

Part 1: The Burden of Vaccine-Preventable Disease: Assessing Risk in Older Adults



Pamela G. Rockwell, DO: Hello, and welcome. My name is Pamela Rockwell, Dr. Rockwell, and I'm a professor of family medicine at the University of Michigan Medical School. I also spent seven years as the American Academy of Family Physicians liaison to the CDC for the Advisory Committee on Immunization Practices. I just handed over the baton now to a younger family physician to take over my role there, but I'll remain on a couple of work groups at the CDC. My scholarly work is in immunizations, but my day-to-day life is a physician in family medicine, teaching medical students and

residents, and I also do inpatient medicine. I'd like to introduce my colleague, Dr. Julio Ramirez, and he can tell you a little bit about himself.

Julio Alberto Ramirez, MD: Thank you. Thank you for the invitation to participate in this series. I'm Julio Ramirez. I was the chief of the Division of Infectious Diseases at the University of Louisville for several years, and now became an emeritus professor in the Division of Infectious Diseases. I recently started a new position as a chief scientific officer here at Norton Infectious Disease Institute in Norton Healthcare. My interest in research has been primarily in the area of pneumonia, primarily community-acquired pneumonia and the different pathogens and outcomes in patients with pneumonia. It's a pleasure to be here with all of you.

Dr. Rockwell: What we're going to talk about is the burden of vaccine-preventable disease in older adults. A quick overview of what we're going to talk about is prevalence and impact of RSV, shingles or herpes zoster, pneumococcal disease. We're going to look into the economic costs of these vaccine-preventable diseases, the health disparities that are seen in these diseases, both in the vaccination of the populations and in health outcomes, the impact of risk factors, and the increased susceptibility to these infections as we age, our older adult population, how to make a good risk assessment, and then go over the immunization schedule in older adults.

First, we'll start with a case. Case number one is a 72-year-old female with a history of COPD. She presents for her annual wellness visit or health maintenance exam. She inquires about vaccination recommendations and has a concern because she's noticed there's been recent outbreaks in her assisted living community. I was wondering, Dr. Ramirez, have you seen this kind of thing happening in your community with outbreaks, say, in nursing home populations or other communities?

Dr. Ramirez: Yes, definitely. As, of course, we all have, now that you mentioned, this reminds me what happened during COVID-19. Now then, the nursing homes or assisted living facilities were the center of patients getting admitted with pneumonia due to SARS-CoV-2, because again, there's a lot of transmission of these respiratory infections.

Then respiratory viruses that get transmitted through droplets or even streptococcal pneumonia that get transmitted through droplets, and then you have all these people in close contact. Yes, this is definitely a concern. Now, since I'm looking at primarily hospitalized patients, then what I see is the most severe forms of these diseases. Then I see the patient, as you see here, respiratory syncytial virus with severe respiratory infection or the case of pneumococcal pneumonia.

Dr. Rockwell: Right. Now, I see hospitalized patients for a week at a time, maybe every two to three months. My primary patient population is in the outpatient. I've been in practice for 30 years, so my patients are growing old with me. I do see a fair number of older adults, day to day in my practice. I strongly recommend vaccines to these folks. As we know, our immune systems are aging with us. We are more susceptible to these diseases.





Risk Factors for RSV

Dr. Ramirez: Then discussing the risk factors, for instance, in this case for respiratory syncytial virus. We know that one of the primary risk factors is age. In young individuals, when you're below 45, 50, usually, respiratory syncytial virus causes upper respiratory infection. The person is going to have a rhinitis or sore throat. We know that as we age, you pass 50, 60, 65, then respiratory syncytial virus is going to cause lower respiratory tract infection. Then we are going to see patients with COPD exacerbation, with pneumonia.

Then of course, not only is age, but if the person is immunocompromised, then you may have problems or hematological disorder, diabetes. As we discussed already, patients living in congregated settings are going to be at a high risk.

Dr. Rockwell: Right. For my patients, like in the outpatient center, who might get RSV, and even though they're over 65, it might be a super bad cold for them. If they have higher risk factors, or they're a smoker or COPD, like Dr. Ramirez said, then they end up in the hospital with lower respiratory tract disease and, worse, conditions that could maybe put them in the ICU.

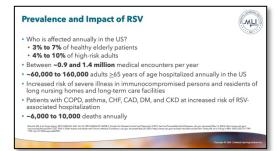
Dr. Ramirez: Then as we discussed, in the case of RSV, one interesting point is that, at least in my experience in patients that are hospitalized, sometimes it's the RSV itself is causing lower respiratory tract infection, not COPD exacerbation, asthma, community-acquired pneumonia. Sometimes what we notice is that the patient gets admitted for a decompensation of an underlying pathology.

Then we've seen a lot of patients, for instance, admitted with congestive heart failure. They have a little bit of cough. We do PCR, and we find RSV. Then the primary reason for hospitalization is an exacerbation of an underlying comorbidity. We assume that it was the RSV last week that gave you a respiratory infection that decompensated congestive heart failure or decompensated diabetes, then sometimes the patient gets admitted not due to RSV, but with RSV that was there one week before.



RSV Clinical Manifestations

Dr. Rockwell: Speaking from a primarily outpatient physician, I can say that RSV presents just like any other cold or viral illness that we're seeing now in the days of COVID and influenza. It's going to be similar, cough, nasal congestion, rhinorrhea, sore throat, and not all these patients end up in the hospital. One interesting fact is that fever is less likely to occur with RSV than with influenza. Not sure on the why with that, but the point is we need to consider RSV when patients are showing up with these viral common symptoms.

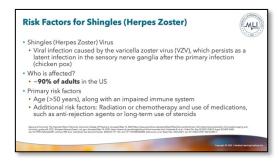


Prevalence and Impact of RSV

I want to take a second just to talk about prevalence and the impact of RSV in the US. In general, the stat is 3% to 7% of all healthy elderly adults in the US will be infected with RSV, and 4% to 10% of high-risk adults. As Dr. Ramirez pointed out, those high-risk results are the older, older adults, those with COPD, underlying immunocompromised, and things like that.

RSV accounts for somewhere in the range of 1 to 1.4 million medical encounters per year, so that's a lot of money spent on healthcare as well. 60,000 to 160,000 US adults over age 65 are hospitalized every year. Then those who are immunocompromised, reside in nursing homes or other long-term care facilities have an

increased risk to actually have more severe illness ending up in the ICU. The current estimate is about 6,000 to 10,000 deaths annually. However, that may be underestimated because we're not testing for it often enough.



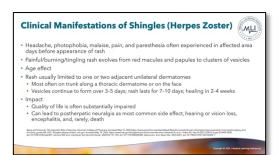
Risk Factors for Shingles (Herpes Zoster)

Dr. Ramirez: I would agree. It's a significant impact for the patients and for the healthcare system. Then we're going to move from respiratory syncytial virus to another virus that is a problem in our adult population, and this is the herpes zoster virus. Then as we all know, at this moment, probably more than 90% of adults in the US have been infected with the varicella-zoster virus, having chickenpox during childhood. This large number of us carrying the varicella-zoster virus is what is going to produce the reactivation

that we recognize as shingles. Now, this reactivation is primarily a manifestation of decreased immune system. Then this reactivation happens in patients more than 50 years of age or whenever our immune system tends to decline.

Dr. Rockwell: Of note, as we age and get into older age, especially over 70, 75, the older you are, the more severe the zoster case can be, and then the higher risk you are to actually get post-herpetic neuralgia. It's very, very important to address this preventable disease with our population, older population, and especially those over 70 and 75.

Dr. Ramirez: Additionally, risk factor besides age, we have the consideration. Really, I would consider here that the CDC defines immunocompromised patients with medical conditions or medical treatments. I may say anyone with medical conditions, HIV, cancer, or primarily treatments now that is chemotherapy. Probably the most important immunocompromised treatment that we are using now is all the biologics. We are using biologics for more and more diseases, rheumatological diseases, dermatological diseases, gastrointestinal diseases. Sometimes we are not aware the patient is taking a biologic, and this person is immunocompromised and this person is going to be at risk for shingles.



Clinical Manifestations of Shingles (Herpes Zoster)

Dr. Rockwell: Just want to go over the clinical manifestation of shingles. If you've been in practice for a while, you've undoubtedly seen a patient with shingles. I have seen a wide variety from people having pain unexplained for days until finally a rash breaks out or showing up in the office with a rash. Preceding any kind of a rash could be a headache, photophobia, malaise, just feeling terrible. Then a painful, described as burning, tingling rash, usually in one dermatome. Could be two adjacent dermatomes, but unilateral,

one side of the body. Then it evolves into papules, going into vesicles, and eventually crusting over.

The most common place in the body for this is going to be in the trunk, but also in the face. When the eye is involved, that becomes a little more dangerous for long-term problems. Vesicles form for about three to five days, tend to crust over in about anywhere from a week to two weeks. Until you see those vesicles all crusted over, the patient is considered contagious. They're not contagious to give shingles to somebody, but they actually could give a primary infection to somebody who's never had chickenpox, or an immune-compromised person.

The impact of all this is quality of life, severely impaired. Most common side effect is post-herpetic neuralgia, where there is a persistent and pretty significant pain along the dermatome, where the zoster occurred. When the eye is involved, you can have vision loss, and the ear could be involved, and you can have hearing loss.

Worst case scenario with those really immunocompromised, it can get systemic, and patients can get encephalitis, and there are cases of death from zoster.

Dr. Ramirez: As you alluded, this long-term sequelae that may be post-herpetic neuralgia, or vision loss, or hearing loss. Now, we are talking months, years of suffering. This is then, when we are looking at this patient and trying to prevent these infections, where we discuss with the patient, it's not just trying to prevent the acute problem. That may be very bad, and you may end up in the hospital. For any one of these infections, we're also trying to prevent the long-term sequelae of infection. Here, these long-term sequelae, sometimes we see this patient with chronic pain, or hearing loss, or vision loss. These are really severe long-term sequelae for this virus.

Dr. Rockwell: Exactly, and we know that vaccination reduces that risk of the long-term side effects.



Prevalence and Impact of Shingles (Herpes Zoster)

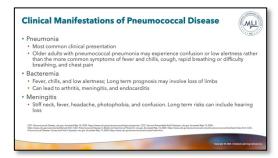
Dr. Ramirez: Regarding the burden of disease, we can estimate that there are 1 million new cases a year. Then if we look at the life span of adults, then this may occur in one into three people in the US, and we discussed that the most severe consequences, hospitalization, and approximately 1% to 4% of people with herpes zoster will be hospitalized for some of these severe acute complications that we're discussing.

Risk Factors for Pneumococcal Disease • Pneumococcal disease • Wide range of infections caused by streptococcus • Age 265 • Risk conditions • Alcoholism • Alcoholism • Alcoholism • Sensor of the streptococcus • Age 265 • Risk conditions • Alcoholism • Alcoholism • Alcoholism • Alcoholism • Alcoholism • Alcoholism • Cerribospinal fluid leak • Chronic heart, kidney, liver, or lung disease • Chronic heart, kidney, liver, or lung disease • Cigarete smoking • Cohlear implant • Diabetes • Immunocompromising condition

Risk Factors for Pneumococcal Disease

Now, we move to the streptococcal pneumonia, the cause of pneumococcal disease. Here, we are going to see something that repeats among all these pathogens. The idea is that as our immune system decline, we have increased incidence of these pathogens. Then the risk factors will be, again, elderly, most of the comorbidities that we have, diabetes, CHF, COPD, because the comorbidities, you have an abnormal immune system. Then at the end of the spectrum, the patient that is immunocompromised, as we discussed.

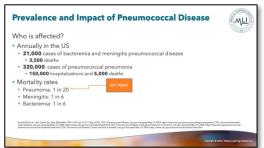
These will be all risk factors for pneumococcal pneumonia. Here, we have two other factors that will be cerebrospinal fluid leak or cochlear implant, that this will be the risk for streptococcal pneumonia to get into the CNS and cause meningitis in adults. Then here, we have the risk factor for meningitis and for comorbidity-acquired pneumonia.



Clinical Manifestations of Pneumococcal Disease

Then the clinical manifestations of streptococcal pneumonia, streptococcal pneumonia colonize the nasopharynx, the oropharynx, and from there, we have microaspiration and the patient develops the most common disease is going to be pneumonia. Sometimes from the oropharynx, the bacteria translocate into the blood and the patient may have bacteremia or can translocate from the blood to the meninges, and the patient may present with meningitis. By far, the most common presentation would be community-acquired pneumonia.

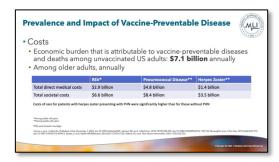




Prevalence and Impact of Pneumococcal Disease

Dr. Rockwell: Well, annually in the US, there are about 31,000 cases of bacteremia and meningitis pneumococcal disease, resulting in about 3,500 deaths, 320,000 cases of pneumococcal pneumonia resulting in 150,000 hospitalizations and 5,000 deaths. Key point in this statistical fact is that the mortality rates for pneumonia, 1 in 20 of those who are hospitalized with severe disease, meningitis, it's 1 in 6, and bacteremia, I've seen anywhere between 1 in 6 and 1 in 8

Dr. Ramirez: Then and also regarding the mortality, this is very important. All this information, as we discussed, is for acute-related mortality. It is difficult for us to still to put a number, but we know that once you have pneumonia, not only you die of pneumonia during the acute event, then you have this long-term mortality that we know that is there associated with pneumonia and is definitely associated with streptococcal pneumonia. Then when we are discussing here the cause of the economic burden, most of the calculations are based on the acute disease.



Prevalence and Impact of Vaccine-Preventable Disease

Even looking at acute disease among older adults, then here we have total direct medical costs, \$2.9 billion for RSV, \$4.8 billion for streptococcal pneumonia, \$1.4 billion for herpes zoster, and the total societal costs that are much increased. Then a significant cost impact just looking at the acute sequelae of these three infections.



Health Disparities in Vaccination for Vaccine-Preventable

Dr. Rockwell: Health disparities occur in vaccination for many vaccine-preventable diseases. Key point is we know the disease burden disproportionately affects some groups. I think I mentioned that earlier. Black patients are more likely to die within the hospital and have a longer length of stay. Lots of reasons behind these disparities, but the key point is that the disease burden disproportionately affects some groups.

Dr. Ramirez: Regarding disparities also in vaccine uptake, probably a key consideration here is that vaccination coverage is lower among adults without health insurance compared with those with health insurance. This brings the point of the socioeconomic position and an issue related to vaccination because again, we know that poverty, one of the reasons that poverty is a factor here, maybe also the fact that poverty is associated with no health insurance. Then we're going to probably address also the cost of vaccination. Again, this is all part of these health disparities in vaccination.

Dr. Rockwell: We know in the US, white elderly adults are significantly more likely to receive vaccinations that are indicated compared to Blacks, Hispanic, and Asian elderly adults. Whether that's because they're not able to access the healthcare system, whether it's not being recommended or they're refusing, that data isn't in this, but the point is there is a huge disparity in vaccine uptake. If you have health insurance, you're more likely to be vaccinated.



Health Disparities in Vaccination for Vaccine-Preventable Disease

Health disparities for vaccine-preventable disease, how do we reduce them? What is the role of social determinants of health?

Really, I have done some reading on this. It requires a broad collaboration over time with multiple things, not just in the medical community. It's housing, it's transportation, it's education, it's employment. We as clinicians have to do our best to always cover

vaccines needed. Dr. Ramirez is in the hospital, and I'm not sure what the practice is there, but I have introduced vaccinating our hospitalized patients into the practice, at least on our teaching service. For sure in the outpatient center, you want to try to vaccinate at every opportunity. We can use evidence-based systems using our IIS, our Immunization Information System. Every state has one.

I'm lucky, state of Michigan has a great one called MICA. We can get involved, improve our public health awareness, and try to like put recall notes or texts or messages out to patients telling them when they're due for vaccines. What we can do as healthcare providers is give a very strong recommendation to vaccinate. Use really presumptive language that you're assuming they're going to vaccinate. Don't ask them, do you want? Just recommend, I highly recommend you get this vaccine.

Dr. Ramirez: Opportunistic pathogens are very low virulence pathogens, Pneumocystis, Jirovecii, cytomegalovirus. Your immune system is very weak. As we discussed, you need to have cancer, you need to have a high dose of steroids, you need to be in immunomodulators. Then we have a group of patients with medical comorbidities that they are not immunocompromised, but the immune system is weak. This is the patient with COPD, with diabetes, with-- this patient has what we call an abnormal immune system without being immunocompromised.

Now another factor is abnormal immune system is age. In a lot of these diseases that we are discussing, for example, RSV and streptococcal pneumonia, we recognize that when we look at the epidemiology of burden of disease, these diseases have this U-shape. This is the immunosenescence. Now immunosenescence has been studied under multiple considerations for why our immune system decreases. It's important for us that above 50, above 60, definitely above 65. Now we know that as we age, our B-cells and our T-cells, the primary defense mechanism of B-cells with antibody production, T-cells going and killing viruses and destroying cells that are infected, they are going to be not working properly. Then we are going to have increased susceptibility with aging for RSV and Streptococcus pneumoniae.

Dr. Rockwell: In addition to all this age-related immune decrease, I just want to add though, it does make a difference also if that older person is exercising, if they're eating well, if they're frail or not, what comorbidities they have. There's a lot that goes into the susceptibility to vaccine-preventable diseases.

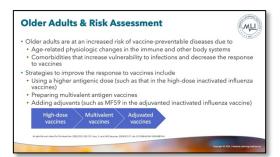
Dr. Ramirez: I completely agree. I may say that there's nothing that we can do for aging, but there's a lot we can do to have a healthy aging. You already mentioned the things that we need to be doing, the exercise, the diet, and the vaccination.

Dr. Rockwell: Let's have a second patient case. Three weeks later, a new patient, age 78, is admitted to the hospital with pneumococcal pneumonia from the same assisted living community from the patient number one. Despite having multiple comorbidities, discussions reveal he was hesitant to receive the recommended vaccines due to misconceptions about the need to be vaccinated. I see this a lot in my patients thinking like, "Oh, I'm healthy. I don't need vaccines. I can have natural immunity by getting the infection."

That's a false statement that we need to try to debunk, that even though some side effects occur with many vaccines, the side effects are preferable to the disease. Maybe Dr. Ramirez can speak to like what would make this particular patient at higher risk to have a severe outcome from disease?

Dr Ramirez: Yes, and I also want to emphasize your point, because when you discuss what patients tell you, I remember a patient that said, I don't need the pneumococcal vaccination because I already have pneumococcal disease. Then some patients believe that the pneumococcal is one bacteria. Then we need to emphasize that every serotype, we develop antibodies specific for every serotype. When patients have multiple comorbidities, you reach the point that you behave the same that you were immunocompromised with AIDS and comorbidities.

Then I may say this patient has multiple factors to have a severe pneumonia. We also recognize that sometimes we have outbreaks of pneumococcal disease. Then this person is coming through an area that seems to be that there's a lot of pneumococcal very active. Definitely, it's not only to protect this patient, we need to go there and we probably need to call the CDC to do an outbreak investigation and make sure everybody gets vaccinated in this assisted living facility.

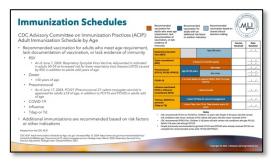


Older Adults & Risk Assessment

One of the challenges that we have in vaccinations in adults is as we discuss, as we get older, our immune system gets weaker. Then our capacity to develop antibodies to a vaccine also gets weaker. Then what is that investigators are doing in an attempt to improve the capacity to our immune system to respond? We have the standard vaccine for everybody, but then we can have vaccines with higher doses for adults. This is one possibility. The other consideration as we learned with COVID, for instance, we were

given one dose for COVID, but then we find out that the person was immunocompromised, didn't develop antibodies, good level of antibodies.

Then we have booster doses. This is another possibility to give more than one dose as your immune system gets weaker. The other consideration sometimes we give adjuvants with the vaccines in an attempt to improve the amount of antibodies. Then there are different considerations that we have in vaccinology in the elderly in an attempt to improve our immune system capacity to respond to the vaccines.



Immunization Schedules

Regarding immunization schedule, one thing that I like from the CDC and the ACIP approach is where we discuss immunization based on age, because this makes life simple for practicing physicians. Then here we see, for instance, that for respiratory syncytial virus, we have one of the vaccines that was just approved for adults more than 50 years of age. It was approved initially for more than 60, but now we decreased to 50 to 59.

Again, with the concept that we discussed that whenever we go beyond 50, we notice that something happened and these viruses started to increase the incidence. For Zoster, it is also above 50. For pneumococcal disease, it's above 65. Then we have age. Now, one thing is important that if a person is immunocompromised, these ages can, as physicians, we need to say, "Oh, I'm a 40-year-old with cancer, chemotherapy." This is a different story. I need to consider to protect these patients regardless of age. In the healthy individual, then we have scheduled based on the age of the patient.

Dr. Rockwell: Moving on to patient case number three. During the recovery, the patient reflects on her peers who have faced similar illnesses, sparking a conversation about the importance of community-wide

immunization efforts to reduce the disease spread, particularly among vulnerable groups. If you can time it, if it's flu season and the patient's open to their flu shot, then go ahead and introduce the other vaccines that they're due for, because studies show it's very safe to give these at the same time. Dr. Ramirez, do you have any way that you frame conversations around vaccines with patients?

Dr Ramirez: What you just mentioned, I think, is important. Of course, these poor patients that already have the pneumococcal pneumonia and survive, then there's nothing better than to have an advocate than a person that has the disease. We know that with all this, we know this happens with SARS-CoV-2, with pneumococcal pneumonia, and then having a person like this returning, it's going to be very important to tell the story of what happened during the disease. Then I would definitely frame the conversation with the other patients and bring in this patient as a real-life situation. Yes.

Dr. Rockwell: Thank you very much, because this brings us to the end of Part 1 of this series, Burden of Vaccine-Preventable Disease in Older Adults. We've taken a look at the health burden of vaccine-preventable diseases, including RSV, respiratory syncytial virus, pneumococcal disease, and herpes, zoster, or shingles, in older adults.

Dr Ramirez: Then I may say that these are, again, very important infectious diseases because, as we already discussed, it's not only that they have acute consequences. For any one of these diseases, patient can be hospitalized for RSV, for streptococcal pneumonia, we are discussing a high rate of mortality. Then these are three diseases that can produce chronic sequelae.

Dr. Rockwell: From my perspective as an outpatient physician, the more we can vaccinate, the fewer infections we'll see. It will lower health costs in general. Perhaps our health insurance will go down. The burden of work loss due to vaccine-preventable diseases. It'll stop the spread of the infection to others in the community. Super important to prevent the disease from the beginning, just for that burden to the health care system, loss and prevention, then to prevent morbidity, mortality, and hospitalization. Please join us in part two of the series, Updates in Vaccine Development.