

Dillon Cason, MD

Department of Internal Medicine,
Lewis Katz School of Medicine,
Temple University, Philadelphia, PA

Paul Williams, MD, FACP

Section of General Internal Medicine,
Lewis Katz School of Medicine,
Temple University Hospital,
Philadelphia, PA

Vaccinating the unvaccinated adult

ABSTRACT

The percent of US children who are not vaccinated has been increasing, and so have the rates of communicable diseases. As the unvaccinated and undervaccinated population ages, practitioners are likely to see more adult patients who have never been vaccinated. This article reviews the recommendations for vaccinating previously unvaccinated patients and addresses potential barriers and concerns adult patients may have about vaccines.

KEY POINTS

The tetanus, diphtheria, and acellular pertussis (Tdap); mumps, measles, and rubella (MMR); and varicella vaccines are recommended for all unvaccinated adults.

Other vaccinations are not routinely recommended unless the patient meets certain criteria, eg, travels internationally, is a healthcare professional, or has no spleen.

Just over 7 in 10 children receive all the recommended vaccinations.

A 24-YEAR-OLD WOMAN with no known medical history presents at our outpatient clinic to discuss getting vaccinated for the first time. She hopes to get the mumps vaccine because of outbreaks at Temple University near her home in Philadelphia, PA. Her parents did not have her vaccinated as a child because of fears of vaccines causing illnesses, and she did not tell them that she wanted to get vaccinated, as she believed it would cause family strife.

She asks about our recommendations for vaccines for her.

■ INCREASING NATIONAL OUTBREAKS AND UNVACCINATED CHILDREN

In the United States, cases of communicable diseases are increasing, even those once considered eliminated. For example, from January 1 to August 1, 2019, 1,172 cases of measles in 30 states were reported to the US Centers for Disease Control and Prevention (CDC), the highest number since 1992, and drastically higher than the 372 cases reported in all of 2018.¹ The number of cases of mumps has also increased significantly during the past several years.²

As cases of measles and similar communicable diseases increase, the percentage of children who are unvaccinated is also increasing. Fortunately, more than 90% of US children age 19 to 35 months have received the vaccines for polio, for measles, mumps, and rubella (MMR), and for hepatitis B, according to the 2017 National Immunization Survey-Child (NIS-Child),³ and more than 7 in 10 children received all the recommended vaccinations. Unfortunately, 1.3% of toddlers had received no vaccinations by 24 months of age, up from 0.3% in 2001.³

Vaccination rates were lowest in uninsured children, those insured by Medicaid, and those residing in more rural areas. While only 2.8% of children were reported as uninsured, they

TABLE 1

Vaccinations recommended for unvaccinated adults

Vaccine	Dosing	Contraindications	Precautions
Tetanus, diphtheria, acellular pertussis (TDaP)	3 doses: 1–2 months between doses 1 and 2 and 6–12 months between doses 2 and 3 Give TD booster every 10 years after initial regimen completed	Prior severe allergic reaction to the vaccine or its components	Moderate or severe acute illness with or without fever For pertussis-containing vaccines only, in patients with progressive or unstable neurologic disorder, uncontrolled seizures, or previous encephalopathy, defer use until a treatment regimen has been established and the condition stabilizes
Measles, mumps, rubella (MMR)	Give 1 dose if born in 1957 or later Give 2 doses (no sooner than 4 weeks after initial dose) to high-risk groups: • Any healthcare personnel • Students entering college • International travelers If pregnant, MMR should be given postpartum	Prior severe allergic reaction to the vaccine or its components Pregnancy or possible pregnancy within 4 weeks Severe immunodeficiency (hematologic and solid tumors, active chemotherapy, congenital immunodeficiency, HIV with severe immunocompromise)	Moderate or severe acute illness with or without fever If blood, plasma, and/or immunoglobulin were given in the last 11 months, follow the ACIP best practices ¹⁴ History of thrombocytopenia or thrombocytopenic purpura
Varicella (chickenpox)	Give 2 doses: second dose 4–8 weeks after first dose; if delayed, do not start over, just give second dose	Prior severe allergic reaction to the vaccine or its components Pregnancy or possible pregnancy within 4 weeks People who are on long-term immunosuppression or are immunocompromised Vaccine can be considered in patients with CD4 count ≥ 200 cells/mm ³	Moderate or severe acute illness with or without fever If blood, plasma, and/or immunoglobulin were given in last 11 months, follow ACIP best practices ¹⁴ Recipient of specific antivirals (acyclovir, famciclovir, valacyclovir) 24 hours before vaccination Use of aspirin-containing products as there is an increased risk of Reye syndrome

ACIP = Advisory Committee on Immunization Practices (part of the US Centers for Disease Control and Prevention); HIV = human immunodeficiency virus

Adapted from reference 16.

made up 17.2% of all unvaccinated children.³

There is evidence that most cases of vaccine-preventable diseases were in the unvaccinated population. A 2016 review of 18 measles studies found that 59.2% of cases (574 of 970 in which vaccination records were available) were in patients who were completely unvaccinated despite being vaccine-eligible, and many more were undervaccinated. Of the patients who were not vaccinated, 70.6% (405 of 574) had nonmedical exemptions to vaccination for various religious or philosophical reasons.⁴

In early 2019, a measles outbreak occurred in Clark County, Washington, with 53 re-

ported cases. Of the patients with measles, 47 (89%) were unvaccinated, 5 had unverified vaccination status, and just 1 had confirmed vaccination. The state of Washington is 1 of 15 US states that allows a philosophical exemption to vaccinations.⁵ For the 2017–2018 school year, nearly 5% of children enrolled in Washington schools were not vaccinated because of philosophical exemptions, with numbers even higher in Clark County (7.9%).⁶

■ WHY ARE VACCINATION RATES SO LOW?

Several reasons account for the rising rates of nonvaccination and undervaccination.

TABLE 2

Vaccinations not routinely recommended for unvaccinated adults

Vaccine	Indications	Dosing	Contraindications
Hepatitis A	<ul style="list-style-type: none"> • Desire to be protected from hepatitis A virus (HAV) • Travel or work outside of United States • Chronic liver disease, use of injected or noninjected drugs, homeless, receiving clotting-factor concentrates, works with HAV in laboratory, food handlers when appropriate • Close contact with international adoptee from country where HAV is endemic during the first 60 days after adoptee's arrival 	2 doses, 6–18 months apart depending on brand If second dose is delayed, do not start over, just give dose	Prior severe allergic reaction to the vaccine or its components Cautions: Moderate or severe acute illness with or without fever
Hepatitis B	<ul style="list-style-type: none"> • Wants to be protected from hepatitis B virus • Has close household contact of hepatitis B surface antigen-positive people, chronic liver disease, injects drugs, sexually active with multiple partners, male who has sex with men, human immunodeficiency virus-positive, hemodialysis patients or may soon need dialysis, diabetes and younger than 60 • Is a healthcare worker or person exposed to blood, inmates of long-term correctional facilities 	Heplisav-B: 2 doses, 1 month apart Engerix-B and Recombivax HB: 3 doses (1 mL each) at 0, 1, 6 months If patient is receiving hemodialysis or is immunocompromised: <ul style="list-style-type: none"> • Recombivax HB: 1 dose of 4 mL at 0, 1, 6 months • Engerix-B: 2 doses of 2 mL given simultaneously at 0, 1, 2, 6 months • Heplisav-B: 2 doses 1 month apart If schedule delayed, do not start over, continue from where schedule was interrupted	Prior severe allergic reaction to the vaccine or its components Cautions: Moderate or severe acute illness with or without fever
<i>Haemophilus influenzae</i> type B	<ul style="list-style-type: none"> • Anatomic or functional asplenia • Undergoing elective splenectomy • Received a hematopoietic stem cell transplant (HSCT) 	Give 1 dose of any <i>H influenzae</i> type B conjugate vaccine If received HSCT, 3 doses at least 4 weeks apart beginning 6–12 months after transplant	Prior severe allergic reaction to the vaccine or its components Cautions: Moderate or severe acute illness with or without fever
Inactivated polio	Plans to travel to areas where exposure to wild-type virus is likely	0, 2, 4, 16 months 4–6 year schedule with minimum interval of 4 weeks between doses	Prior severe allergic reaction to the vaccine or its components Cautions: Moderate or severe acute illness with or without fever; pregnancy
Meningococcal conjugate	<ul style="list-style-type: none"> • Student younger than age 21 living in residence hall • Has anatomic or functional asplenia, is HIV-positive, or has persistent complement component deficiency • Travel to countries where meningococcal disease is endemic • Microbiologist routinely exposed to isolates of <i>Neisseria meningitidis</i> 	If college student age 19–21 living in residence hall, give 1 dose If asplenic, give 2 initial doses at 0 and 2 months with booster every 5 years If traveling or has exposure risk, give 1 initial dose with booster every 5 years	Prior severe allergic reaction to the vaccine or its components Cautions: Moderate or severe acute illness with or without fever
Meningococcal serogroup B	<ul style="list-style-type: none"> • Anatomic or functional asplenia or persistent complement component deficiency • Microbiologist routinely exposed to isolates of <i>N meningitidis</i> • At risk because of a serogroup B meningococcal outbreak 	Bexsero at 0 and 1 months OR Trumenba at 0, 1–2, and 6 months	Prior severe allergic reaction to the vaccine or its components Cautions: Moderate or severe acute illness with or without fever

Adapted from reference 16.

Autism link discredited, but some people still believe it

Foremost in the minds of many vaccine-hesitant parents is a controversial case series published in 1998 that suggested that the MMR vaccine may lead to behavioral regressions and developmental disorders, including autism.⁷ The case series itself was significantly flawed in having a small sample size of 12 patients, an uncontrolled design, and conclusions that were largely speculative.

There was an almost immediate backlash, and several epidemiologic studies refuted the series' conclusions.^{8–10} Shortly afterward, 10 of the 12 coauthors offered a retraction, concluding that no link existed between the vaccine and developmental disorders, including autism. There were further ethical implications after it was revealed that the lead author failed to disclose that he received funding from lawyers involved in lawsuits against vaccine manufacturers.

In 2010, the publisher (*Lancet*) officially retracted the original article,¹¹ and the lead author was removed from the UK medical registry,¹² but by then the damage was done. For example, a review of the 2011 NIS-Child (N = 12,259) found that 21.4% of parents of unvaccinated children and 9.9% of parents of children who received at least 1 MMR dose believed that the vaccine is linked to autism.¹³

Religious and philosophical objections

Many state vaccination laws allow religious exemptions or philosophical exemptions to vaccination.⁵

Lack of access is probably the biggest reason

A 2015 multivariable analysis using data from the 2010–2013 NIS-Child and NIS-Teen suggested that reasons other than negative vaccine-related beliefs accounted for most of the unvaccinated children and adolescents.¹³ In fact, the authors found that 74.6% of parents of unvaccinated children did not have negative opinions of vaccines, and only 34.6% refused vaccines. What they did find was that compared with vaccinated children, unvaccinated children were more likely to be uninsured, to be of lower socioeconomic class, and to have unmarried parents.

This analysis suggests that missed opportunities to vaccinate are more common than parents overtly refusing vaccination. Reviewing a patient's vaccination records at every visit as well as sending patients reminders via cell phone have been shown to improve immunization rates and combat missed vaccine opportunities.¹³

■ Tdap, MMR, AND VARICELLA FOR ALL UNVACCINATED ADULTS

Our patient had asked which vaccines we would recommend for her as a vaccine-naïve adult. The CDC has comprehensive vaccination recommendations on its website¹⁴; however, they do not speak directly to the growing population of unvaccinated adults. The Immunization Action Coalition, a nonprofit organization partially funded by the CDC, has recommendations for adult vaccinations that are more simplified.¹⁵

For our patient, a few vaccines are absolutely recommended (**Table 1**), and some are generally not recommended except under certain circumstances (**Table 2**).¹⁶ Only the tetanus, diphtheria, and acellular pertussis (Tdap), MMR, and varicella vaccines are recommended for all unvaccinated adults.

The Tdap vaccine is given in a 3-dose series, with the second dose 1 to 2 months after the first dose and the third dose 6 to 12 months after the second dose. A tetanus booster should be given every 10 years after the series is completed.

The MMR vaccine is given only if the patient was born in 1957 or later. It is given as a single dose unless the patient works in healthcare, is a student entering college, or travels internationally. In those situations, the patient should receive a second dose 4 weeks after the first dose.

The varicella vaccine is given as a 2-dose series, with the second dose 4 to 8 weeks after the initial dose.

All 3 of the recommended vaccinations can be given safely at the same time.¹⁷

■ OTHER VACCINES, FOR SOME PEOPLE

The remaining vaccinations are not routinely recommended unless the patient meets certain criteria, eg, travels internationally, is a

Only the Tdap, MMR, and varicella vaccines are recommended for all unvaccinated adults

healthcare professional, or is asplenic (Table 2). Patients can receive those vaccinations when specifically requested. Additional vaccinations including influenza, human papillomavirus infection, and pneumococcal vaccines should be encouraged, if indicated.

Providers should also check for contraindications to the live attenuated vaccines (ie, MMR, varicella, herpes zoster, rotavirus, yellow fever, and intranasal influenza vaccines). These vaccines should be avoided in patients who are pregnant or may become pregnant within 4 weeks after administration; these patients should be counseled to use contraceptives for 1 month after vaccination.

Live attenuated vaccines should also be avoided in patients with severe immunodeficiency, including hematologic and solid malignancies, active chemotherapy, congenital immunodeficiencies, and human immunodeficiency virus. Other less common examples of immunosuppression are listed on the CDC website.¹⁸

■ ADDRESSING PATIENT CONCERNS

Patients presenting to discuss vaccinations may have questions, concerns, and anxieties pertaining to the vaccines. They may be concerned about acute postvaccination reactions as well as potential long-term adverse reactions, regardless of their vaccination history. For these patients, it is important to maintain a calming presence while addressing each question and concern honestly. It can be helpful to start by asking, “What specific questions do you have about the vaccines?”

Patients should be assured that they cannot get the disease from the vaccine. They should also be informed that reactions such as soreness and redness at the injection site and low-grade fever, if they occur, are not serious, and usually last no longer than 48 hours.¹⁹ Even patients with known egg allergy can be vaccinated without restriction or observation, as the rate of anaphylaxis is just over 1 in 1 million.²⁰

If patients have questions about vaccine preservatives such as aluminum and mercury-containing thimerosal, you can explain that those preservatives help prevent vaccine contamination or growth of microbes, as

well as allow for multiuse vials. If patients are concerned that preservatives in vaccines can cause diseases such as autism or can lead to mercury poisoning, you can inform them that multiple international studies have found preservatives to be safe in both childhood and adult vaccines.^{21,22} More information on addressing reasons for vaccine reluctance was published in the *Cleveland Clinic Journal of Medicine* in December 2019.²³

With the increasing use of single-dose containers, thimerosal is used much less frequently. In fact, reformulations have focused on significantly reducing mercury-containing preservatives as strictly precautionary measures, not because of safety concerns. If a patient is still hesitant, recommended vaccines are available in formulations that do not contain thimerosal.²⁴

Other patients may be concerned about receiving multiple vaccinations at the same time. As we have mentioned, data show that the recommended vaccinations can be administered together safely. If necessary, vaccinations can be given at different appointments and time intervals based on the patient's specific preferences and availability. There are many online resources for patients that discuss common concerns and misconceptions in simplified language, notably the CDC and the Immunization Action Coalition.^{25–27}

■ VACCINATION IN THE TIME OF COVID-19

The current COVID-19 pandemic and subsequent rapid development and availability of effective COVID-19 vaccines have amplified the discussions around the safety and necessity of adult vaccination. Even before this pandemic, the World Health Organization recognized vaccine hesitancy as a top threat to global health.²⁸

The factors that lead to hesitancy over COVID-19 vaccination are similar to those with other vaccines, but also include the rapidity of vaccine development, as well as political factors that reflect the larger political polarization of the pandemic.²⁹

In a large study of adult Americans,³⁰ over 20% of respondents reported vaccine hesitancy, with racial and ethnic minorities having higher reported vaccine hesitancy in group

Online resources for patients about common concerns and misconceptions, in simplified language, include the CDC and the Immunization Action Coalition

comparisons, as did patients living in rural areas, those with lower household incomes, and those with lower levels of education.

Focus group discussions with Black participants living in communities of high COVID-19 prevalence suggested that vaccine skepticism was driven by a number of factors, including historical mistreatment of the Black community, the accelerated timeline of vaccine development, and limited data on long-term side effects.³¹ These same focus group discussions also demonstrated that acceptance increased if the recommendation for vaccination came from a trusted healthcare provider, a finding that has also been seen in other studies.³²

Ultimately, at the individual clinician level, concerns over the COVID-19 vaccines should be addressed in much the same way as concerns over other vaccines—by eliciting questions and concerns in a nonjudgmental,

patient-centered way, and addressing the concerns compassionately and honestly. In order to address COVID-19 vaccination hesitancy, clinicians will need to be equipped with current, accurate information, which will likely come from both self-directed learning and institutional support and training.²⁹

CASE CONCLUSION

After counseling and reassurance, our patient successfully received the 3 recommended vaccines (MMR, Tdap, and varicella) without issue and is scheduled to return to complete the regimens. The patient agreed to devote time at future visits to discuss human papillomavirus vaccination and to consider an influenza vaccination when it is due.

DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

REFERENCES

- Centers for Disease Control and Prevention. Measles cases and outbreaks. www.cdc.gov/measles/cases-outbreaks.html. Accessed April 7, 2021.
- Centers for Disease Control and Prevention. Mumps cases and outbreaks. www.cdc.gov/mumps/outbreaks.html. Accessed April 7, 2021.
- Hill HA, Elam-Evans LD, Yankey D, Singleton JA, Kang Y. Vaccination coverage among children aged 19–35 months—United States, 2017. *MMWR Morb Mortal Wkly Rep* 2018; 67(40):1123–1128. doi:10.15585/mmwr.mm6740a4
- Phadke VK, Bednarczyk RA, Salmon DA, Omer SB. Association between vaccine refusal and vaccine-preventable diseases in the United States: a review of measles and pertussis. *JAMA* 2016; 315(11):1149–1158. doi:10.1001/jama.2016.1353
- National Conference of State Legislatures. States with religious and philosophical exemptions from school immunization requirements. January 29, 2021. www.ncsl.org/research/health/school-immunization-exemption-state-laws.aspx. Accessed April 7, 2021.
- Nelson R. US measles outbreak concentrated among unvaccinated children. *Lancet Infect Dis* 2019; 19(3):248. doi:10.1016/S1473-3099(19)30074-X
- Wakefield AJ, Murch SH, Anthony A, et al. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 1998; 351(9103):637–641. doi: 10.1016/S0140-6736(97)11096-0. Retraction in: *Lancet* 2010; 375(9713):445. doi:10.1016/S0140-6736(10)60175-4
- Taylor B, Miller E, Farrington CP, et al. Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association. *Lancet* 1999; 353(9169):2026–2029. doi:10.1016/S0140-6736(99)01239-8
- Dales L, Hammer SJ, Smith NJ. Time trends in autism and in MMR immunization coverage in California. *JAMA* 2001; 285(9):1183–1185. doi:10.1001/jama.285.9.1183
- Murch SH, Anthony A, Casson DH, et al. Retraction of an interpretation. *Lancet* 2004; 363(9411):750. doi:10.1016/S0140-6736(04)15715-2
- Editors of *The Lancet*. Retraction—Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. *Lancet* 2010; 375(9713):445. doi:10.1016/S0140-6736(10)60175-4
- BBC News. MMR doctor struck from register. May 24, 2010. news.bbc.co.uk/2/hi/health/8695267.stm. Accessed April 7, 2021.
- Smith PJ, Marcuse EK, Seward JF, Zhao Z, Orenstein WA. Children and adolescents unvaccinated against measles: geographic clustering, parents' beliefs, and missed opportunities. *Public Health Rep* 2015; 130(5):485–504. doi:10.1177/003335491513000512
- Centers for Disease Control and Prevention. ACIP vaccine recommendations and guidelines. www.cdc.gov/vaccines/hcp/acip-recs/index.html. Accessed April 7, 2021.
- Immunization Action Coalition. Vaccinations for adults. www.immunize.org/catg.d/p4030.pdf. Accessed April 7, 2021.
- Immunization Action Coalition. Summary of recommendations for adult immunization (age 19 years and older). www.immunize.org/catg.d/p2011.pdf. Accessed April 7, 2021.
- Centers for Disease Control and Prevention. Timing and spacing of immunobiologics. <https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/timing.html>. Accessed April 7, 2021.
- Centers for Disease Control and Prevention. General recommendations on immunization. <https://www.cdc.gov/vaccines/pubs/pink-book/genrec.html>. Accessed April 7, 2021.
- Centers for Disease Control and Prevention. Possible side effects from vaccines. www.cdc.gov/vaccines/vac-gen/side-effects.htm. Accessed April 7, 2021.
- Centers for Disease Control and Prevention. Flu vaccine and people with egg allergies. www.cdc.gov/flu/prevent/egg-allergies.htm. Accessed April 7, 2021.
- Ball LK, Ball R, Pratt RD. An assessment of thimerosal use in childhood vaccines. *Pediatrics* 2001; 107(5):1147–1154. doi:10.1542/peds.107.5.1147
- Hviid A, Stellfeld M, Wohlfahrt J, Melbye M. Association between thimerosal-containing vaccine and autism. *JAMA* 2003; 290(13):1763–1766. doi:10.1001/jama.290.13.1763
- Mossad SB. How to respond to flu vaccine doubters. *Cleve Clin J Med* 2019; 86(12):782–788. doi: 10.3949/ccjm.86a.19139
- US Food and Drug Administration. Thimerosal and vaccines. <https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/>

- thimerosal-and-vaccines. Accessed April 7, 2021.
25. **Centers for Disease Control and Prevention.** Common vaccine safety questions and concerns. <https://www.cdc.gov/vaccinesafety/concerns/index.html>. Accessed April 7, 2021.
26. **Centers for Disease Control and Prevention.** Making the vaccine decision: addressing common concerns. <https://www.cdc.gov/vaccines/parents/why-vaccinate/vaccine-decision.html>. Accessed April 7, 2021.
27. **Immunization Action Coalition.** Handouts: topic index. <https://www.immunize.org/handouts/vaccine-questions.asp>. Accessed April 7, 2021.
28. **World Health Organization.** Ten threats to global health in 2019. <https://www.who.int/news-room/spotlight/ten-threats-to-global-health-in-2019>. Accessed April 7, 2021.
29. **Finney Rutten LJ, Zhu X, Leppin AL, et al.** Evidence-based strategies for clinical organizations to address COVID-19 vaccine hesitancy. *Mayo Clin Proc* 2021; 96(3):699–707. doi:10.1016/j.mayocp.2020.12.024
30. **Khubchandani J, Sharma S, Price JH, Wiblishauser MJ, Sharma M, Webb FJ et al.** COVID-19 vaccination hesitancy in the United States: a rapid national assessment. *J Community Health* 2021; 46(2):270–77. doi:10.1007/s10900-020-00958-x
31. **Momplaisir F, Haynes N, Nkwihoreze H, Nelson M, Werner RM, Jem-mott J.** Understanding drivers of coronavirus disease 2019 vaccine hesitancy among Blacks. *Clin Infect Dis* 2021; 2021 Feb 9;ciab102. Online ahead of print. doi:10.1093/cid/ciab102
32. **Reiter PL, Pennell ML, Katz ML.** Acceptability of a COVID-19 vaccine among adults in the United States: how many people would get vaccinated? *Vaccine* 2020; 38(42):6500–6507. doi:10.1016/j.vaccine.2020.08.043

Address: Dillon Cason, MD, Department of Internal Medicine, Temple University Health System Inc., 3401 N Broad Street, Philadelphia, PA 19140; dillon.cason@tuhs.temple.edu