What's New?
Highlights from the CDC 2021 STI Treatment Guidelines

Daniela E. DiMarco, MD, MPH

Assistant Professor of Medicine

University of Rochester Medical Center

NYS CEI Sexual Health Center of Excellence

CLINICAL EDUCATION INITIATIVE

NEW YORK STATE DEPARTMENT OF HEALTH AIDS INSTITUTE

Center for Community Practice

CLINICAL EDUCATION INITIATIVE

Objectives

1. Describe updated treatment recommendations for chlamydia, gonorrhea, trichomoniasis, and PID
2. Understand updated recommendations for testing and treatment of *M. genitalium*
3. Identify 3 risk factors associated with syphilis acquisition during pregnancy

CLINICAL EDUCATION INITIATIVE

Find the Guidelines Here:



https://www.cdc.gov/std/treatment-guidelines/

THE STATE OF STDs IN THE UNITED STATES, 2019

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

		NYS
1.8 million CASES OF CHLAMYDIA	19% increase since 2015	124,622 CASES OF CHLAMYDIA — 20% increase since 2015
616,392 CASES OF GONORRHEA	56% increase since 2015	40,901 CASES OF GONORRHEA — 60% increase since 2015
129,813 CASES OF SYPHILIS	74% increase since 2015	10,500 CASES OF SYPHILIS — 35% increase since 2015
1,870 CASES OF SYPHILIS AMONG NEWBORNS	279% increase since 2015	27 CASES OF SYPHILIS AMONG NEWBORNS — 125% increase since 2015

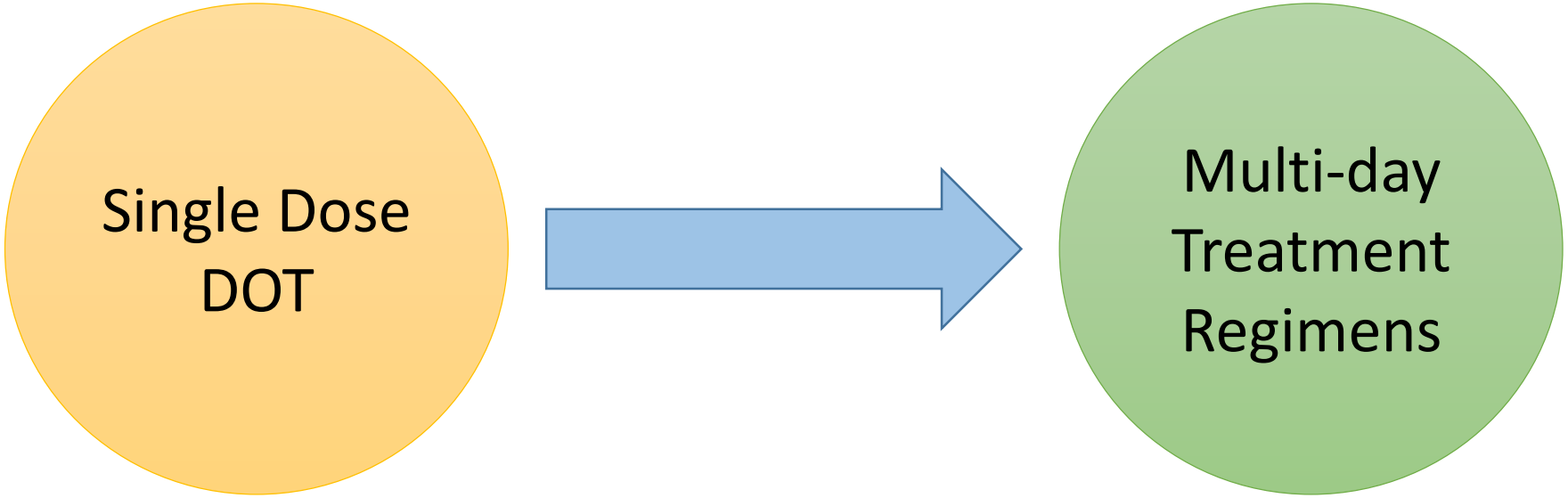
ANYONE WHO HAS SEX COULD GET AN STD, BUT SOME GROUPS ARE MORE AFFECTED

- YOUNG PEOPLE AGED 15-24
- GAY & BISEXUAL MEN
- PREGNANT PEOPLE
- RACIAL & ETHNIC MINORITY GROUPS

CDC

Paradigm Shift

- Goal to improve treatment efficacy



CLINICAL EDUCATION INITIATIVE

Big Picture - Policies, Plans, Guidelines, Guidance

- **New York State**
  - Shift to sexual health, reduction of stigma, health equity focus
  - Revised regulations (minor consent HPV vaccine, PrEP), EPT changes, PEP hotline, PEP via Pharmacies
- **US National**
  - CDC STI Treatment Guidelines (GC out 12/20, Full Guideline 7/22/21)
  - NASEM – STIs: Adopting a Sexual Health Paradigm (3/21/21)
  - HHS – First Ever National Strategic Plan (12/18/20)
  - CDC STI services during COVID (04/06/20, 05/13/20, 09/08/20)
  - CDC Recommendations for Providing Quality Sexual Health Services (1/6/20)

CLINICAL EDUCATION INITIATIVE

Chlamydia

STI

Sexually Transmitted Infections

National Strategic Plan

2021-2025

A. Chlamydia

BOX 3

CHLAMDYIA SNAPSHOT

- Treatable and curable
- Untreated chlamydia can lead to pelvic inflammatory disease (PID), which may cause infertility
- Screening recommended annually for sexually active females < age 25, females ≥ age 25 at increased risk, and MSM; screening in MSM should be based on anatomic site(s) of exposure



Epidemiological Facts

1,758,668 REPORTED CASES (2018)

1,808,703 (2019)

19% RATE INCREASE (2014–2018)

Rates increased among males, females, all geographic regions, and all racial/ethnic groups

80% OF CASES were reported from providers other than STD clinics

Populations Disproportionally Impacted

- Females of reproductive age
- Adolescents and young adults
- Adolescent racial/ethnic minorities

Consequences When Left Untreated

- PID
- Infertility
- Ectopic pregnancy
- Chronic pelvic pain
- Increased risk of HIV
- Epididymitis

Current Challenges

- Asymptomatic infections
- Lack of provider and public awareness about screening recommendations
- Limited resources to support screening
- Lack of an available vaccine

Sources: CDC[1], Workowski and Bolan[35], Jones et al.[66]

Chlamydia – 2021 CDC Guidelines

- Testing Updates:
  - CT rectal testing in men routinely with exposure
  - CT rectal testing in women using a shared decision making approach
    - Consider with exposure history
    - Consider in adolescent females - high rates

NOTE: Concomitant CT rectal infection with cervical infection is common, and not predicted by sexual activity

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Workowski KA et al. MMWR 2015. Jun 5;64(RR-03):1-137

CDC 2021 Treatment Updates

Doxycycline (Preferred) 

Azithromycin (Alternative) 

- Non-Pregnant Adolescents and Adults – all sites
  - First Line - Doxycycline 100 mg po bid x 7 days
    - Dispense on-site/in clinic, first dose DOT
  - Alternative Treatments:
    - Azithromycin 1 gram po x 1 dose, OR
    - Levofloxacin 500mg po daily x7 days
- Pregnancy
  - First Line - Azithromycin 1 gram po x 1 dose
  - Alternative – Amoxicillin 500mg po TID x7 days
- Ofloxacin/Erythromycin removed from alternatives

- Retest in 3 months (all)
- Test of cure at 4 weeks if pregnant
- Offer EPT for partners within 60 days of sx onset

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Workowski KA et al. MMWR 2015. Jun 5;64(RR-03):1-137

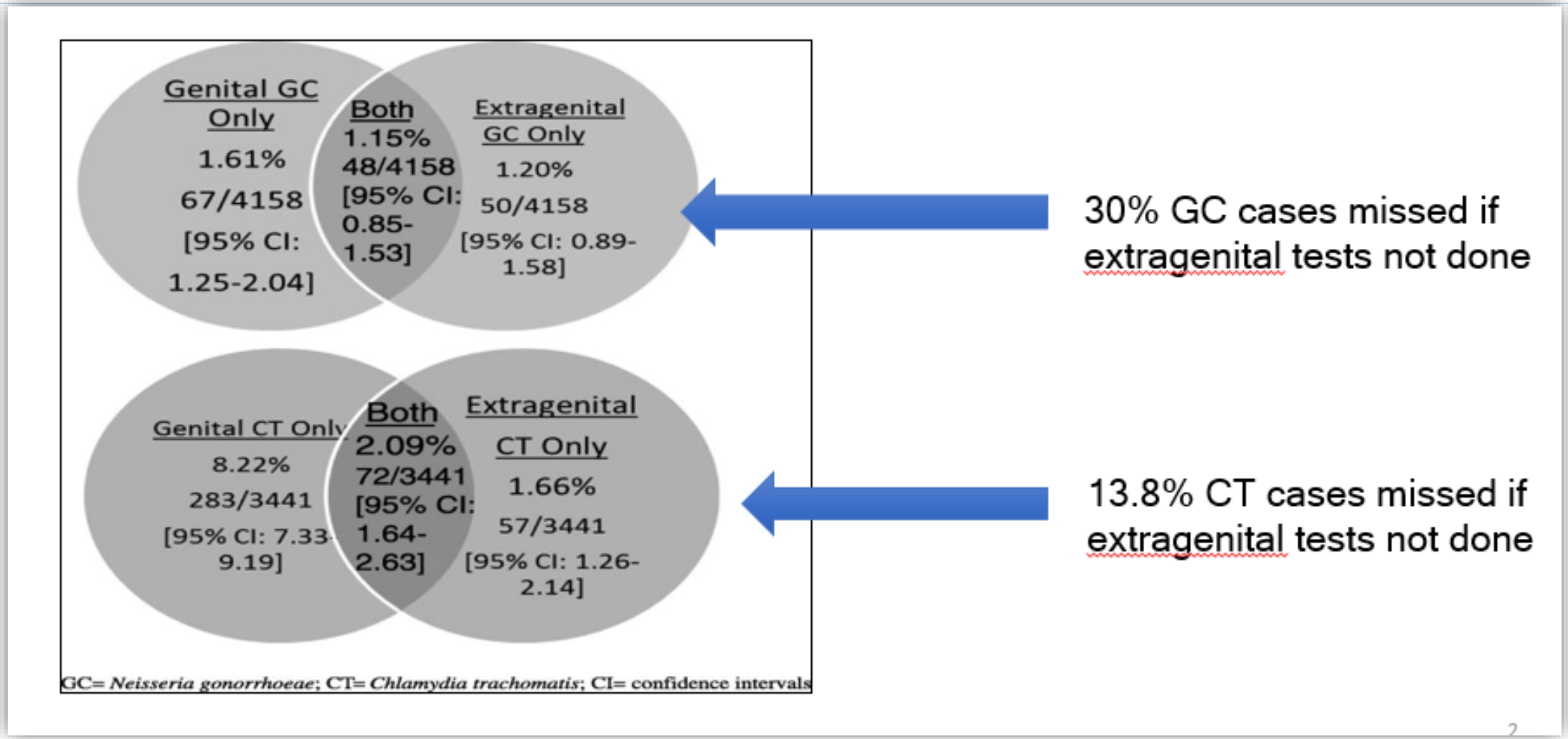


Figure 1 . Genital and extragenital GC (top) and CT (bottom) in women.

Neisseria gonorrhoeae and Chlamydia trachomatis Among Women Reporting Extragenital Exposures.

Trebach, Joshua; Chaulk, C; Page, Kathleen; Tuddenham, Susan; MD, MPH; Ghanem, Khalil; MD, PhD
Sexually Transmitted Diseases. 42(5):233-239, May 2015. DOI: 10.1097/OLQ.0000000000000248
© Copyright 2015 American Sexually Transmitted Diseases Association. Published by Lippincott Williams & Wilkins, Inc.

CLINICAL EDUCATION INITIATIVE

Chlamydia – Why demote Azithromycin now?

Treatment Effectiveness of Azithromycin and Doxycycline in Uncomplicated Rectal and Vaginal *Chlamydia trachomatis* Infections in Women: A Multicenter Observational Study (FemCure)

Nicole H T M Dukers-Muijrers ✉, Petra F G Wolffs, Henry De Vries, Hannelore M Götz, Titia Heijman, Sylvia Bruisten, Lisanne Eppings, Arjan Hogewoning, Mieke Steenbakkers, Mayk Lucchesi ... Show more

Clinical Infectious Diseases, Volume 69, Issue 11, 1 December 2
https://doi.org/10.1093/cid/ciz050

› Clin Infect Dis. 2021 Feb 19;ciab153. doi: 10.1093/cid/ciab153. Online ahead of print.

Doxycycline Versus Azithromycin for the Treatment of Rectal Chlamydia in Men Who Have Sex With Men: A Randomized Controlled Trial

Julia C Dombrowski [1 2], Michael R Wierzbicki [3], Lori M Newman [4], Jonathan A Powell [3], Ashley Miller [5], Dwyn Dithmer [2], Olusegun O Soge [6], Kenneth H Mayer [7 8]

Affiliations + expand

PMID: 33606009 DOI: 10.1093/cid/ciab153

CLINICAL EDUCATION INITIATIVE

Doxycycline Versus Azithromycin for the Treatment of Rectal Chlamydia in Men Who Have Sex With Men: A Randomized Controlled Trial

- RCT in MSM with CT+ rectal infection
- Doxycycline 100 bid x 7 days + azithromycin placebo
- Azithromycin 1000 mg x 1 dose + doxycyline placebo
- TOC at 2 weeks and 4 weeks

Results:

Doxy - 70/70 (**100%**) cured at 4 wks

Azithro - 48/65 (**74%**) cured at 4 wks

Dombrowski JC, et al. CID 2021

FemCure

- Prospective observational cohort study from the Netherlands of heterosexual cisgender women seeking routine care at sexual health clinics
- 416 women with CT + NAAT (vaginal or rectal)
  - Doxy 100mg BID x7d (rectal +)
  - Azithro 1g x1 (vaginal +)

  } Based on initial visit test
- Repeat vaginal and rectal testing at 0, 1, 2, 4, 6, 8, 10, and 12 weeks
- Outcome: Microbiologic cure at 4 weeks

NAAT (+) at Enrollment
Rectal and vaginal - 319
Rectal only - 22
Vaginal only - 75

Cure rates for **rectal** infections
Doxy - 126/132 (**91.0%**)
Azithro - 164/209 (78.5%)

Cure rates for **genital** infections
Doxy - 125/131 (95.4%)
Azithro - 246/263 (95.4%)

Dukers-Muijrers NHTM et al. CID 2019.

CLINICAL EDUCATION INITIATIVE

Gonorrhea

STI

Sexually Transmitted Infections

National Strategic Plan

2021-2025

B. Gonorrhea

BOX 4

GONORRHEA SNAPSHOT

- Treatable and curable
- Gonorrhea can lead to pelvic inflammatory disease (PID), which may cause infertility
- Screening recommended annually for sexually active females < age 25, females ≥ age 25 at increased risk, and MSM; screening in MSM should be based on anatomic site(s) of exposure



Epidemiological Facts

583,405 CASES
(2018)

616,392 (2019)

63% RATE INCREASE
(2014–2018)

137% rate increase among MSM

51% OF ALL ISOLATES
tested in 2018 were resistant to at least one antibiotic

Populations Disproportionally Impacted

- Females of reproductive age
- MSM
- Adolescent racial/ethnic minorities

Consequences When Left Untreated

- PID
- Infertility
- Ectopic pregnancy
- Chronic pelvic pain
- Increased risk of HIV
- Disseminated gonococcal infection
- Epididymitis

Current Challenges

- Antimicrobial resistance—gonorrhea has developed resistance to all but one class of antibiotics, and half of all infections are resistant to at least one antibiotic
- Lack of point-of-care diagnostics to test antibiotic susceptibility
- Asymptomatic infections
- Limited resources to support screening
- Lack of an available vaccine

Sources: CDC[1], Workowski and Bolan[35], Jones et al.[56]

NEW YORK STATE OF OPPORTUNITY. Department of Health

ANDREW M. CUOMO
Governor

HOWARD A. ZUCKER, M.D., J.D.
Commissioner

LISA J. PINO, M.A., J.D.
Executive Deputy Commissioner

To: Sexual Health Providers, Local Health Departments, Family Planning Providers, Hospitals, Emergency Rooms, Community Health Centers, College Health Centers, Community-Based Organizations, and Internal Medicine, Family Medicine, Infectious Disease, OB/GYN, and Primary Care Providers

From: New York State Department of Health, AIDS Institute

Date: February 5, 2021

HEALTH ADVISORY: GONORRHEA INCREASES IN NEW YORK STATE COUNTIES OUTSIDE OF NEW YORK CITY

- **Reported gonorrhea diagnoses increased by 40% from 2019 to 2020.**
- **Increases are higher among females than males (54% increase among females compared to 29% among males from 2019 to 2020).**
- **Increases have occurred among all racial and ethnic groups. Of reported diagnoses in 2020, 47% were among non-Hispanic Black individuals (Age-adjusted rate: 673.2 per 100,000 population), while 22% were among non-Hispanic White individuals (Age-adjusted rate: 52.1 per 100,000 population), and 8% were among Hispanic individuals (Age-adjusted rate: 94.4 per 100,000 population).**
- **Among age groups, the highest proportion of diagnoses in 2020 was seen in individuals aged: 20-29 (49%), 30-39 (22%), and 15-19 (16%).**

While the statewide increases have been noteworthy, counties listed below (in descending order of 2020 diagnoses) have either seen a larger percentage increase in 2020 diagnoses compared to 2019 or diagnoses that have not declined since 2019.

County*	2019	2020**	%Increase
Monroe	2,302	4,073	77%
Erie	1,950	3,042	56%
Onondaga	1,039	1,406	35%
Suffolk	807	1013	26%
Albany	742	775	4%
Niagara	339	504	49%
Schenectady	246	421	71%
Rensselaer	277	366	32%
Orange	291	352	21%
Oneida	162	326	101%
Broome	208	314	51%
Dutchess	212	303	43%
Jefferson	96	225	134%
Wayne	51	161	216%
Saratoga	88	106	20%
Chautauqua	141	142	1%
Chemung	112	113	1%
Sullivan	47	105	123%
Cayuga	62	101	63%
Fulton	28	86	207%
Montgomery	30	77	157%
Ontario	61	76	25%
Oswego	39	52	33%
Columbia	30	48	60%
Cattaraugus	37	48	30%
Orleans	20	47	135%

CDC Issues GC Treatment Changes - MMWR 12/17/20

1. 2-drug therapy no longer routinely recommended
2. Use higher doses of cephalosporin
3. Treat pharyngeal GC with IM ceftriaxone and perform TOC

Diagnostics:

- NAAT remains preferred with culture and sensitivity testing if treatment failure/resistance suspected
- POC resistance testing on the horizon

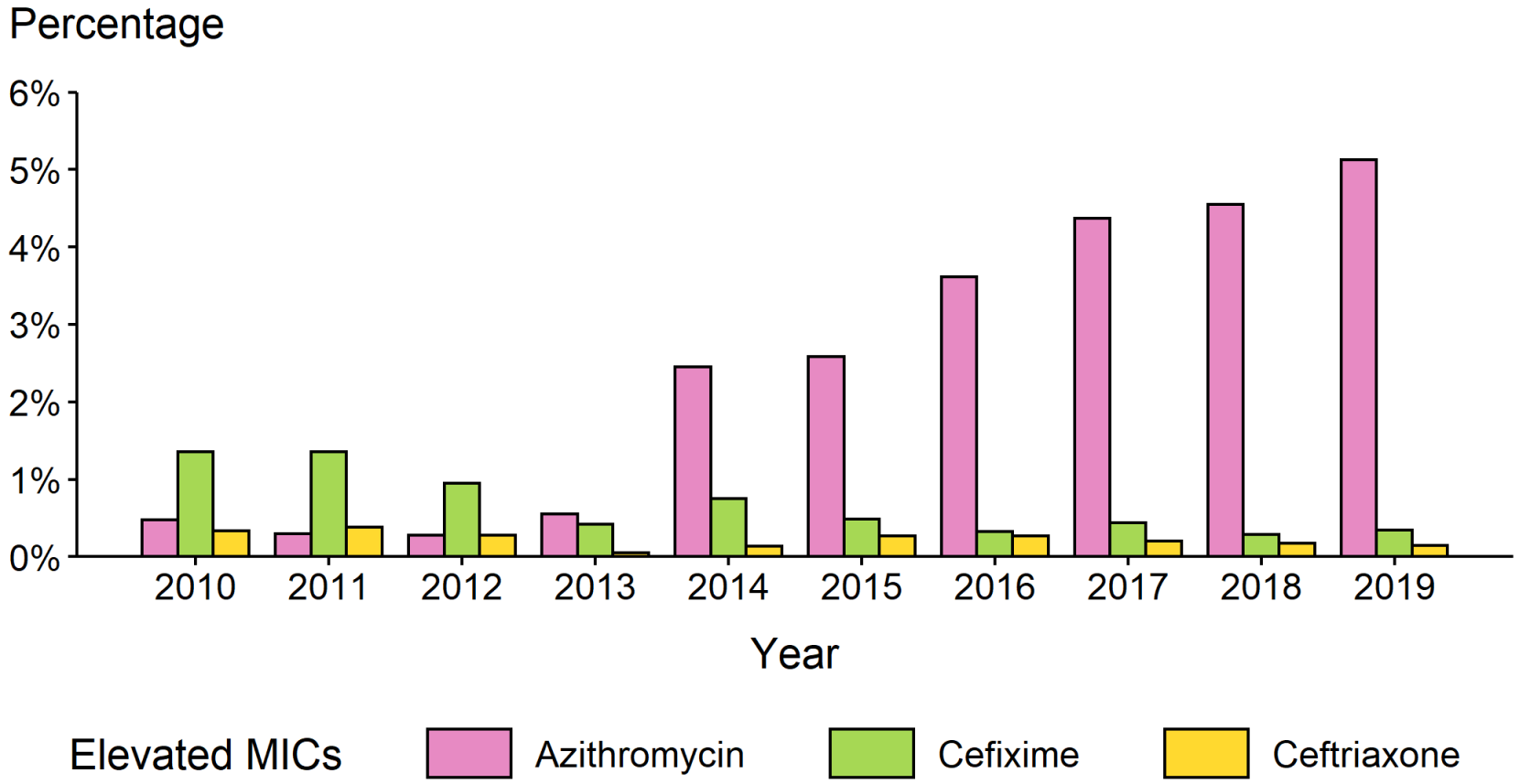
St. Cyr S, et al. MMWR 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6950a6

CDC's Rationale

- Antimicrobial stewardship
  - Macrolide resistance in M. genitalium and S. pneumoniae
  - Azithro resistance in enteric GNRs (e.g. Shigella, Campylobacter)
- Increased azithromycin resistance (GC) based on GISP
- PK/PD
  - Murine model: lowest effective dose of ceftriaxone - 5mg/kg body weight
    - 250mg ceftriaxone dose - 3mg/kg body weight for an 80kg individual
    - Theoretical need for greater time above MIC in pharyngeal tissue

St. Cyr S, et al. MMWR 2020. DOI: http://dx.doi.org/10.15585/mmwr.mm6950a6

Neisseria gonorrhoeae — Percentage of Isolates with Elevated Minimum Inhibitory Concentrations (MICs) to Azithromycin, Cefixime, and Ceftriaxone, Gonococcal Isolate Surveillance Project (GISP), 2010–2019



NOTE: Elevated MIC = Azithromycin: ≥ 2.0 µg/mL; Cefixime: ≥ 0.25 µg/mL; Ceftriaxone: ≥ 0.125 µg/mL

Gonorrhea First Line Regimens

CDC 2015 Guideline

- Ceftriaxone 250mg IM x1 plus 1g single dose oral azithromycin
  - Azithromycin provides dual GC coverage and also covers CT
  - Substitute 1 week of doxycycline for azithro if azithro intolerant

CDC 2020/21 Guideline Updates

- Higher dose ceftriaxone:
  - <150kg: Ceftriaxone 500mg IM x1
  - >150kg: Ceftriaxone 1g IM x1
- If CT not ruled out, treat for CT with oral doxycycline* 100mg twice daily x7d

*If pregnant (or unlikely to complete the 1 week course); use 1g azithromycin

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Workowski KA et al. MMWR 2015. Jun 5;64(RR-03):1-137

Gonorrhea Alternative Regimens

CDC 2015 Guideline

- Cefixime 400mg plus 1g azithromycin oral
  - Azithromycin provides dual GC coverage, and also covers CT
  - Substitute 1 week of doxycycline for azithro if azithro intolerant

CDC 2020/21 Guideline Updates

- Gentamicin 240mg IM plus 2g single-dose oral azithromycin

  OR

- Cefixime **800mg** oral:
  - If CT not ruled out, treat for CT with oral doxycycline* 100mg twice daily x7d

*If pregnant (or unlikely to complete the 1 week course); use 1g azithromycin

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Workowski KA et al. MMWR 2015. Jun 5;64(RR-03):1-137

Gonorrhea of the Pharynx (Uncomplicated)

CDC 2015 Guideline

- Ceftriaxone 250mg IM x1 plus 1g single dose oral azithromycin*

*No TOC unless other regimen used

CDC 2020/21 Guideline Updates

- Higher dose ceftriaxone:
  - <150kg: Ceftriaxone 500mg IM x1
  - >150kg: Ceftriaxone 1g IM x1

*TOC for all pharyngeal GC 7-14 days after treatment.
Obtain GC NAAT and GC culture with susceptibility testing

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Workowski KA et al. MMWR 2015. Jun 5;64(RR-03):1-137

GC Follow Up

- Retest at 3 months
- If suspected treatment failure:
  - Evaluate for re-infection, if suspected, retreat with usual regimen
  - Culture/susceptibility testing
  - If concerned for resistance consider Gentamicin + Azithro
  - TOC with C&S/NAAT at 7-14 days

- *Don't Forget!* - NAAT/Gram stain discrepancy for N. meningitidis

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

CLINICAL EDUCATION INITIATIVE

Real World Impacts – The move to single drug therapy

- What to do about Chlamydia?
  - In STI Clinic setting – co-infection is 25%.
  - POC treatment options for GC, with pending CT result:
    - Treat for GC and CT with Ceftriaxone/Doxy and stop Doxy if test negative
    - Treat only GC and call back for CT treatment with Doxycycline (can work if you know your co-infection rates and have the ability to call patients back)
  - EPT issues are compounded in this setting

CLINICAL EDUCATION INITIATIVE

Pelvic Inflammatory Disease (PID) 2021 CDC Updates

- Proportion of PID cases attributable to GC or CT declining (<50%)
- Consider testing for *M. genitalium*
- **Addition of metronidazole becomes standard**
- Clindamycin + gentamicin dropped to alternative regimen
- Parenteral antibiotic regimens modernized
- Updated Standard IM/PO:
  - Ceftriaxone 500mg (or 1g if >300kg) IM single dose + Doxycycline 100mg po BID x14 days + Metronidazole 500mg po BID x14 days

Pelvic Inflammatory Disease (PID) – 2021 CDC Guidelines

A Randomized Controlled Trial of Ceftriaxone and Doxycycline, With or Without Metronidazole, for the Treatment of Acute Pelvic Inflammatory Disease

Harold C Wiesenfeld ✉, Leslie A Meyn, Toni Darville, Ingrid S Macio, Sharon L Hillier

Clinical Infectious Diseases, Volume 72, Issue 7, 1 April 2021, Pages 1181–1189,
https://doi.org/10.1093/cid/ciaa101

To Effectively Treat Pelvic Inflammatory Disease, Look Beyond Coverage for Gonorrhea and Chlamydia

Caroline Mitchell ✉

Clinical Infectious Diseases, Volume 72, Issue 7, 1 April 2021, Pages 1190–1191,
https://doi.org/10.1093/cid/ciaa103

ACE trial

- RCT with 233 women recruited at several sites in Pittsburgh, PA
- Extensive microbiology testing

Ceftriaxone 250 IM x 1 +
Doxycycline 100 bid x 14 days +
Metronidazole 500 bid x 14 days

or

Ceftriaxone 250 IM x 1 +
Doxycycline 100 bid x 14 days +
Placebo x 14 days

Outcomes:

-3 day
- Clinical improvement

-30 day
- Clinical cure
- Microbiologic results
- Adherence
- Tolerability

Wiesenfeld HC et al. CID 2021. doi: 10.1093/cid/ciaa101

ACE trial

- 116 women in metronidazole arm and 117 in placebo arm
- Clinical improvement at 3 days similar in the two groups

30 Day Outcomes:

Metronidazole group (p< .05):

- Fewer anaerobes recovered
  - 8% vs. 21%
- M. genitalium reduced
  - 4% vs. 14%
- Pelvic tenderness reduced
  - 9% vs. 20%



Conclusion:
Metronidazole should be routinely added to ceftriaxone and doxycycline for the treatment of acute PID

Wiesenfeld HC et al. CID 2021. doi: 10.1093/cid/ciaa101

CLINICAL EDUCATION INITIATIVE

Expedited Partner Therapy (EPT) in NYS

- Delivery of antibiotic therapy to partner by index patient
  - Medications or Prescription
  - Increases partner treatment and decreases re-infections
  - Recommended by CDC since 2006 for GC and CT
  - Legal in NYS for CT only since 2010

<u>New York 2020 EPT Updates</u>

Allowed with clinical or laboratory diagnosis of:

- Gonorrhea
- Chlamydia
- Trichomonas

CLINICAL EDUCATION INITIATIVE

EPT – NYS

Exclusions – No EPT

- Index patient co-infected with syphilis
- Abuse/assault

No Exclusions – EPT OK

- Co-infection with HIV
- Men who have sex with Men

Table 1. Expedited Partner Therapy Recommendations for Index Patients and their Sexual Partners[1]

STI	Treatment for Index Patient	Treatment for Index Patient's Sexual Partner(s)	Follow-up
Chlamydia (Chlamydia Trachomatis)	**Recommended Treatments:** **Azithromycin** 1 gram orally in a single dose OR **Doxycycline** 100 mg orally twice a day for 7 days **Alternative treatments:** **Erythromycin** base 500 mg orally four times a day for 7 days OR **Erythromycin** ethylsuccinate 800 mg orally four times a day for 7 days OR **Levofloxacin** 500 mg orally once daily for 7 days OR **Ofloxacin** 300 mg orally twice a day for 7 days	(same as index patient)	For alternative oral regimens, patients should be counseled that if their symptoms do not improve or resolve within 5-7 days, they should follow-up with the clinic or a medical provider. Patients should be counseled to be tested for STIs. Health departments should remind clients who have been referred for oral treatment to return for comprehensive testing and screening and link them to services at that time.
Gonorrhea[2] (N. Gonorrhoeae)	See Box 1 for CDC recommended regimens for uncomplicated gonococcal infections.	**Recommended Treatments:** **Cefixime** 800mg in a single dose-where concurrent chlamydia infection has been excluded. Otherwise, **Cefixime** 800mg **AND** 100mg of **oral doxycycline** twice daily for 7 days.	
Trichomoniasis (Trichomoniasis Vaginalis)	**Recommended Treatments:** **Metronidazole** 2 grams orally in a single dose OR **Tinidazole** 2 g orally in a single dose **Alternative treatments:** **Metronidazole** 500 mg orally twice a day for 7 days	(same as index patient)	

https://www.health.ny.gov/diseases/communicable/std/docs/ept_guidance.pdf

CLINICAL EDUCATION INITIATIVE

Syphilis

STI

Sexually Transmitted Infections

National Strategic Plan

2021-2025

C. Syphilis

BOX 5

SYPHILIS SNAPSHOT

- Treatable and curable
- Primary and secondary (P&S) syphilis (early-stage disease) may progress to late-stage disease in about 15% of infections, when left untreated
- Screening recommended at least annually for sexually active MSM
- Screening recommended for all pregnant women at the first prenatal visit and, if at high risk for syphilis acquisition during pregnancy, again at 28 weeks and delivery



Epidemiological Facts

115,045 REPORTED CASES OF ALL STAGES (2018) 129,813 (2019)

MSM accounted for 54% of all P&S cases

71% RATE INCREASE OF P&S SYPHILIS (2014–2018)

42% OF MSM WITH P&S SYPHILIS are known to be living with HIV

185% RATE INCREASE IN CONGENITAL SYPHILIS (2014–2018)

Populations Disproportionally Impacted

- MSM
- Pregnant people
- Racial/ethnic minorities

Consequences When Left Untreated

- Ocular and neurologic morbidity
- Cardiovascular, bone, skin, and other organ system morbidity
- Increased risk of HIV
- Congenital syphilis, which can lead to preterm birth, stillbirth, and infant death

Current Challenges

- Lack of provider awareness and training on diagnosis, management, and stages of syphilis
- Need for better diagnostics to detect active infection
- Lack of prenatal screening and timely treatment
- Only one antibiotic available to treat syphilis in pregnancy and newborns
- Shortages of recommended antibiotics for treatment
- Lack of an available vaccine

Sources: CDC[1], Workowski and Bolan[2]

NEW YORK STATE OF OPPORTUNITY. Department of Health

ANDREW M. CUOMO
Governor

HOWARD A. ZUCKER, M.D., J.D.
Commissioner

LISA J. PINO, M.A., J.D.
Executive Deputy Commissioner

To: Sexual Health Providers, Local Health Departments, Family Planning Providers, Hospitals, Emergency Rooms, Community Health Centers, College Health Centers, Community-Based Organizations, and Internal Medicine, Family Medicine, Pediatric, Adolescent Medicine, Dermatology, Infectious Disease, OB/GYN, and Primary Care Providers

From: New York State Department of Health, AIDS Institute, Office of Sexual Health and Epidemiology

Date: June 2, 2021

HEALTH ADVISORY: CONGENITAL SYPHILIS INCREASING IN NEW YORK STATE (NYS) OUTSIDE OF NEW YORK CITY (NYC) [1]

Congenital syphilis diagnoses have been increasing since 2016: Between 2015 – 2017 there were 14 congenital syphilis diagnoses versus 31 congenital syphilis diagnoses in the 2018 – 2020 period.

Syphilis – CDC Guidelines 2021

- **Clinical presentation:**
  - Atypical presentations, including multiple painful lesions (esp. perianal)
  - Emphasis on ocular and otic manifestations
- **Diagnostic Testing:**
  - Reverse vs. Traditional Algorithm Testing – Either OK!
    - Traditional algorithm (RPR/confirmatory specific ab test)
    - Reverse algorithm (Specific ab test/RPR with 2nd specific ab test for discordant results)
  - Repeat CSF exams not needed (for immunocompetent individuals or PLWH on ART) if appropriate serologic (e.g. RPR) response with treatment
  - LP not needed for *isolated* ocular or otic syphilis, doesn't impact treatment

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

Syphilis - CDC Guidelines 2021

New Treatment Alternative:
Primary, Secondary, EL Syphilis:
Ceftriaxone 1 gm IM/IV x 10 days

Do Not Use: Insufficient data
Amoxicillin plus probenecid

Follow Up Serology*: Still want 4 fold decline
Timing of decline adjusted:

- Primary, secondary and early latent – 12 months
- Late latent or unknown duration – 24 months

*Varies by stage, initial titer, age

Be Aware: Titer may not decline if initial titer 1:8 or less

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

Syphilis in Pregnancy - CDC Guidelines 2021

Screening in Pregnancy

1st trimester (all)

AND

Based on Risk and Prevalence

3rd trimester

- 28 Weeks
- At Delivery

Risk factors expanded:

- Multiple partners
- Sex with drug use
- Transactional sex
- Late (≥2nd TM) or no prenatal care
- Methamphetamine or heroin use
- Incarceration (pt or partner)
- Unstable housing

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

Follow Up in Pregnancy - CDC Guidelines 2021

- **Reinfection or treatment failure definition**
  - 4 fold increase in titer post treatment, sustained for 2 weeks
  - Most will not have 4-fold decline by delivery, does not necessarily indicate tx failure
- **When to repeat titers:**
  - If tx ≤24 weeks – repeat at least 8 weeks after treatment (e.g. 32 wks) and at delivery (unless signs of primary or secondary syphilis)
  - If tx >24 weeks – repeat at delivery

Example: 23 year old in first trimester dx with primary syphilis

1/1/21 - RPR 1:4 – Treated with 2.4 million units IM Benz PCN

3/1/21 - RPR 1:16 – no physical findings of syphilis

What if?

3/15/21 - RPR 1:4 – continue to follow

OR

3/15/21 - RPR 1:16 – needs repeat treatment and possibly LP

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

CLINICAL EDUCATION INITIATIVE

M. genitalium Infection



Image Credit: InfectiousDiseaseAdvisor.com

Pathogen

- *M. genitalium;* Bacteria without a cell wall
- Infects epithelial cells of the urogenital tract
- Prevalence 0.5-5% in general population, 5-38% in STD clinic populations

Clinical Manifestations

- Non-purulent urethritis, cervicitis, and PID
- Persistent/relapsing after empiric syndromic treatment
- Many asymptomatic

Diagnosis

- Molecular testing (NAAT)
- Do not screen asymptomatic patients

Treatment

- Resistance-guided
- Doxycycline → Azithromycin
- Doxycycline → Moxifloxacin

M. genitalium

- Had been treated with azithromycin, similar to other Mycoplasma species
  - Now wide-spread macrolide resistance and emerging quinolone resistance
  - Levofloxacin/ofloxacin have lower cure rates than moxifloxacin
- Testing and treatment strategies being adapted to overcome antimicrobial resistance

DIAGNOSTIC UPDATES:
Consider MG if persistent or relapsing symptoms (urethritis, cervicitis, PID)

Rule out re-infection with other STIs and infection with TV

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
DiMarco DE, Urban MA, et al. Guidance: Screening, Diagnosis and Treatment of Mycoplasma genitalium. 2020. https://www.hivguidelines.org/sti-care/m-genitalium-guidance/

Testing Updates

- NAAT +/- Resistance assay
  - Resistance testing not yet available in US
  - Caution with interpretation
- **Recommended in persistent/relapsing urethritis and cervicitis, and consider in PID**
- Screening of asymptomatic individuals is not recommended (unless partner to symptomatic case)

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

CLINICAL EDUCATION INITIATIVE

Two-step Treatment Strategy

- Resistance Guided Therapy – First drug to reduce bacterial load, second drug based on macrolide resistance
  - Doxycycline → Azithromycin
  - Doxycycline → Moxifloxacin
- Used in Australia and the UK, and have been incorporated into their guidelines
- Quinolone resistance assays are also available in some countries
- In some cases, in-vitro resistance does not completely correlate with treatment failure

Clinical Infectious Diseases

MAJOR ARTICLE

Resistance-Guided Antimicrobial Therapy Using Doxycycline–Moxifloxacin and Doxycycline–2.5 g Azithromycin for the Treatment of *Mycoplasma genitalium* Infection: Efficacy and Tolerability

Duygu Durukan,[1,2] Tim R. H. Read,[1,2] Gerald Murray,[3,4] Michelle Doyle,[2] Eric P. F. Chow,[1,2] Lenka A. Vodstrcil,[1,2] Christopher K. Fairley,[1,2] Ivette Aguirre,[2] Elisa Mokany,[5] Lit Y. Tan,[5] Marcus Y. Chen,[1,2] and Catriona S. Bradshaw[1,2]

[1]Central Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Australia; [2]Melbourne Sexual Health Centre, Alfred Health, Carlton, Victoria, Australia; [3]Murdoch Children's Research Institute, Royal Children's Hospital, Parkville, Victoria, Australia; [4]Centre for Women's Infectious Diseases, Royal Women's Hospital, Melbourne, Victoria, Australia; and [5]SpeeDx Pty Ltd, National Innovation Centre, Eveleigh, New South Wales, Australia

- Australian STD clinic 2017-2018 (prior similar study with sitafloxacin)
- 383 patients (cis-males and cis-females, 196 MSM); 82.5% symptomatic, 186 w/urethritis
- Empiric syndromic treatment included doxy 7d, called back if MG positive
- Macrolide susceptible cases given doxy+azithro, resistant cases given doxy+moxi
- Microbial cure w doxy+azithro 95.4% (CI 89.7-98); w/doxy+moxi 92% (CI 88.1-94.6)
- Macrolide resistance 74%, higher in MSM

MG Treatment

CDC 2015

- Azithro 1g x1
- Azithro 500mg x1 followed by 250mg daily x 4 days
- Moxi 400mg daily x7-14 days for treatment failures

CDC 2021

- **Without macrolide resistance testing**
  - **Doxy 100mg BID x7d followed by moxi 400mg daily x7d**
- With macrolide resistance testing:
  - Susceptible- Doxy 100mg BID x7d, then 4d azithro (1g x1d, 500mg x3d)
  - Resistant - Doxy 100mg BID x7d, then moxi 400mg daily x7d
- No discussion on pregnancy

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Workowski KA et al. MMWR 2015. Jun 5;64(RR-03):1-137

CLINICAL EDUCATION INITIATIVE

Summary: Urethritis and Cervicitis Syndromes

- For urethritis, initial tests should be GC and CT
  - TV and MG testing reserved for persistent urethritis (TV only in MSW)
  - Doxycycline for NGU, azithromycin as alternative
- For cervicitis:
  - MG testing for persistent/relapsing cases
  - **Do not test for Ureaplasma or M. hominis, not associated with cervicitis**
  - No data to support antibiotics without etiology (e.g. negative CT, GC, MG, BV, and TV)
- Increased doses of cephalosporin

CLINICAL EDUCATION INITIATIVE

Trichomoniasis

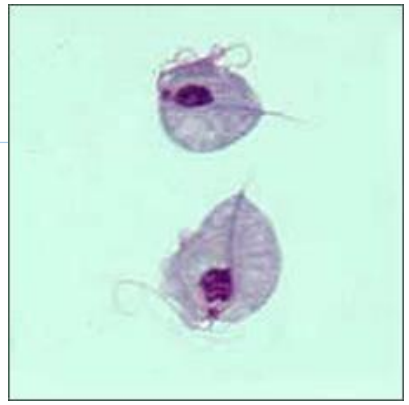


Image Credit: CDC.gov

Pathogen

- *T. vaginalis,* a flagellated protozoan
- Adheres to squamous epithelial cells of the urogenital tract; needs nutrient-rich environment for survival
- Associated w/2-3 fold increased risk of HIV

Clinical Manifestations

- Vaginitis, vulvitis, colpitis macularis
- Urethritis
- Asymptomatic

Diagnosis

- Microscopy (vaginal wet prep)
- Molecular testing (NAAT)
- Culture (limited availability)
- Resistance testing at CDC

Treatment

- Nitromidazoles
- Challenges w/allergy or resistance
- Alternatives with little evidence (boric acid, paromomycin)

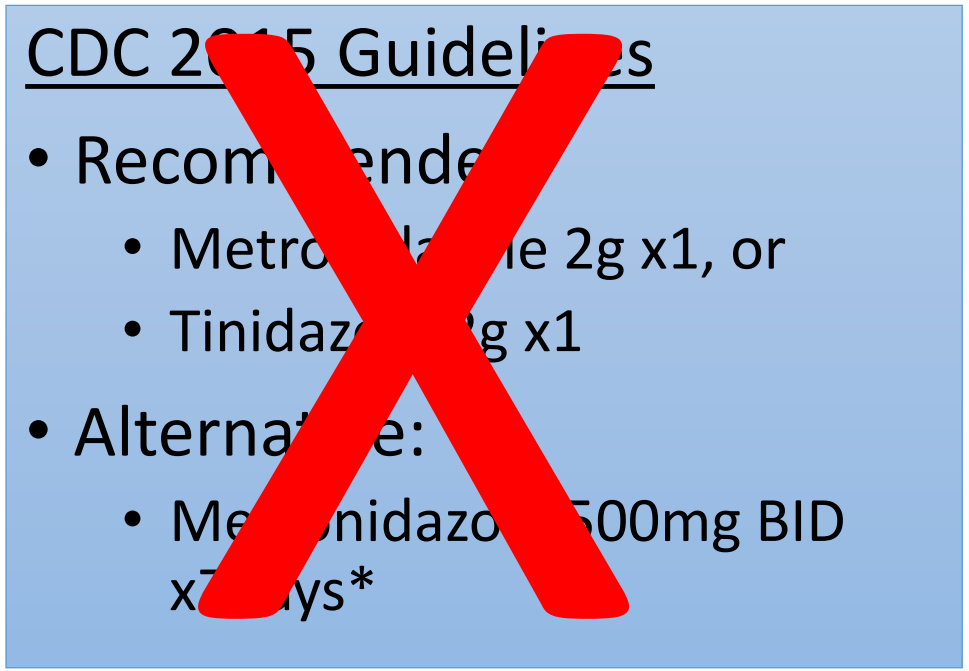
CLINICAL EDUCATION INITIATIVE

Testing Updates

- When to test:
  - Individuals seeking care for vaginal discharge
  - Individuals in high-prevalence areas, persons living with HIV who have receptive vaginal sex, and those otherwise at high risk
  - Individuals with persistent urethritis and negative GC/CT testing
  - Retest at 3 months due to high rates of re-infection
- Clearance of nucleic acid from prior infection can take ~3 weeks, NAAT should not be used for test of cure in immediate post treatment period

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

Trichomoniasis Treatment Updates



CDC 2015 Guidelines

- Recommended:
  - Metronidazole 2g x1, or
  - Tinidazole 2g x1
- Alternative:
  - Metronidazole 500mg BID x7days*

CDC 2021 Updates

- Recommended:
  - Vaginitis - Metronidazole 500mg BID x7days
  - Urethritis – single 2g dose of metronidazole or tinidazole
- Alternative (Vaginitis):
  - Tinidazole 2g x1

*Week long regimen was preferred for women living with HIV

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Workowski KA et al. MMWR 2015. Jun 5;64(RR-03):1-137

Evidence for Multi-day Treatment

- 2017 Meta-analysis – Expansion of multi-day tx to all women, not just women with HIV
  - Reviewed 6 studies that met inclusion criteria (Study sample size ranged from 112-468)
  - Pooled risk for treatment failure higher for single dose compared to multi-dose
    - RR 1.87 (1.2-2.82, P <0.01)
  - Excluding women with HIV, higher risk for treatment failure was sustained
    - RR 1.80 (1.07-3.02; P <0.03)

Howe K et al. Sex Transm Dis 2017.

Antimicrobial Considerations

- Tinidazole has slightly better cure rates (92-100%, compared to 84-98% for metronidazole), and less GI effects
- Metronidazole is generally more cost effective
- Providers - suspect resistance with persistent/recurrent infection after nitromidazole tx once re-exposure has been excluded
- Prevalence of nitromidazole resistance estimated at 4-10%

Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1
Trichomonas vaginalis Antimicrobial Drug Resistance in 6 US Cities, STD Surveillance Network, 2009-2010. Emerg Infect Dis, 2012. doi.org/10.3201/eid1806.111590

CLINICAL EDUCATION INITIATIVE

Updates on Treatment Failure

- Exclude re-infection or other STI
  - Retest with wet prep or culture if short interim
- For persistent vaginal infection:
  - If re-exposure, treat with same 7d metronidazole regimen
  - If no re-exposure, treat with tinidazole 2g daily x7d
- For persistent male urethral infection:
  - If re-exposure, treat with same single dose metronidazole regimen
  - If no re-exposure, treat with metronidazole 500mg BID x7d
- If continued treatment failure despite longer high-dose regimen
  - Send out to CDC for susceptibility testing - Request a trich kit (InPouchTV) by emailing requisition form to CDC

Cudmore SL, Delgaty KL, Hayward-McClelland SF et al. Treatment of Infections Caused by Metronidazole-Resistant Trichomonas vaginalis. Clin Microbiol Rev. 2004. doi: 10.1128/CMR.17.4.783-793.2004
Workowski KA et al. MMWR 2021. DOI: http://dx.doi.org/10.15585/mmwr.rr7004a1

CLINICAL EDUCATION INITIATIVE

Intravaginal Boric Acid

- In-vitro activity against TV that seems independent of acidification
- Also has had success in some instances of treatment refractory Candida vaginitis
- No RCTs; Case reports describe successful eradication
- 2018 review of the literature:
  - Dosing varied from 600mg daily to twice daily
  - Duration varied from 1-5 months
  - Indications for use included severe metronidazole allergy and nitromidazole treatment failure

- Our clinic has had success with BID dosing for as little as 2 weeks

Sex Transm Infect 2018. 2018 Dec;94(8):574-577. doi: 10.1136/sextrans-2017-053343
Sex Transm Dis 2014 Dec;41(12):718-22. doi: 10.1097/OLQ.0000000000000203

CLINICAL EDUCATION INITIATIVE

Future Directions –STIs National Strategic Plan

A. Vision

The United States will be a place where sexually transmitted infections are prevented and where every person has high-quality STI prevention, care, and treatment while living free from stigma and discrimination.

This vision includes all people, regardless of age, sex, gender identity, sexual orientation, race, ethnicity, religion, disability, geographic location, or socioeconomic circumstance.

B. Goals

In pursuit of this vision, the STI Plan establishes five goals:

1. Prevent new STIs
2. Improve the health of people by reducing adverse outcomes of STIs
3. Accelerate progress in STI research, technology, and innovation
4. Reduce STI-related health disparities and health inequities
5. Achieve integrated, coordinated efforts that address the STI epidemic

U.S. Department of Health and Human Services. 2020. Sexually Transmitted Infections National Strategic Plan for the United States: 2021–2025. Washington, DC

CLINICAL EDUCATION INITIATIVE

CDC 2021 Guidelines – Highlighted STI Updates

CHLAMYDIA	GONORRHEA	SYPHILIS
Preferred Tx Adults/Adolescents: • Doxycycline 100mg PO BID x7d **Alternative Tx:** • Azithromycin 1g PO x1 **Tx in Pregnancy:** • Pref. Azithromycin 1g PO x1 • Alt. Amoxicillin 500mg TID x7d Apply updates to associated STI syndromes EPT Available	**Preferred Tx Adults/Adolescents:** • <150kg: Ceftriaxone 500mg IM x1 • >150kg: Ceftriaxone 1g IM x1 **Alternative Tx:** • No reliable alternative to CTX for pharyngeal GC Co-treatment for CT only if not readily excluded Apply updates to associated STI syndromes EPT Available	**Testing:** • LP not indicated if isolated ocular or otic syphilis • Test twice in 3rd trimester for those at elevated risk or tx during pregnancy **Alternative Tx:** • For early syphilis, Ceftriaxone 1g IM/IV daily x10 d (limited evidence) if penicillin allergy • Do not use amoxicillin w/probenecid

CLINICAL EDUCATION INITIATIVE

CDC 2021 Guidelines – Highlighted STI Updates Continued

M. GENITALIUM	TRICHOMONIASIS	PELVIC INFLAMMATORY DISEASE
Preferred Tx Adults/Adolescents: • Doxycycline 100mg PO BID x7d followed by moxifloxacin 400mg PO daily x7d (14d for PID) • Use resistance guided tx if available **Testing:** • Do not screen asymptomatic individuals. • Reserve testing for persistent/relapsing urethritis/cervicitis, or PID. Test current partners of symptomatic cases, treat if positive.	**Preferred Tx Adults/Adolescents with Vaginitis:** • Metronidazole 500mg PO BID x7d **Preferred Tx Adults/Adolescents with Urethritis:** • Metronidazole 2g PO x1 **Alternative Tx:** • Tinidazole 1g PO x1 EPT Available	**Preferred Outpatient Tx Adults/Adolescents:** • Single dose IM ceftriaxone (weight-based), PLUS doxycycline 100mg PO BID x14d AND metronidazole 500mg PO BID x14d **Preferred Inpatient Tx:** • Ceftriaxone 1g IV daily, PLUS doxycycline 100mg PO BID x14d, AND metronidazole 500mg PO BID x14d

QUESTIONS?

NYS Sexual Health
Center of Excellence
853 West Main St. Rochester, New York
585.274.3044

