

GUIDE NO. 3

Evaluation of Acute Diarrhea in Persons with HIV

Gretchen Snoeyenbos Newman, MD¹ / Brian R. Wood, MD² / Jehan Z. Budak, MD² / Aley G. Kalapila, MD³ / Ronald D. Wilcox, MD⁴ / David H. Spach, MD²

TABLE OF CONTENTS

- 2** Definitions and Key Clinical History
- 3** Diagnostic Approach
- 4** Common Causes and Initial Diagnostic Evaluation
- 5** Key Summary Points
- 6** References, Disclosures, Acknowledgment, and Funding

ABOUT THIS HIV SYMPTOM EVALUATION GUIDE

The *HIV Symptom Evaluation Guide* addresses the initial diagnostic evaluation of common problems that occur in persons with HIV. The goal of this decision guide is to provide a practical approach to the initial evaluation and diagnosis of acute or subacute cough and dyspnea in persons with HIV.

Clinical judgment should be used to determine whether hospitalization is required. If needed, clinicians should seek expert consultation for assistance with the diagnostic evaluation or management.

PERMISSIONS

No permission is required when distributing or adapting the images, figures, tables and content for noncommercial purposes. For permission, e-mail support@hiv.uw.edu.

LAST UPDATED

September 15, 2022

AUTHOR AFFILIATIONS

¹ Division of Infectious Diseases / Wayne State University School of Medicine

² Division of Allergy and Infectious Diseases / University of Washington

³ Division of Infectious Diseases / Emory University School of Medicine; Grady Health System

⁴ Health Resources and Services Administration / HIV/AIDS Bureau, Office of Program Support

DEFINITIONS OF ACUTE VERSUS CHRONIC DIARRHEA

Diarrhea is defined as loose or watery bowel movements that occur 3 or more times per day or passage of a greater number of stools of decreased form compared to normal. Acute diarrhea, by definition, has been present for 14 days or less. Diarrhea present for 15 to 30 days is referred to as persistent and greater than 30 days as chronic. This guide will focus on causes of acute diarrhea; occasionally, etiologies described here may cause symptoms that last greater than 14 days (symptoms may be prolonged in the setting of a CD4 count below 200 cells/mm³).

KEY CLINICAL HISTORY

What is the person's most recent CD4 cell count?

Current or recent low CD4 cell count indicates risk for certain opportunistic infections (OIs), such as cryptosporidiosis (CD4 count less than 200 cells/mm³), cytomegalovirus (CMV) colitis (CD4 count less than 50 cells/mm³), or disseminated *Mycobacterium avium* complex (MAC) infection (CD4 count less than 50 cells/mm³).

Does the individual have bloody diarrhea, fever, or other associated symptoms?

Bloody diarrhea, especially associated with fever, suggests a potentially serious infection with a bacterial enteric pathogen or CMV colitis if the CD4 count is less than 50 cells/mm³. Fever, in conjunction with systemic symptoms and weight loss, especially in the setting of a recent CD4 count less than 50 cells/mm³, raises the likelihood of disseminated MAC infection. Fever or respiratory symptoms along with diarrhea may suggest COVID-19 illness at any CD4 cell count.

Have any recent sexual exposures occurred?

It is important to obtain recent sexual history since bacterial enteric infections can be transmitted among persons who have condomless anal sex or oral-anal contact. Rectal sex raises the risk of enteric bacterial infections (e.g., *Campylobacter* sp. and *Shigella* sp.), *Giardia* infection, and chlamydia proctitis (lymphogranuloma venereum [LGV] serovars).

Recently, has there been any of the following: close contact with a person who was sick, ingestion of contaminated food, travel outside the United States, or antibiotic use?

Viral gastroenteritis is commonly transmitted among close contacts. Exposure to contaminated foods may lead to the transmission of diarrheal pathogens. Recent antibiotic use or hospitalization are risk factors for *Clostridioides difficile*-associated diarrhea.

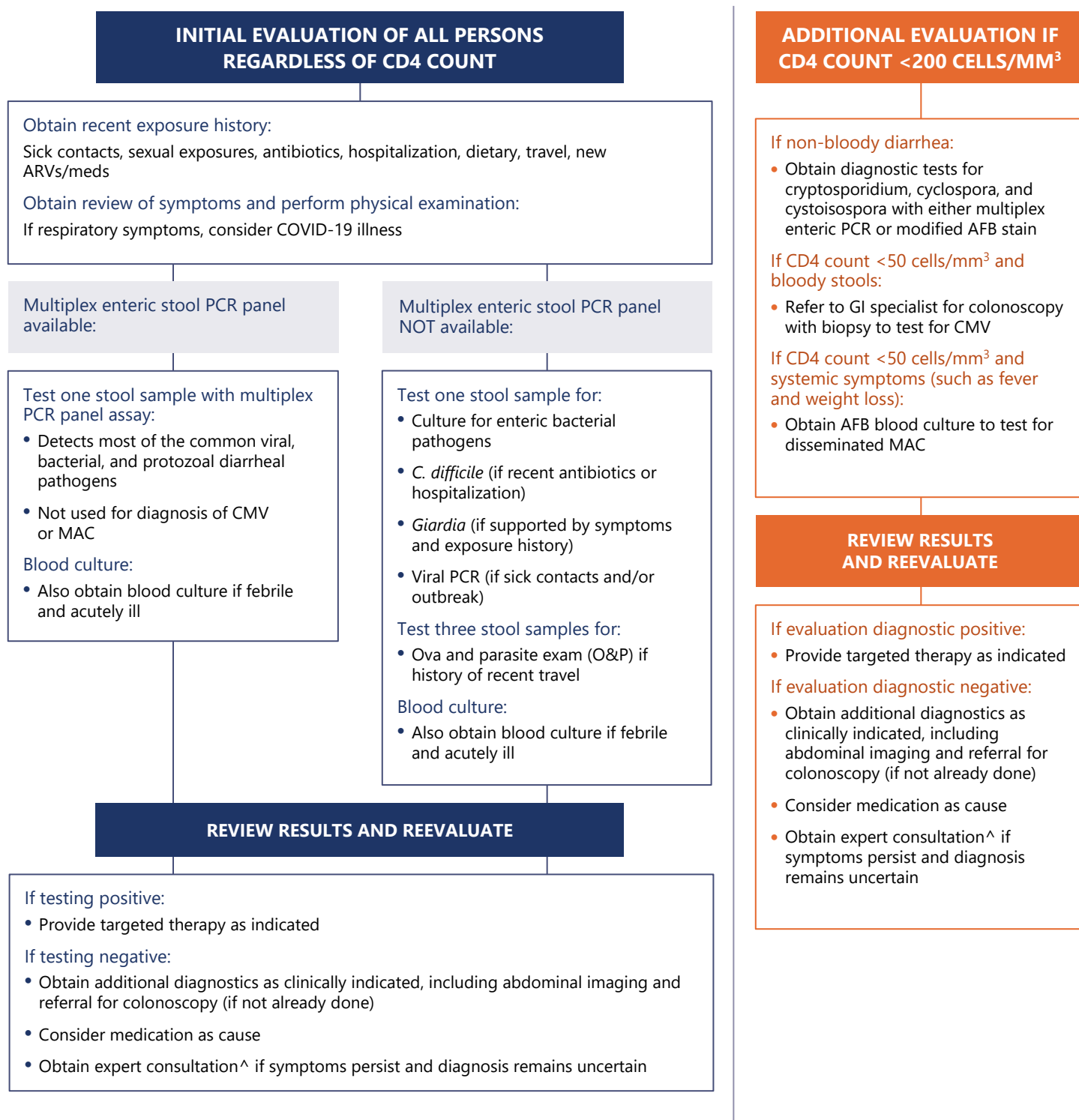
Were there any recent changes in antiretroviral therapy medications?

Certain antiretroviral medications, particularly protease inhibitors and boosting agents (ritonavir and cobicistat), can cause diarrhea and other gastrointestinal symptoms.

Is the person living homeless? If so, do they have documented immunity to hepatitis A?

There have been recent outbreaks of hepatitis A infection, especially in individuals living homeless. Persons who have oral-anal sexual contact also are at increased risk.

DIAGNOSTIC APPROACH TO ACUTE DIARRHEA IN PERSONS WITH HIV



[^] If local expert consultation is not available, consultation can be obtained through the National Clinician Consultation Center (<http://nccc.ucsf.edu/> or 800-933-3413).

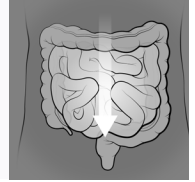
ABBREVIATIONS: AFB = acid-fast bacilli; ARV = antiretroviral; CMV = cytomegalovirus; GI = Gastroenterology; MAC = *Mycobacterium avium* complex; PCR = polymerase chain reaction

COMMON CAUSES AND INITIAL DIAGNOSTIC EVALUATION FOR ACUTE DIARRHEA IN PERSONS WITH HIV

CAUSE (in alphabetical order)	RISK FACTORS AND CHARACTERISTICS	TYPICAL CD4 CELL COUNT	INITIAL DIAGNOSTIC EVALUATION
<i>Clostridioides difficile</i> (<i>C. diff</i>)	Antibiotic or healthcare exposure Typically, watery diarrhea often accompanied by pain	Any	PCR +/- EIA for glutamate dehydrogenase, or toxin A/B; algorithm may vary by institution
Cytomegalovirus (CMV) colitis	Advanced HIV Often bloody diarrhea with abdominal pain and systemic symptoms	<50 cells/mm ³	Colonoscopy with biopsy and pathology Diagnosis should not be made based on stool culture or PCR of stool or blood alone
Disseminated <i>Mycobacterium avium</i> complex (MAC)	Advanced HIV Associated with systemic symptoms and weight loss	<50 cells/mm ³	Blood AFB culture Diagnosis should not be made based on stool PCR or stool culture (stool culture supportive but not diagnostic)
Enteric bacterial pathogens: <i>Campylobacter</i> , <i>Shigella</i> species; <i>Salmonella</i> species; toxigenic <i>E. coli</i> strains	Sexual exposure (primarily rectal sex), food exposure, travel to resource-limited setting Liquid, watery, or bloody diarrhea	Any	Stool enteric multiplex PCR, if available If multiplex PCR NOT available, order stool culture Obtain blood culture if systemically ill
Medication-related	New medication that may cause diarrhea	Any	Other causes ruled out Most common ART: boosting agents (ritonavir and cobicistat) and protease inhibitors
Protozoal infections: <i>Giardia</i> , cryptosporidium, cyclospora, cystoisospora, <i>Entamoeba histolytica</i>	<i>Giardia</i> : travel, sexual exposure Others: travel, local outbreaks Typically, watery diarrhea that may persist for > 14 days	Any	Stool enteric multiplex PCR, if available If multiplex PCR NOT available, order all of the following: Cryptosporidium, cyclospora, cystoisospora: stool modified AFB stain (not detected with O&P test); DFA also available in some labs for cryptosporidium <i>E. histolytica</i> : antigen or PCR <i>Giardia</i> : stool antigen test or PCR
Viral gastroenteritis pathogens: Norovirus (Norwalk virus), rotavirus, enteric adenovirus, SARS CoV-2 (COVID-19)	Group living setting, local outbreaks, food exposure Typically, watery diarrhea Associated respiratory symptoms with COVID-19	Any	Stool enteric multiplex PCR, if available, or Stool viral-specific PCR Respiratory PCR swab if SARS CoV-2 infection suspected

ABBREVIATIONS: AFB = acid-fast bacilli; ART = antiretroviral therapy; EIA = enzyme immunoassay; O&P = ova and parasites; PCR = polymerase chain reaction

KEY SUMMARY POINTS



- For an initial evaluation of acute diarrhea in a person with HIV, consider three main causes: (1) common viral or bacterial infections that are not unique to HIV and may be related to local outbreaks or to sexual transmission, (2) opportunistic gastrointestinal infections that occur in the setting of advanced CD4 T-cell depletion, and (3) noninfectious causes, such as recent ART or other medication or dietary changes.
- At any CD4 count, individuals may contract viral gastroenteritis or may acquire bacterial enteric infections, such as *Campylobacter* or *Shigella*. Bacterial enteric infections may be acquired through sexual contact, particularly anal sex and oral-anal contact.
- The most important causes of diarrhea that occur in persons with HIV and advanced immunosuppression (CD4 less than 50–100 cells/mm³) are cryptosporidiosis, disseminated MAC, and CMV colitis.
- Most viral, bacterial, and parasitic pathogens that cause diarrhea in persons with HIV can be identified on a single stool specimen using a multiplex enteric PCR panel. This test, if available, is highly sensitive and specific and can provide results within 24 hours. However, the multiplex enteric PCR tests should not be used to diagnose CMV or MAC.
- If a multiplex enteric PCR panel is not available, the diagnostic evaluation should consider specific epidemiologic factors and laboratory tests tailored to detect likely pathogens. For example, a stool ova and parasite (O&P) exam is not sufficient to detect cryptosporidium or similar pathogens, so a separate examination of the stool must be requested.
- The diagnosis of CMV colitis requires a compatible clinical syndrome, identification of CMV within tissue on colon biopsies, and histologic changes consistent with CMV infection on a biopsy specimen. Colitis from CMV typically occurs when the CD4 count is less than 50 cells/mm³.
- Diarrhea caused by MAC infection is usually associated with systemic symptoms, including weight loss. A person with disseminated MAC infection may present with acute symptoms, or presentation may be more subacute to chronic. The CD4 count is generally less than 50 cells/mm³. The diagnosis is typically made by a positive AFB blood culture. Imaging of the abdomen by CT may demonstrate lymphadenopathy, hepatosplenomegaly, or small bowel thickening. A stool culture positive for MAC does not establish a diagnosis of MAC infection.
- The most common antiretrovirals to cause diarrhea are protease inhibitors and boosting agents (ritonavir and cobicistat).
- Acute hepatitis A infection should be considered in a person with diarrhea and fever or systemic symptoms, especially if they are homeless and have elevated alanine aminotransferase (ALT) or alanine aminotransferase (AST) levels.
- COVID-19 illness may be associated with GI symptoms, including diarrhea, in 10% or more of cases. If there is associated fever, respiratory symptoms, or known exposure, consider SARS-CoV-2 infection as a potential cause and perform respiratory PCR testing.

REFERENCES

- Cybulski RJ Jr, Bateman AC, Bourassa L, et al. Clinical impact of a multiplex gastrointestinal PCR panel in patients with acute gastroenteritis. *Clin Infect Dis*. 2018;67:1688-96. [PMID: 29697761]
- DuPont HL. Acute infectious diarrhea in immunocompetent adults. *N Engl J Med*. 2014;370:1532-40. [PMID: 24738670]
- Garcia LS, Arrowood M, Kokoskin E, et al. Practical Guidance for Clinical Microbiology Laboratories: Laboratory Diagnosis of Parasites from the Gastrointestinal Tract. Laboratory diagnosis of parasites from the gastrointestinal tract. *Clin Microbiol Rev*. 2018;31:1-81. [PMID: 29142079]
- Logan C, Beadsworth MB, Beeching NJ. HIV and diarrhoea: what is new? *Curr Opin Infect Dis*. 2016;29:486-94. [PMID: 27472290]
- Riddle MS, DuPont HL, Connor BA. ACG Clinical Guideline: diagnosis, treatment, and prevention of acute diarrheal infections in adults. *Am J Gastroenterol*. 2016;111:602-22. [PMID: 27068718]
- Snoeyenbos Newman G, Newman K, Cybulski R, Fang F. Acute gastroenteritis in men who have sex with men in Seattle, Washington, 2017-2018: A cohort study. *Clin Infect Dis*. 2020;71(1):109-115. [PMID: 31621824]

DISCLOSURES

The authors of this symptom guide had no disclosures.

ACKNOWLEDGEMENT

The authors would like to thank Nikolas Johs, MD, Christopher Link, MD, and Julie Weis, MD for their careful review of this symptom guide. The authors also thank Carol Kono-Noble, Mirror-Doc, and Julia Freimund for their design and production work.

FUNDING

The *National HIV Curriculum* is an AIDS Education and Training Center (AETC) Program supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling \$1,021,448 with 0% financed with non-governmental sources. The content in this document is that of the authors and does not necessarily represent the official views of, nor an endorsement by, HRSA, HHS, or the U.S. Government. For more information, visit [HRSA.gov](https://www.hrsa.gov).

