STI Cases

Presenters:

Jason Zucker, MD, MS & Natalie Neu, MD, MPH

Panelists:

Daniela DiMarco MD, MPH

Christine Heumann, MD, MPH

Gretchen Newman, MD

PTC Disclaimer

Some terms in this presentation may have been modified to align with executive order requirements that this CDC-funded grant has received.

Meet Trent

- Trent is a 22 year old male who is a long-time patient of our sexual health program
- Has been on HIV PrEP for the past 5 years, recently switched to LAI with Lenacapavir
  - Has had gonorrhea, chlamydia, and syphilis in the past 2 years
  - Started doxy-PEP 6 months ago
- He walks into sexual health clinic with generalized, intensely itchy rash on abdomen & extremities.
  - Onset: 5 days prior
- Social history: 6 new partners since his last visit

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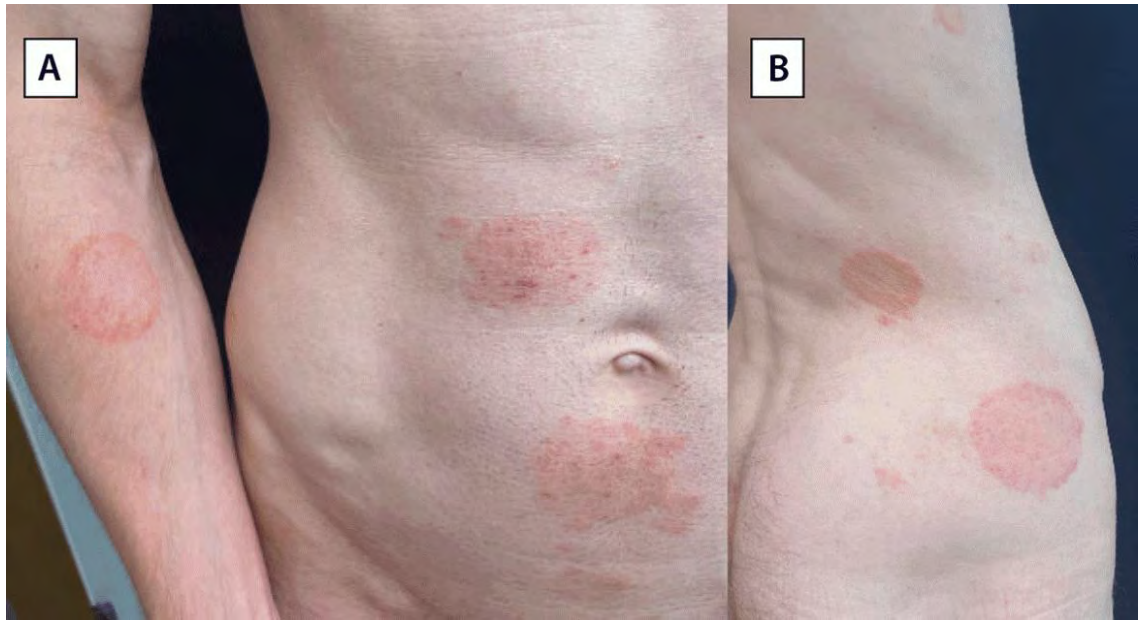

- Similar lesions on his buttocks and genitals

What is Your Differential Diagnosis?

Emerging Infections - Dermatophytes

- **Common Ringworm (Tinea/Dermatophytosis)**
  - Traditionally mild and treatable with standard antifungals
  - Increasing global reports of severe (inflammatory), hard-to-treat cases
  - Emergence of antifungal-resistant strains complicating treatment

Emerging Infections - Dermatophytes

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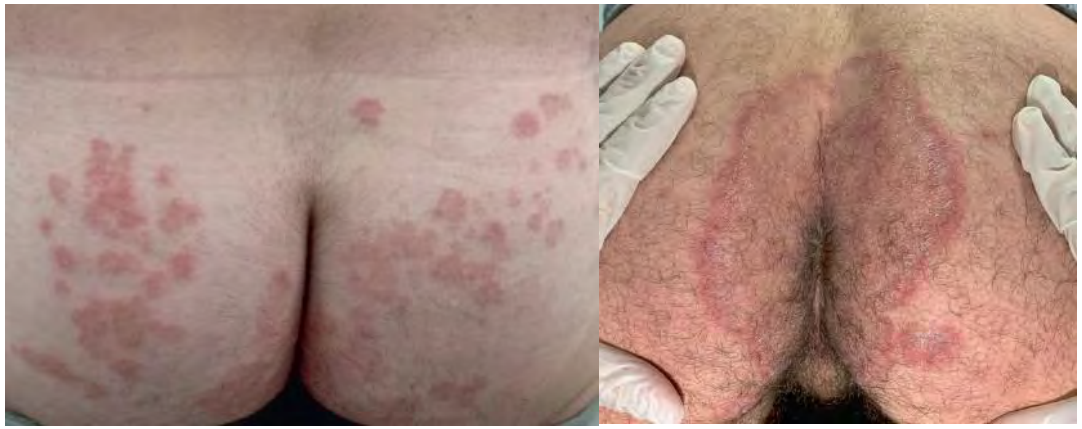
- **Three strains being reported in the US**
  - *Trichophyton indotineae*
  - ***Trichophyton mentagrophytes* genotype type VII**
  - Terbinafine-resistant *Trichophyton rubrum*

Trichophyton mentagrophytes genotype VII (TMVII)

Trichophyton mentagrophytes Genotype VII and Sexually Transmitted Tinea: An Observational Study in Spain

Vicente Descalzo[1,2] | María Teresa Martín[3] | Patricia Álvarez-López[2] | Jorge Néstor García-Pérez[2] | Laura Alcázar-Fuoli[4] | Luis López-Pérez[2] | David Téllez-Velasco[2] | Antonio Carrillo[2] | Elena Sulleiro[3] | Vicenç Falcó[1,2] | Maider Arando[1,2]

[1]Doctoral Programme in Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain | [2]Infectious Diseases, STI/HIV Unit, Hospital Vall d'Hebron, Barcelona, Spain | [3]Department of Microbiology, Hospital Vall d'Hebron, Barcelona, Spain | [4]Mycology Reference Laboratory, Instituto de Salud Carlos III, National Centre for Microbiology, Madrid, Spain



TMVII in Spain (2020–2025)

- 14 confirmed TMVII cases at a Barcelona STI clinic
- All men who have sex with men
- Many HIV-positive (7) or on PrEP (6)
- Frequent STI coinfection (gonorrhea, syphilis, chlamydia, mpox)
- Common sites: pubogenital, buttocks/perianal, beard
- 21 antifungal courses analyzed
  - Oral terbinafine: 45% cure (5/11)
  - Short courses (≤2 weeks): 0% cure
  - Longer courses (3–8 weeks): 80% cure ($p<0.01$)
- Recurrences common without prolonged therapy

Descalzo V, Martín MT, Álvarez-López P, et al. Trichophyton mentagrophytes Genotype VII and Sexually Transmitted Tinea: An Observational Study in Spain. *Mycoses*. 2025;68(4):e70049. doi:10.1111/myc.70049

Trichophyton mentagrophytes genotype VII (TMVII)

Sexually Transmitted *Trichophyton mentagrophytes* Genotype VII Infection among Men Who Have Sex with Men

Arnaud Jabet, Sarah Dellière, Sophie Seang, Aziza Chermak, Luminita Schneider, Thibault Chiarabini, Alexandre Teboul, Geoffroy Hickman, Alizée Bozonnat, Cécile Brin, Marion Favier, Yanis Tamzali, François Chasset, Stéphane Barete, Samia Hamane, Mazzouz Benderdouche, Alicia Moreno-Sabater, Eric Dannaoui, Christophe Hennequin, Arnaud Fekkar, Renaud Piarroux, Anne-Cécile Normand, and Gentiane Monsel

Author affiliations: Assistance Publique-Hôpitaux de Paris, Paris, France (A. Jabet, S. Dellière, S. Seang, A. Chermak, L. Schneider, T. Chiarabini, A. Teboul, G. Hickman, A. Bozonnat, C. Brin, M. Favier, Y. Tamzali, F. Chasset, S. Barete, S. Hamane, M. Benderdouche, A. Moreno-Sabater, E. Dannaoui, C. Hennequin, A. Fekkar, R. Piarroux, A.-C. Normand, G. Monsel); Université de Paris, Paris, France (S. Dellière, E. Dannaoui); Sorbonne Université, Paris, France (F. Chasset, A. Moreno-Sabater, C, Hennequin, A. Fekkar, R. Piarroux)

Main Article

Figure

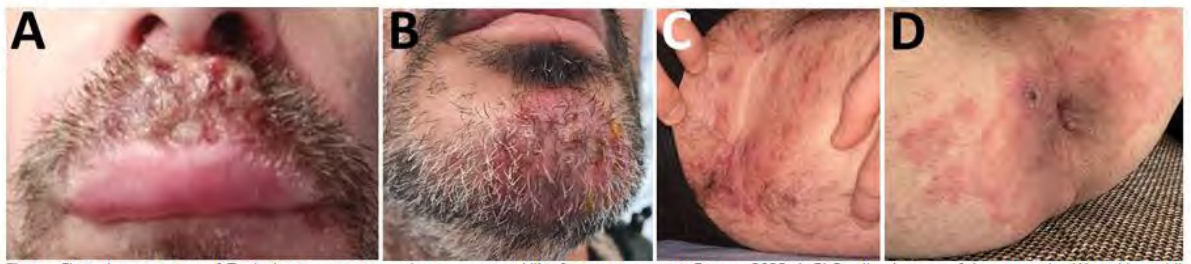


Figure. Clinical appearance of *Trichohpyton mentagrophytes* genotype VII infections in men in France, 2022. A, B) Swollen lesions of the mustache (A) and beard (keric with associated papules and pustules with central umbilication and a large lesion with a central necrotic crust, surrounded by extensive erythemato-squamous circina

TMVII in France (2021–2022)

- 13 confirmed cases reported in France (2021–2022), all men (12 MSM)
- Common sites: genitals, buttocks, and face
- Frequently misdiagnosed as bacterial infection or other STI
- Often co-diagnosed with other STIs
- Not linked to animal exposure — distinct from other T. mentagrophytes
- Transmission consistent with sexual contact

Jabet A, Dellière S, Seang S, et al. Sexually Transmitted Trichophyton mentagrophytes Genotype VII Infection among Men Who Have Sex with Men. *Emerg Infect Dis*. 2023;29(7):1411-1414. doi:10.3201/eid2907.230025

Trichophyton mentagrophytes genotype VII (TMVII)

First U.S. TMVII Cases – NYC (2024)

- 5 confirmed NYC cases (April–July 2024)-
- All men with recent sexual contact with men
- Sites: face, buttocks, groin, penis
- Initially misdiagnosed as eczema or psoriasis

- Zucker J, Caplan AS, Gunaratne SH, et al. Notes from the Field: Trichophyton mentagrophytes Genotype VII - New York City, April-July 2024. MMWR Morb Mortal Wkly Rep. 2024;73(43):985-988. Published 2024 Oct 31. doi:10.15585/mmwr.mm7343a5

Trichophyton indotineae

First U.S. *T. indotineae* Cases

- First U.S. cases: 2 women (NYC, 2021–2023)
- Severe, widespread tinea; both terbinafine-resistant
- One with no travel history → local transmission
- Origin: South Asia, epidemic linked to steroid misuse
- Highly transmissible; often sexually or household-associated

Caplan AS, Chaturvedi S, Zhu Y, et al. Notes from the Field: First Reported U.S. Cases of Tinea Caused by Trichophyton indotineae - New York City, December 2021-March 2023. *MMWR Morb Mortal Wkly Rep*. 2023;72(19):536-537. Published 2023 May 12. doi:10.15585/mmwr.mm7219a4

Trichophyton indotineae

Potential Sexual Transmission of Antifungal-Resistant *Trichophyton indotineae*

Stephanie Spivack, Jeremy A.W. Gold, Shawn R. Lockhart, Priyanka Anand, Laura A.S. Quilter, Dallas J. Smith, Briana Bowen, Jane M. Gould, Ahmed Eltokhy, Ahmed Gamal, Mauricio Retuerto, Thomas S. McCormick, Mahmoud A. Ghannoum

Author affiliations: Temple University Hospital Section of Infectious Diseases, Philadelphia, Pennsylvania, USA (S. Spivack); Centers for Disease Control and Prevention, Atlanta, Georgia, USA (J.A.W. Gold, S.R. Lockhart, P. Anand, L.A.S. Quilter, D.J. Smith); Department of Public Health, Philadelphia (B. Bowen, J.M. Gould); Center for Medical Mycology, Case Western Reserve University and University Hospitals Cleveland Medical Center, Cleveland, Ohio, USA (A. Eltokhy, A. Gamal, M. Retuerto, T.S. McCormick, M.A. Ghannoum)

DOI: https://doi.org/10.3201/eid3004.240115

We describe a case of tinea genitalis in an immunocompetent woman in Pennsylvania, USA. Infection was caused by *Trichophyton indotineae* potentially acquired through sexual contact. The fungus was resistant to terbinafine (first-line antifungal) but improved with itraconazole. Clinicians should be aware of *T. indotineae* as a potential cause of antifungal-resistant genital lesions.

Case:

- Healthy young woman
- Acquired infection after sexual contact abroad.
- Lesions involved genitals, buttocks, and thighs

Spivack S, Gold JAW, Lockhart SR, et al. Potential Sexual Transmission of Antifungal-Resistant Trichophyton indotineae. *Emerg Infect Dis*. 2024;30(4):807-809. doi:10.3201/eid3004.240115

What tests would you consider doing?

Diagnosis of Dermatophytes

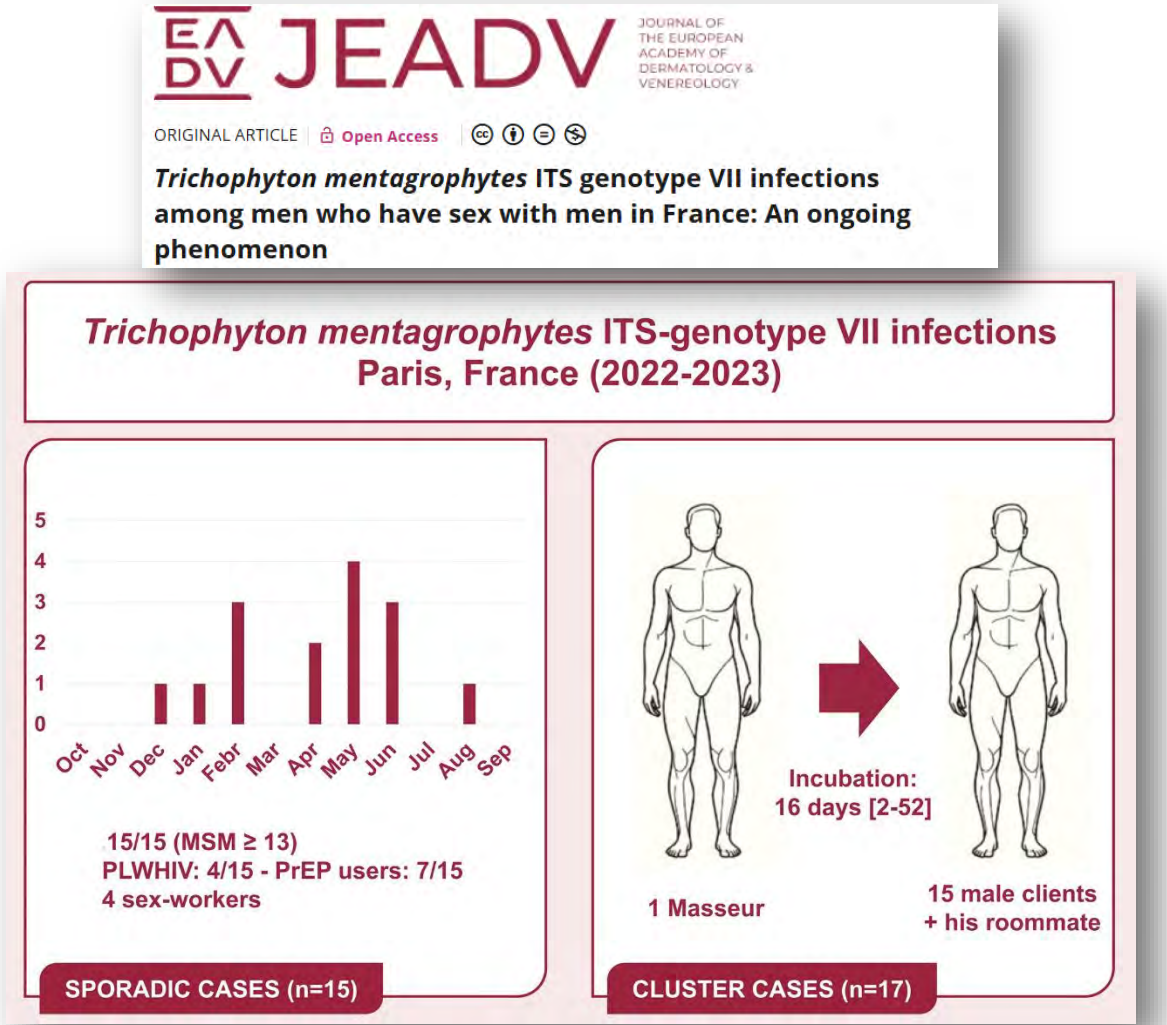
Diagnosis

- **Clinical**: annular, scaly, pruritic plaques (genitals, buttocks, face, torso)
  - Often misdiagnosed as eczema, psoriasis, bacterial infection, or STI rash
- **Point-of-care**: KOH prep (hyphae), fungal culture (slow, may mis-ID)
- **Definitive**: Culture then DNA sequencing (ITS region) to distinguish TMVII vs *T. indotineae*

Poll: What (if any) treatment would you provide at this time?

1. Fluconazole
2. Terbinafine
3. Itraconazole
4. Topical antifungal
5. No treatment at this time

Trichophyton mentagrophytes genotype VII (TMVII)



- 32 cases reported in Paris (Oct 2022–Sept 2023)
- 30 MSM; 4 sex workers
- 17 cases linked to one tantric masseur (15 clients + 1 roommate)
- Lesions: genitals, buttocks, face; frequent STI coinfections
- **Oral terbinafine used in almost all cases; topical therapy alone led to failure**
- **Some remained culture-positive 3–4 weeks into treatment**
- Median incubation: 16 days (range 2–52)-
- Contagiousness may persist during incubation and treatment

- Jabet A, Bérot V, Chiarabini T, et al. Trichophyton mentagrophytes ITS genotype VII infections among men who have sex with men in France: An ongoing phenomenon. *J Eur Acad Dermatol Venereol*. 2025;39(2):407-415. doi:10.1111/jdv.20439

Treatment of Dermatophytes

Treatment

- **TMVII**: usually susceptible to terbinafine; itraconazole as alternative
- **T. indotineae**: often terbinafine-resistant → itraconazole (longer courses, absorption & interaction challenges)
- **Course**: prolonged oral therapy (weeks–months) + topical antifungals
- **Avoid**: corticosteroid creams (worsen infection, cause “tinea incognito”)
- **Partner management**: consider STI-style contact tracing, test/treat partners

Trent

- He was started on fluconazole empirically but switched to terbinafine when he failed to improve over 2 weeks
- Trent's culture grew TM VII
- He completed 8 weeks of Terbinafine with resolution of his lesions

Treatment of Dermatophytes

- **Sexual transmission as a novel route for traditionally non-STI pathogens (dermatophytes).**
  - Circulating in MSM networks across Europe & U.S.
- **Outbreak potential:**
  - Large cluster in Paris linked to tantric masseur
  - Surveillance should adapt to **non-viral, non-bacterial pathogens (i.e. fungal culture)** in sexual health.
- **Transmission dynamics:**
  - Prolonged incubation
  - Contagious even pre-symptom & during treatment
- **Treatment:**
  - TMVII: terbinafine usually effective; itraconazole alternative
  - T. indotineae: often terbinafine-resistant use itraconazole
  - Short courses fail; **prolonged systemic antifungals required (≥3–6 weeks)**
- **Why it matters:**
  - Risk of recurrence, misdiagnosis, spread through sexual and intimate contact
  - Need for STI-style partner management

Julie

- Julie is a 30-year-old woman who presents to urgent care.
- She presents with one-week of thin, white vaginal discharge, and vaginal itching.
- No pelvic pain, genital ulcers or erythema, or systemic symptoms.
- Has a prior history of bacterial vaginosis 2 months ago and thought this might be a recurrence.

Julie

- Sexual Hx:
  - 1 primary male partner
  - 1 new male sex partner
  - Uses condoms consistently with new partners only

What is Your Differential Diagnosis and Work-Up?

Julie

- The multiplex PCR panel comes back:
  - GC/CT – negative
  - Trichomoniasis – negative
  - **Bacterial vaginosis – positive**
  - **Mycoplasma Genitalium – positive**
  - Mycoplasma hominis – negative
  - **Ureaplasma - positive**

What treatment(s) would you offer Julie?

Mycoplasma Genitalium

Characteristics of *Mycoplasma genitalium* Urogenital Infections in a Diverse Patient Sample from the United States: Results from the Aptima *Mycoplasma genitalium* Evaluation Study (AMES)

Lisa E. Manhart,[a,b,c] Charlotte A. Gaydos,[d] Stephanie N. Taylor,[e] Rebecca A. Lillis,[e] Edward W. Hook III,[f,g,h] Jeffrey D. Klausner,[i] Carmelle V. Remillard,[j] Melissa Love,[j] Byron McKinney,[j] Damon K. Getman,[j] on behalf of the AMES Clinical Study Group

TABLE 2 Prevalence of urogenital *M. genitalium* infection in participants reporting symptoms of urogenital sexually transmitted infection and association with symptoms

	M. genitalium infection prevalence			
	Female (n = 1,737)		Male (n = 1,563)	
Patient-reported urogenital symptoms[a]	n/N[b] (%)	OR[c] (95% CI)	n/N (%)	OR[c] (95% CI)
Any reported symptom	122/1,053 (11.6)	1.53 (1.09, 2.14)	104/866 (12.0)	1.42 (1.02, 1.99)
Pain/discomfort in groin or lower belly	17/159 (10.7)	1.07 (0.63, 1.81)	12/149 (8.1)	0.72 (0.39, 1.33)
Pain/burning/discomfort during urination	18/125 (14.4)	1.55 (0.92, 2.62)	39/358 (10.9)	1.05 (0.72, 1.53)
Pain/discomfort during sexual intercourse	11/106 (10.4)	1.03 (0.54, 1.96)	8/65 (12.3)	1.20 (0.48, 2.59)
Genital blisters/sores/bumps/rash/warts	7/69 (10.1)	1.00 (0.38, 2.24)	9/94 (9.6)	0.89 (0.39, 1.82)
Abnormal vaginal odor	65/445 (14.6)	1.82 (1.31, 2.52)		
Vaginal/vulvar itching or irritation	51/429 (11.9)	1.28 (0.90, 1.80)		
Abnormal vaginal bleeding	4/63 (6.3)	0.59 (0.15, 1.63)		
Abnormal vaginal discharge	90/692 (13.0)	1.67 (1.22, 2.28)		
Penile/urethral discharge			56/275 (20.4)	2.77 (1.94, 3.94)
Burning/itching around opening of penis			22/269 (8.2)	0.72 (0.45, 1.15)
Itching/tingling on the inside of penis			13/175 (7.4)	0.65 (0.36, 1.18)

- The overall prevalence of M. genitalium infection was 10.3%
- Prevalence was roughly similar in men and women: 10.1% in women and 10.6% in men

- Manhart LE, Gaydos CA, Taylor SN, Lillis RA, Hook EW 3rd, Klausner JD, Remillard CV, Love M, McKinney B, Getman DK. Characteristics of Mycoplasma genitalium Urogenital Infections in a Diverse Patient Sample from the United States: Results from the Aptima Mycoplasma genitalium Evaluation Study (AMES). J Clin Microbiol. 2020 Jun 24;58(7):e00165-20. doi: 10.1128/JCM.00165-20. PMID: 32321783; PMCID: PMC7315021.

Julie

- Julie gets treatment for BV with metronidazole 500mg twice daily x 7 days and M. Gen with Doxycycline 100mg twice daily x 7 days followed by moxifloxacin 400mg twice daily

Poll: Would you offer her partner treatment?

1. Yes, for both M. Gen and BV
2. Yes, for M. Gen
3. Yes, for BV
4. No, I would not offer her partner treatment

BV and Partner Treatment

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 6, 2025 VOL. 392 NO. 10

Male-Partner Treatment to Prevent Recurrence of Bacterial Vaginosis

Lenka A. Vodstrcil, Ph.D.,[1-3] Erica L. Plummer, Ph.D.,[1,2] Christopher K. Fairley, Ph.D.,[1,2] Jane S. Hocking, Ph.D.,[3] Matthew G. Law, Ph.D.,[4] Kathy Petoumenos, Ph.D.,[4] Deborah Bateson, M.D.,[5] Gerald L. Murray, Ph.D.,[6-8] Basil Donovan, M.D.,[4] Eric P. F. Chow, Ph.D.,[1-3] Marcus Y. Chen, Ph.D.,[1,2] John Kaldor, Ph.D.,[4] and Catriona S. Bradshaw, Ph.D.,[1-3] for the StepUp Team*

- Bacterial vaginosis (BV) affects ~30% of reproductive-aged women globally.
- High recurrence rates (>50% within 3 months) following standard female-only treatment.
- Mounting evidence suggests sexual transmission via male partners contributes to recurrence.
- **Study Objective:** Assess whether treating male partners reduces BV recurrence in women.

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- Open-label RCT in Australia (StepUp trial).
- 164 couples randomized:
  - Partner-treatment group: Woman + male partner treated (oral metronidazole + topical clindamycin).
  - Control group: Woman treated, male partner untreated.
- Primary outcome: BV recurrence within 12 weeks.

Results

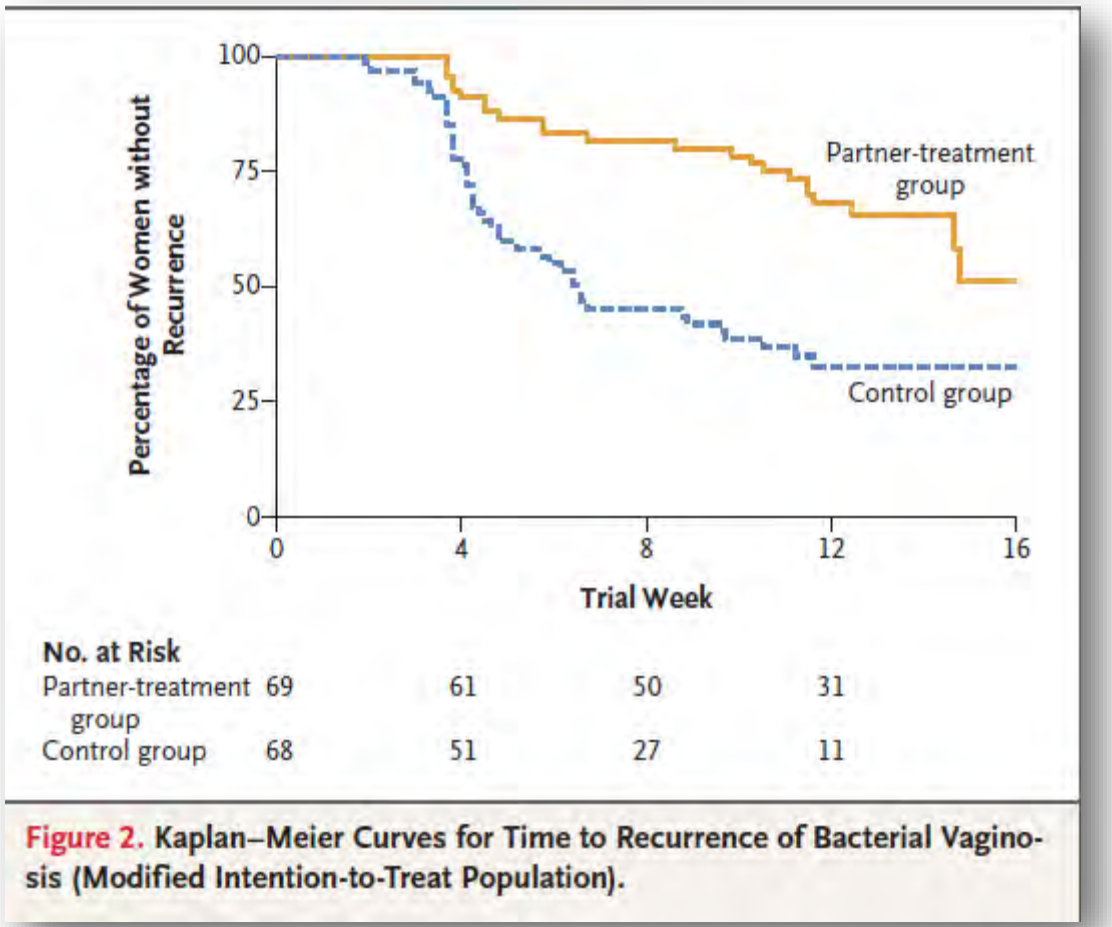


Figure 2. Kaplan–Meier Curves for Time to Recurrence of Bacterial Vaginosis (Modified Intention-to-Treat Population).

Primary Outcome (Modified ITT)

- **Recurrence rate:**
  - 35% in partner-treatment group vs. 63% in control group.
  - Absolute risk difference: –2.6 recurrences/person-year.
  - Hazard ratio: 0.37 (95% CI, 0.22–0.61), $P<0.001$.
  - Longer time to recurrence: 73.9 vs. 54.5 days.

Per-Protocol & Sensitivity Analyses

- Results consistent when accounting for adherence and missing data.
- Lowest recurrence among women whose partners were 100% adherent.

Mycoplasma Genitalium

When to Test

- Recurrent NGU or cervicitis
- Consider testing in PID
- Asymptomatic screening not recommended

How to Test

- FDA approved genital and urine NAAT

Emerging Drug Resistance

- In U.S., Canada, Europe, & Australia, macrolide resistance 44%-90%
- U.S. fluoroquinolone resistance 0-15%

Treatment

- Resistance guided therapy
- **Sex partners of symptomatic persons tested/treated only if positive**

Julie returns

- Julie comes back four weeks later.
- Her symptoms improved briefly but now she has persistent dysuria
- You revisit her history, and she notes no sexual contact since her initial urgent care visit.
- Exam reveals some thin white vaginal discharge, no CMT, slightly erythematous cervix.
- Repeat testing notable for only **positive M. gen**

What treatment(s) if any would you offer Julie?

2nd Line Treatment for M. Gen

Key issues in the U.S:

- No FDA-approved, widely available *M. gen* resistance test → many clinicians can't do resistance-guided therapy.
- Rising macrolide resistance: 40–50% in U.S. surveillance; fluoroquinolone resistance lower but increasing.
- **Limited alternative agents** (e.g., pristinamycin, sitafloxacin) are not available in the U.S.

For treatment failure:

- No established U.S. alternatives

2nd Line Treatment for M. Gen

Alternative Treatments:

Minocycline (100 mg BID x 14 days)

- Slightly lower MICs than doxycycline observed
- Largest case series of 90 patients with macrolide resistant M gen
- 62 had failed treatment with moxifloxacin
- **67% cure rate (90 participants)**

Tinidazole (2g daily x 7 days)

- Single case report of success

Future: Gepotidacin and Zoliflodacin

Not available in the USA

Pristinamycin (1g 3x per day x 10 days + Doxycycline)

- Patients with macrolide resistant M gen
- **75% cure rate (114 participants)**

Sitafloxacin (200mg daily x 7 days)

- **88% cure rate (180 participants)**

Clarke EJ, Vodstrcil LA, Plummer EL, Aguirre I, Samra RS, Fairley CK, Chow EPF, Bradshaw CS. Efficacy of Minocycline for the Treatment of *Mycoplasma genitalium*. Open Forum Infect Dis. 2023 Aug 11;10(8):ofad427.

Read TRH, Jensen JS, Fairley CK, Grant M, Danielewski JA, Su J, Murray GL, Chow EPF, Worthington K, Garland SM, Tabrizi SN, Bradshaw CS. Use of Pristinamycin for Macrolide-Resistant Mycoplasma genitalium Infection. Emerg Infect Dis. 2018 Feb;24(2):328-335.

Julie's course

- Conveniently Julie is going to England for work the following day and decides to go to France to get Pristinamycin
  - She completes a 7-day course of Doxy followed by a 10 day course of Pristinamycin with resolution of her symptoms
- You recommend that both of her sex partners are tested for Mgen
  - One of them tests positive and is treated with doxycycline followed by moxifloxacin

Meet Travis

- Travis is a 37-year-old male who follows with you for general primary care
- 4 days ago, he presented urgently to the ophthalmologist for 1 week of blurred vision
  - Exam at that time showed 20/50 vision in L eye, “panuveitis with placoid macular lesions and focal outer retina punctate lesions”
  - ”appearance most concerning for syphilis
  - Lab workup sent at that visit with close follow up
- Today he notes that his vision is unchanged. He feels otherwise well. No headache, hearing changes, disequilibrium, or eye discomfort.
- Exam notable for mildly decreased visual acuity on Snellen, but otherwise normal, including normal euro exam

The History

- PMH includes HIV diagnosed 12 months prior, CD4 nadir 390/19%, now 629/24% and VLUD
- Meds: TAF/FTC/BIC daily. Valacyclovir PRN for cold sores.
- Allergy: early childhood reaction to penicillin (unsure type--required hospitalization)
- Remote history of gonorrhea urethritis. RPR negative at HIV dx
- Stopped having sex when diagnosed with HIV. 6 months ago, after becoming UD started relationship with one new male partner. Uses condoms inconsistently
- Works as a teacher, lives alone with 2 cats. 3-4 drinks/week, no tobacco or other substance use

The Workup

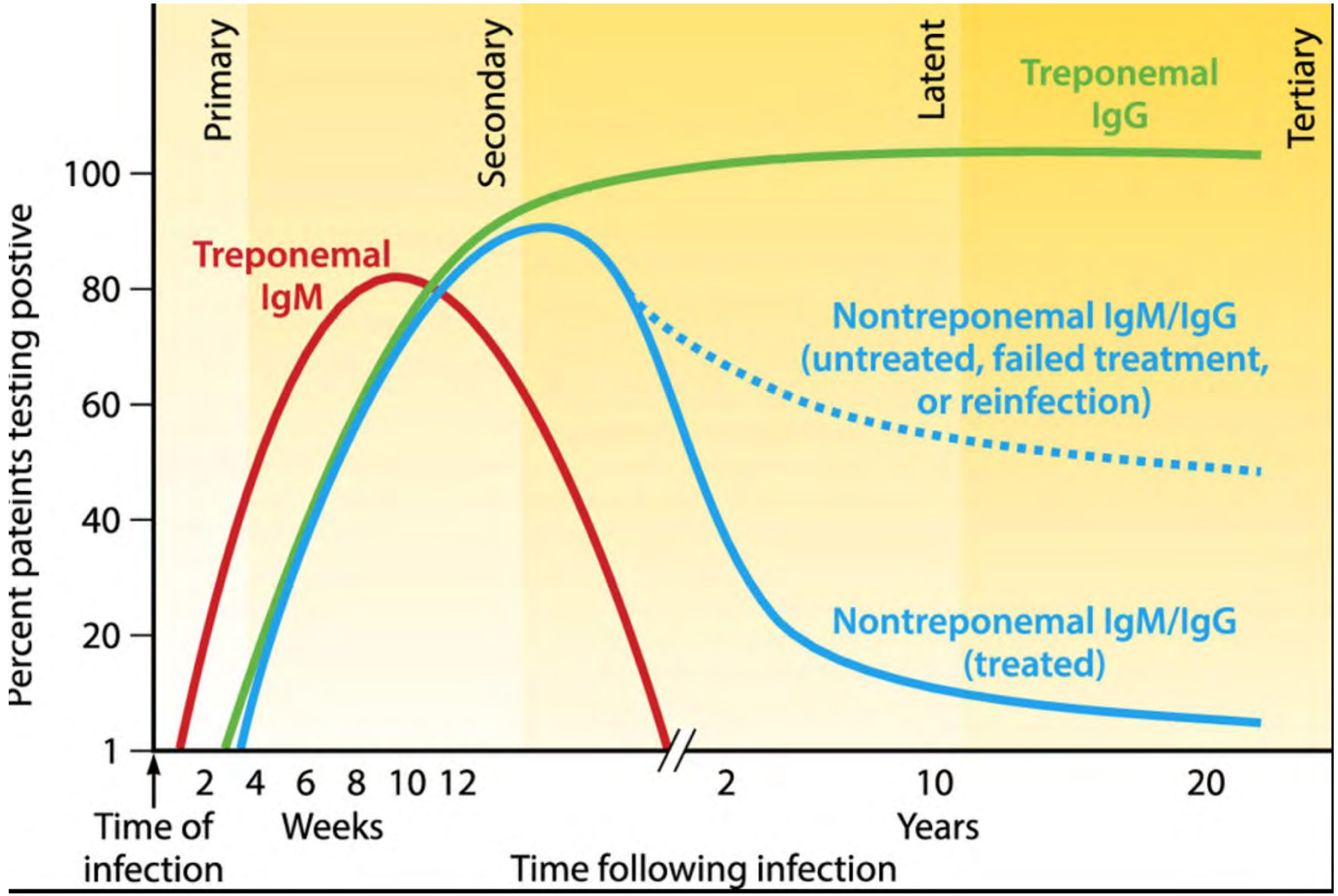
- Quantiferon negative
- Toxoplasma IgG +, IgM negative
- RPR negative
- ESR 25, CRP 4
- Serum ACE pending

Poll: Why is the RPR Negative if We Think This is Syphilis?

1. Infection is too early for seroconversion
2. Alternative infection (Toxoplasma or HSV)
3. False negative syphilis serology due to HIV
4. Prozone effect

Syphilis Serology Timing

- Both treponemal and non-treponemal (RPR) tests imperfectly sensitive in primary syphilis
- Some treponemal tests may convert slightly earlier than RPR
- RPR may wane over time resulting in false negative
- Timeline somewhat suggests against early infection--MAYBE



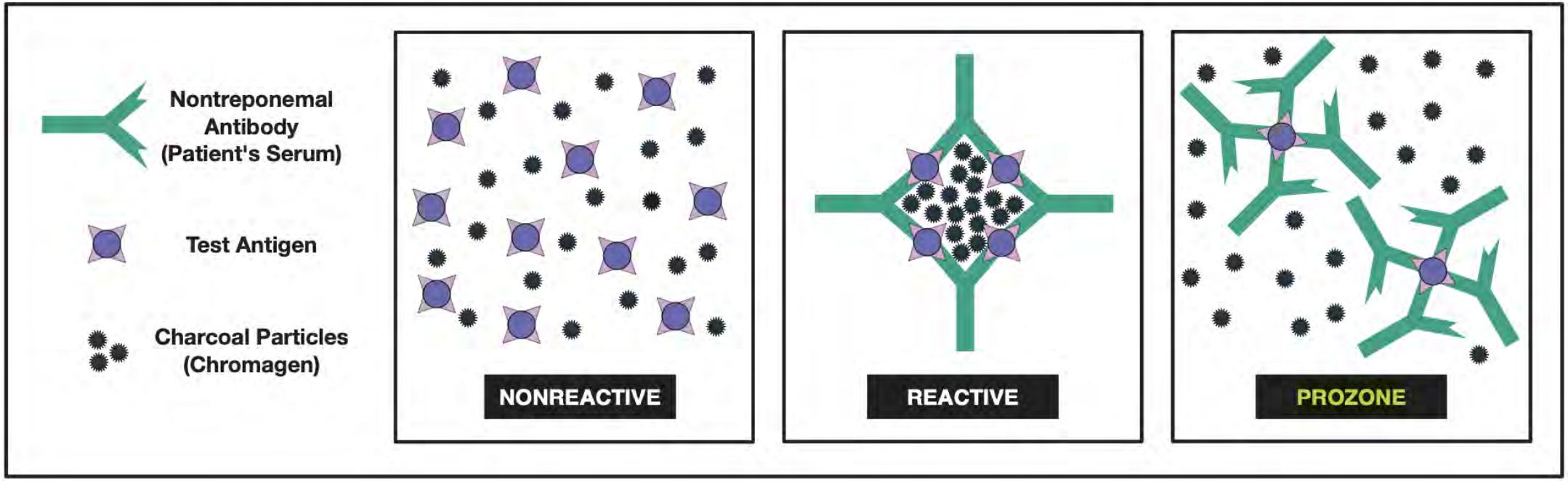
Syphilis Uveitis in HIV

- Broad differential important!
  - Appearance of different infectious pathologies on fundoscopic exam often helps guide differential—ophthalmologist is helpful here!
- Accuracy of serologies for diagnosis is generally reliable
- Inadequate serologic response (< 4-fold decrease) may be more likely

• Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV. National Institutes of Health, HIV Medicine Association, and Infectious Diseases Society of America. 2025.

Prozone!

Figure 7. The Mechanism Underlying Nontreponemal Syphilis Serologic Assays



- False negative RPR due to mismatch between patient antibody and test antigen
- Very high quantity of antibody prevents the lattice formation with antigen that causes visible reactivity

- New York City Department of Health and Mental Hygiene, and the New York City STI/HIV Prevention Training Center. The Diagnosis and Management of Syphilis: An Update and Review. March 2019. A PDF version is available at https://www.publichealth.columbia.edu/file/15568/download?token=exDNYpJ-

Coming Up Empty

- You call up your friendly serology lab to ask them to repeat the RPR with diluted serum to check for prozone
- Sadly, there isn't enough specimen left over to repeat the test
- You're able to get labs again in clinic today

Satyaputra F,Hendry S, Braddick M, Sivabalan P, Norton R, 2021. The Laboratory Diagnosis of Syphilis. J Clin Microbiol 59:10.1128/jcm.00100-21

Poll: What Testing Would You Send?

1. Repeat RPR (traditional algorithm)
2. Reverse sequence syphilis serology (start with e.g. FTA-ABS)
3. LP for CSF VDRL
4. Request vitreous aspirate for T. pallidum PCR

Algorithm Matters

Ocular Syphilis in Patients With Nonreactive Rapid Plasma Reagin and Positive Treponemal Serologies: A Retrospective Observational Cohort Study FREE

Amir M Mohareb ✉, Miriam B Barshak, George N Papaliodis, Lucia Sobrin, Marlene L Durand

Author Notes

Clinical Infectious Diseases, ciae354, https://doi.org/10.1093/cid/ciae354

- 2024 case series of 115 patients with ocular syphilis from MGH/Massachusetts Eye and Ear
  - 25 (22%) had non-reactive RPR with 2 reactive treponemal tests
  - 21 (18%) had RPR <1:8, 69 (60%) had RPR >/= 1:8
- People with low-titer or non-reactive RPR more likely to be older, HIV negative, less likely to have severe ocular inflammation
- A significant proportion of people with ocular syphilis have negative RPR, though more likely less severe/more chronic

• Amir M Mohareb, Miriam B Barshak, George N Papaliodis, Lucia Sobrin, Marlene L Durand, Ocular Syphilis in Patients With Nonreactive Rapid Plasma Reagin and Positive Treponemal Serologies: A Retrospective Observational Cohort Study, *Clinical Infectious Diseases*, 2024;, ciae354

Stuck With Serum

- Remember LP not necessary for people with isolated ocular symptoms and a normal neurologic exam
- PCR tests are promising for diagnosis especially of early syphilis (chancre swab)
  - But no commercially available FDA-approved test
  - Data on use with ocular fluid specimens is limited

New Results

- This time you send the reverse algorithm test
  - T. pallidum Ab +, RPR 1:256

- When you start discussing treatment, he reminds you about his penicillin allergy

Poll: What Treatment Would You Recommend?

1. Hospital admission and for penicillin desensitization, followed by 24 million units/24 hours IV aqueous penicillin G x 10-14 days
2. Doxycycline 200 mg BID x 28 days
3. Ceftriaxone 2 grams daily x 10-14 days
4. Procaine penicillin G IM daily + oral probenecid 4 times daily x 10-14 days

Penicillin or Bust?

- CDC rates intravenous penicillin as the primary recommended therapy
- IM procaine penicillin is no longer available
- Doxycycline is a plausible alternative
  - Good CNS penetration
  - Used in CNS Lyme disease (another spirochete)
  - Data is sparse at the moment, not recommended

Nicolò Girometti, Muhammad H Junejo, Diarmuid Nugent, Alan McOwan, Gary Whitlock, the 56 Dean Street Collaborative Group , Clinical and serological outcomes in patients treated with oral doxycycline for early neurosyphilis, *Journal of Antimicrobial Chemotherapy*, Volume 76, Issue 7, July 2021, Pages 1916–1919

How About Ceftriaxone? Experts Disagree

- From 2021 CDC STI guidelines: “Use of third- and fourth-generation cephalosporins and carbapenems is safe for patients without a history of any IgE-mediated symptoms (e.g., anaphylaxis or urticaria) from penicillin during the preceding 10 years.”

Give Penicillin or Ceftriaxone: Neurosyphilis Does Not Deal in Absolutes FREE

Nicolás W Cortés-Penfield ✉, Daniel M Musher Author Notes

Reply to: Cortés-Penfield and Musher FREE

Matthew Hamill, Khalil G Ghanem ✉, Susan Tuddenham Author Notes

- Some retrospective data suggest that CTX is equivalent or possibly superior to IV penicillin for neurosyphilis
  - However, all have limitations that prevent firm conclusions
- No RCT data yet available
- We continue to recommend IV penicillin for neurosyphilis treatment if at all possible

• Matthew Hamill, Khalil G Ghanem, Susan Tuddenham, Reply to: Cortés-Penfield and Musher, *Clinical Infectious Diseases*, Volume 78, Issue 5, 15 May 2024, Pages 1387–1388

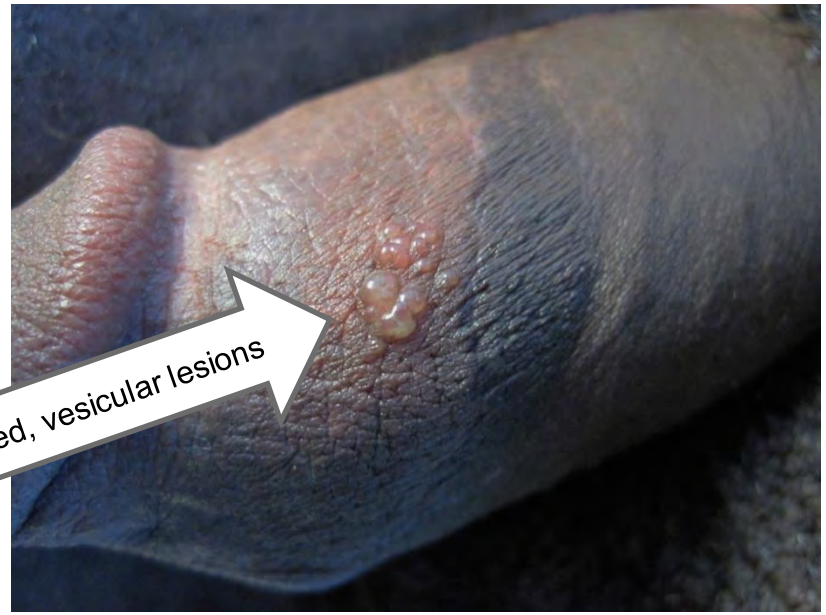
Meet Jasmine

- 24-year-old bisexual female, presents to her OB/GYN with painful vaginal lesions
- They are so painful she is unable to put on her pants
- On exam they “look like herpes”

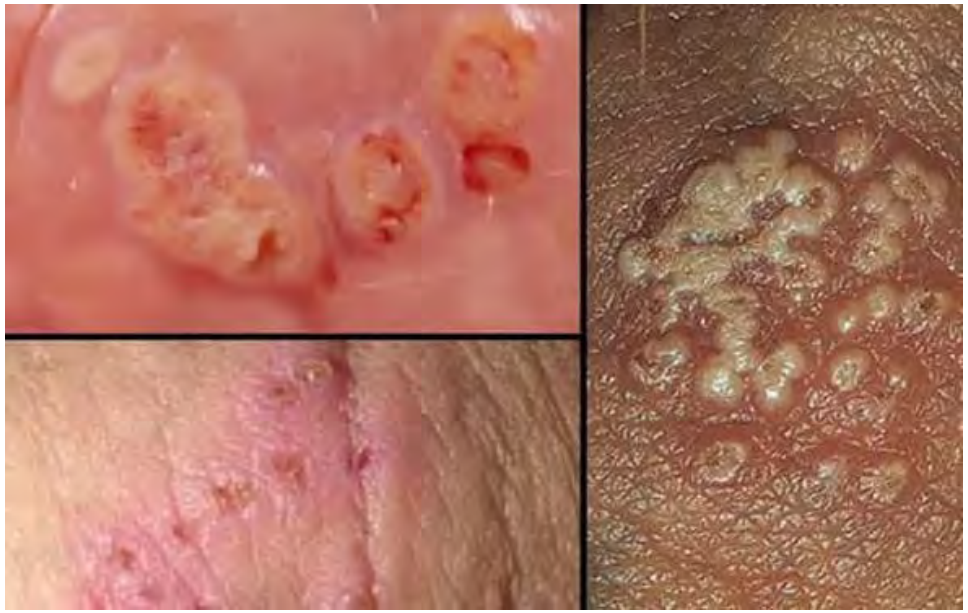
Ulcerative Disease - HSV

Differential

- Syphilis
- **HSV**
- Mpox
- LGV
- Chancroid
- Granuloma inguinale



- **Unique features:** Painful, grouped, often recurrent in same site



- Image from the National STD Curriculum: https://www.std.uw.edu/go/comprehensive-study/genital-herpes/

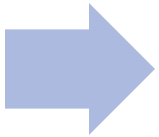
Poll: What should we do for Jasmine?

1. Tell her to come back if the rash recurs so that we can evaluate and send testing at that time
2. Send a serum HSV-1/HSV-2 IgG
3. Prescribe valacyclovir 500 mg BID x 3 days to be taken at the first symptom of a rash
4. Send a lesion swab for HSV-1/HSV-2 PCR
5. Prescribe valacyclovir 1 gram daily to prevent future recurrences

HSV Guidelines

Diagnosis: Virologic Tests (when lesions are present)

Detection of HSV from genital ulcers or mucocutaneous lesions (PCR or viral culture)



HSV PCR is the preferred diagnostic test

- FDA cleared PCR based HSV tests
  - Sensitive and specific
  - Can distinguish HSV-1 from HSV-2

- Viral culture
  - Low sensitivity (especially for recurrent lesions and in healing lesions)
  - Only way to detect acyclovir resistant HSV

HSV Guidelines

- Maybe Useful
  - Recurrent or atypical genital symptoms or lesions with a negative HSV PCR or culture result
  - Clinical diagnosis of genital herpes without laboratory confirmation
  - 12 weeks after suspected acquisition
  - Patient's partner has genital herpes

- Not useful
  - Screening of the general population

Two-Step Serologic Testing

Step 1: EIA Assay (IgG)* (often falsely positive at low index value (<3.0)

Positive EIA

Step 2: Confirm with a second test that uses a different antigen (Biokit/Western blot)

*IgM is not recommended for serologic testing

Jasmine's Course

- 24-year-old bisexual female, presents to her OB/GYN with painful vaginal lesions
- They are so painful she is unable to put on her pants
- On exam they "look like herpes"
- HSV PCR returned positive for HSV-2

Jasmine's Course

- 24-year-old gender bisexual female, presents to her OB/GYN with painful vaginal lesions
- They are so painful she is unable to put on her pants
- On exam they "look like herpes"
- HSV PCR returned positive for HSV-1
- She is started on Valacyclovir 1gm twice daily for 10 days with resolution of symptoms

Jasmine's Course

- One month later she returns with recurrent painful lesions

What should we do for Jasmine Now?

HSV Treatment Options

All patients with first episodes of genital herpes should receive antiviral therapy

1. Acyclovir 400 mg orally 3 times/day for 7–10 days
2. Famciclovir 250 mg orally 3 times/day for 7–10 days
3. Valacyclovir 1 gm orally 2 times/day for 7–10 days

- Treatment can be extended if healing is incomplete after 10 days of therapy.

Treating/Preventing Recurrences of HSV

- **Episodic/Intermittent therapy** - ameliorate or shorten the duration of lesions
  - Recurrences are less frequent after the first episode of HSV-1 genital herpes, and genital shedding rapidly decreases during the first year of infection

- **Suppressive therapy** - reduce the frequency of recurrences
  - Almost all persons with symptomatic first-episode HSV-2 genital herpes subsequently experience recurrent episodes of genital lesions
  - Suppressive therapy can decrease recurrence rate by 70-80% in those with frequent episodes
  - May confer benefits for preventing transmission (more later)

Antiviral Options for HSV

Suppressive

Recommended Regimens

Acyclovir 400 mg orally 2 times/day
OR
Valacyclovir 500 mg orally once a day*
OR
Valacyclovir 1 gm orally once a day
OR
Famciclovir 250 mg orally 2 times/day

* Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens for persons who have frequent recurrences (i.e., ≥10 episodes/year).

Intermittent

Recommended Regimens for Episodic Therapy for Recurrent HSV-2 Genital Herpes*

Acyclovir 800 mg orally 2 times/day for 5 days
OR

Acyclovir 800 mg orally 3 times/day for 2 days
OR

Famciclovir 1 gm orally 2 times/day for 1 day
OR

Famciclovir 500 mg once, followed by 250 mg 2 times/day for 2 days
OR

Famciclovir 125 mg 2 times/day for 5 days
OR

Valacyclovir 500 mg orally 2 times/day for 3 days
OR

Valacyclovir 1 gm orally once daily for 5 days

*Acyclovir 400 mg orally 3 times/day is also effective, but are not recommended because of frequency of dosing.

Dose and/or duration are increased for immunosuppressed people: e.g. valacyclovir 1 gram BID x 7-10 days (intermittent), valacyclovir 500 mg BID for suppression

Preventing Transmission of HSV

- Daily valacyclovir lowers risk of **HSV-2 transmission** from HIV-negative people with symptomatic genital herpes (approx. 50%)
  - Unknown if true for those without a history of symptoms. Not effective/recommended for people with HIV not on ART
- Condoms decrease, but don't eliminate, risk for HSV-2 transmission
- Male medical circumcision
- Caution against HSV acquisition during pregnancy – avoid genital and/or oral sex with partners who have history of orolabial or genital herpes in 3rd trimester, monitor closely peri-delivery
- Pregnant people with a history of genital herpes should be offered suppression starting at 36 weeks to decrease risk of recurrence during delivery, c-section rate, and asymptomatic shedding

Corey L, Wald A, Patel R, Sacks SL, Tyring SK, Warren T, Douglas JM Jr, Paavonen J, Morrow RA, Beutner KR, Stratchounsky LS, Mertz G, Keene ON, Watson HA, Tait D, Vargas-Cortes M; Valacyclovir HSV Transmission Study Group. Once-daily valacyclovir to reduce the risk of transmission of genital herpes. N Engl J Med. 2004 Jan 1;350(1):11-20

Urato AC. ACOG Practice Bulletin No. 220: Management of Genital Herpes in Pregnancy. Obstet Gynecol. 2020 Oct;136(4):850-851

Jasmine's Course

- Jasmine is treated again for 7 days and chooses to go on suppressive therapy 1gm daily

Jasmine's results

- Several years later, Jasmine comes back to your office and lets you know that she's 24 weeks pregnant.
- She already established with OB/GYN at another practice and is getting all recommended prenatal care.
- She hasn't had any recurrences of genital herpes in the past 2 years.
- On further questioning she realizes she forgot to tell her OB-GYN about the herpes since it was so long ago

Poll: What needs to happen for Jasmine?

(Besides making sure her OB finds out this important information)

1. Start suppressive valacyclovir now
2. Tell her to expect delivery by C-section
3. Tell her she'll need to start suppressive valacyclovir at 36 weeks
4. Make sure she still has the valacyclovir you originally prescribed, and tell her to take it only if she develops symptoms
5. No need for any treatment since she's never had another recurrence

Jasmine's course

- With Jasmine's consent, you share her HSV-2 diagnosis and treatment history with her OB-GYN
- She self-monitors for symptoms suggestive of recurrence, but remains asymptomatic
- She is started on suppressive acyclovir at 36 weeks and delivers via NSVD without incident

HSV takeaway points

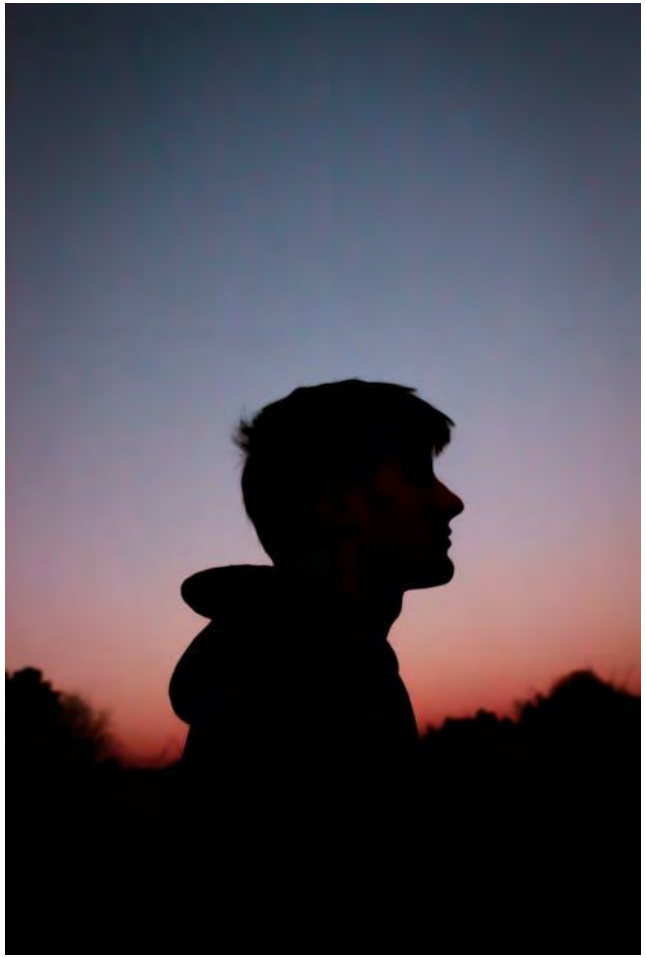
- When possible, HSV diagnosis should be confirmed with PCR testing from an active lesion
  - HSV 1 is an increasingly common cause of genital herpes, especially among younger people, but typically causes fewer outbreaks and less viral shedding
  - HSV 2 causes more frequent outbreaks and increases the risk of HIV transmission
- Serology may help support the diagnosis w/o active lesions, but is not conclusive
- All patients with a first episode of HSV should get antiviral treatment
  - Subsequent outbreaks can be treated with episodic or suppressive therapy
    - Suppressive typically used for those with frequent outbreaks
- Suppressive therapy can reduce outbreak frequency in all patients, and reduce the chances of HSV-2 transmission among people without HIV

Igor

- 29-year-old male
- Takes HIV PrEP for HIV prevention
- Sexually active with men
  - Four condomless partners since his last visit
  - Is a walks into clinic between quarterly visits with 2 days of green penile discharge

- **Routine testing for HIV, syphilis, and three-site gonorrhea/chlamydia testing performed**

- **Treated empirically with Ceftriaxone and Doxycycline**



Igor's Results

Lab results:

HIV Ab/Ag – non-reactive

Urine GC/CT – GC positive

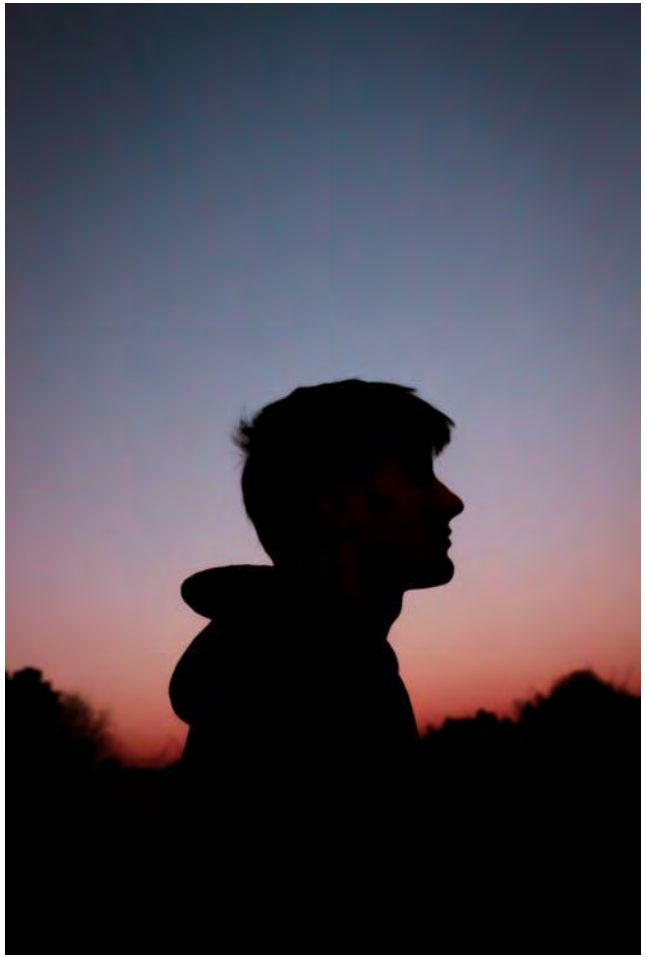
Pharyngeal GC/CT – GC positive

Rectal GC/CT – GC positive

RPR – Negative

Igor

- Returned 6 weeks later saying that, **“I got totally better but now it hurts again when I pee”**
  - Seven condomless partners since his last visit
  - Confident that his regular partners were treated for gonorrhea and syphilis



What Would You Do Now?

Igor

- Returned 6 weeks later saying that, **"I got totally better but now it hurts again when I pee"**
  - Seven condomless partners since his last visit
  - Confident that his regular partners were treated for gonorrhea and syphilis
  - Repeat routine testing for HIV, syphilis, and three-site gonorrhea/chlamydia testing was performed
  - Treated empirically (again) with Ceftriaxone and Doxycycline
  - Started Doxy-PEP

Lab results:

HIV Ab/Ag – non-reactive

Urine GC/CT – GC positive

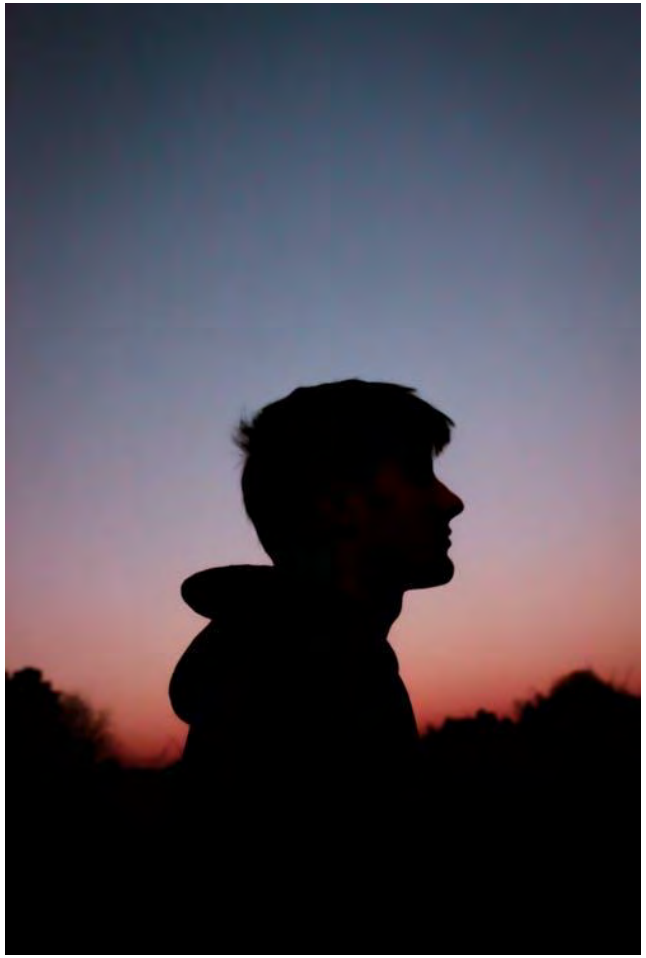
Pharyngeal GC/CT – GC positive

Rectal GC/CT – CT positive

RPR – Negative

Igor

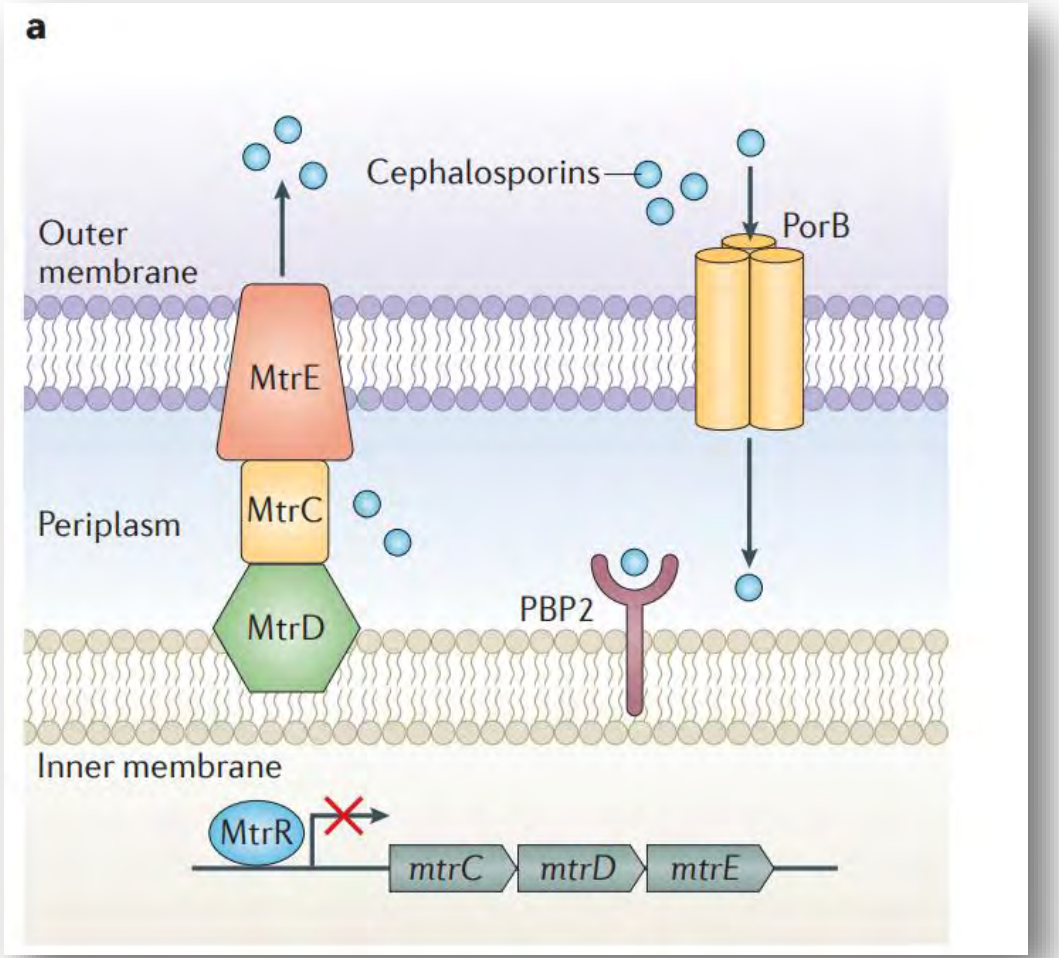
- Returned 3 weeks later saying that, **“I never got totally better but now it hurts really bad again when I pee”**
  - One condomless partner since his last visit
  - Confident that this partner was treated for gonorrhea and syphilis



What Would You Do Now?

GC Has Multiple Mechanisms of Resistance

- PBP2 mutations (penA) → β-lactam resistance
- Efflux pumps (MtrCDE, MtrR) → expel antibiotics
- PorB variations → ↓ permeability, β-lactam resistance
- Plasmid-mediated resistance → blaTEM-1 (β-lactamase), tetM (tetracycline); transferable from commensal Neisseria



• Quillin SJ, Seifert HS. Neisseria gonorrhoeae host adaptation and pathogenesis. Nat Rev Microbiol. 2018 Apr;16(4):226-240. doi: 10.1038/nrmicro.2017.169. Epub 2018 Feb 12. PMID: 29430011; PMCID: PMC6329377.

Worldwide Gonorrhea Resistance

WHO EGASP Surveillance 2023

9 sentinel countries: Cambodia, Philippines, Vietnam, Indonesia, Thailand, Malawi, South Africa, Uganda, Zimbabwe

–**3,498 men with urethral discharge**

–2,491 gonococcal isolates tested

Resistance rates:

– **Ceftriaxone: 3.8% overall (all in Cambodia 15%, Vietnam 20%)**

– **Cefixime**: 8.9% overall (Cambodia 53%, Viet Nam 30%)

– **Azithromycin**: 3.6% overall (Cambodia 21%, Viet Nam 7%)

– **Ciprofloxacin**: 95% (all countries)

– **Dual resistance (CRO + CFM + AZM): Cambodia 9%, Viet Nam 2%**

Ceftriaxone-Resistant Gonorrhea — China, 2022

- **Cases:** 96,313 gonorrhea cases reported nationally
- **Surveillance:** 2,804 isolates collected from 13 provinces
- **Resistance rates:**
  - **Ceftriaxone: 8.1% (↑ from 2.9% in 2017; >10% in 5 provinces, >20% in some)**
  - Cefixime: 16.0%
  - Azithromycin: 16.9%
  - Penicillin: 77.8%
  - Tetracycline: 77.1%
  - Ciprofloxacin: 97.6%
  - Spectinomycin: <1%
  - FC428 clone: internationally disseminated, increasingly dominant

Maatouk I, Vumbugwa P, Cherdtrakulkiat T, Heng LS, Hoffman I, Palaypayon N, Kakooza F, et al.Antimicrobial resistance in Neisseria gonorrhoeae in nine sentinel countries within the World Health Organization Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP), 2023: a retrospective observational study.Lancet Regional Health – Western Pacific. 2025;61:101663. doi:10.1016/j.lanwpc.2025.101663

Zhu X, Xi Y, Gong X, Chen S. Ceftriaxone-Resistant Gonorrhea - China, 2022. MMWR Morb Mortal Wkly Rep. 2024 Mar 28;73(12):255-259. doi: 10.15585/mmwr.mm7312a2. PMID: 38547027; PMCID: PMC10986818.

Worldwide Gonorrhea Resistance

Euro-GASP Surveillance 2022

- **Countries:** 23 EU/EEA countries
- **Sample:**
  - 3,008 isolates tested (linked to epidemiologic data)
- **Resistance rates:**
  - **Ceftriaxone: 0.03% (1 isolate, Germany)**
  - Cefixime: 0.3% (10 isolates, across 6 countries)
  - Azithromycin: 24.9% (↑ from 9% in 2019)
  - Ciprofloxacin: 65.8% (↑ from 57% in 2019)
  - High-level AZM resistance (MIC ≥256 mg/L): rare (0.3%, 9 isolates)
  - Demographics: more cases among women (19% vs 16% in 2019), younger median age (25 yrs vs 31 yrs in men)

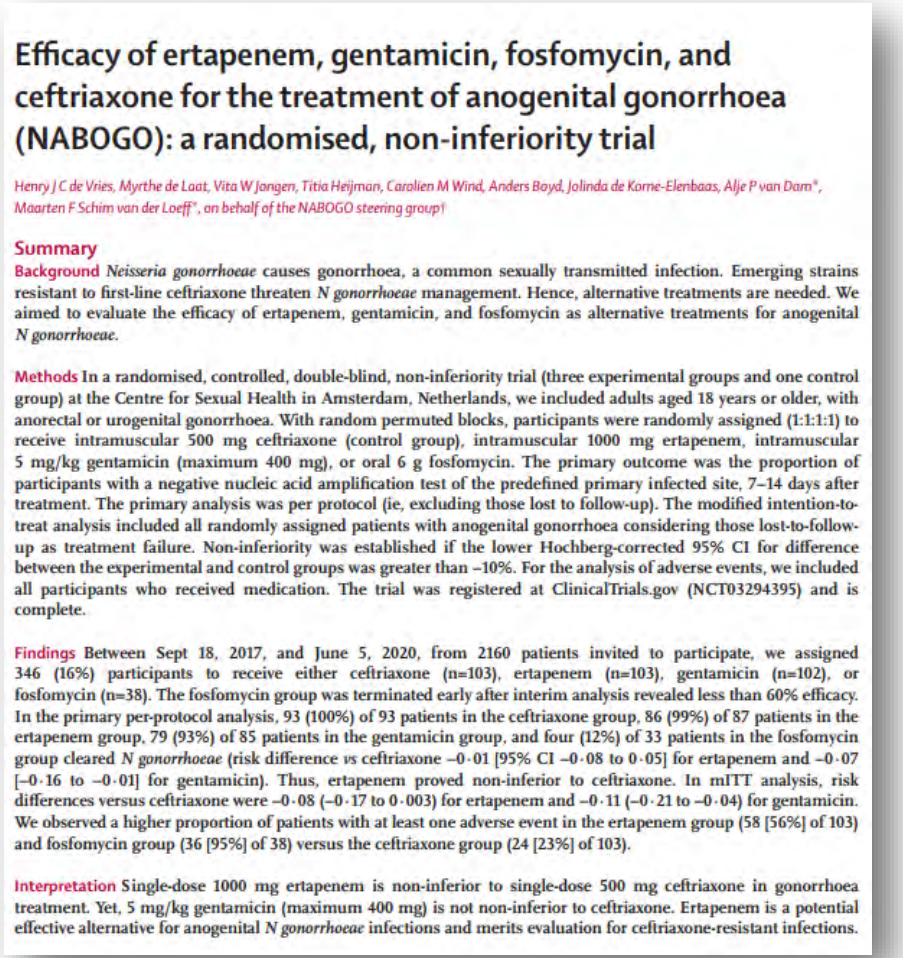
Novel Multidrug Non-Susceptible Gonorrhea — USA, 2022

- **Cases:**
  - First two U.S. cases with mosaic penA 60.001 allele (MLST 8123 lineage)
- **Resistance profile:**
  - Non-susceptible: ceftriaxone (MIC ≥0.5 µg/mL), cefixime, azithromycin
  - Resistant: ciprofloxacin, penicillin, tetracycline
- **Treatment:**
  - Both cases cleared infection after ceftriaxone (500 mg and 1 g regimens)
- **Phylogenetics:**
  - Isolates cluster with emerging international MLST 8123 sublineage, also reported in UK, Europe, Asia

• Maatouk I, Vumbugwa P, Cherdtrakulkiat T, Heng LS, Hoffman I, Palaypayon N, Kakooza F, et al.Antimicrobial resistance in Neisseria gonorrhoeae in nine sentinel countries within the World Health Organization Enhanced Gonococcal Antimicrobial Surveillance Programme (EGASP), 2023: a retrospective observational study.Lancet Regional Health – Western Pacific. 2025;61:101663. doi:10.1016/j.lanwpc.2025.101663

What Alternative Treatment Options Do We Have?

Current Alternative Treatment Options



Efficacy of ertapenem, gentamicin, fosfomycin, and ceftriaxone for the treatment of anogenital gonorrhoea (NABOGO): a randomised, non-inferiority trial

Henry J C de Vries, Myrthe de Laat, Vita W Jongen, Titia Heijman, Carolien M Wind, Anders Boyd, Jolinda de Korne-Elenbaas, Alje P van Dam*, Maarten F Schim van der Loeff*, on behalf of the NABOGO steering group†

Summary

Background *Neisseria gonorrhoeae* causes gonorrhoea, a common sexually transmitted infection. Emerging strains resistant to first-line ceftriaxone threaten *N gonorrhoeae* management. Hence, alternative treatments are needed. We aimed to evaluate the efficacy of ertapenem, gentamicin, and fosfomycin as alternative treatments for anogenital *N gonorrhoeae*.

Methods In a randomised, controlled, double-blind, non-inferiority trial (three experimental groups and one control group) at the Centre for Sexual Health in Amsterdam, Netherlands, we included adults aged 18 years or older, with anorectal or urogenital gonorrhoea. With random permuted blocks, participants were randomly assigned (1:1:1:1) to receive intramuscular 500 mg ceftriaxone (control group), intramuscular 1000 mg ertapenem, intramuscular 5 mg/kg gentamicin (maximum 400 mg), or oral 6 g fosfomycin. The primary outcome was the proportion of participants with a negative nucleic acid amplification test of the predefined primary infected site, 7–14 days after treatment. The primary analysis was per protocol (ie, excluding those lost to follow-up). The modified intention-to-treat analysis included all randomly assigned patients with anogenital gonorrhoea considering those lost-to-follow-up as treatment failure. Non-inferiority was established if the lower Hochberg-corrected 95% CI for difference between the experimental and control groups was greater than –10%. For the analysis of adverse events, we included all participants who received medication. The trial was registered at ClinicalTrials.gov (NCT03294395) and is complete.

Findings Between Sept 18, 2017, and June 5, 2020, from 2160 patients invited to participate, we assigned 346 (16%) participants to receive either ceftriaxone (n=103), ertapenem (n=103), gentamicin (n=102), or fosfomycin (n=38). The fosfomycin group was terminated early after interim analysis revealed less than 60% efficacy. In the primary per-protocol analysis, 93 (100%) of 93 patients in the ceftriaxone group, 86 (99%) of 87 patients in the ertapenem group, 79 (93%) of 85 patients in the gentamicin group, and four (12%) of 33 patients in the fosfomycin group cleared *N gonorrhoeae* (risk difference *vs* ceftriaxone –0·01 [95% CI –0·08 to 0·05] for ertapenem and –0·07 [–0·16 to –0·01] for gentamicin). Thus, ertapenem proved non-inferior to ceftriaxone. In mITT analysis, risk differences versus ceftriaxone were –0·08 (–0·17 to 0·003) for ertapenem and –0·11 (–0·21 to –0·04) for gentamicin. We observed a higher proportion of patients with at least one adverse event in the ertapenem group (58 [56%] of 103) and fosfomycin group (36 [95%] of 38) versus the ceftriaxone group (24 [23%] of 103).

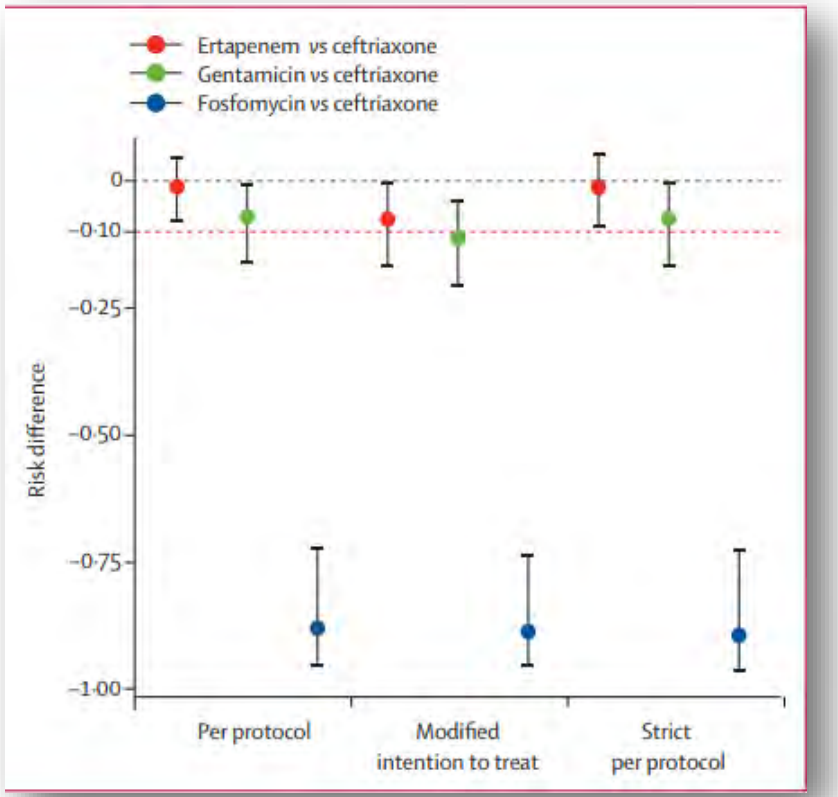
Interpretation Single-dose 1000 mg ertapenem is non-inferior to single-dose 500 mg ceftriaxone in gonorrhoea treatment. Yet, 5 mg/kg gentamicin (maximum 400 mg) is not non-inferior to ceftriaxone. Ertapenem is a potential effective alternative for anogenital *N gonorrhoeae* infections and merits evaluation for ceftriaxone-resistant infections.

- Randomized, controlled, double-blind, non-inferiority trial
- 346 randomly assigned
  - 103 – Ceftriaxone
  - 103 – Ertapenem
  - 102 – Gentamicin
  - 38 - Fosfomycin

de Vries HJC, de Laat M, Jongen VW, Heijman T, Wind CM, Boyd A, de Korne-Elenbaas J, van Dam AP, Schim van der Loeff MF; NABOGO steering group. Efficacy of ertapenem, gentamicin, fosfomycin, and ceftriaxone for the treatment of anogenital gonorrhoea (NABOGO): a randomised, non-inferiority trial. Lancet Infect Dis. 2022 May;22(5):706-717. doi: 10.1016/S1473-3099(21)00625-3. Epub 2022 Jan 19. PMID: 35065063.

Current Alternative Treatment Options

- Single-dose ertapenem 1000 mg **is non-inferior** to single-dose ceftriaxone 500 mg for uncomplicated anogenital gonorrhea
- Single-dose 5 mg/kg gentamicin (max 400mg) is **not non-inferior** to ceftriaxone
- Single-dose oral fosfomycin was ineffective



de Vries HJC, de Laat M, Jongen VW, Heijman T, Wind CM, Boyd A, de Korne-Elenbaas J, van Dam AP, Schim van der Loeff MF; NABOGO steering group. Efficacy of ertapenem, gentamicin, fosfomycin, and ceftriaxone for the treatment of anogenital gonorrhoea (NABOGO): a randomised, non-inferiority trial. Lancet Infect Dis. 2022 May;22(5):706-717. doi: 10.1016/S1473-3099(21)00625-3. Epub 2022 Jan 19. PMID: 35065063.

Near Future Alternative Options

Gepotidacin

- First-in-class triazaacenaphthylene antibacterial
- Dual-targeting: inhibits DNA gyrase (GyrA) and topoisomerase IV (ParC)
  - Binds to a distinct site, different from fluoroquinolones
- Prevents bacterial DNA replication
- Balanced dual-target activity reduces likelihood of single-step resistance

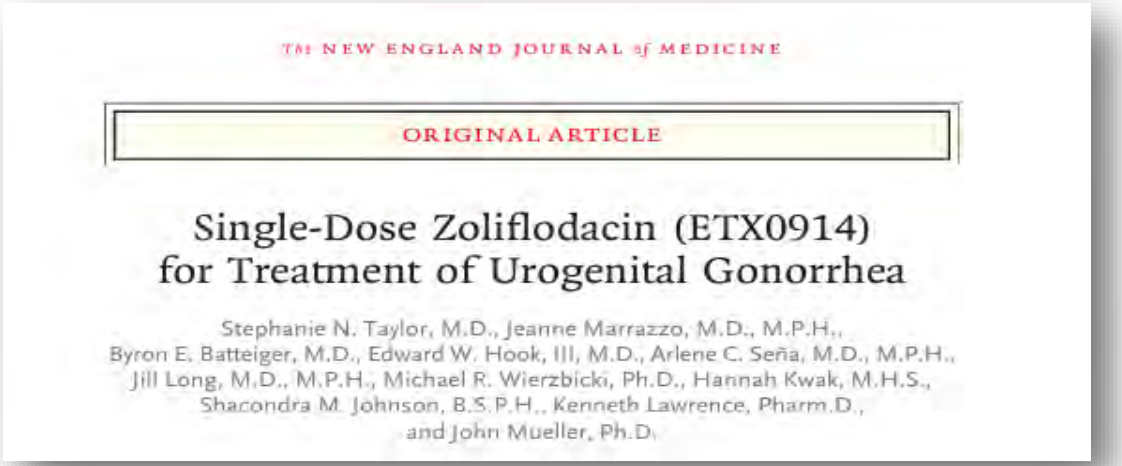
Zoliflodacin

- First-in-class spiropyrimidinetrione antibacterial
- Inhibits DNA gyrase (GyrB subunit)
- Stabilizes the cleaved DNA–enzyme complex → prevents re-ligation
- Blocks DNA biosynthesis, leading to bacterial death
- Active against gonococcal strains resistant to cephalosporins and fluoroquinolones

Near Future Alternative Options

Oral gepotidacin for the treatment of uncomplicated urogenital gonorrhoea (EAGLE-1): a phase 3 randomised, open-label, non-inferiority, multicentre study

Jonathan D C Ross, Janet Wilson, Kimberly A Workowski, Stephanie N Taylor, David A Lewis, Sally Gatsi, William Flight, Nicole E Scangarella-Oman, Charles Jakielaszek, Dan Lythgoe, Marcy Powell, Salim Janmohamed, Judith Absalon, Caroline Perry



THE NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Single-Dose Zoliflodacin (ETX0914) for Treatment of Urogenital Gonorrhea

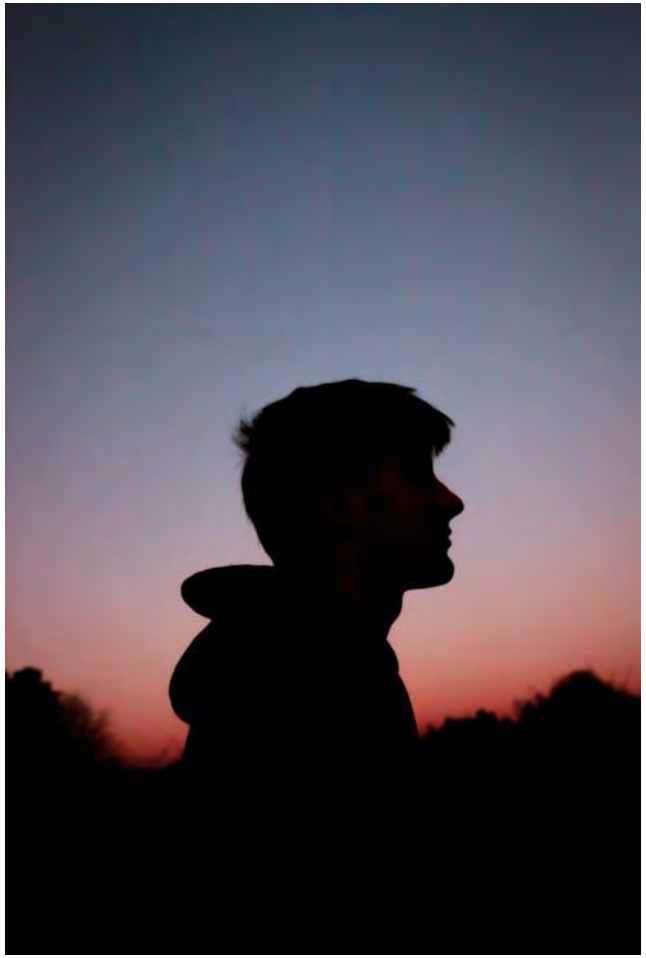
Stephanie N. Taylor, M.D., Jeanne Marrazzo, M.D., M.P.H., Byron E. Batteiger, M.D., Edward W. Hook, III, M.D., Arlene C. Seña, M.D., M.P.H., Jill Long, M.D., M.P.H., Michael R. Wierzbicki, Ph.D., Hannah Kwak, M.H.S., Shacondra M. Johnson, B.S.P.H., Kenneth Lawrence, Pharm.D., and John Mueller, Ph.D.

- The majority of uncomplicated urogenital and rectal gonococcal infections were successfully treated with oral zoliflodacin, but this agent **was less efficacious in the treatment of pharyngeal infections.**

- Gepotidacin demonstrated non-inferiority to ceftriaxone plus azithromycin for urogenital N gonorrhoeae, with no new safety concerns, offering a novel oral treatment option for uncomplicated **urogenital** gonorrhea.

Igor

- Returned 3 weeks later saying that, **“I never got totally better but now it hurts really bad again when I pee”**
  - One condomless partner since his last visit
  - Confident that this partner was treated for gonorrhea and syphilis
  - Repeat routine testing for HIV, syphilis, and three-site gonorrhea/chlamydia testing was performed
    - Plus gonorrhea culture
  - Treated with Gentamicin and Azithromycin



Igor's Results

Lab results:
HIV Ab/Ag - Negative
Urine GC/CT – GC positive
Pharyngeal GC/CT – GC positive
Rectal GC/CT – negative
RPR – 1:4

Lab results:
Azithromycin – susceptible (MIC 0.125)
Ciprofloxacin – resistant (MIC 1)
Ceftriaxone – susceptible (MIC 0.016)
Cefixime – Susceptible (48mm)
Tetracycline – resistant (MIC 12)

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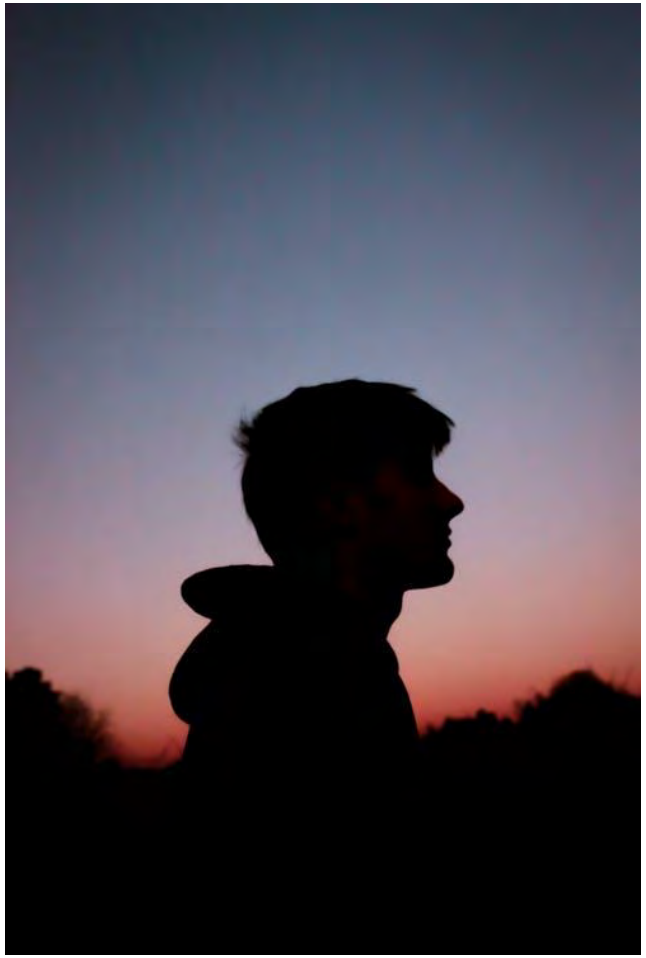
  - **Symptoms resolved**



Gonorrhea Summary

- **Antimicrobial Resistance**
  - CDC: drug-resistant gonorrhea classified as an urgent public health threat since 2013
  - Ceftriaxone resistance rising in Asia (Cambodia, Vietnam, China); sporadic cases in Europe & U.S.
  - tetM plasmid expansion in U.S. (2018–2024) linked to doxycycline use & Doxy-PEP
- **Emerging Treatment Options**
  - **NABOGO**: Ertapenem = non-inferior to ceftriaxone (urogenital); fosfomycin ineffective
  - **EAGLE-1**: Gepotidacin = non-inferior to ceftriaxone+azithro; oral, promising but less effective at pharyngeal site
  - **Zoliflodacin**: Effective at urogenital & rectal sites; reduced efficacy at pharyngeal site
  - **Key challenge remains pharyngeal gonorrhea**
- **Vaccination**
  - UK rollout 2025: first routine gonorrhea vaccination program
  - MenB-4C may offer cross-protection: ~30–50% reduction in GC across observational studies
  - **RCT evidence (DoxyVac) less convincing, highlights need for dedicated gonorrhea vaccine**

17-year-old presents post sexual assault

- 17 yo male presented to ED 48 hrs after a sexual assault; PMhx: MSM, had been on PrEP but not consistent for the past 3 months.
- Patient reports that he passed out at a party, now he has rectal pain and bleeding
- ED evaluation included:
  - GC/CT NAAT (urine, pharyngeal, and rectal)
  - Review of immunization history Hep B
  - Blood testing for HIV, HCV, and syphilis, Hep B; also creatinine, Liver function tests

POLL: what else should be done in the ED?

1. Assess for partner, practice, past STI, protection?
2. Treat for GC with ceftriaxone 500mg IM and Doxycycline 100mg BID x 7 days
3. Treat with Doxycycline 100mg BID x 7 days followed by moxifloxacin
4. Assess for GI pathogens with a PCR test
5. Start HIV PEP with raltegravir + tenofovir / emtricidibine
6. Start HIV PEP with biktarvy

CDC recommended prophylaxis for STIs in Sexual Assault

Recommended Regimen for Adolescent and Adult Female Sexual Assault Survivors

Ceftriaxone 500 mg* IM in a single dose

PLUS

Doxycycline 100 mg 2 times/day orally for 7 days

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Metronidazole 500 mg orally 2 times/day orally for 7 days

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

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STI clinic follow up

Patient tolerated the ceftriaxone and was taking the doxycycline

The HIV medications (raltegravir + tenofovir + emtricitabine) prescribed made him nauseous- so he was inconsistent

Labs:

Labs: GC/CT NAAT negative (oral and urine), **positive CT** in rectal swab;

RPR non-reactive, HIV negative, Hep B Ab+ , Hepatitis C negative, WBC 8K,

75% pmn; CRP 10, ESR 30.

Proctitis or Proctocolitis

- Proctitis Dx: inflammation of rectum (distal 10-12 cm)
  - Symptoms: pain, tenesmus, rectal discharge
  - Diagnostic testing
  - Stool exam for WBC, testing for GC, CT and LGV if PCR available, HSV and syphilis
    - *N. meningitidis* has been identified in some MSM with HIV
- Proctocolitis Dx:
  - Symptoms: diarrhea, abdominal cramping, inflammation extending to 12 cm above the anus
  - Diagnostic testing: wbc in stool. Test for pathogens: campylobacter, shigella, *E. histolytica,* LGV, T pallidum. In HIV +, also consider CMV
- Treatment: acute ceftriaxone 500mg IM + doxycycline x 7 days, if blood, consider LGV and treat for 21 days

Poll: what would you do now?

1. Restart raltegravir + emtricitabine/tenofovir oral (PEP)
2. Change to dolutegravir with emtricitabine/tenofovir
3. Stop PEP as he is inconsistent
4. Phone the PEP hotline
5. Start biktarvy

Follow up

- Changed the PEP regimen to biktarvy
- But couldn't fill the prescription
- Returned 3 months later to test for re-infection for chlamydia
- On discussion, he reports fever, rash, fatigue, and wanted to restart PrEP
- HIV testing performed, HIV Ag/Ab positive, confirmatory negative
  - What do you do next?

Post Exposure Prophylaxis

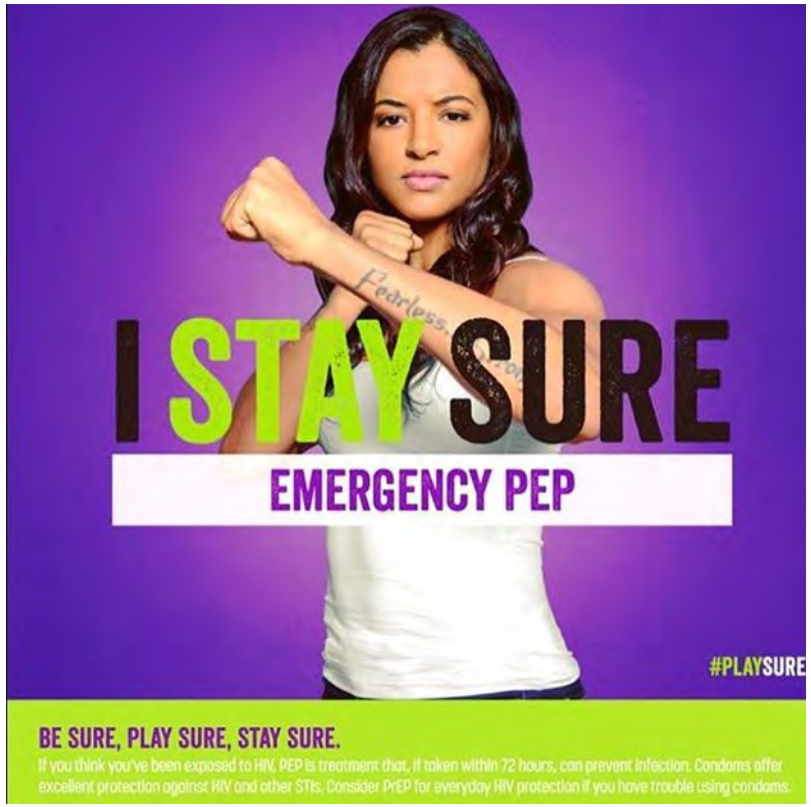
- **Post Exposure Prophylaxis "PEP"**
  - A three-four drug combination therapy given to a patient for 28 days after an HIV exposure, i.e.:
    - Needlestick
    - Sexual encounter (consensual or non-consensual)
    - Significant contact with Blood products that penetrates skin or mucous membrane
  - **Must start within 72 hours of HIV exposure and complete the entire 28 days for medications to be effective**

Post Exposure Prophylaxis

Bictegravir/emtricitabine/tenofovir alafenamide "Biktarvy"
(once a day)
Taken for 28 days

Tenofovir + **Emtricitabine** 200/300mg (once a day)
AND
Dolutegravir 50mg (once a day)
Taken for 28 days

Tenofovir + **Emtricitabine** 200/300mg (once a day)
AND
Raltegravir 400mg (twice a day)
Taken for 28 days

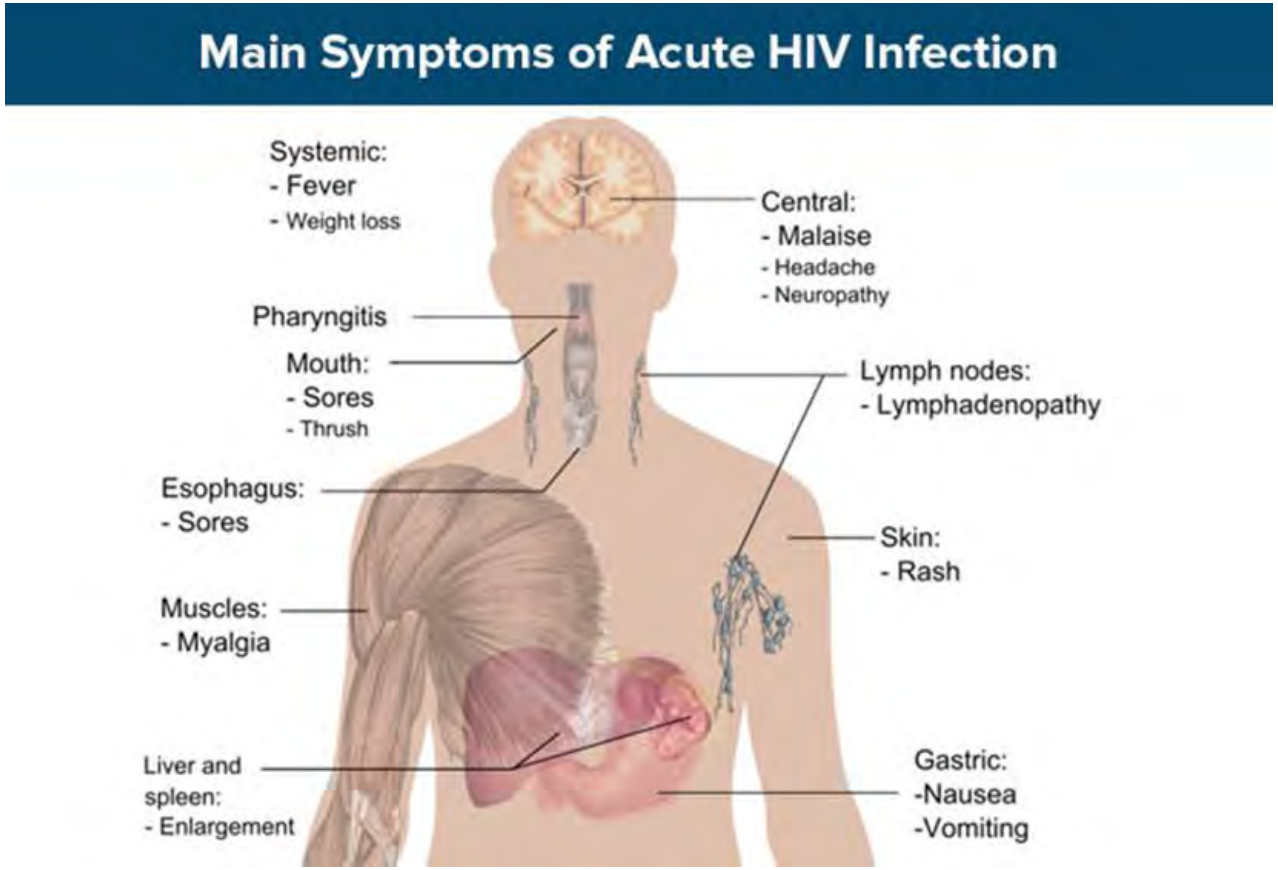


For Alternative Regimens: Dominguez, K. L., Smith, D. K., Thomas, V., Crepaz, N., Lang, K., Heneine, W., . . . Nesheim, S. R. (2016). Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United states, 2016. doi:www.cdc.gov/hiv/risk/pep/ (Appendix 4)

Consider BIC/TAF/FTC for PEP

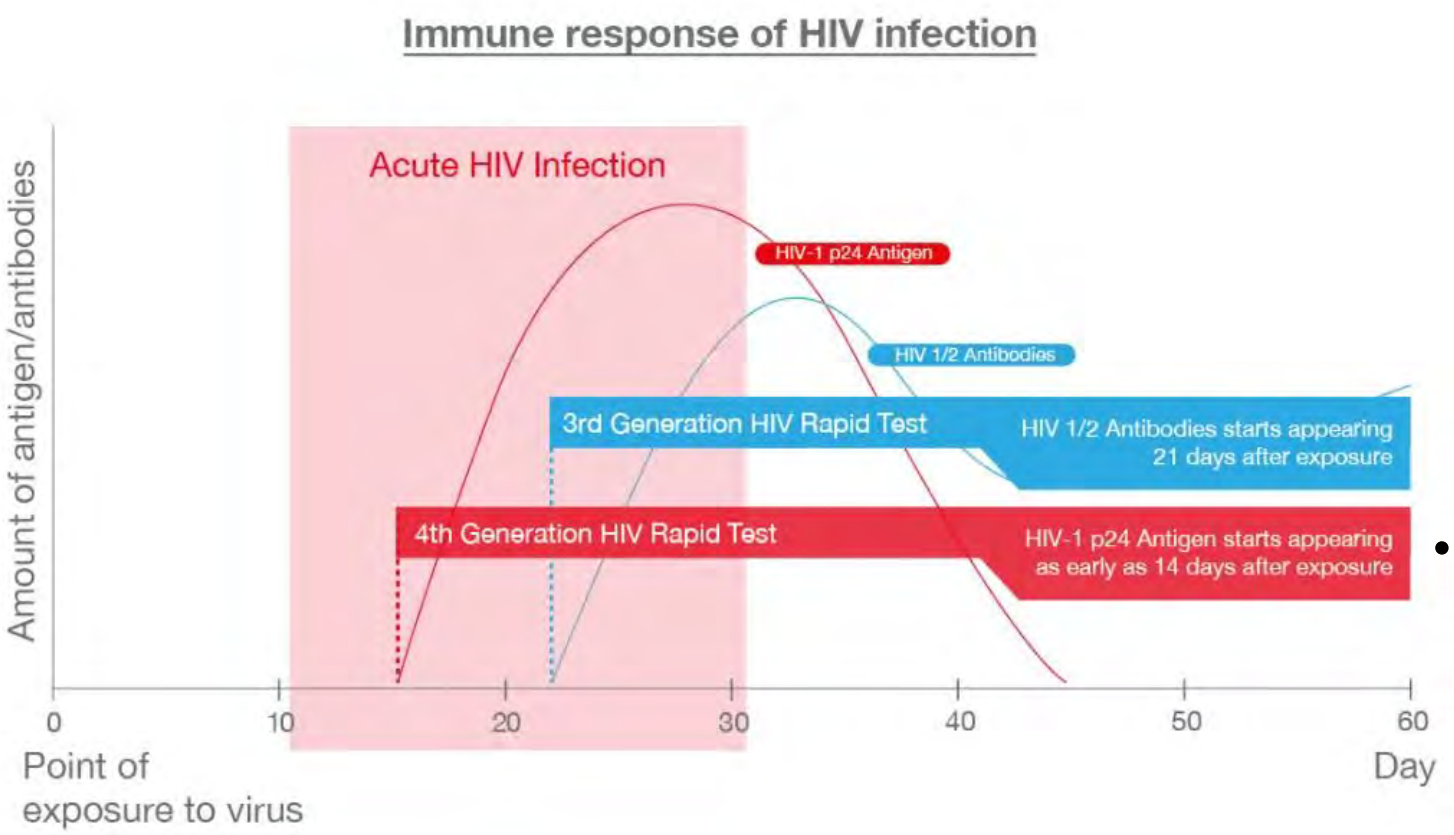
- Efficacy
  - Animal studies demonstrated up to 91% protection with early initiation.
  - Animal studies suggest improved efficacy with late initiation
  - No HIV seroconversions reported in multiple human studies.
- Tolerability
  - Significantly fewer side effects (e.g., diarrhea, fatigue) compared to older PEP regimens.
  - Well-tolerated in both real-world and clinical trial settings.
- Completion Rates:
  - Over 90% regimen completion in multiple studies.
  - Single-tablet regimen enhances adherence.
- Accessibility
  - On most formularies
  - Single manufacturer for patient assistance programs
- Recommended in the NYS AIDS Institute Guidelines and **gaining traction in other jurisdictions**
- Consistent findings across animal, observational, and randomized studies highlight its safety and effectiveness.

Screening for HIV Prevention Services



- Within 2 to 4 weeks after infection with HIV, about two-thirds of people will have symptoms of a flu-like illness
- With 4th generation HIV tests being widely available, someone may present with these symptoms and test positive for HIV

HIV Test Counseling



- **Fourth-generation testing** incorporates HIV-1/HIV-2 antibody and p24 antigen detection; therefore, the window period can be as **early as 14 to 17 days** since exposure
  - Patients at risk should be retested 3-4 weeks after exposure for a definitive negative test
- **Third generation testing** incorporates HIV-1/HIV-2 and starts appearing **between 21- 60 days after exposu**re
  - Over the counter tests are 3rd Generation (Orasure/Oraquick)

Are there other prevention discussions you can have?

- Doxycycline
- 200mg by mouth
- Up to 72 hours after
- A condomless sexual encounter at any anatomic site

Randomized Controlled Trials of Doxy-PEP		
Study	**Population**	**Effectiveness**
IPERGAY	MSM/TGW taking PrEP	**Reduction** in time to first STI HR 0.53 (0.33-0.85) reduction seen in CT and syphilis but **NOT** GC
DoxyPEP	MSM/TGW taking PrEP or PWH	**Reduction** in STI per quarter RR 0.38 (0.24-0.6)
DoxyVac	MSM taking PrEP	**Reduction** in time to first CT or syphilis HR 0.16 (0.08-0.30). Reduction in time to girst GC HR 0.49 (0.32 – 0.76)
dPEP	Females taking PrEP	**No reduction** in STI incidence RR 0.88 (0.6-1.29)

MSM = men who have sex with men, TGW = transgender women, PWH = Persons with HIV, GC = gonorrhea, CT = chlamydia, OR = odds ratio, HR = hazards ratio, RR = relative risk reduction

- Doxycycline **post-exposure prophylaxis** (PEP) is safe and well tolerated
- Doxy-PEP **prevents** STIs in MSM
- Doxy-PEP **did not** prevent STIs in women in the dPEP study
- Future studies in women and others e.g **FoXXyDoxy** – ATN/HPTN trial in women