Vaccines for Health Care Personnel

Melanie D. Swift, MD, MPH, and Amy J. Behrman, MD

Abstract

Medical Center Occupational Health (MCOH) programs must protect health care personnel (HCP) against the occupational risk of vaccine-preventable diseases. This thematic review outlines the rationale for the use of recommended vaccines in HCP; summarizes the available evidence regarding vaccine effectiveness, administration, and assessment of immunity; and provides guidance for MCOH programs navigating challenging situations.

 ■ Mayo Clin Proc. 2019;94(10):2127-2141

> "For at first, neither were the physicians able to cure it, through ignorance of what it was, but died fastest themselves, as being the men that most approached the sick…"
>
> - Thucydides[1]

From the Plague of Athens in 430 BC, to the Ebola epidemic of 2014, health care personnel (HCP) have toiled on the front lines of the battle against infectious disease, often placing themselves in harm's way in the service of their patients. Except for the military, no other occupation involves such pervasive, varied, and unpredictable exposure to workplace hazards, from musculoskeletal strains to workplace violence to psychological stress to chemical and biological agents. Protecting these essential workers requires comprehensive strategies. Safe and effective vaccines are the cornerstone of any Medical Center Occupational Health (MCOH) program.

CLINICAL NEED

MCOH programs must estimate individuals' susceptibility to infectious diseases based largely on vaccination and/or serology records. The need to assess and document likely adult immunity from childhood vaccinations, in the absence of an outbreak or exposure, is perhaps unique to this occupational setting. Key questions for each vaccine-preventable disease (VPD) include the following: Was the correct vaccine administered appropriately? How durable is vaccine-mediated immunity? How reliable is a history of infection? How well do serologic tests correlate with immunity? Are boosters needed? How should facilities manage nonimmune HCP? Although comprehensive guidelines are periodically provided by the Advisory Committee on Immunization Practices (ACIP), most recently, in 2011,[2] recent developments in vaccine formulations and recommendations warrant an updated review.

HCP vaccination programs are needed for several reasons above and beyond protecting health care workers from occupational infection. Vaccines help employers maintain staffing by preventing postexposure furloughs and reducing HCP concerns about working during pandemics.[3] Although available evidence demonstrates that HCP are far more often victim than vector,[4-7] decreasing risk of transmission to patients and others is another important reason to protect HCP.

SCIENTIFIC OVERVIEW OF CLINICAL STUDIES

This review uses the Centers for Disease Control and Prevention (CDC) definition of HCP: "all paid and unpaid persons working in health-care settings who have the potential for exposure to patients and/or to infectious materials, including body substances, contaminated medical supplies and equipment, contaminated environmental surfaces, or contaminated air."[2] In considering the scientific evidence underpinning recommendations for HCP, we must consider vaccine efficacy (VE) for this population, when

For editorial comment, see page 1931

From the Division of Preventive Occupational and Aerospace Medicine, Mayo Clinic, Rochester, MN (M.D.S.) and Department of Emergency Medicine, Perelman School of Medicine, Philadelphia, PA (A.J.B.).

known. As the health care workforce is aging and includes people with chronic diseases, VE estimates for healthy adults below age 65 may overestimate VE in this population.

Hepatitis B Vaccine

Rationale for HCP Vaccination. Hepatitis B virus (HBV) is a highly contagious bloodborne pathogen, with a transmission risk of 10% to 30% via needlestick or other percutaneous exposure.[2] Patients with hepatitis B e antigen or high levels of HBV DNA are the most contagious, although all patients with detectable HBV surface antigen (HBsAg) are infectious.[8] Health care personnel are at occupational risk of exposure to blood or other potentially infectious materials (OPIM).[9] Since 1989, the CDC has recommended HBV vaccination for all HCP. Following implementation of the Occupational Safety and Health Administration's Bloodborne Pathogen Standard in 1991, requiring health care employers to provide vaccination to all potentially exposed HCP,[10] vaccination rates increased dramatically.[11] Occupationally acquired HBV, once common, has become rare.[12] Nevertheless, vaccine coverage remains suboptimal; approximately 25% of US HCP with direct patient contact report never completing a 3-dose series.[13]

Universal childhood vaccination is now the cornerstone of US HBV-elimination strategy.[14] HBV vaccine is highly effective in infants, achieving serologic conversion rates above 95%. The vaccine is less immunogenic in adults.[15] Among HCP aged 18 to 40, the 3-dose series of recombinant HBV vaccine is 86% to 90% effective, but seroconversion rates are lower in HCP older than 40, especially those with chronic diseases.[16]

Vaccine Administration, Formulations, and Boosters. Correct vaccine administration and timing are crucial. Standard recombinant HBV vaccine is administered at 0, 4, and 24 weeks as an intramuscular (IM) injection. Accelerated vaccination schedules are not more effective, and immunogenicity is hampered by delays in the second dose or administration into the gluteus muscle.[17]

A newly approved hepatitis B vaccine, HBsAg-1018, uses a toll-like receptor 9 agonist adjuvant. This vaccine is given in a 2-dose series, administered at 0 and 4 weeks. This formulation produces better seroprotection than the 3-dose vaccine, significantly shortening the vaccination series without sacrificing safety.[18-21] Despite higher cost per dose, the convenience and improved immunogenicity of the 2-dose series makes it a cost-effective option for MCOH programs.[22]

HBV surface antibody (HBsAb) levels wane over time in a large percentage of people vaccinated over 10 years previously; anamnestic responses to vaccine boosters in this population indicate that once established, immune memory is preserved.[23-25] Routine boosters are not necessary.

Serologic Evidence of Immunity. Following the final vaccine dose, HCP should have immunity assessed via serology with IgG for HBsAb. Those lacking seroprotective HBsAb following the initial series should undergo a second series, with another HBsAb 4 weeks after completion. Consideration should be given to using the 2-dose adjuvanted HBsAg-1018 vaccine in adults because of its higher immunogenicity. Following 2 complete series, more than 90% of adults will develop immunity, although there is an inverse association with age.[2]

HCP who fail to develop protective levels of HBsAb after 2 complete series of vaccine are considered "nonresponders." Despite lack of a robust humoral immune response, most nonresponders seem to develop HBsAg-specific memory B cells.[26] Three doses of intradermal recombinant vaccine stimulates seroconversion in a high proportion of nonresponders and is reasonable to offer to this population.[27-29]

Nonresponders and previously unvaccinated nonimmune HCP exposed to blood or OPIM known or suspected to be contagious for HBV should receive postexposure immunoprophylaxis with hepatitis B immune globulin, along with HBV vaccine if incompletely vaccinated, per CDC guidelines.[8]

The phenomenon of waning HBsAb levels presents a quandary for evaluating HCP vaccinated in childhood, as most will not have

previous documentation of seroconversion. Although more than 95% of individuals vaccinated in infancy are likely to have durable immunity, 60% to 85% of those tested more than 10 years after vaccination will have an HBsAb below 10 IU/mL.[23-25] One challenge dose of vaccine will result in an anamnestic response in the vast majority of these adults.[24,25]

Health care facilities have 2 options for managing previously vaccinated HCP without documentation of postvaccine serology: pre-exposure serology for all at-risk employees or immediate postexposure HBsAb for all HCP who report occupational exposures to blood or OPIM. Cost-effectiveness comparisons suggest that pre-exposure assessment is more expensive but prevents more occupational infections. The cost per quality-adjusted life year is high for both strategies and differs with length of employment, with the pre-exposure strategy becoming more cost effective after 3 years.[30]

Measles, Mumps, and Rubella (MMR) Vaccine

Rationale for Vaccination of HCP. Although measles was declared eradicated from the United States in 2000, outbreaks continue to occur because of continued global prevalence, international travel, and lack of uniformly high US vaccination rates.[31] Because people with measles often need medical care, HCP have a relative risk between 2 and 19 of contracting measles compared with the general population.[4] Recently, outbreaks of mumps in communities, colleges, and hospitals have reinforced the need to maintain HCP immunity.[32] Although endemic transmission of rubella was eliminated in the United States in 2004, imported cases of rubella continue to occur. A recent occupational exposure to a nonimmune health care worker emphasizes the ongoing risk.[33]

Vaccine Administration, Formulations, and Boosters. Vaccines against measles, mumps, and rubella were first licensed in 1963, 1967, and 1969, respectively. Trivalent MMR vaccine was licensed in 1971 and has supplanted single-antigen vaccines. ACIP recommended universal childhood vaccination with MMR, which quickly became a standard US school entry requirement.[34] The CDC has recommended HCP MMR vaccination since 1987, evolving to current recommendations of 2 doses of measles and mumps and 1 of rubella for HCP who lack evidence of immunity.[2] Evidence of immunity includes appropriately timed immunization (2 doses after age 12 months, separated by at least 28 days, for measles and mumps; 1 dose after age 12 months for rubella), laboratory evidence of immunity or disease, or birth before 1957. In an outbreak situation, these older HCP should also be vaccinated if they lack laboratory evidence of immunity. Given the logistic challenges and resource constraints facing MCOH programs during outbreaks, facilities may choose to apply the same requirements for all HCP, regardless of age.

Serologic Evidence of Immunity. Case reports of vaccinated HCP contracting measles raise the question of whether vaccination is adequate evidence of immunity.[35-37] Unfortunately, available serologic assays are inadequate to assess immune status fully. Individuals with positive IgG titers have become infected with measles and mumps.[37,38] Vaccine-induced antibody may be effective against vaccine-strain antigens and yet lack efficacy against wild-type virus.[38] Negative serology can underestimate immunity because it cannot detect crucial vaccine-mediated cellular immune responses.[39,40] Among commercially available test methodologies to detect IgG, enzyme immunoassay (EIA) is the most sensitive.[41,42] Although IgG provides reasonable, if imperfect, evidence of immunity, postvaccination serologic surveillance is not recommended.

MCOH programs must often document immunity in newly hired HCP without vaccination records. Cost effectiveness of vaccination vs prevaccination serologic screening will vary with population seroprevalence and costs of laboratory testing and vaccine. Institutions can reasonably select either option, or a combination approach, depending on operational constraints and HCP preferences.[43]

Special Considerations. MMR vaccination must be deferred in (nonimmune) pregnant

and immune-compromised HCP for whom live virus vaccines are contraindicated. Like their patients, these HCP depend on scrupulous attention to isolation and personal protective equipment (PPE) protocols for potentially contagious patients. We strongly advocate implementing precautions for patients whose differential diagnosis includes measles, rubella, or varicella until these diseases are ruled out.

Although MMR contains attenuated virus, no clinically important shedding occurs postvaccination, and there is no need to remove HCP from patient care environments after vaccination. Approximately 5% of vaccine recipients experience a transient postvaccination rash, which is not contagious.

Varicella Vaccine

Rationale for Vaccination of HCP. Occupational exposure to varicella is a serious ongoing hazard to HCP and patients, particularly those with immune compromise.[44-46] Airborne transmission occurs with primary chickenpox and disseminated zoster (which may present atypically in immune-compromised individuals), but case reports have described isolated incidents of apparent airborne transmission from single-dermatome shingles.[45,47] Because transmission can occur before onset of rash, susceptible HCP should be removed from the workplace during the incubation period, days 8 to 21 postexposure.[2] Exposure to varicella in health care facilities is common, expensive, and disruptive. High infectivity and potential staffing impact make establishing HCP immunity an MCOH priority.

Vaccine Administration, Formulations, and Boosters. When varicella vaccine was introduced in 1995, HCP vaccination recommendations immediately followed.[48] This live virus vaccine, administered as a 2-dose series, is 95% effective in children and approximately 80% effective in adults.[48] Vaccine-mediated immunity is less robust than natural immunity and may decrease after 10 to 20 years.[49]

Serologic Evidence of Immunity. As with MMR, commercially available EIAs are somewhat insensitive to varicella vaccine-induced antibodies.[50] Thus, although vaccine is an important tool to protect HCP, increasing childhood and adult vaccination rates complicate serologic interpretation. Although approximately 80% of adults seroconvert following vaccination, 30% may lose serologic evidence of immunity over time.[51] However, negative titers by available EIAs may underestimate clinical immunity.[52] Vaccinated adults develop less disease and less severe disease than unvaccinated controls, likely reflecting cell-mediated immunity and humoral responses not easily measured outside research laboratories.[51] In one study, 70% of vaccinated exposed HCP with negative varicella (VZ) IgG titers by EIA had evidence of immunity by the labor-intensive fluorescent-antibody-to-membrane-antigen assay.[53]

Conversely, vaccine-induced seroconversion doesn't guarantee immunity. Even with a positive VZ IgG by EIA, HCP can have low-avidity antibody and remain susceptible,[52] possibly explaining rare occurrences of primary chickenpox in HCP with positive VZ IgG.[47]

Given the relatively recent introduction of vaccine and high rates of childhood infection, especially among older HCP, much study has focused on the utility of chickenpox disease history. Seroprevalence studies indicate the positive predictive value of history to predict seropositivity is above 95%, whereas the negative predictive value of a negative or uncertain history is quite low.[54-56] However, as younger HCP enter the workforce, seroprevalence in unvaccinated adults will likely decrease.

Multiple cost-effectiveness studies have evaluated strategies to confirm varicella immunity, usually concluding that serologic testing only for HCP without a clear history of chickenpox infection is most cost effective.[57,58] Although a reasonable approach in resource-limited settings, this strategy prevents fewer cases than serologic screening for all unvaccinated HCP. Screening all unvaccinated HCP is cost effective when the impact of patient exposures to infected HCP is considered.[59] Furthermore, cost-effectiveness studies overlook real-life experience in MCOH programs,

Mayo Clin Proc. ■ October 2019;94(10):2127-2141 ■ https://doi.org/10.1016/j.mayocp.2019.01.035
www.mayoclinicproceedings.org

in which many HCP provide previous records. US HCP often have records of vaccination or serologies from previous schools or jobs, lowering employers' costs and making serologic testing for those without documented immunity more feasible. Cost-effectiveness models are also sensitive to susceptible HCP compliance with vaccination, generally assuming a 30% declination rate. However, this depends on facility policy; requiring vaccination in the absence of contraindications would further improve cost effectiveness.

Given the potential impact to coworkers, patients, and operations from any HCP with chickenpox, the ACIP defines evidence of varicella immunity as documentation of 2 doses of vaccine, positive serology, or laboratory diagnosis of disease, not clinical history of disease.[2] Postvaccination serology is not indicated; if performed anyway, and found to be negative, there is no recommendation for a third vaccine.

Special Considerations. Varicella vaccine is a live attenuated vaccine, contraindicated in pregnancy and immune compromise. All HCP, regardless of vaccination or presumptive immunity, should use appropriate infection-control practices and PPE when caring for patients with suspected varicella. Unvaccinated staff without evidence of immunity should not be assigned to potentially contagious patients. Given concerns about relatively increased susceptibility in vaccinated vs previously infected HCP, postexposure management differs slightly for these groups. Whereas exposed HCP with natural immunity require no intervention, and unvaccinated nonimmune HCP require exclusion from the workplace during the incubation period, vaccinated HCP may continue to work after exposure with monitoring and should be evaluated and removed from work if they develop fever or rash illness during the incubation period.

Mild varicella-like rash may occur following vaccination in up to 5% of HCP; vaccine-strain varicella can be isolated from these vesicles. These HCP are not contagious via the respiratory route, so they need not be removed from the workplace entirely, but they should not have direct contact with susceptible patients at risk for varicella complications (eg, pregnant or immune compromised) until the lesions have dried or crusted.

Pertussis Vaccine

Rationale for Vaccination of HCP. Pertussis is an important cause of morbidity and mortality in children, particularly infants too young to be vaccinated. Nosocomial transmission to infants occurs in hospitals,[60] and HCP, especially those caring for children, have occupational risk of contracting pertussis. Although the disease is generally much milder in adults, HCP have experienced serious illness.[61] Pertussis in adults is common, transmissible, frequently subclinical, and often unreported.[62,63]

Pertussis is spread through respiratory droplets, and health care-associated transmission can occur between HCP and coworkers as well as between patients and HCP. The experience of large hospital pertussis outbreaks in which no patients were infected—despite receiving care from infected HCP—demonstrate the effectiveness of droplet precautions.[6,7]

Hospital outbreaks are expensive, nonetheless.[6,64] Contact tracing, notification, education, and offer of postexposure prophylaxis are necessary for exposed HCP and patients. Although several outbreak reports have noted that the costs of outbreak management exceed the costs of vaccinating all HCP in a facility, there is, unfortunately, not a direct trade-off in costs. Few exposures are preventable,[64] and HCP vaccination does not fundamentally change exposure management. Because of imperfect and waning vaccine-induced immunity, vaccinated HCP should be offered postexposure prophylaxis,[65] and symptomatic HCP should be furloughed regardless of vaccine status. HCP vaccination may reduce the number and costs of outbreaks modestly in situations when the index case is a health care worker. Cost-effectiveness models suggest that HCP pertussis vaccination programs are cost saving in facilities that experience at least 1 pertussis outbreak per decade[66] or when the risk of HCP-introduced pertussis exceeds

0.3% per month and the Tdap vaccination rate exceeds 25%.[67]

Vaccination rates among HCP vary widely and are likely still in flux, as the vaccine was introduced relatively recently. Approximately one third of US hospitals had pertussis vaccination policies by 2011, although target population and specific requirements varied widely.[68] Surveys suggest US HCP vaccination rates have risen steeply from 27% in 2011 to 47% by 2014.[69-71] Voluntary vaccination programs have achieved variable results, with some reporting over 90% vaccination.[72] Some US hospitals have instituted Tdap requirements, with predictably high vaccination rates.[73,74]

Despite decades of routine childhood immunization, pertussis remains endemic worldwide. Disease prevalence in adults is increasing. Although enhanced awareness and improved diagnostics may partially account for the increase in reported cases, the most important driver for this trend is likely waning vaccine-induced immunity. Childhood whole-cell pertussis vaccines have largely been supplanted by acellular vaccines, although vaccine types and schedules vary markedly across the globe. The shift to acellular childhood vaccine may decrease the durability of immunity. Among acellular vaccines, there is variability in the number and concentration of pertussis antigens and adjuvants, making direct comparisons difficult. Pertussis vaccines contain different combinations and concentrations of detoxified pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN), and fimbriae serotypes 2 and 3 (FIM2 and FIM3). There is no consensus on ideal antigen composition.

Vaccine Administration, Formulations, and Boosters. Adult pertussis vaccine is combined with tetanus and diphtheria vaccine in Tdap. Two US manufacturers produce Tdap: GlaxoSmithKline (Boostrix) and Sanofi-Pasteur (Adacel). Boostrix contains 8 μg each of PT and FHA antigens and 2.5 μg of PRN, while Adacel contains 2.5 μg of PT, 5 μg of FHA, 3 μg of PRN, and 5 μg of FIM2 and FIM3. In 1 retrospective cohort study, adolescents who received Boostrix demonstrated higher antibody levels and a lower rate of pertussis infection than those receiving Adacel; however, antibody levels fell precipitously over 5 years in both groups. The World Health Organization and CDC currently recommend only 1 adolescent or adult dose of Tdap, followed by regular tetanus/diphtheria boosters at 10-year intervals, except for additional Tdap boosters in every pregnancy for maternal antibody protection of newborns. Additional periodic adult pertussis boosters have not been recommended, but some investigators have suggested that this may be useful,[75] and the safety and short-term immunogenicity of second Tdap boosters have been established.[76]

Serologic Evidence of Immunity. There is no straightforward serologic correlate of protection against pertussis. IgG against PT is the most commonly used indicator, but it is the fastest-waning vaccine-induced antibody, and its absence is often compensated for by cell-mediated immunity. Studies of pertussis seroprevalence and vaccine immunogenicity differ in the antibodies used to define immunity and the cutoff values used, making both comparisons difficult.

Special Considerations. Although only 1 pertussis vaccine is recommended for adults, booster doses are recommended with each pregnancy. For maximal newborn protection, vaccine should be administered at 27 to 36 weeks' gestation. Newly hired HCP in earlier pregnancy stages should be appropriately counseled. For employers requiring pertussis vaccine, it is reasonable to defer vaccination until the optimal stage of pregnancy.

Influenza Vaccine

Rationale for HCP Vaccination. A century ago, the 1918 influenza epidemic raged around the world, with high illness and mortality rates among young adults including HCP. Death rates were higher for HCP tending the sick in the United States than those working overseas in military settings.[77] Influenza in Minnesota HCP drastically

Mayo Clin Proc. ■ October 2019;94(10):2127-2141 ■ https://doi.org/10.1016/j.mayocp.2019.01.035
www.mayoclinicproceedings.org

affected clinical care across the state,[78] mirroring the devastation in other states.

Influenza remains an annual occupational hazard for HCP with concerns for infection, transmission, and absenteeism. Vaccination must be an integral part of comprehensive influenza-prevention programs, although it is less effective than other HCP vaccines. In a metanalysis of VE in adults aged 18 to 65, excluding seasons in which the vaccine did not match circulating strains, the pooled efficacy of trivalent inactivated vaccine was 59%.[79] Despite its modest VE, the benefits of vaccination to HCP are clear, with reductions in both illness and absenteeism.[80] Overall evidence supports—and the CDC recommends—aiming for universal annual immunization of HCP.[81]

Naturally, there is interest in whether HCP vaccination benefits their patients. HCP may be more likely than other professions to work when ill, posing a risk for transmission of influenza and other respiratory illnesses to medically vulnerable patients. Infection-control practices, such as handwashing, likely mitigate this risk. Studies addressing the impact on patients from HCP immunization are strongest in long-term care (LTC) settings, where patients are both most vulnerable to influenza complications and most likely to remain *in situ* during the incubation period. Ironically, HCP vaccination rates are lowest in this setting.[82] Several cluster randomized trials found associations between all-cause mortality and ILI among LTC residents and voluntary HCP vaccination programs achieving modest rates of vaccination.[83-85] The lack of an effect on influenza infection in residents, the presence of bundled educational interventions, and lack of blinding in these studies necessitates a cautious interpretation, especially if extrapolating these findings to different interventions or clinical settings. Comprehensive influenza-control programs, including increased HCP vaccination, have been associated with a decline in nosocomial influenza among patients.[86,87] Systematic reviews have not found strong evidence of a protective effect to patients from HCP influenza vaccine,[88-90] but there may be an interactive effect between vaccination of patients and HCP. Studies in LTC have found an association between influenza outbreaks, HCP vaccination rates, and resident vaccination rates.[91,92]

Vaccine Administrations, Formulations, and Boosters. Influenza vaccines are generally inactivated IM products designed to induce immune protection against the 3 or 4 strains judged most likely to circulate in a coming influenza season.[81] As the majority of vaccines are manufactured in eggs with production cycles of up to 6 months, the strains must be identified well before influenza begins circulating in the United States. Genetic drift and shift during that period can drastically alter vaccine effectiveness year to year. Recently, cell-based and recombinant vaccines have shown promise in terms of shorter production cycles and better immune protection.

Among inactivated IM influenza vaccine products, adjuvanted and high-dose vaccines may confer additional protection for adults older than age 65.[81] There is some evidence that recombinant vaccine may be more effective in adults older than age 50.[93]

In addition to inactivated influenza vaccines, a live attenuated product has been intermittently ACIP-approved for healthy nonpregnant adults below age 50, including HCP.[94] This product has obvious advantages for needle-averse staff; however, there are ongoing concerns about its effectiveness compared with injectible products. Intradermal vaccines have also been ACIP approved during some flu seasons. The spectrum of influenza vaccine products increases every year, and MCOH professionals should consult the most recent recommendations before making purchase decisions.

Special Considerations. Overall, annual influenza immunization rates for US HCP have risen steadily, but only inpatient hospital HCP have met the Healthy People 2020 goal of 90%.[82] Influenza immunization for HCP differs from other immunizations for this population because it must be an annual program. Specific challenges include reaching

TABLE 1. Summary of Recommended Vaccines for Health Care Personnel

Vaccine-preventable disease	HCP group at Risk	Acceptable evidence of immunity	Role of postvaccination serology	Exceptions and caveats
Hepatitis B	HCP at risk of exposure to blood or other potentially infectious material	One complete HBV vaccine series followed by positive HBsAb, or Laboratory evidence of infection. (Two complete HBV vaccine series followed by negative HBsAb signifies vaccine nonresponse and lack of immunity.)	Obtain HBsAb 1 to 2 months postvaccine. Once documented, it does not need to be repeated in immune-competent HCP. Waning antibody titer is expected, but immune memory persists. For HCP with documentation of remote vaccination and no subsequent HBsAb, facilities should select a strategy to determine serologic status, either at hire or postexposure.	HCP who are immune compromised or undergoing hemodialysis should have serial HBsAb with booster vaccination, as needed, to maintain immunity. In nonresponders, perform full hepatitis B serology to rule out infection. Educate all nonresponders about need for HBIG postexposure. Perform risk assessment and management of infected HCP following published guidelines.
Measles	All HCP	Two measles/MMR vaccines, given at least 28 days apart and after 12 months of age, or Positive measles IgG, or Laboratory evidence of infection, or Birth prior to 1957.	Do not perform postvaccination measles IgG. If performed and negative, additional doses of vaccine are not indicated.	In outbreak or exposure situation, birth before 1957 is not adequate evidence of immunity.
Mumps	All HCP	2 mumps/MMR vaccines, given at least 28 days apart and after 12 months of age, or Positive mumps IgG, or Laboratory evidence of infection, or Birth prior to 1957.	Do not perform postvaccination mumps IgG. If performed and results are negative, additional doses of vaccine are not indicated.	In outbreak or exposure situation, birth before 1957 is not adequate evidence of immunity.
Rubella	All HCP	One rubella/MMR vaccine, given after 12 months of age, or Positive rubella IgG, or Laboratory evidence of infection, or Birth prior to 1957.	Do not perform postvaccination rubella IgG. If performed and results are negative, additional doses of vaccine are not indicated.	In outbreak or exposure situation, birth before 1957 is not adequate evidence of immunity.
Varicella	All HCP	Two varicella vaccines, given at least 28 days apart and after 12 months of age, or Positive varicella IgG, or Laboratory evidence of infection.	Do not perform post vaccination varicella IgG. If performed and results are negative, additional doses of vaccine are not indicated.	ACIP guidelines include verification of disease history or clinical diagnosis from any health care provider as acceptable evidence of immunity. However, mild or atypical disease may be incorrectly attributed to varicella, and such clinical details are rarely available to MCOH programs. In our opinion, obtaining a varicella IgG in these situations is reasonable.

Continued on next page

TABLE 1. Continued

Vaccine-preventable disease	HCP group at Risk	Acceptable evidence of immunity	Role of postvaccination serology	Exceptions and caveats
Pertussis	All HCP, especially in pediatric settings	One Tdap vaccine	No serologic correlates of immunity have been established.	
Influenza	All HCP	One influenza vaccine annually	No	
Meningococcal	Microbiologists handling N. meningitidis isolates	Meningococcal ACWY and meningococcal serogroup B vaccination every 5 years while at risk	No	Consult with laboratory medical director to assess ongoing risk of exposure.
Typhoid	Microbiologists handling S. typhi isolates	Live, attenuated oral typhoid vaccine every 5 years while at risk, or inactivated IM typhoid vaccine every 2 years while at risk	No	Consult with laboratory medical director to assess ongoing risk of exposure.

ACIP = Advisory Committee on Immunization Practices; HBIG = hepatitis B immune globulin; HBsAb = hepatitis B surface antibody; HBV = hepatitis B virus; HCP = health care personnel; MCOH = medical center occupational health; MMR = measles, mumps, and rubella vaccine; Tdap = tetanus, diphtheria, and acellular pertussis.

HCP on all shifts, purchasing and deploying vaccine and related supplies, and obtaining adequate staffing to vaccinate during the recommended time frame each year. Factors associated with successful MCOH influenza immunization programs include free and convenient vaccine on all shifts and in all locations, well-advertised special events, adequate staffing, and employee education.[95,96] Employer requirements for annual HCP immunization can dramatically increase annual participation.[74,96,97] Current research efforts to develop influenza vaccines with shorter manufacturing cycles, better effectiveness, more conserved antigenic targets, and durable immunity are promising. The "holy grail" of a universal influenza vaccine would greatly benefit HCP as well as their patients and communities.

Vaccines for Targeted Subpopulations

Although most HCP are exposed to patients or the patient care environment, others may have occupational exposure to more unusual pathogens. Where safe and effective vaccines exist, they should be offered to protect workers from those hazards.

Microbiologists who handle specimens potentially containing meningococcus should be vaccinated with both the ACWY and serogroup B vaccines. Both are inactivated vaccines; for ongoing occupational exposure, boosters every 5 years are recommended.[98] Similarly, microbiologists who manipulate samples likely to contain salmonella typhi should be offered typhoid immunization, available as either a live oral vaccine, which is boosted every 5 years, or as an inactivated IM injection every 2 years.[99] Consultation with laboratory medical directors and infection-prevention personnel is advisable to identify exposure risks for each laboratory.

Recommended vaccines for HCP, with the correlates of immunity and related management strategies reviewed above are summarized in Tables 1 and 2. Vaccinations for research laboratory personnel are complex and outside the scope of this review. MCOH programs serving biomedical research laboratories should work closely with their institutional biosafety officers and research animal

TABLE 2. Dos and Don'ts of Health Care Personnel Vaccine Program Management

- DO obtain complete vaccination records when possible.
- DO document postvaccination serology for hepatitis B, either at hire for all at-risk HCP or upon exposure.
- DO offer postexposure prophylaxis after unprotected exposure to pertussis, regardless of HCP vaccination status.
- DON'T obtain postvaccination serology for measles, mumps, rubella, or varicella.
- DON'T repeat postvaccination HBsAb once seroconversion is documented (absent a bone marrow transplant or hemodialysis)
- DON'T forego PPE in vaccinated staff caring for patients with vaccine-preventable diseases such as respirators for varicella, measles, and high-risk influenza situations.

HBsAb = hepatitis B surface antibody; HCP = health care personnel; PPE = personal protective equipment.

veterinarians to identify research personnel and animal handlers at risk for unusual VPDs, such as vaccinia, diphtheria, and rabies, and enroll all at-risk personnel in vaccination programs.

CHALLENGES AND PITFALLS

The lack of a national immunization information system (IIS) poses a challenge to MCOH programs. State IISs attempt to bridge this information gap, and many are now interoperable with electronic medical records. However, HCP frequently cross state lines during their training and careers, and data interchanges among IISs are typically limited to adjacent states. Adult vaccinations may be missing from IISs. Missing documentation results in needless revaccination with childhood vaccines such as MMR and hepatitis B and complicates serology interpretations. For example, a positive VZ IgG is generally accepted as evidence of immunity, but if it is drawn after only 1 dose of vaccine, immunity is not optimally durable, and a second dose of vaccine would be recommended.

Another challenge to MCOH programs is safeguarding protected health information (PHI) while communicating compliance status clearly to supervisors. Optimal compliance software will default to noncompliant status when additional doses in a vaccine series are overdue, thereby keeping managers updated on employee immunization requirements without sharing PHI. When vaccines are medically contraindicated, compliance software should indicate compliance to managers while allowing MCOH staff to track immune status and manage work restrictions and exposures.

MCOH programs need appropriate resources and authority to respond to evolving HCP vaccine recommendations. For instance, ACIP has recently recommended third doses of MMR during community and campus mumps outbreaks.[100] Compliance software may need to adapt to a third MMR requirement for targeted HCP groups in outbreak situations. Compliance software must accommodate new vaccine products and combinations, vaccine schedule changes (eg, 2-dose HBV vaccine), and institutional policy changes (eg, Tdap requirements for pediatric HCP). Investment in robust and highly flexible MCOH compliance tracking software is vital. Operational requirements for HCP vaccination programs are summarized in Table 3.

Management of nonimmune HCP with vaccine contraindications or refusals poses another challenge to MCOH programs. Although it is preferable to keep known susceptible HCP away from patients with known or suspected VPDs, vaccination never obviates the need for PPE and other precautions. Absent identified threats, such as suspected cases or outbreaks, facilities must make risk-based assessments, considering the community prevalence of the VPD and the HCP's jobs. In most cases, the risk of occupational infection is manageable, and unvaccinated HCP can work with appropriate restrictions. Patient safety must also be considered. Except for seasonal influenza, the risk of nonoccupational VPDs in the United States is low, and asymptomatic HCP do not pose a significant risk to patients absent from known exposure. Even for influenza, routine use of masks to prevent transmission of disease from asymptomatic HCP (vaccinated or not) is not supported by evidence.

CDC recommendations to check HBsAg, HBV core, and surface antibodies only in HCP who have immigrated to the United States from countries with endemic HBV present

Mayo Clin Proc. ■ October 2019;94(10):2127-2141 ■ https://doi.org/10.1016/j.mayocp.2019.01.035
www.mayoclinicproceedings.org

TABLE 3. Requirements of Occupational Vaccine Programs for Health Care Personnel

- ☐ Trained occupational nurses who understand principles of vaccination, immunity assessment, employee rights and requirements, employer obligations, OSHA regulations, and institutional policy
- ☐ Medical direction by physician knowledgeable about vaccine-preventable diseases and the regulatory landscape of occupational medicine
- ☐ Institutional policy that clearly defines required vaccines/tests, optional vaccines, exemption procedures, and consequences of policy noncompliance
- ☐ Onboarding process that includes obtaining complete vaccination records when possible
- ☐ Privacy policy that communicates compliance status to supervisor without disclosing HCP medical information
- ☐ Procedure for evaluating vaccine exemption requests
- ☐ Written protocols for screening records and providing needed services
- ☐ Electronic tracking system for vaccine and serology records with the following:
  - ☐ Daily or real-time update of personnel and jobs from HR system
  - ☐ Routine reports to monitor compliance/completion of onboard screening
  - ☐ Rapid retrieval of data for exposure management
  - ☐ Quality assurance procedures in place to maintain data integrity
  - ☐ Flexibility to adapt to changing immunization formulations, schedules, and requirements
- ☐ Process for ensuring vaccination/immunity for nonpaid or nonemployed personnel (licensed independent practitioners, students, contractors, volunteers, and visiting staff) that mirrors requirements for employed HCP
- ☐ HCP education on infection control practices and reporting of exposures and symptoms

HCP = health care personnel; HR = human resources; OSHA = Occupational Safety and Health Administration.

another MCOH challenge. Facilities must confront concerns about treating immigrant employees differently or imposing additional requirements based on country of origin. If this practice is allowed by the Equal Employment Opportunity Commission, facilities must develop protocols to protect PHI, accommodate reasonable restrictions, and avoid creating adversarial employer—employee relationships at hire.

UNRESOLVED CLINICAL QUESTIONS

Pertussis immunity—whether from infection or vaccine—wanes within a decade, and there is, at present, no recommendation for routine adult boosters, except in pregnancy. HCP working in exposure-prone settings, such as pediatric emergency departments, have only short-term benefit from 1-time vaccination. Research assessing the utility of boosters in at-risk occupational groups is needed.

Varicella zoster (shingles) vaccine is now recommended for adults older than age 50 without prevaccination screening for VZ IgG.[101] However, primary varicella vaccination is still recommended for HCP without evidence of immunity, including those above age 50. Vaccination with 2 doses of shingles vaccine has not been acknowledged as evidence of varicella immunity, so MCOH programs face an awkward recommendation for testing HCP above age 50 for VZ IgG and, if negative, providing low-dose primary varicella vaccine. HCP in this situation need clear guidance for whether and when to obtain shingles vaccines. Research is needed to determine whether 2 doses of shingles vaccine can suffice as evidence of immunity in HCP older than 50 years of age.

Human papillomavirus and other VPDs are found in bioaerosols to which surgical staff may be exposed.[102] Engineering controls to evacuate surgical smoke and respiratory protection programs can mitigate this risk, but the role of HPV vaccine remains unclear in this population. HPV vaccine is not recommended for adults above the age of 26,[103] but the vaccine is newly licensed up to age 45,[104] potentially facilitating its use in occupationally exposed HCP. However, the vaccine's effectiveness for protection against HPV respiratory exposure is unknown.

CONCLUSIONS

MCOH professionals manage complex vaccination programs, not only providing vaccines

but assessing adult immunity from childhood records and serologies based on evolving evidence. These programs are crucial to protect HCP, their families, patients, and employers. Well-trained staff, adequate resources, and robust technology are necessary to deliver evidence-based effective programs. Coordination with a wide variety of stakeholders is needed. Effective HCP vaccination programs follow best practices in immunization and confidentiality, while simultaneously and continuously interfacing with medical-center human resource officers, infection-control staff, and regulatory demands. Doing so requires a range of training, policies, and protocols, many of which are unique to the MCOH setting. More research is needed to resolve common but challenging questions about assessing and maintaining immunity in this adult population with ongoing risk of exposure to VPDs.

Abbreviations and Acronyms: **ACIP** = Advisory Committee on Immunization Practices; **CDC** = Centers for Disease Control and Prevention; **EIA** = enzyme immunoassay; **FHA** = filamentous hemagglutinin; **FIM** = fimbrae; **HBsAb** = hepatitis B surface antibody; **HBsAg** = hepatitis B surface antigen; **HBV** = hepatitis B virus; **HCP** = health care personnel; **HPV** = human papilloma virus; **IIS** = immunization information system; **IM** = intramuscular; **LTC** = long-term care; **MCOH** = medical center occupational health; **MMR** = measles, mumps, and rubella vaccine; **OPIM** = other potentially infectious materials; **PHI** = protected health information; **PPE** = personal protective equipment; **PRN** = pertactin; **PT** = detoxified pertussis toxin; **Tdap** = tetanus, diphtheria and acellular pertussis vaccine; **VE** = vaccine efficacy; **VPD** = vaccine-preventable disease

Potential Competing Interests: The authors report no competing interests.

Publication dates: Received for publication November 15, 2018; revisions received January 16, 2019; accepted for publication January 31, 2019.

Correspondence: Address to Melanie D. Swift, MD, MPH, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 (Swift.melanie@mayo.edu).

The Thematic Review on Vaccines will continue in an upcoming issue.

REFERENCES

1. Sprat T. *The Plague of Athens, Which Hapned [sic] in the Second Year of the Peloponnesian War*. Oxford, UK: H. Hills; 1709.
2. Centers for Disease Control and Prevention. Immunization of health-care personnel: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(7):1-45.
3. Garrett AL, Park YS, Redlener I. Mitigating absenteeism in hospital workers during a pandemic. *Disaster Med Public Health Prep*. 2009;3(suppl 2):S141-S147.
4. Fiebelkorn AP, Seward JF, Orenstein WA. A global perspective of vaccination of healthcare personnel against measles: systematic review. *Vaccine*. 2014;32(38):4823-4839.
5. Torner N, Solano R, Rius C, Dominguez A; MeaslesElimination Program Surveillance Network of Catalonia, Spain. Implication of health care personnel in measles transmission. *Hum Vaccin Immunother*. 2015;11(1):288-292.
6. Leekha S, Thompson RL, Sampathkumar P. Epidemiology and control of pertussis outbreaks in a tertiary care center and the resource consumption associated with these outbreaks. *Infect Control Hosp Epidemiol*. 2009;30(5):467-473.
7. Pascual FB, McCall CL, McMurtray A, Payton T, Smith F, Bisgard KM. Outbreak of pertussis among healthcare workers in a hospital surgical unit. *Infect Control Hosp Epidemiol*. 2006; 27(6):546-552.
8. Schillie S, Vellozzi C, Reingold A, et al. Prevention of hepatitis B virus infection in the United States: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep*. 2018;67(1):1-31.
9. Centers for Disease Control and Prevention. Guidelines for prevention of transmission of human immunodeficiency virus and hepatitis B virus to health-care and public-safety workers: a response to P.L. 100-607, the Health Omnibus Programs Extension Act of 1988. *MMWR Suppl*. 1989;38(suppl 6):1-37.
10. US Department of Labor Occupational Safety and Health Administration. 29 CFR Part 1910.1030. Final rule on occupational exposure to bloodborne pathogens. *Federal Register*. 1991;56(64004).
11. Agerton TB, Mahoney FJ, Polish LB, Shapiro CN. Impact of the bloodborne pathogens standard on vaccination of healthcare workers with hepatitis B vaccine. *Infect Control Hosp Epidemiol*. 1995;16(5):287-291.
12. Mahoney FJ, Stewart K, Hu H, Coleman P, Alter MJ. Progress toward the elimination of hepatitis B virus transmission among health care workers in the United States. *Arch Intern Med*. 1997;157(22):2601-2605.
13. Byrd KK, Lu PJ, Murphy TV. Hepatitis B vaccination coverage among health-care personnel in the United States. *Public Health Rep*. 2013;128(6):498-509.
14. Centers for Disease Control and Prevention. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). *MMWR Recomm Rep*. 1991;40(13):1-25.
15. La Fauci V, Riso R, Facciola A, et al. Response to anti-HBV vaccine and 10-year follow-up of antibody levels in healthcare workers. *Public Health*. 2016;139:198-202.
16. Averhoff F, Mahoney F, Coleman P, Schatz G, Hurwitz E, Margolis H. Immunogenicity of hepatitis B Vaccines. Implications for persons at occupational risk of hepatitis B virus infection. *Am J Prev Med*. 1998;15(1):1-8.
17. Chen W, Gluud C. Vaccines for preventing hepatitis B in healthcare workers. *Cochrane Database Syst Rev*. 2005:Cd000100.
18. Jackson S, Lentino J, Kopp J, et al. Immunogenicity of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant compared with a licensed hepatitis B vaccine in adults. *Vaccine*. 2018;36(5):668-674.
19. Halperin SA, McNeil S, Langley JM, et al. Safety and immunogenicity of different two-dose regimens of an investigational hepatitis B vaccine (hepatitis B surface antigen co-administered with an immunostimulatory phosphorothioate oligodeoxyribonucleotide) in healthy young adults. *Vaccine*. 2012;30(36):5445-5448.

20. Heyward WL, Kyle M, Blumenau J, et al. Immunogenicity and safety of an investigational hepatitis B vaccine with a Toll-like receptor 9 agonist adjuvant (HBsAg-1018) compared to a licensed hepatitis B vaccine in healthy adults 40-70 years of age. *Vaccine*. 2013;31(46):5300-5305.
21. Hyer R, McGuire DK, Xing B, Jackson S, Janssen R. Safety of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant in adults. *Vaccine*. 2018;36(19):2604-2611.
22. Kuan RK, Janssen R, Heyward W, Bennett S, Nordyke R. Cost-effectiveness of hepatitis B vaccination using HEPLISAV in selected adult populations compared to Engerix-B(R) vaccine. *Vaccine*. 2013;31(37):4024-4032.
23. Hartal M, Yavnai N, Galor I, et al. Seroprevalence of anti-HBs antibodies at young adulthood, before and after a booster vaccine dose, among medical personnel vaccinated in infancy. *Vaccine*. 2015;33(38):4878-4885.
24. Bagheri-Jamebozorgi M, Keshavarz J, Nemati M, et al. The persistence of anti-HBs antibody and anamnestic response 20 years after primary vaccination with recombinant hepatitis B vaccine at infancy. *Hum Vaccin Immunother*. 2014;10(12):3731-3736.
25. Behre U, Bleckmann G, Crasta PD, et al. Long-term anti-HBs antibody persistence and immune memory in children and adolescents who received routine childhood hepatitis B vaccination. *Hum Vaccin Immunother*. 2012;8(6):813-818.
26. Valats JC, Tuaillon E, Funakoshi N, et al. Investigation of memory B cell responses to hepatitis B surface antigen in health care workers considered as non-responders to vaccination. *Vaccine*. 2010;28(39):6411-6416.
27. Kalchiem-Dekel O, Grupel D, Bouchnik L, Sikuler E, Ben-Yakov G. Efficacy and long-term durability of intradermal recombinant hepatitis B virus vaccine among intramuscular vaccine nonresponders: a prospective study in healthcare personnel. *J Gastroenterol Hepatol*. 2015;30(12):1782-1787.
28. Ghebrehewet S, Baxter D, Falconer M, Paver K. Intradermal recombinant hepatitis B vaccination (IDRV) for non-responsive healthcare workers (HCWs). *Hum Vaccin*. 2008;4(4):280-285.
29. Playford EG, Hogan PG, Bansal AS, et al. Intradermal recombinant hepatitis B vaccine for healthcare workers who fail to respond to intramuscular vaccine. *Infect Control Hosp Epidemiol*. 2002;23(2):87-90.
30. Hoerger TJ, Bradley C, Schillie SF, Reilly M, Murphy TV. Cost-effectiveness of ensuring hepatitis B protection for previously vaccinated healthcare personnel. *Infect Control Hosp Epidemiol*. 2014;35(7):845-854.
31. Gastanaduy PA, Paul P, Fiebelkorn AP, et al. Assessment of the status of measles elimination in the United States, 2001-2014. *Am J Epidemiol*. 2017;185(7):562-569.
32. Bonebrake AL, Silkaitis C, Monga G, et al. Effects of mumps outbreak in hospital, Chicago, Illinois, USA, 2006. *Emerg Infect Dis*. 2010;16(3):426-432.
33. Wallin T, Holzschuh E, Kintner C. Notes from the field: rubella infection in an unvaccinated pregnant woman - Johnson County, Kansas, December 2017. *MMWR Morb Mortal Wkly Rep*. 2018;67(40):1132-1133.
34. Zimmerman RK, Burns IT. Childhood immunization guidelines: current and future. *Primary Care*. 1994;21(4):693-715.
35. Hahné SJ, Nic Lochlainn LM, van Burgel ND, et al. Measles outbreak among previously immunized healthcare workers, the Netherlands, 2014. *J Infect Dis*. 2016;214(12):1980-1986.
36. de Vries W, Plotz FB, Dorigo-Zetsma JW. Measles infection despite 2-dose vaccination in health care workers. *Pediatr Infect Dis J*. 2014;33(9):992.
37. Gohil SK, Okubo S, Klish S, Dickey L, Huang SS, Zahn M. Healthcare workers and post-elimination era measles: lessons on acquisition and exposure prevention. *Clin Infect Dis*. 2016;62(2):166-172.
38. Gouma S, Ten Hulscher HI, Schurink-van 't Klooster TM, et al. Mumps-specific cross-neutralization by MMR vaccine-induced antibodies predicts protection against mumps virus infection. *Vaccine*. 2016;34(35):4166-4171.
39. Bautista-Lopez N, Ward BJ, Mills E, McCormick D, Martel N, Ratnam S. Development and durability of measles antigen-specific lymphoproliferative response after MMR vaccination. *Vaccine*. 2000;18(14):1393-1401.
40. Charlton CL, Lai FY, Dover DC. How to determine protective immunity in the post-vaccine era. *Hum Vaccin Immunother*. 2016;12(4):903-906.
41. Kumakura S, Shibata H, Isobe T, et al. Comparison of hemagglutination inhibition assay and enzyme immunoassay for determination of mumps and rubella immune status in health care personnel. *J Clin Lab Anal*. 2013;27(5):418-421.
42. Shibata H, Kumakura S, Isobe T, et al. Comparative analysis of a complement fixation assay and enzyme immunoassay to determine the seroprevalence of measles and varicella in a survey of healthcare workers. *J Int Med Res*. 2013;41(1):224-230.
43. Alp E, Cevahir F, Gokahmetoglu S, Demiraslan H, Doganay M. Prevaccination screening of health-care workers for immunity to measles, rubella, mumps, and varicella in a developing country: what do we save? *J Infect Public Health*. 2012;5(2):127-132.
44. Aly NY, Al Obaid I, Al-Qulooshi N, Zahed Z. Occupationally related outbreak of chickenpox in an intensive care unit. *Med Princ Pract*. 2007;16(5):399-401.
45. Saidel-Odes L, Borer A, Riesenberg K, et al. An outbreak of varicella in staff nurses exposed to a patient with localized herpes zoster. *Scand J Infect Dis*. 2010;42(8):620-622.
46. Leung J, Kudish K, Wang C, et al. 2009 varicella outbreak in a Connecticut residential facility for adults with intellectual disability. *J Infect Dis*. 2010;202(10):1486-1491.
47. Johnson JA, Bloch KC, Dang BN. Varicella reinfection in a seropositive physician following occupational exposure to localized zoster. *Clin Infect Dis*. 2011;52(7):907-909.
48. Centers for Disease Control and Prevention. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 1996;45(RR-11):1-36.
49. Burgess MA, Cossart YE, Wilkins TD, Botham S, Fearns G, Chitour K. Varicella vaccination of health-care workers. *Vaccine*. 1999;17(7-8):765-769.
50. Maple PA, Breuer J, Quinlivan M, Kafatos G, Brown KE. Comparison of a commercial Varicella Zoster glycoprotein IgG enzyme immunoassay with a reference time resolved fluorescence immunoassay (VZV TRFIA) for measuring VZV IgG in sera from pregnant women, sera sent for confirmatory testing and pre and post vOka vaccination sera from healthcare workers. *J Clin Virol*. 2012;53(3):201-207.
51. Saiman L, LaRussa P, Steinberg SP, et al. Persistence of immunity to varicella-zoster virus after vaccination of healthcare workers. *Infect Control Hosp Epidemiol*. 2001;22(5):279-283.
52. Behrman A, Lopez AS, Chaves SS, Watson BM, Schmid DS. Varicella immunity in vaccinated healthcare workers. *J Clin Virol*. 2013;57(2):109-114.
53. Rolando L, Schneider WJ, Steinberg S, et al. Effect of varicella-zoster virus (VZV) fluorescent-antibody-to-membrane-antigen (FAMA) testing on sensitivity of determining VZV immunity in healthcare workers and on furlough days. *Infect Control Hosp Epidemiol*. 2010;31(9):972-974.
54. Wu MF, Yang YW, Lin WY, Chang CY, Soon MS, Liu CE. Varicella zoster virus infection among healthcare workers in Taiwan: seroprevalence and predictive value of history of varicella infection. *J Hosp Infect*. 2012;80(2):162-167.
55. Almuneef M, Memish ZA, Abbas ME, Balkhy HH. Screening healthcare workers for varicella-zoster virus: can we trust the history? *Infect Control Hosp Epidemiol*. 2004;25(7):595-598.

56. Urbiztondo L, Bayas JM, Broner S, et al. Varicella-zoster virus immunity among health care workers in Catalonia. *Vaccine*. 2014;32(45):5945-5948.
57. Baracco GJ, Eisert S, Saavedra S, Hirsch P, Marin M, Ortega-Sanchez IR. Clinical and economic impact of various strategies for varicella immunity screening and vaccination of health care personnel. *Am J Infect Control*. 2015;43(10):1053-1060.
58. Chodick G, Ashkenazi S, Livni G, Lerman Y. Cost-effectiveness of varicella vaccination of healthcare workers. *Vaccine*. 2005; 23(43):5064-5072.
59. Gayman J. A cost-effectiveness model for analyzing two varicella vaccination strategies. *AJHP*. 1998;55(suppl 4):S4-S8.
60. Maltezou HC, Ftika L, Theodoridou M. Nosocomial pertussis in neonatal units. *J Hosp Infect*. 2013;85(4):243-248.
61. Kurt TL, Yeager AS, Guenette S, Dunlop S. Spread of pertussis by hospital staff. *JAMA*. 1972;221(3):264-267.
62. Kuncio DE, Middleton M, Cooney MG, Ramos M, Coffin SE, Feemster KA. Health care worker exposures to pertussis: missed opportunities for prevention. *Pediatrics*. 2014;133(1): 15-21.
63. Wright SW, Decker MD, Edwards KM. Incidence of pertussis infection in healthcare workers. *Infect Control Hosp Epidemiol*. 1999;20(2):120-123.
64. Daskalaki I, Hennessey P, Hubler R, Long SS. Resource consumption in the infection control management of pertussis exposure among healthcare workers in pediatrics. *Infect Control Hosp Epidemiol*. 2007;28(4):412-417.
65. Goins WP, Edwards KM, Vnencak-Jones CL, et al. A comparison of 2 strategies to prevent infection following pertussis exposure in vaccinated healthcare personnel. *Clin Infect Dis*. 2012;54(7):938-945.
66. Tariq L, Mangen MJ, Hovels A, Frijstein G, de Boer H. Modelling the return on investment of preventively vaccinating healthcare workers against pertussis. *BMC Infect Dis*. 2015; 15:75.
67. Greer AL, Fisman DN. Use of models to identify cost-effective interventions: pertussis vaccination for pediatric health care workers. *Pediatrics*. 2011;128(3):e591-e599.
68. Miller BL, Ahmed F, Lindley MC, Wortley PM. US hospital requirements for pertussis vaccination of healthcare personnel, 2011. *Infect Control Hosp Epidemiol*. 2011; 32(12):1209-1212.
69. Lu PJ, Graitcer SB, O'Halloran A, Liang JL. Tetanus, diphtheria and acellular pertussis (Tdap) vaccination among healthcare personnel-United States, 2011. *Vaccine*. 2014; 32(5):572-578.
70. O'Halloran AC, Lu PJ, Meyer SA, et al. Tdap vaccination among healthcare personnel: 21 States, 2013. *Am J Prev Med*. 2018;54(1):119-123.
71. Srivastav A, Black CL, Lu PJ, Zhang J, Liang JL, Greby SM. Tdap vaccination among healthcare personnel, internet panel survey, 2012-2014. *Am J Prev Med*. 2017;53(4):537-546.
72. Jiang C, Whitmore-Sisco L, Gaur AH, Adderson EE. A quality improvement initiative to increase Tdap (tetanus, diphtheria, acellular pertussis) vaccination coverage among direct health care providers at a children's hospital. *Vaccine*. 2018;36(2): 214-219.
73. Weber DJ, Consoli SA, Sickbert-Bennett E, Rutala WA. Assessment of a mandatory tetanus, diphtheria, and pertussis vaccination requirement on vaccine uptake over time. *Infect Control Hosp Epidemiol*. 2012;33(1):81-83.
74. Leibu R, Maslow J. Effectiveness and acceptance of a health care-based mandatory vaccination program. *J Occup Environ Med*. 2015;57(1):58-61.
75. Zepp F, Heininger U, Mertsola J, et al. Rationale for pertussis booster vaccination throughout life in Europe. *Lancet Infect Dis*. 2011;11(7):557-570.
76. Mertsola J, Van Der Meeren O, He Q, et al. Decennial administration of a reduced antigen content diphtheria and tetanus toxoids and acellular pertussis vaccine in young adults. *Clin Infect Dis*. 2010;51(6):656-662.
77. Shanks GD, MacKenzie A, Waller M, Brundage JF. Low but highly variable mortality among nurses and physicians during the influenza pandemic of 1918-1919. *Influenza Other Respir Viruses*. 2011;5(3):213-219.
78. Ott M, Shaw SF, Danila RN, Lynfield R. Lessons learned from the 1918-1919 influenza pandemic in Minneapolis and St. Paul, Minnesota. *Public Health Rep*. 2007;122(6):803-810.
79. Osterholm MT, Kelley NS, Sommer A, Belongia EA. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. *Lancet Infect Dis*. 2012;12(1):36-44.
80. Frederick J, Brown AC, Cummings DA, et al. Protecting healthcare personnel in outpatient settings: the influence of mandatory versus monmandatory influenza vaccination policies on workplace absenteeism during multiple respiratory virus seasons. *Infect Control Hosp Epidemiol*. 2018;39(4):452-461.
81. Grohskopf LA, Sokolow LZ, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2018—19 influenza season. *MMWR Recomm Rep*. 2018;67(3):1-20.
82. Black CL, Yue X, Ball SW, et al. Influenza vaccination coverage among health care personnel —United States, 2017-18 influenza season. *MMWR Morb Mortal Wkly Rep*. 2018;67(38): 1050-1054.
83. Lemaitre M, Meret T, Rothan-Tondeur M, et al. Effect of influenza vaccination of nursing home staff on mortality of residents: a cluster-randomized trial. *J Am Geriatr Soc*. 2009; 57(9):1580-1586.
84. Carman WF, Elder AG, Wallace LA, et al. Effects of influenza vaccination of health-care workers on mortality of elderly people in long-term care: a randomised controlled trial. *Lancet*. 2000;355(9198):93-97.
85. Potter J, Stott DJ, Roberts MA, et al. Influenza vaccination of health care workers in long-term-care hospitals reduces the mortality of elderly patients. *J Infect Dis*. 1997;175(1):1-6.
86. Frenzel E, Chemaly RF, Ariza-Heredia E, et al. Association of increased influenza vaccination in health care workers with a reduction in nosocomial influenza infections in cancer patients. *Am J Infect Control*. 2016;44(9):1016-1021.
87. Salgado CD, Giannetta ET, Hayden FG, Farr BM. Preventing nosocomial influenza by improving the vaccine acceptance rate of clinicians. *Infect Control Hosp Epidemiol*. 2004;25(11): 923-928.
88. Thomas RE, Jefferson T, Lasserson TJ. Influenza vaccination for healthcare workers who care for people aged 60 or older living in long-term care institutions. *Cochrane Database Syst Rev*. 2016:CD005187.
89. Dolan GP, Harris RC, Clarkson M, et al. Vaccination of health care workers to protect patients at increased risk for acute respiratory disease. *Emerg Infect Dis*. 2012;18(8):1225-1234.
90. Ahmed F, Lindley MC, Allred N, Weinbaum CM, Grohskopf L. Effect of influenza vaccination of healthcare personnel on morbidity and mortality among patients: systematic review and grading of evidence. *Clin Infect Dis*. 2014;58(1): 50-57.
91. Shugarman LR, Hales C, Setodji CM, Bardenheier B, Lynn J. The influence of staff and resident immunization rates on influenza-like illness outbreaks in nursing homes. *J Am Med Dir Assoc*. 2006;7(9):562-567.
92. Wendelboe AM, Avery C, Andrade B, Baumbach J, Landen MG. Importance of employee vaccination against influenza in preventing cases in long-term care facilities. *Infect Control Hosp Epidemiol*. 2011;32(10):990-997.
93. Dunkle LM, Izikson R, Patriarca P, et al. Efficacy of recombinant influenza vaccine in adults 50 years of age or older. *N Engl J Med*. 2017;376(25):2427-2436.

94. Grohskopf LA, Sokolow LZ, Fry AM, Walter EB, Jernigan DB. Update: ACIP recommendations for the use of quadrivalent live attenuated influenza vaccine (LAIV4): United States, 2018-19 influenza season. *MMWR Morb Mortal Wkly Rep*. 2018;67(22):643-645.
95. Borlaug G, Newman A, Pfister J, Davis JP. Factors that influenced rates of influenza vaccination among employees of Wisconsin acute care hospitals and nursing homes during the 2005-2006 influenza season. *Infect Control Hosp Epidemiol*. 2007;28(12):1398-1400.
96. Hollmeyer H, Hayden F, Mounts A, Buchholz U. Review: interventions to increase influenza vaccination among healthcare workers in hospitals. *Influenza Other Respir Viruses*. 2013;7(4):604-621.
97. Babcock HM, Gemeinhart N, Jones M, Dunagan WC, Woeltje KF. Mandatory influenza vaccination of health care workers: translating policy to practice. *Clin Infect Dis*. 2010; 50(4):459-464.
98. Folaranmi T, Rubin L, Martin SW, Patel M, MacNeil JR. Use of serogroup B meningococcal vaccines in persons aged ≥ 10 years at increased risk for serogroup B meningococcal disease: recommendations of the Advisory Committee on Immunization Practices, 2015. *MMWR*. 2015;64(41):608-612.
99. Jackson BR, Iqbal S, Mahon B. Updated recommendations for the use of typhoid vaccine: Advisory Committee on Immunization Practices, United States, 2015. *MMWR*. 2015;64(11):305-308.
100. Marin M, Marlow M, Moore KL, Patel M. Recommendation of the Advisory Committee on Immunization Practices for use of a third dose of mumps virus-containing vaccine in persons at increased risk for mumps during an outbreak. *MMWR Morb Mortal Wkly Rep*. 2018;67(1):33-38.
101. Dooling KL, Guo A, Patel M, et al. Recommendations of the Advisory Committee on Immunization Practices for use of herpes zoster vaccines. *Am J Transplant*. 2018;18(3):756-762.
102. Alp E, Bijl D, Bleichrodt RP, Hansson B, Voss A. Surgical smoke and infection control. *J Hosp Infect*. 2006;62(1):1-5.
103. Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination: Updated Recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep*. 2016;65(49):1405-1408.
104. US Food and Drug Administration. Gardasil 9. https://www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm426445.htm. Accessed November 12, 2018.