Special Considerations in People With HIV

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Summary Recommendations

Prevention of COVID-19

• The COVID-19 Treatment Guidelines Panel (the Panel) recommends that people with HIV receive COVID-19 vaccines, regardless of their CD4 T lymphocyte (CD4) cell count or HIV viral load, because the potential benefits outweigh the potential risks (AIII).

• The Advisory Committee on Immunization Practices (ACIP) recommends that people with advanced or untreated HIV who received an initial 2-dose series of an mRNA COVID-19 vaccine should receive a third dose of that vaccine at least 28 days after the second dose. Advanced HIV is defined as people with CD4 counts <200 cells/mm³, a history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV.

• People with HIV should receive booster doses of COVID-19 vaccines as recommended by the ACIP.

Diagnosis of COVID-19

• The Panel recommends using the same approach for diagnosing SARS-CoV-2 infection in people with HIV as in people without HIV (AIII).

Management of COVID-19

• Recommendations for the triage, management, and treatment of COVID-19 in people with HIV are the same as those for the general population (AIII).

• Nonhospitalized people with HIV and mild to moderate COVID-19 may be eligible to receive the therapies that are currently recommended for treatment (see Therapeutic Management of Nonhospitalized Adults With COVID-19). However, in situations where there are logistical constraints for administering these therapies, priority should be given to those with very advanced HIV (AIII). See Prioritization of Anti-SARS-CoV-2 Therapies for the Treatment of COVID-19 in Nonhospitalized Patients When There Are Logistical Constraints for details.

• People with HIV who are receiving ritonavir-based or cobicistat-based antiretroviral therapy (ART) can receive the 5-day course of ritonavir-boosted nirmatrelvir (Paxlovid) to treat COVID-19 without altering or interrupting their ART (i.e., they can continue using the ritonavir or cobicistat dose associated with their ART in addition to the dose of ritonavir used with nirmatrelvir).

• In patients with advanced HIV who have suspected or laboratory-confirmed SARS-CoV-2 infection, clinicians should consider HIV-associated opportunistic infections in the differential diagnosis of clinical symptoms and consider consulting an HIV specialist (AIII).

• When starting treatment for COVID-19 in patients with HIV, clinicians should pay careful attention to potential drug-drug interactions and overlapping toxicities among COVID-19 treatments, antiretroviral (ARV) medications, antimicrobial therapies, and other medications (AIII).

• People with HIV should be offered the opportunity to participate in clinical trials of vaccines and potential treatments for COVID-19.

Management of HIV

• People with HIV who develop COVID-19, including those who require hospitalization, should continue their ART and opportunistic infection treatment and prophylaxis whenever possible (AIII).

• Clinicians treating COVID-19 in people with HIV should consult an HIV specialist before adjusting or switching a patient’s ARV medications (AIII).

• An ARV regimen should not be switched or adjusted (i.e., by adding ARV drugs to the regimen) for the purpose of preventing or treating SARS-CoV-2 infection (AIII).

• Clinicians should consult an HIV specialist to determine the optimal time to initiate ART in people who present with COVID-19 and a new diagnosis of HIV.

Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See Guidelines Development for more information.
Introduction

Approximately 1.2 million people in the United States are living with HIV. Most of these individuals are in care, and many are receiving antiretroviral therapy (ART) and have well-controlled disease.\(^1\) Similar to COVID-19, HIV disproportionately affects racial and ethnic minorities and people living in low-income settings in the United States; these demographic groups also appear to have a higher risk of poor outcomes with COVID-19.\(^2\) Many people with HIV have 1 or more comorbidities or conditions that may put them at increased risk for a more severe course of COVID-19.\(^3\)

Information on SARS-CoV-2/HIV coinfection is evolving rapidly. The sections below outline the current knowledge regarding preventing and diagnosing SARS-CoV-2 infection in people with HIV, treatment and clinical outcomes in people with HIV who develop COVID-19, and management of HIV during the COVID-19 pandemic. In addition to these Guidelines, the Guidelines Working Groups of the National Institutes of Health Office of AIDS Research Advisory Council has developed Guidance for COVID-19 and People With HIV.

Clinical Outcomes of COVID-19 in People With HIV

Data are emerging on the clinical outcomes of COVID-19 in people with HIV. In some of the initial case series of people with COVID-19 in Europe and the United States, no significant differences were observed in the clinical outcomes of COVID-19 between people with HIV and people who did not have HIV.\(^4\)-\(^11\)

In contrast, more recent reports suggest worse outcomes for patients with HIV and COVID-19, including increased COVID-19 mortality in cohort studies in the United States, the United Kingdom, and South Africa.\(^12\)-\(^18\) HIV was independently associated with an increased risk of severe and critical COVID-19 in a large World Health Organization platform trial that included data from 24 countries.\(^19\) In a multicenter cohort study of 286 patients with HIV and COVID-19 in the United States, lower CD4 T lymphocyte (CD4) cell counts (i.e., <200 cells/mm\(^3\)) were associated with a higher risk for the composite endpoint of intensive care unit admission, mechanical ventilation, or death.\(^15\) This increased risk was observed even in patients who had achieved virologic suppression of HIV. In a large observational cohort study of people with HIV and COVID-19 in the United States, those with CD4 counts <350 cells/mm\(^3\) were more likely to be hospitalized, require ventilation, or die.\(^18\) Higher levels of viremia were also associated with worse outcomes. In another study of 175 patients with HIV and COVID-19, a low CD4 count or a low CD4 nadir was associated with poor outcomes.\(^16\) In a cohort study conducted in New York, people with HIV and COVID-19 had higher rates of hospitalization and mortality than people with COVID-19 who did not have HIV.\(^17\)

Prevention of COVID-19 in People With HIV

The COVID-19 Treatment Guidelines Panel (the Panel) recommends using the same approach for advising people with HIV on the strategies to prevent SARS-CoV-2 infection that is used for people without HIV (AIII). There is currently no clear evidence that any antiretroviral (ARV) medications can prevent SARS-CoV-2 infection.

The Panel recommends that people with HIV receive COVID-19 vaccines, regardless of their CD4 cell count or HIV viral load, because the potential benefits outweigh the potential risks (AIII). People with HIV were included in the clinical trials of the 2 mRNA vaccines and the adenovirus vector vaccine that are currently available through Emergency Use Authorizations (EUAs) and/or approval from the Food and Drug Administration (FDA);\(^20\)-\(^22\) however, few studies have evaluated the safety and efficacy of these vaccines in people with HIV. Typically, people with HIV who are receiving ART and who have achieved virologic suppression respond well to licensed vaccines. Preliminary data from studies that
used COVID-19 vaccines in people with HIV confirm that people who are receiving ART and have normal CD4 counts have good immunologic responses to the vaccines.23-25

On August 12, 2021, the FDA changed the EUAs for the 2 mRNA vaccines to allow a third dose of an mRNA vaccine to be administered at least 28 days after the second dose to people with advanced or untreated HIV. Advanced HIV is defined as people with CD4 counts <200 cells/mm$^3$, a history of an AIDS-defining illness without immune reconstitution, or clinical manifestations of symptomatic HIV. People with HIV should also receive booster doses of COVID-19 vaccines as recommended by the Advisory Committee on Immunization Practices.26

**Diagnostic and Laboratory Testing for COVID-19 in People With HIV**

**Diagnosis of COVID-19 in People With HIV**

The Panel recommends using the same approach for diagnosing SARS-CoV-2 infection in people with HIV as in people without HIV (AIII). See Testing for SARS-CoV-2 Infection for more information. There is currently no evidence that the performance characteristics of nucleic acid amplification tests (NAATs) and antigen tests differ in people with and without HIV when diagnosing acute SARS-CoV-2 infection. The Panel recommends against the use of serologic testing as the sole basis for diagnosis of acute SARS-CoV-2 infection (AIII). However, if diagnostic serologic testing is performed in a patient with HIV, the results should be interpreted with caution because cross-reactivity between antibodies to SARS-CoV-2 and HIV has been reported.27

**Correlation of CD4 Count in People With HIV and COVID-19**

The normal range for CD4 counts in healthy adults is about 500 to 1,600 cells/mm$^3$. People with HIV who have a CD4 count of $\geq500$ cells/mm$^3$ have similar cellular immune function to those without HIV. In people with HIV, a CD4 count <200 cells/mm$^3$ meets the definition for AIDS. For patients receiving ART, the hallmark of treatment success is plasma HIV RNA below the level of detection by a polymerase chain reaction assay. Lymphopenia is a common laboratory finding in patients with COVID-19; in patients with HIV, clinicians should note that CD4 counts obtained during acute COVID-19 may not accurately reflect the patient’s HIV disease stage.

There have been some reports of people with advanced HIV who have presented with COVID-19 and another co-infection, including *Pneumocystis jirovecii* pneumonia.28,29 In patients with advanced HIV who have suspected or laboratory-confirmed SARS-CoV-2 infection, clinicians should consider HIV-associated opportunistic infections in the differential diagnosis of clinical symptoms and consider consulting an HIV specialist (AIII).

**Clinical Presentation of COVID-19 in People With HIV**

It is currently unknown whether people with HIV have a higher incidence of SARS-CoV-2 infection or a higher rate of progression to symptomatic disease than the general population. Approximately 50% of people with HIV in the United States are aged $>50$ years,30 and many have comorbidities that are associated with more severe cases of COVID-19. These comorbidities include hypertension, diabetes mellitus, cardiovascular disease, a history of smoking, chronic lung disease, chronic liver disease, and cancer.31

There are a number of case reports and case series that describe the clinical presentation of COVID-19 in people with HIV.4-11,32,33 These studies indicate that the clinical presentation of COVID-19 is similar in people with and without HIV. Most of the published reports describe populations in which most of the individuals with HIV are receiving ART and have achieved virologic suppression. Consequently, the
current understanding of the impact of COVID-19 in people with advanced HIV and low CD4 counts or persistent HIV viremia is limited.

Management of COVID-19 in People With HIV

Recommendations for the triage and management of COVID-19 in people with HIV are the same as those for the general population (AIII).

The treatment of COVID-19 in persons with HIV is the same as for those without HIV (AIII). Nonhospitalized people with HIV and mild to moderate COVID-19 may be eligible to receive the therapies that are currently recommended for treatment (see Therapeutic Management of Nonhospitalized Adults With COVID-19). However, in situations where there are logistical or supply constraints for administering these therapies, priority should be given to those with advanced HIV (AIII).

When starting treatment for COVID-19 in patients with HIV, clinicians should pay careful attention to potential drug-drug interactions and overlapping toxicities among COVID-19 treatments, ARV medications, antimicrobial therapies, and other medications (AIII). Therapeutic options for nonhospitalized patients with HIV include ritonavir-boosted nirmatrelvir (Paxlovid), intravenous remdesivir, and molnupiravir.

Drug-drug interactions are a special concern with ritonavir-boosted nirmatrelvir (see Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir [Paxlovid] and Concomitant Medications). People with HIV who are receiving ritonavir-based or cobicistat-based ART can receive the 5-day course of ritonavir-boosted nirmatrelvir to treat COVID-19 without altering or interrupting their ART (i.e., they can continue using the ritonavir or cobicistat dose associated with their ART in addition to the dose of ritonavir used with nirmatrelvir). Before prescribing ritonavir-boosted nirmatrelvir for a patient who is not already on a ritonavir-based or cobicistat-based regimen, clinicians should carefully review the patient’s concomitant medications, including over-the-counter medicines and herbal supplements, and evaluate the potential for drug-drug interactions. Clinicians should utilize resources such as the FDA’s EUA fact sheet for ritonavir-boosted nirmatrelvir and the Liverpool COVID-19 Drug Interactions website for additional guidance on identifying and managing drug-drug interactions.

In hospitalized patients, the appropriate treatment strategy depends on disease severity (see Therapeutic Management of Hospitalized Adults With COVID-19). Both tocilizumab and dexamethasone, which are recommended for some patients with severe or critical COVID-19, are immunosuppressive agents. The safety of using these drugs in patients who are immunocompromised, including those with advanced HIV, has not been studied. Therefore, patients with advanced HIV who are receiving these drugs should be closely monitored for secondary infections.

Dexamethasone is a dose-dependent inducer of cytochrome P450 3A4 and could potentially lower the levels of certain coadministered ARV drugs. More than a single dose of dexamethasone is not recommended for patients receiving rilpivirine as part of their ARV regimen. Clinicians should consult an HIV specialist before administering dexamethasone to these patients. It is currently unknown whether administering ≤10 days of dexamethasone impacts the clinical efficacy of other ARV drugs. Patients with HIV who are receiving dexamethasone as treatment for COVID-19 should follow up with their HIV providers to assess their virologic response.

Although some ARV drugs were studied for the prevention and treatment of COVID-19, no agents have been shown to be effective.

People with HIV should be offered the opportunity to participate in clinical trials of vaccines and...
potential treatments for COVID-19. A variety of immunomodulatory therapies are prescribed empirically or administered as part of a clinical trial to treat severe COVID-19. The data on whether these medications are safe to use in patients with HIV are lacking. If a medication has been shown to reduce the mortality of patients with COVID-19 in the general population, it should also be used to treat COVID-19 in patients with HIV, unless data indicate that the medication is not safe or effective in this population.

Managing HIV in People With COVID-19

People with HIV who develop COVID-19, including those who require hospitalization, should continue their ART and opportunistic infection treatment and prophylaxis whenever possible (AIII). Treatment interruption may lead to rebound viremia, and, in some cases, the emergence of drug resistance. If the appropriate ARV drugs are not on the hospital’s formulary, administer medications from the patient’s home supplies, if available.

Clinicians treating COVID-19 in people with HIV should consult an HIV specialist before adjusting or switching a patient’s ARV medications (AIII). An ARV regimen should not be switched or adjusted (i.e., by adding ARV drugs to the regimen) for the purpose of preventing or treating SARS-CoV-2 infection (AIII). Many drugs, including some ARV agents (e.g., lopinavir/ritonavir, boosted darunavir, tenofovir disoproxil fumarate/emtricitabine), have been or are being evaluated in clinical trials or are prescribed off-label to treat or prevent SARS-CoV-2 infection. To date, lopinavir/ritonavir and darunavir/cobicistat have not been found to be effective.\(^{34,35}\) Two retrospective studies have suggested that tenofovir disoproxil fumarate/emtricitabine may play a role in preventing SARS-CoV-2 acquisition or hospitalization or death associated with COVID-19; however, the significance of these findings is unclear, as neither study adequately controlled for confounding variables such as age and comorbidities.\(^{12,33}\)

For patients receiving an investigational ARV medication as part of their ARV regimen, arrangements should be made with the investigational study team to continue the medication, if possible.

For critically ill patients who require tube feeding, some ARV medications are available in liquid formulations, and some ARV pills may be crushed. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way to continue an effective ARV regimen for a patient with a feeding tube. Information may be available in the drug product label or from the Toronto General Hospital.

For people who present with COVID-19 and have either a new diagnosis of HIV or a history of HIV but are not receiving ART, the optimal time to start or restart ART is currently unknown. For people with HIV who have not initiated ART or who have been off therapy for >2 weeks before presenting with COVID-19, an HIV specialist should be consulted about initiating or reinitiating ART as soon as clinically feasible. If ART is initiated, maintaining treatment and linking patients to HIV care upon hospital discharge is critical. If an HIV specialist is not available, clinical consultation is available by phone through the National Clinician Consultation Center, Monday through Friday, 9 am to 8 pm EST.

References


