



2018 Updates on STD Management: Practical Approaches to the Most Common STD Clinic Patient Concerns

A Monthly Webinar Series

Webinars occur 12-1 pm EST
One Tuesday per month
January – November 2018

Learner Objectives

At the conclusion of this webinar series, participants should be able to:

- Accurately identify patients at risk for STIs and then test, diagnose, and treat according to CDC STD Treatment Guidelines.



Continuing Education Accreditation

This activity has been planned and implemented in accordance with the Essential Areas and the Policies of the Accreditation Council for Continuing Medical Education through the joint providership of the University of Alabama School of Medicine and the Sylvie Ratelle STD/HIV Prevention Training Center.

The University of Alabama School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for participants.

The University of Alabama designates this webinar for a maximum of 1.0 AMA PRA Category 1 Credit™. Participants should claim only the credit commensurate with the extent of their participation in the activity.

These credits are also applicable for registered nurses.



After Today's Webinar

- You will receive an auto-generated email from the National Network of STD Clinical Prevention Training Centers to complete a brief evaluation of today's presentation.
- Within that email, you will find instructions on how to register for and receive CME credits through the University of Alabama School of Medicine.
- Webinars will be archived and available for viewing at www.RatellePTC.org. CME credits will also be available for archived webinars.



Save The Dates: 2018 STD Webinar Schedule

Date	Title	Speaker(s)	Affiliations
Jan 16	Vaginitis: Bacterial Vaginosis, Yeast Vaginitis, Trichomoniasis	Katherine Hsu, MD, MPH	MDPH/Boston Univ. Med. Ctr.
Feb 20	Cervicitis/PID: Chlamydia, Gonorrhea, <i>M. genitalium</i>	Candice McNeil, MD, MPH	Wakeforest Univ.
Mar 20	Motivational Interviewing for STI/HIV Prevention	Thomas Creger, PhD, MPH	Univ. of Alabama at Birmingham
Apr 24	Pregnancy and STIs	Candice McNeil, MD, MPH	Wakeforest Univ.
May 15	Urethritis/Epididymitis/Proctitis: Gonorrhea, <i>M. genitalium</i> , and Lymphogranuloma Venereum	Candice McNeil, MD, MPH	Wakeforest Univ.
Jun 19	Clinician-Health Department Partnerships: Partner Management, Disease Reporting, Presumptive Treatment	Marjorie Kirsch, MD	FL DOH Wakulla County



Save The Dates: 2018 STD Webinar Schedule (cont'd)

Date	Title	Speaker(s)	Affiliations
Jul 17	Genital Lesions: HSV, HPV, Syphilis	Nicholas Van Wagoner, MD, PhD	Univ. of Alabama Sch. of Med.
Aug 21	Management of STI/HIV Coinfection	Katherine Hsu, MD, MPH	MDPH/Boston Univ. Med. Ctr.
Sept 11	Genital Dermatology	Nicholas Van Wagoner, MD, PhD	Univ. of Alabama Sch. of Med.
Oct 16	Approaches with Special Populations: Youth, GLBT	Katherine Hsu, MD, MPH and Nicholas Van Wagoner, MD, PhD	MDPH/Boston Univ. Med. Ctr. and Univ. of Alabama Sch. of Med.
Nov 13	Update on PrEP	Ulyee Choe, DO	FL DOH Pinellas County/Univ. of S. Florida College of Med.



Urethritis, epididymitis, proctitis:

Updates on *N. gonorrhoeae*, *M. genitalium*, & Lymphogranuloma Venereum Infections and Others

Candice J. McNeil, MD, MPH

Clinical Faculty AL/NC STD Training Prevention Center
 Assistant Professor of Medicine
 Wake Forest University School of Medicine



Disclosures

- I have NOT had financial relationships with the manufacturer of any commercial products and/or providers of commercial services for this CME activity.
- This presentation will include the discussion of the following testing technologies that have not been FDA approved but may be validated locally or at a commercial laboratory:
 - extra-genital (rectal and pharyngeal) nucleic acid amplification tests (NAATs) for gonorrhea and chlamydia
 - Testing NAATs for *T. vaginalis* testing in men



Objectives

- At the end of this presentation, participants should be able to:**
- Recommend the appropriate screening in men based on risk
 - Recognize common STI syndromes in men including:
 - urethritis, epididymitis, and proctitis
 - Describe the manifestations of *N. gonorrhoeae* infection and implement appropriate diagnostic testing and treatment in the setting of emerging resistance
 - Describe the potential spectrum of Urethritis and NGU etiologies implications for treatment, and relevant guideline updates
 - Describe the manifestations of Chlamydia including manifestations of LGV serovars and implement appropriate testing and treatment



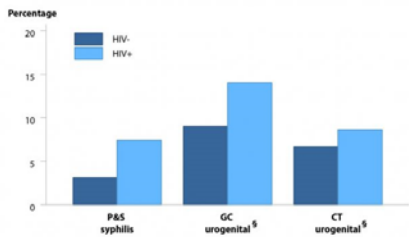
Screening Recommendations – HIV-positive and High-Risk men

STI	Anatomic Site (Test)
Chlamydia	Genital, rectal if exposed (NAAT)
Gonorrhea	Genital, rectal & oral if exposed (culture; NAAT)
Syphilis	Blood (serology)
Hep BsAg	Blood (serology)
Hep C	Blood (serology)
HIV	Blood (serology; viral load)

Source: Primary Care Guidelines for the Management of Persons Infected with HIV, 2015 CDC STD Prevention Guidelines



Proportion of MSM Attending STD Clinics with Primary and Secondary Syphilis, Urogenital Gonorrhea, or Urogenital Chlamydia by HIV Status, STD Surveillance Network (SSuN), 2016



Source: 2016 STD Surveillance Report



The Tip of the Iceberg




Source: WHO Report on global sexually transmitted infection surveillance 2015 (2016)




Detailed Sexual Health Assessment


- 5 P's




Partners




Practices



Past History of STDs




Protection from STDs



Pregnancy Plans

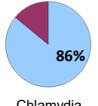
- Comprehensive HEADSSS (Home, Education/employment, peer group Activities, Drugs, Sexuality, and Suicide/depression) *
- Strength Assessment Tool for Psychosocial Screening SSHADESS (strength, school, home, activities, drugs, emotions, sexuality, safety) *

* Tools for adolescents
Source: CDC.gov



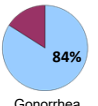
Majority of Rectal Infections in MSM are Asymptomatic

Rectal Infections



Chlamydia
n=316

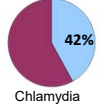
Rectal Infections



Gonorrhea
n=264

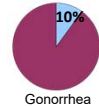
Legend: ■ Asymptomatic ■ Symptomatic

Urethral Infections




Chlamydia
n=315

Urethral Infections

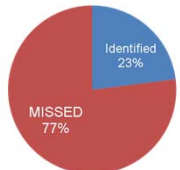


Gonorrhea
n=364

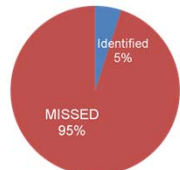
Source: Kent et al, CID, 2005.



Proportion of CT and GC infections MISSED among 3398 asymptomatic MSM if screening only urine/urethral sites, San Francisco, 2008-2009




Chlamydia



Gonorrhea

Source: Marcus et al, STD Oct 2011; 38: 922-4



Centers for Disease Control and Prevention
MMWR Morbidity and Mortality Weekly Report
 Recommendations and Reports / Vol. 63 / No. 2 March 14, 2014

Recommendations for the Laboratory-Based Detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* — 2014

Major conclusions

NAATs recommended for detection of genital tract infections in men and women – with and without symptoms

- highly sensitive and specific compared to culture
- less dependent on specimen collection and handling

Optimal specimen types are:

- First catch urine for men
- Self collected vaginal swabs from women

NAATs recommended for: detection of rectal and oropharyngeal infections but currently not FDA cleared. **Some laboratories have met regulatory requirements**

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Extragenital Collection

Source: <http://www.sfctyclinic.org>

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Self-screening for STIs in the clinic setting

Source: Seattle STD/HIV PTC

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"Triple Dip" for at-risk-MSM

← HIV/Syphilis

← Pharyngeal GC
NAAT/Culture

← Urine GC/CT
NAAT

← Rectal GC (NAAT or
culture)/CT NAAT

- Chlamydia and gonorrhea screening
 - NAAT preferred
 - Multisite testing
- HIV screening
- Syphilis serology
- HepBsAg
- Hep C

Data Source: CDC 2015 STD Treatment Guidelines

Repeat Screening After an STI

- Men with CT or GC should be rescreened at 3 months after treatment
- Patients diagnosed with syphilis should undergo follow-up serology current recommendations

Source: CDC 2015 STD Treatment Guidelines

Expedited Partner Therapy

The delivery of medications or prescriptions by persons infected with an STD to their sex partners without clinical assessment of the partners

Source: <https://www.cdc.gov/std/ept/legal/default.htm>

Case 1

35 y/o transgender female with PMH HIV+. She presents with complaints recent history of perianal ulcer with swollen lymph nodes, lower abdominal and rectal pain with discharge.

Relevant 5 Ps:

- Sex with men - multiple anonymous male partners in the last 2 months
- Anal receptive and insertive sex
- No condom use
- No prior STI testing

Key exam findings:
 Afebrile
 Bilateral cervical LAD
 Anoscopy with friability and gross purulence noted




Image source: CDC Division of STD Prevention


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What syndrome is this?

PROCTITIS

PROCTOCOLITIS

ENTERITIS



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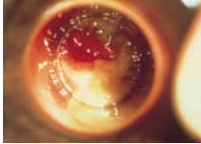
PROCTITIS

Risk factor

- Anal receptive intercourse

Symptoms

- Inflammation of the rectum
- Anorectal pain
- Rectal discharge



Anal Exam/anoscopy:

- mucopurulent discharge,
- spontaneous or easily induced bleeding
- Lab: rectal Gram stain >1 PMN/HPF; STI screens

Source: CDC 2015 STD Treatment Guidelines

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What is your differential for proctitis?

INFECTIOUS

- *Neisseria gonorrhoeae*
- *Chlamydia trachomatis* (serovars D through K)
- Lymphogranuloma venereum
- *Treponema pallidum*
- Cytomegalovirus
- *Mycobacterium tuberculosis*

Ulceration

- Human immunodeficiency virus
- Herpes simplex virus
- *Haemophilus ducreyi* (chancroid)
- *Klebsiella granulomatis* (granuloma inguinale)

NON-INFECTIOUS

Autoimmune conditions

- Crohn's disease
- Ulcerative colitis
- Lymphoid follicular proctitis
- Behçet's syndrome

Trauma

- Foreign bodies
- Chemical proctitis

Lymphoma

Ischemia

Amyloidosis

Idiopathic causes



Source: N Engl J Med 2016;375

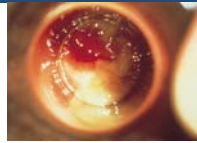
PROCTOCOLITIS

Risk factor(s)

- Anal receptive intercourse
- Oral-anal contact

Symptoms

- Proctitis +
 - Diarrhea
 - Abdominal cramps
 - Inflammation of the colon
 - +/- fecal leukocytes



ID differential diagnosis

- Campylobacter
- Shigella
- *E. Histolytica*
- LGV serovars C, trachomatis
- CMV (ICH)



Source: CDC 2015 STD Treatment Guidelines

ENTERITIS

Risk factor

- Oral anal contact
- Environmental

Symptoms

- Diarrhea
- Abdominal cramping
- No proctitis or proctocolitis

ID Differential diagnosis

- Giardia
- CMV
- *Mycobacterium avium-intracellulare* (MAC)
- *Salmonella* sp.
- *Campylobacter* sp.
- *Shigella* sp.
- *Cryptosporidium*
- *Microsporidium*
- Isospora



Source: CDC 2015 STD Treatment Guidelines

Sexually Transmitted Enteric Pathogens

- Consider sexual transmission of enteric pathogens when outbreaks of GI illness occur in social or sexual networks of MSM
- Syndromes include:
 - proctitis,
 - proctocolitis
 - enteritis
- Evaluation including diagnostic procedures (e.g., anoscopy or sigmoidoscopy, stool examination, culture, STI screens)

Source: CDC 2015 STD Treatment Guidelines



Sexually Transmitted Enteric Pathogens – Summary Disease Manifestations

Pathogen	Disease Manifestations	
	Proctocolitis	Enteritis
<i>Shigella</i> species	X	
<i>Campylobacter</i> species	X	X
<i>Giardia lamblia</i>		X
<i>Entamoeba histolytica</i>	X	
Other	LGV serovars of <i>C. trachomatis</i> ; CMV (immunocompromised hosts)	Non sexual transmission in HIV-infected: CMV, <i>Mycobacterium avium</i> -intracellulare, <i>Salmonella</i> sp., <i>Campylobacter</i> sp., <i>Shigella</i> sp., <i>Cryptosporidium</i> , <i>Microsporidium</i> , and <i>Isospora</i>

Data Source: CDC 2015 STD Guidelines





<https://www.cdc.gov/shigella/resources.html>



Shigella

- Epidemiology:** ~500,000 cases per/yr (3rd, most common bacterial enteric disease)
- About the bug:** 4 serogroups (dysenteriae, flexneri, boydii, sonnei)
- Transmission:** Fecal oral & anoreceptive **VERY contagious** (10-200 organisms ->infection)
- Symptoms:** ~7d bloody diarrhea, abdominal pain, tenesmus, fever,& malaise.
- Diagnosis:** Culture/PCR
- Treatment:** Duration 3-5d based on resistance pattern




Image source: CDC.gov

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Source: CDC.gov

Shigellosis Outbreak Among Men Who Have Sex with Men and Homeless Persons — Oregon, 2015–2016

Jonas Z. Hines, MD^{1,2}; Taylor Pinsent, MPH³; Kathleen Rees, MSPH⁴; Jennifer Vines, MD³; Anna Bowen, MD³; Jacqueline Hurd, MPH³; Richard F. Leman, MD²; Katrina Hedberg, MD²

- Increased number of cases
- 103 cases all adults >18 years
- 77 cases in men of whom **49% MSM**
- Homelessness 63%** non MSM and 8% MSM
- In all **45% hospitalized** no deaths
- Isolates susceptible to Cipro and **resistant to amp, TMP, azithromycin.**

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Source: Hines et al., MMWR 2016 65 (31)

Sexually Transmitted Enteric Pathogens – *Shigella* antibiotic resistance

Table 2. Differences in antimicrobial resistance phenotype by transmission route among clusters of *Shigella* infection, United States, January 2011–December 2015*

Antimicrobial resistance phenotype	MSM-associated transmission, no. (%; 95% CI) [†] , n = 7	Transmission other than MSM-associated, no. (%; 95% CI) [‡] , n = 25	p value [§]
CIP	2 (29, 5–67)	1 (4, 0.2–18)	0.1
CRO	2 (29, 5–67)	0 (0, 0–11)	0.04
AMP	0 (0, 0–96)	1 (4, 0.2–18)	<0.001
AMP, CIP, or CRO	7 (100, 65–100)	2 (8, 1.3–24)	<0.001
AMP and either CIP or CRO	1 (14, 1.2–21)	0 (0, 0–11)	0.007

*AMP, azithromycin; CIP, ciprofloxacin; CRO, ceftriaxone; MSM, men who have sex with men.
[†]95% exact 95% CI of the percentage resistant.
[‡]95% 2-sided Fisher exact test.

- Review of associations b/t transmission route and antimicrobial resistance among US shigellosis clusters 2011–2015.
- Resistance to any of these drugs in all 7 clusters MSM
- Azithromycin resistance more common MSM-associated clusters

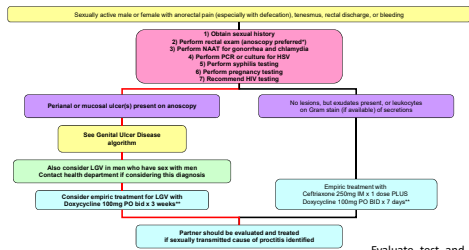
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Source: Bowen et al, EID 2016

Case 1 – Test results...

Rectal NAAT:

- Neisseria gonorrhoea negative
- **Chlamydia trachomatis positive**



N. gonorrhoeae, *C. trachomatis* (including LGV serovars), *T. pallidum*, and HSV are the most common sexually transmitted pathogens involved in proctitis.

*Anoscopes are cheap, disposable, and easy to use.

**Doxycycline not for use in pregnancy.

Lymphogranuloma venereum (LGV)

- **Etiology:** Caused by invasive serovars *Chlamydia trachomatis* L1, L2, or L3
- **Epi:**
 - US and Western Europe: ulcer+LAD + proctitis in MSM.
 - Africa, Asia, Caribbean: ulcer+LAD –proctitis in Heterosexuals
- **Incubation:**
 - Primary 3-12d
 - Secondary 2-6 wk
 - Late
- **Clinical:**
 - painless ulcer (self limited)
 - painful LAD (rare) & rectal pain, tenesmus, rectal bleeding/discharge
 - Reactive polyarthropathy and conjunctivitis (some case reports)
 - Fibrosis and strictures anogenital tract (late)

LGV – Testing

- NAATs: do not distinguish chlamydia serotypes D-K and L1-L3 (LGV)
- Serology: four fold rise of IgM and IgG antibody=active infection. IgM > 1:64 or IgG > 1:256 positive for invasive disease.
- PCR: not widely available

Source: CDC 2015 STD Prevention Guidelines



Recommended Treatment

Proctitis (non LGV):

Ceftriaxone 250 mg IM in a single dose
PLUS
Doxycycline 100 mg PO BID x 7 days

Proctitis or proctocolitis LGV:

Doxycycline 100 mg PO BID x 21 days

Source: CDC 2015 STD Prevention Guidelines



Chlamydia — Epidemiology and Disease Associations

Epidemiology



Disease Associations

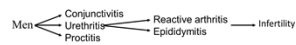


Image source: 2016 CDC STD Surveillance Report

Data source: 2015 CDC STD Prevention Guidelines



Uncomplicated Chlamydia Treatment

<p>Recommended</p> <ul style="list-style-type: none"> • Azithromycin 1 g PO single dose • Doxycycline 100 mg PO BID x 7 days 	<p>Alternative</p> <ul style="list-style-type: none"> • Erythromycin base 500 mg QID x 7 days • Erythromycin ethylsuccinate 800 mg PO QID x 7 days • Levofloxacin 500 mg PO daily x 7 days • Ofloxacin 300 mg PO BID x 7 days
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Source: CDC 2015 STD Treatment Guidelines

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Reactive Arthritis








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Reactive Arthritis

Clinical Syndrome Triggered by an infectious agent in a genetically susceptible host

<p>Enteric</p> <ul style="list-style-type: none"> •M:F 1:1 •Dysentery – Epidemic •<i>Yersinia</i> •<i>Shigella</i> •<i>Campylobacter</i> •<i>Salmonella</i> 	<p>ARTHRITIS</p> <ul style="list-style-type: none"> ☐ Immune response important ☐ Autoimmune vs response to disseminated antigen ☐ HLA-B27 (3/4 of patients) 	<p>STI</p> <ul style="list-style-type: none"> •M:F 99:1 •Urethritis –Sporadic •<i>C. trachomatis</i> (1-3%) •<i>N. gonorrhoeae</i> •<i>U. urealyticum</i>
CONJUNCTIVITIS		URETHRITIS

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Reactive Arthritis Syndrome – Diagnostic Criteria

- Seronegative asymmetric arthritis with one or more of the following:
 - urethritis or cervicitis
 - dysentery
 - inflammatory eye disease
 - mucocutaneous disease
- Rule out disseminated GC



Reactive Arthritis – Clinical Manifestations

- Asymmetrical arthritis (knee, ankle)
- Other musculoskeletal pain (heel, LBP)
- Mucocutaneous Lesions
 - Balanitis circinata (23-50%)
 - Keratoderma blennorrhagica (30%)
- Ocular lesions (conjunctivitis, uveitis)
- Urethritis/Cervicitis



Epididymitis – Epidemiology

Inflammation of epididymis usually due to infection

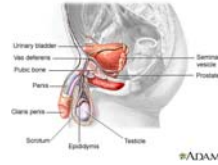
- True prevalence unknown
- ~600,000 cases per year
- Studies have demonstrated:
 - Bimodal distribution peaks 16-30 and 51-70 years of age
 - Correlation between epididymitis and high STIs in southern US

Source: Taylor, SN, CID 2015:61 (suppl 8)



Epididymitis – Diagnosis

- Diagnosis is based on **clinical exam findings**
 - Testicle in **normal anatomic position**
 - **Prehn sign +**: elevation of the testes or scrotum when standing decreases pain (not reliable/consistent)
 - **Cremasteric reflex present**: ipsilateral elevation of testicle with contraction of cremasteric muscle
- Consider **urine studies and grams stain** if concurrent urethritis



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Source: Taylor, SN. CID 2015:61 (suppl 8)

Epididymitis – Clinical Presentation

- **Clinical presentation**: gradual onset **posterior testicular pain**, usually **unilateral**, occasionally radiates to the abdomen
- **Other Signs and Symptoms**: discharge, dysuria, frequency, urgency, erythema of scrotal skin, fever



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Source: Taylor, SN. CID 2015:61 (suppl 8)

Epididymitis – Etiology

- **Age < 14**: urinary pathogens i.e. E. coli or viral illness
- **Age 14-35 or > 35 MSM and sexually active**: GC, CT, +/- coliforms i.e. E. coli
- **Age > 35**: urinary pathogens i.e. E. coli : bacteriuria due to outlet obstruction BPH; urinary instrumentation; prostatic biopsy; or urologic surgery
- **Other**:
 - Anatomic abnormalities may be associated with anaerobic bacteria
 - Chronic infections can be caused by hematogenous spread TB
 - Systemic illness, inflammatory conditions, and medications may be associated

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Source: Taylor, SN. CID 2015:61 (suppl 8)

Epididymitis Management

Likely *N. gonorrhoeae* or *C. trachomatis*:


- Ceftriaxone 250mg IM x 1 + Doxycycline 100mg PO x 10 days

STD or enteric

- Ceftriaxone 250mg IM x 1 + Ofloxacin 300mg PO BID
- OR Ceftriaxone 250mg IM x 1 + Levofloxacin 500mg PO QD x 10 days

Likely enteric bacteria:


- Levofloxacin 500mg PO QD x 10 days
- OR Ofloxacin 300mg PO BID

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Source: CDC 2015 STD Treatment Guidelines

Epididymitis Management cont.

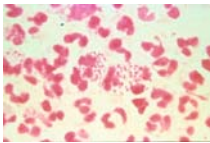
- Bed rest, scrotal elevation, and analgesics
- Sexual partner referral for evaluation and treatment
- Schedule follow-up appointment in 72 hours
- **Hospitalize IF**
 - Severe pain suggesting complications or other diagnoses
 - Fever
 - Noncompliant
- Rescreen for CT or GC at 3 months if identified


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CDC 2015 STD Treatment Guidelines

Case 2 – Gram stain dilemma?

- Your patient presents with painful urination and penile discharge
- You perform a urethral gram stain and discuss treating the patient; however he insists on waiting on all of his labs to come in first
- The next day his report reads Negative gonorrhea NAAT and Negative chlamydia NAAT



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Increase in *Neisseria meningitidis*-Associated Urethritis Among Men at Two Sentinel Clinics — Columbus, Ohio, and Oakland County, Michigan, 2015

Jose A. Bazan, MD^{1,2}, Amy S. Peterson, MPH^{1,2}, Robert D. Korbkade, MD^{1,2}, Elizabeth C. Bizon, MD^{1,2}, Courtney Marshall, MPH^{1,2}, Abigail Noelle Tarron, PhD^{1,2}, Denise B. Lamm, PhD^{1,2}, Nichole Parker, MPH^{1,2}, Amanda Stevenson, MPH^{1,2}, Melissa Frutin¹, Laura Johnson, MD¹, Barbara Whittemann, PhD¹, Patricia Kackert, MD¹, Nao Wang, PhD¹, Cecilia R. Korte, PhD¹, A. Jeanette Abrams, PhD¹, David L. Tross, PhD¹, Carlos Ekl Biso, MD¹, David S. Stephens, MD¹, Yun-Ling Tseng, PhD¹, Mary DiCenso, MD¹, Myahika Williams Roberts, MD¹

Uhh another *Neisseria*...

- *Neisseria meningitidis* (NM) urethritis is on the rise in heterosexual men
- Columbus OH clinic: 0 NM urethritis until 2 in Dec 2014, Jan-Sept. 2015 52 confirmed
- Oakland County MI: 2 NM urethritis in 2013, 8 in 2014, and 15 through Oct. 2015
- 67 cases in 2015: all but one symptoms and heterosexual, majority oral sex
- All cases were non groupable
- 8 individuals had h/o meningococcal vaccine (incomplete data)
- Majority rx for N. gonorrhoea based on gram stain with CDC recommended rx

Source: Bazan et al., MMWR 2016 65 (21)



Uhh another *Neisseria*...

- *N. Meningitis* (NM) urethritis has been reported in MSM with oral sex exposure
 - Cases HIV-infected and uninfected
 - A diversity of serogroups have been reported in the literature
- Urogenital and rectal carriage of NM may be asymptomatic w/ potential for invasion
- Concurrent *N. Gonorrhoea* may be present

Source : Hayakawa et al., EID 2017; Harrison et al, STI 2017



Neisseria meningitides – Management

- Test and treat patient & partners w/ CTX + Azithromycin same as N. gonorrhoea
- IF men with urethritis w/ Gram stain suggests GC infection but NAAT testing is negative REMEMBER *N. meningitidis* is a possibility
- Vaccinate against meningococcal disease according to current ACIP recommendations



Case 3 – “It hurts when I pee”

Patient is a 20 y/o HIV + male PMH significant for CT infection at the age of 18 and multiple episodes of urethral complaints (pain and burning with urination) over the last 2 years. He reports 2 female partners in the last year. Intermittent condom use.

- What is this syndrome?
- What is your differential diagnosis?
- How would you diagnosis his condition?
- How would you treat?



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Characteristics of Urethritis in Men

- **Incubation:** days to weeks
- **Discharge:** watery to purulent
- **Dysuria**
 - may be only symptom
 - may not be present
- **Penile tingling**

Source: CDC 2015 STD prevention guidelines

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Etiologies of urethritis

Infectious

- *N. gonorrhoeae* (~5-20%)
- NGU (15-40%)
 - *C. trachomatis* (15-40%)
 - *U. urealyticum* (inconsistent reports)
 - *M. genitalium* (15-25%)
 - *T. vaginalis* (variable depending on geographic location/risk)
 - HSV (2-3% in the absence of skin lesions)
 - Other bacteria (i.e. GNR, anaerobes)
 - UNKNOWN! (20-40%)

Non Infectious (? Frequency)

- Chemical
- Allergic
- Autoimmune

Sources: CDC 2015 STD prevention guidelines; Bachmann et al. CID 2015-61 (suppl8)

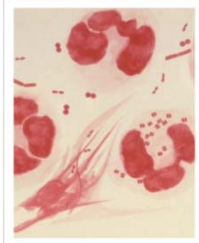
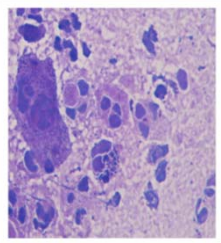
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Are there alternative POC tests to assist in the clinical diagnosis of urethritis (in symptomatic men)?

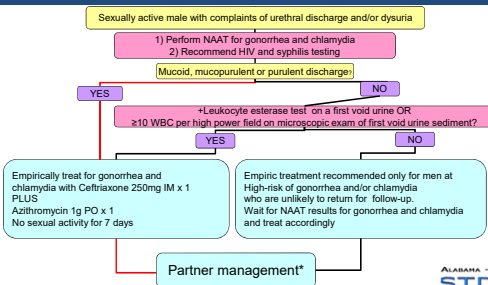
- **Methylene Blue/Gentian Violet (MB/GV) smear**
 - alternative to Gram stain
 - single step after drying= faster than Gram stain
 - similar performance characteristic to Gram stain:
 - sensitivity of Gram stain and MB/GV both 97.3%, with specificity of 99.6% (100% correlation)
- **Evidence/Recommendation: Moderate/B**
 - Methylene Blue/Gentian Violet (MB/GV) smear should be considered as an alternative to Gram stain for clinical diagnosis of urethritis



Methylene Blue vs Gram Stain



Management Urethritis – Gram Stain Unavailable



Case 3 – Test results...

Urine NAAT:

- **Neisseria gonorrhoea positive**
- Chlamydia trachomatis positive

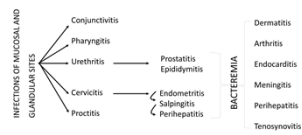


Gonorrhea — Epidemiology and Disease Associations

Epidemiology



Disease Associations



Source: CDC 2014 STD Surveillance





Gonorrhea *Dual* Therapy Uncomplicated Genital, Rectal, or Pharyngeal Infections

Ceftriaxone 250 mg IM in a single dose **PLUS***

Azithromycin 1 g orally (preferred) or Doxycycline 100 mg BID *7 days

- **Dual therapy:** regardless of CT test result
- **Retest:** within 3-6 months IF high-risk
- **Partner management:** evaluate, test, and treat partners within the last 60 days

Source: CDC 2015 STD Treatment Guidelines

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Case 3 – Follow up visit

Since his last visit he was seen in the ED for urethral complaints X 2 **GC/CT testing was negative** on both occasions. The **ED treated him with IM ceftriaxone and doxycycline** on most recent visit. He reports that he has **one female partner. Condom use? "Sometimes Doc."**

Today he reports **penile discharge and itching**

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Are symptoms resolved?

YES NO

Objective signs of urethritis still present?*

YES NO

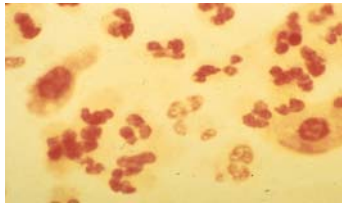
Probable persistent or recurrent NGU.
*** Consider re-infection, azithromycin-resistant *M. genitalium*, or *T. vaginalis* infection in men who have sex with women

Value of extending duration of antimicrobials in persons without objective signs of Urethritis has not been demonstrated

Source: Sylvie Ratelle STD/HIV Prevention Training Center

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THE GRAM STAIN SHOWS...



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Gram stain PMN cutoff for clinical diagnosis of urethritis in men with urethral signs and/or symptoms

Gram stain stratum	Number	CT+	%	95% CI
0	2612	126	4.8	4.0-5.7
1	1083	71	6.6	5.2-8.1
2	284	46	16.2	12.2-20.8
3	627	93	14.8	12.2-20.8
4	753	136	18.0	15.4-20.9
5	609	156	25.6	22.2-29.2
6	297	103	34.7	29.4-40.2
7	249	61	24.4	19.4-30.0
8	358	122	34.0	29.3-39.0
9	139	54	38.8	31.0-47.1
10	533	220	41.2	37.1-45.4
>10	3878	1699	43.8	42.3-45.5

Source:
Reitmeijer Sex
Trans Dis
2012;39(1):18-
20

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Summary Non gonococcal Urethritis (NGU)
Diagnosis

Clinical syndrome characterized by:

- Urethral inflammation
- Symptoms: urethral discharge, dysuria, meatal pruritus

Lab criteria include (any):

- Mucopurulent or purulent discharge.
- Gram stain of urethral secretions demonstrating ≥ 2 WBCs per oil immersion field**
- Positive leukocyte esterase test on first-void urine or microscopic examination of first-void urine sediment demonstrating >10 WBCs per high power field.


Source: CDC 2015 STD Treatment Guidelines

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Etiologies of urethritis

<p>Infectious</p> <ul style="list-style-type: none"> - <i>N. gonorrhoeae</i> (~5-20%) - NGU (15-40%) <ul style="list-style-type: none"> • <i>C. trachomatis</i> (15-40%) • <i>U. urealyticum</i> (inconsistent reports) • <i>M. genitalium</i> (15-25%) • <i>T. vaginalis</i> (variable depending on geographic location/risk) • HSV (2-3% in the absence of skin lesions) • Other bacteria (i.e. GNR, anaerobes) • UNKNOWN! (20-40%) 	<p>Non Infectious (? Frequency)</p> <ul style="list-style-type: none"> • Chemical • Allergic • Autoimmune
---	---


Sources: CDC 2015 STD prevention guidelines; Bachmann et al. CID 2015:61 (suppl8)



M. genitalium – Associated Conditions

- Urethritis
 - 15%–20% of NGU
 - 20%–25% of nonchlamydial NGU
 - 30% of persistent or recurrent urethritis
- Infertility (?)
- Anogenital tract syndromes
 - Epididymitis (?)
 - Proctitis (does not appear to be associated)


Sources: CDC 2015 STD prevention guidelines



M. genitalium – An Emerging Issue?

- National retrospective survey of all *M. genitalium* testing performed in Denmark (Jan 2006-Dec 2010)
 - Macrolide resistance screening 2007 onward
- A total of 31 600 specimens from 28 958 patients were tested for *M. genitalium*, with an increasing trend from 3858 per year in 2006 to 7361 in 2010.
- The majority (54%) of the patients were tested in general practice.
- For both sexes, the positive rate increased significantly, from 2.4% to 3.8% for women and from 7.9% to 10.3% for men (P < .0005).
- Macrolide resistance was detected in 38% (385/1008) of the *M. genitalium*-positive patients, and the highest rate was found in patients tested at sexually transmitted disease clinics (43%)

Source: Salado-Rasmussen and Jensen. CID 2014; 59 (1): 24-30



Diagnosis of *M. genitalium*

- MG culture and MG serology not used for diagnosis
 - MG culture takes weeks to months to grow
- NAAT is the preferred method for MG detection
- **No commercially available MG NAAT currently FDA approved in the US**
- Research settings/academic setting/commercial labs: in-house NAATs often used (urine, urethral, vaginal, and cervical swabs and through endometrial biopsies)
- Multiple NAATs are under study

Source: CDC 2015 STD Treatment Guidelines



T. vaginalis Diagnostic Testing in Men

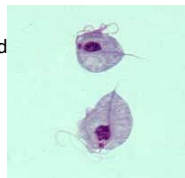
- Wet prep is not a sensitive test and no point of care tests are available
 - Culture testing of urethral, urine, or semen specimens is one diagnostic option however TV NAAT has superior sensitivity for diagnosis in men (Hologic Gen-Probe APTIMA Combo 2® ; Roche COBAS® AmpliCor PCR)
 - TV NAAT not currently FDA-approved in men – **Some laboratories have met regulatory requirements**
 - TV has not been detected in the oral cavity and rectal prevalence is low in MSM – thus oral and rectal testing are not currently recommended

Source: 2015 CDC STD Treatment Guidelines



What about *T. vaginalis* in men?

- Associated w/ urethritis, epididymitis, & prostatitis
- Urethral infections are associated w/ increased shedding of HIV in HIV-infected individuals
- Highly transmissible
 - Male to female 85%
 - Female to male
 - 20-60% (Krieger, 1995)
 - 70% (Sena, 2003)



T. vaginalis Prevalence in Men

Population	No.	Location, year	Prevalence (%)	Diagnostic method used
Nongonococcal urethritis	141	Butler, US, 1980 ²¹	10	Culture
	415	Qutbilgin, Egypt, 1994 ²²	21	Culture, microscopy
STD clinic patients	447	Krieger, US, 1995 ²³	11	Culture
	454	Jayner, US, 2000 ²⁴	2.9	Culture
	204	Borchardt, US, 1995 ²⁵	12	Culture, microscopy
	140	Schwebke, US, 2001 ²⁶	4.3	Culture, PCR
			17	
Adolescents at high risk	85	Saxena, US, 1991 ²⁷	58	Culture, microscopy
Contacts of infected women	93	Weston, UK, 1963 ²⁸	45	Culture, microscopy

Source: Soper et al., American Journal of Obstetrics and Gynecology, 2004



Case 3: Test results...

W Leukocytes	800	800
W Count	Microscopic necessary	8000
W Bacteria	None	None
W Red Blood Cells	0-10	0 - 3 /HPF
W White Blood Cells	0-10	0 - 5 /HPF
Urine Rithelial Cells	PPK	PPK /HPF

SureWebb®: Mycoplasma genitalium, PCR
 SureWebb®: Mycoplasma genitalium, PCR
M. genitalium DNA Detected Not Detected



NGU Treatment

Recommended

- Azithromycin 1 gm PO x 1 dose
- OR**
- Doxycycline 100 mg PO BID x 7 days

Alternative

- Erythromycin base 500 mg PO QID x 7 days
- Erythromycin ethylsuccinate 800 mg PO QID x 7 days
- Levofloxacin 500 mg PO QD x 7 days
- Ofloxacin 300 mg PO BID x 7 days

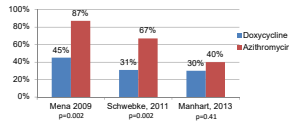
Source: CDC 2015 STD Treatment Guidelines



Is AZM(1g) superior to doxycycline 100mg bid x 7d for *M. Genitalium*?

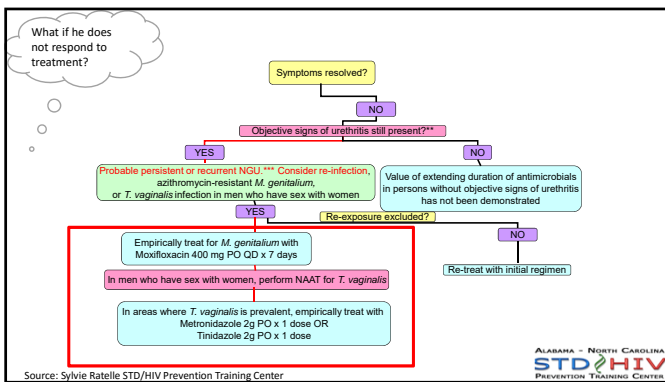
- Observational studies – DOX (7 studies); AZM (18 studies)
 - Microbiologic cure rates (eradication)
 - Doxycycline (7-9 days) : range 17% to 94%
 - Azithromycin (1g): 91% range 72% to 100%

• RCTS – 3 comparing DOX (100mg bid x 7d) to AZM (1g)



• **CONCLUSION:** AZM (1g) is superior to DOX (100mg bid x 7d). However, efficacy of AZM is not consistently high and may be declining

Source: Manhart et al. CID 2015:61 (suppl 8)



Persistent NGU Treatment

IF azithromycin NOT given for 1st episode:

- Azithromycin 1 g orally in a single dose
- PLUS
- Metronidazole 2 g orally in a single dose OR
- Tinidazole 2 g orally in a single dose

IF azithromycin given for 1st episode:

- Moxifloxacin 400 mg orally daily x 7d
- PLUS
- Metronidazole 2 g orally in a single dose OR
- Tinidazole 2 g orally in a single dose

Source: CDC 2015 STD Treatment Guidelines



M. genitalium Treatment

Treatment in the context of syndromic management

- Urethritis
 - Recommended: Azithromycin 1g PO [RESISTANCE EMERGING]
 - Alternative: Azithromycin 500 mg PO x1 then 250 mg PO x 4 days
Moxifloxacin 400 mg PO x 7 days (if rx failure)

Follow-up

- IF validated *M. genitalium* testing available in persons with persistent urethritis accompanied by persistent detection of *M. genitalium* might be treated with moxifloxacin
- Routine TOC in asymptomatic persons are not recommended.

Management of Sex Partners

- Sex partners should be managed according to guidelines
- IF access to validated *M. genitalium* tests, partner testing and treatment of identified infections might be considered.

Source: CDC 2015 STD Treatment Guidelines



Summary

- The new **2015 CDC STD Guidelines** are the best resource for routine STD management. **Get the App!**
<https://itunes.apple.com/us/app/std-tx-guide/id655206856?mt=8>
<https://play.google.com/store/apps/details?id=gov.cdc.stdtxguide&hl=en>
- **Screen MSM at all sites of exposure for GC/CT** and include **HIV and syphilis** screening at intervals of 3-6 months if high-risk. **Manage partners!**
- **CT has a spectrum of manifestations** from local mucosal invasion to GU tract disease and reactive arthritis
- **Epididymitis** is diagnosed based on **exam findings and treated based on risk**
- **LGV** is caused by L1-L3 serovars of chlamydia is associated with **proctitis and proctocolitis** requiring **3 weeks of doxycycline**
- **Enteric pathogens** may be associated with proctitis and proctocolitis in MSM
- Due to the rising **threat of GC resistance, dual therapy with ceftriaxone/azithro.** should be used to treat infections due to Neisseria regardless of CT results
- New guidance on **NGU** highlight a lower threshold **≥ 2 PMN/HPF** for diagnosis
- Consider **TV infections in high risk heterosexual males** and recurrent NGU
- **M. genitalium** is an **emerging pathogen** associated with urethritis which may not respond to traditional regimens



Thank you for all of the work that you do!



Questions: cmcneil@wakehealth.edu



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**2018 Updates on STD Management:
Practical Approaches to the Most
Common STD Clinic Patient Concerns**


A Monthly Webinar Series

Webinars occur 12-1 pm EST
One Tuesday per month
January – November 2018

Learner Objectives

At the conclusion of this webinar series, participants should be able to:

- Accurately identify patients at risk for STIs and then test, diagnose, and treat according to CDC STD Treatment Guidelines.



Continuing Education Accreditation

This activity has been planned and implemented in accordance with the Essential Areas and the Policies of the Accreditation Council for Continuing Medical Education through the joint providership of the University of Alabama School of Medicine and the Sylvie Ratelle STD/HIV Prevention Training Center.

The University of Alabama School of Medicine is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for participants.

The University of Alabama designates this webinar for a maximum of 1.0 *AMA PRA Category 1 Credit*[™]. Participants should claim only the credit commensurate with the extent of their participation in the activity.

These credits are also applicable for registered nurses.



After Today's Webinar

- You will receive an auto-generated email from the National Network of STD Clinical Prevention Training Centers to complete a brief evaluation of today's presentation.
- Within that email, you will find instructions on how to register for and receive CME credits through the University of Alabama School of Medicine.
- Webinars will be archived and available for viewing at www.RatellePTC.org. CME credits will also be available for archived webinars.



Save The Dates: 2018 STD Webinar Schedule

Date	Title	Speaker(s)	Affiliations
Jan 16	Vaginitis: Bacterial Vaginosis, Yeast Vaginitis, Trichomoniasis	Katherine Hsu, MD, MPH	MDPH/Boston Univ. Med. Ctr.
Feb 20	Cervicitis/PID: Chlamydia, Gonorrhea, <i>M. genitalium</i>	Candice McNeil, MD, MPH	Wakeforest Univ.
Mar 20	Motivational Interviewing for STI/HIV Prevention	Thomas Creger, PhD, MPH	Univ. of Alabama at Birmingham
Apr 24	Pregnancy and STIs	Candice McNeil, MD, MPH	Wakeforest Univ.
May 15	Urethritis/Epididymitis/Proctitis: Gonorrhea, <i>M. genitalium</i> , and Lymphogranuloma Venereum	Candice McNeil, MD, MPH	Wakeforest Univ.
Jun 19	Clinician-Health Department Partnerships: Partner Management, Disease Reporting, Presumptive Treatment	Marjorie Kirsch, MD	FL DOH Wakulla County



**Save The Dates:
2018 STD Webinar Schedule (cont'd)**

Date	Title	Speaker(s)	Affiliations
Jul 17	Genital Lesions: HSV, HPV, Syphilis	Nicholas Van Wagoner, MD, PhD	Univ. of Alabama Sch. of Med.
Aug 21	Management of STI/HIV Coinfection	Katherine Hsu, MD, MPH	MDPH/Boston Univ. Med. Ctr.
Sept 11	Genital Dermatology	Nicholas Van Wagoner, MD, PhD	Univ. of Alabama Sch. of Med.
Oct 16	Approaches with Special Populations: Youth, GLBT	Katherine Hsu, MD, MPH and Nicholas Van Wagoner, MD, PhD	MDPH/Boston Univ. Med. Ctr. and Univ. of Alabama Sch. of Med.
Nov 13	Update on PrEP	Ulyee Choe, DO	FL DOH Pinellas County/Univ. of S. Florida College of Med.