Vaccines and Prevention

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Literature review current through June 2024
Last updated June 2024

Educational Objectives:
1. Discuss the indications for different forms of pneumococcal vaccine
2. Review indications and contraindications for the influenza vaccine
3. Review indications for vaccination in patients with splenectomy
4. Review indications and contraindications for the COVID-19 vaccine
5. Review indications and contraindications for the RSV vaccine

Scenario 1:
Mrs. Smith is a 64-year-old woman with diabetes with an additional past medical history of Hodgkin’s Lymphoma in the 1970s s/p mantle radiation, complicated by systolic and restrictive cardiomyopathy with LVEF 30% and radiation pulmonary fibrosis. She is coming to you to establish care and evaluate her chronic dyspnea.

Question 1: Is Mrs. Smith at high risk for pneumonia? What vaccinations would you consider for her?

Mrs. Smith meets criteria to receive the pneumococcal conjugate vaccine (PCV), influenza, and COVID-19 vaccines. There should also be shared decision-making regarding potentially receiving the RSV vaccine.

She is considered at increased risk for pneumonia due to her congestive heart failure and chronic lung disease. Under the current ACIP recommendations, she meets criteria to receive 1 dose of PCV, either PCV20 or PCV15. When PCV15 is used, it should be followed by a dose of PPSV23. ACIP recommends pneumococcal vaccination before age 65 for individuals with alcoholism, chronic heart, liver, or lung disease, chronic renal failure, cigarette smoking, cochlear implant, congenital or acquired asplenia, cerebrospinal fluid leak, diabetes mellitus, generalized malignancy, HIV, Hodgkin disease, immunodeficiency, iatrogenic immunosuppression, leukemia, lymphoma, or multiple myeloma, nephrotic syndrome, solid organ transplant, sickle cell disease, or other hemoglobinopathies.

All persons older than 6 months should receive annual influenza vaccination if they do not have a contraindication (history of severe allergies to a vaccine ingredient or prior flu vaccines), so the influenza vaccine should be recommended to her. Additionally, her cardiopulmonary conditions put her at higher risk for severe illness due to influenza, so vaccination is especially important in her case.
She should also receive one of the available COVID-19 vaccines. Based on her age, she should receive 1 or 2 doses of a COVID-19 vaccine, depending on her previous vaccination status and the vaccine that is administered.

As she is over age 60, shared decision-making regarding the RSV vaccine should also occur. Risk factors for severe RSV disease include cardiopulmonary disease, kidney disorders, liver disorders, neuromuscular disorders, hematologic disorders, diabetes mellitus, immunocompromise, frailty, advanced age (especially >75), and long-term care residents. Studies of these vaccines reported a reduction in symptomatic lower respiratory tract RSV disease by approximately 80% in the first season after vaccination, and 50-75% in the second season after vaccination.

**Question 2: Mrs. Smith has now returned for follow-up and reports that she just turned 65. Does she need any updates on her vaccinations?**

In 2022, the ACIP changed guidance to recommend use of either PCV20 alone or PCV15 in series with PPSV23 for all adults aged ≥65 years. When PCV15 is used, the recommended interval between administration of PCV15 and PPSV23 is ≥1 year. A minimum interval of 8 weeks can be considered for adults with an immunocompromising condition, cochlear implant, or cerebrospinal fluid leak to minimize the risk for IPD caused by serotypes unique to PPSV23 in these vulnerable groups. For Ms. Smith, it is important to let her know that her chronic heart and lung disease, as well as her diabetes, puts her at increased risk. 24 per 100,000 US adults get pneumococcal pneumonia each year, accounting for 9.3% of community-acquired pneumonia hospitalizations.
Question 3: What is the recommended pneumococcal vaccination schedule for adults greater than 65?

<table>
<thead>
<tr>
<th>Medical indication group</th>
<th>Specific underlying medical condition</th>
<th>19–64</th>
<th>≥65</th>
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<tbody>
<tr>
<td>None</td>
<td>None</td>
<td>None</td>
<td>1 dose of PCV20 or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 years later*</td>
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<tr>
<td>Underlying medical conditions or other risk factors</td>
<td>Alcoholism</td>
<td>1 dose of PCV20 or 1 dose of PCV15 followed by a dose of PPSV23 ≥1 years later*</td>
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<tr>
<td></td>
<td>Chronic heart disease†</td>
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<td>Chronic liver disease†</td>
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<td>Chronic lung diseases†</td>
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<td>Cigarette smoking</td>
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<td>Diabetes mellitus</td>
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<td>Cochlear implant</td>
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<td>CSF leak</td>
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<td>Congenital or acquired asplenia</td>
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<td>Sickle cell disease or other hemoglobinopathies</td>
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<td></td>
<td>Chronic renal failure**</td>
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<td></td>
<td>Congenital or acquired immunodeficiencies***</td>
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<td></td>
<td>Generalized malignancy**</td>
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<td>HIV infection**</td>
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<td>Hodgkin disease**</td>
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<td>Latrogenic immunosuppression**</td>
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<td>Leukemia**</td>
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<td>Lymphoma**</td>
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<td>Multiple myeloma**</td>
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<td>Nephrotic syndrome**</td>
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<td>Solid organ transplant**</td>
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</table>

**Abbreviations:** CSF = cerebrospinal fluid; PCV15 = 15-valent pneumococcal conjugate vaccine; PCV20 = 20-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.
* Adults with immunocompromising conditions, cochlear implant, or CSF leak might benefit from shorter intervals such as ≥8 weeks. These vaccine doses do not need to be repeated if given before age 65 years.
† Includes congestive heart failure and cardiomyopathies.
‡ Adults with Immunocompromising conditions, cochlear implant, or CSF leak might benefit from shorter intervals such as ≥8 weeks.
§ Includes chronic obstructive pulmonary disease, emphysema, and asthma.
** Indicates Immunocompromising conditions.
†† Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).
§§ Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.

Question 4: Mrs. Smith asks if she should be receiving the influenza vaccination. Is she in a high-priority group?

Mrs. Smith has several indications for the influenza vaccination. Adults over age 50 are high priority. Furthermore, she has chronic respiratory and cardiac conditions. Even though at the current time concern is highest for COVID-19 infection, it is important to acknowledge the long history of influenza as a common cause of serious illness and the likelihood that it will re-emerge in the future. Since she is 65, it is reasonable to give the high dose influenza vaccination. The following are high priority groups:

a. Populations at Higher Risk for Medical Complications Attributable to Severe Influenza
   1. Children 6 through 59 months
   2. Persons ≥50 years
   3. Those with chronic pulmonary (including asthma) or cardiovascular (except isolated hypertension), renal, hepatic, neurologic, hematologic, or metabolic disorders (including diabetes mellitus)
   4. Immunocompromised due to any cause (including immunosuppression caused by medications or by HIV infection);
   5. Pregnant women
   6. Children and adolescents receiving aspirin or salicylates
7. Nursing home/long-term care facility residents
8. American Indians/Alaska Natives

b. People who live with or care for those at risk for Influenza-related complications:
   1. Health care personnel
   2. Household contacts (including children) and caregivers of children <5 years and adults ≥50 years old
   3. Household contacts (including children) and caregivers of persons with high-risk medical conditions

**Question 5: What is the high dose influenza vaccination? What is the difference between it and the regular influenza vaccination? Are there any other flu vaccines I should know about?**

In the past, both trivalent and quadrivalent influenza vaccines were available, and quadrivalent was superior. As of the 2023-2024 season, all available influenza vaccines in the USA were quadrivalent.

For adults over age 65, high-dose or regular-dose adjuvanted influenza vaccination is recommended. Adjuvanted vaccination includes the same amount of antigen as the regular quadrivalent vaccine but includes an adjuvant to stimulate a stronger immune response. High-dose influenza vaccines contain 4 times the amount of influenza antigen as regular vaccines. These vaccines stimulate a stronger immune response, and lead to more side effects after vaccination (such as headache, myalgias, injection site pain, etc), but also stimulate more effective immune responses in older adults. For patients younger than 65, non-adjuvanted regular-dose tetravalent vaccines are recommended.

Currently available flu vaccines are propagated either in eggs or in cell culture (canine kidney cells).

Available influenza vaccines include both live attenuated nasal spray vaccines, and inactivated (killed) vaccines. The live attenuated vaccines should only be used in patients ages 2-49 without a contraindication (such as immunocompromise or pregnancy, etc).

**Question 6: Mrs. Smith has an egg allergy. What are her influenza vaccine options?**

The guidelines for influenza vaccination in patients with egg allergies were updated in August 2023 for the 2023-2024 season. Previously, patients with egg allergies were recommended to receive influenza vaccination in an inpatient or outpatient setting supervised by a health care provider. As of August 2023, egg allergy alone does not necessitate any difference in vaccination recommendation, regardless of the severity of the egg allergy. Any influenza vaccine, including egg-based vaccines, can be used. A systematic review and GRADE of evidence supported this recommendation, available at: https://www.cdc.gov/vaccines/acip/recs/grade/influenza-egg-allergy.html

**Question 7: Mrs. Smith also reports that she had a splenectomy during her treatment for lymphoma. Now what changes to her care are needed?**

All patients who are anatomically or functionally asplenic are at high risk for encapsulated organisms including *S. pneumoniae*, *H. influenzae* and *N. meningitidis*. Ideally these
patients are vaccinated > 2 weeks prior to splenectomy; if not possible they can be vaccinated as soon as they are stable after the procedure. In Mrs. Smith’s case, we need to confirm that she received this series of vaccines.

For S. pneumoniae, asplenic individuals should receive either a single dose of PCV20 or PCV15 followed by PPSV23 >1 year later (may consider >8 weeks later).

Americans over the age of 5 years old are almost entirely immune to H. influenzae type B. Nevertheless, all patients >15 months who are undergoing splenectomy and who are not immunized should receive one dose of Hib vaccine.

The ACIP recommends vaccination against N. menigitidis with meningococcal quadrivalent conjugate vaccine (Menveo or Menactra) AND serotype B vaccination (Trumenba or Bexsero) for patients >2 years of age.

Also, asplenic individuals are at risk for fulminant sepsis from Capnocytophaga canimorsus, severe babesiosis, and should not receive the live active influenza vaccination. They CAN receive other live vaccinations.

**Question 8: Mrs. Smith tells you she is about to become a grandmother. In addition to what has already been discussed, what other vaccination might she consider?**

In addition to the previously discussed influenza vaccination, you may recommend a Tdap vaccine. Babies are at risk for serious complications from Influenza and Pertussis. They are not eligible for influenza vaccination until 6 months of age, and are not eligible for Pertussis vaccination until 2 months of age.

a. Tdap vaccination recommendations:
   1. All pregnant women during each pregnancy
   2. Adults over age 19 who have not been vaccinated to address waning pertussis immunity. This should be repeated every 10 years.

**Question 9: What about the COVID-19 vaccine?**

COVID-19 vaccination is recommended for all people 6 months of age and older. At the time of this writing in the Spring 2024, the recommendations for ideal protection depend on whether the patient is considered immunocompetent, or moderately to severely immunosuppressed. According to the CDC, examples of patients who may be considered moderately to severely immunosuppressed include patients who fit the following descriptions:

- Active treatment for solid tumor and hematologic malignancies
- Hematologic malignancies associated with poor responses to COVID-19 vaccines regardless of current treatment status (e.g., chronic lymphocytic leukemia, non-Hodgkin lymphoma, multiple myeloma, acute leukemia)
- Receipt of solid-organ transplant or an islet transplant and taking immunosuppressive therapy
- Receipt of chimeric antigen receptor (CAR)-T-cell therapy or hematopoietic cell transplant (HCT) (within 2 years of transplantation or taking immunosuppressive therapy)
• Moderate or severe primary immunodeficiency (e.g., common variable immunodeficiency disease, severe combined immunodeficiency, DiGeorge syndrome, Wiskott-Aldrich syndrome)

• Advanced HIV infection (people with HIV and CD4 cell counts less than 200/mm³, history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV) or untreated HIV infection

• Active treatment with high-dose corticosteroids (i.e., 20 mg or more of prednisone or equivalent per day when administered for 2 or more weeks), alkylating agents, antimetabolites, transplant-related immunosuppressive drugs, cancer chemotherapeutic agents classified as severely immunosuppressive, tumor necrosis factor (TNF) blockers, and other biologic agents that are immunosuppressive or immunomodulatory (e.g., B-cell-depleting agents)

This list is not exhaustive, and a thoughtful approach should be taken when classifying an individual patient. Additional resources to help classify patients’ degree of immunosuppression include ACIP’s General Best Practice Guidelines for Immunizations, the CDC Yellow Book, and the Infectious Diseases Society of America policy statement, 2013 IDSA Clinical Practice Guideline for Vaccination of the Immunocompromised Host.

For patients who are not moderately or severely immunocompromised, similar to this patient, the recommended dosing schedule is as follows:

<table>
<thead>
<tr>
<th>TABLE 1. Recommended COVID-19 vaccination schedule for persons aged 6 months–4 years who are not moderately or severely immunocompromised,* by COVID-19 vaccination history — United States, September 2023</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous COVID-19 vaccination history (before updated mRNA vaccine)</td>
</tr>
<tr>
<td>Unvaccinated</td>
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<tr>
<td></td>
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<tr>
<td>Received Moderna vaccine</td>
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<tr>
<td>Received Pfizer-BioNTech vaccine</td>
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</tbody>
</table>

* Additional clinical considerations, including detailed schedules and tables by age and vaccination history for those who are and are not moderately or severely immunocompromised, are available. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

For patients who are not moderately or severely immunocompromised, similar to this patient, the recommended dosing schedule is as follows:

<table>
<thead>
<tr>
<th>TABLE 2. Recommended COVID-19 vaccination schedule for persons aged ≥5 years who are not moderately or severely immunocompromised,* by COVID-19 vaccination history — United States, September 2023</th>
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</thead>
<tbody>
<tr>
<td>COVID-19 vaccination history before updated vaccine</td>
</tr>
<tr>
<td>Unvaccinated</td>
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<tr>
<td>Novavax (aged ≥12 yrs only)</td>
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<tr>
<td>Received ≥1 COVID-19 vaccine dose, including Moderna, Pfizer-BioNTech, Novavax (aged ≥12 yrs only), or Janssen</td>
</tr>
<tr>
<td>Johnson &amp; Johnson (aged ≥18 yrs only)</td>
</tr>
<tr>
<td>Novavax (aged ≥12 yrs only)</td>
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</tbody>
</table>

* Additional clinical considerations, including detailed schedules and tables by age and vaccination history for those who are and are not moderately or severely immunocompromised, are available. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Source: US Department of Health and Human Services | Centers for Disease Control and Prevention | MMWR | October 20, 2023 | Vol. 72 | No. 42 (Regan JJ et al. in references).

These recommendations are likely to evolve as more is learned about the optimal boosting strategy or as vaccines for variants undergo further study. As of Spring 2024, all people 65 and older are recommended to have 1 additional dose of the 2023-2024 formula of a COVID-19 vaccine (Moderna, Pfizer-BioNTech, or Novavax).
A person is considered fully vaccinated against COVID-19 ≥2 weeks after receipt of the second dose in a 2-dose series (Pfizer-BioNTech, Moderna, or Novavax). Immunity wanes with time.

**Question 10: Mrs. Smith asks you about the differences among the different manufactured COVID vaccines available in the USA.**

The 2023-2024 formulation for all available COVID-19 vaccines (Moderna, Novavax, and Pfizer-BioNTech) are monovalent vaccines based on the Omicron XBB.1.5 sub-lineage of SARS-CoV-2. The vaccines based on the original strains of SARS-CoV-2 should no longer be used.

The Pfizer-BioNTech and Moderna vaccines are lipid nanoparticle-formulated, nucleoside-modified mRNA vaccines encoding the prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19. Novavax is also based on the spike protein, but it is a protein subunit vaccine. It is composed of recombinant, purified spike protein and an adjuvant derived from saponin extracts of the soap bark tree. The Janssen vaccine, which is no longer recommended in the United States, is a recombinant replication-incompetent adenovirus type 26 (Ad26) vector encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2. None of the currently authorized COVID-19 vaccines are live virus vaccines.

According to the CDC, **none of the COVID-19 vaccines affect or interact with our DNA** and the following are **not** included in the vaccines:

- **No preservatives** such as thimerosal or mercury or any other preservatives.
- **No antibiotics** such as sulfonamide or any other antibiotics.
- **No medicines or therapeutics** such as ivermectin or any other medications.
- **No tissues** such as aborted fetal cells, gelatin, or any materials from any animal.
- **No food proteins** such as eggs or egg products, gluten, peanuts, tree nuts, nut products, or any nut byproducts. (COVID-19 vaccines are not manufactured in facilities that produce food products).
- **No metals** such as iron, nickel, cobalt, titanium, or rare earth alloys. They also do not have any manufactured products like microelectronics, electrodes, carbon nanotubes or other nanostructures, or nanowire semiconductors.
- **No latex.** The vial stoppers used to hold the vaccine also do not contain latex.

All three of the currently approved vaccines reported efficacy of 95-100% for preventing severe COVID-19 disease in their original formulations. Preclinical evidence was used to support the updated formulations, which are based on more recently circulating strains of COVID-19.

**Question 11: She also asks you about vaccine co-administration. What do you tell her regarding recommendations for receiving more than one vaccine at a time?**

According to the CDC, the COVID-19 vaccine may be co-administered with other vaccines, including influenza and RSV vaccines. Data on coadministration with pneumococcal vaccines is emerging, and coadministration is not discouraged. Influenza and pneumococcal vaccinations remain effective when given together, without an increase in adverse reactions.

PCV and PPSV vaccines should not be given together. When both are given (e.g. PCV15 then PPSV23), the PPSV23 should be given 1+ years after PCV. An alternative is a single dose of PCV-20.
References:


11. Preventing Tetanus, Diphtheria, and Pertussis Among Adults: Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and Recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for Use of Tdap Among Health-Care Personnel. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5517a1.html


