Trichomoniasis: Testing and Treatment Update

Arlene C. Sena, MD, MPH
Medical Director, Durham County Health Department
Associate Professor, University of North Carolina
Infectious Diseases

Acknowledgements: Marcia Hobbs, PhD

Outline

• Epidemiology of T. vaginalis infections
• Clinical presentations of trichomoniasis
• T. vaginalis detection and improved diagnostic methods
• Treatment considerations
• HIV interactions

What’s in a name?

From the Greek:
• trichos, hair
• monas, unit, single

Trichomonads in vaginal discharge first described by Alfred Donné in 1863

Trichomoniasis and other vaginal infections in women — Initial visits to physicians’ offices: United States, 1966–2008

Note: The relative standard error for trichomoniasis estimates range from 16% to 27% and for other vaginitis estimates range from 8% to 13%.

Trichomoniasis prevalence estimates in women

- Miller et al. 2005, US, Add Health
- Sutton et al. 2007, US, NHANES
- Hollman et al. 2010, NYC
- Keesee et al. 2010, Zimbabwe
- Kraishin et al. 2010, US
- Munson et al. 2008, US
- Hapert et al. 2007, US
- Crucitti et al. 2010, Zambia
- Freeman et al. 2010, SF, CA jails

Trichomoniasis prevalence estimates in men

- Price et al. 2004, Malawi, Dermatol.
- Huq et al. 2010, Bangladesh, SFV clients
- Black et al. 2006, South Africa, VCT
- Black et al. 2006, South Africa, urethritis

Associations with Trichomoniasis

- HIV
- Risk of other STDs (gonorrhea, HSV)
- Cervical neoplasia (HPV)
- Tubal infertility
- Post-hysterectomy infection
- Atypical PID
- Preterm birth

Screening for trichomoniasis criteria?

Community-based study in remote northern Australia
Proportion of asymptomatic trichomoniasis

- 77% asymptomatic
- 73% symptomatic

Symptoms included penile or vaginal discharge or itching, dysuria, or lower abdominal pain.

Clinical presentation in women

- Common sites of *T. vaginalis* infection include the vagina, urethra, and endocervix
- Symptoms include vaginal discharge, itching, odor, dysuria (though commonly asymptomatic)
- Elevated vaginal pH, amines
- Frothy discharge and strawberry cervix are classic findings on exam

Clinical presentation in men

- Non-gonococcal, non-chlamydial urethritis
- Symptoms include urethral discharge, dysuria (though commonly asymptomatic)
- *T. vaginalis* can be isolated from men with chronic prostatitis

*T. Vaginalis* Diagnostics

- Wet mount microscopy
- Culture
- Rapid antigen detection
- Nucleic acid amplification tests (NAATs)
  - in-house polymerase chain reaction (PCR)
  - commercially available transcription mediated assays (TMA)
Wet mount microscopy

- Performed on vaginal swab specimens (or male urine sediment) resuspended in a drop or 2 of saline
- Organisms must be viable and motile
- Must be performed within 15 minutes of specimen collection
- 50 - 70% sensitivity with expert microscopist

T. vaginalis culture

- Trich grows best in microaerophilic or anaerobic environments
- CO₂ incubator or anaerobe jars, 35 - 37°C, pH 5 - 7.5
- Diamond’s medium with antifungal and antibacterial additives
- InPouch™ TV (Biomed)
- Cultures examined daily for up to 5 days
- Sensitivity estimates:
  70 - 90% in women
  < 50 - 70% in men

InPouch TV cultures from men require long incubation periods

Rapid antigen detection

- Dipstick from Genzyme
- Antibodies on stick capture T. vaginalis antigen in specimen
- Sensitivity slightly better than wet mount microscopy ~80%
- Only validated in women
Recent advances in *T. vaginalis* detection (NAATs)

- Numerous in-house PCR assays in the literature
  - gel detection
  - ELISA detection
  - real-time PCR
- Gen-Probe, Inc. now has a commercial (not FDA cleared) Analyte Specific Reagent test using transcription-mediated amplification (TMA)
- NAATs are more sensitive than other tests for *T. vaginalis* (~90 - 100%)
- Non-invasive specimens
  - urine
  - self-collected vaginal swabs

*Trich detection in Malawian men*

- *T. vaginalis* is seldom included in studies of STDs in men.
- When it is sought, a urethral swab OR urine is usually collected for culture.
- The organism can be recovered from urethral swabs, urine, semen and rarely from the external genitalia.
**Treatment of Trichomoniasis**

- Metronidazole 2 gm orally once
- Metronidazole 500 mg orally twice daily x 7 days
- Metrogel NOT recommended; ≤ 50% efficacious than oral regimens

**Tinidazole**

- Tinidazole 2 gm orally once also recommended regimen
- Clinical trials found cure rates between 86-100% in women, 83% in men.
- Compared to metronidazole, tinidazole has:
  - Higher clinical and microbiological cure rates
  - Less frequent side effects
  - Substantially higher cost (2gm @$11 compared to $.15)
Treatment during Pregnancy and Lactation

- Pregnancy
  - Metronidazole 2gm orally once
  - Tinidazole safety NOT well evaluated (category C)
- Breast-feeding
  - Metronidazole - withhold breastfeeding during treatment and for 12-24 hours after last dose
  - Tinidazole – withhold breastfeeding during treatment and for 3 days after last dose

Treatment in HIV-infected Persons

- CDC Treatment Guidelines 2006 recommend:
  - Same treatment as those who are HIV negative
- Randomized phase IV trial of metronidazole single dose vs. 7 day dose for treatment of trichomoniasis among HIV-infected women
  - Involved 3 US sites
  - Conducted test-of-cure visit at 6-12 days post-treatment

Metronidazole Allergy

- Helms, 2008 reported hypersensitivity in 59 women: 47% with urticaria; 11% with facial edema
- 15 women had metronidazole desensitization and all were cured.
- 27 women had alternative intravaginal treatments (i.e., betadine douche, paromomycin, clotrimazole) and only 29.4% had cure
- Tinidazole also a nitroimidazole, not recommended

Metronidazole-Resistant T. vaginalis

- Clinical failures reported since 1962
- Treatment failures - give 7 day regimen, then metronidazole 2 gm orally each day for 3-5 days
- Tinidazole has proven effective in a limited number of treatment failures from metronidazole
- Can consider tinidazole 2gm orally each day for 5 days
- If no improvement or persistent positive tests with no possibility of reinfection, contact CDC for susceptibility testing
Trich and HIV Interactions

- In four African cities, cross sectional study
  - Low HIV (4-8%) = Low TV (3-17%)
  - High HIV (31-35%) = High TV (29-34%)
  Buve et al., 2001 AIDS 15:s89-s96
- Pregnant Congolese:
  - HIV-: TV 10%
  - HIV+: TV 18.6% (OR 2.0, 95% CI 1.1-3.6)
  Sutton et al., 1999 Am J Obstet Gynecol 181:656-662
- HSV-2+ women in Zimbabwe
  - HSV-2 only: TV 11%
  - HSV-2 + HIV: TV 27% ($\chi^2 P = 0.022$)
  Cowan et al., 2006 AIDS 20:261-267

TV and HIV Acquisition

- Among 1335 HIV seronegative women in Kenya
  - TV incidence was 23.6/100 py
  - 1.52-fold increased risk of HIV infection (95% CI: 1.04 – 2.24)
  McClelland et al. 2007 J Infect Dis 196:650
- Among 4450 HIV seronegative women in Uganda and Zimbabwe
  - TV prevalent among women who seroconverted was 11.3% vs 4.5% in controls
  - OR for HIV acquisition = 2.74 (95% CI 1.25 – 6.0)
  Van Der Pol et al. 2008 J Infect Dis 197:548
- Among 4968 HIV seronegative women in South Africa and Zimbabwe
  - TV incidence was 6.5/100 py
  - HR for HIV acquisition = 2.05 (95% CI 1.05 – 4.02)
  - HR for TV acquisition among HIV+ women = 2.12 (95% CI 1.35 – 3.32)
  Mavedzenge et al. 2010 Sex Transm Dis 37:460

TV and HIV Transmission

- Treatment of trichomoniasis reduces HIV RNA in vaginal fluid
  Wang et al. 2001 JID 183:1017-1022

The canary in the coal mine?

- Among 1578 HIV+ women on HAART
  - Magnus et al. 2003
  - Retrospective cohort study in HIV outpatient program in New Orleans 1990 – 2000
  - TV detected by wet-mount microscopy
  - Urine-based nucleic acid detection for CT/NG
  - Genital warts diagnosed clinically
Trichomoniasis is highly prevalent, including among HIV+ women
- Testing guidelines not well-defined
  - who should be screened?
  - what tests should be used?
- Better diagnostics available, but cheaper tests are needed
- Options limited for metronidazole allergic or resistant infections
- T. vaginalis may contribute to HIV acquisition and transmission