Emerging Laboratory Diagnostic Options for Sexually-transmitted Infections

Erik Munson
Wheaton Franciscan Laboratory
Marquette University
Milwaukee, Wisconsin

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OBJECTIVES

I. Appreciate the changing epidemiology of trichomoniasis and clinician ordering patterns on the basis of improved laboratory diagnostics

II. Characterize the distribution of *Mycoplasma genitalium* infection in women and men on the basis of a new diagnostic option

III. Describe the evolution of molecular screening for human papillomavirus and application to cervical cytology

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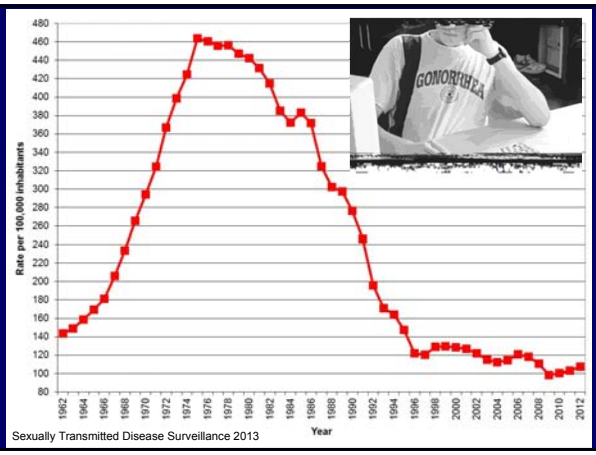

Sexually Transmitted Disease Surveillance 2013

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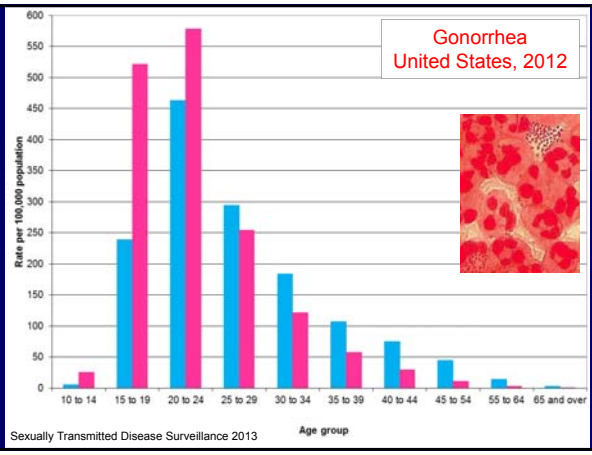

Sexually Transmitted Disease Surveillance 2013

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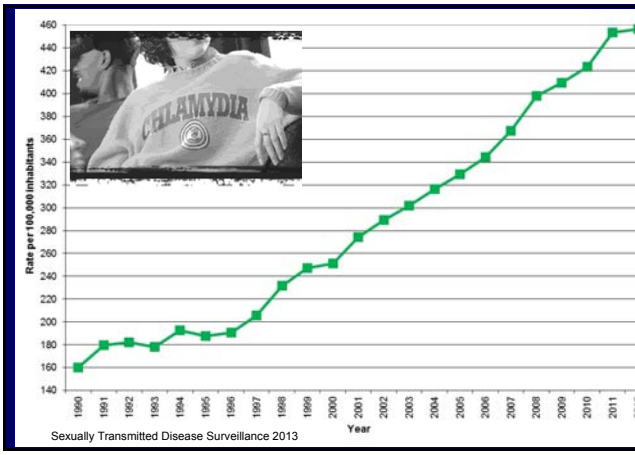

Sexually Transmitted Disease Surveillance 2013

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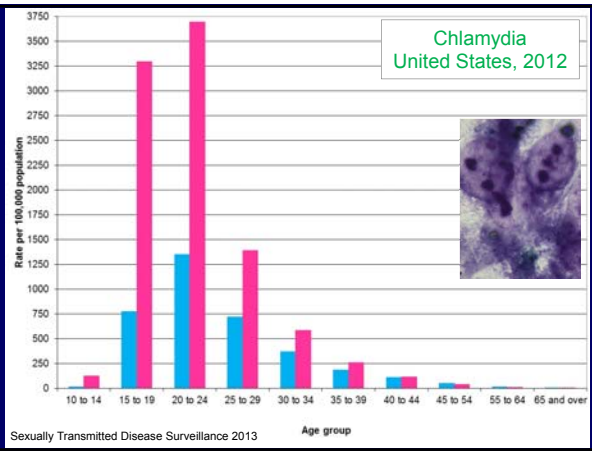

Sexually Transmitted Disease Surveillance 2013

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JOURNAL OF CLINICAL MICROBIOLOGY, Mar. 2005, p. 1372–1373 Vol. 43, No. 3
0095-1137/05/$08.00+0 doi:10.1128/JCM.43.3.1372–1373.2005

Confirming Positive Results of Nucleic Acid Amplification Tests (NAATs) for *Chlamydia trachomatis*: All NAATs Are Not Created Equal

J. Schachter,[1]* E. W. Hook,[2] D. H. Martin,[3] D. Willis,[4] P. Fine,[5] D. Fuller,[6] J. Jordan,[7] W. M. Janda,[8] and M. Chernesky[9]

University of California, San Francisco, California[1]; University of Alabama, Birmingham, Alabama[2]; Louisiana State University Medical Center, New Orleans, Louisiana[3]; Florida State Department of Health, Jacksonville, Florida[4]; Planned Parenthood Foundation of Houston and Southeast Texas, Houston, Texas[5]; Wishard Memorial Hospital, Indianapolis, Indiana[6]; Magee-Womens Research Institute, Pittsburgh, Pennsylvania[7]; University of Illinois, Chicago, Illinois[8]; and St. Joseph's Health Care Regional Virology and Chlamydiology Laboratory, Hamilton, Ontario, Canada[9]

Received 4 August 2004/Returned for modification 7 October 2004/Accepted 14 November 2004

In vitro CHALLENGE *C. trachomatis*

Elementary Bodies	TMA Result		PCR Result
	Light Units (x1000)	Interpretation	
200	1217	detected	detected
20	1111	detected	detected
2	1062	detected	not detected
0.2	878	detected	not detected
0.02	288	detected	*not tested*
0.002	12	not detected	*not tested*
0.0002	14	not detected	*not tested*
0.00002	13	not detected	*not tested*

J. Med. Microbiol. **54:** 357-360; 2005

EXTRA-UROGENITAL GONOCOCCUS

Source	Modality	Sensitivity (%)	Specificity (%)
Pharynx	Culture	60.0	100.0
	DNA amplification (PCR)	60.0	78.9
	RNA amplification (TMA)	95.0	100.0
Rectum	Culture	50.0	100.0
	DNA amplification (PCR)	44.4	99.5
	RNA amplification (TMA)	100.0	99.5

Sex. Transm. Dis. **35:** 635-642; 2008

EXTRA-UROGENITAL TMA (since '10)

Gender	Source	n	Detection Rate (%)	
			C. trachomatis	*N. gonorrhoeae*
Female	Pharynx	167	1.2	1.8
	Rectum	51	3.9	2.0
Male	Pharynx	3910	1.0	3.8
	Rectum	1864	7.0	7.0

Wheaton Franciscan Laboratory In-house Data

CHLAMYDIA TRENDING

Metropolitan Statistical Area	Mean Annual Rank	Aggregate Rate/100,000
Memphis	1.22	792.5
Milwaukee	2.00	678.0
Virginia Beach-Norfolk	4.11	566.0
Philadelphia	9.44	474.3
Indianapolis	10.33	480.1
Jacksonville	10.78	462.2
San Antonio	10.78	468.6
Richmond	11.22	466.6
Saint Louis	11.33	464.4
Birmingham	11.56	476.1
United States	NA	382.3

Expert Rev. Anti Infect. Ther. **11:** 845-863; 2013

"Trich is just an itching disease; why should I care?"

SOCIAL/PUBLIC HEALTH I

- HIV transmission facilitated by *T. vaginalis* infection

Sex. Transm. Dis. **31:** 541-547; 2004

- 2.57 relative risk for per-act probability of HIV transmission for *T. vaginalis*-positive women at start of two-year surveillance (*P* = 0.002)

J. Infect. Dis. **205:** 358-365; 2012

- Estimated $167 million for *T. vaginalis*-attributable HIV infection

Sex. Transm. Dis. **31:** 541-547; 2004

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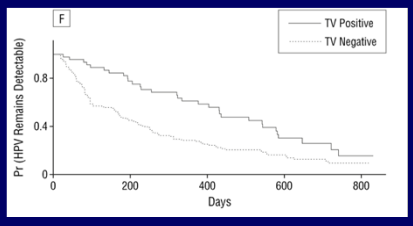
SOCIAL/PUBLIC HEALTH II

- Human papillomavirus (HPV) / cervical neoplasia
- Difference in median time to clear HPV infection



Arch. Pediatr. Adolesc. Med. **160:** 151-156; 2006

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MOLECULAR DETECTION RATES

STI Agent	Percentage Detection from Females	
	Initial Validation (n = 1086)	Community Audit (n = 7277)
Chlamydia trachomatis	9.5	5.7
Neisseria gonorrhoeae	6.1	1.4
Trichomonas vaginalis	14.5	9.3

J. Clin. Microbiol. **46:** 3368-3374; 2008
J. Clin. Microbiol. **49:** 4190-4194; 2011

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OTHER *T. vaginalis* DETECTION

Modality	Performance Indices (%)		
	Sensitivity	Specificity	Reference
Wet mount microscopy	48.1	99.8	1
	47.1	100.0	2
Antigen detection	78-84	99-100	3
	35.1	99.9	4
Nucleic acid hybridization	63.4	99.9	5

[1]J. Clin. Microbiol. **46:** 3368-3374; 2008
[2]Diagn. Microbiol. Infect. Dis. **68:** 66-72; 2010
[3]Sex. Transm. Infect. **86:** 514-519; 2010
[4]J. Clin. Microbiol. PMID 26659216
[5]J. Clin. Microbiol. **49:** 4190-4194; 2011

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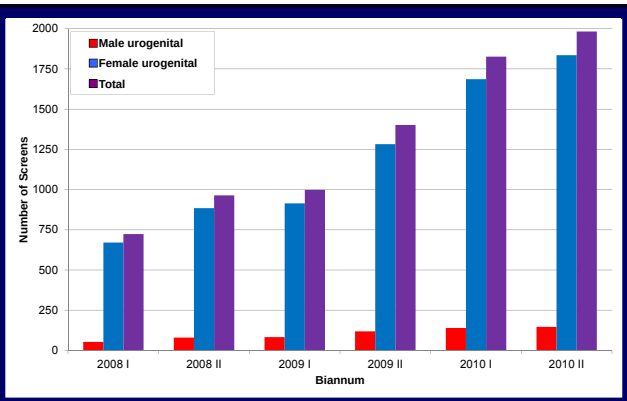

J. Clin. Microbiol. **49:** 4190-4194; 2011

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ORDERING PRACTICES

Testing Modality	Percentage of Female Genital Swabs		
	2004-2007	2008-2010	*P* value
Any wet mount preparation	66.2	57.7	< 0.0002
Point-of-care wet mount preparation	27.8	22.4	< 0.0002
Any assessment for *Trichomonas vaginalis*	66.2	83.6	< 0.0002
Chlamydia trachomatis/*Neisseria gonorrhoeae* TMA	80.4	83.7	< 0.0002

Wisc. Med. J. **111:** 233-236; 2012

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DETECTION RATE

Specimen	Percentage Detection		
	Trichomonas vaginalis	*Chlamydia trachomatis*	*Neisseria gonorrhoeae*
Endocervix	8.9	5.7	1.3
Vagina	8.6	4.8	0.4
Female urine	12.6	6.0	2.6

J. Clin. Microbiol. **49:** 4190-4194; 2011

DETECTION RATE

Specimen	Percentage Detection		
	Trichomonas vaginalis	*Chlamydia trachomatis*	*Neisseria gonorrhoeae*
Endocervix	8.9	5.7	1.3
Vagina	8.6	4.8	0.4
Female urine	12.6	6.0	2.6

P = 0.85

J. Clin. Microbiol. **49:** 4190-4194; 2011

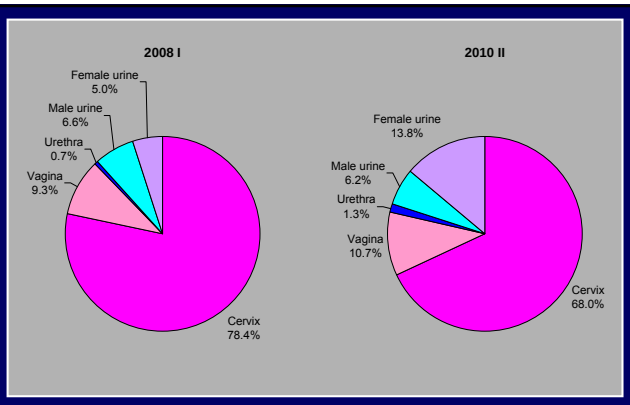
DETECTION RATE

Specimen	Percentage Detection		
	Trichomonas vaginalis	*Chlamydia trachomatis*	*Neisseria gonorrhoeae*
Endocervix	8.9	5.7	1.3
Vagina	8.6	4.8	0.4
Female urine	12.6	6.0	2.6

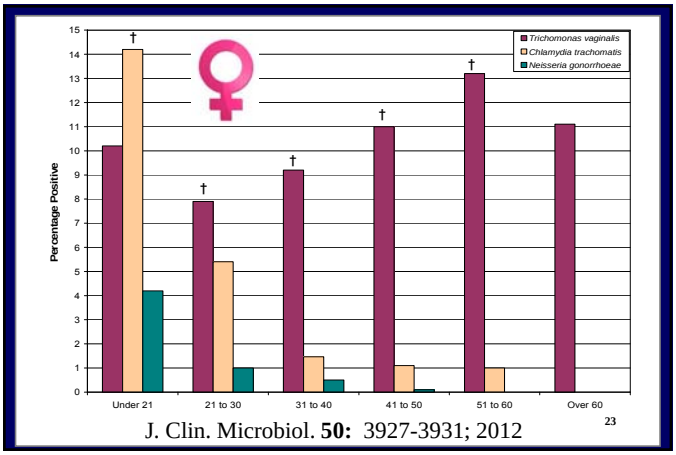
P = 0.85

P < 0.0004

J. Clin. Microbiol. **49:** 4190-4194; 2011



J. Clin. Microbiol. **49:** 4190-4194; 2011



J. Clin. Microbiol. **50:** 3927-3931; 2012

Testing of Males for *T. vaginalis*

CLINICAL/PUBLIC HEALTH

- Non-gonococcal urethritis; persistent, scant, mucoid discharge; prostatitis

  Sex. Transm. Dis. **7:** 135-136; 1980
  J. Chemother. **14:** 537-538; 2002

- Complications include infertility, hypogonadism

  J. Clin. Microbiol. **13**: 880-881; 1981

- HIV transmission

Clinical condition	Median copies HIV RNA/mL semen
T. vaginalis urethritis	3.45 x 10^5
Non-*T. vaginalis* urethritis	0.05 x 10^5

Sex. Transm. Dis. **26**: 381-387; 1999

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POPULATION STUDIES/PROSTATE

- 13% of prostate cancer pts. with *T. vaginalis* Ab
  9% of age-matched controls with *T. vaginalis* Ab

  Cancer Epidemiol. Biomarkers Prev. **15**: 939-945; 2006

- 0.97 odds ratio for prostate cancer in men with *T. vaginalis* seropositivity

  Int. J. Cancer. **124**: 2082-2087; 2009

- 1.25 odds ratio for prostate cancer in physicians with *T. vaginalis* seropositivity

J. Natl. Cancer. Inst. **101**: 1406-1411; 2009

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INCREASED CARCINOGENICITY?

- Increased risk of advanced-stage prostate cancer diagnosis in men with positive *T. vaginalis* serostatus

  Cancer Epidemiol. Biomarkers Prev. **15**: 939-945; 2006

- Odds ratio of 6.4 (95% CI 1.5-27.9) for diagnosis of lethal prostate cancer in seropositive patients with documented history of *T. vaginalis* infection

  J. Natl. Cancer. Inst. **101**: 1406-1411; 2009

- Prostate carcinogenesis mechanism undefined

PLoS Pathog. **8**: e1002801; 2012

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EVOLVING REFERENCE STANDARD

Diagnostic method and specimen	Number of specimens: True positive	False positive	False negative	True negative	Sensitivity: %	95% CI	Specificity: %	95% CI	Predictive value (%): Positive	Negative
	Infected patient status algorithm									
Culture	12	0	0	286	100	69.9-100	100	98.3-100	100	100
PCR - Urethral swab	11	13	1	273	91.7	59.8-99.6	95.5	92.2-97.5	45.8	99.6
PCR - Urine	11	9	1	277	91.7	59.8-99.6	96.9	93.9-98.5	55.0	99.6
ATV - Urethral swab	11	38	1	248	91.7	59.8-99.6	86.7	82.1-90.3	22.5	99.6
ATV - Urine	11	23	1	263	91.7	59.8-99.6	91.9	88.0-94.7	32.1	99.6
	Molecular resolved algorithm									
Culture	12	0	30	256	28.6	16.2-44.8	100	98.2-100	100	89.4
PCR - Urethral swab	23	0	19	256	54.8	38.8-69.8	100	98.2-100	100	93.1
PCR - Urine	20	0	22	256	47.6	32.3-63.4	100	98.2-100	100	92.0
ATV - Urethral swab	40	9	2	247	95.2	82.6-99.2	96.5	93.2-98.3	81.7	99.2
ATV - Urine	31	4	11	252	73.8	57.7-85.6	98.4	95.8-99.5	88.6	95.8

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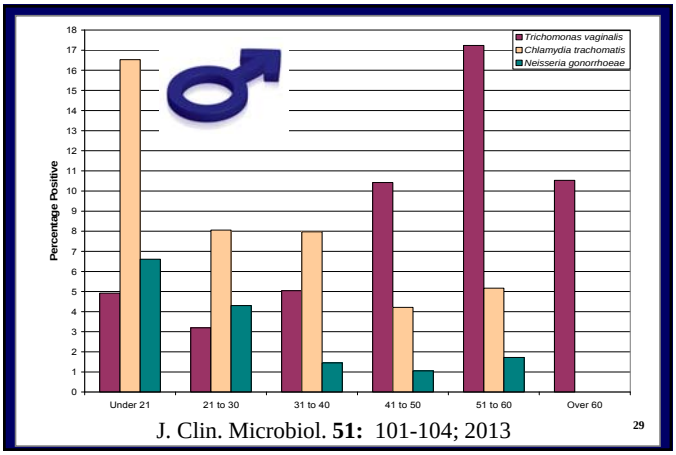
Am. J. Obstet. Gynecol. **200:** 188.e1-188.e7; 2009 (adapted)



J. Clin. Microbiol. **51:** 101-104; 2013

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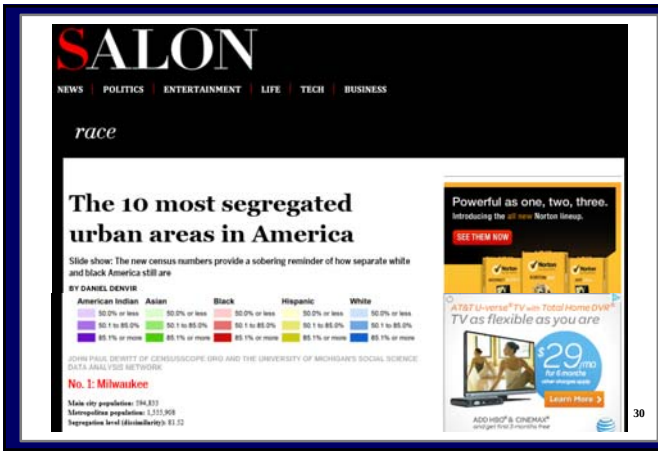

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11 MILWAUKEE COUNTY ZIP CODES

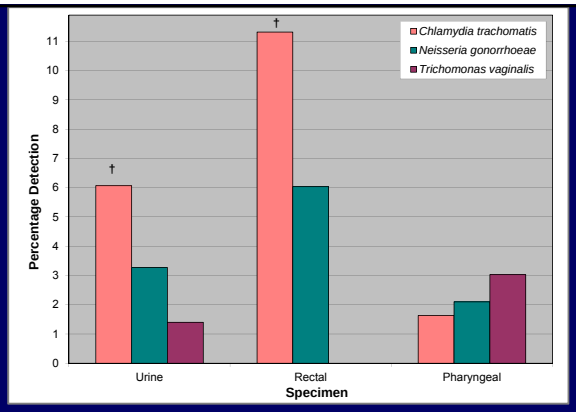
African American (7): Mean difference between African American and Caucasian populations was 43.9% per ZIP

Caucasian (4): Mean difference between Caucasian and African American populations was 32.6% per ZIP

RACE/ETHNICITY (Males)

Parameter	Geographical Region Race Majority		
	African American	Caucasian	*P* value
Percentage urine submissions	78.4	72.3	0.16
Mean screenings per ZIP code	49.7	34.8	0.26
Percentage detection of:			
Trichomonas vaginalis	8.9	5.0	0.15
Chlamydia trachomatis	8.4	9.4	0.74
Neisseria gonorrhoeae	3.7	4.3	0.78

J. Clin. Microbiol. **51:** 101-104; 2013



J. Clin. Microbiol. **51:** 1855-1860; 2013

Mycoplasma genitalium

Int. J. Syst. Bacteriol. **33:** 387-396; 1983

CLINICAL SIGNIFICANCE (MALES)

- Increased *M. genitalium* molecular detection in males with acute non-gonococcal urethritis (NGU) than in males without NGU

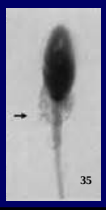
  J. Eur. Acad. Dermatol. Venerol. **18:** 1-11; 2004

- *M. genitalium*-positive males more likely to exhibit urethritis than *C. trachomatis*-positive males

  Sex. Transm. Infect. **80:** 289-293; 2004

- Male infertility; spermatozoa motility

  Clin. Microbiol. Rev. **24:** 498-514; 2011

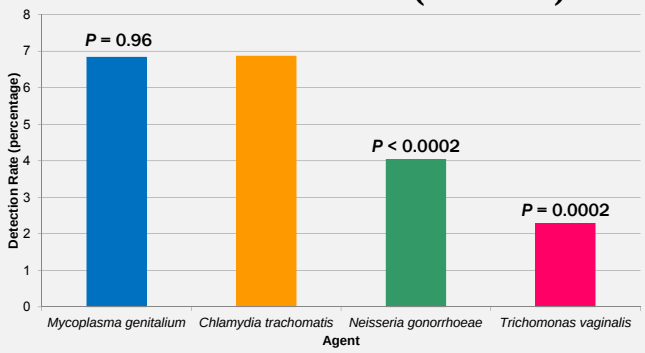


ASSESSMENT OF MALES

- Prospective sampling of 2750 residual urines via *M. genitalium* research-use only TMA
- Previous TMA testing: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Trichomonas vaginalis*
- Source of specimens

  Outpatient clinics (community setting)
  Milwaukee STI clinic (demographics, history available)

DETECTION RATE (MALES)



Diagn. Microbiol. Infect Dis. **82:** 194-198; 2015

AGE OF POSITIVE MALES

Agent	Median	Mean	Range
Mycoplasma genitalium	29	30.81	14-74
Chlamydia trachomatis	26	27.80	15-64
Neisseria gonorrhoeae	29	31.14	15-66
Trichomonas vaginalis	42	41.60	16-85

All mean detection age comparison $P \leq 0.006$, except *N. gonorrhoeae* vs. *M. genitalium* ($P = 0.78$)

Diagn. Microbiol. Infect Dis. **82:** 194-198; 2015

STI CLINIC; *M. genitalium* ONLY

- Preferences 58.9% heterosexual
  8.4% bisexual
  32.6% homosexual
- Partners median 4
  mean 5.18
  range 1-30
- 60.6% symptomatic for urogenital disease

Discharge	49.1%	Dysuria	14.0%
Burning/tingling	35.1%	Itching	14.0%

Diagn. Microbiol. Infect Dis. **82:** 194-198; 2015

STI Phenotype				Percentage of Patients Delineated by Healthcare Setting		
M. genitalium	*Chlamydia*	*Neisseria*	*Trichomonas*	STI Clinic	Outpatient	*P* value
+	-	-	-	36.5	22.0	0.0007
+	+	-	-	6.4	4.8	0.45
+	-	+	-	3.4	1.0	0.08
-	+	-	-	25.9	32.1	0.14
-	+	+	-	3.8	6.2	0.22
-	-	+	-	16.5	12.4	0.21
-	-	-	+	5.3	18.7	< 0.0002
Any detection of *Mycoplasma genitalium*				47.4	29.7	0.0002
Any detection of *Chlamydia trachomatis*				36.5	44.0	0.10
Any detection of *Neisseria gonorrhoeae*				25.6	20.6	0.20
Any detection of *Trichomonas vaginalis*				7.1	21.1	< 0.0002

Diagn. Microbiol. Infect Dis. **82:** 194-198; 2015

CLINICAL SIGNIFICANCE (FEMALES)

- Females with high-burden *M. genitalium* more likely to shed HIV-1 DNA than *M. genitalium*-negative females

J. Infect. Dis. **197:** 733-736; 2008

- Associated w/ reproductive disease (meta-analysis)

Cervicitis	pooled OR 1.65
PID	pooled OR 2.53
Pre-term birth	pooled OR 2.33
Spontaneous abortion	pooled OR 1.82

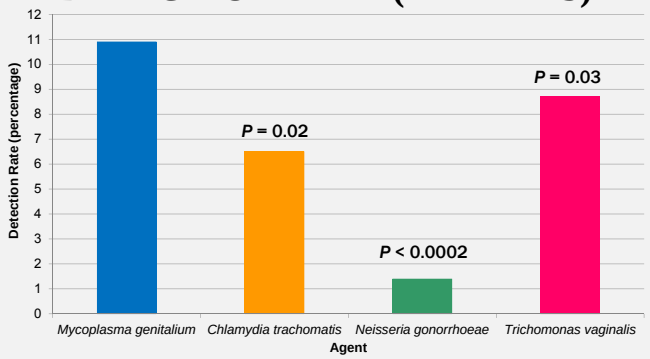
Clin. Infect. Dis. **61:** 418-426; 2015

ASSESSMENT OF FEMALES

- Retrospective/random selection of 2478 urine, cervical, or vaginal specimens via *M. genitalium* research-use only TMA
- Previous TMA testing: *Chlamydia trachomatis*
  Neisseria gonorrhoeae
  Trichomonas vaginalis
- Assessment of study set via comparison to 6-month audit of routine *C. trachomatis* TMA

  age, location, detection rate, specimen source

DETECTION RATE (FEMALES)



J. Clin. Microbiol. PMID 26659209

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AGE OF POSITIVE FEMALES

Agent	Median	Mean	Range
Mycoplasma genitalium	23	24.74	14-65
Chlamydia trachomatis	21	22.75	14-54
Neisseria gonorrhoeae	21	23.47	15-46
Trichomonas vaginalis	28	30.09	15-68

Mean *M. genitalium*, *N. gonorrhoeae* ages *P* = 0.30
Mean *C. trachomatis*, *N. gonorrhoeae* ages *P* = 0.56

J. Clin. Microbiol. PMID 26659209

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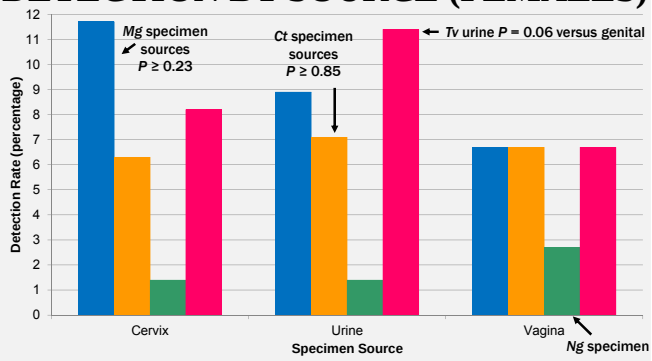
DETECTION BY SOURCE (FEMALES)



J. Clin. Microbiol. PMID 26659209

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EMERGENT VERSUS "SUBACUTE"

Setting	n	*M. genitalium* detection (%)	*T. vaginalis* detection (%)	*P* value
Emergency Department	755	14.6	13.0	0.37
Non-Emergency Department	1723	10.0	7.2	0.004

J. Clin. Microbiol. PMID 26659209

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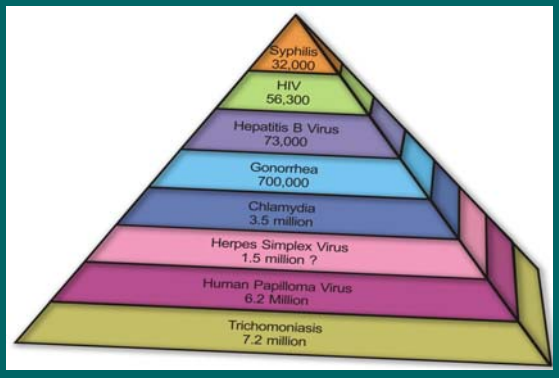

Courtesy of Charlotte Gaydos, Dr.Ph. (via Fred Jones, Ph.D.)

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HPV AND CANCER

- 90% of cervical cancers caused by HPV

Int. J. Cancer. **52:** 743-749; 1992

- High-risk HPV types:

16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68

Obstet. Gynecol. **79:** 328-337; 1992

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EVOLUTION OF HPV DIAGNOSTICS

Chemistry	Product	Manufacturer	Mechanism
Hybrid capture	H_c2	Digene (Qiagen)	DNA hybridization
Invader®	Cervista™	Third Wave (Hologic)	DNA hybridization
PCR	Cobas® 4800	Roche	DNA amplification
TMA	APTIMA HPV	Gen-Probe (Hologic)	RNA transcription

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Comparison of Three Management Strategies for Patients With Atypical Squamous Cells of Undetermined Significance: Baseline Results From a Randomized Trial

Diane Solomon, Mark Schiffman, Robert Tarone

For the ALTS Group

Background: More than 2 million U.S. women receive an equivocal cervical cytologic diagnosis (atypical squamous cells of undetermined significance [ASCUS]) each year. Effective colposcopy triage strategies are needed to identify the minority of women who have clinically significant disease while avoiding excessive follow-up evaluation for others. *Methods:* The ASCUS/LSIL (i.e., low-grade squamous intraepithelial lesion) Triage Study (ALTS) is a multicenter, randomized trial comparing the sensitivity and specificity of the following three management strategies to detect cervical intraepithelial neoplasia grade 3 (CIN3+): 1) immediate colposcopy (considered to be the reference standard), 2) triage to colposcopy based on human papillomavirus (HPV) results from Hybrid Capture 2™ (HC 2) and thin-layer cytology results, or 3) triage based on cytology results alone. This article summarizes the cross-sectional enrollment results for 3488 women with a referral diagnosis of ASCUS. All statistical tests are two-sided. *Results:* Among participants with ASCUS, the underlying prevalence of histologically confirmed CIN3 was 5.1%. Sensitivity to detect CIN3 or above by testing for cancer-associated HPV DNA was 96.3% (95% confidence interval [CI] = 91.6% to 98.8%), with 56.1% of women referred to colposcopy. Sensitivity of a single repeat cytology specimen with a triage threshold of HSIL or above was 44.1% (95% CI = 35.6% to 52.9%), with 6.9% referred. Sensitivity of a lower cytology triage threshold of ASCUS or above was 85.3% (95% CI = 78.2% to 90.8%), with 58.6% referred. *Conclusions:* HC 2 testing for cancer-associated HPV DNA is a viable option in the management of women with ASCUS. It has greater sensitivity to detect CIN3 or above and specificity comparable to a single additional cytologic test indicating ASCUS or above. [J Natl Cancer Inst 2001;93:293-9]

J. Natl. Cancer Inst. **93:** 293-299; 2001

ALTS

Use molecular testing to triage ASC-US patients

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Test Performance	H_c2	
Participants	5000	
Mean Age	29	
Colposcopies	1149	
% with no lesion (no biopsy)	25	
% with no pathology upon biopsy	49	
% CIN1	15	
% CIN2+	11	
Detection of CIN2+ (%) via HPV DNA	96	
Detection of CIN3+ (%) via HPV DNA	96	
Negative predictive value for CIN2+ (%)	98.9	
Negative predictive value for CIN3+ (%)	99.5	
Referral to colposcopy (%)	57	
PCR concordance (%)	82.7	

J. Natl. Cancer. Inst. **93:** 293-299; 2001

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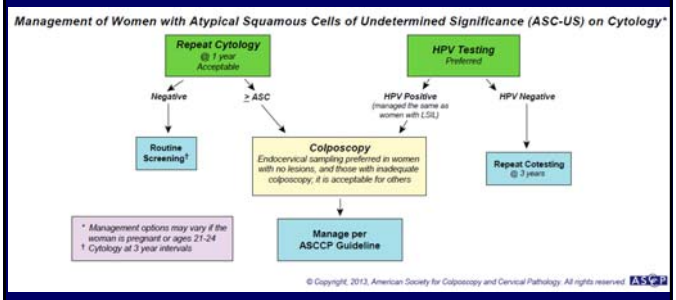

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CERVISTA EVALUATION

Cytologic Classification	Percentage Detection		*P* value
	Cervista™	H_c2	
HSIL	90.0	90.0	1.00
LSIL	57.1	78.6	0.22
ASC-US	36.4	42.9	0.18
NILM	11.8	12.6	0.82
Total	30.2	35.2	0.17

Diagn. Microbiol. Infect. Dis. **71:** 230-235; 2011

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Test Performance	H_c2	Cervista™
Participants	5000	~3500
Mean Age	29	33
Colposcopies	1149	1347
% with no lesion (no biopsy)	25	28
% with no pathology upon biopsy	49	53
% CIN1	15	14
% CIN2+	11	5
Detection of CIN2+ (%) via HPV DNA	96	93
Detection of CIN3+ (%) via HPV DNA	96	100
Negative predictive value for CIN2+ (%)	98.9	99.1
Negative predictive value for CIN3+ (%)	99.5	100.0
Referral to colposcopy (%)	57	57
PCR concordance (%)	82.7	86.1

Gynecol. Oncol. **118:** 116-122; 2010

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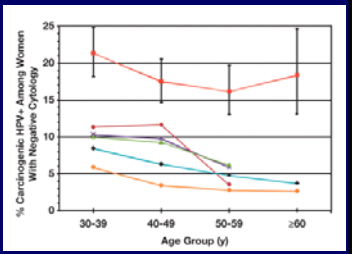
CERVISTA "TOO POSITIVE"??

Special Commentary

Patient Safety and the Next Generation of HPV DNA Tests

Walter Kinney, MD,[1] Mark H. Stoler, MD,[2] and Philip E. Castle, PhD, MPH[3]



Am. J. Clin. Pathol. **134:** 193-199; 2010

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SUMMARY OF METHODS

- 2386 ThinPrep vials for H_c2 performance at reference laboratory during nine months of 2008-2009
- 2380 ThinPrep vials for Cervista™ performance in-house during nine months of 2009-2010

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FREQUENCY OF DIAGNOSIS

Cytologic Classification	Percentage Diagnosis		*P* value
	Cervista™ arm	H_c2 arm	
HSIL	0.4	0.8	0.13
LSIL	2.4	1.8	0.17
ASC-US	22.8	16.7	<0.0002
NILM	73.7	80.2	<0.0002

J. Clin. Microbiol. **51:** 1057-1058; 2013

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RETROSPECTIVE COMPARISON

Cytologic Classification	Percentage Detection		*P* value
	Cervista™	H_c2	
HSIL	70.0	72.2	0.90
LSIL	79.3	79.5	0.98
ASC-US	40.3	43.0	0.41
NILM	9.1	7.7	0.14

J. Clin. Microbiol. **51:** 1057-1058; 2013

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RETROSPECTIVE COMPARISON

Cytologic Classification	Percentage Detection		*P* value
	Cervista™	H_c2	
ASC-US; age < 30	54.1	61.3	0.24
ASC-US; age ≥ 30	29.0	30.6	0.77
NILM; age < 30	16.2	21.8	0.42
NILM; age ≥ 30	8.9	7.0	0.10

J. Clin. Microbiol. **51:** 1057-1058; 2013

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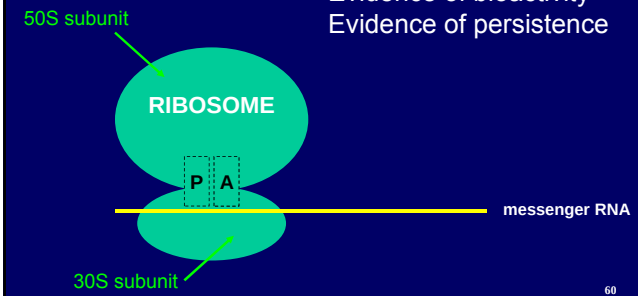
TRANSCRIPTION

Evidence of bioactivity
Evidence of persistence



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A NEW PARADIGM

- Detection of E6/E7 (RNA) transcripts from high-risk HPV
- Potential to ascribe (precursory) oncogenic function to HPV nucleic acid detected in ThinPrep specimens

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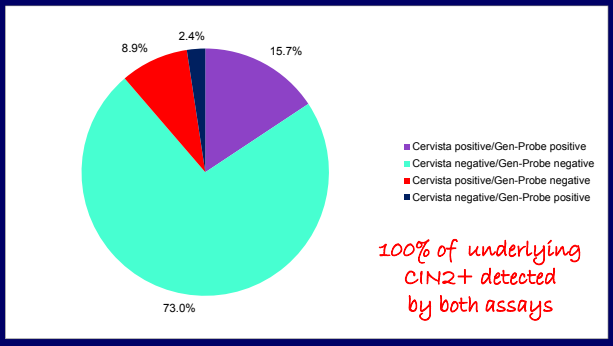
PROSPECTIVE COMPARISON



J. Clin. Microbiol. **52:** 331-334; 2014

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HPV PCR

- 226 ThinPrep vials subjected to Cervista™; also HPV PCR via Cobas® 4800
- 25.7% concordant positive
  56.7% concordant negative
  2.7% Cervista™ negative; Cobas® positive
  15.0% Cervista™ positive; Cobas® negative

112th General Meeting American Society for Microbiology

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ADJUDICATION

Of 5 COBAS® 4800 negative/ Cervista positive specimens, HPV sequencing revealed 3 low-risk HPV and 2 HPV-negative results

112th General Meeting American Society for Microbiology

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RETROSPECTIVE COMPARISON

Cytologic Classification	Percentage Detection		*P* value
	Cervista™	Gen-Probe HPV	
HSIL	94.7	100.0	0.31
ASC-H	80.0	80.0	1.00
LSIL	78.7	73.8	0.98
ASC-US	49.3	43.9	0.02
NILM	13.7	6.6	< 0.0002
Cumulative	24.5	18.0	< 0.0002

J. Clin. Microbiol. **52:** 331-334; 2014

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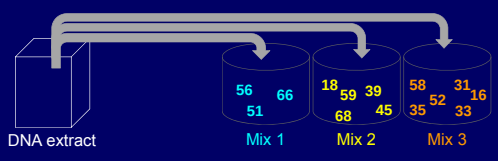
CERVISTA POSITIVES

- Pool of 14 high-risk HPV oligonucleotides distributed among three mixes



- Hybridization signal versus background:

  Positive if one or two mixes exceeds 1.525
  Positive if all three exceed 1.92 (triple-positive; TP)

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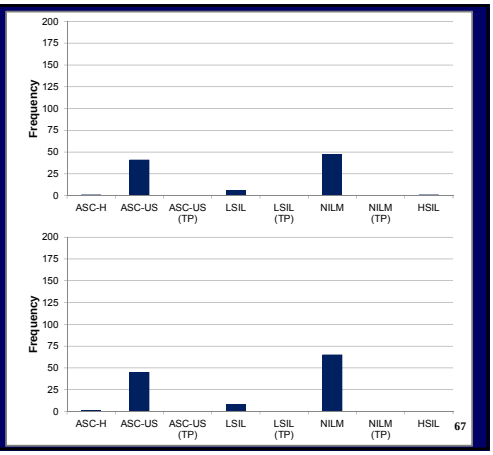
Cervista negative/
Gen-Probe positive



Cervista positive/
Gen-Probe negative

J. Clin. Microbiol. **52:** 331-334; 2014

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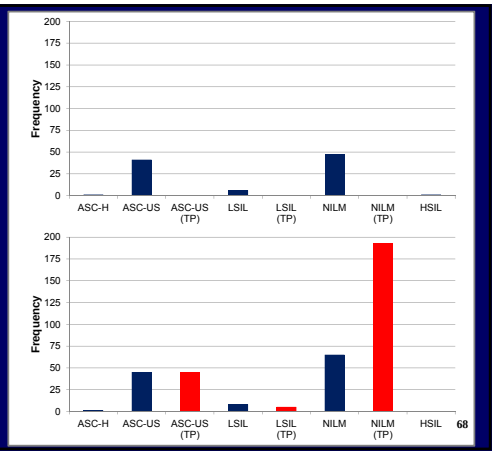
Cervista negative/
Gen-Probe positive



Cervista positive/
Gen-Probe negative

J. Clin. Microbiol. **52:** 331-334; 2014

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RELATIVE LUMINESCENT OUTPUT

Gen-Probe Result	n	Mean Cervista™ Luminescence from:[a]			
		Mix 1[b]	Mix 2[b]	Mix 3[b]	Genomic DNA
positive	19	5.69	5.02	5.44	17.58
negative	244	3.29[c]	2.61[c]	3.14[c]	19.40[d]

[a]From Cervista™ TP specimens
[b]TP hybridization signal versus background exceeds 1.92 for all three mixes
[c]$P < 0.0001$ versus mean luminescence from Gen-Probe positive specimens
[d]$P = 0.05$ versus mean luminescence from Gen-Probe positive specimens

J. Clin. Microbiol. **52:** 331-334; 2014

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BASIS FOR GENOTYPING

- HPV high-risk types 16, 18, 45 most associated with cervical cancer
  - 75% of squamous cell carcinoma
  - 94% of adenocarcinoma
- Co-detection of high-risk types 18, 45 more common in adenocarcinoma (44%) than squamous cell carcinoma (14%)

Lancet Oncol. **11:** 1048-1056; 2011

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BASIS FOR GENOTYPING

- Mean age of patients with cervical cancer

Type 45:	46.8	Type 16:	50.0
Type 18:	48.2	Other types:	56.0

Lancet Oncol. **11:** 1048-1056; 2011

- Integration frequency predictive of quicker progression to invasive cancer

Type 18:	92-100%
Type 45	83%
Type 16:	55-80%
Type 33:	37%
Type 31:	14%

J. Med. Virol. **67:** 574-582; 2002
J. Pathol. **212:** 356-367; 2007
Cancer Res. **68:** 307-313; 2008

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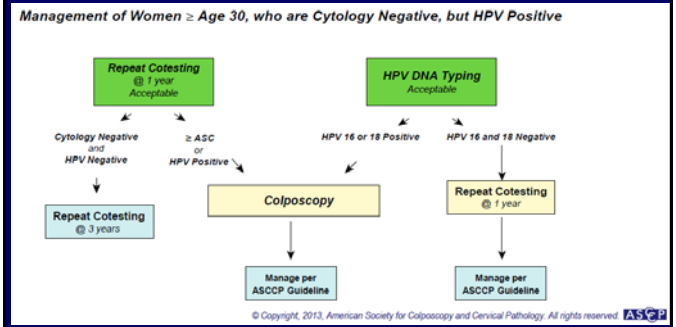

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GEN-PROBE GENOTYPING

Cytologic Classification	Percentage Positive HPV High-risk 16[a]	
	< 30 years	≥ 30 years
NILM[b]	7.9	12.7
Non-NILM[c]	19.7	19.6

Cytologic Classification	Percentage Positive HPV High-risk 18/45[a]	
	< 30 years	≥ 30 years
NILM[b]	8.9	10.4
Non-NILM[c]	10.6	15.6

[a]Dataset derived from HPV high-risk screen-positive specimens
[b]745 total NILM specimens
[c]816 total non-NILM specimens

Wheaton Franciscan Laboratory In-house Data

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SUMMARY

- Changing epidemiology of trichomoniasis on basis of highly-accurate molecular assay
- *M. genitalium* dichotomy within females and males on basis of novel molecular assay
- Cervista™ and Gen-Probe HPV acceptable triage performance; Gen-Probe HPV specificity
- Benefits for HPV 16, 18/45 genotyping

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