to some soreness. And you can take a look. I mean, it's 70% you're surprised why it wouldn't be 100%. Stick a needle in somebody's arm and their adulthood, it's going to be painful. But it's actually very short lived pain.

The key here, I think, to stress is that there are systemic manifestations from getting this vaccination. And it's largely coming from the adjuvant component, the muscle aches, the headaches, and the fatigue. That's important to tell individuals so that they don't get worried. And also they may want to time their vaccination, especially those individuals who are 50 to say 70, they may still be working, that is very practical information for them to have. What are the generalized symptoms, and of course the localized symptoms?

One of the common questions I get is, "Can I then workout?" And the answer is yes, you can. Should they take Tylenol before getting the vaccination, is another question that I get. Bill, did you want to say something about that? I see a big smile coming across your face.

William Schaffner:

No. I knew it was coming. Go ahead. I'm thinking these are all the questions that the family doctor gets.

Iris Gorfinkel:

This is a common question that I get. And generally speaking, my advice is against taking Tylenol. But you have to understand, I have a bit of a minimalist philosophy, trying keep medications down if I can, especially in my older patients, just so that we can see what their reaction is. Understand that if somebody does take Tylenol, it will only give them four to six hours of analgesia anyway. So it's kind of nice to know what is their reaction to the vaccine. And just to refer back to the old slide that we've seen, as patients get older, they have less of a reaction. It's the very immuno-competent patient, the patient who's 50 to say 60, 70, those patients who aren't well into immunosenescence, they are more likely to react to the vaccine.

I don't think we have a slide demonstrating age, but that is what was noted. And if we move on to the next slide-

Anthony Cunningham:

Before you go Iris, I think you were going to say it in the next slide, but it is worthwhile emphasizing this paper that we published, that if you have severe local pain that impairs daily activities, that there's only about a one third chance of this recurring in the second dose. And there is no increased severity at all in people who get the second dose, which I think is important. In the trials, 96% of people came back for the second dose, which is another important issue.

Iris Gorfinkel:

I think that's absolutely critical.

William Schaffner:

While we've got you on the podium, Tony, we know that many of our patients have medical comorbidities. We've been talking about that, you have before. Do these comorbidities impact the safety or effectiveness of the vaccine?

Anthony Cunningham:

Just let, Bill... Iris, did you want to say anything about quality of life and duration of reactogenicity before I go on to that?

Iris Gorfinkel:

Thank you, Tony. It's just a very small point. But I figured it was important to understand that when patients do experience systemic symptoms, that those systemic symptoms are in fact short lived. They're not going to last a long time. We're talking two or three days. But again, when it comes to counseling patients around RZV, it is important to tell them to expect those, those can happen. But when we compare it to the risks of having shingles, it is a very small price to pay.

Anthony Cunningham:

Okay. Now Bill, to answer your question, there are conditions that both have an increased risk of herpes zoster, immunosuppressive conditions, mainly because of the drugs that they're taking. But there is some intrinsic susceptibility as well. And you can imagine that these are diseases that disturb the immune system, and also those that may have local effects on herpes zoster. The question is, in these sort of mild cases, are we going to see any diminished effect of the RZV, the recombinant zoster vaccine? And the answer is no. And in 80% of the people that we saw over the age of 70, and Iris would certainly know this, they had multiple comorbidities, and that is predictive of frailty. And we've now actually looked at the efficacy and the reactogenicity of a vaccine in people specifically with frailty.

And there is no diminished effect, which is really important because zoster can tip people over the edge, tip them into aged care. And this is on the brink of frailty, boom, over they go and into aged care, and I've certainly seen quite a lot of that. So the vaccine will prevent that.

Iris Gorfinkel:

Tony, I so appreciate you're making that point, because I think a lot of family doctors, especially those with minimalist perspective such as my own, might be inclined to think, "Oh, this patient is frail, this patient has an immunosuppressive condition or an autoimmune condition like rheumatoid or lupus. And should I really vaccinate that patient with RZV?" These are precisely the patients we want vaccinated. These are precisely the patients who are at highest risk.

William Schaffner:

So, let me move on to where patients can get vaccinated. Obviously, we've been speaking about vaccinating patients in physicians' offices. But I'd like to get in a plug for our colleagues, the pharmacists because they can help us distribute this vaccine to many, many people. In fact, early on when there was a bit of a shortage and a great demand for this vaccine, our health care system had run out, and my internist directed me to a pharmacist. And that's where I got my shingles vaccine. And they sent me a notice saying, "It's time, Bill, for your second dose." I showed up. They'd saved that dose for me in a time of scarcity. And I was very happy to get it. So it's a combined activity. Pharmacists are very, very willing, and able to provide this vaccine.

And as we may get into a little bit later, there're quirks of funding of vaccines, such that for people aged 65 and older, it's actually easier for them to get the vaccine in the pharmacist. It's more difficult than a doctor's office. And our physicians at Vanderbilt send many of their patients to pharmacies in order to get their shingles vaccine, but they insist that their patients get the vaccine. So that works pretty well.

Iris Gorfinkel:

I love that concept of using the pharmacists to help. And I think it's actually underutilized. I think we have to look at ourselves as a team along with the pharmacists to ensure that patients are receiving their doses, especially the second one.

William Schaffner:

We're all part of the immunization neighborhood, as we say. Now, this is a very effective vaccine. But you can drive a tree into a car, a car into a tree. So some errors can occur. And it would be well to let folks know about them so they're aware of them, and can avoid them. So Iris, do you want to start and talk about some errors, and then Tony can chime in?

Iris Gorfinkel:

Thank you, Bill. By far and away, the most common error that I see is missing that second dose. Personally, what I try to do is try to, as soon as I'm giving that first dose, I make the appointment for the second dose, and I aim for the two-month mark. In the ZOE-50 and 70 trials, that's precisely what we did. It was given at the two-month mark. However, later data clearly demonstrated that the patient can get it even a year later. The problem is, people forget, doctors forget, we don't have mechanisms in place to necessarily remind patients. That's definitely an advantage of getting it in the pharmacy, that it's if you put that order in, put a refill on the prescription, this is just basic stuff, the patient will get an automatic recall.

Iris Gorfinkel:

Otherwise, we have to ensure to set up systems in our office that have automatic recalls for patients to ensure that they do in fact get that second dose on time. What's surprising is that the data shows that people are not necessarily preparing it correctly, and reconstituting vaccination correctly. And it is important to remember that unlike the live vaccination, which has given subcutaneously, many of you will probably still have that in your vaccine fridges. This is given intramuscularly. We do see errors where patients are, in fact, given it subcutaneously. Big mistake.

Tony, you were saying something about, if this vaccination is given subcutaneously what happens?

Anthony Cunningham:

So, thanks very much Iris. I think to give you some scientific reasoning behind particularly points one and three, missing the second injection, we often get asked about just simply what happens if you get only one injection. Well, what happens is you only get two-thirds of the immune response and that's not enough. That will actually drop your responsiveness remarkably. So this is essentially a two-injection vaccine. Now, when you actually inject in the muscle, within 30 minutes the immunostimulant, the adjuvant, and the antigen, flow into the lymph node, those nice reactions between multiple cell types occur, outcomes the antibody, outcomes the T cells, exactly what you want. Put it into fat and it's stuck there. It just does not get into the lymph node, and do what it's meant to do. So that's the scientific rationale behind the importance of these key points.

William Schaffner:

Thank you. Thank you, both. We know that vaccination is important, but we also recognize in the real world we're all so busy, and frontline providers have so many things they need to do to evaluate the vaccination status of their patients. So let me ask the audience. What percentage of the time do you discuss vaccination for shingles with your patients who are 50 years of age or older?

Iris Gorfinkel:

We need to make a conscious effort to discuss vaccination. That's not a theoretical fund. Vaccination is low lying fruit. And it forms what is the standard of care for patients. As Bill initially said, this is now a recommendation. And it's actually pretty much in the entire OECD, the entire western world is recommending this for patients over 50. It forms the standard of care. So I would ask you, if a patient is to get shingles, and they have not been told about the vaccination, they may get just a little upset, especially if there's postherpetic neuralgia. The data speaks for itself. It's extremely strong. It takes a common condition and turns it into a rare condition.

So the way we approach vaccination makes a big difference. I personally do not say, "So would you like to get the shingles vaccine? Have you read about it?" I think that's important that they do read about it. But my way of approaching it is, and this is actually the evidence based way, which is, "I see you're missing your shingles vaccine today, Tony. Would you like to get it in the office today? You're here. Let's just get it done." If you have it, and that patient has insurance coverage for it.

Anthony Cunningham:

Yes, doctor.

Iris Gorfinkel:

Oh my gosh, you're my kind of patient. I like that. But here, I have this brochure. I want you to read about it. I want you to feel confident that this is the standard of care across North America. And I want you to know that I'm giving you this vaccination, I'm going to reduce the likelihood of disease by 97%. Note my level of confidence on it. If I'm confident, I can share that with patients. Vaccination is one the key things we have to offer them. It is one of the single most evidence based practices. And we need to be thinking about that, especially in this time of COVID-19.

William Schaffner:

So I'm going to send out a little signal to my colleagues. I've just been told that we have many, and I've looked already, many questions awaiting us. So I'm going to ask us all to be a little more brief. But while we're talking about vaccine hesitancy, Iris just say a few words about that.

Iris Gorfinkel:

What compromises the great majority of vaccine hesitancy are reasonable concerns, and they're concerns about side effects, they're concerns about wallet effects, they're concerns about what a person can expect in the days to come. And these are the questions that we can easily answer. And I'm hoping this webinar will provide you with that necessary information. It is only a small percentage of patients who are genuinely anti-vaxxers. And in Canada, that number represents approximately 2.5%. I don't know what COVID-19 will bring. But the trials ZOE-50, and ZOE-70 are beacons. These are examples of how research should be done. They lasted... It's 30,000 patients for four years. And now there's an ongoing trial for an additional six years to help us understand just how long the immunity will last. The 97% reduction we see in disease speaks for itself. The numbers are highly compelling.

William Schaffner:

Thank you. So Tony, give us a few tips about how we can make sure to get that second dose into our patients. Because as you said before, it's very important for a number of reasons.

Anthony Cunningham:

I'll leave some of the practical issues to Iris, who deals with this on a daily basis. But I think that when we took a survey of doctors and patients, the thing that really matters to patients is the confidence of their doctor that this vaccine is highly efficacious. If you've got a vaccine that's only around about 30, 40%, as sometimes occurred with influenza, actors are a bit ambivalent. But when you're dealing with a vaccine like this, it's very important that doctors portray the confidence in vaccines because that is conveyed to their patients. Patients trust their doctors. That's what we learned from the survey. Please do convey that sense of confidence to your patients. Iris.

Iris Gorfinkel:

I will point out that it is a one-off, basically the patients are getting the vaccination in two doses, and they are done. They are done for the foreseeable future. And the older patients especially, 70 or 80 years old, we're not going to be vaccinating them again in a decade even. It's a one-off. So I think that's an important thing to do. Having the mechanism in place to ensure they get the vaccination in a timely way, matters. And I think the sooner, like hugging that two-month mark, is a good clinical practice.

William Schaffner:

So very good. Now it's time to go back to some of those questions, and we'll get the answers.

Anthony Cunningham: So we have 42%, who are extremely confident post. And 40% who are confident. And only 3% who are not all confident in implementing shingles immunization. That's a pretty good result. We've got 16% who was somewhat confident. Perhaps we can work on that.

William Schaffner: Well, we've certainly been reminded about the significant burden imposed by shingles and therefore the need to implement vaccination protocols that increase uptake, Iris, again, what are some important messages that you would like for clinicians to take away from our discussion today?

Iris Gorfinkel:

Suggest a vaccination visit, a visit that is devoted only to vaccinations. Understand that patients have a tremendous number of problems that are competing for that limited time, and vaccination remains relatively low lying fruit. And when I talk about RZV vaccination, it's not limited to that, as we well know. We're talking about vaccinations against pneumonia, vaccinations against influenza. These diseases should not be viewed as standalone entities, but rather as one feeds into the next. Influenza is a risk factor for COVID-19, and vice versa. It forms a pre-existing one disease. If a patient should get shingles across their chest and unable to cough, that in itself becomes a risk factor and a preexisting disease that feeds into the potential for worse outcomes for pandemics.

So I think that that's one way to look at it. A separate vaccination visit. Of course, address vaccine hesitation. Try to understand if a patient is hesitating about it, where are they coming from? And that way, we can better address their own concerns. Is it the money? Is it the pain? Is it the fear of getting a shot? Because these are all different answers depending on what that fear is. And of course, having mechanisms in place to remind them of the second dose is tremendously important. Because the data is showing that people are forgetting about the second dose. So a good practice is to book that second dose.

If it's being given in the clinic, book it at the same time. That becomes the practice for all vaccinations that require a booster. It's booked at the same time, and even giving them a reminder call the night before is a good clinical practice. Giving it at the pharmacy, great idea because pharmacies have those mechanisms in place already.

William Schaffner:

Well, all of you... Thank you, Iris. All of you have been very enthusiastic about submitting questions. So I'm just going to alternate amongst us about with these questions. So let's start with Tony. If you had chickenpox vaccine, can you get shingles?

Anthony Cunningham:

If you have chickenpox vaccine, it's certainly a lot, it's about a 14th of the dose of the live attenuated vaccine. So the vaccine itself can give rise, very rarely, to shingles. And in fact, the vaccine strain of virus has been identified. It's pretty rare. And it's more likely you're going to get breakthrough from the wild zoster, rather than actually the shingles vaccine strain itself.

William Schaffner:

So thank you. And this one's for Iris. So if you've had shingles already, and you're over 50, should you now get a recombinant vaccine?

Iris Gorfinkel:

Yes, absolutely. That's the standard of care. So whether or not a person who's got shingles, whether or not a person suffers from an autoimmune condition, or if they have immunosenescence because of age, or if they're seriously immunosuppressed, it is virtually every population that needs vaccination over the age of 50. So whether or not they've had shingles... I was showing some of the data and it's interesting. If I just had shingles say last week, I do have some immunity from getting it again in the near future. But with every passing month, the chances of my getting shingles a second time actually increases. And we see that especially as we approach the 50th month, the 60th month, it just continues to go up in a linear fashion.

So the key is, if you're thinking it, vaccinate when you're thinking about it. It's better to get it on board earlier, rather than waiting and taking a chance. Because people get other conditions as they go along.

William Schaffner:

So if my colleagues who are not in the United States will bear with me, here's a question. Why wasn't recombinant zoster vaccine put into Medicare? So let me give a somewhat long-ish answer to that. The short answer is, for purely fiscal reasons. It was put into Part D, which is the prescription drug benefit. Every Medicare recipient does not elect Part D. And if you're in a part D, if you do elect it, you have to elect a plan. All of those plans must offer shingles vaccine, recombinant vaccine. But some of them have deductibles. And some of them have co-pays, and others you have to pay up front, bill the insurance company, and three months later you get a check.

So it's much more complicated to administer zoster vaccine in a physician's office than it is in a pharmacy. Because after all, they're set up for this. It was originally part D, the prescription drug benefit. And that's why our internist sends people who are aged 65 and older, to the pharmacy to get the vaccine. It's another reason if you needed one to start vaccinating at age 50, because there it's included in medical insurance. A word to the wise.

So here are a few others. How long should one wait to give shingles vaccination after a shingles attack? Iris since you answered that other question.

Iris Gorfinkel:

I don't think the answer to that is a single answer. I think it depends on the patient. If I'm seeing a patient who's at very high risk because of immunosuppression, or on immunosuppressants, or facing the possibility of starting immunosuppressant drugs, I would be inclined to give that sooner rather than later. If I'm seeing a young patient, say in their early 50s, who had it, I think it's reasonable to wait six months. There is no set answer to that. Because we know and understand what the rules does increase with every passing month. But they will have some immunity after having initially zoster. But exactly when you give that, I think depends on the age and the concomitant medical conditions that they have, as well as what drugs they're on.

So it's not just a slam dunk single answer to that. But if you're thinking about it, and you're worried about it. And of course, the patient's own concerns will play a role in that as well. If they saw their mother go through it twice, they're almost certainly going to demand it. And I think it's better to side on caution rather than waiting. That would be my own inclination.

Anthony Cunningham:

There is a trial that's been run on this and published, but it was published way out at about five years. And the concern there at the time was safety, and it's completely safe. And five years is too long. Aaron and I used to recommend three years. But I think right hours you can go earlier than that. And while people are thinking about shingles, good idea to be immunized.

William Schaffner:

So Tony-

Iris Gorfinkel:

While the iron is hot.

William Schaffner:

Exactly. So Tony, while I have you, we have an aspiring molecular virologist here. This person understands that the chickenpox virus remains dormant and then reactivates later to cause zoster, obviously, but they want to know, is this really the same virus, or has it mutated in some way to cause this distinctive illness?

Anthony Cunningham:

No, it's the same virus. We do know with both herpes simplex and varicella that you can actually get multiple strains in the various dorsal root ganglia. But we can see this, as I mentioned before, with the rare cases of zoster that occur after varicella immunization, that you can see the same mutations in that particular virus. So the issue here is the immune system. There's also some very interesting information. Send up astronauts, and under their stress, they'll reactivate virus in their saliva without varicella, without actually getting shingles. So it's not quite like herpes simplex which reactivates regularly, but it's probably reactivating a little more commonly than we thought. And it's being controlled by the immune system throughout. Bill, until you get that immunosenescence.

William Schaffner:

So, here are a couple of questions for the family practitioner. Iris, they have to do with the concurrent immunizations. So the patient needs recombinant vaccine, but they're also due for tetanus booster, or perhaps it's time of the year they need their influenza immunization. Can we give them simultaneously or concurrently? And if so, how?

Iris Gorfinkel:

My own practice is to give them separately. And I do that... Again, it's consistent with a minimalist philosophy. It's also consistent with patient expectation. So I think a lot of things go into building patient confidence. It is, you can get away with doing that. Would I do it? No, because I want to see if a patient has a reaction, precisely what is that reaction and what are they reacting to. Incidentally, I apply the same rule for drugs as patients get older. One drug at a time. You do it, and you see what the reaction is. And that way you can better gauge.

Otherwise, you're dealing with what is A, what is B, what is A plus B. And patients have difficulty around that. And also the vaccine hesitant patient may have great problems with that. So can you get away with it? Yes, you can. But is it always necessary? When you don't have to, I think it's better practice to do them individually if you can. If there is a problem with that, send them to the pharmacy to do that there.

Iris Gorfinkel:

But I think it's better received by patients when we ourselves, say, "Okay, this is going to cause some... It has the potential for some systemic reaction to last a couple of days. Let's see what your reaction is. We're just going to give you one vaccine and we'll see how you do. We will prioritize getting all your vaccines done. They must be done. We should be doing them. Let's try to work out a schedule that works with your schedule." That's the way I approach it.

William Schaffner:

And look at that. Yeah, go ahead, Tony.

Anthony Cunningham:

That's a counselor perfection, but there are some GPs, certainly here, who will give both together. And you do get good immunogenicity with both if you use opposite arms. Because the effect of the adjuvant and the antigen is local. It occurs in one lymph node group in this arm versus that. I think what Iris is saying is that this systemic reactogenicity can be confusing, and it may be worthwhile differentiating them. But you can do it at the same time, and there are trials which show that.

Iris Gorfinkel:

Thanks so much for that, Tony. One thing I want to mention too, is that, and this may seem like a small point, when giving the vaccination, that should always be given in the non-dominant arm. It's just a matter of practicality. Why would you vaccinate a right-hander in the right arm? Like that's the arm they're going to experience more soreness in when they're using it. So just a very practical consideration. It is important to go for the non-dominant arm.

William Schaffner:

Good point. Nice. So Tony, take a chance at this. Do you think there will be a need for re-immunization? The writer calls it a booster of recombinant vaccine.

Anthony Cunningham:

Yeah, I think ultimately, there probably will. If you get immunized at age 50, then my bet is that this vaccine might last 15 to 20 years. And just like we do this now with pertussis in older people, and tetanus. But I think it'll be a long-lasting vaccine, Bill. But we'll find out how long it lasts with these follow up studies.

Iris Gorfinkel:

This is such an important point that needs emphasizing. We don't know how long it lasts until we get to that time point. So that again, we're holding hands with COVID-19 because there are some parallels happening in the vaccination world. This study, I think it's as optimal as a study gets. I'm going to repeat it. Forgive me. 30,000 individuals over four years. Now looking at it another six years. How do we know how long the immunity lasts? We have to get to that time point in order to know how long the immunity lasts. And that's just as true for COVID-19 as it is for shingles.

Anthony Cunningham:

But our indication is that the immunogenicity, the immune response goes out to nine to 10 years. So nine years at present. So, fingers crossed, and we'll watch the efficacy.

William Schaffner:

Yeah, exactly. So we don't certainly recommend that people get varicella titers before people are vaccinated against shingles using recombinant vaccine. But this person asks, is there a relationship at all between varicella titers and the need for shingles vaccine?

Anthony Cunningham:

There is a really good paper in the Journal of Infectious Diseases by a guy named Cunningham, who, as first author, you should have a look at and the answer is no, there's not. But one thing that we have not done, and Myron Levine and I have discussed this, is to actually look at baseline levels of T cells and correlate that with responsiveness. And even look over the years if you can see little spikes of T cells when people relapse, recur asymptomatically, which we think they do. That'd be a lovely study to do. Thank you.

Iris Gorfinkel:

Tony, I'm going to stick my neck out on that question and just ask, because I didn't quite even understand your answer. But if I say as a family doctor, I have a patient who says I've never had chickenpox. I do the titers, I see their titers is zero. They in fact have never had chickenpox. To my knowledge, the standard of care would still be to vaccinate that patient against shingles. But your perspective is, is there a theoretical risk? Yes, they could get chickenpox. But is there a theoretical risk that they could get zoster anyway despite having no titers?

Anthony Cunningham:

So, this is something that's been debated a lot. Seeing the vaccine RZV has been so successful, should we actually use it particularly for chickenpox in immune compromised patients? And there are no plans to do that study. And the big question is, is the shingles vaccine so effective? Because it builds on the fact that a person has been exposed either to wild chicken pox or to the chickenpox vaccine with all of the viral proteins that are involved. We don't know the answer to that. So really interesting question. So I don't think anybody is the key issue here. It's actually the T cell levels. And some of the people who failed the RZV had very low T cell levels, not enough for us to draw conclusions. But they have very low T cell levels.

Iris Gorfinkel:

And a practical level, I generally will tell patients, some 97% and some studies are suggesting higher, have had natural disease, of the older patient population when you're talking 50-plus. Now the younger group will have to wait and see. But I'm just sharing with you. On a practical level, the chances are even when they don't remember having had the disease, they actually did have it.

Anthony Cunningham:

And we do know that anybody can drop off from T cell level stage, just like size one.

William Schaffner:

So, Tony, we're going to kind of end this on a note here. So you've told us that a senescent immune system is probably the single predictor, or it's the circumstance in which recurrence occurs, in which herpes zoster occurs. The virus comes out of its cave, it's been hibernating, and it causes illness. But the question wants to know, because there's a lot of folklore about this, are there triggers that set this off? A stressful life or exposure to either heat or cold? Is there anything to those bits of folklore out there?

Anthony Cunningham:

Well, I think this is relating back to the well-known expresses for recurrence of herpes simplex. And I've had a stressful life, and I've never got shingles, just in joking. But clearly, the issue of the astronauts asymptomatically extreme chickenpox virus in their saliva without disease indicates the importance of the immune response, and particularly the T cell immune response. So, we know very clearly there are precipitants for occurrences of herpes simplex that are not documented for recurrences of zoster, other than immunosuppression.

Iris Gorfinkel:

Well, it's interesting though, we come back to the bio psychosocial model. And this speaks to the heart of me as a family physician. If someone is really stressed, what's going to happen? They may not sleep as well. What happens when they don't sleep as well? They become immunocompromised to some degree. And this brain of this particular GP, stress holds hands with every disease. And I think that we need to recognize that, and embrace that, and try if we can and when we can, to approach disease in that light.

William Schaffner:

Well, on that note, we don't want to overly stress our organizers here because we've come to the end of time. So receive CME and CE credit for today's program. Click on evaluations tab to complete the post test, and print your certificate. As a reminder, if you'd like to claim this activity as a CME for MIPS improvement activity, follow the steps described on this slide. And thank you both Iris, Tony. This has been a wonderful, rich discussion.

Thank you our audience for all the great questions you sent in. I wish we could have gotten to more of them. We hope that you will be able to use the strategies that we've shared to implement shingles vaccination protocols in your respective clinical settings. Don't forget your pharmacist colleagues, they're there to help. Also, please stay tuned to CMEOutfitters.com, as we will launch three additional shingles activities. Each title is a 15-minute podcast, targeting best practices for implementing your shingles protocol in either primary care settings, pharmacies, or in specialty settings.

Thank you again for participating. Thank you for providing the best care for patients. And everyone out there, please stay safe.