Sexually Transmitted Bacterial Infections

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Objectives

1. Review sexually transmitted bacterial pathogens epidemiology, sequelae, and symptoms.
2. Describe laboratory testing of these pathogens.
Overview

Pathogenesis

Epidemiology

Diagnosis

Laboratory tests
Why STIs Are Important

- All communities impacted by STIs
- Individuals directly or indirectly pay for costs
- Difficult to control because people are reluctant to discuss sexual behavior
- Lack easy solutions because they are rooted in human behavior
Epidemiology

15 to 24 ages = 25% of the sexually experienced population

Represent nearly half of all new infections

Disproportionate burden of disease among African Americans and Hispanics
Increasing STIs

- Earlier initiation age for sexual relations
- Longer delay to marriage
- Multiple partners
- Unprotected intercourse
- Higher risk partners
Prevalence and Incidence in US

WHAT’S THE DIFFERENCE?
PREVALENCE VS INCIDENCE

Prevalence is the estimated number of infections – new or existing – in a given time. Incidence is the estimated number of new infections – diagnosed or undiagnosed.
26.2 Million Incident STI Infections in 2018

67.6 Million prevalent In 2018

45% of 2018 Incident STIs in 15-24 years old
THE U.S. IS EXPERIENCING STEEP, SUSTAINED INCREASES IN SEXUALLY TRANSMITTED DISEASES

Combined diagnoses of chlamydia, gonorrhea, and syphilis increased sharply over the past five years.

**Total Cases**
- 1.8 Million in 2013
- 2.3 Million in 2017

**Gonorrhea**
- 333,004 in 2013
- 555,608 in 2017
- 67% Increase

**Syphilis**
- 17,375 in 2013
- 30,644 in 2017
- 76% Increase

**Chlamydia**
- 1.7 MILLION

In 2017* chlamydia was the most common condition reported to CDC

*Preliminary data
$16 BILLION
in direct medical costs

Women
25%
of total costs

$1.1 BILLION
direct medical costs attributed to
CHLAMYDIA GONORRHEA & SYPHILIS
common, preventable infections

Youth aged 15-24
26%
of total costs

Direct Medical Costs by Infection...

HBV $46 M
HSV-2 $91 M
Trichomoniasis $144 M
Syphilis $174 M
Gonorrhea $271 M
Chlamydia $691 M
HPV $775 M
HIV $13.7 B
UNDIAGNOSED STDs CAN LEAD TO SEVERE HEALTH PROBLEMS

Diagnosed cases of chlamydia, gonorrhea, and syphilis represent just a small fraction of the true disease burden. Left untreated, these STDs can produce severe, adverse effects.

ECTOPIC PREGNANCY INFERTILITY INCREASED HIV RISK

CONTINUED CONCERNS ABOUT ANTIBIOTIC RESISTANT GONORRHEA

Gonorrhea is expected to eventually wear down our last highly effective antibiotic. Lab tests show a small but growing fraction of gonorrhea samples have signs of emerging antibiotic resistance. CDC recommends a two-drug combination to preserve our last highly effective antibiotic.

For more information, visit cdc.gov/nchhstp/newsroom
Consequences

- Chronic pelvic pain
- Infertility
- Poor birth outcomes and death
- Increases risk of HIV
- Quality of life
- Billions of $$$
Pelvic Inflammatory Disease — Initial Visits to Physicians’ Offices Among Females Aged 15–44 Years, United States, 2007–2016

* In thousands.

NOTE: The relative standard errors for these estimates are 23%–16%. See section A2.5 in the Appendix and Table 44.

Ectopic Pregnancy — Ratio* Among Commercially Insured Females with Live Births Aged 15–44 Years by Age Group, 2006–2017

* Ratios represent the number of ectopic pregnancy diagnoses per 100,000 live births.

Chlamydia and Gonorrhea — Rates of Reported Cases Among Infants <1 Year of Age by Year and Specimen Source, United States, 2014–2018
Diseases that Produce Genital Ulcers

- Syphilis
- Chancroid
- Lymphogranuloma venereum
Syphilis Epidemiology

- 115,000 cases of syphilis in 2018
- Increased 14.9% during 2017–2018
- MSM 54% of cases-42% HIV
- Congenital 40% increase in 2018
Syphilis — Rates of Reported Cases by Stage of Infection, United States, 1941–2018

* Per 100,000.

NOTE: See section A1.3 in the Appendix for more information on syphilis case reporting.
Primary and Secondary Syphilis — Distribution of Cases by Sex and Sex of Sex Partners, United States, 2018

- Women (n = 4,995) - 14%
- Men who have sex with women only (n = 5,416) - 15%
- Men who have sex with men only (n = 16,905) - 48%
- Men without data on sex of sex partners (n = 5,858) - 17%
- Cases with unknown sex (n = 34) - 0%
- Men who have sex with men and women (n = 1,855) - 5%
Primary and Secondary Syphilis — Rates of Reported Cases by Sex and Male-to-Female Rate Ratios, United States, 1990–2018

* Per 100,000.
† Log scale.
Primary and Secondary Syphilis — Reported Cases by Sex and Sex of Sex Partners and HIV Status, United States, 2018

ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSW = Men who have sex with women only.
Syphilis: *Treponema pallidum*

- Darkfield wet mount
- Screen with a nontreponemal test
  - Rapid plasma reagin (RPR)
  - Venereal Disease Research Laboratory (VDRL)
- Confirm with treponemal test
  - FTA-ABS
  - TPPA
  - EIA

Public Health Image Library (PHIL)
http://phil.cdc.gov/phil/details.asp
Primary Syphilis: Chancre

Public Health Image Library (PHIL)
http://phil.cdc.gov/phil/details.asp
Secondary Syphilis Rash
Latent Syphilis

- No signs or symptoms
- Detected by serological tests
Tertiary Syphilis

Develops in 30% of untreated individuals

Cardiac

Neurologic

Ophthalmic

Auditory

Gummatous lesions
Neurosyphilis

- Occurs 5-15 years after secondary syphilis
- Symptoms of pain, general paresis (incomplete paralysis), tabes dorsalis (staggering, wide-base gait), and optic atrophy and pupillary changes
- Diagnosis by increased WBCs in CSF and positive VDRL on CSF
Pregnant Women

69% of untreated infected pregnant women

Adverse pregnancy outcomes

• 25% stillbirth
• Serious birth defects
• Low birth weight
• Prematurity
Congenital Syphilis

- Clinical course variable
- Symptoms of secondary and tertiary syphilis
- Rash
- Damage to bones, mucous membranes, eyes, teeth, and auditory nerves
- Neurosyphilis and gummas
**Congenital Syphilis**

- 26% increase 2013-18—1,306
- 52.5% in South
- 33% liveborn & symptomatic
- 6% stillborn

Louisiana Department of Health’s STD/HIV Program worked with policymakers in 2014 to pass a state law requiring syphilis screening in the first and third trimesters of pregnancy for all women, as well as at delivery for women at high risk.
Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Females Aged 15–44 Years, United States, 2009–2018

ACRONYMS:
- CS = Congenital syphilis
- P&S = Primary and secondary syphilis
Missed Preventative Opportunities

- No timely prenatal care and no timely syphilis testing 28%
- No timely syphilis testing despite receipt of timely prenatal care 9%
- No adequate maternal treatment despite a timely syphilis diagnosis 31%
- Late identification of seroconversion during pregnancy 11%
Primary and secondary syphilis:

- positive darkfield exam is definitive
- Presumptive diagnosis by a positive nontreponemal serology test (VDRL or RPR) ~80% Positive primary
- 100% secondary
- Confirmed by FTA-ABS or TPPA
- Nontreponemal tests become negative with successful treatment
U.S. Preventative Services Task Force

Recommendations for testing

- All pregnant women
- Persons at increased risk
  - MSM
  - Commercial sex workers
  - Exchange sex for drugs
  - Adult correctional institutions
  - Persons with other STIs

PPV falls when testing other populations
Direct Microscopy

Visualized in darkfield microscopy of a wet mount of chancre as corkscrew movement with flexion.

Mount must be visualized immediately to see characteristic motility.

DFA

Cannot be cultured.
Timing of Serological Response

![Graph showing the timing of serological response to syphilis infection.](image)

- **FTA-Abs**
- **TPHA**
- **VDRL/RPR**
- **IgM**
- **Untreated**
- **Treated**

% of patients who test positive

- **Time of infection**
  - 2
  - 4
  - 6
  - 8
  - 10
  - 12

- **Time post infection**
  - 2
  - 10
  - 20

**Clinical stages of syphilis**

- **Primary lesion**
- **Secondary lesion**
- **Latent (Asymptomatic)**
- **Tertiary**

Syphilis stages & possible test results*

Primary Chancre
- Dark Field +
- RPR +/–
- VDRL +/–

Secondary Eruptions
- RPR +
- VDRL +
- TP-PA +
- AIA +
- FTA +

Tertiary Disease
- RPR +/–
- VDRL +/–
- TP-PA +
- AIA +
- FTA +

- 10-90 days
- 6 weeks to 6 months
- 10-30 years after primary
- Period of latency

*excludes CSF

Courtesy: Michael Pentella, PhD
Traditional Algorithm

- **RPR or other nontreponemal test**
  - [ ] +
    - **TPPA or other treponemal test**
      - [ ] +
        - **Syphilis (past or present)**
          - Evaluate clinically:
            - Past infection and treatment?
            - Current infection risk?
            - Administer therapy according to CDC’s Sexually Transmitted Diseases Treatment Guidelines, 2010 if not previously treated.
      - [ ] -
        - **Syphilis unlikely**
          - If at risk, repeat RPR in several weeks.
  - [ ] -
    - **Syphilis unlikely, or too early to detect.**
    - If clinical signs point to incubating or suspected primary syphilis, treat with benzathine penicillin G.
Automated EIA

- More expensive, less labor
- Unable to distinguish between current and former infection
Reverse Algorithm

EIA or CIA

- Quantitative RPR or other nontreponemal test
  - Syphilis (past or present)
    Evaluate clinically:
    • Past infection and treatment?
    • Current infection risk?
    • Administer therapy according to CDC’s Sexually Transmitted Diseases Treatment Guidelines, 2010 if not previously treated.
  - TP-PA
    - If at risk for syphilis, repeat RPR in several weeks
- If clinical signs point to incubating or suspected primary syphilis, treat with benzathine penicillin G
Tertiary Syphilis Diagnosis

- 70% positive by nontreponemal tests
- ~100% positive by treponemal tests
- Negative nontreponemal tests followed by treponemal tests when symptoms indicate
Neurosyphilis Diagnosis
Congenital Syphilis

- Spirochetes visualized from rash or mucocutaneous lesions by darkfield
- Silver stain of placenta
- Molecular tests
- RPR or VDRL positive, confirmed by FTA-ABS or TPPA with 4-fold rise in titer over 3 weeks
- Drop in RPR or VDRL titer after successful antibiotic treatment
## Curbing a Syphilis Outbreak in Alaska

<table>
<thead>
<tr>
<th>2017-18 300% increase in Anchorage</th>
</tr>
</thead>
<tbody>
<tr>
<td>88% men 87% MSM</td>
</tr>
<tr>
<td>71% of MSM reported using online dating apps</td>
</tr>
<tr>
<td>Only 60% reported being screened</td>
</tr>
<tr>
<td>Migration, travel, tourism, substance abuse and homelessness</td>
</tr>
<tr>
<td>Outreach: free syphilis screening, provider webinars, condom giveaways</td>
</tr>
</tbody>
</table>
Chancroid caused by *Haemophilus ducreyi*

- Uncommon STD in U.S.
- Asia, Africa, Caribbean
- Occasionally causes outbreaks
- Most common in uncircumcised males, HIV
Chancroid — Reported Cases by Year, United States, 1941–2018

NOTE: See section A1.3 in the Appendix for more information on chancroid case reporting.
Symptoms of Chancroid

- Painful genital ulcers, may be multiple
  - Necrotic base and irregular borders
- Enlarged, tender, inguinal lymph nodes
- Combination of symptoms is diagnostic with no evidence of syphilis or herpes
Laboratory Diagnosis

- Culture is difficult
- Gram stain of ulcer or lymph node material reveals pleomorphic gram negative coccobacilli that have been described as “school of fish” formations
- Poor sensitivity
Lymphogranuloma venereum

- Caused by serovars L1, L2, or L3 of *Chlamydia trachomatis*
- Tender unilateral inguinal and/or femoral lymphadenopathy
- Rare in U.S.
  - Primarily in MSM
- Common in Africa, Asia, and South America
- Prostitution, immigration, global travel
LGV

Symptoms

- Rapidly healing, nonpainful, ulcerating papule at the site of inoculation
- Fever, headache, and myalgia
- Inguinal lymphadenopathy
- Proctitis
- Chronic colorectal fistulas and strictures
Transmission of LGV

Because lesion is painless and resolves quickly, infection may not be recognized.

Seldom diagnosed before lymph node involvement is obvious.

Therefore, transmitted to others when infection is unknown.
Diagnosis

- Serology -- Four-fold rise in titer
- Rule out other causes of inguinal lymphadenopathy
- Cell culture, direct immunofluorescence, or nucleic acid detection
LGV 2015-16 MSM

- 38 cases in Michigan
- 29 years (19-60)
- 6 newly diagnosed HIV
- 4 HCV
- 6 syphilis
- 8 gonorrhea
- 50% proctitis
STDs Characterized by Urethritis, Cervicitis, and Vaginitis

Gonorrhoea
*Chlamydia* infections
*Mycoplasma genitalium*
Neisseria gonorrhoeae Epidemiology

- 1.14 million/year
- 550,00 resistant to at least one antimicrobial
- >17,000 unique samples in specimen bank
- Second most common notifiable condition
- Rates among women increased 3.6% during 2017–2018 and 45.2% during 2014–2018
- Rates among men increased 6.0% 2017–2018 and 78.7% 2014–2018
Neisseria gonorrhoeae

- Gram negative diplococci
- Gram stain is useful for diagnosing symptomatic males if intracellular GNDs
- Fastidious
Gonorrhea — Rates of Reported Cases by Year, United States, 1941–2018

* Per 100,000.

NOTE: See section A1.3 in the Appendix for more information on gonorrhea case reporting.
Gonorrhea — Proportion of STD Clinic Patients* Testing Positive by Age Group and Sex and Sex of Sex Partners, STD Surveillance Network (SSuN), 2018

* Results are based on data obtained from unique patients with known sex of sex partners (n=77,314) attending SSuN STD clinics who were tested ≥1 time for gonorrhea in 2018.

NOTE: See section A2.2 in the Appendix for SSuN methods.

ACRONYMS: MSM = Gay, bisexual, and other men who have sex with men; MSW = Men who have sex with women only.
Symptoms

- Urethral discharge and dysuria in males
- Vaginal discharge or asymptomatic in females
- Pharyngitis
- Proctitis
Fig. 38-6. Yellowish green frothy purulent discharge emanating from the cervical os, demonstrative of trichomonas vaginitis.

(Courtesy Centers for Disease Control and Prevention, Atlanta, Ga.)
Complications

- Disseminated or invasive disease
  - Septic arthritis
  - Rash
  - Heart

- Females: infection with GC or Chlamydia causes salpingitis—30% of female infertility—1.5 million

- Blockage leads to pelvic inflammatory disease (PID)—10-20% from gonorrhea
Pelvic Inflammatory Disease

- 20-40% of infected women develop PID
- Infertility 20%
- Ectopic pregnancy 9%
  - 20 case/1000 pregnancies
  - Highest in 20 years
- Chronic abdominal pain 18%
- # of episodes = risk of TFI
Complications in Neonates

- Ophthalmia neonatorum
  - Eye infection in infants
  - If untreated, may cause blindness
Risk from Oral Sex

- Gonorrhea in the throat
- Disseminated infections
- More difficult cure than genital or rectal infections

Can be treated with recommended antibiotics

85% of sexually active adults aged 18-44 years reported having had oral sex at least once with a partner of the opposite sex
Diagnosis

- Males with discharge-gram stain
- Culture
- DNA probe
- Nucleic Acid Amplification
Male Specimen Collection

- If symptomatic, swab pus
- If asymptomatic, insert swab in urethra, rotate, and leave it in place
- Inoculate directly to medium in a “Z”
- Transport to the laboratory immediately
- Urine for NAAT
Female Cultures for GC

- Visualize the cervix with a warmed speculum w/out lubricant
- Remove mucus and/or secretions from cervix with a swab and discard
- Firmly, yet gently, sample endocervical canal by inserting the swab a few millimeters and rotate
Treatment

- Uncomplicated: single 500 mg IM dose of ceftriaxone and oral doxycycline 100 mg twice daily for 7 days
- Gonococcal expedited partner therapy 800 mg oral dose of cefixime and oral doxycycline 100 mg twice daily for 7 days
- No test of cure except oropharyngeal
- Retest at 3 months
Antimicrobial Resistance

- Azithromycin resistance increasing concern
- Results from multiple mechanisms
- Increased >7-fold over 5 years (from 0.6% in 2013 to 4.6% in 2018)
- MSM-- 8.6%; 2.9% among men who have sex with women only

Resistance

Elevated MICs

<table>
<thead>
<tr>
<th>Year</th>
<th>Azithromycin</th>
<th>Cefixime</th>
<th>Ceftriaxone</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>0.5%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2010</td>
<td>1%</td>
<td>0%</td>
<td>0%</td>
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<tr>
<td>2011</td>
<td>1.5%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2012</td>
<td>1%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2013</td>
<td>0.5%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2014</td>
<td>2%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2015</td>
<td>3%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2016</td>
<td>4%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2017</td>
<td>5%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>2018</td>
<td>4%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

%  

Year
**Chlamydia trachomatis**

- Small intracellular bacterium
- Gram negative cell wall
- Elementary bodies— infectious stage
- Reticulate bodies— inclusion in epithelial cells
Chlamydia Epidemiology

- 1,758,668 cases in 2018—most common
- 1 in 10 adolescents infected
- Exceeds all other notifiable infectious diseases in U.S
- 70% asymptomatic

* Per 100,000.
Chlamydia — Rates of Reported Cases by State and Territory, United States, 2018

NOTE: See Section A1.11 in the Appendix for more information on interpreting reported rates in US territories.
Chlamydia — Rates of Reported Cases by Sex, United States, 2000–2018

* Per 100,000.
NOTE: See sections A1.3 and A1.8 in the Appendix for more information on chlamydia case reporting and interpreting trends in chlamydia case reports.
Chlamydia — Positivity Among Females Aged 14–39 Years by Race/Hispanic Ethnicity and Age Group in Clinics* Providing Family Planning and Reproductive Health Services, STD Surveillance Network (SSuN), 2018

* Includes clinics (n=26) that tested >100 females for chlamydia in 2018 and testing coverage was >60%.

NOTE: See section A2.2 in the Appendix for SSuN methods.
Chlamydia — Proportion of STD Clinic Patients Testing Positive* by Age Group and Sex and Sex of Sex Partners, STD Surveillance Network (SSuN), 2018
Chlamydia trachomatis

- 15-20% of men seen in STD clinics
- 3-5% of men seen in general medical practice
- Seropositivity asso. infertility & ectopic pregnancy
- No visible tubal pathology 33% lower pregnancy rate
- Increased risk of impaired development & implantation
Sequellae

- In pregnant women
  - Premature birth
  - Low birth weight
  - Can be spread to the baby during delivery
  - Can cause eye infection
  - Infection of respiratory tract that can develop into pneumonia
Sequellae

In men:

• Epididymitis: painful condition that may lead to scarring

In everyone:

• Arthritis
• Conjunctivitis
• Rash on the soles of the feet or elsewhere
The Chlamydia infection causes a build-up of scarring that can block the fallopian tube and prevent fertilisation.
PID

- 10%--15% of untreated chlamydial infections result in diagnosed clinical PID
- 7.4% of married females aged 15--44 years infertile
- 750,000 cases diagnosed each year
- Infertility costs estimated at $701 million annually
Chlamydia Screening

- Recommend annual screening for all sexually active females aged <25 years
- Females aged ≥25 years if they are at increased risk for infection
- Rescreen after 3 mo.
- Targeted male screening in high prevalence settings
Diagnosis of *Chlamydia*

- Culture
- Enzyme immunoassay
- Direct fluorescent antibody
- Gene probe
- Amplification of nucleic acid
## FDA Approved Tests

<table>
<thead>
<tr>
<th>NAAT</th>
<th>Producer</th>
<th>Detected Pathogen</th>
<th>Methods Used</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aptima Combo 2 assay</td>
<td>Hologic Inc.</td>
<td>CT/NG</td>
<td>TMA</td>
<td>NG, specific regions in 16S rRNA; CT, specific regions in 23Sr rRNA.</td>
</tr>
<tr>
<td>Aptima CT assay</td>
<td>Hologic Inc.</td>
<td>CT</td>
<td>TMA</td>
<td>Specific regions in 16S rRNA.</td>
</tr>
<tr>
<td>Aptima NG assay</td>
<td>Hologic Inc.</td>
<td>NG</td>
<td>TMA</td>
<td>Specific regions in 16S rRNA.</td>
</tr>
<tr>
<td>Abbott RealTime CT/NG</td>
<td>Abbott</td>
<td>CT/NG</td>
<td>real-time PCR</td>
<td>CT, two specific regions in cryptic plasmid; NG, specific sequence in OPA gene.</td>
</tr>
<tr>
<td>cobas 4800 CT/NG Test</td>
<td>Roche Diagnostics</td>
<td>CT/NG</td>
<td>PCR</td>
<td>CT, two targets, one incryptic plasmid and one in chromosome; NG, direct repeat (DR) 9 specific regions</td>
</tr>
<tr>
<td>ProbeTec ET CT/GC Amplified DNA assay</td>
<td>Becton Dickinson</td>
<td>CT/NG</td>
<td>SDA</td>
<td>CT, specific region in cryptic plasmid (ORF); NG, pilin gene inverting protein homolog.</td>
</tr>
<tr>
<td>ProbeTec CT QX Amplified DNA assay</td>
<td>Becton Dickinson</td>
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<td>Becton Dickinson</td>
<td>NG</td>
<td>SDA</td>
<td>Specific region in pilin gene.</td>
</tr>
<tr>
<td>Xpert CT/NG</td>
<td>Cepheid</td>
<td>CT/NG</td>
<td>real-time PCR</td>
<td>CT, specific chromosomal DNA sequence; NG, two specific chromosomal DNA sequences (both should be detected for a positive result).</td>
</tr>
<tr>
<td>Aptima Mycoplasma genitalium Assay</td>
<td>Hologic Inc.</td>
<td>MG</td>
<td>TMA</td>
<td>Specific regions in 16s rRNA.</td>
</tr>
</tbody>
</table>
Advantages of Amplified Tests

- 37% more sensitive than probes
- 25-30% more sensitive than culture
- Urine specimens: first catch, no cleansing
- Vulva swabs can be collected by patient
- Tampons
**Mycoplasma genitalium**

- Fastidious organism of *Mollicutes*, smallest prokaryote
- First isolated in 1981
- 15-20% acute and chronic non-gonococcal urethritis (NGU) in men
- 30% of persistent or recurrent urethritis
- Cervicitis—10-30% and 13-16% PID in women
- Adverse pregnancy outcomes

<table>
<thead>
<tr>
<th>Disease</th>
<th>Level of disease association*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urethritis</td>
<td>++++</td>
</tr>
<tr>
<td>Cervicitis</td>
<td>+++</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>-</td>
</tr>
<tr>
<td>Endometritis and/or Pelvic Inflammatory Disease (PID)</td>
<td>+++</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>+/-</td>
</tr>
<tr>
<td>Infertility (women)</td>
<td>+</td>
</tr>
</tbody>
</table>

* ++++ strong association, +++ association in most studies, + association from a few studies, +/- conflicting results (adapted from WHO 2013)
M. genitalium Epidemiology

- Majority remain asymptomatic and clear infection without developing disease
- Duration 1-3 months
- Antibodies correlate to TFI in 9%
- 4% develop PID
- Asymptomatic screening not recommended
Prevalence

- Symptomatic: Female 10%, Male 10%
- Asymptomatic: Female 9%, Male 9%

Years of age:
- 15-17: Female 0%, Male 0%
- 18-20: Female 26.2%, Male 15.1%
- 21-30: Female 11.7%, Male 14.1%
- 31-40: Female 7.2%, Male 12.4%
- 41-50: Female 3.8%, Male 5.9%
- 51-60: Female 1.1%, Male 2.5%
- 61-70: Female 1.5%, Male 1.5%
- 71-82: Female 0%, Male 0%
M. genitalium Epidemiology

- Similar incidence to Chlamydia trachomatis: 1% in sexually active heterosexuals
- Higher in MSM and STI clinics
- 1,001 asymptomatic MSM, 95 had M. genitalium; 84.2% were macrolide resistant, and 17% were co-infected with Neisseria gonorrhoeae or Chlamydia trachomatis
- Rectal positivity 7%; 2.7% urine
- NGU but not proctitis
Diagnosis

- Difficult to culture
- NAAT preferred
- Hologic’s Aptima Mycoplasma genitalium Assay
  - Transcription mediated amplification
  - FDA approved 2019
  - Urine, urethral, penile meatal, endocervical or vaginal swab samples
- Roche Cobas
Treatment

- Lacks cell wall
- Resistance to macrolides
- Doxycycline less effective
- Fluorinated quinolones
Bacterial Vaginosis

- *Gardnerella vaginalis*/
  *Atopobium vaginae* and other bacteria
- Change in normal vaginal flora with increase pH
Causes of Dysbiosis

- Hormonal changes
- Age
- Sexual practices
- Antimicrobial drugs usage
- Vaginal douching
Atopobium vaginae

Anaerobic GPR

Higher risk of preterm birth

Very rarely found without the presence of Gardnerella

Gardnerella is scaffold

R to metronidazole
## Prevalence

<table>
<thead>
<tr>
<th>Description</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most common vaginal condition in ages 15-44</td>
<td>29.2%</td>
</tr>
<tr>
<td>21.2 million</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td></td>
</tr>
<tr>
<td>19% report no sex</td>
<td></td>
</tr>
<tr>
<td>25% pregnant</td>
<td></td>
</tr>
<tr>
<td>Increases based on lifetime sex partners</td>
<td></td>
</tr>
</tbody>
</table>
Adverse Outcomes

- Miscarriage
- Premature labor, preterm birth, preterm prelabor rupture of membranes
- Chorioamnionitis, intrauterine infection
- Post-caesarean endometritis
- Upper genital tract infections & PID
- 1 in 5 infertile have BV

Synergistic interactions between BVAB such as G. vaginalis and Atopobium vaginale significantly enhanced the severity of BV by increasing bacterial burden.

Polymicrobial biofilm formation mainly by G. vaginalis thicker.

Dysbiosis associated with HPV.

Decreased Lactobacillus–increased incidence for all STIs.

Increased HIV shedding and acquisition.
Diagnosis

- Homogenous, grey discharge
- Clue cells seen microscopically
- Fishy amine odor elicited by adding a drop of KOH to secretions
- pH greater than 4.5
Clue Cell Identification

- Wet mount:
  - Sloughed epithelial cells
  - Numerous tiny bacteria coating epithelial cells
  - No WBCs
Clue Cells
Gram Stain of Clue Cells
Clue Cell Gram Stain

- Normal vaginal flora includes *Lactobacillus*, large, straight, gram positive bacilli
- Vaginosis has no *Lactobacillus* and numerous small, gram-variable coccobacilli
Vaginosis Discharge
## Scoring Vaginal Smears

<table>
<thead>
<tr>
<th>Organism Morphotype</th>
<th>Number/oil field</th>
<th>Score</th>
<th>Organism Morphotype</th>
<th>Number/oil field</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactobacillus</td>
<td>&gt;30</td>
<td>0</td>
<td>Gardnerella</td>
<td>&gt;30</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5-30</td>
<td>1</td>
<td></td>
<td>5-30</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>1-4</td>
<td>2</td>
<td></td>
<td>1-4</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&lt;1</td>
<td>3</td>
<td></td>
<td>&lt;1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>4</td>
<td></td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Add score and interpret:

<table>
<thead>
<tr>
<th>Score</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>Normal</td>
</tr>
<tr>
<td>4-6</td>
<td>Intermediate, retest</td>
</tr>
<tr>
<td>7-10</td>
<td>Bacterial vaginosis</td>
</tr>
</tbody>
</table>
Treatment

- Vaginal microbiota transplantation (VMT) could be effective in treating problematic vaginal infections
- Reconstitute Lactobacillus-dominated microbiota with no observable adverse effects in recurrent-BV patients
- Combined therapy metronidazole with Lactobacillus successfully treated 88% vs 40% recovery with only metronidazole
Case 1

- 7-week-old with “snuffles,” mucocutaneous lesions and slight fever
- Radiological studies revealed periostitis of bones
- Confirmed by serology with difficulty
- Parents also treated
Case 2

- 15-year-old practicing gay male
- 24-hour history of dysuria, pus-like drainage from his penis, and tender left knee joint
- Gram stain revealed the causitive organism
Case 3

- 30-year-old woman was the contact of man who tested positive at the STD clinic but was asymptomatic
- Pelvic examination demonstrated pus
- Two weeks later, she developed PID
Case 4

- 40-year-old male had a painless ulcer on his penis two weeks after visiting a local prostitute
- She had no visible lesions
- No lymphadenopathy was noted
Case 5

- 24 y o pregnant woman
- Presented at PA with a foul smelling, gray, homogenous discharge
- No pain, itching, or other symptoms
- Gram stain revealed numerous epithelial cells covered by small gram variable rods
Case 6

- 43 y. o. female
- Tender inguinal lymph nodes
- No lesions were found and her cervix normal
- Not had sex with anyone but her husband
- Husband frequently travels overseas
- Nothing seen on gram stain of the lymph fluid