

# Behind Closed Doors: CDI, STI, & HIV

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*The Alabama Society of Health System Pharmacists*

*Annual Clinical Meeting*

*November 5, 2021*

# Disclosures

These individuals have *nothing to disclose* concerning financial or personal relationships with commercial entities (or their competitors) that may be referenced in this presentation:

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# Objectives

- Review recently updated *Clostridioides difficile* treatment guidelines
  - Recognize medication changes to the treatment of gonorrhea and chlamydia
  - Discuss recent updates in HIV management
-

# *Clostridioides difficile* Infection

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# Introduction



## Epidemiology

- Between 2001 and 2012 rates of infection are increasing
  - 43% increase in Clostridioides difficile (C. diff) infection (CDI)
  - 188% increase in recurrent C. diff infection (rCDI)
- > 450,000 cases occur annually in the US
  - Associated with ~ 14,000 deaths
- 225,000 cases occur in hospitalized patients
  - Most common healthcare-associated infection in the US
- Costs the healthcare system ~ \$1 billion each year

## Risk Factors

- Initial infection
  - Antibiotic therapy
  - Previous hospitalization
  - Immunosuppression
  - Advanced age (> 65 years)
  - Acid suppressing therapy
  - Chronic renal disease
  - Chronic hepatic disease
  - Malnutrition
- Recurrent infection
  - Recent antibiotic exposure
  - Advanced age (> 65 years)
  - Acid suppressing therapy



# Characteristics of Recurrent CDI

- CDI is associated with a 15% - 25% rate of recurrence
- After first CDI episode, the rate of recurrence increases
- rCDI is associated with higher rates of:
  - Cost
    - Adjunctive / investigational therapies
  - Hospitalization
    - 2.5-fold higher rate of hospital admission
    - 8 day longer length of stay
  - Morbidity
    - Significant impact on quality of life
  - Mortality
    - 33% higher than those without rCDI



# CDI Guideline 2021 Updates: So...what's the *diff*?

- May 18
    - ACG Clinical Guidelines: Prevention, Diagnosis, and Treatment of *Clostridioides difficile* Infections
  - June 14
    - Clinical Practice Guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 Focused Update Guidelines on Management of *Clostridioides difficile* Infection in Adults
  - October 19
    - European Society of Clinical Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for *Clostridioides difficile* infection in adults
-

# CDI Episode: Initial (Non-severe)

## ACG

- Preferred: vancomycin (strong/low) or fidaxomicin (strong/moderate)
- Alternative: metronidazole (low risk patients)

## IDSA/SHEA

- Preferred: fidaxomicin (Conditional/moderate)
- Alternative: vancomycin (metronidazole if other agents unavailable)

## ESCMID

- Preferred: fidaxomicin (strong/moderate)
- Alternative:
  - Fidaxomicin based on risk stratification
  - Vancomycin when above is not available or feasible
  - Metronidazole when above options not available or feasible

## WWJD (What would Jonathan do?)

- Preferred: fidaxomicin based on risk stratification or vancomycin
- Alternative: vancomycin



# Risk Stratification Tool for Fidaxomicin

Age > 65 years plus one of the following risk factors:

- Healthcare-associated CDI
- Prior hospitalization in the previous three months
- Use of concomitant antibiotics
- Proton pump inhibitor (PPI) therapy *plus* a prior CDI episode

\*The risk of recurrence is assumed to be higher when more risk factors are present

# CDI Episode: Initial (Severe)

## ACG

- Preferred: vancomycin (strong/low) OR fidaxomicin (conditional/very low)

## ESCMID

- Preferred: vancomycin or fidaxomicin (Good practice statement)

## IDSA/SHEA

- Preferred: fidaxomicin (conditional/moderate)
- Alternative: vancomycin

## WWJD

- Preferred: vancomycin
- Alternative: fidaxomicin

# CDI Episode: Fulminant (Severe-complicated)

## ACG

- High dose vancomycin + IV metronidazole (conditional/very low)
- Add vancomycin enema if ileus present (conditional/very low)
- Alternative: fecal microbiota transplantation (FMT) (strong/low)

## IDSA/SHEA

- High dose vancomycin + IV metronidazole
- Add vancomycin enema if ileus present

## ESCMID

- Vancomycin or fidaxomicin (Good practice statement)
- Add IV tigecycline when patient is deteriorating or progressing to severe-complicated CDI

## WWJD

- High dose vancomycin + IV metronidazole
- Add vancomycin enema if ileus is present

# CDI Episode: **First Recurrence**

## ACG

- Vancomycin tapered or pulsed regimen (strong/very low) OR fidaxomicin - if initially treated with an alternative (strong/moderate)

## IDSA/SHEA

- Preferred: fidaxomicin standard or extended-pulsed regimen (conditional/low)
- Alternative:
  - Vancomycin tapered or pulsed
  - Vancomycin standard regimen (if initially treated with metronidazole)

## ESCMID

- Preferred: Fidaxomicin - if initially treated with an alternative (strong/low)
- Alternative:
  - Fidaxomicin (good practice) OR vancomycin (weak/moderate) + bezlotoxumab
  - Vancomycin tapered or pulsed when fidaxomicin or bezlotoxumab not available (weak/very low)

## WWJD

- Preferred: fidaxomicin
- Alternative:
  - Vancomycin tapered or pulsed
  - Vancomycin +/- bezlotoxumab

# CDI Episode: Subsequent recurrence

## ACG

- FMT (strong/moderate)

## IDSA/SHEA

- Preferred: fidaxomicin standard or extended-pulsed regimen (conditional/low)
- Alternative:
  - Vancomycin tapered or pulsed
  - Vancomycin standard regimen followed by rifaximin
  - FMT

## ESCMID

- FMT after pre-treatment with fidaxomicin OR vancomycin (weak/moderate)
- Fidaxomicin OR vancomycin + bezlotoxumab (weak/low)

## WWJD

- FMT after pre-treatment with fidaxomicin OR vancomycin

# Adjunctive Therapy: Bezlotoxumab

## ACG

- Consider in those who are at high risk of recurrence (conditional/moderate)

## ESCMID

- Patients with increased risk of recurrence when fidaxomicin is not an option (weak/moderate)

## IDSA/SHEA

- Patients with rCDI within the last 6 months - with logistical issues (conditional/very low)
- Patients with an initial CDI episode and at least one risk factor for recurrence - without logistical issues
  - Age  $\geq$  65 years
  - Immunocompromised host
  - Severe CDI on presentation

## WWJD

- Patients with rCDI or those at increased risk of recurrence when vancomycin used
  - Age  $\geq$  65 years
  - History of CDI in previous 6 months
  - Immunocompromised
  - Severe CDI on presentation
  - CDI caused by strains that are associated with poorer outcomes (027, 078, 244)

# Key Considerations for Implementation

- Guidelines place high priority on the prevention of recurrence
- There is still uncertainty as to the best way to prevent recurrence
- Cost of treatment remains a significant barrier
  - Acquisition cost
  - Cost to the patient
  - Insurance coverage
  - Cost-effectiveness analysis
- Level of evidence regarding recommendations
- Feasibility

# Sexually Transmitted Infections

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**Program Director: Jonathan Edwards, PharmD, BCPS, BCGP, BCIDP**

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# What's New?

## Treatment updates for:

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis*
- *Trichomonas vaginalis*
- Pelvic Inflammatory Disease (PID)
- Bacterial vaginosis

## Management of *Mycoplasma genitalium*

## Human Papillomavirus (HPV) vaccine recommendations

THE  
**STATE OF STDs**  
IN THE  
**UNITED STATES,**  
2019

STDs increased for the  
6th year, reaching a  
new all-time high



**1.8 million**  
CASES OF CHLAMYDIA  
19% increase since 2015



**616,392**  
CASES OF GONORRHEA  
56% increase since 2015



**129,813**  
CASES OF SYPHILIS  
74% increase since 2015



**1,870**  
CASES OF SYPHILIS  
AMONG NEWBORNS  
279% increase since 2015

LEARN MORE AT: [www.cdc.gov/std/](http://www.cdc.gov/std/)

LEFT UNTREATED, STDS CAN CAUSE:



INCREASED RISK OF GIVING  
OR GETTING HIV

LONG-TERM  
PELVIC/ABDOMINAL PAIN

INABILITY TO GET PREGNANT OR  
PREGNANCY COMPLICATIONS



# Gonococcal Infections

- Second most reported bacterial communicable disease
- Can be complicated by resistance to antimicrobials
  - During 2006-2011, minimum concentrations of cefixime needed to inhibit in vitro growth of strains circulating in the United States increased
  - Resistance to azithromycin is also emerging
- Dual therapy for gonococcal infection with ceftriaxone and azithromycin recommended previously could have mitigated emergence of reduced susceptibility to ceftriaxone in *N.gonorrhoeae*

# Gonococcal Treatment

If chlamydial infection has been excluded:

- Ceftriaxone 500mg IM\* in a single dose

If chlamydial infection has NOT been excluded:

- Ceftriaxone 500mg IM\* in a single dose + doxycycline 100mg PO BID x 7 days

Alternative:

- Gentamicin 240mg IM in a single dose + Azithromycin 2g PO single dose OR  
Cefixime 800mg PO single dose

\*1g IM dose should be used for  $\geq 150$ kg

# Chlamydial Infections

- Most frequently reported bacterial infectious disease in the US
- Site of infection matters

## Doxycycline

- Urogenital
- Rectal
- Oropharyngeal

## Azithromycin

- Urogenital

# Chlamydial Infections

## First-Line Therapy

- Doxycycline 100mg BID PO x 7 days

## Alternative

- Azithromycin 1g PO single dose
- Levofloxacin 500mg PO QD x 7 days

## Pregnancy

- Azithromycin 1g PO single dose (preferred)
- Amoxicillin 500mg PO TID x 7 days

# Trichomoniasis

- Most prevalent nonviral STI worldwide
- Treatment is determined by patient specific factors
- Oral therapy matters!

## Women

- Metronidazole  
500mg PO BID  
x 7 days

## Men

- Metronidazole  
2g PO single  
dose

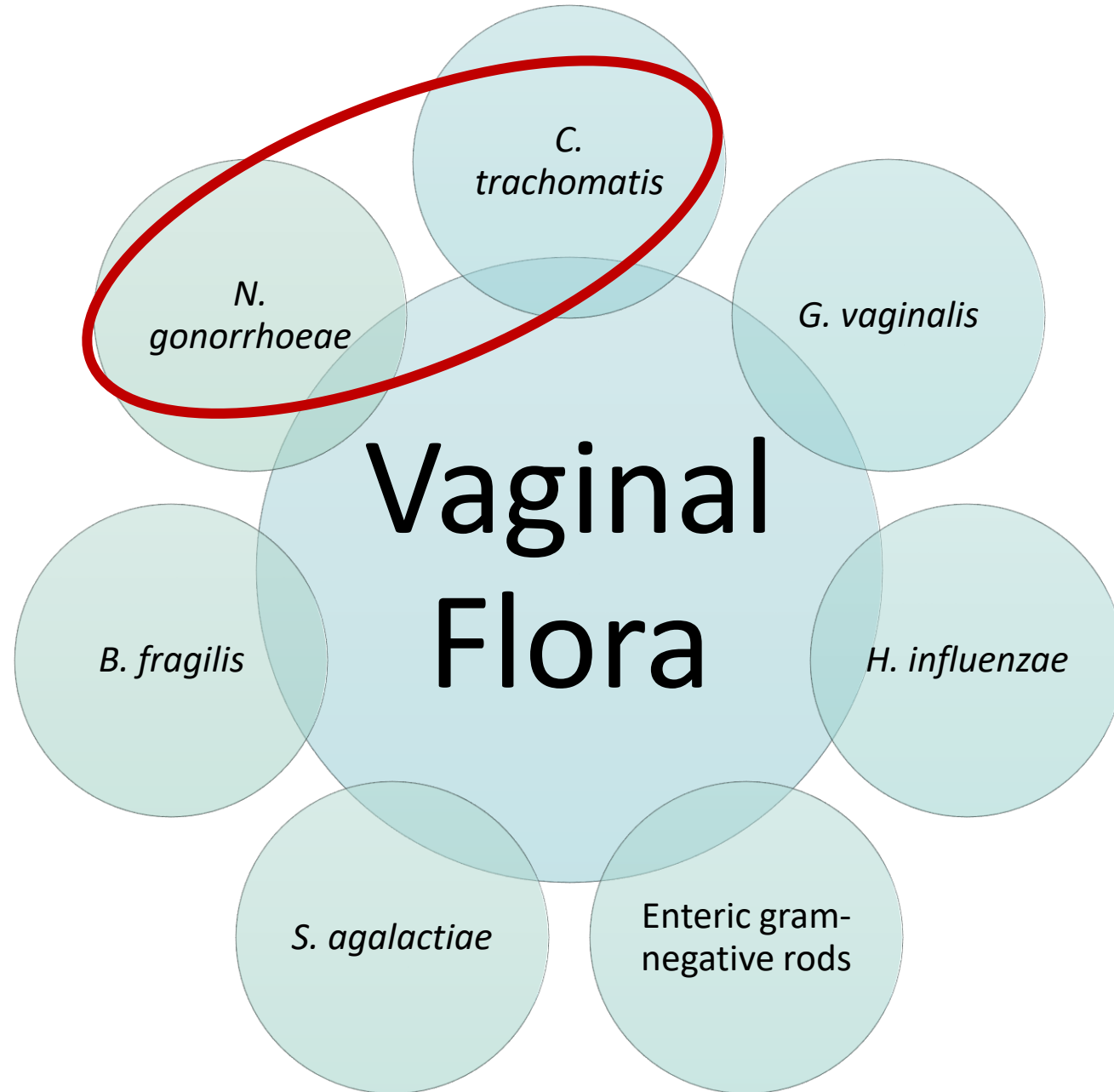
## Alternative

- Tinidazole 2g  
PO single dose

## Allergic

- Desensitization

# Pelvic Inflammatory Disease (PID)





# Pelvic Inflammatory Disease (PID)

## Parenteral Regimens

- Ceftriaxone 1gm QD + doxycycline 100mg BID + metronidazole 500mg BID
- Cefotetan 2gm BID + doxycycline 100mg BID
- Cefoxitin 2gm QID + doxycycline 100mg BID

## Intramuscular/Oral Therapy

- Ceftriaxone 500mg IM single dose + doxycycline 100mg BID and metronidazole 500mg BID x 14 days
- Cefoxitin 2gm IM single dose + probenecid 1gm PO single dose (administered concurrently with cefoxitin) + doxycycline 100mg BID and metronidazole 500mg BID x 14 days
- Parenteral 3rd generation cephalosporin + doxycycline 100mg BID and metronidazole 500mg BID x 14 days

## Alternative Regimens

- Ampicillin-sulbactam 3gm IV QID + doxycycline 100mg IV BID
- Clindamycin 900mg IV TID + gentamicin 2mg/kg IV or IM then 1.5mg/kg TID (can also use 3-5mg/kg QD)

# Bacterial Vaginosis

- Highly prevalent condition and the most common cause of vaginal discharge
- Treatment is recommended to those with symptoms

Metronidazole  
500mg BID PO x 7  
days

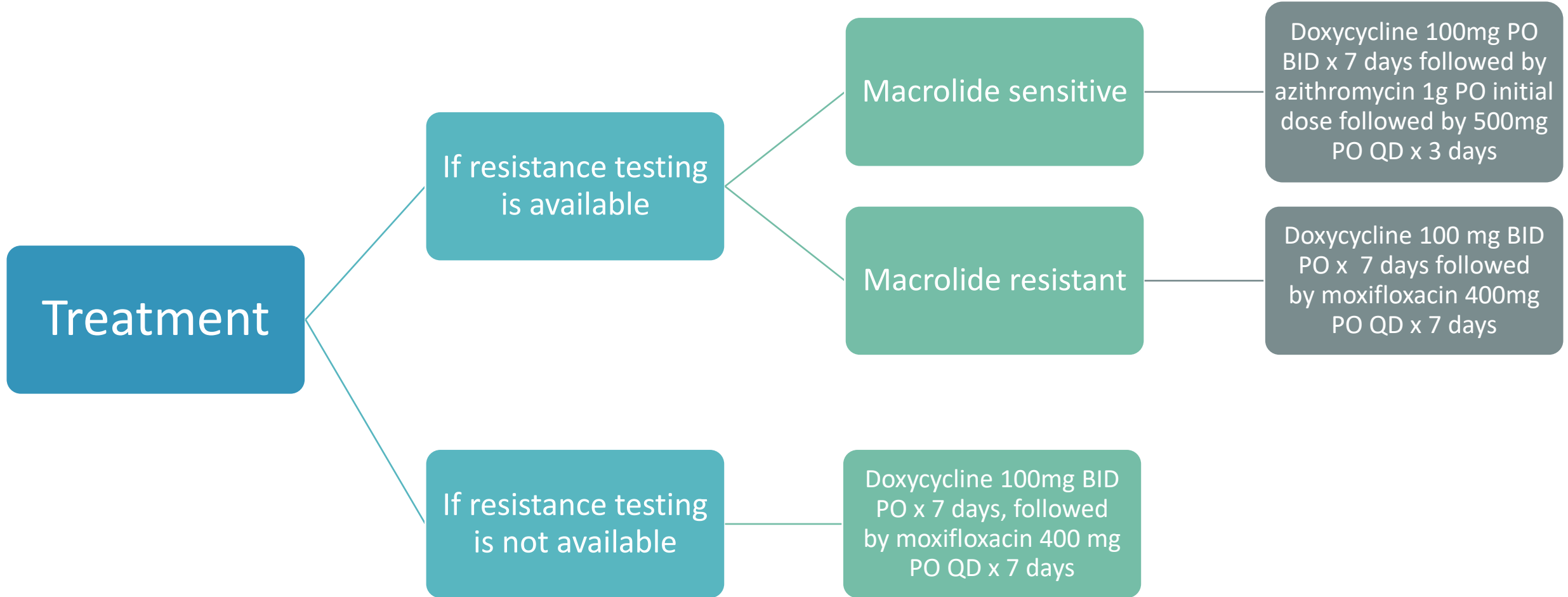
Metronidazole gel  
0.75%  
intravaginally once  
daily x 5 days

Clindamycin cream  
2% intravaginally at  
bedtime x 7 days

# *Mycoplasma genitalium*

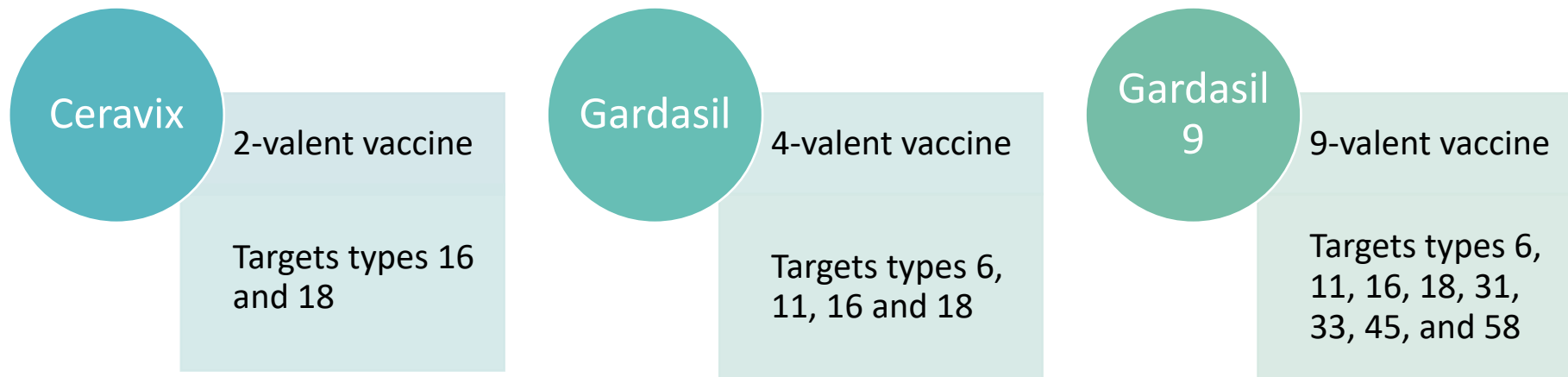
- Associated with cervicitis, PID, pre-term delivery, spontaneous abortion, and infertility
- *M. genitalium* lacks a cell wall – antibiotics that target cell-wall biosynthesis are **ineffective**
- Resistance to azithromycin has rapidly increased
- Resistance-guided therapy is recommended for treatment due to cure rates > 90%

# *Mycoplasma genitalium*



# Human Papillomavirus Infection

- Three HPV vaccines are licensed in the US: Cervix, Gardasil, Gardasil 9
- HPV types 16 and 18 account for 66% of all cervical cancers



# Human Immunodeficiency Virus

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# Guideline Updates

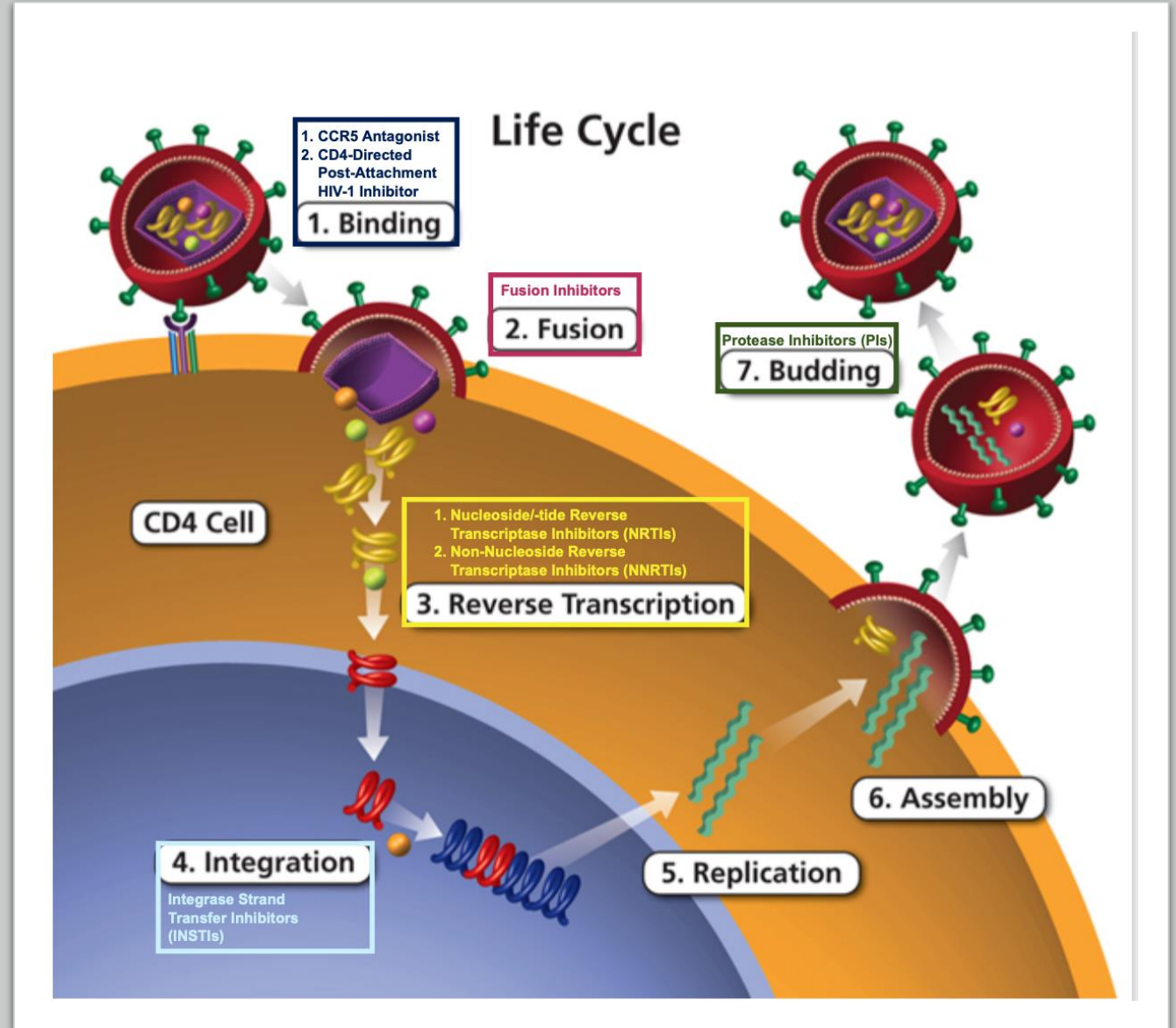
- **Department of Health and Human Services**

- What to start
- Optimizing antiretroviral (ARV) therapy in the setting of viral suppression
- Tuberculosis/HIV coinfection
- Virologic failure
- Hepatitis C Virus/HIV coinfection
- Poor CD4 recovery and persistent inflammation
- Adolescents and young adults with HIV
- Women with HIV
- Substance use disorder and HIV
- Cost considerations and antiretroviral therapy

- **World Health Organization**

- Prevention
- Advanced HIV disease
- Treatment monitoring
- HIV Testing
- Palliative care & pain management

# Review: HIV Life Cycle, Antiretroviral Mechanism





# What to Start: Initial Combination Regimens for the Antiretroviral Naïve Patient

Initial Regimens for <i>Most</i> People with HIV	
INSTI plus 2 NRTIs	BIC/TAF/FTC DTG/ABC*/3TC DTG plus (TAF or TDF) plus (FTC or 3TC)
INSTI plus 1 NRTI	DTG/3TC**
<i>Select</i> Initial Regimens in <i>Certain Clinical Situations</i>	
INSTI plus 2 NRTIs	<b>RAL</b> plus (TAF or TDF) plus (FTC or 3TC)
Regimen to consider when ABC, TAF, & TDF cannot be used or are not optimal	DRV/r plus <b>RAL</b> twice a day***

INSTI: Integrase Strand Transfer Inhibitor, NRTI: Non-nucleoside Reverse-Transcriptase Inhibitor, BIC: bictegravir, TAF: tenofovir alafenamide, FTC: emtricitabine, DTG: dolutegravir, ABC: abacavir, 3TC: lamivudine, TDF: tenofovir disoproxil fumarate, RAL: raltegravir, DRV: darunavir

\*If HLA-B\*5701 negative

\*\*Not recommended for individuals with HIV RN >500,000 copies/mL, HBV co-infection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

\*\*\*If HIV RNA <100,000 copies/mL and CD4 count >200 cells/mm<sup>3</sup>

# What to Start:

## Weight Gain & Antiretroviral Therapy

Data from studies showing increased weight gain with select antiretroviral medications – *clinical significance still unknown*

Sax et al. (September 2020)

- Pooled analysis of weight gain in 8 RCTs of treatment-naïve people with HIV
- **Baseline demographic factors:** ↓ CD4 cell count, ↑ HIV type 1 RNA, no injection drug use, female sex, black race
- INSTIs associated with more weight gain than protease inhibitors or NNRTIs
  - **INSTIs:** Dolutegravir and bictegravir > elvitegravir/cobicistat
  - **NNRTIs:** Rilpivirine > efavirenz
  - **NRTIs:** Tenofovir alafenamide > tenofovir disoproxil fumarate, abacavir, zidovudine

# Optimizing Antiretroviral Therapy in the Setting of Viral Suppression: **CABENUVA**



**FDA Approved January 21, 2021**

- Cabotegravir 200 mg/mL + rilpivirine 300 mg/mL
- **Extended-release injectable** suspensions
- Indicated for HIV-1 infection in adults
  - Virologically suppressed
  - Currently on a stable antiretroviral regimen
  - No history of treatment failure
  - No known/suspected resistance to either agent
- Dosing
  - Requires oral lead-in dosing
  - Initially, cabotegravir 600 mg + rilpivirine 900 mg IM (*one-time dose*)
  - Cabotegravir 400 mg + rilpivirine 600 mg IM every month thereafter

CABENUVA package insert. Research Triangle Park, NC: ViiV Healthcare; 2021 January.

Image: <https://www.businesswire.com/news/home/20210121005951/en/ViiV-Healthcare-announces-FDA-approval-of-Cabenuva-cabotegravir-rilpivirine-the-first-and-only-complete-long-acting-regimen-for-HIV-treatment>

# Optimizing Antiretroviral Therapy in the Setting of Viral Suppression: CABENUVA

## Drug Interactions

Substrate of UGT 1A1 and CYP 3A4

Inducers will decrease the concentration of CABENUVA, rendering it less effective

Drugs with a known risk of Torsades de Pointes

Antiarrhythmic medications (ex. amiodarone),  
Macrolide antibiotics (ex. Azithromycin)

## Adverse Drug Events

- Injection site reactions
- Pyrexia
- Fatigue
- Headache
- Musculoskeletal pain
- Nausea
- Sleep disorders
- Dizziness
- Rash

# CABENUVA: Missed Dose

- Planned missed injections
  - If miss dose by > 7 days
    - Take daily oral therapy to replace **up to 2 consecutive monthly** injection visits
    - First dose of oral therapy should be taken ~ 1 month after the last injection dose of CABENUVA & continued until the day injection dosing is restarted
    - Oral regimen: cabotegravir 30 mg (VOCABRIA) and rilpivirine 25 mg (EDURANT) daily
- Unplanned missed injections
  - If monthly injections are missed & oral therapy is not taken in the interim
    - **Less than or equal to 2 months:** resume cabotegravir 400 mg and rilpivirine 600 mg IM monthly injections ASAP
    - **Greater than 2 months:** re-initiate with cabotegravir 600 mg and rilpivirine 900 mg IM injections then continue with cabotegravir 400 mg and rilpivirine 600 mg IM injections thereafter

# Tuberculosis/HIV Coinfection

TB Regimen	Antiretroviral Therapy (ART) Regimen
Daily isoniazid (alone for 6 or 9 months)	Any ART regimen can be used
<b>Once-weekly isoniazid plus rifapentin x 3 months</b>	<p>Efavirenz 600 mg once daily or raltegravir 400 mg twice daily (in combination with either abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine)</p> <p><b>Dolutegravir (DTG) 50 mg once daily may be used for those in whom once-daily DTG is appropriate*</b></p>
<b>Once-daily isoniazid &amp; rifapentine x 1 month</b>	<b>Efavirenz 600 mg once daily (in combination with either abacavir/lamivudine or tenofovir disoproxil fumarate/emtricitabine)</b>

*\*NOT recommended for patients who require twice-daily DTG therapy (e.g., those with certain INSTI-associated resistance substitutions or clinically suspected INSTI resistance)*

# Virologic Failure

- **Virologic failure:** the inability to achieve or maintain suppression of viral replication to HIV RNA level <200 copies/mL
- "A new regimen can include **two fully active drugs** if at least one with a high resistance barrier is included (e.g., dolutegravir or boosted darunavir)"
- Fostemsavir (**RUKOBIA**):  
gp120-directed attachment inhibitor



# Prevention

## **Dapivirine vaginal ring**

- Non-nucleoside reverse transcriptase inhibitor
- Monthly administration
- Shown to reduce HIV risk by 39% (HOPE Trial)
- Eastern and Southern Africa primary sites seeking urgent approval
- Under review by the United States FDA



# Advanced HIV Disease: Histoplasmosis

## Overview of clinical management of histoplasmosis

Induction Therapy

Liposomal amphotericin B 3 mg/kg x 2 weeks  
(preferred)

Deoxycholate amphotericin B 0.7-1.0 mg/kg x 2 weeks

Maintenance Therapy

Itraconazole 200 mg twice daily x 12 months

Timing of Antiretroviral Therapy

Antiretroviral therapy should be **initiated as soon as possible** among people with disseminated histoplasmosis for whom central nervous system involvement is not suspected or proven



# HIV- Update Recap

- Dolutegravir recommended option for people of childbearing potential
  - Raltegravir recommended option in “certain clinical situations”
  - Weight gain associated with some INSTIs and TAF & certain populations (i.e., women, black race)
  - CABENUVA, an extended-release injectable option for virally suppressed patients
  - Recommended ART regimens for patients with TB/HIV coinfection
  - Virologic failure & RUKOBIA
  - Prevention & dapivirine vaginal ring
  - Recommendations for histoplasmosis treatment & ART
-

# Behind Closed Doors: CDI, STI, & HIV

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