NOTE: The total rate of gonorrhea for the United States and outlying areas (Guam, Puerto Rico, and Virgin Islands) was 103.1 per 100,000 population.
Gonorrhea—Rates by Race/Ethnicity, United States, 2002–2011

GC Epidemiology: Key Points
- US has high rates for developed country
- GC concentrated among adolescents/young adults and among racial/ethnic minorities
- GC geographically concentrated in SE US, especially in cities

GC: Pathogenesis
- Gram-negative diplococcus
- Oxidase positive
- Utilizes glucose but not sucrose, maltose or lactose
- Infects cuboidal or columnar epithelial surfaces (conjunctiva, urethra, rectum, endocervix)
- Divides by binary fission (every 20-30 minutes)
GC Manifestations: Men

- **Urethritis:**
  - ~70% overt, symptomatic disease
  - Incubation period: 3-7 days, usually within 10-14 days after exposure
  - Symptoms: purulent urethral discharge and/or dysuria

Clinical Manifestations: Men

- **Epididymitis**
  - Most common local complication
  - Symptoms: unilateral testicular pain and swelling concurrent with urethritis

- **Uncommon Complications:**
  - penile edema and lymphangitis
  - “bull-headed clap”
  - accessory gland infection
  - urethral strictures, prostatitis

GC Manifestations: Women

- **Cervicitis:**
  - 50% have NO symptoms
  - Incubation period unclear: usually 10 days
  - Symptoms: vaginal discharge, bleeding
GC Manifestations: Women

- Urethritis: dysuria
- Skene’s or Bartholin’s Abscesses
- PID
  - Endometritis, salpingitis and peritonitis
  - Symptoms: lower abdominal pain, dyspareunia, spotting, fever

Anorectal Gonorrhea

- Acquired by anal intercourse
- In women: cervicovaginal secretions can contaminate perianal region
- Most cases **asymptomatic**
- Symptoms: anal irritation, painful defecation, constipation, rectal bleeding and/or discharge, tenesmus

Pharyngeal Gonorrhea:

**% Asymptomatic**
Diagnostics for GC

- Gram-negative intracellular diplococci on Gram's stain of discharge
- Culture
- Non-amplified molecular tests
- NAAT (PCR, TMA, SDA)

What is the best specimen type to screen for genital gonorrhea and chlamydia?

**Women**
- A vaginal swab for NAATs testing is preferred
- Endocervical swabs and urine are acceptable alternate specimen types for NAATs testing
- Endocervical swabs are the only acceptable specimen type for gonorrhea cultures

**Men**
- First-catch urine for NAATs testing is preferred
- Urethral swabs are acceptable alternate specimen types for NAATs testing
- Urethral swabs are the only acceptable specimen type for gonorrhea cultures

Who should be screened for gonorrhea?

**Women**
- USPSTF
  - All sexually active women, including those who are pregnant, if they are at increased risk for infection
- CDC
  - All sexually active women ≥15 years annually
  - High-risk older women annually
  - All pregnant women irrespective of age at first prenatal visit

**Men**
- USPSTF
  - Insufficient evidence to recommend for or against routine screening in men at increased risk for infection
- CDC
  - All sexually active MSM annually at all sites of exposure

- Multiple current sex partners, new sex partner, inconsistent condom use, sex work, drug use, history of gonococcal infection or other STI, living in a community with a high prevalence of gonorrhea
- Repeat screening in third trimester if risk factors persist or new risk factors emerge
Gonorrhea therapy

- Ceftriaxone 250 mg intramuscularly + Azithromycin 1 g orally OR Doxycycline 100 mg orally twice daily for 7 days
  - Azithromycin is preferred over doxycycline but both are acceptable
  - Use dual therapy even if CT is ruled out!
- Alternative regimens
  - Cefixime 400 mg orally + Azithromycin 1 g orally OR Doxycycline 100 mg orally twice daily for 7 days
  - Azithromycin 2 g orally
    * Azithromycin is the only regimen currently available to treat persons who is unable to tolerate cephalosporins
  - MMWR Recomm Rep. 2011;60(1):18

Gonococcal cephalosporin resistance

- Combined effects of several chromosomal mutations
- Oral cephalosporin resistance documented in the U.S. MICs increasing to injectable cephalosporins
- Oral and injectable cephalosporin resistance documented in the Far East and Europe

Distribution of Minimum Inhibitory Concentrations (MICs) of Azithromycin Among Neisseria gonorrhoeae Isolates, Gonococcal Isolate Surveillance Project (GISP), 2007–2011

- MMWR 2011 Jul 8;60(26):873-7
Antimicrobial Drugs Used to Treat Gonorrhea Among Participants, Gonococcal Isolate Surveillance Project (GISP), 1988–2011

NOTE: For 2011, “Other” includes no therapy (1.2%), azithromycin 2g (2.3%), and other less frequently used drugs.

Test of cure

• If an alternate regimen is used to treat GC, patients should return for a test of cure 1 week after therapy
• Test of cure
  – Culture (≥72 hours after re-treatment), if culture is not available, NAAT (≥7 days after re-treatment). If the test of cure NAAT is positive, a specimen for culture should be obtained to both ensure that the NAAT result is reliable and to allow for antimicrobial susceptibility testing

Treatment failure with alternate regimens

• Culture relevant clinical sites and perform antimicrobial susceptibility testing using disk diffusion, E-test, or agar dilution
• Treat with intramuscular ceftriaxone 250 mg + azithromycin 2g orally as a single dose
• Evaluate sex partners from the preceding 60 days with culture from all exposed sites and treat with above enhanced regimen
• The laboratory should retain the isolate for possible further testing
Treatment failure with ceftriaxone-based regimen

- Culture relevant clinical specimens and perform antimicrobial susceptibility testing
- Consult an ID specialist, an STD/HIV Prevention Training Center (http://www.nnptc.org), or CDC (404-639-8859) for treatment advice, and report the case to CDC through the local or state health department within 24 hours of diagnosis
- A test-of-cure should be conducted 1 week after re-treatment
- Evaluate sex partners from the preceding 60 days and treat with the same antimicrobial regimen with which the index patient was re-treated

Disseminated Gonococcal Infections (DGI)

- Gonococcal bacteremia of strains that usually cause minimal genital inflammation
- Petechial or pustular acral skin lesions, asymmetrical arthralgia, tenosynovitis, or septic arthritis
- Rarely perihepatitis, endocarditis, meningitis

Other Management Issues

- Person should be screened for syphilis & HIV
- Refer all sex partners in past 60 days for evaluation and treatment
- HIV infected: same strategy
- Clinicians should advise patients with gonorrhea to be retested 3 months after treatment.
DGI Therapy

- Hospitalize and treat parenterally until 24-48 hr after improvement begins
- Recommended:
  - Ceftriaxone 1g IM or IV every 24 hours
  - Alternate is Cefotaxime 1 g IV or Ceftizoxime 1 g IV every 8 hours
- Regimen should be continued for 24-48 hours after improvement begins
- Then switch to following to complete a full week course:
  - Cefixime 400 mg PO BID (if organism is susceptible)

Retesting to detect repeat infections

- Reinfection with GC and CT is common in both men and women
- All persons treated for GC and/or CT should be re-tested in three months because of high reinfection rates regardless of whether their partner was treated

Chlamydia
Chlamydia—Rates by Sex, United States, 1991–2011

Rate (per 100,000 population)

Year

Chlamydia—Rates by Region, United States, 2002–2011

Rate (per 100,000 population)

Year

Chlamydia—Rates by Age and Sex, United States, 2011

Men | Rate (per 100,000 population) | Women
--- | --- | ---
4000 | 14.5 | 34.6
3200 | 10.0 | 21.4
2400 | 6.5 | 12.2
1600 | 3.5 | 10.5
800 | 2.5 | 10.5
0 | 1.5 | 10.5
0-14 | 103.3 | 285.2
15-19 | 15.3 | 32.3
20-24 | 11.3 | 16.4
25-29 | 15.8 | 28.3
30-34 | 15.8 | 28.3
35-39 | 14.6 | 30.5
40-44 | 11.0 | 20.4
45-49 | 7.5 | 10.5
50-54 | 3.5 | 10.5
55-64 | 2.5 | 10.5
65+ | 2.5 | 10.5
Total | 146.6 | 346.6

NOTE: As of January 2000, all 50 states and the District of Columbia have regulations that require the reporting of chlamydia cases.
Serological classification

- A, B, Ba, C (Trachoma)
- D-K (Genitourinary and ocular infections)
- L1-L3 (Lymphogranuloma venereum)

Infections in Men (D-K)

- Urethritis with dysuria
- Discharge classically mucopurulent
- Often asymptomatic
Infections in Men: Epididymitis

- Up to 70% of sexually transmitted cases are due to chlamydia, others to GC
- Usually improve rapidly with antibiotic treatment

Infections in Women: Cervicitis

- Most often no signs or symptoms
- If present signs include
  - Discharge, ectopy, edema, induced bleeding
- 30-50% have mucopurulent cervicitis (>30 PMNs per oil immersion field)

Proctitis

- Caused by direct inoculation from unprotected anal sex
- Serovar D-K or LGV types
- Symptoms may include
  - Rectal bleeding and pain
  - Mucous discharge
  - Diarrhea
Other infections

- Conjunctivitis
- Acute urethral syndrome in women
- Bartholinitis
- Endometritis
- Salpingitis
- Perihepatitis
- Reiters Syndrome
  - Urethritis, conjunctivitis, arthritis, skin lesions

Sequelae for Untreated CT

Among women:
- PID
- Ectopic pregnancy
- Infertility

Among men:
- Prostatitis
- Epidydimitis

Lymphogranuloma venereum

- Strains are more invasive
- Causes thrombolymphangitis
- Appear to replicate more efficiently in macrophages
- Early disease: transient genital ulcer, buboes, inflammation
- Late disease: abscesses, fistulas, elephantiasis, frozen pelvis
Sensitivity and specificity of diagnostic tests for the detection of Chlamydia trachomatis

<table>
<thead>
<tr>
<th>Diagnostic Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tissue Culture</td>
<td>70-85%</td>
<td>100%</td>
</tr>
<tr>
<td>Direct Fluorescent Antibody</td>
<td>80-85%</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>Enzyme Immunoassay</td>
<td>53-76%</td>
<td>95%</td>
</tr>
<tr>
<td>Hybridization (Pace2)</td>
<td>65-83%</td>
<td>95%</td>
</tr>
<tr>
<td>Ligase Chain Reaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>94.4-96.4%</td>
<td>95.5-100%</td>
</tr>
<tr>
<td>Female Urine</td>
<td>93-98%</td>
<td>90-100%</td>
</tr>
<tr>
<td>Male Urine</td>
<td>96.4%</td>
<td>94-100%</td>
</tr>
<tr>
<td>Polymerase Chain Reaction (COBAS)</td>
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<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>89.7%</td>
<td>99.4%</td>
</tr>
<tr>
<td>Female Urine</td>
<td>89.2%</td>
<td>99.0%</td>
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<tr>
<td>Male Urine</td>
<td>90.3%</td>
<td>98.4%</td>
</tr>
<tr>
<td>Strand Displacement Amplification</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervical</td>
<td>92.8%</td>
<td>98.1%</td>
</tr>
<tr>
<td>Female urine</td>
<td>80.5%</td>
<td>98.4%</td>
</tr>
<tr>
<td>Male urine</td>
<td>93.1%</td>
<td>93.9%</td>
</tr>
</tbody>
</table>

Gaydos, C - 2002

LGV Diagnosis

- Routine NAATs do not distinguish between D-K and L1-L3 serotypes
  - Additional testing (e.g. multiplex PCR, sequencing) by the lab is necessary to distinguish between the strains
- Serological testing for LGV antibodies available but not standardized for rectal LGV
Who should be screened for chlamydia?

**Women**

- **USPSTF**
  - All sexually active women ≤24 years annually (at first prenatal visit if pregnant)*
  - High-risk older women annually* (at first prenatal visit if pregnant*)
- **CDC**
  - All sexually active women ≤25 years annually
  - High-risk older women annually*
  - All pregnant women irrespective of age at first prenatal visit *

**Men**

- **USPSTF**
  - Current evidence is insufficient to assess the balance of benefits and harms of screening
- **CDC**
  - All sexually active MSM annually at all sites of exposure
  - Targeted screening in correctional facilities, adolescent clinics, and STD clinics (if funds available)

---

* Multiple current sex partners, new sex partner, inconsistent condom use
* Repeat screening in third trimester if risk factors persist

---

**Recommended Regimens: CT (D-K)**

- Azithromycin 1 g PO
  - or
- Doxycycline 100 mg PO BID for 7 days

**Alternative Regimens: 7 Day Course of:**

- Erythromycin base 500 mg PO QID
- Erythromycin ethylsuccinate 800 mg QID
- Ofloxacin 300 mg PO BID

---

**Recommended Regimens: CT (LGV)**

- Doxycycline 100 mg PO BID for 21 days

- Azithromycin 1g PO q week X 3 weeks
Other Considerations for *Chlamydia* Infections

- TOC - 3 weeks AFTER completion of Rx with erythromycin
- *Re-screen women for Ct 3-4 months after treatment*
- Refer all sex partners in last 60 days for evaluation, testing and therapy
- No sex until patient AND partner (s) are cured

Pregnancy and *Chlamydia*

- Screen all pregnant women in 1st trimester. If high-risk, repeat in 3rd
- Doxycycline and ofloxacin are contraindicated
- Recommend Regimens:
  - Azithromycin 1 g PO
  - Amoxicillin 500 mg PO TID for 7 days
  - Erythromycin base 500 mg PO QID for 7 days

Extragenital gonorrhea (GC) and chlamydia (CT) infections

- The majority of cases of pharyngeal and rectal GC and CT are asymptomatic
- Studies suggest that up to 65% of cases of gonorrhea and 50% of cases of chlamydia among MSM may be missed if genital-only testing were performed.
- In women, 10% of CT and 31% of GC infections would have been missed if extragenital testing were not done
- Rectal and pharyngeal infections are of public health significance
Extragenital STI diagnostics

- All persons should be tested for rectal gonorrhea and chlamydia and pharyngeal gonorrhea if they report rectal or pharyngeal exposures
- Sensitivity of culture <50% to detect rectal and pharyngeal GC vs. >90% sensitivity for NAATs (this can vary by NAAT type)
- The CDC recommends that NAATs be used to detect these extragenital infections
- Although none of the NAATs are FDA cleared to use with extragenital specimens, most large laboratories have established performance specifications to satisfy compliance to Clinical Laboratory Improvement Amendments

Other References