



# Postexposure prophylaxis for occupational exposure to selected pathogens for healthcare personnel

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## Purpose of review

Timely postexposure prophylaxis is important after an occupational exposure. Here we review select organisms, exposure opportunities in the healthcare setting, and postexposure prophylaxis regimens.

## Recent findings

Needlestick injuries pose a risk of exposure to bloodborne pathogens, such as HIV, Hepatitis B, and Hepatitis C. Risk mitigation strategies should be reexamined in light of newer vaccines and therapeutics. Increased vaccine hesitancy and vaccine denialisms may foster the re-emergence of some infections that have become extremely uncommon because of effective vaccines. With increasing occurrences of zoonotic infections and the ease of global spread as evidenced by COVID-19 and mpox, healthcare exposures must also consider risks related to emerging and re-emerging infectious diseases.

## Summary

Early recognition and reporting of occupational exposures to pathogens with available postexposure prophylaxis is key to mitigating the risk of transmission. Providers should be able to evaluate the exposure and associated risks to provide prompt and appropriate postexposure prophylaxis.

## Keywords

needlestick, occupational health, postexposure prophylaxis

## INTRODUCTION

Occupational exposures to pathogens unfortunately occur relatively commonly in the healthcare workplace. The purpose of this paper is to address current postexposure interventions known to be effective in mitigating the risk for transmission of selected pathogens following occupational exposures in the healthcare workplace.

The management of these exposures lies primarily in the purview of the occupational medicine team in any healthcare facility; however, some institutions lack a 24-h presence for occupational medicine, and, in such institutions, the emergency department often assumes this role. Often, the healthcare epidemiology team and infectious diseases consultants also will be called on to provide expertise in managing occupational exposures in the healthcare setting.

One of the most challenging issues is determining whether an exposure has occurred. Curiously, this may be the most difficult determination in postexposure management. Accordingly, we have attempted to provide information about exposures for the relevant pathogens. The paper is organized by pathogen, routes of exposure, approaches to

postexposure prophylaxis, and recent developments with respect to each pathogen. Current approved prophylactic regimens are outlined in Table 1.

## BACTERIAL DISEASES

### Meningococcal disease

Exposure – Healthcare personnel (HCP) may become exposed by having direct, close contact with

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## KEY POINTS

- Postexposure prophylaxis for occupational exposures to infectious diseases in the healthcare workplace is a key component of occupational medicine in healthcare settings; staff need to be informed of and the risks for, management of, and postexposure treatment for pathogens commonly encountered in the healthcare workplace.
- In light of the steady increase in the prevalence in the United States of vaccine hesitancy and vaccine denialism, healthcare professionals should be vigilant about the possible reappearance of pathogens such as diphtheria, pertussis and tetanus for which effective postexposure prophylaxis interventions exist.
- Determining whether an exposure has occurred is often challenging and timing of prophylaxis is critical; in general, prophylaxis should be administered as soon as possible once an exposure determination has been made.
- Pathogens are prone to develop resistance to commonly used agents over time; staying current with public health recommendations is key to successful postexposure interventions.
- Whereas potentially effective agents may exist for postexposure prophylaxis to some pathogens, in some instances, low rates of transmission and highly effective, curative therapies may argue for monitoring and early therapy, rather than immediate postexposure prophylaxis (e.g., hepatitis C).

mucous membranes or secretions from a patient who has documented meningococcal disease (e.g., such as by providing mouth-to-mouth resuscitation or inserting or manipulating an endotracheal tube while not wearing appropriate personal protective equipment). Lesser contact with an infected patient (e.g., being in the same room, same hallway, or having encounters other than face-to-face, delivering meals, or even performing a history and physical) is not classified as an exposure. Additionally, having unprotected direct contact with respiratory secretions or saliva of a person who is colonized with *N. meningitidis*, but who does not have clinical disease, also is not considered an exposure.

Prophylaxis – according to the Centers for Disease Control and Prevention (CDC), chemoprophylaxis with rifampin (600 mg every 12 h for 48 h), ceftriaxone (250 mg intramuscularly) or ciprofloxacin (500 mg orally), are between 90% and 95% effective in eradicating nasopharyngeal carriage of *N. meningitidis* [1,2]. Azithromycin is an acceptable alternative when one anticipates ciprofloxacin-resistance [3].

Newer developments – though not directly related to postexposure prophylaxis, the past year has seen the Food and Drug Administration (FDA) approval [4] and Advisory Committee on Immunization Practices (ACIP) endorsement [5] of a new pentavalent conjugate vaccine for individuals 10–25 years of age that provides immunoprophylaxis coverage for meningococcal serogroups ABCW and Y. The vaccine received FDA approval in October 2023 and was endorsed by the ACIP later that October. In addition, because of increasing ciprofloxacin resistance, CDC issued new prophylaxis guidelines that suggest the use of rifampin, ceftriaxone, or azithromycin instead of ciprofloxacin when two or more ciprofloxacin-resistant meningococcal disease cases are reported in a defined area [3].

## Anthrax

Exposure – HCP may become exposed by handling cutaneous lesions without appropriate personal protective equipment (PPE). Concern has also been expressed for inhalation exposure due to bioterrorism.

Prophylaxis – Recently issued CDC guidelines provide evidence for antimicrobial prophylaxis efficacy [6]. Current FDA-approved agents for prophylaxis are: doxycycline (100 mg orally every 12 h), ciprofloxacin (500 mg orally every 12 h) and levofloxacin (500 mg orally every 24 h). The appropriate duration of postexposure prophylaxis is unknown, but because spores persist for extended periods of time, the current recommendation is for at least 7 days of prophylaxis for cutaneous exposure and at least 60 days of prophylaxis for inhalation exposures. In addition, in the past few years both monoclonal (Obiltoxaximab and Raxibacumab) and polyclonal (anthrax immunoglobulin intravenous) antitoxins have become available. The polyclonal product is harvested from the sera of individuals who have been immunized with anthrax vaccine. The antitoxins have demonstrated efficacy in animal models, but are not quite as effective as antimicrobials. If effective antimicrobials are not available, the antitoxins offer a reasonable alternative.

Newer developments – New candidate vaccines have shown promise in animal studies in the past 18 months [7,8] and CDC issued a revised and updated set of guidelines for the prevention and treatment of anthrax in late 2023 [6].

## Diphtheria

Exposure – Diphtheria transmission occurs through direct contact with respiratory secretions (or, if the

**Table 1.** Recommended postexposure prophylaxis for occupational exposure to selected pathogens

Organism	Modes of transmission	Status of HCP	PEP	Notes
<b>Bacteria</b>				
<i>Neisseria meningitidis</i>	Droplet	Regardless of immunization status if managing an airway or direct contact with respiratory secretions within 7 days of symptom onset	<ul style="list-style-type: none"> <li>Rifampin 600 mg p.o. every 12 h × 48 h</li> <li>Ceftriaxone 250 mg i.m. × 1</li> <li>Ciprofloxacin<sup>a</sup> 500 mg p.o. × 1</li> <li>Azithromycin<sup>b</sup> 500 mg p.o. × 1</li> </ul>	<ul style="list-style-type: none"> <li>Rifampin: review drug interactions</li> <li>Rifampin, Ciprofloxacin: Not for pregnant women</li> </ul>
Anthrax	Contact	Direct contact with cutaneous lesions	<ul style="list-style-type: none"> <li>Doxycycline 100 mg p.o. every 12 h</li> <li>Ciprofloxacin 500 mg p.o. every 12 h</li> <li>Levofloxacin 500 mg p.o. every 24 h</li> </ul>	<ul style="list-style-type: none"> <li>Cutaneous: ≥ 7 days</li> <li>Inhalation: ≥ 60 days</li> <li>Consider antitoxin if no antimicrobials are available</li> </ul>
Diphtheria	Droplet, Contact	Direct contact with respiratory secretions or cutaneous lesions	<ul style="list-style-type: none"> <li>Diphtheria vaccine</li> <li>Benzathine penicillin G 1.2 million units i.m. × 1</li> <li>Erythromycin 250 mg p.o. every 6 h × 7–10 days</li> </ul>	<ul style="list-style-type: none"> <li>Depends on vaccination status</li> </ul>
Pertussis	Droplet	Regardless of immunization status after direct contact with respiratory secretions	<ul style="list-style-type: none"> <li>Azithromycin 500 mg × 1 on Day 1, then 250 mg p.o. daily Days 2–5</li> <li>Erythromycin 500 mg p.o. every 6 h × 10 days</li> <li>Clarithromycin 500 mg p.o. every 12 h × 7 days</li> <li>Trimethoprim 160 mg/ sulfamethoxazole<sup>c</sup> 800 mg p.o. every 12 h × 14 days</li> </ul>	
<b>Viruses</b>				
HIV	Bloodborne	Parenteral exposure to blood or splashes of blood into mucous membranes	<ul style="list-style-type: none"> <li>Raltegravir 400 mg p.o. twice a day AND</li> <li>Tenofovir disoproxil fumarate 300 mg p.o. daily AND</li> <li>Emtricitabine 200 mg p.o. daily</li> </ul>	
HBV	Bloodborne	Parenteral exposure to blood or splashes of blood into mucous membranes	<ul style="list-style-type: none"> <li>Hepatitis B vaccine</li> <li>HBIG 0.06 mL/kg</li> </ul>	<ul style="list-style-type: none"> <li>Depends on vaccination status and response to vaccinations</li> </ul>
Influenza	Droplet	Large droplets within 6 feet or indirect contact from a contaminated surface or object	<ul style="list-style-type: none"> <li>Oseltamivir 75 mg p.o. daily × 7 days</li> <li>Zanamivir 10 mg (two 5-mg inhalations) daily × 7 days</li> <li>Baloxavir 40 mg p.o. × 1 (if weight &lt; 80 kg) or 80 mg p.o. × 1 (if weight ≥ 80 kg)</li> </ul>	<ul style="list-style-type: none"> <li>Depends on underlying medical conditions and vaccine status and anticipated response to vaccination</li> <li>For PEP after exposure to avian influenza, twice a day dosing for oseltamivir or zanamivir</li> </ul>
Mpox	Contact	Contact with patient's lesions, bodily fluids, respiratory secretions, or contaminated environment	<ul style="list-style-type: none"> <li>JYNNEOS</li> <li>ACAM2000</li> </ul>	
Rabies	Contact	Bite or contact between a patient's saliva and a person's mucous membranes or broken skin	<ul style="list-style-type: none"> <li>HDCV</li> <li>PCECV</li> <li>HRIG 20 international units/kg</li> </ul>	
VHF	Contact	Contact with patient's blood, bodily fluids, respiratory secretions, or contaminated environment	<ul style="list-style-type: none"> <li>None</li> </ul>	
<b>Parasites</b>				
Malaria	Bloodborne	Parenteral exposure to blood or splashes of blood into mucous membranes	<ul style="list-style-type: none"> <li>None</li> </ul>	<ul style="list-style-type: none"> <li>Consult with Occupational Health and Infectious Diseases</li> </ul>

i.m., intramuscular; KG, kilogram; PEP, postexposure prophylaxis; p.o., per os (by mouth).

<sup>a</sup>If no fluoroquinolone-resistant strains identified in the community.

<sup>b</sup>Alternative if sustained fluoroquinolone-resistant strains identified in the community.

<sup>c</sup>Alternative if macrolide allergy or if known macrolide-resistant strain.

patient has cutaneous disease, direct contact with lesions, wounds, or skin exudate) from a patient infected with *Corynebacterium diphtheriae*. For HCP, diphtheria exposure is defined as unprotected (i.e., the HCP was not wearing appropriate PPE),

close, face-to-face contact with an infected patient or the patient's secretions [9].

Prophylaxis – Postexposure prophylaxis for occupational diphtheria exposures includes the administration of a dose of diphtheria vaccine as

well as the administration of either a single dose of benzathine penicillin G (1.2 million units intramuscularly) or a 10-day course of oral erythromycin (250 mg every 6 hours) [9].

Newer developments – Substantial outbreaks of diphtheria have occurred during the past 18 months in Nigeria [10<sup>a</sup>], Pakistan [11], and Australia [12].

## Pertussis

Exposure – Direct face-to-face contact with an infected person (while not wearing appropriate PPE) or contact with secretions from an infected individual constitutes exposure to pertussis.

Prophylaxis – Since immunity to pertussis is known to wane over time, postexposure prophylaxis for occupational pertussis exposures should be administered to all exposed providers. Acceptable agents for prophylaxis include: azithromycin (a 500 mg first dose, followed by 250 mg orally per day for 5 days); erythromycin (500 mg orally every 6 h for 10 days); clarithromycin (500 mg orally every 12 h for 7 days); or trimethoprim-sulfamethoxazole (160 mg trimethoprim/800 mg sulfamethoxazole every 12 h for 14 days) [13].

Newer Developments – The last 18 months have seen the development and testing of vaccines designed to produce mucosal immunity to pertussis [14<sup>a</sup>,15], but the duration of protection for the new vaccines is unknown. Pertussis immunity in health-care personnel remains a concern around the world. Most recently, a large study of pertussis immunity in China found that >57% of healthcare workers had no immunoglobulin G (IgG) directed against *Bordetella pertussis* [16<sup>a</sup>].

## VIRAL DISEASES

### Human immunodeficiency virus (HIV)

Exposure – Healthcare-associated occupational exposures to HIV are most commonly associated with parenteral exposures to blood or other blood-containing fluids from patients infected with HIV. In addition, splashes of blood or blood-containing fluids onto mucous membranes are also considered occupational exposures. Exposures of intact skin to such materials are not considered an exposure.

Prophylaxis – Numerous animal studies, studies of postpartum prophylaxis and a retrospective case-control study published by CDC in the late 1990s [17] all suggest efficacy of postexposure antiretroviral chemoprophylaxis for occupational HIV exposures. The most recently published guidelines published in 2013 [18<sup>a</sup>] recommend a combination of raltegravir (400 mg orally twice daily) plus

tenofovir disoproxil fumarate (300 mg orally once daily) plus emtricitabine (200 mg orally once daily). (The tenofovir disoproxil fumarate and emtricitabine are available as one pill – Truvada). Several possible alternative regimens are provided.

Newer developments – The CDC's postexposure prophylaxis guidelines are currently under revision. The new guidelines will take into consideration the many new, improved, and less-toxic antiretroviral agents and combination pills that have become available since the previous guidelines were written. Although no definitive recommendations have been published, we anticipate that the updated guidelines will recommend an integrase strand transfer inhibitor plus two nucleotide/nucleoside reverse transcriptase inhibitors. Newer preparations combine all three agents into one pill. The new guidance is also likely: to emphasize the administration of antiretroviral postexposure prophylaxis as soon as practical following an HIV occupational exposure; to suggest that exposed staff should receive counseling and testing for HIV, hepatitis B and hepatitis C as soon as possible after the exposure to establish baselines; to emphasize that exposed staff should be reevaluated within 72 h of the exposure and should be monitored regularly for drug toxicity during the course of treatment; to advocate that, when possible, testing should employ fourth generation HIV antigen/antibody tests at baseline, when any symptoms consistent with acute infection occur, and at three months following the exposure; to suggest that qualitative nucleic acid tests also be performed at the completion of therapy (i.e., three months following the exposure).

### Hepatitis B virus (HBV)

Exposure – As is the case for both HIV and HCV, healthcare-associated occupational exposures to HBV are most commonly associated with parenteral exposures to blood or other blood-containing fluids from patients infected with HIV. In addition, splashes of blood or blood-containing fluids onto mucous membranes are also considered occupational exposures. Exposures of intact skin to such materials are not considered an exposure.

Prophylaxis – Prior to the development of the hepatitis B vaccine, hepatitis B was a major occupational hazard for healthcare personnel whose jobs entail handling or processing blood or blood-containing materials. Serologic studies of healthcare personnel and controls conducted in the 1970s suggested that healthcare personnel were at a tenfold increased risk for hepatitis B infection. In 1991 the Department of Labor's Occupational Safety and Health Administration published its Bloodborne



Pathogen Standard that required all healthcare employers to offer HBV vaccine to all employees at risk for exposure to blood or blood-containing fluids. This requirement combined with the immunization of mothers and their infants has had a marked effect on the epidemiology of HBV in the United States. According to CDC, HBV infection among healthcare personnel declined by 98% from 1983 to 2010 [19]. Nonetheless healthcare personnel who have not been immunized, those who fail to respond to immunization and some of those whose antibody titers have become undetectable are at risk. Vaccine nonresponders (i.e., a provider who fails to respond to six doses of the vaccine) who have documented exposure should be given two doses of hepatitis B immune globulin (HBIG) 0.06 ml/kg, with one month between the doses. Postexposure prophylaxis for providers who have received three doses of vaccine, but their antibody status is unknown should immediately be tested for antibody to hepatitis B surface antigen (anti-HBs). If the provider has >10 mIU/ml, no further treatment is needed; if <10 mIU/ml, the provider should be given one dose of HBIG (0.06 ml/kg), followed by the traditional three dose vaccine series (at 0, 1 and 6 months). Unvaccinated or incompletely vaccinated providers who have exposure should receive a dose of HBIG (0.06 ml/kg) followed by the three dose vaccine series. Providers who receive HBIG prophylaxis should receive baseline tests for HBV infection as soon as possible after exposure, and follow-up testing approximately 6 months later. At baseline, these providers should be tested for antibody directed at the hepatitis B core antigen (anti-HBc) and tested again if symptoms develop or at 6 months following the exposure for both hepatitis B surface antigen (HBs) as well as for antibody to HBc.

Newer developments – The past decade has seen the development and licensing of several antivirals capable of suppressing HBV (e.g., entecavir, tenofovir alafenamide, tenofovir disoproxil fumarate, lamivudine, and adefovir). Although these agents have been used successfully in preventing the relapse of HBV infection in immunosuppressed patients, they are not recommended for postexposure prophylaxis for occupational exposures.

### **Influenza**

Exposure – Exposure to influenza virus occurs via large droplets (e.g., coughing, sneezing, talking) typically over distances <6 ft. Indirect contact transmission also occurs by hand transfer via a contaminated surface or object to a person's facial mucosal surface (e.g., nose, mouth). Airborne transmission

via small droplets may also occur, though this is not known to occur over longer distances [20].

Prophylaxis – Several antivirals are available for postexposure prophylaxis, including oral oseltamivir, inhaled zanamivir, and oral baloxavir [21<sup>■</sup>]. Postexposure prophylaxis can be considered for HCP who are at high risk for complications from influenza infection and in whom influenza vaccine is contraindicated or anticipated to have low effectiveness [22]. It is recommended all HCP receive influenza vaccine annually unless they have a medical contraindication [23,24].

Newer developments – With ongoing outbreaks of highly pathogenic avian influenza (HPAI) A virus infection in animals, occasional animal-to-human transmission, and the known pandemic potential, HCP must be on high alert when caring for patients who are in close contact with infected animals. Patients suspected or confirmed to have HPAI infection should be placed on airborne and contact precautions with eye protection. For chemoprophylaxis after exposure to avian influenza, twice a day dosing of oseltamivir or zanamivir is recommended over daily dosing [25<sup>■</sup>]. Due to concerns of novel influenza A oseltamivir-resistance, treatment with zanamivir or baloxavir should be considered in persons who become symptomatic after chemoprophylaxis with oseltamivir [25<sup>■</sup>].

### **Mpox**

Exposure – CDC recommends postexposure prophylaxis for risk levels of exposure that are intermediate or high. An intermediate exposure includes unprotected contact with a patient (e.g., contact with a patient's skin lesions or bodily fluids, contact with a patient's soiled materials, or unmasked within 6 ft for a total of 3 or more cumulative hours). A higher risk level of exposure is if the exposure occurs to the person's broken skin or mucous membranes (e.g., eyes, mouth) or being in the room during an aerosol-generating procedure or resuspension of dried exudates (e.g., shaking of soiled linens) without wearing appropriate PPE [26<sup>■</sup>].

Prophylaxis – Two vaccines, ACAM2000 and JYNNEOS are available for PEP. ACAM2000 is approved in the United States for smallpox, but available under an Expanded Access Investigational New Drug (EA-IND) protocol. JYNNEOS is approved for smallpox and mpox. It is currently being distributed by the Administration for Strategic Preparedness & Response (ASPR), but the company plans for commercial distribution in 2024.

Newer developments – Cases from the global outbreak of mpox that began in 2022 [27] continue. In addition, Democratic Republic of Congo is

currently experiencing its largest outbreak affecting many of its provinces including the capital city of Kinshasa (<https://emergency.cdc.gov/han/2023/han00501.asp>).

## Rabies

**Exposure** – Healthcare setting exposure of rabies virus could occur after a bite by an infected patient or contact between the patient's saliva and a person's mucous membranes (e.g., eyes, mouth) or broken skin. Exposure to wildlife on the premises of a healthcare facility is also possible. Caring for a patient with rabies does not meet criteria for an exposure.

**Prophylaxis** – For previously unvaccinated persons, a single dose of human rabies immune globulin (HRIG) (20 international units/kilogram body weight) should be administered [28]. Previously unvaccinated persons should also receive four doses of rabies vaccine, human diploid cell culture rabies vaccine (HDCV) or purified chick embryo cell culture rabies vaccine (PCECV). Previously vaccinated persons should receive two doses of HDCV or PCECV [29,30].

**Newer developments** – ACIP provided updated guidance for preexposure prophylaxis in May 2022, including two-dose rabies vaccination replacing the previous three-dose schedule [31]. While intradermal (or intramuscular) vaccination is recommended by WHO [32], rabies vaccines in the United States are only approved for intramuscular administration [33]. Studies have also evaluated a potential one-dose rabies vaccination for preexposure prophylaxis [34]. Monoclonal antibodies have potential for PEP [35,36].

## Viral hemorrhagic fevers (e.g., Ebola, Marburg, Lassa, Crimean Congo Hemorrhagic Fever, the South American Hemorrhagic Fevers)

**Exposure** – Healthcare setting exposures to viral hemorrhagic fevers (VHF) result from contact with the blood or body fluids of a patient or, in some instances, with the contaminated patient-care environment.

**Prophylaxis** – No products are currently approved for postexposure prophylaxis after exposure to the viruses causing VHF. Two approved vaccines are available for Ebola preexposure prophylaxis, and some animal studies have suggested possible efficacy when used for postexposure prophylaxis; however, a more recently conducted macaque study failed to demonstrate improved outcomes associated with the postexposure administration of vesicular stomatitis virus-Ebola virus

vaccine [37]. Animal studies have also demonstrated efficacy of monoclonal antibodies raised against Ebola targets, though these data have not been replicated in human studies. Though ribavirin has long been considered for the treatment and postexposure prophylaxis of some VHF, including Crimean Congo hemorrhagic fever; it is not formally approved nor recommended by CDC for postexposure prophylaxis.

**Newer developments** – The COVID-19 pandemic stimulated a major effort in antiviral drug development. Several studies of repurposed antivirals or monoclonal antibodies are in development for several of the agents of VHF. One promising compound is obeldesivir, demonstrated in animal studies to be 100% protective when administered as postexposure prophylaxis against Ebola, Marburg, and Sudan virus [38\*\*].

## PARASITIC DISEASES

### Malaria

**Exposure** – While transmission typically occurs via mosquitos, healthcare exposures may occur after exposure to blood likely through parenteral exposure [39,40].

**Prophylaxis** – There is no standard regimen for postexposure prophylaxis for healthcare exposures to malaria; administration of effective antimalarial agents following a documented parenteral occupational exposure may be considered after consultation with occupational health and infectious diseases.

**Newer developments** – In 2021, the first malaria vaccine was recommended by the World Health Organization (WHO) and currently two are recommended: RTS,S/AS01 and R21/Matrix-M. As yet, no malaria vaccine has been approved by the FDA. In the United States, locally acquired malaria, while uncommon, has occurred as recently as 2023 [41\*].

## CONCLUSION

Substantial progress has been made in the four decades since postexposure prophylaxis for occupational exposures to HIV was initially offered. Assuring that staff are fully informed about the risks for occupational exposure and that they are aware the actions to take should such an exposure occur; making certain that access to Occupational Medicine/Employee Health is readily available; and making certain that exposures are managed in a timely, scientifically based manner are the key components of effective postexposure management strategies in

the healthcare setting. New agents and vaccines and more studies of safety and efficacy are needed to establish effective postexposure interventions for a variety of pathogens for which no approved interventions exist.

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## Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- ■ of outstanding interest

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