STIs 101: GC, CT and Common STI Syndromes

Natalie Neu, MD, MPH Professor of Pediatrics Medical Director, NYC STD Prevention Training Center



STIs Are Not Benign



- Pelvic inflammatory disease
- Chronic pelvic pain
- Infertility
- Adverse pregnancy outcomes
 - Prematurity
 - Stillbirth
- Urethral strictures
- Gastrointestinal fistulas
- Peri-rectal abscesses
- Severe complications of syphilis
 - Permanent hearing or vision impairment



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What do we do when we see patients? Jack....

- 16-year-old
- Presents to clinic as a walk-in
- Feels like he just wants to get tested for STIs
- No specific complaints







Jack's History

- Partners
 - 6 male partners in the past 2 months
 - Meets partners on an app
 - 1 regular female partner
- Practices
 - Oral (gives and receives), vaginal and anal intercourse (insertive and receptive)
- Protection from STIs
 - Condoms "sometimes", doesn't like the sensation
- Past history of STIs
 - Chlamydia in the past

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- Pregnancy intention
 - Doesn't want kids but does not know what his female partner uses





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General STI Screening Recommendations

Population	Recommendations
Men who have sex with men	At least annually, <u>test at each site of exposure (urethra, rectum)</u> for sexually active MSM regardless of condom use or every 3-6 months if at increased risk.
Patients taking PrEP	All patients starting and taking oral PrEP should have genitourinary and extra-genital testing performed at baseline and every 3 months.
Persons living with HIV	For sexually active individuals, screen at first HIV evaluation and at least annually thereafter. More frequent screening might be appropriate depending on individual risk behaviors and local epidemiology
Non-pregnant Women	Test at least annually for sexually active women under 25 years of age and those aged 25 years and older if at increased risk Rectal chlamydial testing can be considered in females based on sexual behaviors and exposure through shared clinical decision making.
Men who have sex with women***	Consider screening young men in high prevalence clinical settings (adolescent and STI clinics and correctional facilities)
Pregnant Women	All pregnant women under 25 years of age and those aged 25 years and older if at increased risk. retest during 3rd trimester if under 25 years of age or at risk.





Why an Emphasis on Extragenital Testing



Extragenital Gonorrhea and Chlamydia Among Men and Women According to Type of Sexual Exposure

David M. Bamberger, MD, *†‡ Georgia Graham, MD,*§ Lesha Dennis, BA,† and Mary M. Gerkovich, PhD‡

Kansas City Department of Health STD Clinics - 9,646 clinical encounters

Missed Diagnosis

Change in Management





Emphasis on Extra-Genital Testing



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Bamberger DM, Graham G, Dennis L, Gerkovich MM. Extragenital Gonorrhea and Chlamydia Among Men and Women According to Type of Sexual Exposure. Sex Transm Dis. 2019 May;46(5):329-334. doi: 10.1097/OLQ.000000000000967. PMID: 30676485.



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Emphasis on Extra-Genital Testing



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Emphasis on Extragenital Testing



- Most cases of GC and CT in MSM would have been missed had extragenital testing not been performed
- A third of cases of extragenital GC and CT in MSW and WSM would have been missed had only urogenital testing been performed





Jack's Work-Up

- Well, he does have some discharge
- Its mild and comes and goes
- Let's do a gram stain then...







Gonorrhea (Neisseria gonorrhea)

Gram stain from urethral discharge

Gram-negative intracellular diplococci



Rates of Reported Cases by Age Group and Sex, United States, 2023







Gonorrhea — Estimated Proportion of Cases by Sex and Sex of Sex Partners and Jurisdiction, STI Surveillance Network (SSuN), 2023



NOTE: Estimate based on weighted analysis of data on sex of sex partners obtained from interviews (n=5,705) conducted among a random sample of gonorrhea cases reported to participating SSuN jurisdictions during January to December 2023. Includes ten SSuN sites reporting completed case investigations in 2023 for at least 1% of all reported cases.

What is the best treatment for his positive gonorrhea test?

- Ceftriaxone 250 mg IM once
- Ceftriaxone 500 mg IM once
- Ceftriaxone 250 mg IM once with azithromycin 1 gram by mouth once
- Ceftriaxone 500 mg IM once with doxycycline 100 mg by mouth twice daily for 7 days



Gonorrhea Treatment Guidelines

Ceftriaxone <u>500</u> mg IM x 1 for persons weighing <150kg*

*For persons weighing ≥ 150kg, 1 g of IM ceftriaxone should be administered

If chlamydia has **not** been excluded, treat for chlamydia with:

Doxycycline 100 mg PO twice daily x 7 days

*For pregnancy, allergy, or concern for nonadherence 1g PO Azithromycin can be used

No longer recommending dual therapy with azithromycin



Gonorrhea — Estimated Proportion of Cases Treated with Recommended Regimen by Jurisdiction, STI Surveillance Network (SSuN), 2023



NOTE: Includes SSuN jurisdictions with treatment and dosage data ascertained for at least 80% of sampled, investigated cases. In 2023, the recommended treatment for uncomplicated gonorrhea was ceftriaxone 500 mg, intramuscular.

Alternative Gonorrhea Treatment

Uncomplicated infections of the cervix, urethra, and rectum if ceftriaxone is not available .:

IF chlamydia has <u>not</u> been excluded, treat for chlamydia with:

Cefixime **<u>800</u>** mg PO x 1

Doxycycline 100 mg PO BID x 7 days

For pregnancy, allergy, or concern for nonadherence, 1g PO azithromycin x 1 can be used

Cephalosporin allergy: Gentamicin 240 mg IM + azithromycin 2 g PO

No reliable alternative treatments are available for pharyngeal gonorrhea



Source: Update to CDC's Treatment Guidelines for Gonococcal infection, MMWR 202

Why Make This Change for Gonorrhea

- 1. Antimicrobial stewardship
 - *a) N. gonorrhoeae* resistance
 - b) Rising resistance in other pathogens
 - c) Selection for non-macrolide resistance
- 2. Pharmacokinetics and pharmacodynamics
 - a) Rising MICs = Increase Dose Needed
 - b) Pharynx





Antimicrobial Stewardship

- 1. Antimicrobial stewardship
 - a) N. gonorrhoeae resistance
 - b) Rising resistance in other pathogens
 - c) Selection for non-macrolide resistance
- 2. Pharmacokinetics and pharmacodynamics
 - a) Rising MICs = Increase Dose Needed
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Prevalence of Tetracycline, Penicillin, or Fluoroquinolone Resistance or Cefixime, Ceftriaxone or Azithromycin Decreased Susceptibility, by Year, GISP, 1987–2019*





Antimicrobial Stewardship

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- 1. Antimicrobial stewardship
 - *a) N. gonorrhoeae* resistance
 - b) Rising resistance in other pathogens
 - c) Selection for non-macrolide resistance
- 2. Pharmacokinetics and pharmacodynamics
 - a) Rising MICs = Increase Dose Needed
 - b) Pharynx



infections each year

each vea



Purpura L, Zucker J, LaSota E, et al. Prevalence of Gastrointestinal Pathogens Detected by Multiplex Polymerase Chain Reaction in a Prospective Cohort of Men Who Have Sex With Men Taking Human Immunodeficiency Virus Preexposure Prophylaxis-New York City, 2019-2020. Open Forum Infect Dis. 2021;8(8):ofab411. Published 2021 Aug 3. doi:10.1093/ofid/ofab411

DRUG-RESISTANT

CAMPYLOBACTER

THREAT LEVEL SERIOUS

Antimicrobial Stewardship

- 1. Antimicrobial stewardship
 - *a) N. gonorrhoeae* resistance
 - b) Rising resistance in other pathogens
 - c) Selection for macrolide and nonmacrolide resistance
- 2. Pharmacokinetics and pharmacodynamics
 - a) Rising MICs = Increase Dose Needed
 - b) Pharynx

	36 Months		48 Months	
Macrolides		7.36 (4.02-16.73)		7.46 (3.76-23.14)
Aminocoumarins	•	- 3.70 (1.03-NR)	•	- 3.61 (0.96-NR)
Aminoglycosides		2.32 (1.33-4.57)	֥	1.63 (0.85-4.29)
Bacitracin		3.21 (1.42-12.10)		1.55 (0.61-8.75)
Beta-lactams		2.13 (1.33-4.02)	—	1.98 (1.10-4.57)
Cationic peptides		2.37 (1.33-4.88)	֥	1.66 (0.85-4.88)
Elfamycins		2.00 (1.10-7.20)		1.72 (0.90-4.29)
Fluoroquinolones		2.09 (1.17-5.21)	÷	1.77 (0.85-6.33)
Metronidazole		2.32 (0.90-5.93)		3.59 (1.73-8.20)
Multidrug resistance		2.10 (1.25-4.57)	֥	1.72 (0.85-4.88)
Rifampin	•	3.06 (1.03-19.05)	•	2.14 (0.85-14.70)
Sulfonamides	•	2.75 (0.85-13.78)	•	2.09 (0.79-15.68)
Tetracyclines		1.68 (1.10-3.31)		1.75 (1.03-4.02)
Trimethoprim	0.5 1.0 2.0 4.0 8.0 16.0	2.22 (1.25-5.21)	0.5 1.0 2.0 4.0 8.0 16.0	1.61 (0.85-4.29)

Figure 4. Antibiotic-Resistance Determinants in the Gut of Children at the 36-Month and 48-Month Samples.

The difference in antibiotic-resistance determinants in the azithromycin-treated group as compared with the group that received placebo is shown, with associated 95% confidence intervals. The 36-month samples were obtained 6 months after the sixth distribution, and the 48-month samples were obtained 6 months after the eighth distribution. NR denotes not reached.



Pharmacokinetics and Pharmacodynamics

- 1. Antimicrobial stewardship
 - *a) N. gonorrhoeae* resistance
 - b) Rising resistance in other pathogens
 - c) Selection for non-macrolide resistance
- 2. Pharmacokinetics and pharmacodynamics
 - a) Rising MICs = Increase Dose Needed
 - b) Pharynx

- Ceftriaxone levels need to be > GC strain MIC for ~24 hours
- Increasing MIC means increasing dosage needed



Pharmacokinetics and Pharmacodynamics

- 1. Antimicrobial stewardship
 - *a) N. gonorrhoeae* resistance
 - b) Rising resistance in other pathogens
 - c) Selection for non-macrolide resistance
- 2. Pharmacokinetics and pharmacodynamics
 - a) Rising MICs = Increase Dose Needed
 - b) Pharynx

- Screened less
- Ceftriaxone concentrations more variable
 - *N. gonorrhoeae* likely requires longer times above the strain's MIC





When should the patient follow-up for re-testing?

- 1-2 weeks
- 4 weeks
- 8 weeks
- 12 weeks
- 24 weeks



Gonorrhea Follow-up

Abstain from sex until 7 days after completing treatment

Assess for treatment failure if persistent symptoms at 3-5 days with culture (with AST) and NAAT

Test of cure recommended for all pharyngeal infections at 7-14 days

Test of cure at 4 weeks if pregnant

Rescreen everyone at 3 months for re-infection



Test of Cure for Pharyngeal Infections

- Persistent nonviable organisms may cause a false positive NAAT
- Reinfection from re-exposure is a common cause of persistent positive GC tests

RNA NAAT

DNA NAAT

тос		Pers	sistent			Pharyngeal GC	
						persistenceDNA NAAT	
Pharynx*	Ν	Ν	(%)	OR	(95% CI)		% (95% Cl)
0-7 days	309	27	(8.7)	1 -		7 days	13 (6.4-19.6)
8-14 days	367	8	(2.2)	0.23	8 (0.1-0.52)	14 days	8 (2.7-13.3)
15-28 days	105	1	(1.0)	0.10) (0.01-0.75)	All cultures neg	gative

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Hananta IPY, De Vries HJC, van Dam AP, van Rooijen MS, Soebono H, Schim van der Loeff MF. Persis tence after treatment of pharyngeal gonococcal infections in patients of the STI clinic, Amsterdam, the Netherlands, 2012-2015: a retrospective cohort study. Sex Transm Infect. 2017 Nov;93(7):467-471. doi: 10.1136/sextrans-2017-053147. Epub 2017 Aug 19. PMID: 28822976; PMCID: PMC5739854.. Bissessor M, Whiley DM, Fairley CK, Bradshaw CS, Lee DM, Snow AS, Lahra MM, Hocking JS, Chen MY. Persis tence of Neisseria gonorrhoeae DNA following treatment for pharyngeal and rectal gonorrhea is influenced by antibiotic sus ceptibility and reinfection. Clin Infect Dis. 2015 Feb 15;60(4):557-63. doi: 10.1039/cid/ciu873. Epub 2014 Nov 3. PMID: 25371490.

What if this patient's test of cure were positive?

- Most suspected treatment failures are reinfections
- If re-infection is unlikely:
 - Obtain simultaneous NAAT and gonorrhea culture
 - Alert public health authorities
 - Treat with either ceftriaxone or gentamicin/azithromycin







Case 2: Jill

- A 18-year-old female in New York City
- She is sexually active with several male partners
 - One of them was recently diagnosed with chlamydia







What Do You Ask Jill?



Gender Neutral – 5Ps

- Partners
- Practices
- Protection from STIs
- Past history of STIs
- Pregnancy intention





Jill's History

- Partners
 - 6 male partners in the past 2 months
 - 1 female partner
- Practices
 - Oral (gives and receives), vaginal and anal intercourse "a few times"
- Protection from STIs
 - Condoms 50% of the time, never for oral sex
- Past history of STIs
 - Chlamydia x 2 in the past
- Pregnancy intention

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- Does not want kids
- Uses oral contraceptives (when she remembers to take them)

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Jill's Work-up

- HIV Testing (HIV Ab/Ag test)
- Hepatitis C testing
- Gonorrhea and chlamydia testing
 - 3 site GC/CT NAAT
 - Gram stain (if able)
- Trichomonas testing
- Syphilis testing (RPR)

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- Pregnancy test
- Offer of HIV biomedical HIV prevention services (PrEP +/- PEP)





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Non-Gonococcal Urethritis



Etiology

- C. trachomatis (15-40%)
- *M. genitalium* (15-25%)
- *T. vaginalis* (1-8%)
- HSV (3%)
- N. meningitidis
- Other bacteria (i.e. *H. influenzae*)
- Other viruses (i.e. adenovirus, EBV)
- UNKNOWN (~50%)!





Chlamydia — Rates of Cases by Age and Sex, 2023



https://www.cdc.gov/sti-statistics/media/files/2024/11/2023-STI-Surveillance-Report

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Testing for STIs in Women

- New: Consider extragenital testing for GC/CT rectal and GC in the pharynx
- Data: 2016, review of 33 studies included women
 - Rectal GC 0.6- 35.8% (median 1.9%)
 - Pharyngeal GC 0-29.6% (median 2.1%)
 - Rectal CT 3-77.3% (median 8.7%)
 - Pharyngeal CT 0.2-3.2% (median 1.7%)
- Conclusions:
 - Extragenital screening can increase detection of GC/CT from 6-50% compared with urine alone



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Sexual history taking Shared decision making



Treatment Guidelines - Chlamydia

Preferred

Alternative

Doxycycline 100 mg PO twice daily x 7 days

Azithromycin 1g orally once*

*Preferred during pregnancy **Pregnancy alternative: Amoxicillin 500mg orally 3 times per day for 7 days

OR

Levofloxacin 500mg orally x 7 days





Genitourinary infection

 Microbiologic failure higher among men

Rectal infection

- Doxycycline superior to azithromycin (20%-26%)
- Rectal infection not uncommon among women with genitourinary infection (33%-83%)





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Genitourinary infection

 Microbiologic failure higher among men

Rectal infection

- Doxycycline superior to azithromycin (20%-26%)
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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Azithromycin versus Doxycycline for Urogenital Chlamydia trachomatis Infection

William M. Geisler, M.D., M.P.H., Apurva Uniyal, M.A., Jeannette Y. Lee, Ph.D., Shelly Y. Lensing, M.S., Shacondra Johnson, B.S.P.H., Raymond C.W. Perry, M.D., M.S.H.S., Carmel M. Kadrnka, D.O., and Peter R. Kerndt, M.D., M.P.H.

- Efficacy of azithromycin was 97%
- Efficacy of doxycycline was 100%
- Non-inferiority of azithromycin was not established



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Genitourinary infection

 Microbiologic failure higher among men

Rectal infection

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- Doxycycline superior to azithromycin (20%-26%)
- Rectal infection not uncommon among women with genitourinary infection (33%-83%)

Clinical Infectious Diseases

MAJOR ARTICLE



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

Julia C. Dombrowski,¹² Michael R. Wierzbicki,³ Lori M. Newman,⁴ Jonathan A. Powell,³ Ashley Miller,⁵ Dwyn Dithmer,² Olusegun O. Soge,⁶ and Konneth H. Mayer²⁴

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Azithromycin or Doxycycline for Asymptomatic Rectal *Chlamydia trachomatis*

7-day course of doxycycline was significantly

Dor more Weffective than a cisingle here of azithromycin Treatment of Rectal Chlamydia in Men Who Have Sex With Men. A gradomized Controlled Tral. Clin

Infect Dis. 2021;73(5):824-831. doi:10.1093/cid/ciab153

Lau A, Kong FYS, Fairley CK, et al. Azithromycin or Doxycycline for Asymptomatic Rectal *Chlamydia trachomatis*. *N Engl J Med*. 2021;384(25):2418-2427. doi:10.1056/NEJMoa2031631



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Genitourinary infection

 Microbiologic failure higher among men

Rectal infection

NITIM RIA

- Doxycycline superior to azithromycin (20%-26%)
- Rectal infection not uncommon among women with genitourinary infection (33%-83%)

Doxycycline versus azithromycin for the treatment of anorectal @ *Chlamydia trachomatis* infection in women concurrent with vaginal infection (CHLAZIDOXY study): a multicentre, open-label, randomised, controlled, superiority trial

Olivia Peuchant, Edouard Lhomme, Pervenche Martinet, Anne Grob, Dounia Batta, Claire Bernier, Sophie Anne Gibaud, Isabelle Le Hen, Erwan Le Naour, Nathalie Trignol-Viguier, Philippe Lanotte, Philippe Lefebvre, Anne Vachée, Thomas Girard, Julien Loubinoux, Cécile Bébéar, Bellabes Ghezzoul, Caroline Roussillon, Marion Kret, Bertille de Barbeyrac, and the CHLAZIDOXY Study Group*



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Azithromycin vs Doxycycline



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Ease

Access

 Only 57.7% (95%Cl, 50.9-64.5) of adolescents with STI diagnosis in an ED filled their prescription

Adherence

 Studies suggest doxycycline self-reported adherence 60%-90%

Confidentiality

Side Effect Profile



Azithromycin vs Doxycycline



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Indications for Azithromycin

- Pregnant or may be pregnant
- History of allergy or intolerance to doxycycline
- Unlikely to be adherent
- Unlikely to be able to obtain doxycycline and azithromycin is available at point of care



Chlamydia Shared Decision Making



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Chlamydia Follow-up



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What Did We Do For Jill?

Prescription Pad Dr. Z Sexual Health Clinic			
Doxycycline 100mg PO Q12 x 7 days			
HIV testing			
Hepatitis C Ab testing			
3 Site GC/CT testing			
Syphilis Testing			
HIV prevention counseling and offer of services			
Pregnancy testing, counseling and services			





Sally has a discharge





The college roommate text... help....



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Vaginitis: itching, burning, irritation, odor, and discharge

#1 Bacterial vaginosis:

May be considered an STI based on new study showing treatment of partners leads to less recurrences.*

Dysbiosis resulting from replacement of normal lactobacillus in the vagina with other anaerobic bacteria such as *Gardnerella vaginalis*, *prevotella*, *mobiluncus*

Asymptomatic pregnant women should not be screened -> no data on risk to fetus or pregnancy

Risk factors:

multiple sex partners

female partners

douching

Copper IUD





Diagnosing Bacterial Vaginosis

BV Diagnostic Scores

- Nugent score (#) (from vaginal gram stain of the concentration of organisms (0-3 normal)
 - # > 4 consistent with Gardnerella; #
 >6= BV
- Amsel's Clinical criteria (3 out of 4 below)
 - Milk-like discharge, Clue cells (e.g., vaginal epithelial cells studded with adherent bacteria), pH of vaginal fluid >4.5, fishy odor of vaginal discharge before or after addition of 10% KOH (i.e., the whiff test)

Near and Point of Care Testing

- Point of Care testing
 - Osom BV Blue test (detects vaginal sialidase activity)
 - Affirm VP III- detects Gardnerella (most useful in those with symptoms)
 - FemExam Test Card- measures vaginal pH, and other aminopeptidases in Gardnerella
- NAAT testing- high sensitivity and specificity
 - Max Vaginal Panel, Aptima BV- FDA cleared
 - NuSwabVG, OneSwab BV panel PCR and SureSwab BV



Bacterial Vaginosis

Risks and Sequelae

- High likelihood of recurrence
- Can complicate GYN surgeries
- May increase risk of other STIs (MG, HSV2, and HPV)
- Certain BV associated bacteria may increase HIV susceptibility
 - Prevotella bivia, Leptotrichia/Sneathia, Parvimonas 1&2, M. hominis, Eggerthella spp.

Prevention and Protection

- male circumcision
- condom use
- lack of sexual activity
- hormonal contraception
- probiotics (Cohen, et al. NEJM 2020; 382: 1906-15) Lactin-V to prevent recurrence



Treatment of BV

Recommended Regimens for Bacterial Vaginosis

- Metronidazole 500 mg orally 2 times/day for 7 days
- OR
- Metronidazole gel 0.75% one full applicator (5 g) intravaginally, once a day for 5 days OR
- Clindamycin cream 2% one full applicator (5 g) intravaginally at bedtime for 7 days (preferred for allergy)

Alternative Regimens

- PO options:
 - Clindamycin 300 mg orally 2 times/day for 7 days (preferred for allergy)
 - Secnidazole 2 g oral granules in a single dose (53% cure rate)
 - Tinidazole 2 g orally once daily for 2 days or Tinidazole 1 g orally once daily for 5 days
- Suppository options:

Clindamycin ovules 100 mg* intravaginally once at bedtime for 3 days (may weaken latex)

NEW: SINGLE DOSE: metronidazole 1.3% gel and Clindesee 2% vaginal cream (37% cure rate)

Bacterial Vaginitis Vodstrcil, L. etal

N Engl J Med 2025;392:947-957

Kaplan-Meier Curves for Time to recurrence of BV (Mod ITT population)



- Prevalence: college students (5-25%) and 12-61% of STI patients
- Treatment response: 30-60%
- Diagnostics:
 - Wet mount: clue cells- Amsel criteria
 - CLIA waived POC testing vaginal sialidase activity
 - BV NAAT
- Screening: symptomatic women, female partners of women with BV, women prior to surgical abortion
- Treatment:
 - Metronidazole 500 mg orally twice a day for 7 days, OR
 - Metronidazole gel 0.75%, one full applicator x 5 days OR
 - Clindamycin cream 2%, one full applicator x 7 days
 - <u>Alternative treatmen</u>t: clindamycin 300mg 2 times/day x 7 days, secnidazole 2 gm single dose, tinidazole 2 gm daily x 2 days or tinidazole 1 gm daily x 5 days or clindamycin 100mg ovules vaginally x 3 days



Treatment of male partners with metronidazole 400mg BID and clindamycin cream BID lead to fewer recurrences of BV within 12 weeks. The trial was stopped early.

More Vaginal Discharge: Trichomonas

- Why is it important:
 - Meta-analysis OB outcomes associated with trichomonas
 - PROM 1.4, preterm birth 1.4, endometritis 2.2, HIV acquisition 1.5
- Testing
 - Asymptomatic- many and screening only for women in correctional facility
 - Symptoms: Testing done
 - Men: urethritis, epididymitis, prostatitis; persistent symptoms (MSW)
 - Women: malodorous discharge; strawberry cervix
- Re-testing
 - Persistent infection (resistance testing + combination therapy)
 - Clearance by NAAT up to 3 weeks



Trichomoniasis: Diagnostic comparisons

Nucleic Acid Amplification Tests

 can order on same GC/CT specimen
 Sens/Spec :88-100%, 97-99.9%

Point-of-care tests

- OSOM trichomonas rapid antigen test (Genzyme)
- Affirm VP III (BD)

OSOM **Sens/**Spec: **67-100%**, 92-100% Affirm VP **Sens**/Spec: **~63 %**

Sens/Spec: 75-95%, 100%

Saline Wet Mount

- Motile trichomonads
- pH >4.5
- Whiff test may be +

Sens/Spec: **36-70**%, ~100%

Culture

- Diamond's
- InPouch TV, BioMed Diagnostics

Diagnosis: NAAT

- vaginal discharge and women with HIV;
- Men
 - consider testing (high prevalence settings, high risk of infection)

Miller & Nyirjesy, Curr Infect Dis Rep 2011

Schwebke, JCM 2011

APHL, Advances in Laboratory Detection of T. Vaginalis (Updated) 2016

Trichomonas Treatment

Preferred Regimen For Women

Metronidazole 500mg twice daily for 7 days

Preferred Regimen For Men

•Metronidazole 2g once

ALTERNATIVE Regimen

Tinidazole 2g x 1

Regimens for TV Persistence

- Metronidazole or tinidazole 2 g daily x 7 days
- Tinidazole 2 g daily + intravaginal tinidazole
 500mg 2 times/day x 14 days
- Tinidazole 1 g 3 times/day + intravaginal paromomycin (4 g of 6.25% intravaginal paromomycin cream nightly) x 14 days

NEW Treatments

Trichomonas Treatment

Metronidazole 500 mg PO x 1 vs 7 days

Single-dose versus 7-day-dose metronidazole for the treatment of trichomoniasis in women: an open-label, randomised controlled trial

Patricia Kissinger, Christina A Muzny, Leandro A Mena, Rebecca A Lillis, Jane R Schwebke, Laura Beauchamps, Stephanie N Taylor, Norine Schmidt, Leann Myers, Peter Augostini, William E Secor, Martina Bradic, Jane M Carlton, David H Martin

- Multicenter, open-label, randomized controlled trial (2014-2017 published 2018)
- Block randomization
- 632 women enrolled
- Primary outcome was infection at test-of-cure 4
 weeks after completion of treatment
- Patients in the 7-day-dose group were less likely to be positive at test-of-cure than those in the single-dose group 11% vs 19%
 - Relative risk 0.55, 95% CI 0.34–0.70; p < 0.0001



Construction

NEW Treatments

Vulvovaginal Candidiasis (VVC)

- Non specific symptoms: dysuria, pruritis, dyspareunia, vaginal discharge
- 75% of women will have at least one episode

Uncomplicated	Complicated
Sporadic or infrequent	Recurrent (> 3 episodes per year)
Mild to moderate VVC	Severe
Likely candida albicans	Non- albicans
Non- immunocompromised women	Women with diabetes, immune compromise (HIV), immunodeficiency, or on steroids



Vulvovaginal Candidiasis

- Testing
 - Wet prep, saline, 10% KOH- to see budding yeast or
 - hyphae on microscope
 - Culture remains standard (susceptibility testing)
 - *C. albicans* azole resistance more common
 - PCR testing for yeast- most not FDA cleared
- Recurrent VVC (≥3 episodes/year) large economic burden
 - Fluconazole (100-mg, 150-mg, 200-mg oral dose) weekly for 6 months







VVC Treatment: Uncomplicated Infection

- Over the counter agents (clotrimazole, miconazole, etc)
- Prescription intravaginal applications (oil based and weaken condoms)
 - Butoconazole 2% cream (single dose), 5 g
 - Terconazole 0.4% cream; 5 g daily x 7 days
 - Terconazole 80mg vaginal suppository daily x 3 days
- Prescription orals
 - Fluconazole 150 mg oral single dose



VVC Treatment: Complicated Infection

- 7-14 days of topical or every 3rd day for 3 doses (Day 1,4,7)
- Recurrent VVC (≥3 episodes/year) large economic burden- for prevention
 - Fluconazole (100-mg, 150-mg, 200-mg oral dose) weekly for 6 months
- Fluconazole use in pregnancy
 - Increase risk of congenital anomalies
 - Spontaneous abortion

Molgaard-Neilsen. JAMA 2016: 315: (1): 58-67.

- Retrospective study, Denmark; nationwide registry 1997-2013
- 1,405,663 pregnancies; fluconazole exposed at weeks 7-22 in pregnancy
- 1:4 Oral fluc vs unexposed- match on propensity score, maternal age, year, gestational age
- Increased risk for spontaneous abortion in exposed group:
 - HR 1.48; 95% CI, 1.23-1.77
 - 147 out of 3315 women exposed vs 563 out of 13,246 unexposed women
- No impact on still births



Case #3: BB has pain

- BB presents with dysuria and abdominal pain 2 months after having CT infection
- Exam with cervical motion tenderness consistent with mild PID





Cervicitis→ Concern for PID due to symptoms

- Mild to moderate pelvic inflammatory disease (PID). No new information on the definition of this condition.
- Clinical diagnostic criteria (minimum 3 criteria)
 - Temperature >38.3C
 - Abnormal mucopurulent cervical discharge
 - WBC in vaginal saline microscopy (wet prep)
 - Elevated ESR and CRP
 - + test for GC/CT





PID Treatment





PID Treatment

NEW Treatments

Clinical Infectious Diseases MAJOR ARTICLE



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

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(See the Editorial Commentary by Mitchell on pages 1190-91.)

Background. Anaerobic organisms are important pathogens in acute pelvic inflammatory disease (PID). The currently recommended PID regimen of a single dose of ceftriaxone and doxycycline for 14 days has limited anaerobic activity. The need for broader anaerobic coverage is unknown and concerns have been raised about metronidazole tolerability.

Methods. We conducted a randomized, double-blind, placebo-controlled trial comparing ceftriaxone 250 mg intramuscular single dose and doxycycline for 14 days, with or without 14 days of metronidazole in women with acute PID. The primary outcome was clinical improvement at 3 days following enrollment. Additional outcomes at 30 days following treatment were the presence of anaerobic organisms in the endometrium, clinical cure (absence of fever and reduction in tenderness), adherence, and tolerability,

Results. We enrolled 233 women (116 to metronidazole and 117 to placebo). Clinical improvement at 3 days was similar between the 2 groups. At 30 days following treatment, anaerobic organisms were less frequently recovered from the endometrium in women treated with metronidazole than placebo (8% vs 21%, P < .05) and cervical Mycoplasma genitalium was reduced (4% vs 14%, P < .05). Pelvic tenderness was also less common among women receiving metronidazole (9% vs 20%, P < .05). Adverse events and adherence were similar in each treatment group.

Conclusions. In women treated for acute PID, the addition of metronidazole to ceftriaxone and doxycycline was well tolerated and resulted in reduced endometrial anaerobes, decreased M. genitalium, and reduced pelvic tenderness compared to ceftriaxone and doxycycline. Metronidazole should be routinely added to ceftriaxone and doxycycline for the treatment of women with acute PID.

Clinical Trials Registration. NCT01160640. Keywords. pelvic inflammatory disease; anaerobes; metronidazole.

- Double-blind placebo-controlled trial •
- 233 cis-females •
- Outcomes: Symptom improvement at 3 • days and presence of anaerobic organisms in the endometrium
- Findings at Day 30 post treatment • WITH metronidazole vs. placebo:
 - Endometrial anaerobes reduced (8% vs • 21%, P < .05)
 - Pelvic tenderness less common (9% vs 20%, • P < .05)
- Decreased cervical M. genitalium (4% vs Wiesenfeld HC, Meyn LA, Darville T, Macjo IS, Hillier SL, A Randomized Controlled Trial of Ceftriaxone and Daxy opcline, With Gravit Pout

Metronidazole, for the Treatment of Acute Pelvic Inflammatory Disease. Clin Infect Dis. 2021 Apr SUMIAL-AQVERSE EVENTS 10.1093/cid/ciaa101. PMID: 32052831; PMCID: PMC8028096.



Summary: what's new for vaginitis and PID

- Bacterial vaginosis:
 - <u>Single dose regimens for non-pregnant women</u> (secnidazole 2 g oral, metro gel & clindesse cream)
 - No data linking nitroimidazole and alcohol adverse effect
- Trichomonas:
 - Test out option for women in correctional facilities
 - Treatment for <u>7 days recommended (males still have single dose treatment option)</u>
- Candida
 - Review PCR treatment options (may not be FDA cleared yet)
 - Review data on fluconazole and spontaneous abortions (first trimester data)
- PID:
 - No new data refining diagnosis

Treatment includes <u>metronidazole</u> and clindamycin/gent demoted to alternative regimen

NYC STI Prevention Training Center (PTC)

The CDC-funded NYC STD Prevention Training Center at Columbia University provides a continuum of education, resources, consultation and technical assistance to health care providers, and clinical sites. https://www.publichealth.columbia.edu/nycptc

Didactic Presentations

Webinars, conferences, trainings and grand rounds presentations to enhance and build knowledge

Technical Assistance

Virtual and on-site technical assistance regarding quality improvement, clinic implementation and best practices around sexual health provision

For more information please contact: nycptc@cumc.columbia.edu

Clinical Consultation Warmline

Clinical guidance regarding STD cases; no identifying patient data is submitted www.stdccn.org

Resources

Clinical guidance tools regarding the STD treatment guidelines, screening algorithms and knowledge books, such as the **Syphilis**

Monograph.

To download a copy:

https://www.publichealth.columbia.edu/file/15 568/download?token=exDNYpJ-



