Bacterial Infections

Updated: November 21, 2024
Reviewed: November 21, 2024

Panel's Recommendations
• Status of vaccination should be reviewed at every clinical encounter and indicated vaccinations provided, according to the established recommendations for immunization of children with HIV (AIII).
• Routine use of antibiotics solely for primary prevention of serious bacterial infections is not recommended (BIII). Discontinuation of antibiotic prophylaxis is recommended for children with HIV who are receiving antibiotics for the purpose of primary or secondary prophylaxis of serious bacterial infections once they have achieved sustained (≥3 months) immune reconstitution (CD4 T lymphocyte [CD4] cell percentage ≥25% if <6 years old; CD4 percentage ≥20% and CD4 count >350 cells/mm^3 if ≥6 years old) (AII).
• Intravenous immune globulin is recommended to prevent serious bacterial infections in children with HIV who have hypogammaglobulinemia (IgG <400 mg/dL) (AI).
• Children with HIV whose immune systems are not seriously compromised (Stages 1 and 2) and who are not neutropenic can be expected to respond the same as children without HIV and should be treated with the usual antimicrobial agents recommended for the most likely bacterial organisms (AIII).
• Severely immunocompromised children with HIV and invasive or recurrent bacterial infections require expanded empiric antimicrobial treatment covering a broad range of resistant organisms (AIII).
• Initial empiric therapy for children with HIV with suspected intravascular catheter sepsis should target both gram-positive and enteric gram-negative organisms, with combinations that have activity against *Pseudomonas* spp. and methicillin-resistant *Staphylococcus aureus* or MRSA (AIII).
Rating of Recommendations: A = Strong; B = Moderate; C = Optional
*Rating of Evidence: I = One or more randomized trials **in children**† with clinical outcomes and/or validated endpoints; I* = One or more randomized trials **in adults** with clinical outcomes and/or validated laboratory endpoints with accompanying data **in children**† from one or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; II = One or more well-designed, nonrandomized trials or observational cohort studies **in children**† with long-term outcomes; II* = One or more well-designed, nonrandomized trials or observational studies **in adults** with long-term clinical outcomes with accompanying data **in children**† from one or more similar nonrandomized trials or cohort studies with clinical outcome data; III = expert opinion*
†Studies that include children or children/adolescents but not studies limited to postpubertal adolescents

Epidemiology

Before antiretroviral therapy (ART) was available, serious bacterial infections were the most commonly diagnosed opportunistic infections in children with HIV, with an event rate of 15 per 100 child-years.[1] Acute pneumonia, often presumptively diagnosed in children, was associated with increased risk of long-term mortality in children with HIV in one study from the pre-ART era.[2] Pneumonia was the most common serious bacterial infection (11 per 100 child-years), followed by bacteremia (3 per 100 child-years), and urinary tract infection (2 per 100 child-years).[1] Other serious bacterial infections—including osteomyelitis, meningitis, abscess, and septic arthritis—occurred at rates of <0.2 per 100 child-years.[1] Less serious bacterial infections, such as otitis media and sinusitis, were particularly common (17–85 per 100 child-years) in untreated children with HIV.[3]

Since the advent of combination ART in the late 1990s and universal guidelines recommending the rapid initiation of ART for all people with newly diagnosed HIV (including infants, children, and adolescents),[4,5] opportunistic infections among children with HIV in the United States have become exceedingly rare. Among children born during 1997 to 2016, the number of infants experiencing their first opportunistic infections decreased significantly from 432 during 1997 to 2001 to 24 during 2012 to 2016, with the biggest decrease in the number of diagnoses of *P. jirovecii* pneumonia (PCP).[6] Despite the overall decrease in the numbers of hospitalizations among children with HIV, the rates and adjusted odds of many bacterial outcomes (pneumonia, pneumococcal disease, bacterial infections/sepsis, methicillin-resistant *Staphylococcus aureus* [MRSA] infections) were still higher among hospitalized children with HIV compared with children without HIV from 2003 to 2012.[7] Additionally, children with HIV who are not receiving ART and present with pneumonia are more likely to be bacteremic and to die than children without HIV with pneumonia.[8,9] Children with chronic lung disease, including bronchiectasis and complicating repeated episodes of infectious pneumonia, also referred to as lymphocytic interstitial pneumonitis (LIP),[10,11] are more susceptible to infectious exacerbations (similar to those in children and adults with bronchiectasis or cystic fibrosis) caused by typical respiratory bacteria (*Streptococcus pneumoniae*, non-typeable *Haemophilus influenzae*) and *Pseudomonas* spp.

Streptococcus pneumoniae

Before the introduction of the first conjugate pneumococcal vaccine in the United States in 2000 and the use of ART in a substantial proportion of children with HIV in 1997, *S. pneumoniae* was the most prominent invasive bacterial pathogen in children with HIV, accounting for >50% of bacterial bloodstream infections in children with HIV.[1,12-14] Before the licensure of the 7-valent pneumococcal conjugate vaccine (PCV7) in 2000, the incidence of invasive pneumococcal disease (IPD) in children with HIV decreased by more than 80% from 1.9 per 100 person-years before ART to 0.3 per 100 in the ART era.[15] During the ART era, the rate of hospitalization for IPD in children and youth with HIV also declined by 62.5% since the introduction of PCV7.[16] Despite this significant decline in overall pneumococcal bacteremia, the odds of having pneumococcal disease as a discharge code was almost four times higher among children with HIV compared to children without HIV in 2012.[7] In children with IPD, study results vary on whether penicillin-resistant pneumococcal strains are more commonly isolated from people with HIV versus people without HIV, although these variabilities could reflect differences in the study setting.[17-20] Invasive disease caused by penicillin-nonsusceptible pneumococcus was associated with longer duration of fever and hospitalization but not with greater risk of complications or poorer outcome in a study of children without HIV[21]; however, most IPD in children with HIV is caused by susceptible pneumococci.[15] In 2010, PCV7 was replaced by a 13-valent pneumococcal conjugate vaccine (PCV13) for routine use in all children, including children with HIV.[22] Following the introduction of PCV13, the proportion of IPD caused by non-PCV13 serotypes increased.[23,24] The indications for 15-valent and 20-valent pneumococcal conjugate (PCV15 and PCV20) vaccines were recently expanded by the U.S. Food and Drug Administration in 2022 and 2023, respectively, for use in children aged 6 weeks and older,[25,26] thus providing an additional 10.6% to 38.2% coverage against IPD beyond serotypes contained in PCV13.[24] Among children with HIV, PCV15 elicited comparable levels of immunogenicity compared to PCV13 for the 13 shared serotypes[27] and was immunogenic for the two additional serotypes that are contained in PCV15. There has been reported variability in the efficacy of 23-valent pneumococcal polysaccharide vaccine (PPSV23) in preventing IPD and pneumonia in adults with HIV.[28-30] The ultimate effectiveness of PCV15, PCV20, and PPSV23 in preventing IPD in children with HIV is not yet known. The current recommendation is for children to receive the four-dose series with PCV15 or PCV20; if PCV15 is used, a dose of PCV20 or PPSV23 should be given at least 8 weeks later.[31]

Haemophilus influenzae *Type b*

Children with HIV are at increased risk of invasive *Haemophilus influenzae* type b (Hib) infection. In a study in South African children who had not received Hib conjugate vaccine, the estimated relative annual rate of overall invasive Hib disease in children aged <1 year was 5.9 times greater in those who had HIV than those who did not have HIV, and children with HIV were at greater risk for Hib bacteremic pneumonia.[32] Routine Hib immunizations in the United States and other countries has dramatically reduced invasive Hib infections in children.[33,34]

Neisseria meningitidis *(Meningococcus)*

HIV infection is associated with an increased risk of meningococcal disease.[35-39] In a population-based study of invasive meningococcal disease in New York City,[39] the average annual incidence rate of disease was high among people with HIV (15–64 years of age; 3.4 cases per 100,000 population) compared to people without HIV (0.34 cases per 100,000 population). As expected, the risk for invasive meningococcal diseases was 5.3 times higher among those with CD4 T lymphocyte (CD4) cell counts <200 cells/L compared with those with CD4 counts ≥200 cells/L. There are no studies of meningococcal disease risk in children with HIV in the United States. However, in a population-based surveillance study in South Africa, HIV infection significantly increased the risk of meningococcal bacteremia, which was associated with increased risk of death in all ages, but especially in children; very few children with HIV were receiving ART at the time of this study.[35] A more recent population-based cohort study in the United Kingdom between 2011 and 2013 reported that children and adolescents with HIV had a higher risk of meningococcal group B disease, and adults were at increased risk of groups C, W, and Y disease.[37]

Methicillin-Resistant Staphylococcus aureus

HIV infection appears to be a risk factor for MRSA infections in children and adults, but findings are conflicting about the relative contribution of immunosuppression versus the impact of social determinants of health to this increased risk.[7,40-44] Limited data suggest that children with HIV, like their uninfected counterparts, experience predominantly non-invasive, skin, and soft tissue infections as a result of community-associated MRSA strains and that greater immunosuppression may not confer greater risk of MRSA.[45] *S. aureus* (both methicillin-susceptible and MRSA) should be considered in people with a recent viral infection (especially influenza) or complicated pneumonia.

Other Pathogens

Other pathogens, including *Pseudomonas aeruginosa* and enteric organisms, cause infection in children with HIV, especially those who have indwelling vascular catheters or advanced immunosuppression or are not on ART.[13,46-49] The most commonly isolated pathogens in catheter-associated bacteremia in children with HIV are similar to those in children without HIV with indwelling catheters, including coagulase-negative staphylococci, *S. aureus*, enterococci, *P. aeruginosa*, gram-negative enteric bacilli, *Bacillus cereus*, and *Candida* spp.[12,48] In a cohort of 680 children with HIV in Miami, Florida, 10.6% had 95 episodes of gram-negative bacteremia between 1980 and 1997, of which 25% of children had two or three episodes of gram-negative bacteremia, and only six episodes were associated with an indwelling vascular catheter. The predominant organisms were *P. aeruginosa*, non-typhoidal *Salmonella*, and *E. coli* (15%).[46] More than 70% had advanced immunosuppression, and the overall case-fatality rate was 43%. In Kenyan children with bacteremia, HIV infection increased the risk of non-typhoidal *Salmonella* and *E. coli*

infections.[47] Rates of bacterial enteric infections have declined substantially among people with HIV with the use of combination ART,[50] but should be considered in children with persistent diarrhea without an alternative etiology.[51] In most cases, the treatment of bacterial enteric infections in children with HIV does not differ from that of children without HIV. The optimal duration of treatment for *Salmonella* enteritis in children with advanced HIV has not been defined. Please refer to the American Academy of Pediatrics Red Book for more details on specific bacterial etiologies and their diagnosis and management.[52]

Please refer to the *Pneumocystis jirovecii* Pneumonia and *Mycobacterium avium* Complex Disease sections of the Pediatric Opportunistic Infections Guidelines for information on the prevention and treatment of these conditions.

Children Who Were Exposed to Maternal HIV (But Uninfected)

Data are conflicting about whether infectious morbidity increases in children who have been exposed to but not infected with HIV. In studies in developing countries, infants who were exposed to HIV but uninfected (HEU) had higher mortality (primarily because of bacterial pneumonia and sepsis) than did those born to uninfected mothers.[53-55] Observational studies from South Africa and Europe have also shown a higher risk of invasive Group B Streptococcus disease in children who were HEU compared to children without HIV exposure.[56-58] Advanced maternal HIV infection has been associated with infant mortality.[53,54] In a study in Latin America and the Caribbean, 61% of 462 infants who were HEU experienced infectious disease morbidity during the first 6 months of life, with the rate of neonatal infections (particularly sepsis) and respiratory infections higher than rates in comparable community-based studies.[59] However, in a study from the United States, the rate of lower respiratory tract infections in children who were HEU was within the range reported for healthy children during the first year of life.[60] In a more recent study of children born during 2006 to 2017 in the United States, children who were HEU had approximately two times greater rates of infection-related hospitalization in the first 2 years of life compared to children who had not been exposed to HIV.[61] In addition to the potential of children who were HEU to experience increased severity in infections, data suggest that children who were HEU may be less likely to respond to treatment than children who have not been exposed to HIV, particularly in resource-limited settings.[62-64] There is increasing evidence for insufficient maternally derived antibody levels in infants who were HEU that put those infants at increased risk of pneumococcal and other vaccine-preventable infections.[65,66] However, at this time, there is no evidence to suggest that children who were HEU should receive vaccines on a different schedule from children without HIV exposure.

Clinical Manifestations

Clinical presentation depends on the particular type of bacterial infection (e.g., bacteremia/sepsis, osteomyelitis/septic arthritis, pneumonia, meningitis, sinusitis/otitis media)[67]; children with HIV who have an invasive bacterial infection typically have a clinical presentation similar to children without HIV.[68-70]

The classical signs, symptoms, and laboratory test abnormalities that usually indicate invasive bacterial infection (e.g., fever, elevated white blood cell count) are usually present but may be lacking in children with HIV who have reduced immune competence.[67,68] One-third of children with HIV not receiving ART who have acute pneumonia have recurrent episodes.[2] Bronchiectasis and other chronic lung damage that occurs before ART initiation can predispose an individual to recurrent pulmonary infections, even in the presence of combination ART.[10] Lower respiratory tract

bacterial infections in children with LIP most often are a result of the same bacterial pathogens that cause lower respiratory infection in children with HIV without LIP, manifesting as fever, increased sputum production, and respiratory difficulty superimposed on chronic pulmonary symptoms and radiologic abnormalities.[71]

In studies in Malawi and South Africa before the availability of ART, the clinical presentations of acute bacterial meningitis in children with and without HIV were similar.[72,73] However, in a study from Malawi, children with HIV were 6.4-fold more likely to have repeated episodes of meningitis than were children without HIV, although the study did not differentiate relapses from new infections.[72] In both studies, children with HIV were more likely to die from meningitis than were children without HIV.

Diagnosis

When evaluating children with HIV with a suspicion of a bacterial infection, pediatric infectious diseases should be consulted. Non-bacterial pathogens must also be considered as possible diagnoses in immunocompromised children with HIV.

Attempted isolation of a pathogenic organism from normally sterile sites (e.g., blood, cerebrospinal fluid, pleural fluid) is strongly recommended, as identification and antimicrobial resistance testing will guide effective treatment. Depending on its availability and pretest probability, molecular diagnostic testing of nasopharyngeal swabs, stool samples, or cerebrospinal fluid can be considered to aid in the diagnosis of children presenting with concerns for infection.[74-76] These molecular diagnostic testing panels also aid in the detection of antibiotic resistance markers, which can facilitate treatment management.[77]

In children presenting with respiratory symptoms, the diagnosis of pneumonia is often based on clinical symptoms and can be supported by an abnormal chest radiograph. The use of molecular diagnostic testing can aid in differentiating viral from bacterial pneumonia and has the potential to decrease hospitalizations and empiric antibiotic use.[78] Even after diagnosis with a viral infection, the clinician must consider that a secondary bacterial pneumonia can occur following the initial phase of a viral respiratory infection or during the recovery phase.[79] Blood and fluid from pleural effusion (if present) should be cultured. The differential for children with HIV and pneumonia must include *Mycobacterium tuberculosis* (TB) even if they are receiving ART, and must include PCP if they are not receiving combination ART. Presence of wheezing makes acute bacterial pneumonia less likely than other causes, such as viral infections, asthma exacerbation, atypical bacterial infections, or aspiration.[80] Children with LIP often have recurrent episodes of bacterial respiratory infection superimposed on chronic respiratory symptoms of cough and mild tachypnea.[81]

In children with bacteremia, a source should be sought. In addition to routine chest radiographs, other diagnostic imaging may be necessary in children with HIV with compromised immune systems to identify less apparent foci of infection (e.g., bronchiectasis, internal organ abscesses).[82-84] In children with suspected bacteremia and central venous catheters, blood culture should be obtained through the catheter and (if possible) peripherally.[85]

Prevention Recommendations

Children with HIV who are not receiving combination ART are at high risk for acquiring opportunistic infections. Regardless of their treatment status and CD4 count, children with well-

controlled HIV have a higher risk for certain infections, such as pneumococcal disease, compared to children without HIV.[86,87] The recommendations below are applicable to all children with or without HIV, but special considerations should be paid to children with HIV who are not receiving appropriate ART or are immunosuppressed.

Preventing Exposure

Because *S. pneumoniae* and *H. influenzae* (other than type b) commonly colonize the upper respiratory tract of children, no effective way exists to eliminate exposure to these bacteria. However, routine use of conjugated pneumococcal and Hib vaccines in the United States has dramatically reduced vaccine-type nasopharyngeal colonization in children, thus decreasing the risk of exposure to vaccine-type pathogens.[88-92]

Food

To reduce the risk of exposure to potential gastrointestinal bacterial pathogens, health care providers should advise that children with HIV avoid eating the following raw or undercooked foods (including other foods that contain them): eggs, poultry, meat, seafood (especially raw shellfish), and raw seed sprouts **(BIII).** Unpasteurized dairy products and unpasteurized fruit juices also should be avoided **(BIII).** Hands, cutting boards, counters, and knives and other utensils should be washed thoroughly after contact with uncooked foods to avoid unknowingly transferring bacteria from hands to chidren's food, milk, or formula or directly to children **(BIII).** Produce should be washed thoroughly before being eaten **(BIII).** These precautions are especially important for children who are not receiving combination ART.

Pets

When obtaining a new pet, caregivers should be aware that pets, especially puppies and kittens, can sometimes carry germs that can make people sick, even if the pet appears healthy. Proper veterinary care should be recommended for all pets to help ensure the risk of zoonotic disease transmission is minimized **(BIII).**[93] Children and adults with HIV should always wash their hands with soap and water after handling pets, especially before eating, and avoid contact with pets' feces **(BIII).**[94] Additionally, people with HIV should avoid contact with animals with diarrhea when possible; when not possible, they should use personal protective equipment like gloves. Due to the risk of infections such as salmonellosis, children younger than 5 years and immunosuppressed children should have limited exposure to reptiles (e.g., snakes, lizards, bearded dragons, turtles), live poultry (e.g., chicks, duckings), and rodents **(BIII).**[95,96] Reptiles and pet food should be kept out of the kitchen and anywhere that food is prepared, stored, served, or eaten to avoid cross-contamination of infectious pathogens. Any wounds sustained from pets, including bites or scratches that may seem minor, should be washed with warm soapy water immediately, and health care providers should be contacted.[97]

Travel

The risk of foodborne and waterborne infections in immunosuppressed people with HIV is magnified during travel to resource-limited settings. All children who travel to such settings should avoid foods and beverages that might be contaminated, including raw fruits and vegetables, raw or undercooked seafood or meat, cooked foods that have been allowed to cool without refrigeration, tap water, ice made with tap water, unpasteurized milk and dairy products, and items sold by street

vendors **(AIII).** Foods and beverages that are usually safer include steaming hot foods, fruits that are peeled by the traveler, untampered bottled (including carbonated) beverages, and water brought to a rolling boil for 1 minute. Treatment of water with iodine or chlorine may not be as effective as boiling and will not eliminate *Cryptosporidia.* However, iodine or chlorine treatment can be used when boiling is not practical.[98] These precautions are especially important for children who are not receiving combination ART.

Preventing Disease

Immunization

In addition to ART, one of the most important interventions to prevent bacterial infections in children with HIV is to ensure that they are immunized according to the HIV-specific recommended schedule (see the Center for Disease Control and Prevention's [CDC's] Child and Adolescent Immunization Schedule by Medical Indication) **(AII).**[99] Vaccines that protect against bacterial pathogens directly (e.g., pneumococcal, Hib, meningococcal, pertussis) and indirectly (e.g., influenza, COVID-19) have been demonstrated to be safe and immunogenic in children with HIV.[100-107] Children with HIV are at increased risk of under-immunization,[108] likely due to multiple factors, including those related to social determinants of health.[109] Therefore, vaccination status should be reviewed at every clinical encounter and indicated vaccinations provided, according to the established recommendations for immunization of children with HIV **(AIII).** Combination ART instituted before immunization offers the best means to optimize response to immunization.[110] Lack of combination ART and low CD4 counts may reduce the magnitude, quality, or duration of immunologic response and likely impair memory response. Greater number or strength of vaccine doses are recommended in some circumstances to overcome suboptimal response.

For the most up-to-date information on immunization, please refer to CDC's Child and Adolescent Immunization Schedule by Medical Indication.

Hib Vaccine

Children with HIV aged ≤5 years should receive Hib vaccine on the same schedule as that recommended for children without HIV, including for catch-up immunization **(AII).** See CDC's Child and Adolescent Immunization Schedule by Age for more information. Depending on the vaccine product, children should receive either a three-dose series with PedvaxHIB at ages 2 months, 4 months, and 12 to 15 months, or a four-dose series with ActHIB, Hiberix, Pentacel, or Vaxelis at ages 2 months, 4 months, 6 months, and 12 to 15 months. Vaxelis is not recommended for the fourth (booster) dose given at age 12 to 15 months; a different Hib-containing vaccine should be used.[111] Children with HIV between 1 and 5 years of age who have not received any Hib vaccine doses or who have only received one dose before the age of 12 months should receive two Hib vaccine doses 8 weeks apart. If they have received two or more doses before the age of 12 months, they should receive one additional dose at least 8 weeks after the previous dose. Children with HIV aged ≥5 years who have received less than the routine Hib series before age 14 months or have not previously received the Hib vaccine after age 14 months should receive one dose of any Hib conjugate vaccine **(AIII).**[112]

Pneumococcal Vaccines

Despite strong evidence on the efficacy of pneumococcal conjugate vaccine (PCV) among children (<7 years old) with and without HIV, its effectiveness against IPD among children with HIV was

notably limited in a meta-analysis of 10 studies that were mainly from South Africa.[113] As of June 2023, the CDC's Advisory Committee on Immunization Practices (ACIP) recommended the use of PCV15 or PCV20 for routine vaccination in children <2 years.[114] Children with HIV aged <2 years should receive routine pneumococcal conjugate vaccines (either PCV15 or PCV20) on the same schedule as that recommended for children without HIV **(AII).**[31] A four-dose series of either PCV15 or PCV20 is recommended for routine administration to children aged 2 months, 4 months, 6 months, and 12 to 15 months.

Children aged 2 to 6 years with HIV who have incomplete PCV vaccination status should receive either PCV15 or PCV20 according to currently recommended dosing and schedules. If they have received three conjugate vaccine doses before age 12 months but have not received their fourth booster dose, they should receive an additional dose at least 8 weeks after any prior PCV15 or PCV20 dose. If they have received any incomplete schedule of fewer than three conjugate vaccine doses before age 2 years, they should receive two doses of PCV15 or PCV20 (8 weeks after the most recent dose and administered 8 weeks apart).[20]

In addition, children with HIV aged ≥2 years who have received all recommended PCV doses using PCV13 or PCV15 should receive either a dose of PCV20 or PPSV23 (≥8 weeks after their last PCV dose). If PPSV23 is administered, either a dose of PCV20 or a second dose of PPSV23 is recommended 5 years after the first PPSV23 **(AII).**[31] Children with HIV aged ≥2 years who have received at least one dose of PCV20 do not need additional pneumococcal vaccine doses. Children with HIV aged 6 to 18 years with no prior history of PCV13, PCV15, or PCV20 should receive one pneumococcal conjugate vaccine dose (PCV15 or PCV20). If PCV15 is used, it should be followed by a dose of PPSV23 at least 8 weeks later if not previously given.[114]

Meningococcal Vaccine

All children with HIV age ≥2 months should routinely receive the age-appropriate series of the meningococcal ACWY (MenACWY) conjugate vaccine **(AIII).**[115] In contrast to the two-dose primary series for adolescents without HIV, children with HIV aged <2 years should be vaccinated according to the age-appropriate multidose schedule with MenACWY-CRM (Menveo) (see CDC's Child and Adolescent Immunization Schedule by Medical Indication). Children with HIV aged ≥2 years who have not received any meningococcal conjugate vaccines should receive a primary series of MenACWY conjugate vaccine of two doses given at least 8 weeks apart.[115] For booster doses, children aged <7 years should get a single dose at 3 years after the primary series and every 5 years thereafter. Children aged ≥7 years should receive a single dose at 5 years after primary vaccination and every 5 years thereafter.[115]

At this time, serogroup B meningococcal (MenB) vaccine is not routinely indicated for children with HIV, but may be administered to persons aged ≥10 years who are at increased risk for serogroup B meningococcal disease (e.g., persons with complement deficiencies) and is recommended for adolescents ≥16 years on the basis of shared clinical decision-making.[116]

Influenza Vaccine

Because influenza increases the risk of secondary bacterial respiratory infections,[117,118] annual influenza vaccination for influenza prevention can be expected to reduce the risk of serious bacterial infections in children with HIV **(AIII).**[119] Children with HIV should receive annual influenza vaccination according to the HIV-specific recommended immunization schedule **(AII)** (see CDC's Child and Adolescent Immunization Schedule by Medical Indication).[120] Live attenuated influenza

vaccines are contraindicated in people with HIV; children with HIV should receive inactivated influenza vaccines.[121]

COVID-19 Vaccine

COVID-19 has been associated with bacterial coinfections, and a bacterial coinfection with COVID-19 is a major risk of mortality and morbidity.[122-124] All children with HIV should receive the COVID-19 vaccine regardless of their CD4 count or HIV viral load; for current COVID-19 vaccination recommendations, please visit the Interim Clinical Considerations for Use of COVID-19 Vaccines in the United States.

Chemoprophylaxis

Among children with HIV who have an indication for PCP prophylaxis, daily trimethoprim-sulfamethoxazole (TMP-SMX) may decrease the rate of serious bacterial infections (predominantly respiratory) **(BII).**[125,126] For people who cannot tolerate TMP-SMX, alternative prophylactic regimens include dapsone **(BI*),** aerosolized pentamidine with a Respirgard II nebulizer **(BI*),** and atovaquone plus azithromycin **(AI).** Atovaquone combined with azithromycin, which provides prophylaxis for *Mycobacterium avium* complex (MAC) as well as PCP, is well tolerated, and is as effective as TMP-SMX in preventing serious bacterial infections in children with HIV.[127] For more detail on when to initiate primary prophylaxis, please refer to the *Pneumocystis jirovecii* Pneumonia and *Mycobacterium avium* Complex Disease sections of the Pediatric Opportunistic Infection Guidelines. Routine use of antibiotics solely for primary prevention of serious bacterial infections (i.e., when not indicated for PCP or MAC prophylaxis or other specific reasons) promotes development of drug-resistant organisms and is therefore not routinely recommended **(BIII).** Intravenous immune globulin (IVIG) is recommended to prevent serious bacterial infections in children with HIV who have hypogammaglobulinemia (immunoglobulin G <400 mg/dL) **(AI).**[128]

Discontinuation of Primary Prophylaxis

The Pediatric AIDS Clinical Trials Group (PACTG) Protocol 1008 demonstrated that discontinuation of MAC and/or PCP antibiotic prophylaxis in children with HIV who achieved sustained (≥16 weeks) immune reconstitution (CD4 cell percentage >20% to 25%) while receiving ART did not result in excessive rates of serious bacterial infections.[129] In support of discontinuing primary prophylaxis, multiple observational and randomized studies in adults have demonstrated a low incidence of PCP and MAC in adults who discontinued prophylaxis after receiving ART with sustained CD4 count recovery for >3 months.[130-133] Antibiotics for primary prophylaxis of serious bacterial infections should be discontinued in children with HIV once they have achieved sustained (i.e., ≥3 months) immune reconstitution (CD4 percentage ≥25% if aged <6 years; CD4 percentage ≥20% or CD4 count >350 cells/mm^3 if aged ≥6 years) **(AII).**

Treatment Recommendations

Treating Disease

The principles for treating serious bacterial infections are the same in children with and without HIV. Specimens for microbiologic studies should be collected before initiation of antibiotic treatment. However, in those with suspected serious bacterial infections, therapy should be administered empirically and promptly without waiting for the results of such studies; therapy can be adjusted once results become available. The local prevalence of antibiotic-resistant bacteria (e.g., penicillin-

resistant *S. pneumoniae*, MRSA) and the recent use of prophylactic or therapeutic antibiotics should be considered when initiating empiric therapy. When the organism is identified, antibiotic susceptibility testing should be performed, and subsequent therapy should be based on the results of susceptibility testing **(AIII).** The involvement of antibiotic stewardship programs when managing people with bacterial infections is also essential in ensuring appropriate antibiotic use and making sure that the development of antibiotic resistance is minimized.[134,135]

Children with HIV whose immune systems are not seriously compromised (Stages 1 and 2; see HIV Infection Stage table in the Introduction) and who are not neutropenic can be expected to respond similarly to children without HIV, and they should be treated for the most likely bacterial organisms **(AIII).** Based only on expert opinion, mild-to-moderate community-acquired pneumonia in children with HIV on ART with only mild or no immunosuppression who are fully immunized (especially against *S. pneumoniae* and Hib) can be treated with oral antibiotics (usually oral amoxicillin) according to the same guidelines as for healthy children **(BIII).** However, many experts have a lower threshold for hospitalizing these children to initiate treatment. In addition, broader-spectrum antimicrobial agents for initial empiric therapy are sometimes chosen because of the potentially higher risk of non-susceptible pneumococcal infections in children with HIV.[15,17-19,136,137] Thus, options for empiric therapy for children with HIV outside of the neonatal period who are hospitalized for suspected community-acquired bacterial pneumonia or bacteremia include ampicillin or an extended-spectrum cephalosporin (e.g., ceftriaxone), respectively **(AIII).**[138-140] The addition of vancomycin or other antibiotic for suspected bacterial meningitis should follow the same guidelines as for children without HIV.[141] The addition of a macrolide or fluoroquinolone can be considered for hospitalized individuals with pneumonia to treat other common community-acquired pneumonia pathogens (*M. pneumoniae, C. pneumoniae*). If MRSA is suspected or the prevalence of MRSA is high (i.e., >10%) in the community, clindamycin, TMP-SMX, or vancomycin can be added (choice based on local susceptibility patterns and adjusted according to culture results).[142-146] Neutropenic children also should be treated with an appropriate antipseudomonal drug if infection with *Pseudomonas* spp. is likely. Severely immunocompromised children with HIV and invasive or recurrent bacterial infections require expanded empiric antimicrobial treatment covering a broad range of resistant organisms similar to that chosen for suspected catheter sepsis pending results of diagnostic evaluations and cultures **(AIII).**

Initial empiric therapy for children with HIV with suspected intravascular catheter sepsis should target both gram-positive and enteric gram-negative organisms, with combinations that include agents with anti-*Pseudomonas* activity (e.g., ceftazidime, cefepime) and vancomycin **(AIII),** taking into consideration the person's history of drug-resistant infections or colonization. Factors such as response to therapy, clinical status, identification of pathogen, and need for ongoing vascular access will determine the need for and timing of catheter removal.[85]

Monitoring and Adverse Events (Including IRIS)

The response to appropriate antibiotic therapy should be similar in children with and without HIV. A clinical response is usually observed within 2 to 3 days after initiation, and radiologic improvement in individuals with pneumonia may lag behind clinical response.

Immune reconstitution inflammatory syndrome (IRIS) has not clearly been described in association with treatment of typical bacterial infections in children. Reports of bacterial infections in children during the first several weeks of combination ART have been associated with IRIS;[147,148] however, more recent data report mycobacterial (e.g., TB) and non-bacterial causes (e.g., cytomegalovirus,

cryptococcal meningitis) to be more commonly attributed to IRIS.[149] Suspicion of IRIS in a child being treated for a bacterial infection should raise concern for the presence of a different or additional infection or for inadequately treated infection mimicking IRIS.

Preventing Recurrence

Status of vaccination against Hib, pneumococcus, meningococcus, influenza and COVID-19 should be reviewed and updated, according to the recommendations outlined above and in the HIV-specific recommended immunization schedule from the Panel and ACIP **(AIII).** Refer to CDC's Child and Adolescent Immunization Schedule by Medical Indication for more information.

Among children with HIV who have an indication for PCP or MAC secondary prophylaxis, TMP-SMX (administered daily or three times per week for PCP prophylaxis) with either azithromycin or clarithromycin (administered for MAC prophylaxis) may reduce the recurrence of serious bacterial infections. Administration of antibiotic chemoprophylaxis to children with HIV who have frequent recurrences of serious bacterial infections despite ART (e.g., more than two serious bacterial infections in a 1-year period despite ART) can be considered **(CIII);** however, caution is required when using antibiotics solely to prevent recurrence of serious bacterial infections because of the potential for developing drug-resistant microorganisms and drug toxicity. In rare situations in which ART and antibiotic prophylaxis are not effective in preventing frequent recurrent serious bacterial infections, IVIG prophylaxis can be considered for secondary prophylaxis **(CI).**[128]

Discontinuing Secondary Prophylaxis

PACTG 1008 demonstrated that discontinuing MAC and/or PCP antibiotic prophylaxis in children with HIV who achieved sustained (i.e., ≥16 weeks) immune reconstitution (CD4 percentage >20% to 25%) while receiving ART did not result in excessive rates of serious bacterial infections.[129] In support of discontinuing secondary prophylaxis, multiple observational and randomized studies in adults demonstrated a low incidence of PCP and MAC in individuals who discontinued prophylaxis after receiving ART with sustained CD4 cell count recovery for >3 months.[131,132,150,151] Antibiotics for secondary prophylaxis of serious bacterial infections should be discontinued in children with HIV who have achieved sustained (i.e., ≥3 to 6 months) immune reconstitution (CD4 percentage ≥25% if ≤6 years old; CD4 percentage ≥20% or >350 cells/mm^3 if >6 years old) **(AII).**

Dosing Recommendations for Prevention and Treatment of Invasive Bacterial Infections

Indication	First Choice	Alternative	Comments/Special Issues
Primary Prophylaxis *S. pneumoniae* and other invasive bacteria	• Pneumococcal, meningococcal, and Hib vaccines • IVIG 400 mg/kg body weight every 2–4 weeks (only in cases of hypogammaglobulinemia, IgG <400 mg/dL)	TMP-SMX 75/375 mg/m^2 body surface area per dose by mouth twice daily	See CDC website for detailed immunization schedule. Criteria for Discontinuing IVIG • Resolution of hypogammaglobulinemia Criteria for Restarting IVIG • Relapse of hypogammaglobulinemia
Secondary Prophylaxis *S. pneumoniae* and other invasive bacteria	TMP-SMX 75/375 mg/m^2 body surface area per dose by mouth twice daily	IVIG 400 mg/kg body weight every 2–4 weeks	Secondary Prophylaxis Indicated • More than two serious bacterial infections in a 1-year period in children who are unable to take ART Criteria for Discontinuing Secondary Prophylaxis • Sustained (≥3 months) immune reconstitution (CD4 percentage ≥25% if ≤6 years old; CD4 percentage ≥20% or CD4 count >350 cells/mm^3 if >6 years old) Criteria for Restarting Secondary Prophylaxis • More than two serious bacterial infections in a 1-year period despite ART
Treatment Bacterial pneumonia; *S. pneumoniae*; occasionally *S. aureus*, *H. influenzae*, *P. aeruginosa*	• Amoxicillin 90 mg/kg/dose orally divided every 8 or 12 hours (max 1 g/dose) for outpatient management, *or* • Ampicillin 200–400 mg/kg/day divided every 6 hours (max 2 g/dose) (use higher dose if *S. pneumoniae* MIC ≥4 mcg/mL), *or* • Ceftriaxone 50–100 mg/kg body weight per dose once daily, or 25–50 mg/kg body weight per dose twice daily IV or IM (max 4 g/day)	• Ceftazidime 200–300 mg/kg/day divided every 8 hours IV or IM (max 12 g/day), *or* • Cefepime 50 mg/kg/dose every 8 hours IV or IM (max 2 g/dose)	Alternative treatment should be determined based on local antimicrobial susceptibility patterns or that of the bacterial isolate, if available. For children who are receiving combination ART, have mild or no immunosuppression, and have mild-to-moderate community-acquired pneumonia, oral therapy option would be amoxicillin 45 mg/kg/dose twice daily (maximum dose: 4 g per day). Add azithromycin for hospitalized patients to treat other common community-acquired pneumonia pathogens (*M. pneumoniae, C. pneumoniae*).

Indication	First Choice	Alternative	Comments/Special Issues
			Add clindamycin or vancomycin if methicillin-resistant *S. aureus* is suspected (base the choice on local susceptibility patterns). For patients with neutropenia, chronic lung disease other than asthma (e.g., LIP, bronchiectasis) or indwelling venous catheter, consider regimen that includes activity against *P. aeruginosa* (such as ceftazidime or cefepime instead of ceftriaxone). Consider PCP in patients with severe pneumonia or more advanced HIV disease. Evaluate for tuberculosis, cryptococcosis, and endemic fungi as epidemiology suggests.

Key: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; Hib = *Haemophilus influenzae* type b; IgG = immunoglobulin G; IM = intramuscular; IV = intravenous; IVIG = intravenous immune globulin; LIP = lymphocytic interstitial pneumonia; MIC = minimum inhibitory concentration; PCP = *Pneumocystis jirovecii* pneumonia; TMP-SMX = trimethoprim-sulfamethoxazole

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