Postexposure management of healthcare personnel to infectious diseases

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Abstract
Healthcare personnel (HCP) are at risk of exposure to various pathogens through their daily tasks and may serve as a reservoir for ongoing disease transmission in the healthcare setting. Management of HCP exposed to infectious agents can be disruptive to patient care, time-consuming, and costly. Exposure of HCP to an infectious source should be considered an urgent medical concern to ensure timely management and administration of postexposure prophylaxis, if available and indicated. Infection control and occupational health departments should be notified for management of exposed HCP, identification of all contacts of the index case, and application of immediate infection control measures for the index case and exposed HCP, if indicated. This article reviews the main principles of postexposure management of HCP to infectious diseases, in general, and to certain common infections, in particular, categorized by their route of transmission, in addition to primary prevention of these infections.

Introduction
Healthcare personnel (HCP) are at risk of exposure to various pathogens through their daily tasks. They may serve as a reservoir for ongoing nosocomial transmission, particularly highly contagious infections such as varicella and measles [1]. Nosocomial transmission can result in infection of susceptible patients, outbreaks, work and patient care disruption, and increased cost [2,3]. An occupational exposure is defined as an exposure of HCP to a material containing an infectious agent in a healthcare setting [1]. The exposure can occur in inpatient settings (e.g. patient rooms and laboratories), in outpatient settings (e.g. medical offices and dialysis units), and in nontraditional facilities (e.g. emergency medical and skilled nursing facilities) [1]. HCP include all paid and unpaid persons working in healthcare settings who can potentially be exposed to patients and/or to infectious materials, including body substances (e.g. blood, tissue, and specific body fluids), contaminated medical supplies and equipment, contaminated environmental surfaces, or contaminated air [1]. The infectious organism can be transmitted to HCP from a patient, another HCP, hospital visitor, or the environment by several routes (Table 1) [1].

There are several strategies to prevent infections among HCP. These include vaccination of HCP who are at risk of infection and are close to or in frequent contact with high-risk patients; education and implementation of infection prevention and control measures (Table 1); and timely delivery of postexposure prophylaxis (PEP) to susceptible HCP in the event of exposure [4,5]. PEP involves administration of anti-infective agents, vaccines, or immunoglobulin as soon as possible to HCP potentially exposed to a pathogen in order to reduce the risk of infection [1,4]. Management of HCP exposure to infectious agents is paramount not only to prevent or attenuate the infection in the HCP but also to prevent secondary transmission to their contacts [1].

General principles of postexposure management
HCP who have had unprotected exposure to an infectious source should notify their supervisor and seek prompt medical evaluation. Infection control and occupational health departments should be notified for postexposure management of HCP, identification of all contacts of the index case, application of immediate infection control measures for the index case and exposed HCP, if indicated, and for deciding on whether exposed HCP can continue to provide patient care [1,4]. The HCP should be evaluated by an experienced clinician in the occupational health or emergency department as per institution policy. Postexposure management includes assessing the risk of transmission through a thorough history and laboratory testing, if necessary, with follow up, if indicated, timely administration of appropriate PEP, if available, and general and psychological counseling of exposed HCP [1,4]. The clinician can determine the need for PEP after exposure to an infectious agent based on the following: infectivity of the source patient or material at the time of
Table 1. Recommended hospital infection control precautions.

| Standard precautions | Contact precautions | Droplet precautions<sup>ab</sup> | Airborne precautions<sup>ac</sup> |
|----------------------|--------------------|-------------------------------|-------------------------------|
| Wash hands with soap and water or alcohol-based hand disinfectant before and after patient contact, before aseptic procedures, and after contact with body fluids, mucous membranes or non-intact skin. Wear gloves if contact with blood, any body fluids or contaminated items. Wear gowns during procedures and patient-care activities if contact with blood, body fluids, secretions, or excretions is anticipated. Wear masks, goggles, face shields, and combinations during procedures and patient-care activities that are likely to generate splashes or sprays of blood, body fluids, secretions, and excretions. Cough etiquette (cover nose or mouth when coughing, promptly dispose used tissues, and practice hand hygiene after contact with respiratory secretions). Safe disposal or cleaning of instruments and linen. Recommended for all patients | Isolate patients in a single room or cohort those with same active infection or colonized with the same organism. Wear nonsterile gloves for all patient contact. Wear gowns during direct patient contact or contact with contaminated material or surfaces. Use dedicated equipment for a single patient or clean and disinfect prior to use for another patient. | Isolate patients in a single room or cohort with patients who have the same active infection or are colonized with the same organism. Wear a surgical mask and eye protection within 6–10 feet of the infectious patients. Infectious patients must wear a surgical mask during transport. | Isolate patients in a single room with special air handling and ventilation systems (e.g. monitored negative pressure, at least 6–12 air exchanges per hour, exhaust must be appropriately discharged outdoors or passed through a high-efficiency particulate air filter before recirculation within the hospital). Wear a fit-tested certified N95 or higher-level respirator before entering the room of infectious patients. Infectious patients must wear a surgical mask during transport. |
| Isolate patients in a single room or cohort those with same active infection or colonized with the same organism. Wear nonsterile gloves for all patient contact. Wear gowns during direct patient contact or contact with contaminated material or surfaces. Use dedicated equipment for a single patient or clean and disinfect prior to use for another patient. | Recommended for patients with the following infections: MRSA, VRE, ESBL-producing organisms, CRE, enteric infections, *Clostridium difficile* infection, cutaneous anthrax, localized cutaneous herpes zoster, cutaneous or mucocutaneous herpes simplex infection (dissiminated or severe primary infection), RVV, enterovirus, parainfluenza, scabies, and lice | Recommended for patients with the following infections: Respiratory viral infections (e.g. influenza, adenovirus, rhinovirus) mumps, rubella, VHF's (e.g. Lassa fever, Marburg), diphtheria, iGAS, invasive meningococcal disease including meningitis, pertussis, pneumatic and meningal plague, *Haemophilus influenzae* type B (meningitis), and Mycoplasma pneumoniae | Recommended for patients with the following infections: tuberculosis (pulmonary, laryngeal), measles, varicella-disseminated herpes zoster, smallpox<sup>d</sup>, SARS-associated coronavirus<sup>d</sup>, avian influenza, and Ebola<sup>d</sup> |

<sup>a</sup>Certain procedures can generate droplets and aerosols including administration of aerosolized or nebulized medication, diagnostic sputum induction, bronchoscopy, airway suctioning, endotracheal intubation, positive pressure ventilation via facemask, high frequency oscillatory ventilation, grinding, centrifugation, and vigorous shaking of laboratory specimens, and bone-sawing during autopsy.

<sup>b</sup>Contact precautions also are required for infectious patients with respiratory viruses such as influenza, and iGAS infections.

<sup>c</sup>Contact precautions required for infectious patients with varicella, disseminated herpes zoster, smallpox, SARS-associated coronavirus, and MERS-CoV.

<sup>d</sup>Contact and droplet are the main routes of transmission for smallpox, SARS-associated coronavirus, and MERS-CoV.

<sup>e</sup>Patients with Ebola should be placed in a single private room with a closed door and a private bathroom. HCP entering the room should wear a single-use fluid-resistant or impermeable gown that extends to at least mid-calf or single-use shoe covers, and fit-tested N95 respirator in combination with a single-use surgical hood extending to shoulders and a single-use full face shield or powered air-purifying respirator (PAPR) with full face shield, helmet, or headpiece.

Abbreviations: CRE = Carbapenem-resistant Enterobacteriaceae; ESBL = Extended spectrum β-lactamase; HCP = Healthcare personnel; iGAS = Invasive group A streptococcal disease; MERS-CoV = Middle East respiratory syndrome coronavirus; MRSA = Methicillin-resistant *Staphylococcus aureus*; RVV = Respiratory syncytial virus; SARS = Severe acute respiratory syndrome; VHF = Viral hemorrhagic fever; VRE = Vancomycin-resistant enterococci.

Information from references [1,6,21-23,32,39,45,48,50,51,54-56,68,88].
exposure, extent and type of exposure, susceptibility of the HCP to the infectious disease of concern, and whether the exposed HCP is at a greater risk of complications than the general population [1,4]. Vaccines should be given to the exposed HCP even if they present beyond the time indicated for PEP administration. All nonimmune HCP should be vaccinated against hepatitis B virus (HBV), seasonal influenza, measles, mumps, rubella, pertussis, and varicella [4,5]. The HCP should be counseled on risk of infection acquisition and transmission to others, particularly if they decline PEP, benefits of treatment, importance of adherence to the drug regimen, possible adverse effects of the PEP regimen, and follow-up plan [1,4].

The exposed HCP should be counseled to immediately stop working or not to report to work, notify infection control and occupational health, and seek prompt medical attention if they develop fever or symptoms and signs of the infection of concern. They should comply with work restriction or exclusion until they are no longer deemed infectious to others by the occupational health department [1,4].

Healthcare institutions should have protocols available to HCP for the management of occupational exposures to infectious diseases. Federal law requires covered employers to ensure that all medical evaluations and procedures, vaccines, and PEP are made available to the employee within a reasonable timeframe, at a reasonable location, and at no cost to the employee [1,4,6]. The employer is responsible for establishing and implementing policies to protect the confidentiality of both the exposed employee and the source [6].

In the following section, we will review postexposure management of common and serious infectious agents encountered in the healthcare setting, categorized by route of transmission. We will discuss initial assessment and testing, PEP regimen and its adverse effects, follow-up testing, and work restriction. We will also briefly discuss primary prevention, infection prevention and control precautions and vaccination for each infection.

**Postexposure management of blood-borne infections**

Percutaneous injuries sustained by hospital-based HCP occur at a rate of 19.5 injuries per 100 occupied beds [7]. Exposure of HCP to blood-borne pathogens commonly occurs as a result of needlestick injuries, with operating rooms, patient rooms, and emergency departments being the most common sites [7]. Exposures that pose a risk of transmission of blood-borne pathogens include percutaneous (e.g. needlestick), ocular, mucous membrane, or non-intact skin (e.g. human bites, traumatized skin) exposures to blood, tissue, or other potentially infectious body fluids. There are several pathogens that can be transmitted following exposure to blood [8]. Other body fluids that can transmit blood-borne pathogens are cerebrospinal, pericardial, pleural, peritoneal, synovial, amniotic fluid; semen, cervical, or vaginal secretions; and visibly bloody fluids, excretions, or secretions. Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus cannot transmit blood-borne pathogens unless they contain blood [1,9,10].

We will discuss the management of exposure to HBV, hepatitis C virus (HCV), and HIV since they are the most commonly encountered [8].

**Initial management of exposure to blood-borne pathogens**

Following exposure to blood-borne pathogens, the exposed area should be immediately washed with soap and water and cleansed with an antiseptic (e.g. chlorhexidine gluconate). The exposed mucous membranes should be flushed with copious amounts of water and the eyes irrigated with saline or water [1].

The risk factors and baseline status for HIV, HBV, HCV, and other blood-borne pathogens should be assessed in both the source and the exposed HCP. It is not necessary to test the source patient if the status of HIV, HBV, or HCV is known to be positive [9-11]. If the status for these infections is unknown through history and medical records, testing to determine the disease status of both source and exposed HCP should be performed promptly. The recommended tests are hepatitis B surface antigen (HBsAg), hepatitis C antibodies, and HIV antibodies. It is not recommended to test needles or sharp instruments implicated in the exposure [9-11].

PEP for HIV and HBV, if nonimmune, should be given to HCP as early as possible while waiting for further information or test results if the exposure is associated with risk of transmission [9-11]. However, hepatitis B vaccine should be given to nonimmune exposed HCP who are at future exposure risk even if presenting >7 days after exposure [9,11].

The exposed HCP should be counseled about modifying sexual practices (for HIV), avoiding breastfeeding and pregnancy (HIV), and refraining from donating blood, plasma, organs, tissue, or semen until these infections have been ruled out [9-11].

**HIV**

The average risk of HIV transmission after percutaneous and mucocutaneous exposure to HIV-infected blood in healthcare settings is approximately three and one per 1000 exposures, respectively [12]. The risk of transmission of HIV after percutaneous exposure to HIV-infected blood is increased with deep injury, visible blood on the device, procedures involving a needle in an artery or vein, and high HIV viral load. Low level of HIV viral load in the blood and the use of antiretroviral therapy (ART) are associated with a reduction of the risk of HIV transmission [13].

Selection of a three-drug regimen for HIV PEP should be guided by proven efficacy, tolerability and side effect and toxicity profiles, ease of administration, and known or suspected resistance of the source virus to ART [9,11]. The preferred HIV PEP regimen is tenofovir, emtricitabine, and raltegravir, based on their proven efficacy in treatment of HIV infection and tolerability (Table 2) [9,11,14,15].

HIV PEP should be continued until the result of HIV testing is available. If the source patient is known or confirmed to be HIV-infected, PEP should be continued for 28 days. If HIV antibody testing is negative in the source patient, PEP
| Pathogen | Disease status of source patient | Disease status of exposed HCP | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|----------|---------------------------------|-----------------------------|-------------|-----------------------------------------------|-------------------|-------------------------------|
| HIV<sup>b</sup> | HIV-infected patients<sup>c</sup> | HIV-negative HCP | One of the following oral regimens started as early as possible for 28 days<sup>5</sup>: Tenofovir-emtricitabine 300/200 mg/day<sup>e</sup> OR Zidovudine 300 mg twice daily with lamivudine 150 mg twice daily<sup>d</sup> PLUS Raltegravir 400 mg orally twice daily<sup>c</sup> OR Atazanavir/ritonavir 300/100 mg/day orally OR Darunavir-ritonavir 800 mg/100 mg/day orally OR Lopinavir/ritonavir (400/100 mg) 2 tablets orally twice daily<sup>1</sup> | For source patient: -Anti-HIV1/HIV2, if status is unknown<sup>6</sup> For exposed HCP: -Anti-HIV1/HIV2 at baseline, 6 weeks, and 12 weeks postexposure -Pregnancy test for females of reproductive age -Complete blood count, urea, creatinine, liver function tests, serum glucose (if on PIs), and creatine phosphokinase (if on raltegravir) at baseline, 2 weeks, and 4 weeks after initiating ARV drugs | Follow standard precautions for HIV-infected patients unless they have other infections that require additional precautions (e.g., airborne precautions for pulmonary tuberculosis) | Tenofovir: asthenia, nausea, vomiting, diarrhea, headache, dizziness, and nephrotoxicity; avoid in patients with creatinine clearance <50mL/min Emtricitabine and lamivudine: nausea, vomiting, headache, rash and skin hyperpigmentation. For chronic Hepatitis B patients: risk of acute hepatitis exacerbation on withdrawal of tenofovir, emtricitabine or lamivudine Zidovudine: nausea, vomiting, headache, insomnia, fatigue, anemia, and neutropenia Raltegravir: insomnia, nausea, vomiting, headache, dizziness, severe skin and hypersensitivity reaction, increased creatine phosphokinase and rhabdomyolysis PIs (atazanavir, darunavir, lopinavir, ritonavir): nausea, vomiting, diarrhea, hyperglycemia, dyslipidemia, PR and QTc prolongation, hepatotoxicity, hyperbilirubinemia (atazanavir), nephrolithiasis (atazanavir), increased risk of bleeding in patients with hemophilia, rash (darunavir), and multiple drug interactions -Darunavir is not recommended for patients with severe liver disease -Avoid use of darunavir in patients with significant sulfonamide allergy All ARV therapy listed are safe in pregnancy |
| HBV<sup>b</sup> | Patients with positive HbsAg | Unvaccinated or previously vaccinated HCPs that are nonresponders to first three-dose vaccine series<sup>5</sup> | A single dose of HBIG, 0.06 mL/kg IM, followed by hepatitis B vaccine series (given at 0, 1–2 months, and 6 months)<sup>j</sup>, injected at a different site than HBIG, within 24 hours but no later than 7 days post-exposure HBIG 0.06 mL/kg IM twice, the first dose to be given within 24 hours of exposure, second dose 1 month later A single dose of HBIG 0.06 mL/kg IM, followed by completion of the three-dose hepatitis B virus vaccine series<sup>1</sup> | For source patient: HbsAg For exposed HCP: -HbsAg, Anti-HBs, anti-HBe<sup>k</sup> -Pregnancy test for female of reproductive age -HbsAg and anti-HBe at 6 months after baseline<sup>5</sup> -Check anti-HBs 1–2 months following the last dose of vaccine for HCP at risk for occupational percutaneous or mucosal exposures | Follow standard precautions for HBV-infected patients All nonimmune HCP at reasonably anticipated risk for blood or body fluid exposure should receive a 3-dose primary series of hepatitis B vaccine on a 0-, 1-, and 6-month schedule<sup>3</sup> | Hepatitis B vaccine: local injection site reactions or systemic reaction (fever) -Contraindicated for persons with a history of anaphylactic allergy to Baker’s yeast or any vaccine component HBIG: headache, erythema, pain at injection site, malaise, myalgia, nausea, and vomiting -Contraindicated in cases of previous anaphylactic or severe systemic reaction to human globulin preparations Hepatitis B vaccine and HBIG are safe during pregnancy |
| HBV<sup>b</sup> | Patients with positive HbsAg | Previously vaccinated, nonresponder to a second three-dose vaccine series<sup>5</sup> | None required | | | |
| HBV<sup>b</sup> | Patients with positive HbsAg | Currently receiving first three-dose vaccine series | | | | |
| HBV<sup>b</sup> | Patients with positive HbsAg | Previously infected or vaccinated with adequate response<sup>1</sup> | Test exposed HCP for anti-HBs; if serum level of anti-HBs ≤10 mIU/mL, PEP is not required; if serum level of anti-HBs <10 mIU/mL, a single dose of HBIG 0.06 mL/kg IM, followed by hepatitis B vaccine booster injected at different sites | | | |
| HBV<sup>b</sup> | Patients with positive HbsAg | Previously vaccinated with unknown antibody response | | | | |
| Pathogen | Disease status of source patient | Disease status of exposed HCP | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|----------|---------------------------------|------------------------------|-------------|-----------------------------------------------|-------------------|-------------------------------|
| HCVb     | Patients with HCV infection (both positive HCV antibody and HCV RNA) | HCV-negative HCP | None | For source patient: anti-HCV, HCV-RNA, if status is unknown | Follow standard precautions for HCV-infected patients |

**Notes:**

1. Postexposure management and testing should be performed according to the institution policy following informed consent if indicated. If the status is unknown both source and exposed HCP should be tested for HIV (Anti-HIV1/HIV2), HBV (HbsAg), and HCV (anti-HCV).

2. There is no need for work restriction or modification for exposed asymptomatic noninfected HCP.

3. HIV-infected source who has confirmed positive HIV antibody by EIA assay with HIV1/HIV2 antibody differentiation immunoassay, rapid HIV testing, or positive HIV RNA (>5000–10,000 c/mL, if the source patient has been at risk of HIV exposure in the previous 6 weeks).

4. ARV drugs that should be avoided due to severe drug adverse effects and toxicity include efavirenz, nevirapine, abacavir, stavudine, didanosine, nelfinavir, indinavir, tipranavir, and enfuvirtide.

5. This is the preferred HIV PEP regimen, whereas others are considered alternative regimens.

6. Zidovudine-lamivudine and lopinavir-ritonavir is the alternative PEP regimen in pregnancy.

7. Information about known HIV-infected source’s stage of infection (i.e. asymptomatic, symptomatic, or AIDS), CD4+ T-cell count, HIV viral load, current and previous ARV drugs, and results of any genotypic or phenotypic viral resistance testing should be used in choosing an appropriate HIV PEP regimen.

8. Serum level of anti-HBs <10 mIU/mL.

9. Serum level of anti-HBs ≥10 mIU/mL.

10. Day 0 is the day of administration of first dose of vaccine; administer hepatitis B vaccine in deltoid muscle using a 1–1.5 inch needle at a dose of 20 μg (1.0 mL) for Engerix-B OR 10 μg (1.0 mL) for Recombivax.

11. HbsAg and anti-HBc should be monitored only in previously unvaccinated, vaccinated with inadequate response, vaccinated nonresponders, vaccinated with unknown status, or HCP undergoing vaccination if only the source patient is HbsAg-positive or unknown status.

12. The presence of anti-HCV indicates past or present HCV infection and HCV RNA testing is recommended to ascertain present true infection.

13. Follow-up blood testing for HCV is not required for the exposed HCP, if the source is anti-HCV-negative or anti-HCV-positive but HCV RNA is undetectable.

Abbreviations: Anti-Hbc = Antibody to hepatitis B core antigen; anti-HCV = Antibodies to hepatitis C virus; Anti-HBs = Antibody to hepatitis B surface antigen; ARV = Antiretroviral; HBV = Hepatitis B virus; HCP = Healthcare personnel; HCV = Hepatitis C virus; HbsAg = Hepatitis B surface antigen; HBIG = Hepatitis B immunoglobulin; IM = Intramuscular; PEP = Postexposure prophylaxis; PIs = Protease inhibitors.

Information from references [1,4,5,9-11,16,20].
should be discontinued and no follow-up HIV testing for the exposed HCP is required. However, if the source patient is at a risk of HIV exposure in the previous 6 weeks and acute retroviral syndrome is clinically suspected, plasma HIV RNA testing is recommended. PEP should be continued until results of the plasma HIV RNA assay are available [9,11].

Rapid HIV testing is the recommended test to be utilized in decision-making regarding PEP, if the HIV status of the source is unknown. A fourth-generation HIV antigen/antibody combination test is the preferred serologic screening test, if the rapid HIV test is positive, and as a follow-up test for the exposed HCP. All positive HIV antibody tests should be confirmed by supplemental tests such as the HIV1/HIV2 antibody differentiation immunoassay [9,11,16].

Exposed HCP should be followed in an outpatient clinic 3 days after initial assessment, every 1–2 weeks until the end of PEP treatment and for blood testing (Table 2). If the exposed HCP develop an acute illness consistent with primary HIV infection such as febrile or mononucleosis-like illness, testing for HIV with a fourth-generation enzyme immunoassay and HIV RNA assay is recommended [9,11]. If HIV antibody testing is positive at baseline or at any time during follow up, HCP should be referred to a clinician experienced with HIV care for further management and treatment, and the incident should be reported to the local health department if occupationally acquired [9,11].

HBV

The risk of HBV transmission after percutaneous exposure to blood from an HBV-infected patient is approximately 23%–62% [17]. The need and type of PEP for HBV is based on type of exposure, HBsAg status of the source patient, disease status of the exposed HCP, and vaccination status and vaccine-response status of the exposed HCP (Table 2) [4,10]. HBV vaccine and hepatitis B immunoglobulin are 70%–90% effective in preventing HBV infection if given within 12–24 hours of exposure [18,19].

HCV

The risk of transmission of HCV following percutaneous exposures to blood from HCV-infected source patients is estimated to be 1.8% per exposure [8,11]. Since there is no effective PEP regimen to prevent HCV transmission, the goal is early identification of infection and, if present, referral for follow up, and evaluation of treatment options with an experienced clinician (Table 2) [11,20].

If the serum alanine aminotransferase level is elevated at follow up, HCP should be tested for HCV RNA to assess for acute HCV infection; if the HCP become acutely infected with hepatitis C, immediate referral to a specialist experienced in the treatment of hepatitis C is strongly recommended [11,20].

Primary prevention

Primary prevention of occupational infection with blood-borne pathogens can be achieved by preventing exposures to blood and body fluids through infection control precautions, use of safety devices, safer work practices and engineering controls, improved surgical techniques, education of HCP on prevention of needlestick injury, and postexposure care and vaccination against HBV [6,10].

Postexposure management of infections transmitted by the airborne route

Person-to-person transmission of these air-borne infections occurs via inhalation of droplet nuclei (airborne particles 1–5 μm in diameter) containing infectious agents that remain infective over time and distance. These droplets are usually generated by infectious patients through coughing, sneezing, and shouting, in addition to other sources such as aerosol-generating procedures (Table 1) [1,21-23].

Tuberculosis

HCP are at higher than average risk of acquiring tuberculosis (TB), particularly in TB-prevalent areas. The estimated latent TB infection (LTBI) rates among HCP in countries with low, intermediate, and high TB incidence are 3.8%, 6.9%, and 8.4%, respectively [24]. Patients with unrecognized TB disease who are not promptly placed in appropriate airborne precautions are the major risk factor for transmission of Mycobacterium tuberculosis in healthcare settings [21]. The risk of transmission is higher following contact with patients with cavitary pulmonary or laryngeal TB, acid-fast bacilli (AFB) smear positive sputum, cough, and those who are not on effective anti-TB treatment or have just initiated treatment [21].

When a new case of infectious TB is identified in the healthcare setting, all contacts prior to implementing infection control measures should be identified and evaluated for TB disease and LTBI [21]. The highest priority for contact evaluation should be given to HCP with medical risk factors for TB disease (e.g. HIV infection or immunocompromised) and those present during aerosol-producing procedures (e.g. bronchoscopies, sputum induction, or autopsies) (Table 3) [21].

Any HCP exposed to a potentially infectious TB source should be evaluated promptly with a symptom screen for TB and a tuberculin skin test (TST) or IFN-γ release assay (IGRA). TST or IGRA should not be performed in exposed HCP who have had a previous positive test result or a history of treatment for LTBI or TB disease [21]. The TST or IGRA and symptom screen should be repeated 8–12 weeks later, if the initial TST or IGRA result is negative and HCP is asymptomatic. Repeating TST is not contraindicated, unless the test was associated with severe ulceration or anaphylactic shock; in such cases, IGRA is the recommended test. IGRA is also preferred in previously Bacillus Calmette-Guérin (BCG) vaccinated HCP [21,25-27].

The choice of the cut point for a positive TST result after exposure to an active TB index case will depend on the baseline TST result if known and whether the exposed HCP has an immunocompromising condition. Prior BCG vaccination status should not be used in the interpretation of TST in the setting of contact investigations [25-27]. The result of the TST should be read by a designated and trained clinician 48–72 hours after the TST is placed and should be
| Infection | Disease status of source patient | Disease status of exposed HCP and type of exposure | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|-----------|---------------------------------|-----------------------------------------------|-------------|-----------------------------------------------|-------------------|--------------------------------|
| TB        | Patients with untreated pulmonary or laryngeal TB | All HCP with unprotected exposure, regardless of prior history of TB or vaccination with BCG | One of the following regimens for treatment of LTBI should be considered:  
Isoniazid 5 mg/kg/day orally PLUS vitamin B6 25–50 mg/day orally for 9 months  
OR  
Rifampicin 10 mg/kg (maximum dose of 600 mg/day) orally for 4 months  
OR  
Isoniazid 900 mg orally once weekly PLUS vitamin B6 25–50 mg/day orally PLUS rifapentine 900 mg orally once weekly for 3 months  
OR  
Isoniazid 5 mg/kg/day orally PLUS vitamin B6 25–50 mg/day orally for 6 months  
OR  
Isoniazid 900 mg orally twice weekly PLUS vitamin B6 25–50 mg/day orally for 9 months  
OR  
Isoniazid 900 mg orally twice weekly PLUS vitamin B6 25–50 mg/day orally for 6 months  
OR  
Rifampicin 10 mg/kg orally PLUS isoniazid 900 mg/kg orally twice weekly PLUS vitamin B6 25–50 mg/day orally for 3 months | Notify infection control and occupational health departments to identify contacts of the index case  
Screen exposed HCP for symptoms and signs of TB disease  
Perform TST or IGRA in exposed HCP who have no history of prior positive TST or IGRA  
Screen exposed HCP with prior positive TST or IGRA or documented history of LTBI or TB disease for symptoms and signs of TB disease and chest radiography  
Repeat TST or IGRA 8–12 weeks postexposure, if the initial test and screen for symptoms and signs of TB disease are negative  
Rule out TB disease by symptom and sign screen and chest radiography, if initial or follow up TST or IGRA are positive  
Perform baseline and monthly liver function tests for HCP on treatment of LTBI  
No work restriction or modification required for exposed asymptomatic HCP with or without LTBI or with extrapulmonary TB without lung or laryngeal involvement or draining lesions  
Symptomatic HCP with infectious pulmonary or laryngeal TB should be excluded immediately from work and can return to work when they are considered noninfectious by occupational health and infection control departments | Patients with suspected or confirmed pulmonary laryngeal TB, or extrapulmonary TB with draining lesions should be placed in contact and airborne precautions  
Patients with extrapulmonary TB without draining lesions require only standard precautions | Isoniazid: nausea, vomiting, hepatotoxicity, and peripheral neuropathy  
Rifampin and rifapentine: nausea, vomiting, hepatotoxicity, red-orange discoloration of urine, tears, sweat, and stool, drug interactions, thrombocytopenia, and rash |
| Infection                                | Disease status of source patient | Disease status of exposed HCP and type of exposure | PEP regimen                                                                 | Initial assessment and follow up of exposed HCP | Primary prevention                                                                                                                                 | Adverse effects of PEP regimen |
|-----------------------------------------|---------------------------------|---------------------------------------------------|----------------------------------------------------------------------------|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------|
| Varicella and disseminated herpes zoster (HZ) | Patients with active infection from 1–2 days before rash onset for varicella and from onset of rash for HZ until all lesions have crusted (for vesicular rash) or disappeared (for maculopapular rash) | Nonimmune HCP with direct, face-to-face contact, not transitory, with patients with varicella or disseminated HZ | Two doses of varicella vaccine 1 month apart SC for exposed immunocompetent HCP within 5 days of exposure A single dose of VariZIG 125 units/10 kg IM/IV (to a maximum of 625 units) for exposed pregnant or immunocompromised HCP as soon as possible, ideally within 96 hours of exposure OR Immune globulin 400 mg/kg IV if VariZIG is not available OR Acyclovir 40–80 mg/kg orally in four divided doses, famciclovir 500 mg orally 3 times daily, or valacyclovir 1 g orally 3 times daily on postexposure days 3–22, or on postexposure days 3–28 in HCP who has received VariZIG or immunoglobulin PEP is not recommended | Monitor exposed HCP daily for fever, skin rash, or systemic symptoms from days 8–21 after exposure (from days 8–28, if they received VariZIG) No work restriction or modification for asymptomatic exposed immune HCP or recently vaccinated HCP Exposed HCP who are nonimmune, vaccinated with a single dose of varicella vaccine, or received the second dose of varicella vaccine >5 days postexposure should be excluded from work from days 8–21 (from days 8–28, if they received VariZIG) after last exposure Exposed symptomatic HCP should be excluded immediately from work until lesions are dry and crusted 2 | Patients with varicella or disseminated HZ, or immunocompromised patients with cutaneous HZ should be placed in contact and airborne precautions until all lesions are dry and crusted 2 | Varicella vaccine: injection-site reactions (pain, tenderness, swelling), fever, rash, and thrombocytopenia VariZIG: injection-site reactions, headache, chills, anaphylactic/hypersensitivity reaction, and noncardiogenic pulmonary edema Acyclovir: nausea, vomiting, diarrhea, headache, acute renal failure, agitation, tremors, delirium, hallucinations, and myoclonus Famciclovir: nausea, malaise, rash, and headache Valacyclovir: nausea, headache, increased liver function tests, and thrombotic microangiopathy Varicella vaccine is contraindicated in HCP who are pregnant or might become pregnant within 4 weeks of vaccination and in immunocompromised HCP (with hematologic malignancies, or on immunosuppressive drugs such as such as systemic steroids >2 mg/kg body weight) Varicella vaccine can be administered to HIV-infected HCP with a CD4+ T-lymphocyte count ≥ 200 cells/mL or immunocompetent HCP with immunocompromised patients in their households Contraindications to VariZIG include history of anaphylactic or severe systemic reactions to human immunoglobulins, and IgA-deficient patients with antibodies against IgA and a history of hypersensitivity Acyclovir, famciclovir, and valacyclovir are classified as category B in the FDA use-in-pregnancy rating |
### Table 3. (Continued)

| Infection | Disease status of source patient | Disease status of exposed HCP and type of exposure | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|-----------|---------------------------------|-----------------------------------------------|--------------|---------------------------------|------------------|--------------------------------|
| Measles   | Patients with active infection, from 4–5 days before appearance of the rash until 4 days after rash onset | Nonimmune HCP or documentation of 1 vaccine dose | A single dose of immunoglobulin, 0.5 mg/kg IM (maximum dose 15 mL) or 400 mg/kg IV, for pregnant women or severely immunocompromised HCP within 6 days of exposure | Give exposed immunocompetent HCP the second dose of live measles virus-containing vaccine, if indicated, at least 28 days after the first dose of MMR or at least 3 months after the first dose of MMRV | Patients with measles should be in airborne precautions until 4 days after onset of rash, or for duration of illness in immunocompromised individuals | Live measles virus-containing vaccines (MMR, MMRV): pain, redness, or swelling at the injection site, fever, transient rashes, transient lymphadenopathy, arthralgia/transient arthritis, parotitis, thrombocytopenia, febrile seizures, and encephalitis |
|          |                                  | Immune contacts<sup>k</sup>                  | Live measles virus-containing vaccine (MMR or MMRV) SC for exposed immunocompetent HCP within 3 days of exposure | Exposed nonimmune HCP should be excluded from work from days 5–21 postexposure; HCP with a documented history of 1 vaccine dose may receive the second dose and remain at work | All nonimmune HCP should be vaccinated with two doses of live measles virus-containing vaccines (MMR, MMRV) | Contraindications to live measles virus containing vaccines include history of anaphylactic reactions to neomycin, history of severe allergic reaction to any component of the vaccine, pregnancy, and immunosuppression |
|          |                                  |                                              | A single dose of immunoglobulin, 0.5 mg/kg IM (maximum dose 15 mL) or 400 mg/kg IV, exposed immunocompromised HCP within 6 days of exposure<sup>l</sup> | Exposed symptomatic HCP should be excluded immediately from work until ≥4 days post-onset of rash | | MMR vaccine, not MMRV vaccine, can be administered to HIV-infected patients who are well controlled and on effective antiretroviral therapy |
| MERS-CoV  | Patients with MERS-CoV infection | HCP who have close contact with infectious patients<sup>m</sup> | No PEP available | Consider excluding HCP with unprotected exposure to a MERS-CoV patient for 14 days following the last exposure; or HCP should wear a facemask at all times while in the healthcare facility | Patients with MERS-CoV infection should be placed in contact and airborne precautions | Consultation with expert, local or state health department, or CDC is strongly recommended; site and vaccine complications |
| Ebola     | Symptomatic patients with Ebola  | All HCP with high-risk exposure<sup>n</sup> | None | No work restriction for asymptomatic HCP during temperature surveillance period | Duration of precautions should be determined on a case-by-case basis, in conjunction with local and state public health authorities and CDC | |
| Avian influenza (H5N1, H7N9) | Patients with symptomatic H5N1 or H7N9 infection | All HCP within moderate risk exposure group<sup>o</sup> | One of the following regimens could be given within 48 hours of exposure: Oseltamivir 75 mg/day orally once for 7 days, if H5N1, or twice daily for 5 days for limited exposure | Counsel HCP to measure temperature daily for 7–10 days following the last known exposure to the patient | Patients suspected of having avian influenza should be placed in contact and airborne precautions with face/eye protection | |

<sup>k</sup> Immune contacts: A single dose of immunoglobulin, 0.5 mg/kg IM (maximum dose 15 mL) or 400 mg/kg IV, for pregnant women or severely immunocompromised HCP within 6 days of exposure. Exposed nonimmune HCP should be excluded from work from days 5–21 postexposure; HCP with a documented history of 1 vaccine dose may receive the second dose and remain at work. Exposed symptomatic HCP should be excluded immediately from work until ≥4 days post-onset of rash.

<sup>l</sup> Immunocompromised HCP: Live measles virus-containing vaccine (MMR or MMRV) SC for exposed immunocompetent HCP within 3 days of exposure. Live measles virus-containing vaccine (MMR, MMRV): pain, redness, or swelling at the injection site, fever, transient rashes, transient lymphadenopathy, arthralgia/transient arthritis, parotitis, thrombocytopenia, febrile seizures, and encephalitis.

<sup>m</sup> Close contact: A single dose of immunoglobulin, 0.5 mg/kg IM (maximum dose 15 mL) or 400 mg/kg IV, for pregnant women or severely immunocompromised HCP within 6 days of exposure. Exposed nonimmune HCP should be excluded from work from days 5–21 postexposure; HCP with a documented history of 1 vaccine dose may receive the second dose and remain at work. Exposed symptomatic HCP should be excluded immediately from work until ≥4 days post-onset of rash.

<sup>n</sup> High-risk exposure: A single dose of immunoglobulin, 0.5 mg/kg IM (maximum dose 15 mL) or 400 mg/kg IV, for pregnant women or severely immunocompromised HCP within 6 days of exposure. Exposed nonimmune HCP should be excluded from work from days 5–21 postexposure; HCP with a documented history of 1 vaccine dose may receive the second dose and remain at work. Exposed symptomatic HCP should be excluded immediately from work until ≥4 days post-onset of rash.

<sup>o</sup> Moderate risk exposure: A single dose of immunoglobulin, 0.5 mg/kg IM (maximum dose 15 mL) or 400 mg/kg IV, for pregnant women or severely immunocompromised HCP within 6 days of exposure. Exposed nonimmune HCP should be excluded from work from days 5–21 postexposure; HCP with a documented history of 1 vaccine dose may receive the second dose and remain at work. Exposed symptomatic HCP should be excluded immediately from work until ≥4 days post-onset of rash.
Table 3. (Continued)

| Disease status of source patient | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|---------------------------------|-----------------------------------------------|-------------------|--------------------------------|
| Infection                       | Exposure status of exposed HCP and type of exposure | PEP regimen       | for 10 days for ongoing exposure and for 10 days for ongoing exposure (if H1N1 or H2N2 influenza) |
|---------------------------------|-----------------------------------------------|-------------------|--------------------------------|
| -                               | -                                             | -                 | -                             |
| C or other symptoms should be considered for H1N1 or H2N2 influenza. For patients with HIV infection, use of antiretroviral therapy may be considered. |
| Disease status of source patient | Exposure status of exposed HCP and type of exposure | PEP regimen       | for 10 days for ongoing exposure and for 10 days for ongoing exposure (if H1N1 or H2N2 influenza) |
| -                               | -                                             | -                 | -                             |
| Close contact is defined as being within 6 feet or within the room or care area for a prolonged period of time (not a brief interaction such as walking by) or having direct contact with infectious secretions such as respiratory while not wearing PPE. |
| Close contact, particularly if at high risk of complications of avian influenza, within 6 feet with a confirmed or probable case during bronchoscopy or intubation; while performing tracheal suctioning, delivering nebulized drugs, or handling inadequately screened or sealed body fluids without use of recommended PPE; or following a recognized breach in PPE procedure or a laboratory workers with unprotected exposure to a virus-containing sample. If PEP cannot be started within 48 hours of exposure, antiviral treatment with oseltamivir 75 mg orally twice daily for 7 days can be given. |
| Close contact with an infected patient. Low-risk exposures include: HCP in facilities with infected patients who have been in care areas of infected patients without recommended PPE. |
| Close contact, particularly if at high risk of complications of avian influenza, within 6 feet with a confirmed or probable case during bronchoscopy or intubation; while performing tracheal suctioning, delivering nebulized drugs, or handling inadequately screened or sealed body fluids without use of recommended PPE; or following a recognized breach in PPE procedure or a laboratory workers with unprotected exposure to a virus-containing sample. If PEP cannot be started within 48 hours of exposure, antiviral treatment with oseltamivir 75 mg orally twice daily for 7 days can be given. |
| Close contact with an infected patient. Low-risk exposures include: HCP in facilities with infected patients who have been in care areas of infected patients without recommended PPE. |
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| Close contact with an infected patient. Low-risk exposures include: HCP in facilities with infected patients who have been in care areas of infected patients without recommended PPE. |
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| Close contact with an infected patient. Low-risk exposures include: HCP in facilities with infected patients who have been in care areas of infected patients without recommended PPE. |
| Close contact with an infected patient. Low-risk exposures include: HCP in facilities with infected patients who have been in care areas of infected patients without recommended PPE. |
documented in millimeters, not simply as negative or positive. A positive TST in a contact of a known infectious TB patient is defined as ≥5 mm in HCP with a previous TST result of 0 mm or an increase of ≥10 mm in HCP with a previous TST result between 0 mm and 10 mm. In immunocompromised HCP, a TST ≥5 mm on baseline or follow-up testing is considered positive [21,25-27].

All exposed HCP with positive TST or IGRA should be evaluated by screening for symptoms and signs of TB disease and chest radiography to rule out TB disease. If TB disease is ruled out, treatment for LTBI should be considered [21]. Treatment of LTBI significantly reduces the risk of progression from infection with *M. tuberculosis* to TB disease by 60%–90% (Table 3) [28-31].

Exposed immunocompromised HCP (e.g. HIV infection, organ transplantation) should be evaluated by screening for symptoms and signs, TST or IGRA, and chest-X-ray; if all the tests are normal, they should be started on treatment for LTBI due to the high risk of developing active disease. If the repeat TST or IGRA at 8–12 weeks is negative, treatment for LTBI can be discontinued. Clinicians may choose to complete the treatment course for LTBI in that situation since TST and IGRA may not be reliable in severely immunocompromised conditions [21].

If exposed HCP develop symptoms or signs of TB (e.g. fever, weight loss, hemoptysis) during follow up, chest X-ray and AFB smear and culture should be performed and the HCP should be treated for TB disease if indicated [21].

Prevention of TB among HCP can be accomplished through education regarding TB symptoms, transmission, and prevention, and by providing training in the proper donning and doffing of personal protective equipment (PPE) such as respirators and N95 masks. In addition, annual screening for symptoms or signs of TB disease, baseline (for all HCPs in low- and medium-risk settings) and annual (for medium-risk settings) TB screening for HCP with negative TST or IGRA, and treatment of HCP who have LTBI is recommended [21,25-27].

### Varicella and herpes zoster

Varicella, caused by varicella-zoster virus (VZV), is highly contagious, with secondary attack rates up to 90%. It is transmitted via direct contact with vesicles and inhalation of aerosols from vesicular fluid or respiratory tract secretions of a patient with varicella or disseminated herpes zoster (HZ) [22]. HZ is much less contagious than varicella [22,32]. Varicella can still occur in vaccinated exposed persons, but the infection is usually milder and less infectious than in the unvaccinated ones [22]. Nosocomial transmission, which is uncommon, is usually due to delay in the diagnosis, incorrect diagnosis, or late implementation of infection control precautions [4,22,32].

PEP regimens for varicella and HZ include varicella vaccine, varicella zoster immune globulin (VariZIG), and oral antiviral agents (Table 3) [22,32,33].

Varicella vaccine, not zoster vaccine, is effective in prevention of varicella infection (risk reduction of 60%–90%) and development of severe disease due to vaccine-induced VZV-specific T-cell proliferation if given within 3–5 days of exposure to an index case of varicella or zoster [34]. The disease is usually mild in vaccinated persons who did not seroconvert or who lost detectable antibody and developed varicella after exposure to VZV [4,35]. Any HCP who develops vaccine-related rash should avoid contact with susceptible patients until resolution of the rash [4,22].

Varizig is effective in prevention and disease modification of varicella in exposed susceptible persons if given ideally within 96 hours, and up to 10 days, of exposure [36,37].

It should be noted that none of the PEP regimens are completely effective in preventing the disease after exposure and breakthrough infections have been reported [22].

### Measles

Measles is a highly contagious disease with a secondary attack rate of 90%. The majority of measles cases occur in either unvaccinated HCP or HCP with unknown vaccination status. It still can occur in immunized persons after exposure to an index case [4,38,39].

Measles vaccine may prevent and attenuate the severity of the disease if given within 3 days of exposure in limited contact settings such as schools, childcare, and medical offices [40,41]. Immunglobulin products are effective in preventing and modifying the infection, in addition to reducing the mortality by 75%, in persons who are nonimmune if administered within 7 days of exposure [42].

Measles, mumps, and rubella vaccine is highly effective in primary prevention of measles, with a two-dose vaccine effectiveness of 99% [4,39,43].

### Ebola

Ebola is an infection caused by *Ebolavirus*, part of the family Filoviridae. Although the natural reservoir host is unknown, the virus can be transmitted from person-to-person and can result in outbreaks. There are 20,129 cases of Ebola with 7879 deaths in the current outbreak of Ebola in West Africa [44].

The virus is transmitted through direct contact (through broken skin or mucous membranes) with blood, body fluids, tissues, or skin of symptomatic infected patients or persons who have died of the disease. The risk of transmission is particularly high during the later stages of infection, when viral loads are high. Transmission is not possible during the incubation period when the patient is asymptomatic [45-47]. HCP caring for Ebola patients are in the highest risk of infection if not wearing appropriate PPE.

Unfortunately, there is no available PEP for Ebola. Exposed HCP should stop working immediately and report to occupational health and their supervisors. They should monitor their temperature twice daily for 21 days after the last exposure and report any temperature >101°F (38.3°C) or symptoms/signs of Ebola infection. Clinicians should follow the updated information available at Centers for disease control and prevention, World Health Organization, and other health organization websites [45-47].
Emerging respiratory viruses

Postexposure management of avian influenza and Middle East respiratory syndrome coronavirus are summarized in Table 3 [48-52].

Postexposure management of infections transmitted by the droplet route

Droplet transmission occurs when respiratory droplets carrying infectious agents travel directly from the respiratory tract of the infectious person to susceptible mucosal surfaces of the exposed person. Respiratory droplets are >5 μm in diameter, do not remain suspended in air, are generated mainly during coughing, sneezing, and talking by the infectious person or during procedures such as suctioning, and are typically transmitted across short distances (3–6 feet) from the infectious person (Table 1) [1].

Invasive group A streptococcal infection

Healthcare-associated severe group A streptococcal (GAS) infection occurs at rate of 5%–12%. Surgical, obstetrics and gynecology, and burn units are the wards most commonly involved in hospital outbreaks of GAS infections [53-55]. The issue of treating the contacts of invasive GAS (iGAS) index cases is debated because it is unknown if antibiotic therapy will decrease risk of acquiring GAS infection. It is generally agreed that PEP should not be routinely given to all contacts of iGAS cases. The decision to use PEP for contacts will be based on clinician’s assessment of the risk associated with each HCP and guidance from local institutions (Table 4) [53-55].

All HCP in contact with an index case of iGAS infection should be screened for GAS if they develop sore throat, skin infection, skin lesions, vaginitis, or pruritus within 7 days of contact with the index case [55]. In outbreaks of GAS infection, the infection control department may decide to screen asymptomatic HCP for GAS. Screening for GAS should be performed from throat and skin lesions and, if negative, from nose, anus, and vagina. Screened HCP found to be positive for GAS should receive antibiotic eradication therapy (Table 4). Screening for GAS should be repeated 7–10 days after completion of therapy and, if still positive for GAS, HCP should be retreated and their household contacts should be screened [53-55].

Neisseria meningitidis

Nosocomial transmission of N. meningitidis is rare due to adherence to infection control practices. HCP can acquire the organism through contact with respiratory secretions of infected patients or in laboratory settings [4,56]. Antibiotic therapy used as PEP is effective in preventing infection after exposure and eradicating nasopharyngeal carriage of N. meningitidis (Table 4) [57].

Quadrivalent (A, C, W-135, Y) meningococcal polysaccharide vaccine (MPSV4) and conjugate meningococcal vaccines (MenACWY-D, MenACWY-CRM) protect against 75% of disease among adults by induction of detectable bactericidal antibodies, which decline 3–5 years post-vaccination [4,56]. Meningococcal vaccines can be used in the routine vaccination schedule of high-risk HCP (Table 4) and during institutional outbreaks (defined as the occurrence of ≥2–3 confirmed or probable primary cases of meningococcal disease caused by the same serogroup in ≤3 months). During an outbreak, HCP should be vaccinated with a meningococcal vaccine that contains the responsible serogroup [4,56]. The recently approved meningococcal vaccine for serogroup B is indicated for individuals 10–25 years of age and its role for HCP vaccination is not clear [58].

Pertussis

Pertussis is a highly contagious disease with a secondary attack rate of 80%, which may turn into an outbreak [4,59]. Pertussis is most communicable in the first 2 weeks of illness during the catarrhal and early paroxysmal stages. Transmission is negligible after about 3 weeks of untreated infection or 5 days after initiation of effective antibiotic therapy [59].

The benefits of PEP for exposed HCP to pertussis are not well supported with strong evidence (Table 4) [4,60-62]. However, it is generally recommended that unvaccinated HCP with significant exposure to an infectious patient should be given PEP. On the other hand, vaccinated HCP can be given the option of either taking PEP or monitoring for symptoms for 21 days after last contact with infectious index patient. Providing PEP is preferred for vaccinated HCP at high risk of severe disease or HCP working with patients at high risk of severe disease, such as neonates or pregnant women [60,63].

Effectiveness of pertussis-containing vaccines (e.g. tetanus-diptheria-acellular pertussis, diphtheria-tetanus-acellular pertussis) for primary prevention of pertussis ranges from 66% to 78% but the duration of immunity is unknown [4,5,59,63-65].

Influenza

Influenza is a large burden in healthcare settings since it is a common infection and can cause outbreaks of severe respiratory illness among hospitalized patients and long-term-care residents [4,66]. Viral shedding typically occurs from 1 day before symptom onset until 5–10 days after onset, although young children and immunocompromised patients may shed virus for longer durations [67]. Antiviral agents have been shown to be effective as PEP after unprotected exposure to influenza and particularly in outbreak situations. However, because of concern of antiviral resistance, it is usually preferred to watch the exposed HCP and to initiate treatment early if symptoms develop [67-69]. If it is decided to give PEP, it should be for HCP contacts who are at high risk of influenza complications or in contact with persons at high risk of influenza complications (Table 4) [67].

The effectiveness of influenza vaccine to prevent influenza varies and depends on the age and health status of the person and the match between the circulating strains and the strains
Table 4. Postexposure management of HCP to infections transmitted by droplets route.

| Pathogen                                                                 | Disease status of source patient                                                                 | Disease status of exposed HCP and type of exposure                                                                 | PEP regimen                                                                                           | Initial assessment and follow up of exposed HCP | Primary prevention                                                                 | Adverse effects of PEP regimen |
|--------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|------------------------------------------------|----------------------------------------------------------------------------------|-------------------------------|
| iGAS infection (e.g. streptococcal toxic shock syndrome, necrotizing fasciitis, myositis, or gangrene) | Patients with iGAS infection from 7 days prior to onset of symptoms until 24 hours after an effective antibiotic therapy | HCP whose mucous membrane or non-intact skin was in contact with secretions from the nose, mouth, wound, or skin of an infected patient. Colonized asymptomatic HCP implicated in a nosocomial cluster or an outbreak | One of the following regimens should be given within 24 hours and up to 7 days after the last contact with an infectious case: Cephalexin 25–50 mg/kg (maximum of 1 g/day) orally in 2–4 divided doses for 10 days OR Penicillin V 500 mg orally 4 times daily for 10 days OR Amoxicillin 500 mg orally 3 times daily for 10 days OR Clindamycin 20 mg/kg (maximum of 900 mg/day) orally three times daily for 10 days OR Azithromycin 12 mg/kg/day (maximum of 500 mg/day) orally for 3–5 days | No need for work restrictions or modifications for exposed asymptomatic HCP | None of the above HCP require contact and droplet precautions until 24 hours after an effective antibiotic therapy | Cephalexin: nausea, vomiting, diarrhea, abdominal pain, and rash Penicillin V and amoxicillin: nausea, vomiting, diarrhea, abdominal pain, and rash Clindamycin: nausea, vomiting, diarrhea, and CDI |
| Invasive meningococcal infection (Neisseria meningitidis) meningitis, pneumonia with bacteremia |
| Patients with invasive meningococcal infection from 7 days prior to onset of illness until 24 hours after effective antibiotic therapy, other than penicillins | HCP directly and significantly exposed to oral or respiratory secretions of a patient during the infectious period regardless of vaccination status | One of the following regimens should be administered as soon as possible and up to 14 days after last contact: Ciprofloxacin 500 mg orally as a single dose OR Ceftriaxone 250 mg IM as a single dose OR Azithromycin 500 mg orally as a single dose OR Rifampin 600 mg orally twice daily for 2 days | No need for work restrictions or modifications for asymptomatic HCP | Patients with invasive meningococcal disease should be placed in droplet precautions until 24 hours after effective antibiotic therapy, other than penicillins OR HCP with anatomic or functional asplenia, persistent complement component deficiencies, HIV, or microbiologists who are routinely exposed to N. meningitidis should receive a two-dose series, 8–12 weeks apart, of conjugate meningococcal vaccines HCP over the age of 55 with any of the above risk factors should receive the quadrivalent meningococcal polysaccharide vaccine (MPSV4) HCP who remain in a group at increased risk should receive a booster dose every 5 years after the primary series | Ciprofloxacin: nausea, vomiting, diarrhea, headache, QT prolongation, tendon rupture, neurologic abnormalities, and CDI; contraindicated in pregnancy Ceftriaxone: nausea, diarrhea, abdominal pain, and reversible gallbladder disease Rifampin: nausea, vomiting, hepatotoxicity, red-orange discoloration of body fluids and stool, drug interactions, and thrombocytopenia |
| Pathogen | Disease status of source patient | Disease status of exposed HCP and type of exposure | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|---------|---------------------------------|---------------------------------------------------|-------------|-------------------------------------------|-----------------|-------------------------------|
| Pertussis | Symptomatic patients in the first 3 weeks of illness | HCP in direct contact with respiratory, nasal or oral secretions or with a face-to-face exposure within 3 feet of infected patient during the infectious period, regardless of vaccination status | One of the following regimens administered as early as possible but no later than 3 weeks after onset of cough in the source index case: Azithromycin 500 mg orally on day 1 followed by 250 mg/day on days 2 through 5 OR Clarithromycin 500 mg orally twice daily for 7 days OR TMP-SMX one double-strength tablet (TMP 160 mg, SMX 800 mg) orally twice daily for 14 days | Complete primary vaccination series of unvaccinated or incompletely vaccinated HCP with age-appropriate pertussis containing vaccine (DTaP, Tdap) No need for work restrictions or modifications for asymptomatic HCP Symptomatic exposed HCP should be excluded from work until 5 days after effective antibiotic therapy or negative microbiologic testing | Patients require droplet precautions until clinical improvement and 5 days after effective antibiotic therapy All HCP should receive a single dose of Tdap IM if they have not previously received it followed by Td booster doses every 10 years Adults with an unknown or incomplete history of completing a 3-dose primary vaccination series with Td-containing vaccines should begin or complete a primary vaccination series including a Tdap dose at 0, 4 weeks, and 6–12 months | TMP-SMX: gastrointestinal disturbance, hypersensitivity reaction, nephrotoxicity, hyperkalemia, rash, and myelosuppression; contraindicated in the last trimester of pregnancy and breastfeeding; avoid in patients with severe renal and hepatic disease |
| Plague (*Yersinia pestis*) | Patients with pneumonic or meningeal plague who have not received at least 48 hours of effective antibiotic therapy | All HCP in close contact with a pneumonic or meningeal plague patient or direct contact with infected body fluids or tissues, regardless of vaccination status | One of the following regimens should be given within 7 days of exposure for 7 days: Doxycycline 100 mg orally twice daily OR Ciprofloxacin 500 mg orally twice daily OR Levofloxacin 500 mg/day orally for 10 days OR Trimethoprim-sulfamethoxazole one double-strength (TMP 160 mg, SMX 800 mg) tablet orally twice daily | No need for work restriction for asymptomatic HCP | Patients with pneumonic plague require droplet precautions until 48 hours after effective antibiotic therapy | No need for work restriction for asymptomatic HCP |
| Influenza | Symptomatic patients with laboratory-confirmed seasonal influenza A or B infection, from 1 day before onset of symptoms until 24 hours after the fever ends | Unvaccinated HCP or vaccinated with either a poor matching vaccine with circulating strain or expected poor response to the vaccine | One of the following regimens administered within 48 hours after exposure: Oseltamivir 75 mg/day orally for 10 days and in case of an outbreak for a minimum of 2 weeks and up to 1 week after diagnosis of the last case OR Zanamivir 10 mg/day (2 inhalations) for 10 days and in case of an outbreak for a minimum of 2 weeks and up to 1 week after diagnosis of the last case | No need for work restriction for asymptomatic HCP HCP who develop symptomatic influenza should be suspended from patient care until afebrile ≥24 hours without the use of antipyretics | Patients with influenza require contact and droplet precautions for 7 days from symptom onset or until resolution of symptoms, whichever is longer Annual influenza vaccination recommended for all HCP who have no contraindications to the approved vaccines | Oseltamivir: nausea, vomiting, diarrhea, abdominal pain, esophagitis, skin hyperpigmentation, skin hypersensitivity, headache, and dizziness |
| | | | | | | | Zanamivir: headache, throat pain, cough, nasal discharge, bronchospasm, nausea, and vomiting; zanamivir is not approved for use in patients with underlying cardiac or respiratory disease |
| Pathogen | Disease status of source patient | Disease status of exposed HCP and type of exposure | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|----------|---------------------------------|--------------------------------------------------|-------------|-----------------------------------------------|-------------------|-------------------------------|
| Mumps    | Patients with laboratory-confirmed mumps infection from 7 days before onset of parotitis to 9 days after | Nonimmune HCP\(^k\) or vaccinated with only one dose of mumps-containing vaccine who have unprotected exposure, within 3 feet of an infectious patients | None | No need for work restriction for asymptomatic HCP who are either fully vaccinated or received one dose of the MMR vaccine Unvaccinated exposed HCP should be excluded from work from day 12 after first unprotected exposure through day 25 after last exposure Acutely infected HCP with mumps should be excluded immediately from work for 9 days after onset of parotitis | Patients with mumps require droplet precautions until 9 days after symptom onset All nonimmune HCP should receive two doses of MMR vaccine given at least 28 days apart | HRIG: local (pain, tenderness, erythema, and induration) and systemic reactions (headache, hypersensitivity reactions) HRIG can be used in pregnancy Rabies vaccines: local reactions (e.g. pain at injection site, redness, swelling), and rarely systemic reactions (e.g. fever, headache, myalgia, dizziness, and gastrointestinal symptoms), systemic hypersensitivity reactions, and Guillain-Barré syndrome Both types of vaccines are safe for use in pregnancy |
| Rubella  | Patients with confirmed rubella, from 1 week before to 7 days after onset of rash | Nonimmune HCP\(^k\) | None | Perform acute and convalescent serology in susceptible pregnant HCP who are exposed; if seroconversion occurs, counsel regarding risk of congenital rubella syndrome Susceptible exposed HCP should be excluded from work from day 5 after first exposure to day 23 after last exposure, regardless of whether they received post-exposure vaccine Acutely infected HCP with rubella should be excluded from work immediately until 7 days after rash onset | Patients with rubella should be placed in droplet precautions until 7 days after symptom onset All nonimmune HCP should receive two doses of MMR vaccine given at least 28 days apart | Standard precautions are sufficient when caring for patients with rubella Preexposure vaccination is recommended for all HCP who work with rubies virus or infected animals or engage in diagnostic, production, or research activities with rubies virus |
| Rabies   | Infected patients with rabies from 2 weeks before onset of symptoms | Previously unvaccinated HCP with mucous membrane or non-intact skin exposure to infectious material (saliva, tears, CSF, neural tissue)\(^i\) Previously vaccinated HCP with mucous membrane or non-intact skin exposure to infectious material (saliva, tears, CSF, neural tissue)\(^i\) | Single dose of HRIG 20 IU/\(k\)o AND Rabies vaccine (4 doses of 1 mL) IM on days 0, 3, 7, 14, and 28 (for immunocompromised only)\(^o\) Rabies vaccine IM on days 0 and 3\(^o\) | Prompt and thorough mucous membrane irrigation with copious amount of water and wound cleansing with soap and water No need for work restrictions or modifications for asymptomatic HCP | Standard precautions are sufficient when caring for patients with rabies Preexposure vaccination is recommended for all HCP who work with rabies virus or infected animals or engage in diagnostic, production, or research activities with rabies virus |
Nosocomial GAS infection clusters is defined as ≥2 cases caused by the same strain and identified within a 6-month period.

Cases of necrotizing fasciitis and other cases of GAS infection where there is a significant discharge of infected body fluids; mothers and neonates on maternity units and patients on burn units should be isolated until culture negative.

PEP is not recommended for close contacts of patients with *N. meningitidis* isolated only from nonsterile sites, such as oropharyngeal swab, endotracheal secretions, or conjunctival swab.

Penicillins are ineffective in the eradication of *N. meningitidis* from the nasopharynx due to their inability to achieve high levels in nasopharyngeal secretions.

Exposure to oral or respiratory secretions such as mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management. PEP should not be administered to HCP with brief contact not involving exposure to oral or respiratory secretions, since the risk of transmission is low.

Azithromycin is not recommended as a first-line agent for PEP but it is an option in areas where fluoroquinolone-resistant strains of *N. meningitidis* have been identified.

TMP-SMX should be used as an alternative agent to macrolides in patients who are allergic to macrolides or cannot tolerate them, or who are infected with a macrolide-resistant strain of *B. pertussis*.

Although contraindicated in pregnancy, doxycycline and fluoroquinolones can be used as PEP because of the potential severity of plague and lack of effective alternatives.

HCP contacts who are ≥65 years of age, or pregnant in their third trimester or 2 weeks postpartum, morbidly obese (BMI ≥40), or have chronic comorbid condition such as cardiopulmonary and renal disorder, or immunocompromised condition or who are in close contact with persons at high risk of influenza complications.

HCP who provide care to high-risk patients such as hematopoietic stem cell transplant patients should be either work reassigned or excluded from work for 7 days from symptom onset or until resolution of respiratory symptoms, whichever is longer.

Due to absence of either prior infection or vaccination.

Contact with blood, urine, or feces of an infected patient, or contact of intact skin with saliva of an infected patient are not associated with risk of transmission of rabies and therefore PEP is not recommended.

HCP are considered vaccinated if they received a complete series of a cell culture vaccine (i.e. three 1-mL doses administered intramuscularly in the deltoid area on days 0, 7 and 21 or 28) or other types of vaccine (e.g. duck embryo vaccine, Semple™ rabies vaccine) with previously documented protective titer of rabies virus neutralizing antibodies (>0.5 IU/mL or complete virus neutralization at a 1:5 serum dilution by RFFIT).

Full dose of HRIG should be infiltrated in and around the wound if anatomically feasible, with the rest administered IM into the deltoid muscle, lateral or anterior thigh, or the gluteal region in a separate syringe and site from the vaccine. If HRIG is not administered when active vaccination is begun, it can be administered until day 7 but not after 7 days since the immune response to rabies vaccine would have developed by that time.

Day 0 is the day when the first dose of vaccine was given. Rabies vaccine should be given in deltoid muscle but never in gluteal muscle due to the resulting titer of neutralizing antibodies is lower than expected.

If protective neutralizing antibodies are not attained (>0.5 IU/mL or complete virus neutralization at a 1:5 serum dilution by RFFIT), additional doses of vaccine could be on days 7 and 14.

Abbreviations: CDI = *Clostridium difficile* infection; CSF = Cerebrospinal fluid; DTaP = Diphtheria-tetanus-acellular pertussis; HCP = Healthcare personnel; HRIG = Human rabies immune globulin; iGAS = Invasive group A streptococcal; IM = Intramuscular; MMR = Measles, mumps, and rubella; PEP = Postexposure prophylaxis; RFFIT = Rapid fluorescent focus inhibition test; Td = Tetanus-diphtheria toxoids adsorbed; Tdap = Tetanus-diphtheria-acellular pertussis; TMP-SMX = Trimethoprim-sulfamethoxazole.

Information from references [1,4,5,39,53-57,59-61,63,64,67,68,70,76,79,80].
Table 5. Postexposure management of HCP to infections transmitted by contact route.

| Pathogen/infection | Disease status of source patient | Disease status of exposed HCP | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|---------------------|----------------------------------|-------------------------------|-------------|-----------------------------------------------|-------------------|-------------------------------|
| HAV                 | Patients with acute HAV infection confirmed serologically (presence of serum anti-HAV IgM antibodies), from the incubation period (15–50 days) until 7 days after onset of jaundice | Nonimmune HCP reporting close contact with index patients if an epidemiologic investigation indicates HAV transmission has occurred between patients and HCP | Two doses of hepatitis A vaccine 6–18 months apart (1440 EL.U in 1 mL for HAVRIX and 1 mL for VAQTA vaccine) IM in the deltoid muscle OR A single dose of Ig 0.02 mL/kg IM in the deltoid or gluteal muscle | No need for work restriction or modification for asymptomatic exposed HCP Infected exposed HCP should be excluded from patient care, patient environment, or food handling until 7 days after onset of jaundice | Patients with hepatitis A infection require standard precautions HCP should be vaccinated with two doses of hepatitis A vaccine, 6–12 months apart, if at high risk of future exposure or when the vaccine is indicated (e.g., travelers to endemic areas, injection drug users, MSM, patients with chronic liver disease) | Hepatitis A vaccine: fever, injection-site reactions, rash, and headache IG: injection-site reactions, muscle rigidity and cramps at injection site, body aching, and gastrointestinal symptoms |
| HSV 1,2             | Patients with active lesions | HCP who have unprotected contact with skin lesions or with virus-containing secretions, such as saliva, vaginal secretions, or amniotic fluid | None | No need for work restriction or modification of asymptomatic exposed HCP Symptomatic exposed HCP should be evaluated by occupational health to determine if they can continue providing patient care | Patients with mucocutaneous, disseminated, severe extensive HSV infection or neonates with HSV infection require contact precautions until all lesions are dry and crusted Standard precautions for patients with other types of HSV infection | |
| Scabies             | Patients with untreated infestation | HCP in close contact with infested patients | Permethrin 5% cream (apply from neck to toe, wash off after 8–14 hours, repeat in 1–2 weeks) OR Crotamiton 10% cream or lotion (after a bath, apply from shin to toes; repeat in 24 hours) OR Sulfur 5%–10% ointment (apply for 3 consecutive days) OR Lindane 1% lotion (apply from neck down, wash off after 8–12 hours; do not repeat; do not apply immediately after a bath or shower) OR Ivermectin 200 µg/kg orally two doses 2 weeks apart | No need for work restriction or modification of asymptomatic exposed HCP Symptomatic HCP should be excluded from work until treated and deemed to be free of infestation by occupational health | Patients with scabies require contact isolation until 24 hours after effective treatment Rooms used by patients infested with scabies should be vacuumed and cleaned thoroughly; patients’ bedding, linens, and towels should be washed in hot water and dried at high heat cycle, or dry cleaned | Permethrin 5% and crotamiton 10% cream, lotion; skin irritation Sulfur 5%–10% ointment: dryness, malodor, and staining fabrics; safe in pregnancy Lindane 1% lotion; skin irritation and dryness, aplastic anemia, and neurotoxicity such as seizures Lindane is contraindicated in patients with extensive dermatitis, pregnant and lactating women Ivermectin: pruritus, tachycardia, dizziness, edema, arthralgia, nausea, diarrhea, increased liver function tests, Ivermectin should be avoided in pregnant and lactating women |
The influenza vaccine is ~90% serologically effective in HCP but the vaccine impact on clinical illness among HCP and their contacts is not well established [71-74].

Postexposure management of other infections transmitted by the droplet route are summarized in Table 4 [39,75-80].

Postexposure management of infections transmitted by the contact route

Direct contact transmission occurs when infectious agents are transferred from an infected person to another person without a contaminated intermediate object or person. Indirect contact transmission occurs when infectious agents are transferred from an infected person to another through a contaminated intermediate object or person (e.g. hands of HCP, shared patient-care devices such as electronic thermometers and glucose monitoring devices, or inadequately cleaned instruments such as endoscopes and surgical instruments) [1].

There are several organisms that can be transmitted by this route (Table 1). Unfortunately, there is no effective PEP regimen for the majority of these organisms. Therefore, standard precautions including hand hygiene are the cornerstone of prevention and control of these infections [1].

Scabies

Scabies, which is caused by the mite Sarcoptes scabiei, has resulted in many outbreaks in different healthcare settings [81]. Scabies is transmitted primarily by skin-to-skin contact via an infected person. Casual scabies, in which millions of scabies mites infect a single host, is more contagious than solitary infestations. Rooms used by patients infected with scabies should be vacuumed and cleaned thoroughly; patients’ bedding, linens, and towels should be washed in hot water and dried at high heat cycle, or dry cleaned.

PEP should not be given for exposed HCP who lack signs of infestation. In case of a continuing outbreak, PEP for scabies can be given to asymptomatic HCP contacts in consultation with the infection control and occupational health departments (Table 5) [1,83,84].

| Disease status of source patient | Disease status of exposed HCP | PEP regimen | Initial assessment and follow up of exposed HCP | Primary prevention | Adverse effects of PEP regimen |
|---------------------------------|-----------------------------|-------------|----------------------------------------------|------------------|--------------------------------|
| Patients with untreated infestation | HCP in contact with the skin or clothing of infested patients | None | No need for work restriction or modification of asymptomatic exposed HCP | Patients with pediculosis require contact isolation until 24 hours after effective treatment | Adverse effects of PEP regimen |

Postexposure management of infections transmitted by the contact route is summarized in Table 5 [1,85-89].

Conclusion

Postexposure management is the responsibility of the HCP, occupational health provider, and employer, and is made possible through awareness of the risks and potential interventions both before and after exposure. There are several challenges in the postexposure management of HCP to infectious sources. These include evaluation of an unknown source patient or a source patient who refused testing, difficulties in determining levels of risk of transmission for exposure incidents, availability of rapid diagnostic tests for exposure incidents, sensitivity and specificity of diagnostic tests for source individual, uncertainty of related information, and adherence to the prescribed PEP regimen. There is an urgent need for PEP for serious infections such as HCV and Ebola.
Having established protocols for postexposure management, a multidisciplinary team approach, and accessible expert consultation may solve some of these challenges.

Declaration of interest
The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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