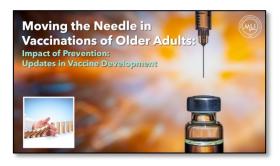




Part 2: Impact of Prevention: Updates in Vaccine Development



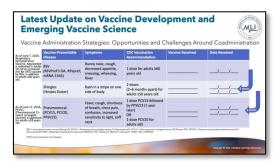
Pamela G. Rockwell, DO: Hello, I'm Dr. Pamela Rockwell, Professor of Family Medicine at the University of Michigan Medical School. I also served for the past seven years at the American Academy of Family Medicine, liaison to the ACIP or Advisory Committee on Immunization Practices through the CDC. I also chair our Human Health and Resources Division of Immunizations at our state level, and I'm happy to be here today.

Myron J. Levin, MD: I'm Myron Levin. I'm an infectious diseases doctor, both pediatric and adult infectious diseases at the University of Colorado School of Medicine. Here on campus, I have a vaccine research clinic, and I've been involved in vaccinology for a long time, and I actually was chair and a member of the ACIP in the past.

Dr. Rockwell: Today, our overview and updates in vaccine development is on vaccine science for RSV, respiratory syncytial virus, shingles or zoster, and pneumococcal disease. We're going to go over vaccine administration schedules, managing vaccine side effects, clinical workflows, and patient-focused strategies.

Case number one, you're treating a 75-year-old male with a history of hypertension. After a recent outbreak in his community, he receives his RSV vaccine. Among adults in my practice, the rates of RSV right now are non-existent because the RSV season is over. However, we had a significant outbreak during the traditional sort of flu season, and our outbreak where RSV was actually outnumbering influenza cases in our community. I don't know about your community, Dr. Levin.

Dr. Levin: The same. I think RSV had a higher peak, and I look at the statewide data in our hospital compared to influenza.



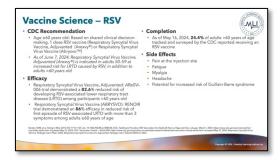
Latest Update on Vaccine Development and Emerging Vaccine Science

Dr. Rockwell: Unfortunately, RSV vaccinations have not reached those of influenza vaccinations. I'm just going to speak a few minutes on a reminder of the three diseases. We started talking about what the common symptoms are and then what the CDC recommendation is to prevent those diseases.

RSV, we have two different RSV vaccine options. Symptoms are anywhere from runny nose, cough, and cold symptoms, sneezing, coughing, all the way up to hospitalization. The CDC recommendation is one dose, adults 60 years and older, okay? Then shingles or herpes zoster vaccine, you usually see a painful, puritic, rash, one dermatome, unilateral. It's two-dose series, two to six months apart, and that's for adults over age 50.

Then the pneumococcal vaccines that are available, that can be a little more severe with lower respiratory tract symptoms, fever, cough, shortness of breath, getting pneumonia. It's one dose of PCV15 followed by a dose of PPSV23 a year later, if that is what you have in your office or hospital, or if that is what the patient has already had, or it's one dose of the PCV20 for adults over age 65.





Vaccine Science – RSV

Dr. Levin: The recommendation is that people who are 60 and older should get a dose of RSV vaccine before the season starts, which basically is, for RSV, is just a little bit after, in general, the influenza. It tends to be more predictable. Influenza can start later in the year than RSV. It varies from year to year. Basically, in the fall, we should be protected against both.

RSV vaccine is also recommended for people that are at high risk for lower respiratory disease if their age is 50 to 59. These recommendations are accompanied by clinical decision-making. The reason for that is that there was some signal that there might be some serious adverse events from it. Very, very rare neurologic disease. It wasn't certain whether or not this is vaccine-related or not. Because of that, it was felt that the physicians ought to discuss with their patients the decision to give the vaccine or not.

In terms of efficacy, currently, there are two vaccines. They have different types of platforms. One is adjuvanted, one is not. They are both, in the first year, were shown an efficacy, as shown here, somewhere in the order of 80% for lower respiratory disease. I'd point out that the way the studies were done were really different between the two vaccines, so it's very hard to compare one with the other. Is one better than the other? Right now, I would say they're about the same.

The two-year data is in. One vaccine looks a little better than the other in the two-year data, but it doesn't matter because they were done differently. I think the bottom line is they were both effective at preventing serious disease. We're, right now, in the throes of finding out if there'll be additional protection after two years or whether a booster dose will be needed.

We know a booster dose is safe, and we know it's also immunogenic, and it probably will be something that we'll hear more about. As I think I pointed out in the previous comments in the previous slide, the uptake has been slow for RSV vaccine. This shows 24%. I think we do a little better around here. It depends on the age group. As far as side effects go, I think they're like any other vaccine that we give to older people.

I'd like to talk about the shingles vaccine, which I really have been working with since the 1980s. One vaccine we actually developed and now has been replaced by a much better one. I would say it's really a good vaccine. It's recommended to prevent shingles in people over the age of 50 because that's where the risk starts to become severe. It's a two-dose vaccine separated by a couple of months or more, up to six months. Even a year would be okay, actually. It's extremely effective.

I've studied vaccines in older people for a long time, and we always find that the older you are, the less well you respond to a vaccine, and the quicker you lose the response. That's not true of this vaccine. It doesn't matter how old you are. You're still protected almost as well as a younger person, and at last now we know for 10 or 11 years we have data. I think this is an excellent vaccine. You basically convince people to take their two shots, and it's done, and they're protected lifelong.

As you can see under efficacy, the efficacy is really very, very high, remarkable for older people, and it stays high even as they get older. As I said, there's no age effect, and there's long-term protection. Again, I'm disappointed with all vaccines that we're giving these days that we haven't done a better job of getting everybody immunized. Everybody over the age of 50 should be vaccinated against shingles. It's a disease we don't want our patients to get, we don't want to get, and way more than one in two should be vaccinated.



<u>Vaccine Science – Shingles (Zoster)</u>

Dr. Levin: What about adverse events? The shingles vaccine has been labeled as being more reactogenic than other vaccines, let's say a flu vaccine, and it's true. I think you'll see slightly more adverse events that are not serious adverse events, but feeling poorly for a 24-hour period, not feeling up to doing the usual work during the day. These are all things that happen, and all I can tell my patients is if they feel these things, it's going to be done with, and they're

going to be protected. I feel confident they'll be protected against shingles probably for the rest of their life, so it's really worth it.

They need to get two doses. One dose will protect them for a short period of time, but to have lifelong protection, you clearly need to get two doses. Even if you have side effects from the first dose that you don't like, you may not have them with the second dose and vice versa, but in any case, the side effects are tolerable. I certainly can attest to that, and it's worth it in terms of the lifelong benefit.

As the rest of the slide says, the mild side effects, I think lasting two to three days is probably a stretch. Usually, it's a 24-hour period in my experience, but it could be longer. Very often, it's not anywhere near as long as that.

Dr. Rockwell: I just want to add, Dr. Levin, a key point here is that I have seen this in practice that even if you had a moderately serious side effect with myalgias, feeling so sick you couldn't go to work, there is no evidence that you're going to have the same reaction with the second shot. It's true, it's proven, it's evidence-based. You do need to remind your patients that if they're hesitant to complete the series.

Dr. Levin: Yes, it's published in very good data.

Dr. Rockwell: Case number 2, your patient returns with mild side effects following his shingles vaccination, and you must counsel him, addressing his concerns and managing the side effects appropriately. I think the most reported adverse events are what we've already been talking about, myalgia, maybe low-grade fever, just feeling punky, not having a lot of energy. I think it helps, and studies show that if you tell people ahead of time, they may experience this, they're less likely

Vaccine Science – Pneumonia

Efficacy of Pneumococal Conjugate Vaccines (PCV)

PCV15 (Vaxneuvance) and PCV20
(Prevnar20)

Approved by the FDA for adults 3-65 years old

Inactivated vaccines that contain
polyaccharide antigens bound to protein
carrier (RM197)

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Adv Michacy against vaccine type neumococcal
pneumococal vaccination at least 1 years of a study enrollment

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then, to have to come back and seek medical care because of the side effects.

Vaccine Science - Pneumonia

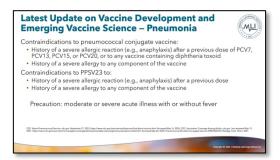
Dr. Levin: As shown here, we have two conjugate vaccines. The conjugate vaccines are the ones that are used almost exclusively nowadays. PCV-15, as it protects against 15 types of pneumococcal disease, PCV-20 obviously against

20, they don't exactly overlap entirely. I would say that PCV-20 has replaced PCV-15 because you basically get more for your money with PSV. Both of these are approved for people over the age of 65, and they are non-live vaccines, so they can be given to people who are somewhat immune-compromised. The efficacy has been well established in a blinded, randomized trial.

You see the efficacy there against both pneumococcal pneumonia, pneumococcal bacteremia, and otherwise invasive disease. I think that understates the value of them because even if these things occur that are shown there, they tend to be less severe in people who are vaccinated versus people who are not. They get what I call breakthrough disease. If they get it in spite of vaccination, it tends to be attenuated. All vaccines, in general, tend to do that kind of thing. The field is rapidly changing, and we're going to see new pneumococcal vaccines in the next year or two.

Now, what's disappointing in terms of completion in the last bullet is that it's more like influenza. We basically are able to give 70% of people who need this vaccine, as we do for influenza. Influenza is a little bit less right now. We're only about two-thirds being successful, and we should do better.

Dr. Levin: What about the side effects of pneumococcal vaccines? Right now, I would say they're similar to most other vaccines that we give to older people. Influenza might be the best. They're less than we see with the shingles vaccine. They're similar to what we see with influenza. I don't think there are any surprises here, and there's nothing specific you need to alert your patients to.



<u>Latest Update on Vaccine Development and Emerging Vaccine Science - Pneumonia</u>

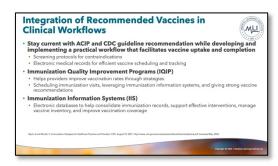
Dr. Rockwell: There are contraindications to pneumococcal conjugate vaccines and they're like contraindications to other vaccines. A history of a severe reaction like anaphylaxis after a previous dose of another pneumococcal vaccine or any vaccine containing diphtheria toxoid, and so that is no different than any other vaccine if you're allergic to one of the components, a known allergy. Other than that,

there are no contraindications.

Case variation number three. The same patient later inquires about the RSV and pneumococcal vaccines. You must navigate the patient's existing vaccination schedule and co-administration guidelines to recommend the most appropriate course of actions. Well, many vaccines can be co-administrated, and very few have any stipulation on what shouldn't be given together. In this case, I would recommend that this patient get both the RSV and their pneumococcal vaccine on the same day, opposite arms.

There are a lot of factors that go into why somebody might have a vaccine-associated side effect ranging from the vaccine administrator like did they inject too fast, too shallow of a vaccine if it should have been intramuscular. There is some user expertise involved in giving the vaccine. If it's an adjuvanted vaccine, sometimes they cause a little more local side effects. If somebody is much older and their immune system is down, they may not have as many side effects as a younger person who is getting the same vaccine. There are a lot of factors that go into why somebody might have a vaccine-associated local side effect.

The key point to understanding co-administration of vaccines is there's so much advantage to giving two vaccines at once to increase compliance, to increase coverage. You might have a little bit of increased reactogenicity overall, but I can assure you ACIP has looked at those studies when there is co-administration, especially with a new vaccine coming out, and it really is not significant enough to put out a warning or to have us recommend to separate these vaccines. The key point is co-administer vaccines when able.



<u>Integration of Recommended Vaccines in Clinical Workflows</u>

Dr. Rockwell: For integration of the recommended vaccines in clinical workflows, make sure to stay up-to-date with ACIP and CDC guidelines. There are plenty of online and apps available that are free to look at that. There are some screening protocols for contraindications for some vaccines more than others. Use your electronic medical record when possible. Use your quality improvement programs and your

state immunization system whenever possible. Manage your vaccine inventory and have somebody in your office or your environment be in charge of all your vaccines.



<u>Integration of Recommended Vaccines in Clinical Workflows</u>

There are some patient-focused strategies like we give a strong recommendation to vaccinate. If there's hesitation, answer questions appropriately, address concerns, look for any barriers the patient might have to getting vaccinated. If you don't have that vaccine, in your office it would be a barrier for them to go to another place to get that. Reduce missed opportunities, as I've mentioned before, no matter

what the patient is coming in for, aside from high fever and severe illness, consider vaccinating for things that they're up-to-date for. Keep accurate immunization records for your patients and use your own reminder system, whatever is available to you in your healthcare system, whether it's a BPA in your electronic health record or maybe even written notes that the medical assistant puts on the chart prior to rooming the patient.

Case variation number 4. Upon reviewing the patient's electronic medical records, it's discovered this patient missed his second dose of the herpes zoster vaccine. You need to adjust the workflow to accommodate.

How can your workflow help in your office? In our office, the electronic health record has now put out a yellow alert that the patient is due and overdue for their vaccine. You can also query your state immunization roster to see which patients are behind or overdue for vaccines.

Thank you. This brings us to the end of Part 2 of this series, Updates in Vaccine Development. We've looked at the latest clinical data, safety profiles, efficacy rates, and administration schedules for new and emerging vaccines. This is super important to keep our elderly population and general community healthy and prevent diseases that would otherwise possibly put them in the hospital or because morbidity and death. Please join us in Part 3 of the series, Improving Vaccine Uptake.