OI Guidelines Update

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Disclosures

No conflicts of interest or relationships to disclose

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Disclaimer

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AETC AIDS Education & Training Center Program Mountain West

Objectives

Review recent updates in the Guidelines for Prevention and Treatment of Opportunistic Infections in Adults/Adolescents with HIV

- Toxoplasmosis
- Pneumocystis Pneumonia
- Vulvovaginal Candidiasis
- Bacterial Enteric Infections
- MAC

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Toxoplasmosis

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Toxoplasmosis

- Limit baseline serologic screening and measures to prevent exposure to individuals with CD4 T lymphocyte cell counts <200 cells/mm^3
- Added trimethoprim-sulfamethoxazole as a preferred regimen for acute infection

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Toxoplasmosis

Limit baseline serologic screening and measures to prevent exposure to individuals with CD4 T lymphocyte cell counts <200 cells/mm^3

Recommendations:

For individuals with CD4 counts < 200

advise to avoid raw/undercooked meat

wash hands after contact with raw meat and after gardening

wash raw fruits/vegetables prior to eating

avoid changing cat litter (or wearing gloves/washing hands if do)

Rationale:

Seroprevalence of toxo IgG varies (in US 11%, non-US 40-80%)

Clinical disease rare in people with CD4 count > 200 (<50 being at highest risk)

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Toxoplasmosis

Trimethoprim-sulfamethoxazole is a preferred regimen for acute infection

Treating *Toxoplasma gondii* Encephalitis

Preferred Regimens for Acute Infection

- Pyrimethamine 200 mg PO once, followed by weight-based dosing **(AI)**:
  - Body weight ≤60 kg: pyrimethamine 50 mg PO daily + sulfadiazine 1,000 mg PO every 6 hours + leucovorin 10–25 mg PO daily (can increase to 50 mg daily or twice daily)
  - Body weight >60 kg: pyrimethamine 75 mg PO daily + sulfadiazine 1,500 mg PO every 6 hours + leucovorin 10–25 mg PO daily (can increase to 50 mg daily or twice daily)

or

- TMP-SMX (TMP 5 mg/kg and SMX 25 mg/kg) (IV or PO) twice daily **(AII)**

Note: If pyrimethamine is unavailable or cannot be obtained without delay due to costs or other factors, TMP-SMX should be used in place of pyrimethamine-sulfadiazine **(AII).**

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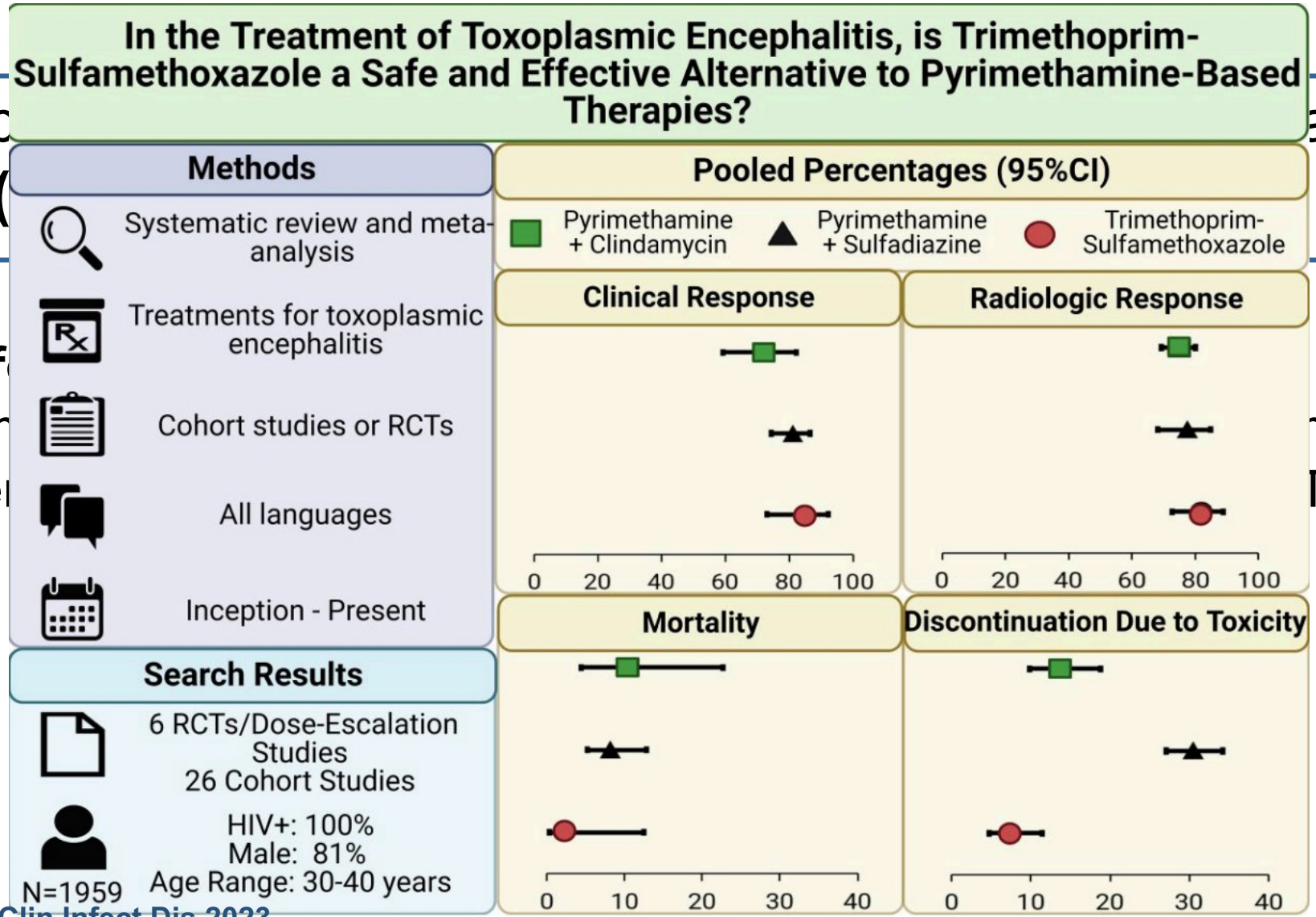
Toxoplasmosis

Trimethop acute infection (

Rationale f

Pyrimetham mendation

Given exper TMP/SMX exists



Source: Prosty C et al. Clin Infect Dis 2023

Pneumocystis Pneumonia

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Pneumocystis pneumonia

- Simplified indications for starting primary prophylaxis
- Intravenous pentamidine added as an alternative for prophylaxis

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Pneumocystis pneumonia

Simplified indications for starting primary prophylaxis

Recommendations for Preventing First Episode of *Pneumocystis* Pneumonia (Primary Prophylaxis)

Indications for Initiating Primary Prophylaxis

- CD4 count 100–200 cells/mm^3, if plasma HIV RNA level above detection limits **(AI),** *or*
- CD4 count <100 cells/mm^3, regardless of plasma HIV RNA level **(AIII)**
- **Note:** Patients who are receiving pyrimethamine-sulfadiazine for treatment or suppression of toxoplasmosis do not require additional prophylaxis for PCP **(AII).**

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Pneumocystis pneumonia

- Intravenous pentamidine added as an alternative for prophylaxis

Preferred Therapy

- TMP-SMX, 1 DS tablet PO daily **(AI),** *or*
- TMP-SMX, 1 SS tablet PO daily **(AI)**
- **Note:** TMP-SMX also confers protection against toxoplasmosis and some protection against many respiratory bacterial infections.

Alternative Therapy

- The following regimens can be used for people who are seropositive or seronegative for *Toxoplasma gondii*:
  - TMP-SMX 1 DS tablet PO three times weekly **(BI),** *or*
  - Dapsone[a] 50 mg PO daily with pyrimethamine 50 mg plus leucovorin 25 mg PO weekly **(BI),** *or*
  - Dapsone[a] 200 mg plus pyrimethamine 75 mg plus leucovorin 25 mg PO weekly **(BI),** *or*
  - Atovaquone 1,500 mg PO daily with food **(BI)**
- The following regimens should only be used in people who are seronegative for *Toxoplasma gondii*:
  - Dapsone[a] 100 mg PO daily or dapsone 50 mg PO twice a day **(BI)**, *or*
  - Aerosolized pentamidine 300 mg via Respirgard II nebulizer every month **(BI)**, *or*
  - Intravenous pentamidine 300 mg every 28 days **(CIII)**

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Pneumocystis pneumonia

- Intravenous pentamidine added as an alternative for prophylaxis

Rationale:

- IV pentamidine has been studied in immunosuppressed people without HIV (limited data in people with HIV)
- Need negative pressure room to administer aerosolized pentamidine
- Pyrimethamine expensive and availability limited
- Atovaquone bioavailability varies (also more expensive, taste not preferred)

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Candidiasis

2 New Agents Added for the Treatment of Candidiasis

Ibrexafungerp added for treatment of vulvovaginal candidiasis

Oteseconazole added for the treatment of recurrent vulvovaginal candidiasis

- No data in people with HIV
- Can we extrapolate to other uses – ie esophageal or oropharyngeal? – no recommendations, however

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Ibrexafungerp

- Oral b-glucan synthase inhibitor
- FDA approved in 2021 after phase 2 and 3 clinical trials for uncomplicated vulvovaginal candidiasis
- For uncomplicated vulvovaginal candidiasis:
  - Ibrexafungerp 300 mg PO twice daily for 1 day **(BI)**

Oteseconazole

- New tetrazole antifungal
- FDA approved in 2022 for recurrent vulvovaginal candidiasis
- For severe or recurrent vulvovaginal candidiasis:
  - Oteseconazole 600 mg PO at Day 1, 450 mg at Day 2, followed by once weekly 150 mg dosing starting at Day 14 for 11 weeks **(AI)** (for those who are not of reproductive potential)

Bacterial Enteric Infections

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Bacterial Enteric Infections

- Updated information on antimicrobial resistance among bacterial enteric pathogens.
- Updated recommended regimens for empiric therapy pending susceptibility results, including a recommendation to consider empiric carbapenem therapy in people with advanced HIV and severe diarrhea where campylobacter bacteremia is suspected.

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Bacterial Enteric Infections

Updated information on antimicrobial resistance among bacterial enteric pathogens

- Antimicrobial prophylaxis to prevent bacterial enteric illness **is not routinely recommended,** including for travelers **(AIII)**
- Because of toxicity associated with fluoroquinolone use (e.g., CDI, tendinitis) and increasing rates of antimicrobial resistance among enteric bacterial pathogens outside of the United States, routine use of fluoroquinolones for prophylaxis is discouraged **(AIII)**

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Bacterial Enteric Infections - Empiric

Updated recommended regimens for empiric therapy pending susceptibility results, including a recommendation to consider empiric carbapenem therapy in people with advanced HIV and severe diarrhea where campylobacter bacteremia is suspected

Empiric Treatment of Bacterial Enteric Infections (Pending Diagnostic Studies and Antimicrobial Resistance Testing)

For People With HIV and CD4 >500 cells/mm^3, With 1–2 Days of Loose Stools Without Fever or Blood

- Oral hydration; no further work-up and no treatment is needed.

For People With HIV and CD4 Count 200–500 cells/mm^3, With Diarrhea Severe Enough to Compromise Quality of Life or Ability to Work

- Azithromycin 500 mg PO daily for 5 days **(BIII)**, *or*
- Ciprofloxacin 500–750 mg PO every 12 hours for 5 days **(BIII)**

For People With HIV and Severe Disease (e.g., people with CD4 count <200 cells/mm^3 or concomitant AIDS-defining illnesses), With Clinically Severe Diarrhea (≥6 liquid stools/day or bloody stool and/or accompanying fever or chills)

- Hospitalization for inpatient diagnostic evaluation and IV antibiotics
- Ceftriaxone 1–2 g IV every 24 hours **(BIII)**[a] until antimicrobial susceptibility is available, then treatment can be changed based on sensitivity results.
  - If *Campylobacter* or *Shigella* bacteremia is suspected, a carbapenem is preferred for empiric therapy **(BIII).**

Increase in XDR Shigella

April 5, 2024

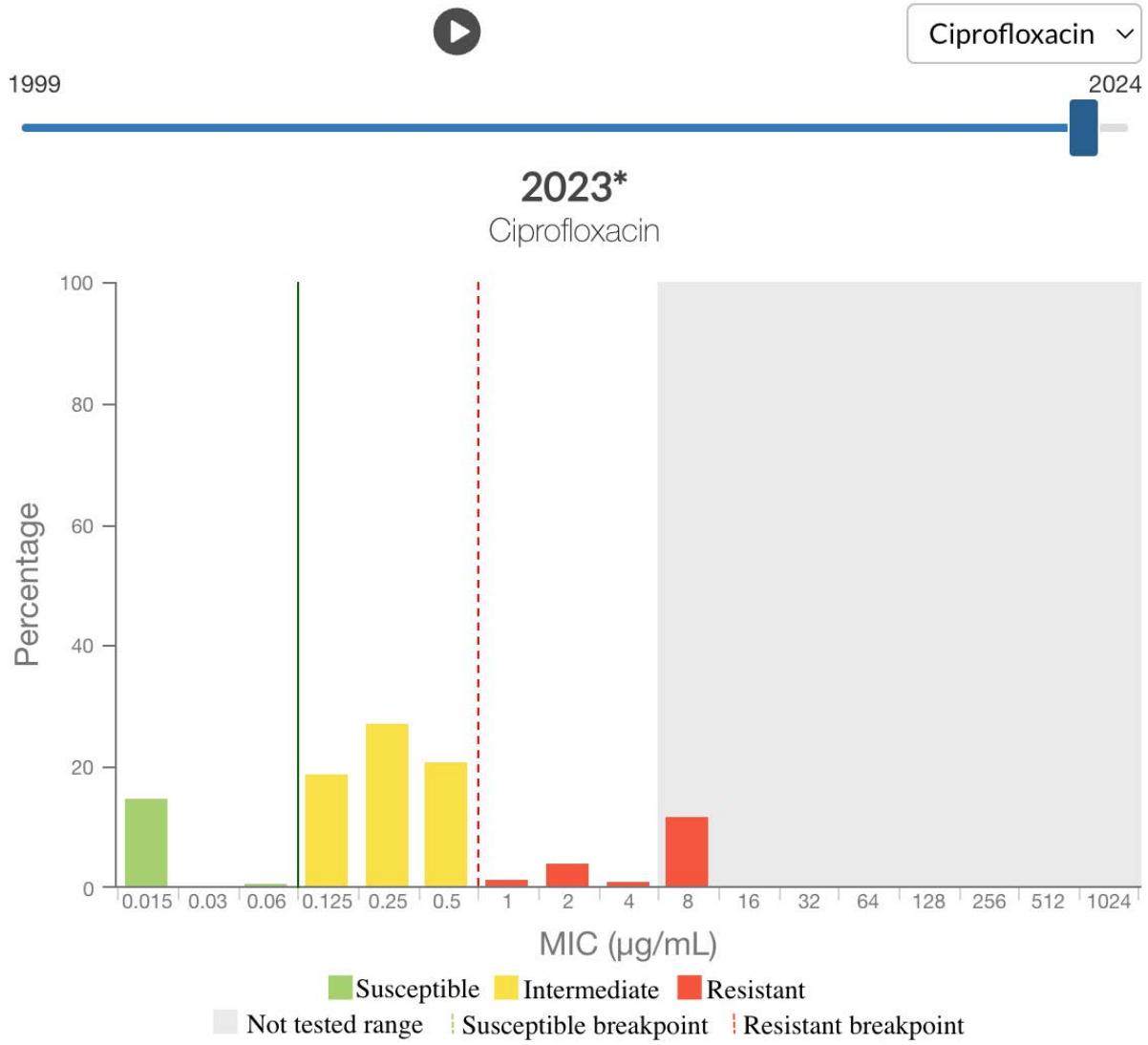
Suspected Local Transmission of Extensively Drug-Resistant (XDR) Shigellosis in King County

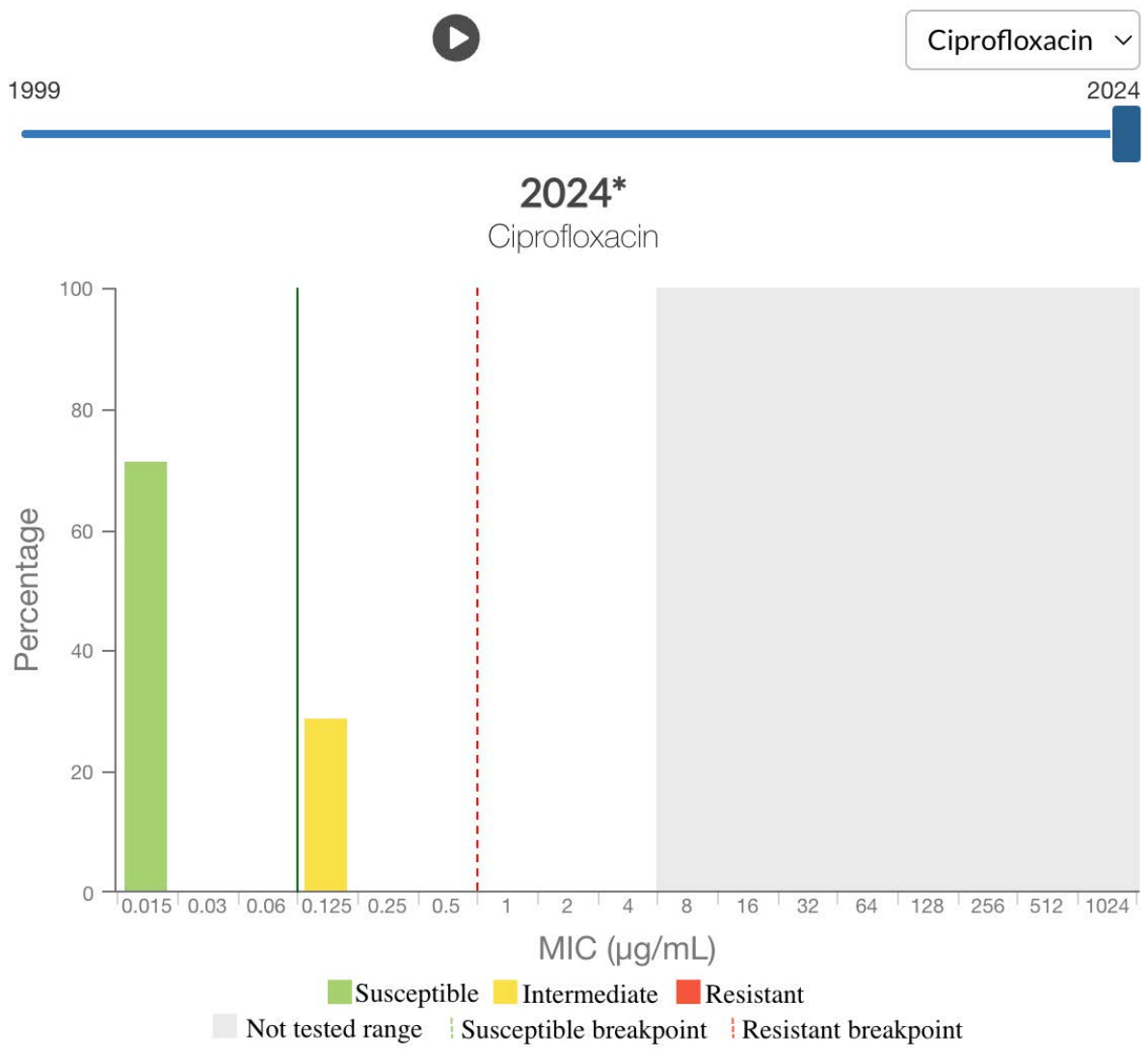
Actions requested

- Be aware of four cases of extensively drug-resistant (XDR) shigellosis detected in King County during 2023–2024 with suspected local transmission.
- Consider *Shigella* infection in patients with acute diarrhea, especially among people with higher risk for *Shigella* infection, including:
  - People experiencing homelessness or unstable housing;
  - International travelers;
  - Immunocompromised persons;
  - People living with HIV;
  - Men who have sex with men (MSM);
  - Young children

Source: https://kingcounty.gov/en/dept/dph/health-safety/disease-illness/health-advisories/2024/april-5

Shigella Antimicrobial Susceptibility





Source: https://wwwn.cdc.gov/narmsnow/

Bacterial Enteric Infections - Shigella

Updated recommended regimens for empiric therapy pending susceptibility results, including a recommendation to **consider empiric carbapenem therapy** in people with advanced HIV and severe diarrhea where campylobacter bacteremia is suspected

Treating Shigellosis

In Severely Ill Patients Requiring Empiric Parenteral Therapy While Awaiting Susceptibility

- Initiate a carbapenem until antimicrobial susceptibilities are available **(BIII).**

Preferred Therapy (If Susceptible)

- Ciprofloxacin 500–750 mg PO (or 400 mg IV) every 12 hours if MIC <0.12 µg/mL for 5 to 10 days **(AIII)**

Alternative Therapy (If Susceptible)

- Levofloxacin 750 mg (PO or IV) every 24 hours if MIC <0.12 ug/mL for 5 to 10 days **(BIII),** *or*
- Trimethoprim 160 mg/sulfamethoxazole 800 mg PO or IV every 12 hours for 5 to 7 days **(BIII),** *or*
  - Note: TMP-SMX **is not recommended** for bacteremia.
- Azithromycin 500 mg PO daily for 5 days **(BIII)**
  - Note: Azithromycin **is not recommended** for bacteremia **(AIII)**
- Ceftriaxone 1–2 g IV every 24 hours **(BIII)**

Duration of Therapy

- Gastroenteritis: 5–7 days **(AIII)** (except ciprofloxacin [5 to 10 days] and azithromycin [5 days])
  - 7–10 days of therapy may be reasonable in patients who are severely immunosuppressed with poor clinical response to antibiotics.
- Bacteremia: ≥14 days **(BIII)**
- Recurrent infections: up to 6 weeks **(BIII)**

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Mycobacterium Avium Complex

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MAC

Updated information to prioritize the initiation of effective antiretroviral therapy and to refrain from primary prophylaxis for *Mycobacterium avium* Complex (MAC) except for people with HIV who are not receiving antiretroviral therapy (ART), remain viremic on ART, or have no options for a fully suppressive ART regimen.

Preventing First Episode of Disseminated MAC Disease (Primary Prophylaxis)

- Primary prophylaxis **is not recommended** for adults and adolescents who immediately initiate ART **(AII).**

Indications for Primary Prophylaxis

- CD4 count <50 cells/mm^3 **AND** not receiving ART or remains viremic on ART or has no options for a fully suppressive ART regimen **(AI)**
- Before primary prophylaxis is initiated, disseminated MAC disease should be ruled out by clinical assessment, and if appropriate, by obtaining a blood culture for MAC **(AI).** If blood culture is obtained, prophylaxis should be delayed until results are available to avoid exposing patients to monotherapy and the attendant risk of drug resistance **(AI).**

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Updates Coming Soon

- Histoplasmosis
- Cryptococcosis
- Coccidioidomycosis
- Community acquired pneumonia

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Take Home Points

- TMP/SMX is a preferred regimen for toxoplasmosis
- Intravenous pentamidine added as an alternative for PCP prophylaxis
- New antifungals available for treatment of vulvovaginal candidiasis (ibrexafungerp and oteseconazole)
- Empiric carbapenem now recommended for severe shigella infection while susceptibilities pending due to increasing antimicrobial resistance
- MAC primary prophylaxis not indicated in people initiating ART

Questions?

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