Trichomoniasis: Testing and Treatment Update

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Outline

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

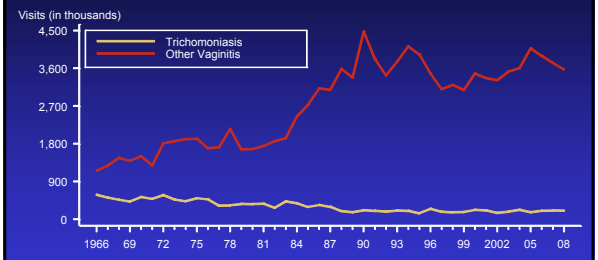
What's in a name?

From the Greek:
- *trichos,* hair
- *monas,* unit, single

Trichomonads in vaginal discharge first described by Alfred Donné in 1863

Medical Parasitology, 3rd. edition. Edward K. Markell & Henrietta Voge. Filmstrip II, Frame 34

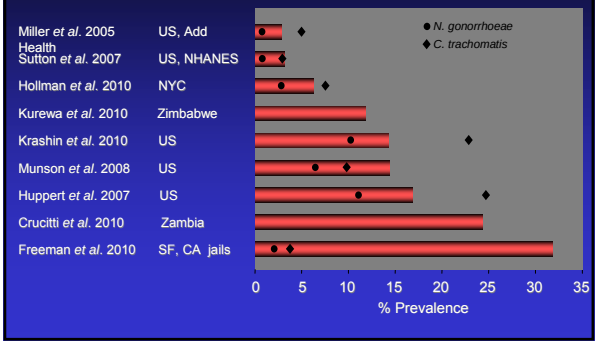
Trichomoniasis and other vaginal infections in women — Initial visits to physicians' offices: United States, 1966–2008



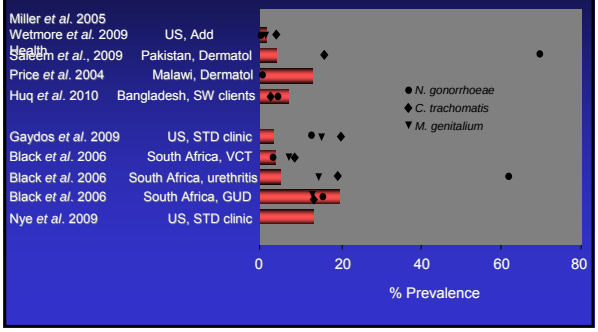
Note: The relative standard error for trichomoniasis estimates range from 16% to 27% and for other vaginitis estimates range from 8% to 13%.

SOURCE: IMS Health, Integrated Promotional Services, IMS Health Report, 1966-2008 Hardcopy

Trich prelavence estimates in women



Trich prevalence estimates in men

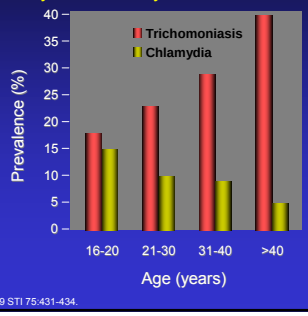


Associations with Trichomoniasis

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

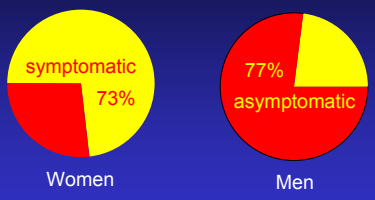
Screening for trichomoniasis criteria??

Community-based study in remote northern Australia



From Bowden *et al.*, 1999 STI 75:431-434.

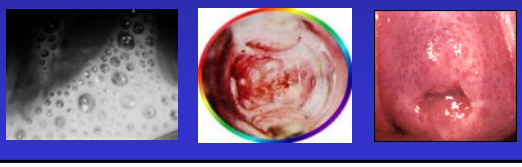
Proportion of asymptomatic trichomoniasis



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

Clinical presentation in women

- Common sites of *T. vaginalis* infection in 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

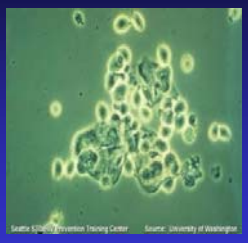
- Non-gonococcal, non-chlamydial urethritis
- Symptoms include urethral discharge, dysuria (though commonly asymptomatic)
- *T. vaginalis* can be isolated from men with chronic prostatitis

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

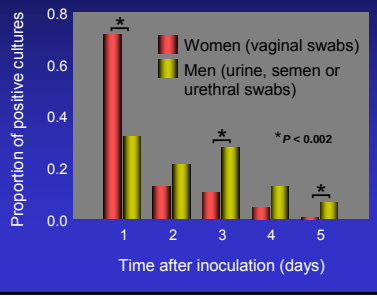
- Performed on vaginal swab specimens (or male urine sediment) resuspended in a drop or 2 of saline
- Organisms must be viable *and* motile
- Must be performed within 15 minutes of specimen collection
- 50 - 70% sensitivity with expert microscopist



T. vaginalis culture

- Trich grows best in microaerophilic or anaerobic environments
- CO_2 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

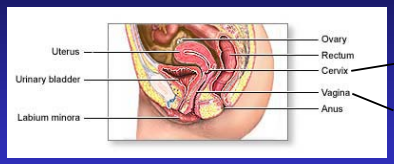
osom Trichomonas Rapid Test

- 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

TV detection in conjunction with CT and NG in women

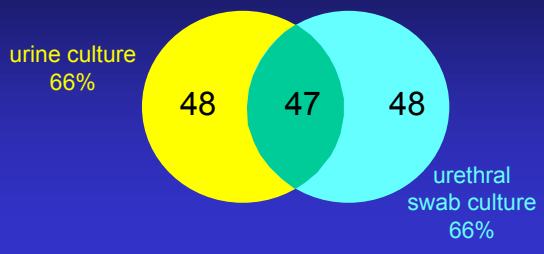


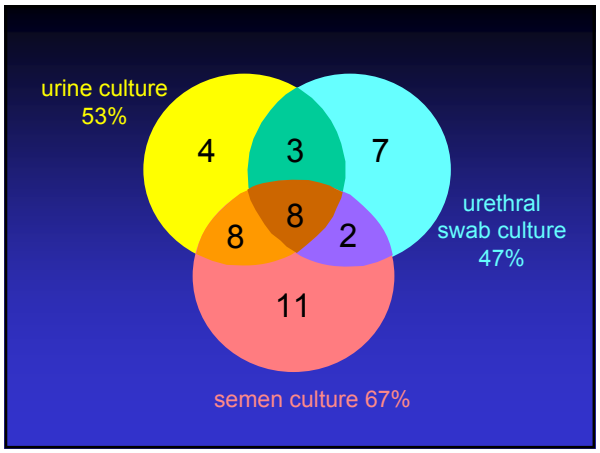
CT, NG and TV are 'bystanders' in urine.
TV can be detected in vaginal and cervical swabs.

T. vaginalis detection in men: where are the parasites?

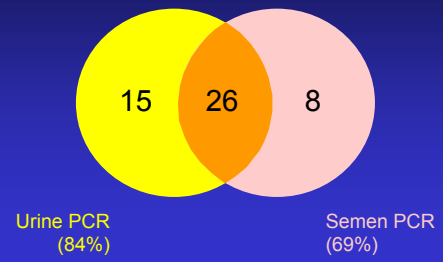
- *T. vaginalis* is seldom included in studies of STDs in men.
- When it *is* sought, a urethral swab OR urine is usually collected for culture.
- The organism can be recovered from urethral swabs, urine, semen and rarely from the external genitalia.

Trich detection in Malawian men





T. vaginalis detection by PCR in men attending US STD clinics



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% (χ^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 195:698
- Among 4450 HIV seronegative women in Uganda and Zimbabwe
  - TV prevalence among women who seroconverted was 11.3% vs 4.5% in controls
  - OR for HIV acquisition = 2.74 (95% CI 1.25 – 6.0)

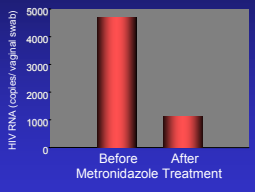
  Van Der Pol *et al.* 2008 J Infect Dis 197:548
- Among 4968 HIV seronegative women in South Africa and Zimbabwe
  - TV incidence was 6.5/100 py
  - HR for HIV acquisition = 2.05 (95% CI 1.05 – 4.02)
  - HR for TV acquisition among HIV+ women = 2.12 (95% CI 1.35 – 3.32)

  Mavedzenge *et al.* 2010 Sex Transm Dis 37:460

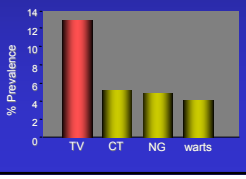
TV and HIV Transmission

- 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

T. vaginalis
"no longer a minor STD"

- 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