

Developments in STD testing:  
*A collaborative discussion for  
clinicians and laboratorians*

Jessica Dalby, MD  
Alana Sterkel, PhD

July 29, 2020

## Welcome

- Welcome to the jointly sponsored Health Care Education and Training (**HCET**) and Wisconsin State Laboratory of Hygiene's (**WSLH**) Wisconsin Clinical Laboratory Network (**WCLN**) webinar -

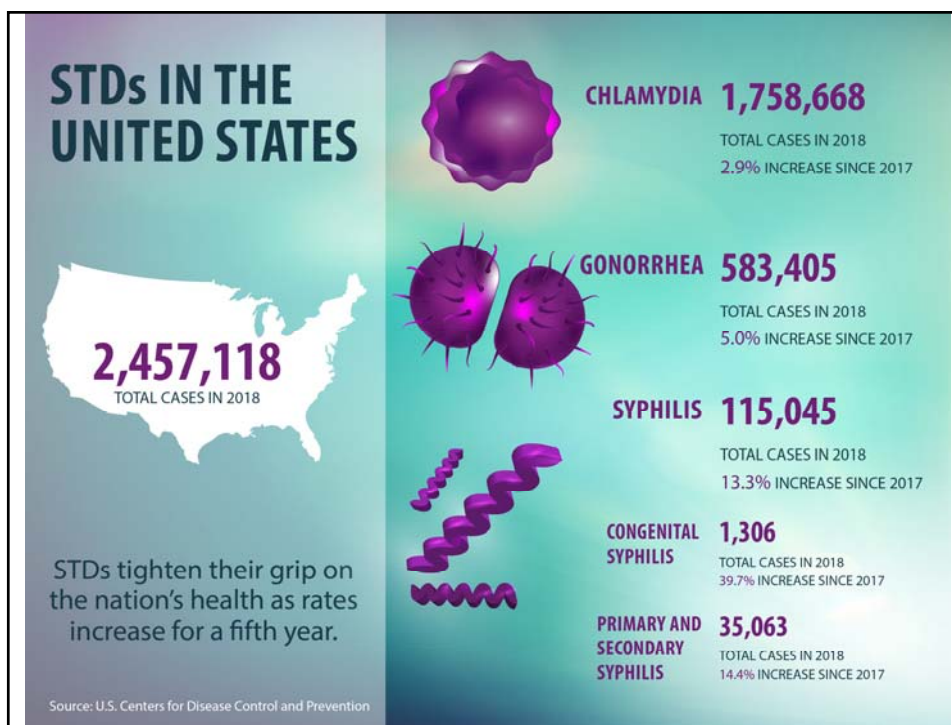
***"Developments in STD Testing - a  
Collaborative Discussion for Clinicians and  
Laboratorians"***

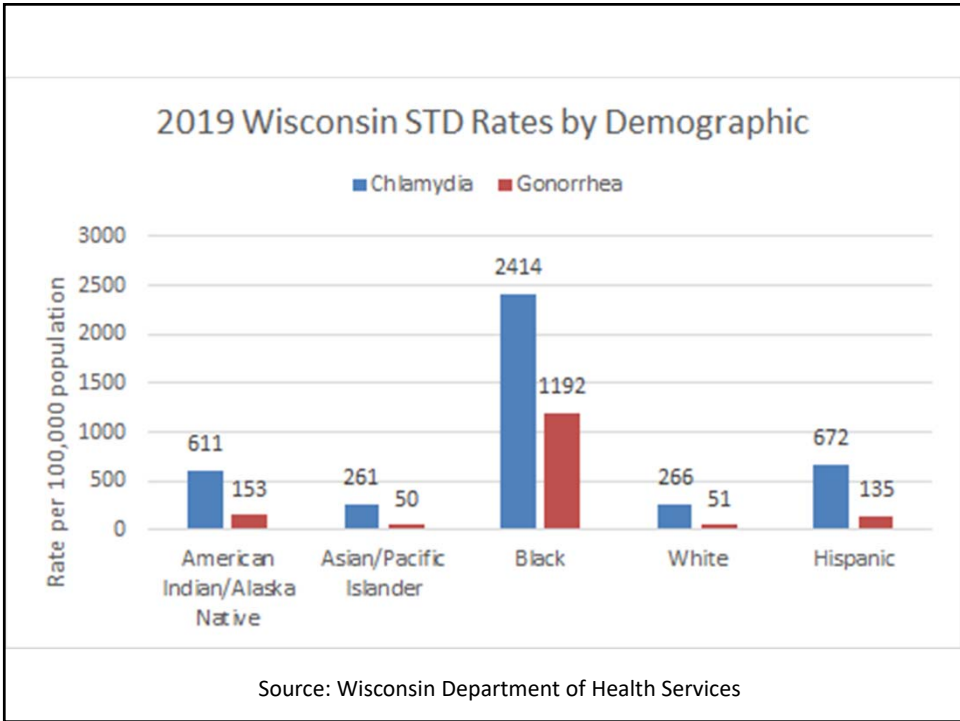
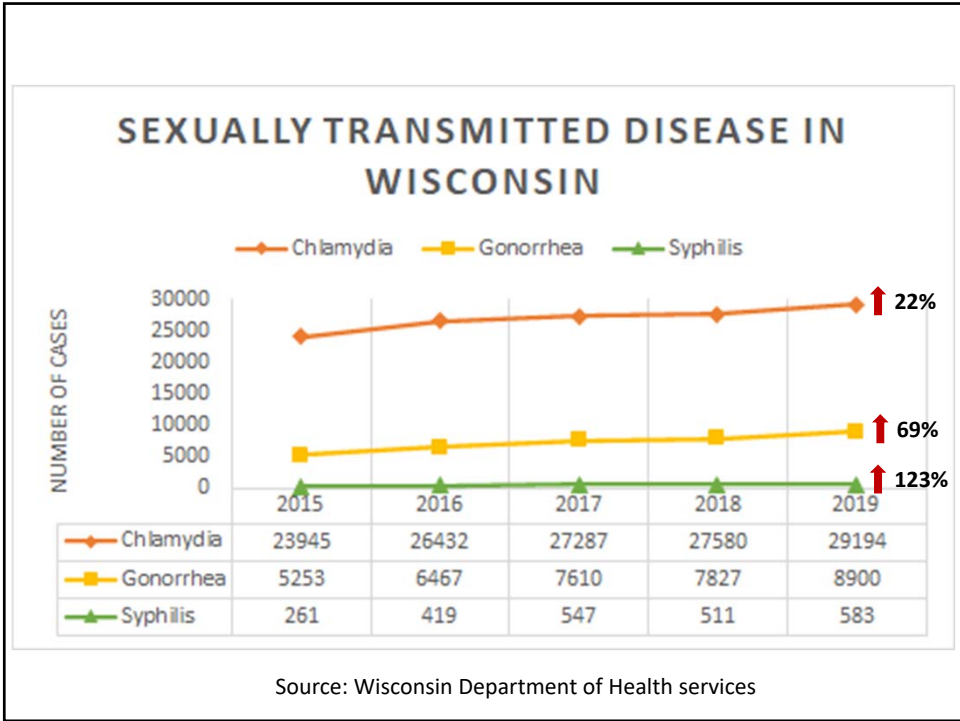
- **Thank you for joining us today!**



## Objectives

- Discuss the importance of extragenital testing
- Consider implementation of self-collection
- Share the clinical implications and testing strategies for *Mycoplasma genitalium*
- Advocate for testing and treating males with Trichomoniasis
- Review the platforms FDA cleared for this new type of testing





# Extragenital


## Extragenital testing

- Definition: Collecting samples from rectum and pharynx
- Remember the 5 “P”s of sexual history
  - Partners
  - **Practices**
  - Protection from STDs
  - Past STDs
  - Pregnancy prevention


Centers for Disease Control and Prevention  
**MMWR** | **MSM\* & STDs: TEST MORE THAN GENITALS**

**STDs IN THE THROAT AND RECTUM**


- **MSM AT HIGH RISK**
- **OFTEN NO SYMPTOMS**
- **DETECT BY SCREENING**
- **INCREASES HIV RISK**



**OF MSM SCREENED FOR CHLAMYDIA & GONORRHEA\*\*:**




**1 IN 8 HAD AN STD IN THROAT OR RECTUM**



**1/3 NOT SCREENED IN LAST 12 MONTHS**

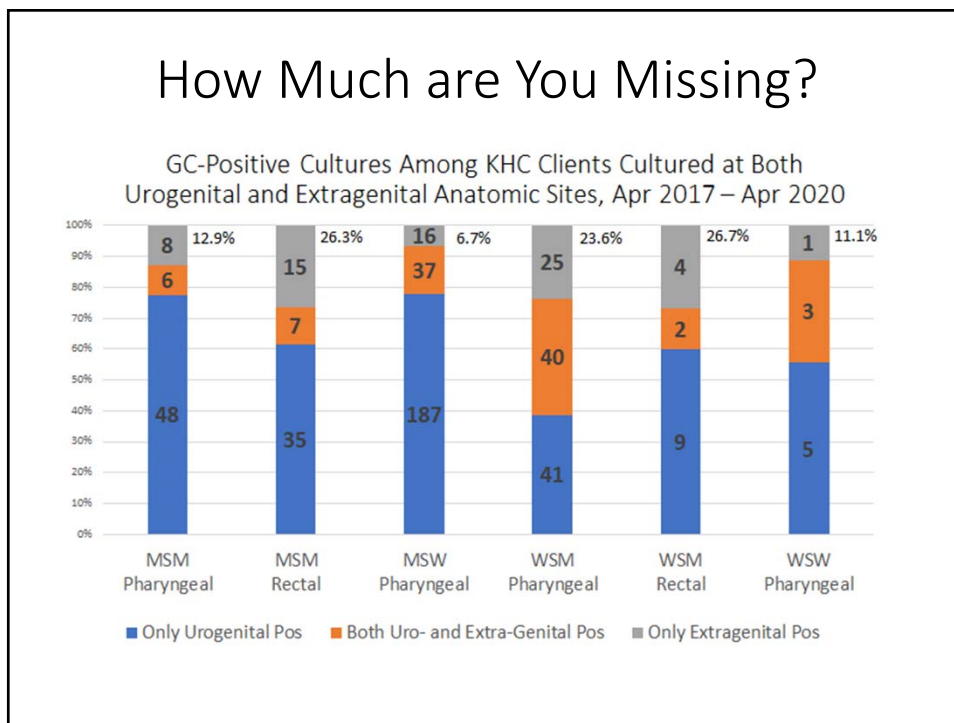
**SCREEN SEXUALLY ACTIVE MSM FOR STDs!**

- **AT LEAST 1X/YEAR**
- **HIGHER RISK? EVERY 3-6 MONTHS**
- **IF INDICATED, TEST THROAT & RECTUM**

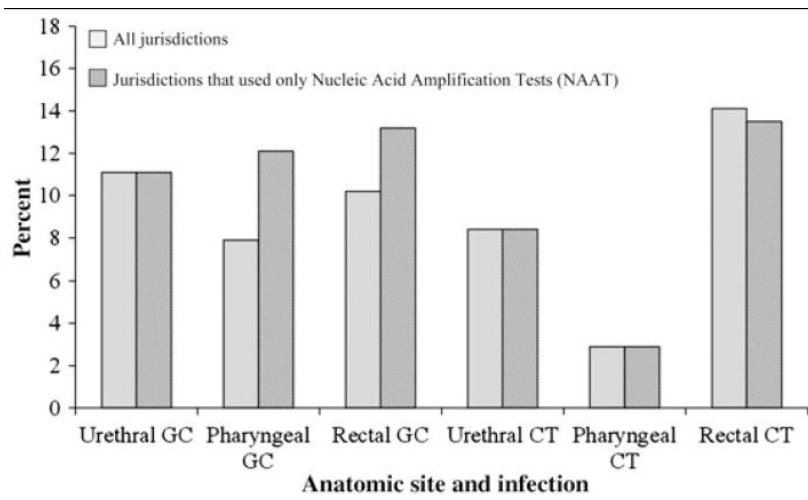


Data from National HIV Behavioral Surveillance (NHBS) as published in Johnson Jones et. al. MMWR 2019.  
 \* Men who have sex with men  
 \*\* MSM recruited from social venues in 5 cities provided data and self-collected swabs  
 doi://CDCVA24  
 © 2019-20

[WWW.CDC.GOV](http://WWW.CDC.GOV)



## Extragenital CT and GC



Patton et al. Clin Infect Dis 2014

## Oral and Rectal Testing

- CT/GC now FDA approved on 3 different platforms!

- Panther
- Cobas
- GeneXpert



## Self collection

### Self Collected Vaginal

- 3867 women at an urban sexual health centre (10.2% CT positive)
- Self-collected vulvovaginal swabs were significantly more sensitive than endocervical swabs (97% vs 88%;  $P < .00001$ )
- Using endocervical samples rather than vaginal swabs would have missed 9% of infections
- 90% of women found it very easy to self-collect a vaginal swab, and 67% preferred a vaginal swab over a pelvic examination

Sarah A. Schoeman. British Medical Journal. 2012;345:e8013

## Self Collected Penile Meatal

- 203 paired urethral and penile meatal self collected swabs
- More infections detected with self-collection
  - CT: 96.8% sens, 98.8% spec.
  - NG: 100% sens, 98.9% spec.
  - TV: 85.0% sens, 96.7% spec.
  - MG: 79.3% sens, 99.4% spec.
- 90.1% of men reported it was easy or very easy and are willing to collect their own swab sample

Diaz et al. *Diag. Micro Inf Dis.* 2016. <https://doi.org/10.1016/j.diagmicrobio.2016.07.018>

## Self Collected Extragenital More people willing to test

- Urban HIV clinic implemented self-testing program for asx clients. Compared testing and yield along with patient acceptability before and after self-testing implemented
- Increased testing: 32% more pharyngeal, 33% more rectal
- Increased detection: 50% more gonorrhea, 47% more chlamydia
- 95% of participants collected samples appropriately
- 92% rated self-testing experience as “good” or “very good”

Barbee et al. Implementation and Operational Research: Effectiveness and Patient Acceptability of a Sexually Transmitted Infection Self-Testing Program in an HIV Care Setting. *J Acquir Immune Defic Syndr.* 2016;72(2):e26-e31.



## Self Collected Rectal

- 1458 MSM and 936 women at Dutch STI clinics who report rectal receptive intercourse
- Self-collected versus clinician collected **rectal** sample for NAAT testing
- Results:
  - MSM 11% +CT and 7% +GC, W 9% +CT and 2% +GC;
  - Concordance for CT 98% in MSM and W
  - Concordance for GC 98% in MSM and 99.4% in W
  - 57% MSM and 62% W preferred self swab

van der Helm et al. High performance and acceptability of self-collected rectal swabs for diagnosis of Chlamydia trachomatis and Neisseria gonorrhoeae in men who have sex with men and women. *Sex Transm Dis.* 2009;36(8):493-497.

## Self Collected Pharyngeal

- 480 MSM in San Francisco STD clinic
- Self-collected versus clinician collected **pharyngeal** sample for NAAT testing
- Results:
  - 6.7% GC and 1.3%CT
  - Concordance for GC 96.6%
  - Concordance for CT 99.4%

Freeman AH et al. Evaluation of self-collected versus clinician-collected swabs for the detection of Chlamydia trachomatis and Neisseria gonorrhoeae pharyngeal infection among men who have sex with men. *Sex Transm Dis.* 2011;38(11):1036-1039.

## Testing by Self Collection

- Many STIs now widely available for self collected vaginal testing!
    - Panther- CT/GC/TV/MG/CV/BV
    - Cobas- CT/GC/TV/MG
    - BD Max- CT/GC/TV
    - BD Viper- CT/GC/TV
    - Alinity M- CT/GC/TV
    - GeneXpert- CT/GC/TV
- \*No FDA approved oral/rectal self collection yet
- Self collected penile meatal now FDA approved
    - Panther- MG
    - Cobas- MG

## What about pooled specimens from multiple sites?

- 489 female sex workers sampled from vagina, rectum and pharynx. After vortex, aliquot from each sample pooled into single vial.
- 6.5% positive CT and 3.5% positive GC
- Testing only vaginal samples would have missed 40% of CT and 60% of GC
- Of 42 positive women on non-pooled sample, only 5 were negative on pooled sample (due to single site infections with low bacterial load)
  - sensitivity of 94% (95% CI 79% to 99%) for CT and 82% (95% CI 57% to 96%) for NG

Verougstraete et al. To pool or not to pool? Screening of *Chlamydia trachomatis* and *Neisseria gonorrhoeae* in female sex workers: pooled versus single-site testing. *Sex Transm Infect.* May 13 2020.

## Pooling

- In the right setting this can be useful to maximize limited supplies.
- Pooling dilutes the sample so pools should not have more than 5 samples.
- It can delay the time to report a positive since each positive needs to be tested twice.
- If the disease prevalence is greater than 5% the amount of testing is no longer time or cost effective
- It is challenging for some LIMS to deal with pooling
- Pooling is not approved in current FDA assays.

**\*Talk to the lab!**

## Lab Developed Test

- Requires much more extensive in lab validation
- May require IRB approval for human subject research
- Time consuming and expensive

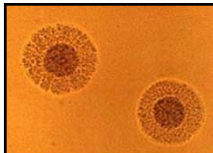
# *Mycoplasma genitalium*

## Mycoplasma genitalium: The Basics

- Symptoms similar to chlamydia (NSU, cervicitis)
- Common in urogenital system, also rectum; uncommon in pharynx
- Prevalence in general population 1-2%, in STI clinic attendees 4-38%
- Infection may persist for months or years

## Guideline Comparison

Guideline	USA (2015 - CDC)	Canada (2019?)	European (2016 - IUSTI)	Australian (2018 – ASHM)	British (2018 – BASHH)
Who to test?	Symptomatic men and women (urethritis, cervicitis, PID)	Persistent or recurrent urethritis, cervicitis, or PID despite empiric treatment when initial tests for gonorrhea and chlamydia are negative.	Symptomatic clients (including vaginal discharge) ALSO High-risk sexual behavior ALSO prior to abortion or IUD insertion	Symptomatic clients and their contacts	Symptomatic (NGU and PID)



## M gen Diagnostics

- Gram Stain not useful (no cell wall)
- Culture not useful
  - *M. genitalium* can take up to 6 months grow
  - Requires special media
  - Only a few labs in the world able to grow M gen
- The optimal detection method is molecular
  - Nucleic Acid Amplification Test (NAAT)

Mycoplasma tests					
Vendor	Platform	Test	Targets	Sample	Status
Roche	Cobas 6800/8800	TIB MOLBIOL	MG/TV	Urine, Swabs (vaginal, self vag., endocervical, meatal, and self meatal)	FDA approved
Hologic	Panther	Aptima Mycoplasma Genitalium Assay	MG	Urine, Swabs (endocervical, cervical, vaginal, self vag., urethral, and self meatal)	FDA approved
Abbott	Alinity M	STI Assay	CT/GC/TV/MG	Swab (endocervical)	FDA approved
BD	BD MAX	Mycoplasma – Ureaplasma OSR	MH/MG/UU/UP	Thin-prep	CE-IVD in Europe
BioFire	BioFire	FilmArray STI	CT/GC/TV/MG/UU/UP/syphilis, H. ducreyij, herpes 1+2	Urine, Swabs (cervical, vaginal, urethral, ulcer, oral, and rectal)	RUO
Bio-Rad	qPCR, multiple	CT/NG/MG Assay	CT/NG/MG	Urine, Swabs (endocervical, vaginal, anorectal, self vag.)	Dev.
Diagenode	qPCR, multiple	DIA-MG-050 vs2	MG/TV	Urine, Swabs (vaginal, urethral)	CE in Europe
Pathofinder	qPCR, multiple	RealAccurate TVMGres	TV/MG MG Az Res	Urine, Swabs (vaginal)	CE-IVD in Europe
Speedx	qPCR, multiple	ResistancePlus MG assay	MG + 5 Res genes	Urine, Swabs (anal, cervical, endocervical, and vaginal)	CE in Europe

## Antibiotic Resistance



- *M. genitalium* lacks a cell wall, and thus antibiotics targeting cell-wall biosynthesis (e.g., beta-lactams including penicillins and cephalosporins) are ineffective against this organism.
- Due to challenges of culture, antibiotic resistance testing not clinically available
- Resistance often detected by treatment failure

## Growing Antibiotic Resistance

- Are we increasing the prevalence of antibiotic resistant M gen with presumptive treatment of urethritis (NSU/NGU)?
  - Azithromycin 1g cures 85% in macrolide susceptible infections (more recent study with cure rates of just 40%)
    - Macrolide resistance highly variable, 30-50%, up to 80% in MSM in one Australian study
    - Estimated 10% of susceptible infections develop resistance during treatment course
  - Doxycycline cures 30-40%
    - lowers bacterial burden, does not cause resistance
  - Moxifloxacin cure rate approaches 100% in susceptible infections (more recent studies 89%)
    - Moxifloxacin resistance ~30% in Asia-Pacific region, 10-15% in Australia
- Risk of fluoroquinolones
  - Moxifloxacin cannot be used in pregnancy, and is associated with diarrhea, occasional tendinopathy and rare neurological and cardiac events

<https://www.cdc.gov/std/tg2015/emerging.htm>

Jensen et al. 2016 European guideline on Mycoplasma genitalium infections.

## Treatment Guidelines

Guideline	USA (2015 - CDC)	Canada (2019?)	European (2016 - IUSTI)	Australian (2018 - ASHM)	British (2018 - BASHH)
<b>Initial Treatment</b>	Azithromycin (1g once vs 5-day: 500mg +250mgx4)	Azithromycin 5 day: 500mg + 250mgx4	Azithromycin (5 day: 500mg + 250mgx4) OR Josamycin 500mg TID x 10d	Doxycycline 100mg BID x 7d followed by Azithromycin 1g + 500mgx3	Doxycycline 100mg BID x 7d followed by Azithromycin 1g + 500mgx2  Alternative: Pristinamycin
<b>Persistent sx</b>	Moxifloxacin 400mg 7,10 or 14 days	Moxifloxacin 400mg x 7 days (14 days PID)	Moxifloxacin 400mg 7-10 d (14d PID) (3rd line: doxycycline 100mg BID x 14 days)	Doxycycline 100mg BID x 7d followed by Moxi 400mg x 7d	Moxifloxacin 400mg x 10d (14d PID)

## Milwaukee Health Department Data

- 12 Months (March 2019 to February 2020)
  - **1254 Male patients with urethritis symptoms**
    - 327 + GC (26%)
    - 295 + MG (24%)
    - 228 + CT (18%)
    - 56 + TV (4%)

Analyte tested	CT	GC	MG	TV	CT/GC	CT/MG	CT/TV	CT/GC/MG	CT/GC/TV	CT/MG/TV	GC/MG	MG/TV	GC/MG/TV
Positive	228	327	295	56	49	43	4	23	3	0	58	4	1

CT = Chlamydia; GC = Gonorrhea; MG = M Gen; TV = Trichomoniasis

## Milwaukee Health Department Protocol

- Clients with NSU/NGU now treated with doxycycline 100mg BID x 7 days as first-line replacing 1g Azithromycin based on higher rate of M gen than Chlamydia in this population at our STD clinic



## Partner Treatment?

Guideline	USA (2015 - CDC)	Canada (2019)	European (2016 - IUSTI)	Australian (2018-ASHM) *primary care	British (2018-BASHH)
<b>Follow up</b>	No TOC	Insufficient data, Maybe in areas of known high prevalence AR	TOC for all patients – no sooner than 3 weeks from tx initiation	TOC – no sooner than 14 days from completion of tx	TOC for all patients 5 weeks (no sooner than 3 weeks) from tx initiation
<b>Partner tx?</b>	Consider partner testing	Treat current partners (testing not necessary)	Test and treat OR just treat	Test and treat current partners	Test and treat (OR just treat)

## Controversy: Asymptomatic Screening?

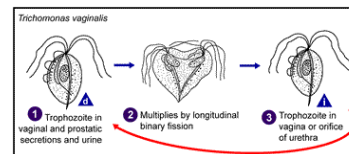
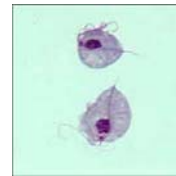
### BASHH 2018 Guidelines:

- The evidence suggests that the majority of people infected with *M. genitalium* in the genital tract do not develop disease.
- Current treatments are imperfect and associated with development of antimicrobial resistance.
- There is no evidence that screening asymptomatic individuals will be of benefit, and indeed is likely to do harm at a population level.

# Trichomoniasis

## *Trichomonas vaginalis*

- Flagellated parasite
- Feeds through absorption and ingestion of bacteria
- Can survive in urine, semen, or water for up to 24 hours



## Trich Diagnostics

- **Microscopy** used routinely (twitching motility)
  - 1-24 Hours (50-70% sensitive)
- **Culture** often successful and more sensitive
  - 2-8 Days (~80% sensitive), most appropriate in abuse cases
- **Antigen detection** variable, not recommended for asymptomatic women
  - 1-3 Days (67-95% sensitive)
- **Molecular** assays highly sensitive and specific, samples tolerate shipping.
  - 1-3 Days (85-98% sensitive)
- **Antimicrobial susceptibility testing**
  - No guidelines, testing rare at CDC

## NAAT for Male Trich

- Urine testing now available on 3 platforms
  - Cobas
  - Alinity M
  - GeneXpert
- Not yet available on urethral swabs

## 2015 CDC guidelines for TV testing

- Symptomatic women
- Screening in persons living with HIV
- Screening “might be considered” for individuals receiving care in settings with high prevalence (eg, prisons and sexually transmitted disease [STD] clinics) and for individuals engaged in high-risk behaviors (eg, multiple sex partners and illicit drug use)

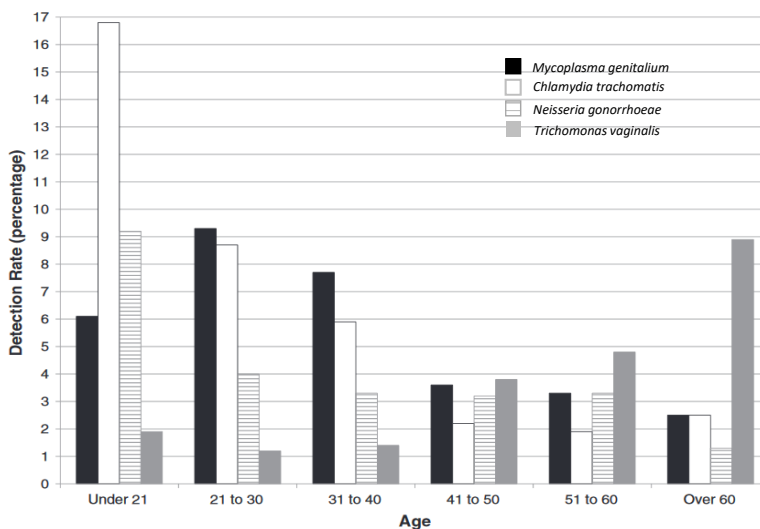
## Racial Disparities

- 4057 men and woman participating in the 2013–2014 National Health and Nutrition Examination Survey
- Urine sample for Trich NAAT
- Results
  - 71 of 4057 +TV (1.2%)
  - Significant racial disparities: 6.8% black vs 0.4% other

Patel et al. Prevalence and Correlates of *Trichomonas vaginalis* Infection Among Men and Women in the United States. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, 67(2), 211–217. 2018.

## STI rates of Men at Milwaukee Clinics

M. Napierala et al. / *Diagnostic Microbiology and Infectious Disease* 82 (2015) 194–198



Napierala M, Munson E, Wenten D, Phipps P, Gremminger R, Schuknecht MK, Munson KL, Boyd V, Hamer D, Schell RF, Hryciuk JE. *Diagn Microbiol Infect Dis*. 2015

## Milwaukee Health Department Data

- 12 Months (March 2019 to February 2020)
  - **1254 Male patients with urethritis symptoms**
    - 327 + GC (26%)
    - 295 + MG (24%)
    - 228 + CT (18%)
    - 56 + TV (4%)

Analyte tested	CT	GC	MG	TV	CT/GC	CT/MG	CT/TV	CT/GC/MG	CT/GC/TV	CT/MG/TV	GC/MG	MG/TV	GC/MG/TV
Positive	228	327	295	56	49	43	4	23	3	0	58	4	1

CT = Chlamydia; GC = Gonorrhea; MG = M Gen; TV = Trichomoniasis

## Importance of Trichomoniasis Screening and Treatment in Men

- TV infection is strongly linked to an increased risk of human immunodeficiency virus (HIV) acquisition and transmission
- Association with preterm delivery
- Treatment of all sexual partners can prevent recurrences in the index cases, reduce transmission, and prevent new cases in the community.

Lab Testing summary

## Molecular Diagnostics



BD Viper



Hologic Panther



Cepheid Gene Xpert  
Male urine FDA approved



Roche Cobas



Abbott Alinity M



BD MAX

## STD/Women's Health Platforms by Pathogen

	<i>Chlamydia trachomatis</i>	<i>Neisseria gonorrhoea</i>	<i>Trichomonas vaginalis</i>	<i>Mycoplasma genitalium</i>	<i>Herpes simplex virus</i>	<i>Candida vaginitis</i>	Bacterial vaginosis	Human papillomavirus	Hepatitis C virus	Group B Strep	HIV	Hepatitis B virus
BD Viper	X	X	X	-	X	-	-	-	-	-	-	-
BD Max	X	X	X	-	-	X	X	-	-	X	-	-
Panther	X	X	X	X	X	X	X	X	X	X	X	X
Cobas	X	X	X	X	X	-	-	X	X	X	X	X
Alinity m	X	X	X	X	-	-	-	X	X	-	X	X
Xpert	X	X	X	-	-	-	-	X	-	X	-	-

**Key**  
Available  
Not Available

## STD Platforms by Specimen Type

	Female Urine	Male urine	Endocervical	Urethral	Pap	Vaginal	Self Vag	Self meatal	Throat/Oral	Rectal	Ulcer	Vag/anal	Blood
BD Viper	CT/GC/TV	-	CT/GC/TV/HSV	CT/GC	-	-	CT/GC/TV	-	-	-	HSV	-	-
BD Max	CT/GC/TV	CT/GC	CT/GC/TV	CT/GC	CT/GC	-	CT/GC/TV	-	-	-	HSV	GBS	-
Panther	CT/GC/MG	CT/GC/MG	CT/GC/TV/MG	CT/GC/MG	CT/GC/TV/HPV	CT/GC/TV/MG/CV/BV	CT/GC/TV/MG/CV/BV	MG	CT/GC	CT/GC	HSV	GBS	HCV/HIV/HBV
Cobas 6800	TV/MG	CT/GC/TV/MG	CT/GC/TV/MG	CT/GC	CT/GC/TV/HPV	CT/GC/TV/MG	CT/GC/TV/MG	MG	CT/GC	CT/GC	HSV	GBS	HCV/HIV/HBV
Alinity m	CT/GC/TV	CT/GC/TV	CT/GC/TV/MG	-	CT/GC/TV/HPV	CT/GC/TV	CT/GC/TV	-	-	-	-	-	HBV/HCV/HIV
GeneXpert	CT/GC/TV	TV	CT/GC/TV	-	-	-	CT/GC/TV	-	CT/GC	CT/GC	-	GBS	-

CT	Chlamydia trachomatis	
GC	Neisseria gonorrhoea	
TV	Trichomonas vaginalis	
MG	Mycoplasma genitalium	
HSV	Herpes Simplex virus	Key
HPV	Human papilloma virus	Available
HCV	Hepatitis C virus	Not Available
HIV	Human immune deficiency virus	
GBS	Group B Streptococcus	
CV	Candidia vaginosis	
BV	Bacterial Vaginosis	

Testing update at wslh



## WSLH Switching to Panther

### How does this impact you?

- New collection kits
- New pathogen
  - *Mycoplasma genitalium*
- New sample types
  - Oral and rectal CT/GC
  - Self collected penile meatal for *Mycoplasma genitalium*
  - Male urine for CT/GC and *Mycoplasma genitalium*
  - Clinician collected vaginal- CT/GC/TV/MG
- Faster time to results

## Communication

- Webinar
- Updates in the newsletter
- Letters to submitters
- Posted announcements on WSLH webpage
- Updates to the WSLH reference manual
- Presented/handouts at STD Conferences

## Summary

- Extragenital testing
  - *If they use it, you should test it! Offer rectal and pharyngeal testing.*
- Self collection
  - *They may be more willing to test and you will find more to treat!*
- *Mycoplasma genitalium*
  - *This is a common cause of urethritis in males. There are serious concerns with antibiotic resistance.*
- Male *Trichomonas vaginalis*
  - *Keep this on your differential for men with symptoms and consider testing high-risk men without symptoms. More prevalent with increasing age, significant racial disparities with higher rates in black people.*
- New FDA testing and update at WSLH

## Questions?

## Thank You!

- Thank-you to Dr. Dalby and Dr. Sterkel for sharing their expertise on this important subject and giving a wonderful presentation today!
- Thank-you to HCET for partnering with the WCLN to provide today's webinar.
- If you are a WI laboratorian and have any questions after we've concluded today's webinar, you may email Erin Bowles, the Wisconsin Laboratory Network Coordinator at [erin.bowles@slh.wisc.edu](mailto:erin.bowles@slh.wisc.edu) and she will forward your question to the appropriate speaker.

## Archived Presentation

- This webinar has been recorded. It will be posted along with the presentation slides on the WSLH Laboratory Networks and Surveillance Training Events web page for this event within a day or two.
- Here is the link to the web page:  
<http://www.slh.wisc.edu/event/wcln-webinar-developments-in-std-testing-a-collaborative-discussion-for-clinicians-and-laboratorians/>

## Obtaining ASCLS P.A.C.E. CEU

1. Go to the training event webpage for this event:  
<http://www.slh.wisc.edu/event/wcln-webinar-developments-in-std-testing-a-collaborative-discussion-for-clinicians-and-laboratorians/>
2. Click on the link to the "ASCLS CE Organizer" website.
3. Click on the correct box for "Member" or "Non-Member".
4. Login to your account or create an account.
5. Click on "Claim Credit" at the top of the page.
6. Click on the "ASCLS State and Regional Events" tab.
7. Scroll down to ASCLS-Wisconsin and click on "View Region".
8. Click on the blue box to the far right for this webinar event.
9. Scroll to the bottom of the list of offerings and click on "Next".
10. Enter the code **2558** and click on "Next".
11. Complete the program evaluation and click on "Complete Survey".
12. Click on "Download Certificate Now" and save or print your certificate.