

## An Update for Generalists: The 2015 CDC STD Treatment Guidelines

Edward W. Hook III M.D.  
Departments of Medicine,  
Epidemiology, and Microbiology  
Univ. of Alabama at Birmingham  
Birmingham, Alabama



---

---

---

---

---

---

---

---

Edward W. Hook, III, M.D.

### Disclosures

Grant/Research Support: NIH, CDC, WHO, Becton Dickinson, Cepheid, Hologic/Gen-Probe, Roche Molecular,

Consultant: None

Speakers Bureau: None

---

---

---

---

---

---

---

---

### Off-Label Disclosure

This presentation will include discussion of the following non-FDA-approved or investigational uses of products/devices:

Oral and rectal testing for *N. gonorrhoeae* and *C. trachomatis* with NAAT

Testing for *T. vaginalis* by NAAT (in men)

Testing for *M. genitalium* utilizing NAAT

---

---

---

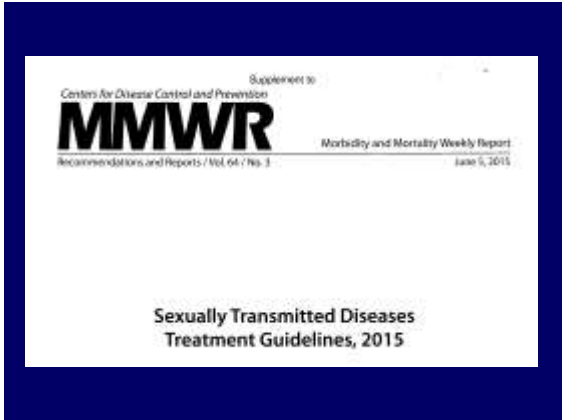
---

---

---

---

---



---

---

---

---

---

---

---

---

**2015 CDC STD Treatment Guidelines**

---

**“Typical” Guidelines Subjects NOT Covered in This Talk**

Adolescents

HPV

Tests You Do Not Do  
Darkfield Microscopy  
Gram Stain

---

---

---

---

---

---

---

---

**2015 CDC STD Treatment Guidelines**

---

**Emerging Topics**

STI Assessment and Management for the Generalist

Sex Partner Status – GLBTQ Awareness

*Mycoplasma genitalium*

Hepatitis C as an STI

---

---

---

---

---

---

---

---

## Lecture Overview

- I. Sexual Health- A subtle but high impact paradigm shift
- II. Changes to the CDC Treatment Guidelines/Hot Topics
  - A. Gonococcal Antimicrobial Resistance
  - B. Extragenital Testing
  - C. Urethritis Diagnosis
  - D. Trichomoniasis – NAATs/ Males
  - E. *Mycoplasma genitalium*- an emerging pathogen

---

---

---

---

---

---

---

---

## Sexual Health Changing the Paradigm

Why are rates of curable STIs (Gonorrhea, Chlamydia, Syphilis) Higher in the U.S Than in Any Other Developed nation on Earth??

---

---

---

---

---

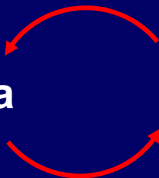
---

---

---

Stigma

Intolerance



---

---

---

---

---

---

---

---

## Evolving Foci for STI Management Efforts

	<u>Major Focus</u>
Pre-1960s	Syphilis
1960s & 70s	Gonorrhea, Syphilis
1970s & 80s	Chlamydia, Gonorrhea, Syphilis (Herpes)
1990s	Chlamydia, Gonorrhea, Syphilis, HPV (Herpes)
21st Century	>25 STIs including Chlamydia, Gonorrhea, Syphilis, HPV, Herpes, Trichomonas and Dysbiotic STI Syndromes

---

---

---

---

---

---

---

---

## Widely Held Beliefs About STDs

“Nice” (normal?) people do not get STDs

If you are not “promiscuous” you will not get STDs, unless your partner betrays you

Testing for STDs is warranted primarily for persons with risks for STD

When STDs are present, its obvious

Discussion of the need for STD testing is offensive to patients

---

---

---

---

---

---

---

---

## Sexual Health Changing the Paradigm

Sexually Transmitted Infections,  
Not Diseases

~~STD~~ STI

---

---

---

---

---

---

---

---

## Consequences of STI-Related Stigma

### Personal (Individual)

- Delays in using or seeking preventative health care
  - Condoms
  - Vaccines
  - Screening
- Delays in seeking care for perceived problems
- Ineffective partner notification

### Provider

- Hesitancy in seeking relevant information
- Differential testing
- Changes to provider-client interactions

### Population

- Guilt by association
- Differential Care
- Profiling

---

---

---

---

---

---

---

---

## Sexual Health

Sexual health is a broad perspective that spans the entire lifespan encompassing topics which include:

- |                             |  |
|-----------------------------|--|
| Sex Education               | Family Planning                            |
| STD/HIV Management          | Reproductive Tract Care                    |
| Interpersonal Relationships | Erectile Dysfunction/<br>Diminished Desire |

---

---

---

---

---

---

---

---

A sexual health framework shifts the approach from a more traditional loss frame approach to a gain frame

Framing – influenced by context; anticipated to have selective influence on perception, encouraging certain interpretation, discouragement, others (Wikipedia)

Gain frame – Emphasizes positives, benefits

Loss frame – Emphasizes risks, potential harm, potentially fueling shame and stigma

---

---

---

---

---

---

---

---

The New Yorker



*"If I ask you something, will you promise not to get mad?"*

---

---

---

---

---

---

---

---

### Loss Frame/Gain Frame Examples Sexual History

#### Loss Frame

##### Partner Type

Have you ever had homosexual sex?

##### Sites of exposure

Have you had oral or rectal sex, or just regular sex?

#### Gain Frame

##### Partner Type

Are your partners men, women or both?

##### Sites of exposure

When you have sex, what sites are exposed- oral, rectal or genital?

---

---

---

---

---

---

---

---

### A Sexual Health "Litmus Test" for Clinicians

Have you ever apologized to a patient for making a diagnosis of chlamydia, trichomoniasis or HIV?

---

---

---

---

---

---

---

---

## Three Question Sexual History for Adults

### Take the history, assess risks

- When was the last time you had sex?
- How many partners have you had in the past year?
- Were they men, women or both?

**Don't hesitate to screen. STI screening is not judgemental it is health promoting**

**Routinely provide STI prevention messages as part of continuing care**

---

---

---

---

---

---

---

---

THE NEW YORKER



*"What's the next best medicinal?"*

---

---

---

---

---

---

---

---

Supplement to  
Centers for Disease Control and Prevention

**MMWR**

Morbidity and Mortality Weekly Report  
Recommendations and Reports / Vol. 64 / No. 1  
June 5, 2015

**Sexually Transmitted Diseases  
Treatment Guidelines, 2015**

---

---

---

---

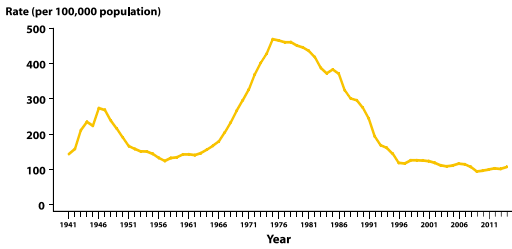
---

---

---

---

## Gonorrhoea — Rates of Reported Cases by Year, United States, 1941–2014




---

---

---

---

---

---

---

---

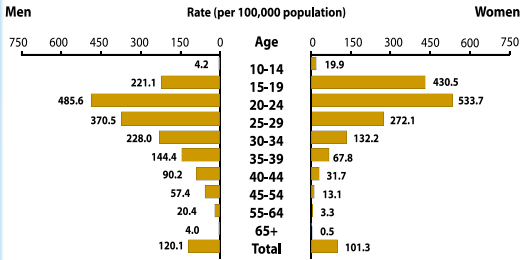
---

---

---

---

## Gonorrhoea — Rates of Reported Cases by Age and Sex, United States, 2014




---

---

---

---

---

---

---

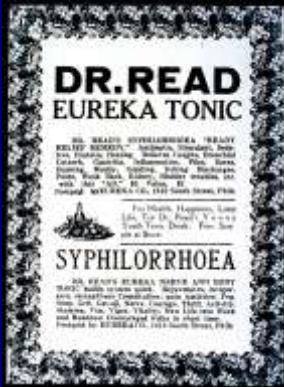
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

---

---



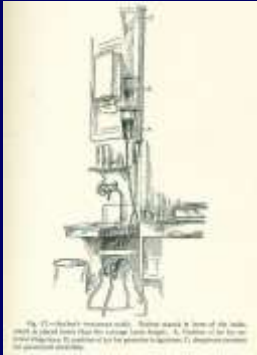


Fig. 12—(Coffey's) steam sterilizer. (1) Steam enters in front of the boiler, which is placed lower than the chamber; (2) steam enters the chamber; (3) chamber is closed; (4) chamber is heated; (5) chamber is cooled; (6) chamber is opened; (7) chamber is emptied.

---

---

---

---

---

---

---

---



Fig. 28—The composition of the middle and ring fingers is then released and the entire anterior surface is irrigated.

---

---

---

---

---

---

---

---

## Emerging Gonococcal Antimicrobial Resistance – Deja Vu

Pre-1937	Antiseptic Irrigation With Potassium Permanganate, Silver Salts, Mercurochrome
1937	Sulfonamide Therapy
1943	Penicillin Therapy (Mahoney <i>et al</i> )
1944	35% Treatment Failure With Sulfonamides
1972	Penicillin Regimen Increased to 4.8 Million Units Plus Probenecid

---

---

---

---

---

---

---

---

## GONORRHEA THERAPY – HISTORICAL PERSPECTIVE

- Previously Recommended Medications For Gonorrhea Therapy
  - Sulfonamides
  - Penicillins
  - Macrolides
  - Tetracyclines
  - Aminoglycosides
  - Spectinomycin
  - Fluroquinolones

---

---

---

---

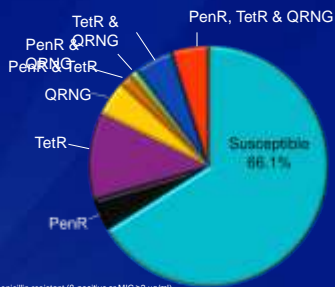
---

---

---

---

### Penicillin, Tetracycline, and Ciprofloxacin Resistance, 2013



PenR = penicillin resistant (B-positive or MIC ≥ 2 µg/ml)  
QRNG = ciprofloxacin MIC ≥ 1 µg/ml  
TetR = tetracycline resistant (MIC ≥ 2 µg/ml)

---

---

---

---

---

---

---

---

PRELIMINARY  
COMMUNICATION

JAMA 2013;309(2):163-170

*Neisseria gonorrhoeae* Treatment Failure and Susceptibility to Cefixime in Toronto, Canada

Cephalosporin-Resistant Gonorrhea in North America

---

---

---

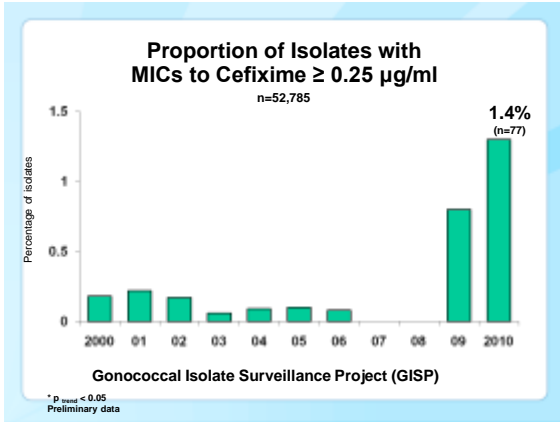
---

---

---

---

---




---

---

---

---

---

---

---

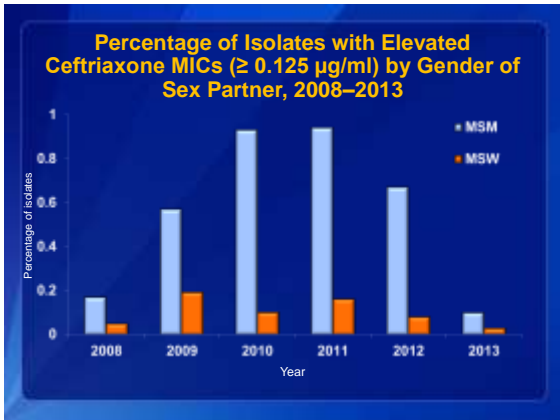
---

---

---

---

---




---

---

---

---

---

---

---

---

---

---

---

---

## ***N. Gonorrhoeae* Treatment Failures to Cefixime, Toronto, Canada**

**Rx failure overall – 6.8% (95% CI – 3.1-12.5%)**  
 If cefixime MIC  $\geq 0.12$  – 25% (95% CI 10.7-44.9%)  
 If cefixime MIC  $< 0.12$  – 1.9% (95% CI 0.23-6.7%)  
 RR 13.13 (95% CI 2.9-59.72)

**Treatment failures:**  
 4 of 76 urethral (5.3%)  
 2 of 7 pharyngeal (28.6%)  
 3 of 39 rectal (7.7%)

Neisseria gonorrhoeae Treatment Failure and Susceptibility to Cefixime in Toronto, Canada, JAMA. 2013;309(2):163-170.

---

---

---

---

---

---

---

---

---

---

---

---

**2015 CDC STD TREATMENT GUIDELINES**  
**Uncomplicated Gonorrhea**

Ceftriaxone 250 mg IM

PLUS

Azithromycin 1.0 g Single Dose ~~or~~  
~~Doxycycline 100 BID x 7d~~  
Even if chlamydia negative

---

---

---

---

---

---

---

---

**Alternative GC Treatment**  
**2015 CDC STD Treatment Guidelines**

Cefixime 400mg po x 1  
Plus  
Azithromycin 1gm po x  
1

+ TOC in ~~1 week~~ 14d

~~If cephalosporin  
allergy:  
Azithromycin 2gm po  
x 1~~

~~+ TOC in 1 week 14d~~

---

---

---

---

---

---

---

---

**Gonorrhea Treatment-**  
**What's Next**

Salvage Therapy:

Gentamicin 240 IM/ Azithromycin 2.0g PO  
(IM Administration/Toxicity)

Gemifloxacin 340 mg/Azithromycin 2.0g PO  
(GI Toxicity)

On The Horizon:

Solithromycin

~~Delafloxacin~~

AZ D0914

Others

---

---

---

---

---

---

---

---

## Reasons for STD Treatment Failure

Reinfection

Wrong Therapy

Wrong diagnosis

Wrong dosage/duration

Self medication

Resistant Organisms

Other

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---

## Changing Paradigms For Urogenital Specimen Collection

Pre-NAAT's: Specimen Quality Critical  
- Endocervical Or Urethral Swabs  
- Swab Order Impacts Test Results

: Culture > Non-Amplified Nucleic Acid Detection > Antigen Detection

NAAT's: More Forgiving Specimen Collection  
- Vaginal Swab  $\geq$  Endocervical Swab  $\geq$  initial Void Urine

---

---

---

---

---

---

---

---

## How common are extra-genital sexual behaviors?

### ♣ Males:

- Active oral
  - Lifetime 77%
  - Last sex 27%
- Passive oral
  - Lifetime 79%
  - Last sex 28%

### ♣ Females

- Active oral
  - Lifetime 68%
  - Last sex 19%
- Passive oral
  - Lifetime 73%
  - Last sex 28%

Michael RT, Gagnon JH, Laumann EO, Kolata G. Sex in America: A Definitive Survey. Little, Brown and Co. UK. 1994.

---

---

---

---

---

---

---

---

---

---

---

---

## Performance of NAATs for Diagnosis of Pharyngeal *N. Gonorrhoeae* and Infections

Pharyngeal Gonococcal Infections (N=961)		
	% Sensitivity (95%)	% Specificity (95% CI)
ProbeTec (SDA)	97.1 (85.1-99.9%)	94.2 (92.5-95.6%)
Amplicor (PCR)	91 (78.1-98.3%)	71.8 (68.7-74.6%)
Aptima Combo2 (TMA)	100 (89.7-100%)	96.2 (98.1-99.6%)
Culture	65.4 (50-78%)	99.0 (98.1-99.6%)

Bachmann, et al. J Clin Micro. 2009;47:902-907.

---

---

---

---

---

---

---

---

---

---

---

---

## Performance of NAATs for Diagnosis of Pharyngeal *N. Gonorrhoeae* and Infections

Pharyngeal Gonococcal Infection By Site	
Site	No (%) Individuals
Genital and Oral	23 (28%)
Genital Only	28 (34.1%)
Oral Only	31 (37.8%)
Total Genital or Oral	82 (100%)

Bachman, et al. J Clin Micro. 2009; 47:902-907.

---

---

---

---

---

---

---

---

---

---

---

---

## Performance of NAATs for Diagnosis Rectal *N. Gonorrhoeae* Infections

Gonococcal Rectal or Genital Infections By Site	
Site	No. (%) Individuals
Genital and Rectal	12 (31.6%)
Genital Only	11 (28.9%)
Rectal Only	15 (39.5%)
Genital or Rectal	28 (100%)

Bachmann, et al. J Clin Micro, 2010, 48: 1827-32 .

---

---

---

---

---

---

---

---

## Performance of NAATs for Diagnosis of Rectal *C. trachomatis* Infection

Chlamydial Rectal or Genital Infections By Site	
Site	No. (%) Individuals
Genital and Rectal	20 (40.8%)
Genital Only	6 (12.2%)
Rectal Only	23 (46.9%)
Genital or Rectal	49 (100%)

Bachmann, L et al. J. Clin Microbiol. 2010;48(5):1827-1832

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---

## Case 1

**History:** 29yo male presents to your office with urethral "itching" 7 days. Two weeks ago while at a business convention he had unprotected sex with a colleague.



---

---

---

---

---

---

---

---

## Case 1 (Cont)

The most likely cause of his symptoms is:

1. Gonorrhea
2. Non gonococcal Urethritis (NGU)
3. Human Papillomavirus Infection
4. Post Coital Remorse

---

---

---

---

---

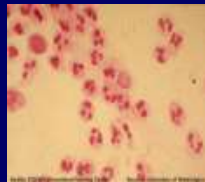
---

---

---

## Case 1(Cont.)

**History:** 29yo male presents to your office with urethral "itching" 7 days. Two weeks ago while at a business convention he had unprotected sex with a colleague.



**Diagnosis:** NGU

---

---

---

---

---

---

---

---



## Urethritis Diagnosis Updates 2015 CDC STD Treatment Guidelines

- NGU cutoff will be lowered to  $\geq 2$  WBC/hpf
- *T. vaginalis* testing could also be considered in areas or populations of high prevalence
  - No FDA-cleared NAAT for *T. vaginalis* detection in men in the U.S.
  - Several large reference labs have performed the necessary CLIA validation of a urine-based *T. vaginalis* NAAT for men
- Currently no commercially available diagnostic test for *M. genitalium* cleared by the FDA for use in the U.S.
  - Some medical centers and commercial labs have developed a *M. genitalium* NAAT
- Methylene Blue/Gentian Violet (MB/GV) smear should be considered as an alternative to Gram stain for clinical diagnosis of urethritis

---

---

---

---

---

---

---

---

---

---

### 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

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

---

---

---

---

---

---

---

---

---

---

## Urethritis: Etiologies

- |   |   |
|---|---|
| <p>† Infectious</p> <ul style="list-style-type: none"> <li>- <i>N. gonorrhoeae</i></li> <li>- NGU                             <ul style="list-style-type: none"> <li>• <i>C. trachomatis</i></li> <li>• <i>U. urealyticum</i></li> <li>• <i>M. genitalium</i></li> <li>• <i>T. vaginalis</i></li> <li>• HSV</li> <li>• Other bacteria (i.e. GNR, &lt;5%)</li> <li>• UNKNOWN! (20-30%)</li> <li>• Dysbiotic Origin?</li> </ul> </li> </ul> | <p>† Non-infectious</p> <ul style="list-style-type: none"> <li>- Chemical</li> <li>- Allergic</li> <li>- Autoimmune</li> </ul> <p>† ? Frequency</p> |
|---|---|

---

---

---

---

---

---

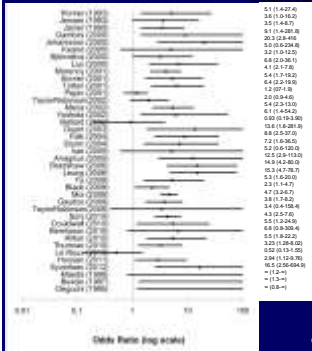
---

---

---

---

## Does MG cause Male Urethritis?



- † Acute urethritis – 38 studies
  - 15% MG+ (median) in urethritis cases
  - 22% MG+ (median) in NCNGU cases
- † Persistent urethritis – 6 studies
  - 12-14% MG+ men with persistent/recurrent urethritis

Compliments: Lisa Manhart

---

---

---

---

---

---

---

---

---

---

## NGU Treatment Updates 2015 CDC STD Treatment Guidelines

- Azithromycin and doxycycline regimens remain recommended for initial NGU treatment
- In areas with high *T. vaginalis* prevalence, heterosexual men with persistent/recurrent urethritis should be presumptively treated
- *M. genitalium* should be suspected in persistent/recurrent urethritis
  - Moxifloxacin 400mg daily x  $\geq 7$  days should be considered for subjects failing azithromycin treatment
- Persistent or recurrent NGU after presumptive treatment for *M. genitalium* or *T. vaginalis* should be referred to a urologist

---

---

---

---

---

---

---

---

---

---

## Persistent/Recurrent Urethritis Treatment 2015 CDC STD Treatment Guidelines

- If azithromycin NOT given for 1<sup>st</sup> 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 1<sup>st</sup> episode:**
- ❖ Moxifloxacin 400 mg orally qd x 7d PLUS
  - ❖ Metronidazole 2 g orally in a single dose OR
  - ❖ Tinidazole 2 g orally in a single dose

---

---

---

---

---

---

---

---

---

---



---

---

---

---

---

---

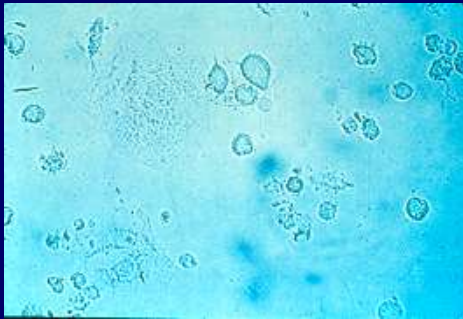
---

---

---

---

## TRICHOMONAS WET PREP



---

---

---

---

---

---

---

---

---

---

### MAJOR ARTICLE

## Added Benefit of Nucleic Acid Amplification Testing for the Diagnosis of *Trichomonas vaginalis* Among Men and Women Attending a Sexually Transmitted Diseases Clinic

Eleonora A. Wilson,<sup>1</sup> Prashil J. Bhambhani,<sup>1</sup> Richard J. Stealy,<sup>2</sup> Ernie L. Smith,<sup>2</sup> and Jane R. Yehoshua<sup>1</sup>  
<sup>1</sup>Division of Infectious Diseases, Department of Medicine, University of Medicine and Dentistry, Newark, New Jersey, and <sup>2</sup>Family, Translational, and Systems Impact, Jefferson School of Population Science, Philadelphia, PA

See the Editorial Commentary by Taylor on page 802-810.

**Background.** *Trichomonas vaginalis* (TV) is the most common cause of sexually transmitted infections (STI) in the world. However, TV is not a reportable STI and, with the exception of HIV-positive women, there are no guidelines for screening in women or men. The objective of this study was to determine the added value of nucleic acid amplification tests (NAATs) for detection of TV in men and women at high risk for trichomonas as well as correlation of infection.

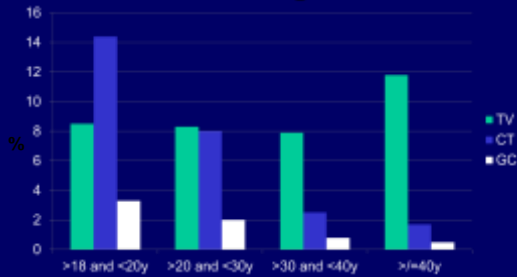
**Methods.** This was a review of clinical and laboratory data of men and women presenting to the Jefferson County Department of Health Sexually Transmitted Diseases (STD) Clinic and receiving a TV NAAT.

**Results.** During 2012-2013, 6,039 patients (3,025 women and 3,014 men) received a TV NAAT on endospermated, urethral, or urine specimens. Overall TV prevalence was 26.2% in women and 9.8% in men. Correlation of TV among men included age >40 years, African American race, and 25 polypropyleneacrylate cells per high-power field on urethral Gram stain. Age >40 years, African American race, leukorrhea on wet mount, elevated vaginal pH, positive white blood cell count, and concurrent gonococcal infection were positively associated with TV among women. TV NAAT detected approximately one-third more infections among women than wet mount alone.

**Conclusions.** TV prevalence among men and women was high in this study, suggesting that both groups should be routinely screened, including those aged <40 years. Improved detection of TV by routine implementation of NAATs

Downloaded from <http://jama.com/> on September 10, 2014. For information on this article, visit [jama.com](http://jama.com).

## STI Prevalence in Women by Pathogen and Age



Ginocchio et al. J Clin Microbiol 2012, 50(8):2601

---

---

---

---

---

---

---

---

---

---

## Trichomoniasis Treatment 2015 CDC STD Treatment Guidelines

### New Episode

Tinidazole 2 g PO single dose OR  
Metronidazole 2 g PO single dose  
Metronidazole 500 mg po BID for 7d (alternative, rec if HIV+)

### Treatment Failure of 2 g metronidazole single dose

Metronidazole 500 mg BID x 7d

### Treatment Failure – Additional Options

Tinidazole or Metronidazole 2 g PO daily x 5d 7d  
Tinidazole 2-3g PO daily x 14d plus intravaginal tinidazole

### Treatment Failure – Alternative Additional Options

High-dose tinidazole + intravaginal paromomycin  
Nitazoxanide PO  
Intravaginal boric acid-

---

---

---

---

---

---

---

---

---

---

## Off-Label Disclosure

This presentation will include discussion of the following non-FDA-approved or investigational uses of products/devices:

Oral and rectal testing for *N. gonorrhoeae* and *C. trachomatis* with NAAT

Testing for *T. vaginalis* by NAAT (in men)

Testing for *M. genitalium* utilizing NAAT

---

---

---

---

---

---

---

---

---

---



\"BMM, Zog! ... Here come one now!\"

---

---

---

---

---

---

---

---

## Acknowledgement

Laura Bachmann, MD, MPH  
William M. Geisler MD, MPH

## Resources



[www.stdptc.org](http://www.stdptc.org)



[www.nnptc.org](http://www.nnptc.org)

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---