

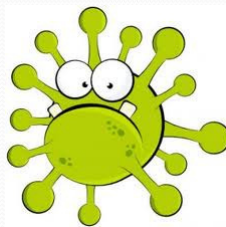
Gonococcal and Chlamydial Infections and Associated Syndromes

October 2012



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Gonorrhea



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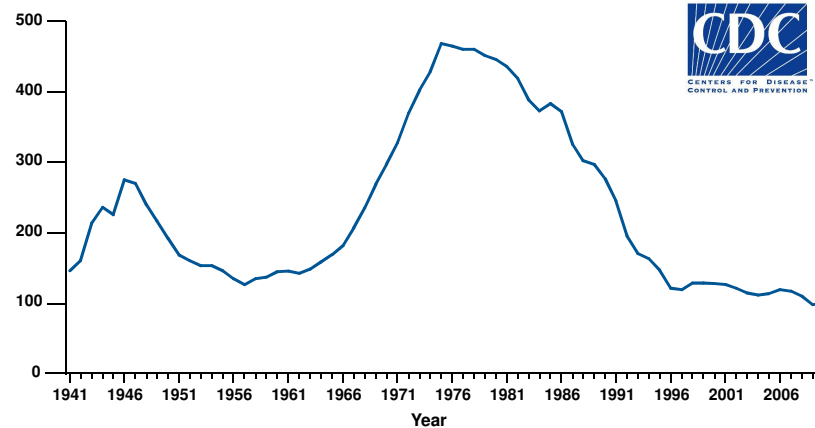
Gonorrhea – Epidemiology

- Incidence geographically variable
 - Highest in South, Lower in West
 - Ever-increasing rates among MSM
 - Peak incidence
 - Men – 20-24 years
 - Women – 15-19 years
 - High rates
 - Black, Hispanic, & Native Americans
 - Many Risk Factors
 - Multiple* or new sex partners
 - Lack of barrier precautions
 - Young age
 - Urban residence
 - Exchange of sex for drugs/money
 - Core population
- * Defined as > 1 in a six-month period

3

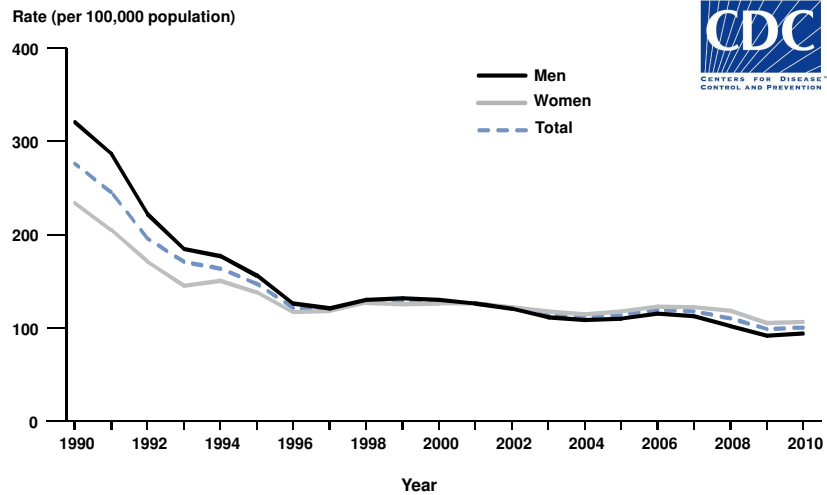
US GC Rates – 1941-2010

Rate (per 100,000 population)

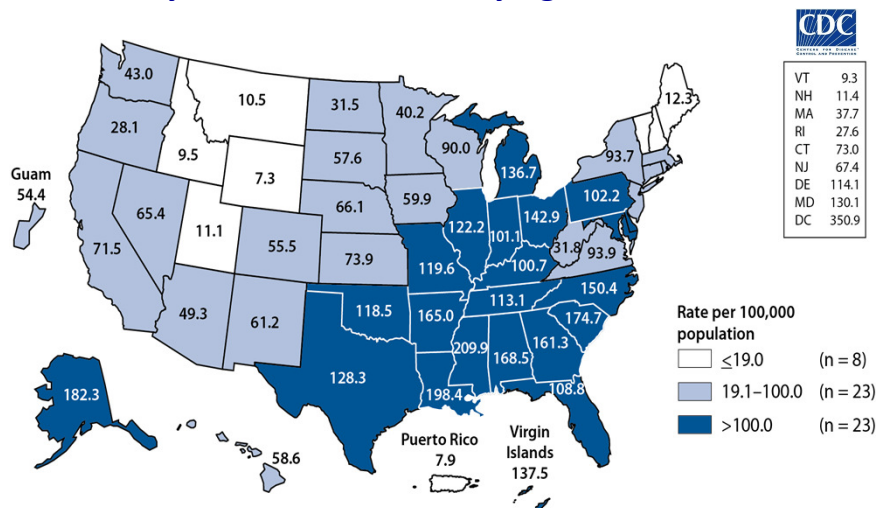


GC Culture became available in 1962 & NAATs became available in late 1990s

US GC Rates by Sex – 1990-2010

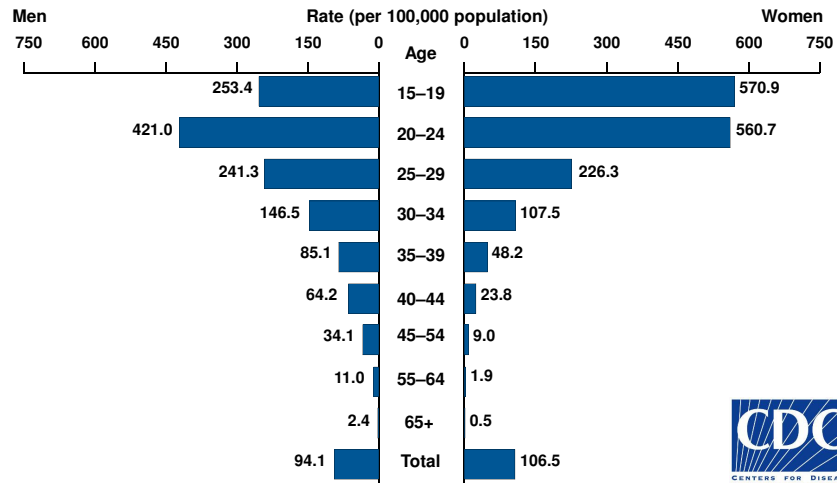


GC Rates by State – US and Outlying Areas – 2010

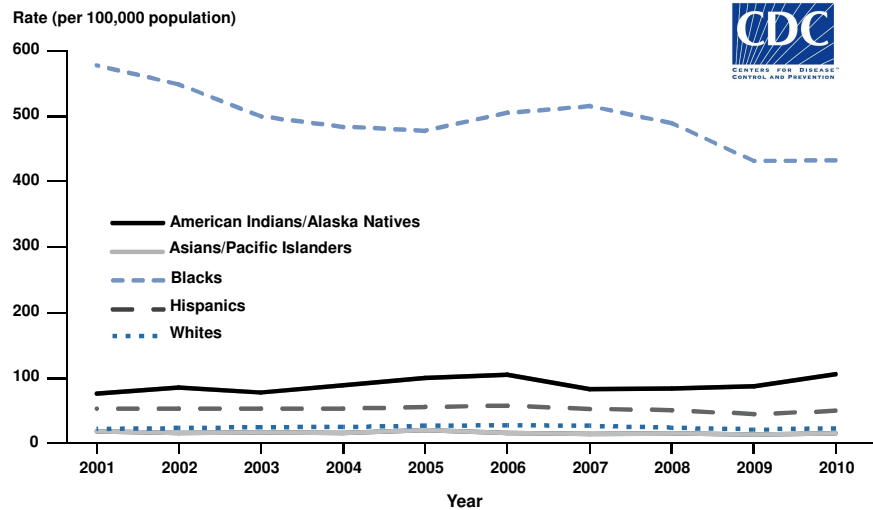


NOTE: The total rate of GC for the US & Outlying Areas (Guam, PR, VI) was 99.6 per 100,000 population

US GC Rates by Age and Sex – 2010



US GC Rates by Race/Ethnicity – 2001-10



GC – Epidemiology

- Gram negative intracellular diplococcus known as *Neisseria gonorrhoeae*
- Attaches to non-ciliated columnar epithelial cells
- Detected by visualization (Gram's Stain), growth (culture), or detection of bacterial products (EIA, NAATs, etc)
- Antimicrobial resistance possible – plasmid or chromosomal

* **Currently this is a critical problem with GC – more to follow**

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GC – Transmission

- Efficiently transmitted by
 - Male to female via semen
 - Female to male urethra
 - Rectal intercourse
 - Fellatio (pharyngeal infection)
 - Perinatal transmission (mother to infant)
- GC is associated with increased transmission of & susceptibility to HIV infection
 - One of the more likely HIV facilitators, due to the inflammatory response to this infection

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Males – GC Urethritis

- Incubation
 - Typically 3-7 days but asymptomatic infection may occur (10%)
- Symptoms
 - Dysuria & purulent or mucopurulent discharge
- Signs
 - Purulent yellowish discharge is classic but it could be mucoid or mucopurulent



Note the erythema of the glans & foreskin secondary to the irritation due to the discharge

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Females – GC Cervicitis

- Incubation
 - Unknown but S/S generally develop by 10 days
- Symptoms
 - Present in 50% of cases & they are non-specific, including vaginal discharge, dysuria, cervical bleeding
- Signs
 - Exam is highly variable (normal to frank purulent discharge)

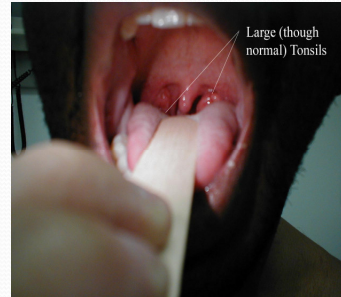


Classic GC mucopurulent cervical discharge – pathognomonic – but not commonly seen

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Gonococcal Pharyngitis

- Incubation
 - Unknown
- Symptoms
 - Rarely present but may include non-exudative pharyngitis, cervical adenitis



** May be only site of infection & is more difficult to eradicate with Rx – mounting evidence that treating pharyngeal GC is increasingly challenging*

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October 2012 Issue of *Rolling Stone* has article on GC



Oral Sex Is No Longer Safe Sex

October 24, 2012

"The list of things we've had to learn to live without – polar ice caps, Bengal tigers, jobs that pay a living wage, the White Stripes – grows longer every day. But now things are really getting out of hand: According to the New England Journal of Medicine..."



Read more

<http://www.rollingstone.com/search?q=gonorrhea#ixzz2A8WuiH96>

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GC – Other Sites Complications and Other Syndromes

- PID
- Epididymitis
- Anorectal disease
- Genital abscesses
 - Classically Bartholin's or Skene's Glands
- Eye disease
- Disseminated Gonococcal Infection (DGI)

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Bartholin's Gland Abscess

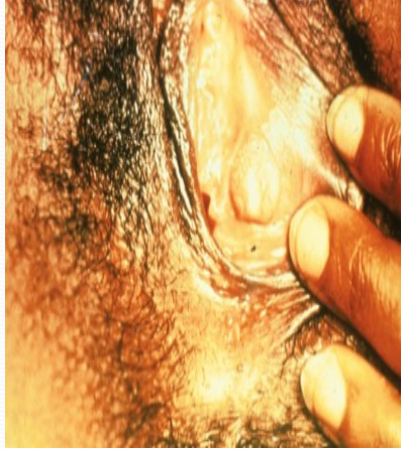


- This large abscess is intact – it could rupture spontaneously or would likely require an I & D
 - Some use a Word Catheter as a drain after performing an I & D
 - A GC culture should be done



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Bartholin's Gland Abscess



- This abscess is draining purulent discharge – which should be cultured for GC
 - Some abscesses rupture spontaneously & others require I & D

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Gonococcal Ophthalmia – Adult

- Incubation
 - 3-19 days – often there could be a Hx of urethral Sx (males) within the past 1-3 weeks; often transmitted by auto-inoculation
- Symptoms
 - Profuse purulent discharge with severe inflammation
- Signs
 - Discharge, injection of conjunctiva, lid swelling, & occasionally periorbital erythema
 - Characterized by rapid onset; preseptal cellulitis & corneal involvement do occur – though quite rare



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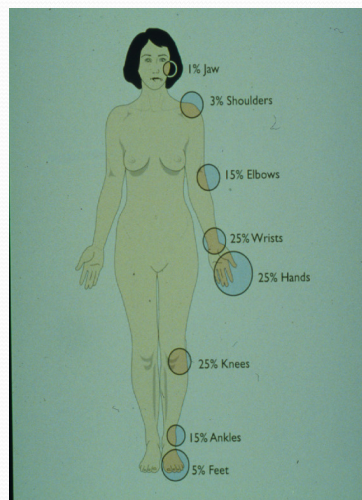
Disseminated Gonococcal Infection

- DGI is usually related to 0.5-3% untreated mucosal GC
- DGI is a Dermatitis-Arthritis Syndrome
 - Tender, necrotic pustules (variable)
 - Asymmetrical Arthritis
 - Tenosynovitis
- Risk of Endocarditis or meningitis exists

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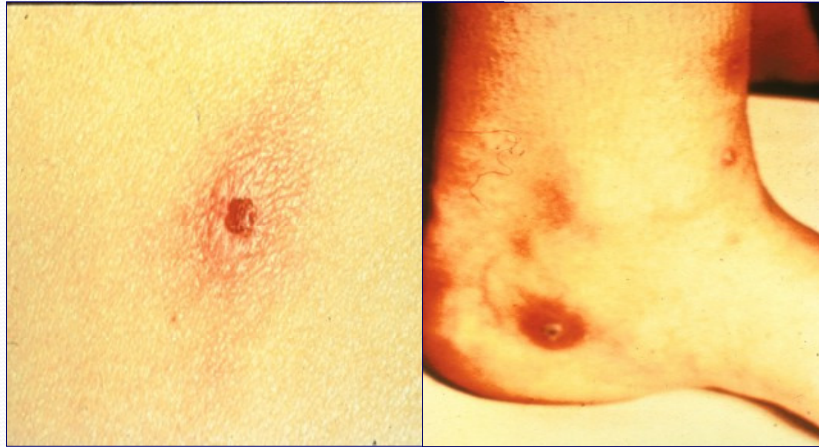
Joint Involvement in DGI

- A hot, swollen, painful, & exquisitely tender joint is often the 1st indication of DGI
 - It is important that a case that presents without Hx of trauma or other known cause should be tested for GC (culture)
- Emergency Department &/or Orthopedic surgeons are often the providers who see this patient first & unfortunately they do not always collect a GC culture



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DGI – Skin Lesions



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DGI – Tenosynovitis



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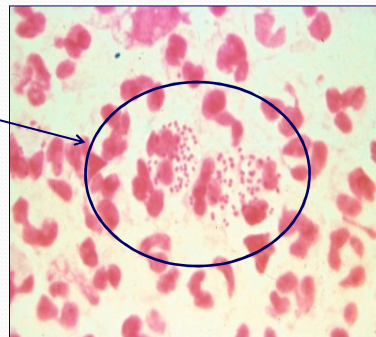
GC – Methods of Detection

- Gram's Stain
 - Sensitivity – 95% male urethral smear
 - Sensitivity – 50% cervical smear
- **Culture (Gold Standard)** – allows for susceptibility testing
- Non-Amplified Assays
 - DNA probe – *GenProbe*™
 - EIA
- **Amplification Assays (NAATs)**
 - Polymerase chain reaction (PCR) – Roche *Amplicor*™ Transcription-mediated amplification (TMA) – *Gen-Probe Aptima*®
 - Strand displacement amplification (SDA) – Becton-Dickinson BD *ProbeTec ET*™

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GC – Gram Stain of Male Urethral Discharge

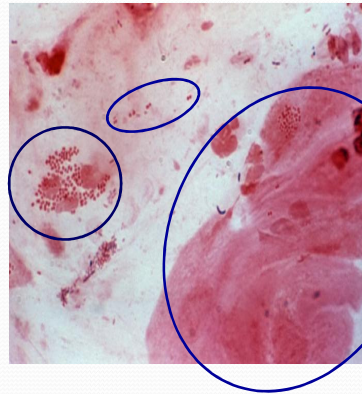
- Note the intracellular Gram Negative diplococci
- Also, note the numerous pmns



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GC – Gram Stain of Cervical Discharge

- This is a **particularly** clear stain showing Gram Negative intracellular diplococci (also some extracellular)
 - Note how the cervical stain has many organisms & other cells (e.g., an epithelial cell) as compared to the male urethra
 - A cervical Gram Stain is not sensitive, though it is specific



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GC/CT – and – HIV

- Increased risk of PID/acute salpingitis
- Increased risk of tubo-ovarian abscess
- PID presents with lower WBC count
- Immunosuppressed HIV-infected women with PID – inpatient Rx with optimal anaerobic coverage
- Severely immunocompromised patients are at risk for
 - GC proctitis
 - Rectal abscess
 - Sepsis

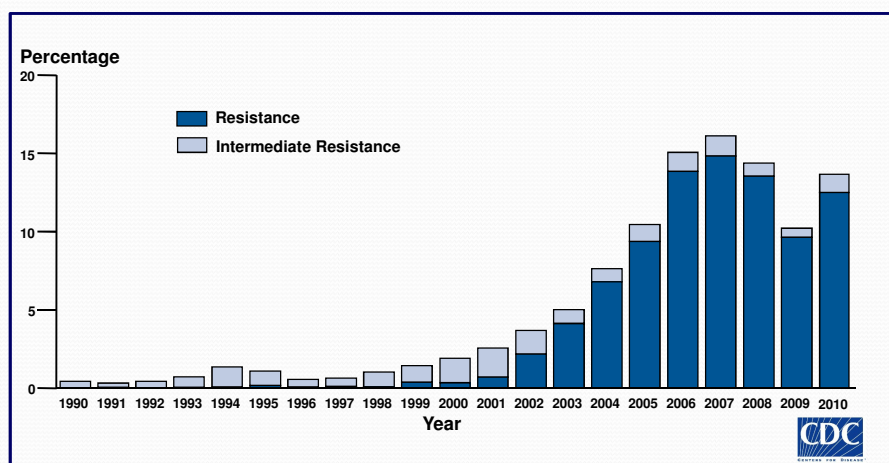
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Antimicrobial Susceptibility of *N. gonorrhoeae*

- Fluoroquinolone resistance is widely disseminated throughout the US & the world
- Approximately 25% of isolates are resistant to penicillin or tetracycline or both
- Approximately 0.5% of isolates show decreased susceptibility to azithromycin
- Sporadic cases of decreased susceptibility to ceftriaxone & cefixime have been reported recently

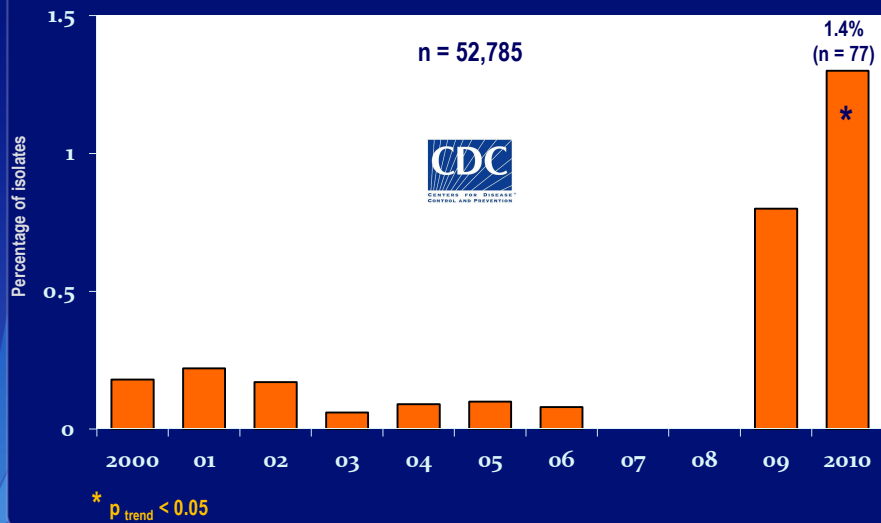
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Gonococcal Isolate Surveillance Project (GISP) – % of *N gonorrhoeae* Isolates with Resistance or Intermediate Resistance to Ciprofloxacin – 1990-2010

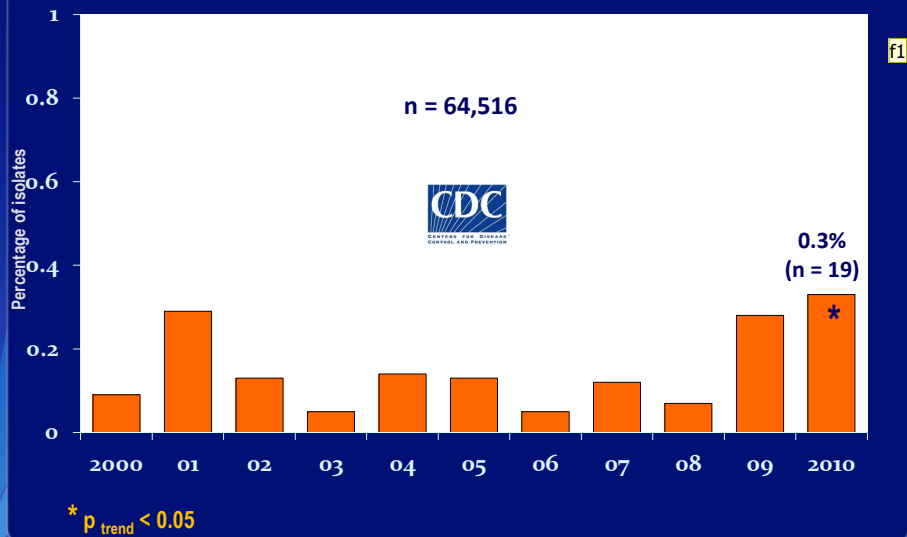


NOTE: Resistant isolates have ciprofloxacin minimum inhibitory concentrations (MICs) >1 µg/ml; those with intermediate resistance have ciprofloxacin MICs of 0.125–0.5 µg/ml; susceptibility to ciprofloxacin was first measured in GISP in 1990

GISP Data – Proportion of Isolates with Elevated Cefixime MICs ($\geq 0.25 \mu\text{g/ml}$) – US – 2000-10



GISP – Proportion of Isolates with Elevated Ceftriaxone MICs ($\geq 0.125 \mu\text{g/ml}$) – US – 2000-10



Slide 30

f1 inserted new slide
fve0, 8/19/2011

GC Antibiotic Resistance

**Guidelines for GC Rx
were updated this past
August by the CDC**



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**Updated CDC Recommendations
Issued August 11, 2012**



For uncomplicated GC infections of the cervix, urethra, & rectum

Recommended regimen	Alternative regimen If Ceftriaxone unavailable
- Ceftriaxone 250 mg IM x one + - Azithromycin 1 gm PO x one <u>or</u> Doxycycline 100 mg PO BID x 7 days *	- Cefixime 400 mg PO x one + - Azithromycin 1 gm PO x one <u>or</u> Doxycycline 100 mg PO BID x 7 days * + ➤ Test-of-cure (TOC) in 1 week *
* Because of the high prevalence of Tetracycline resistance among GISP isolates, particularly those with elevated Cefixime MICs, use of Azithromycin as 2nd antimicrobial is preferred. ✗ Every effort should be made to use gonorrhea <u>culture</u> for TOC.	

If Rx Failure is suspected/confirmed – contact an ID Specialist & notify the DoH

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For uncomplicated GC infections of the cervix, urethra, & rectum

If Severe Cephalosporin Allergy

- Azithromycin 2 gm PO x one

+

➤ **TOC in 1 week ***

✕ Every effort should be made to use gonorrhea culture for TOC.

**If Rx Failure is suspected/confirmed – contact an
ID Specialist & notify the DoH**

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For uncomplicated GC infections of the pharynx

Recommended regimen

- Ceftriaxone 250 mg IM x one

+

- Azithromycin 1 gm PO x one or
Doxycycline 100 mg PO BID x 7
days *

Alternative regimen

- Azithromycin 2 gm PO x one

+

➤ **TOC in 1 week**

* Because of the high prevalence of Tetracycline resistance among GISP isolates, particularly those with elevated Cefixime MICs, use of Azithromycin as 2nd antimicrobial is preferred.

**If Rx Failure is suspected/confirmed – contact an
ID Specialist & notify the DoH**

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GC Treatment – CDC Guidelines

- Still stress single dose, dispensed therapy
- Treat all patients with GC for co-existing/incubating CT **infection regardless of CT test result**
- Resistance on the rise – use increased dose of Ceftriaxone, i.e., the full 250 mg dose (Use the “Intern Rule”: 250 mg comes in the vial – use the whole vial!)
 - **Oral cephalosporin is not an equivalent choice anymore**
- Azithromycin another alternative agent for Rx



Special Considerations – Pregnancy

- Treat with recommended Cephalosporin-based **combination** therapy
- If Cephalosporin is not tolerated, treat with Azithromycin 2 g PO x 1
 - A **TOC** should be performed 1 week after treatment
- Pregnant women should not be treated with Quinolones or Tetracyclines; Spectinomycin is not commercially available



If Penicillin-Allergic *

- Azithromycin 2 g orally
 - **Plus TOC in 1 week**

* **Desensitization is impractical in most settings**

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Treatment Follow-Up – Test of Cure

- A TOC is **not** considered necessary (nor recommended) as long as the CDC recommended Cephalosporin-based regimen is administered
- **A TOC is recommended if an alternative regimen is administered**
- If symptoms persist, perform culture for *N gonorrhoeae*
 - Any gonococci isolated should be tested for antimicrobial susceptibility at site of exposure
- Repeat testing in 3 months

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GC Rx – DGI

Ceftriaxone 1g IV/IM q 24 hours – until improved x 2 d

~ or ~

Cefotaxime 1g IV q 8 hours

~ or ~

Ceftizoxime 1g IV q 8 hours

Followed by

Cefixime 400 mg PO BID – to finish 7 days

~ plus ~

Azithromycin 1 gm PO x 1

~ or ~

Doxycycline 100 mg PO BID x 7

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GC – Test-of-Cure vs Re-Screening

- Test-of-Cure *
 - As noted – any time a non-recommended GC Rx is given, or if patient does not recover
- Re-screening *
 - 3-4 months post-Rx – or when they next present for care within next 12 months
 - Population statistics show that ~ 35% of persons Rx'd for GC will have infection again within 3-4 months
 - Thus re-screening might detect these re-infected persons

* If using NAAT – not before 3 weeks post-Rx

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Chlamydia



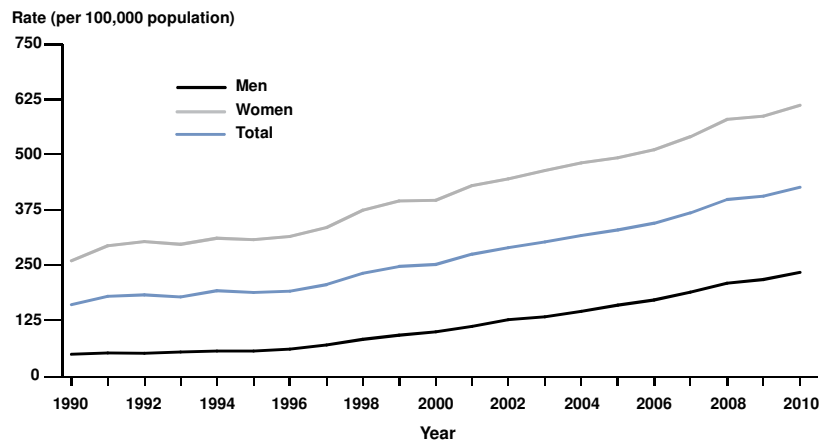
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***Chlamydia trachomatis* Incidence**

- Estimated 3 million cases in US annually
- Most frequently reported STD in US
- Reported rates 3 times higher in females than in males
- Rule of thumb – 3 times more Chlamydia (CT) than GC in most communities

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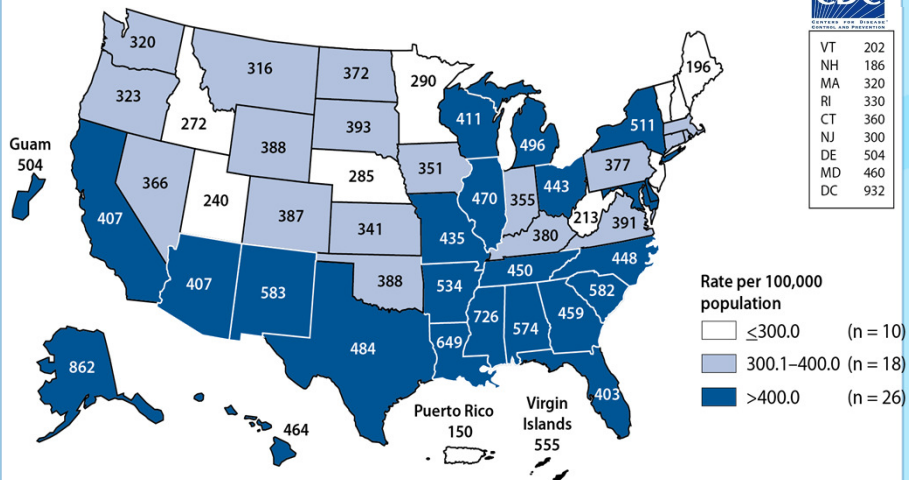
CT US Rates by Sex – 1990-2012



NOTE:

As of January 2000, all 50 states & Wash DC require the CT reporting CT

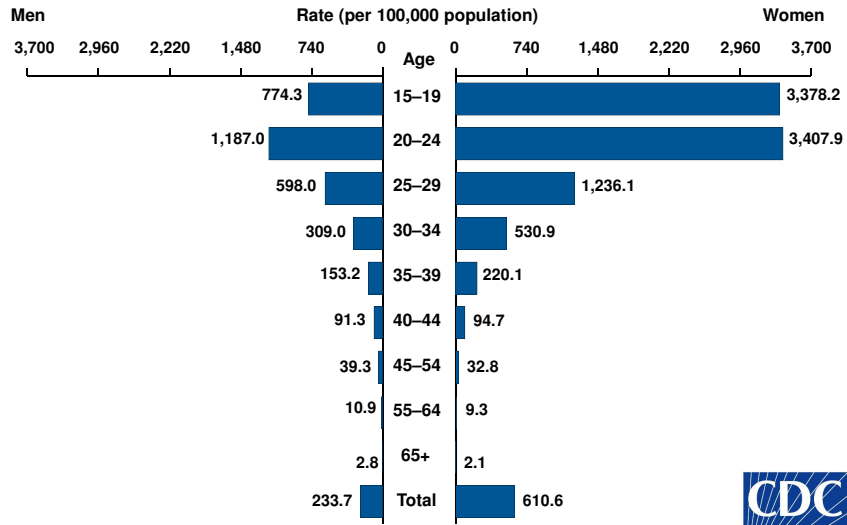
CT Rates by State – US and Outlying Areas – 2010



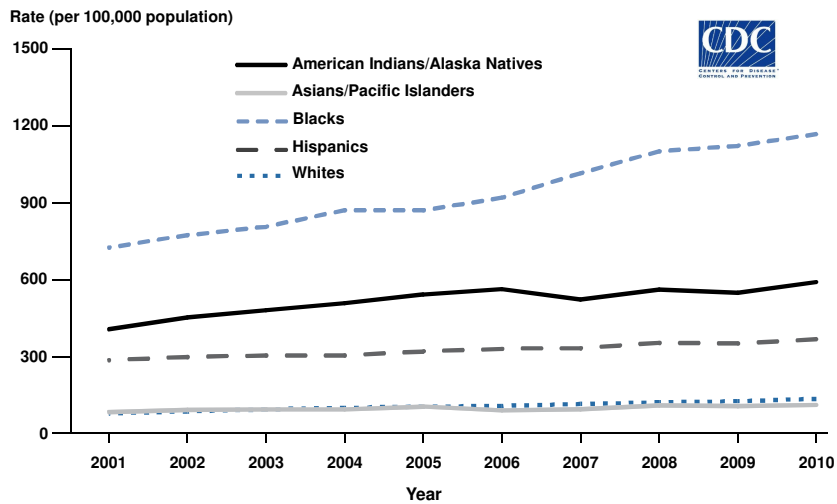
NOTE:

The total rate of CT – US & Outlying Areas (Guam, PR, VI) – was 422.6 per 100,000 population

US CT Rates – By Age and Sex – 2010

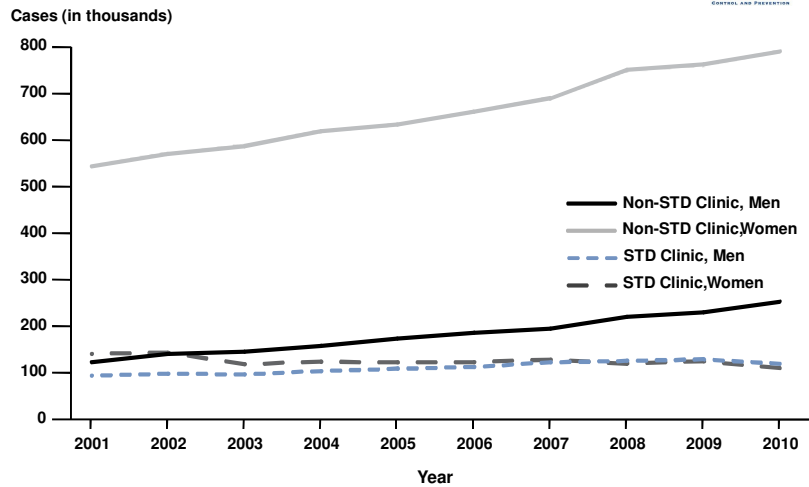


US CT Rates – By Race/Ethnicity – 2001-10



Prevalence is an important contributing factor for disproportionately high rates of STDs

US CT Cases – Reporting Source and Sex – 2001-10



CT – Risk Factors

- Adolescence
- New or multiple* sex partners
- History of STD infection
- Presence of another STD
- Oral contraceptive user
- Lack of barrier contraception

* Defined as > 2 in a 6-month period

CT – Transmission

- Transmission is **sexual** ~ or ~ **vertical**
- Highly transmissible
- Incubation period 7-21 days
- Significant asymptomatic reservoir exists in the population
 - Prevalence is an important factor that drives this infection
- Re-infection is common

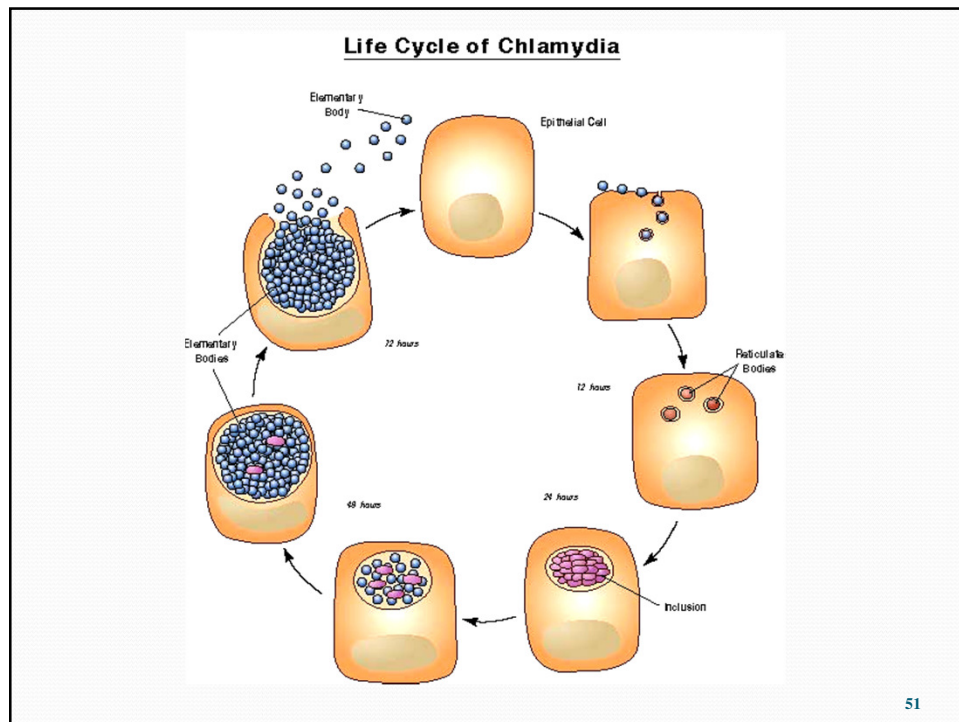
* **Defined as > 2 in a 6-month period**

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CT – Microbiology

- Obligatory intracellular bacteria
- Infect columnar epithelial cells
- Survive by replication that results in the death of the cell
- Takes on two forms in its life cycle
 - Elementary body (EB)
 - Reticulate body (RB)

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Chlamydiaceae Family Species that Cause Disease in Human	
Species (genus)	Disease
<i>C trachomatis</i> 2 biovars, non-LGV LGV	• Conjunctivitis, • Trachoma, • Sexual Transmission: NGU, MPC, PID, • Infant pneumonia • LGV
<i>C pneumoniae</i>	• Pharyngitis • Bronchitis • Pneumonia
<i>C psittaci</i>	• Psittacosis

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Clinical Syndromes Caused by *C trachomatis*

	Local Infection	Complications	Sequelae
Males	Conjunctivitis Urethritis Proctitis Prostatitis (?)	Reiter's Syndrome Epididymitis	Chronic Arthritis (rare) Infertility (rare)
Females	Conjunctivitis Urethritis Cervicitis Proctitis	Endometritis Salpingitis Perihepatitis Reiter's Syndrome	Ectopic Pregnancy Infertility Chronic Pelvic Pain Chronic Arthritis (rare)
Infants	Conjunctivitis Pneumonitis Pharyngitis Rhinitis	Chronic Lung Disease (?)	Rare (if any)

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CT – Urethritis

Most Common Manifestation in Males

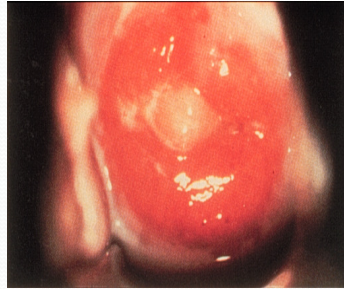
- Incubation
 - Unknown – 5-10 days in symptomatic, but > 50% asymptomatic
- Symptoms
 - Urethral discharge, dysuria, meatal erythema
- Signs
 - None or clear, mucoid, or mucopurulent discharge



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CT – Cervicitis

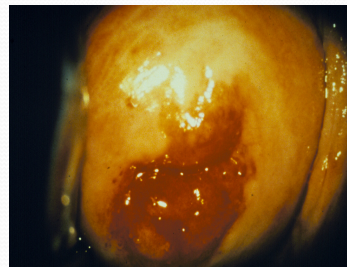
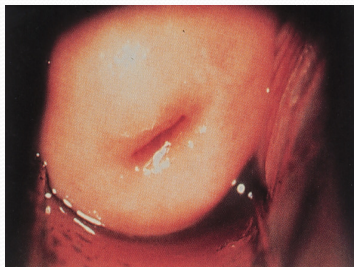
- Incubation
 - Unknown – with > 80% asymptomatic
- Symptoms
 - Non-specific – vaginal discharge or spotting, dyspareunia
- Signs
 - 30-50% with signs of MPC, including endocervical discharge, edematous cervical ectopy, cervical friability



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CT – Cervical Infection

- A CT-infected cervix can look entirely normal – healthy, pink, with clear mucus
- Friability can be seen with CT
 - Defined in different ways, but usually as 1+, 2+, or 3+
 - Here, it is 3+



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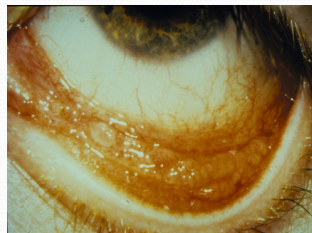
CT – Other Manifestations

- Females
 - Urethritis
 - Usually asymptomatic, frequently with cervicitis, may cause “sterile” pyuria
 - Pelvic Inflammatory Disease
 - Perihepatitis (Fitz-Hugh-Curtis)
 - May be due to GC (30%) or CT (70%)
 - Presents like PID plus RUQ pain/nausea/fever
- Males
 - Epididymitis
 - 70% of STD-associated epididymitis is due to CT

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CT – Other Manifestations

- Conjunctivitis
 - Auto-inoculation
 - Follicular conjunctivitis
 - Rarely purulent in adults
- Proctitis/Proctocolitis
- LGV (*Lymphogranuloma venereum*)
 - Caused by serovars L1-L3
 - Rare in the US
 - Presents with tender adenopathy that may suppurate & sometimes a painless ulcer (often not detected)
 - Recent outbreaks in MSM – presents like proctitis



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LGV – Lymphadenopathy



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CT – Other Manifestations

- Reiter's Syndrome
 - More common in males
 - Syndrome of conjunctivitis, urethritis, oligoarticular arthritis, & spondyloarthritis
 - May occur 3-6 weeks after infection
 - Associated with HLA-B27



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CT – Methods of Detection

- Culture
- Non-Amplified Assays
 - Direct Fluorescent Antibody (DFA)
 - ELISA/EIA
 - DNA probe – *GenProbe*™
- Amplification Assays (NAATs)
 - Becton Dickinson *BDProbeTec*™
 - Gen-Probe *AmpCT*™, *Aptima*™
 - Roche *Amplicor*™
- Serology

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CT – Methods of Detection – Culture

- Historically the “gold standard”
- Variable sensitivity – 50-80%
- Depending on the laboratory – culture might be the only way to test for CT in non-genitourinary sites (e.g., eye, rectum)
- High specificity
- Used in legal investigations
- Not suitable for widespread screening



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CT – Methods of Detection – Nucleic Acid Amplification Tests

- NAATs amplify & detect organism-specific genomic or plasmid DNA or RNA
- FDA cleared for urethral swabs from men/women, urine from men/women, and cervical & vaginal swabs
- Significantly more sensitive than other tests
- Downside is cost, possible false positives, no approval for non-genital sites
 - However, as noted – the FDA has approved NAATs for non-genitourinary sites, but specific lab competencies must be fulfilled

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CT – Methods of Detection – Serology

- Rarely used for uncomplicated infections
 - The results difficult to interpret
- Criteria used in LGV diagnosis
 - Complement fixation titers > 1:64 suggestive
 - Complement fixation titers > 1:256 diagnostic
 - Complement fixation titers < 1:32 rule out



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Laboratory Diagnosis of CT		
	Sensitivity (%)	Specificity (%)
Culture	52-92	99-100
Antigen detection ~ or ~ Nucleic Acid Hybrid	50-70	95-99
PCR (NAAT)	65-95	> 99
LCR (NAAT)	85-95	> 99
Serology	85-100	< 65

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Rx of Uncomplicated CT Infection

- Standard Rx
 - Azithromycin 1 gm PO in a single dose
 - ~ or ~
 - Doxycycline 100 mg PO BID for 7 days
- Alternative Agents
 - Erythromycin 500 mg PO QID for 7 days
 - Ofloxacin 300 mg PO BID for 7 days
 - Levofloxacin 500 mg PO QD for 7 days



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Rx of CT Infection in Pregnancy

- Standard Rx

Azithromycin 1 gm PO as a single dose

~ or ~

Amoxicillin 500mg TID PO for 7 days

- Alternative Agents

Erythromycin base 500 mg PO QID for 7 days

Erythromycin base 250 mg PO QID for 14 days

Erythromycin ethylsuccinate 800 mg PO QID for 7 days

Erythromycin ethylsuccinate 400 mg PO QID for 14 days



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CT – Test-of-Cure vs Re-Screening

- Test-of-Cure *

- Pregnancy
- Therapeutic compliance is in question

- Re-screening *

- 3-4 months post-Rx – or when they next present for care within next 12 months
- Population statistics show that ~ 35% of persons Rx'd for CT will have infection again within 3-4 months
 - Thus re-screening might detect these re-infected persons

* If using NAAT – not before 3 weeks post-Rx

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Rx of Lymphogranuloma Venereum (LGV)

- Recommended regimen
 - Doxycycline 100 mg PO BID for 21 days
- Alternative regimen
 - Erythromycin base 500 mg PO QID for 21 days
 - ? Azithromycin 1 gm weekly x 3 doses

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GC/CT – and – HIV

- Increased risk of PID/acute salpingitis
- Increased risk of tubo-ovarian abscess
- PID presents with lower WBC count
- Immunosuppressed HIV-infected women with PID – inpatient Rx with optimal anaerobic coverage
- Severely immunocompromised patients are at risk for
 - GC proctitis
 - Rectal abscess
 - Sepsis

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Why Screen for Chlamydia?

- Screening can reduce the incidence of PID by more than 50%
- Most infections are asymptomatic
- Screening decreases the prevalence of infection in the population
- Screening reduces the transmission of disease

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CT – Screening Recommendations Non-pregnant Women

- Sexually active women age ≤ 25 years should be screened annually (HEDIS recommendations ≤ 24 yr)
- Women >25 years old should be screened if risk factors are present
- Repeat screening of women 3-4 months post-Rx for CT infection, especially adolescents
- Repeat screening of all women treated for CT when they next present for care

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Screening Recommendations Pregnant Women

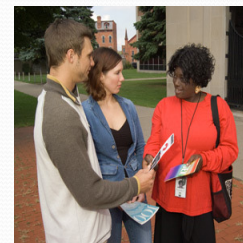
- Screen all pregnant women at the first prenatal visit
- Pregnant women aged < 25 years & those at increased risk for CT should be screened again in the 3rd trimester



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Partner Management

- Sex partners should be evaluated, tested, & treated if they had sexual contact with the patient during the 60 days preceding the onset of symptoms or diagnosis of GC or CT
- The most recent sex partner should be evaluated & treated even if the time of the last sexual contact was > 60 days before symptom onset or diagnosis
- **DoH Partner Services** – Disease Investigation Specialists (DIS) – can be extremely helpful
 - To find & bring in patients that have been lost to follow-up
 - To find partner(s) & get them into care for screening & Rx



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Expedited Partner Therapy for CT and GC

- Delivery of antibiotic therapy by index (original) patient – either by prescription or medication
- Male partners – inform female partners about still seeking care for assessment of possible PID
- Partners of patients with GC should receive CT co-Rx
- Not routinely recommended for MSM due to co- morbidities (other STDs, HIV)
- Recommended by CDC * since 2006 – what about your state?

* www.cdc.gov/std/treatment/EPTFinalReport2006.pdf

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EPT Studies

- Schillinger et al. (STD (2003), 30)
 - 20% reduction in CT re-infection among women ($P = 0.102$)
- Golden et al. (NEJM (2005), 352)
 - 73% reduction in GC re-infection among men & women ($P < 0.01$)
 - 17% reduction in CT re-infection ($P = 0.17$)
- Kissinger et al. (Clin Inf Dis (2005), 41)
 - 46% reduction in GC &/or CT infection among men with urethritis ($P < 0.001$)

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Patient Education and Counseling

- Nature of infection
 - Asymptomatic
 - Risks of complications
- Transmission issues
 - Increased risk of HIV acquisition
 - Need to have partner treated
 - Need to complete therapy before sexual activity
- Risk Reduction Strategies
 - Safer sex, mutual monogamy with an uninfected partner, abstinence
 - Develop individualized plans – does patient believe that s/he is at risk/vulnerable?
 - Moreover – does the patient see a need to change behaviors?
 - Need for repeat screening



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DoH Reporting – Which STDs?

- GC & CT are reportable STD in all states & jurisdictions (also syphilis)
- Report cases to the local or state STD program
- The Health Department uses reported info to assure Rx of the index case & contacting sexual partners for screening & treatment (for the health of the public)
 - Partner Services



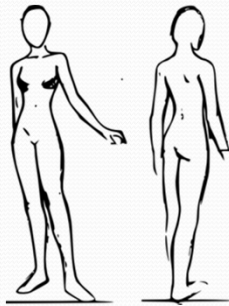
Department of Community Health



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Females and STDs

Syndromes



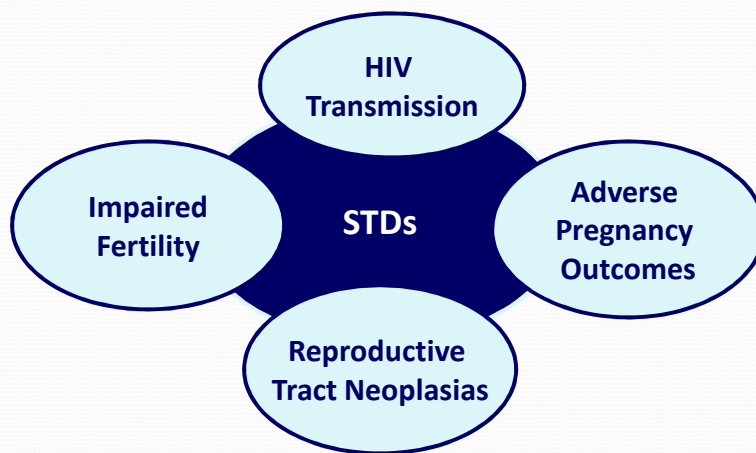
79

STDs & Women

- Disproportionately affect women
- More easily infected – biological bias for infection acquisition – compared to males (consider the anatomy)
- More likely to develop complications
- Perinatal & neonatal complications
- Teenagers biologically most vulnerable – due to “immature” cervix (i.e., presence of ectopy)

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CDC's Strategic Common Element in Maternal Child Health



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Female STD Syndromes

Cervicitis

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Cervicitis

- Common STD syndrome
 - S & S previously discussed
- Not as well-studied as male counterpart – urethritis
- **Significantly under-diagnosed**
 - **This is associated with potential complications & long-term sequelae**
- Can lead to PID/infertility

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Cervicitis – Etiology

- Known Causes
 - GC 5-10%
 - CT 30-40%
 - HSV
- Unknown Causes
 - 50-70%
 - **Mycoplasmas** (increasingly implicated – see STD Rx Guidelines for discussion & references), **Streptococci**, or simply inflammation

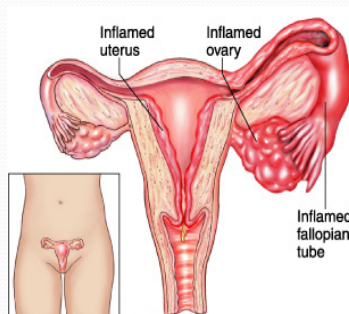
84

Cervicitis – Some Specifics re Chlamydia

- Women infected with CT more than once are at higher risk of developing PID
- Reinfection rates have a 3 times greater prevalence than from primary screening
- Recommendation to re-screen all women with CT (& GC) – as previously noted – 3-4 months after Rx
 - Based on population-based statistics, ~ 35% of those with CT &/or GC become re-infected within 3-4 months
- Re-screening is a critical tool for infertility prevention, particularly in young women

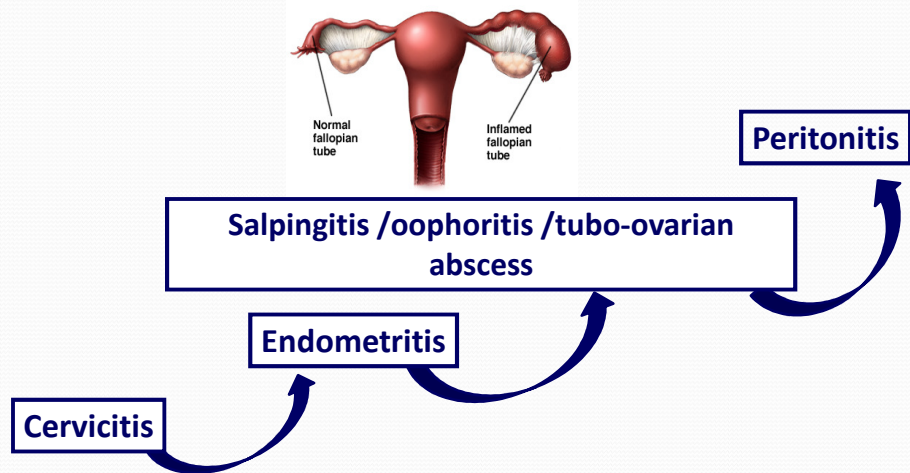
85

Female STD Syndromes Pelvic Inflammatory Disease



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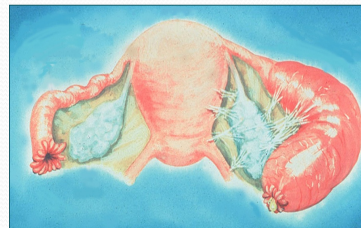
PID's Pathway of Ascendant Infection



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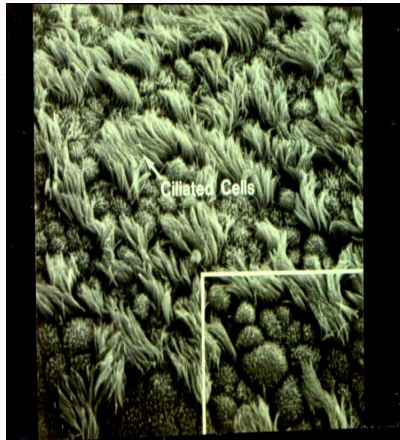
Pelvic Inflammatory Disease

- Acute First Episode
 - Considered to be due to STD etiology (GC or CT) unless recent surgery, abortion (spontaneous or therapeutic), or instrumentation
- Acute Recurrent
- Chronic

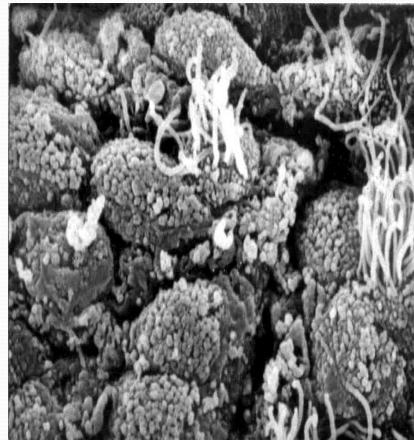


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Fallopian Tube Tissue – Normal and Infected

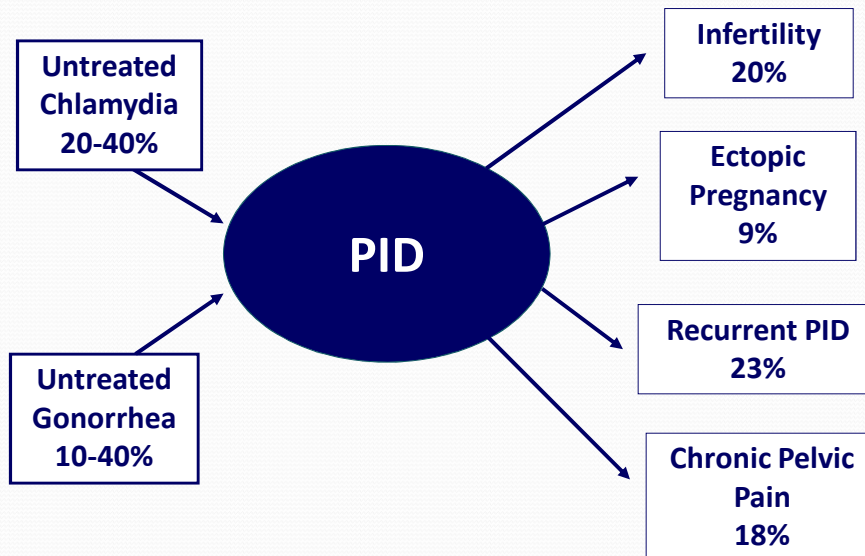


Normal Ciliated Cells
electron microscope

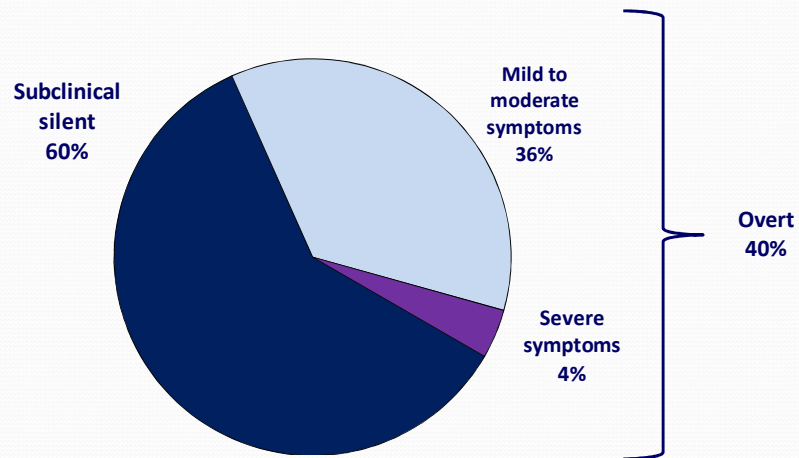


CT-infected
electron microscope

Sequelae of Untreated GC & CT in Women



PID – Classification



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PID – Etiology

STD Etiology

- *Neisseria gonorrhea*
- *Chlamydia trachomatis*
- *Mycoplasma hominis*
(not considered to be true STD)
- ? *Mycoplasma genitalium* ?

Opportunistic Contributors

- Group B Streptococcus
- Peptostreptococci
- *Escherichia coli*
- *Bacteroides* – several different Sp
- *Clostridium* Sp

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PID – Symptoms

- Abdominal pain – may be described or identified as “cramps” or “worse than usual” menstrual “cramps”
- May be abnormal vaginal discharge, including spotting
- Sometimes women c/o vague urinary symptoms (lower abdominal pain that changes before/during urination)
- Dyspareunia (most likely due to moving the cervix during intercourse)



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PID – Clinical Criteria

- Lower abdominal tenderness – during abdominal exam
- Tenderness – during bimanual exam
 - Uterus, tubes, &/or ovaries
- Possibly cervical motion tenderness (CMT)
- Possibly, mucopurulent cervical discharge
 - Elevated temperature (> 101 F), leukocytosis, elevated Sed Rate or C-reactive protein **are not necessary** for the clinical diagnosis – **nor is laboratory documentation of GC &/or Chlamydia**

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PID – Minimum Clinical Criteria

- Uterine &/or adnexal tenderness ~ **or** ~ cervical motion tenderness (CMT) – often called a Positive Chandelier Sign; CMT is
 - Patient has pain when the cervix is moved during bimanual examination
- Absence of other causes of pelvic inflammation, specifically
 - Ectopic or other abnormal pregnancy, appendicitis, ovarian cyst – **be sure to R/O pregnancy!**

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PID – Differential Diagnosis

- Mittelschmerz (ovulation related)
 - Ovarian Cyst
 - Acute Appendicitis
 - Ectopic Pregnancy
 - Ruptured, Bleeding, Torsion of Ovary
 - Pelvic Endometriosis
 - Inflammatory Bowel Disease (mesenteric lymphadenitis, regional ileitis, enteritis)
 - Urinary Tract Infection
 - Renal/Ureteral Stones
- These are 3 conditions are life-threatening – be sure to R/O (testing/imaging)

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Outpatient PID Treatment Regimens *

Ceftriaxone 250 mg IM in a single dose

~ or ~

Cefoxitin 2g IM in a single dose & Probenecid 1gm PO

~ plus ~

Doxycycline 100 mg PO BID for 14 days

~ with or without ~

Metronidazole 500 mg PO BID x 14 days

**** No need to remove IUD unless recently inserted ****

* Based on 2010 CDC Rx Guidelines

Outpatient PID Rx Regimen Alternatives

Azithromycin 2 gm PO x 1 dose

~ plus ~

Levofloxacin* 500 mg PO QD x 14 days

~ or ~

Levofloxacin 500* mg PO QD x 14 days

~ with or without ~

Metronidazole 500 mg PO BID x 14 days

➤ If risk of GC low or if rates of quinolone resistance in GC is low

* Based on 2010 CDC Rx Guidelines

PID – Pregnancy – This is Rare



- PID in pregnancy is rare because of local cervical immunity during pregnancy, but it does happen occasionally
 - Should be diagnosed with help of obstetrical provider (including probably ultra-sound, blood work, others)
- Pregnancy & PID – from to CDC Guidelines
 - “Because of the high risk for maternal morbidity and preterm delivery, pregnant women who have suspected PID should be hospitalized and treated with parenteral antibiotics.” (p 67)

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Males and STDs

Syndromes



Urethritis – Gonococcal

- Bacterial, curable
 - **Except now increasingly challenging to cure** (as noted)
- Common male STD syndrome
 - S & S previously discussed
- Responsible for about 10-15% of all urethritis, depending on location
 - Check the epidemiology of the geographical area in which you work

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Urethritis – Non-Gonococcal

- Very Common STD syndrome
 - Much more common than GC Urethritis
- NGU is typically bacterial – so curable
 - Though there is known viral cause as well as unknown causes – see next slide
- Incidence is stable – however, since it is not reportable – tracking this is through research & sentinel screening sites
 - **There is one exception – if CT test is positive – then the infection (not the syndrome) gets reported**



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NGU – Etiology

Incidence	Cause	Comments
~ 35%	<i>Chlamydia trachomatis</i>	Males < 35 years
~ 30%	<i>Ureaplasma urealyticum</i> (a <i>Mycoplasma</i>)	In all males
Unknown	<i>Mycoplasma genitalium</i>	Likely a major etiologic organism
Up to 10%	Herpes simplex Virus (HSV)	In some studies
< 5%	< 5% <i>Trichomonas</i> – Rare	Trich does not stay in urethra – so probably less (<2%)
Up to 10%	Inflammation from unknown causes	

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NGU – Signs

- Urethral erythema (seen here)
- Urethral discharge
 - Mucoid (seen here)
 - Purulent (next slide)
- Discharge is spontaneous or may only be seen with stripping
- Often no clinical signs



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NGU – Chlamydia Urethral Discharge – If has Any



Purulent
Discharge



Erythematous
Meatus

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GC Urethritis ~ and ~ NGU – Symptoms

- Urethral Sx can vary from mild to severe – NGU is typically milder while GC is more symptomatic
 - Burning – can be mild to severe (GC likely more so)
 - Irritation – sometimes described as “itching” or “tingling” (vague Sx are usually associated with NGU)
- GC Sx can appear within 48 hours of infection – NGU causes usually appear after several days to ~ 2 weeks
- Urethral discharge by patient history
- **NGU often has no Sx**
 - This is another reason to conduct routine screening

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NGU – Diagnostic Criteria

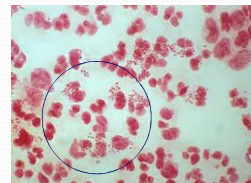
Must Meet criteria either 1 or 2 ~ & ~ 3

1. Laboratory evidence of ≥ 4 pmns /oil immersion field (1000X) in a urethral Gram Stain
2. Clinical sign of abnormal urethral discharge with erythema on examination
3. Exclusion of gonorrhea (i.e., Gram negative intracellular diplococci)

NGU



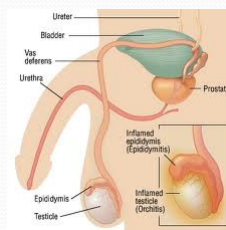
GC



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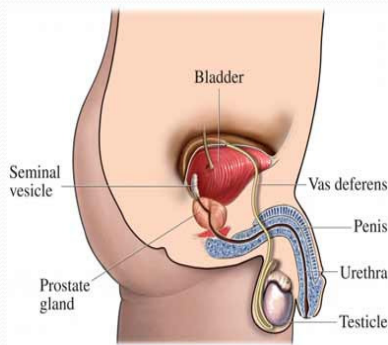
Male STD Syndromes

Epididymitis



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Epididymitis – Recall the Male Anatomy

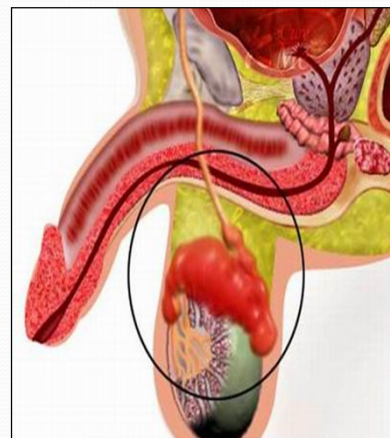


- Closed & protective
- Deeper structures are protected – unlike the “open system” of the female reproductive system
- Epididymitis is the male counterpart of PID – however – it is much less common due to the male anatomy as it is more “closed”

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Epididymitis

- Complication of GC, Ct, or any other NGU
- May result in infertility
- **Less common than PID – but a counterpart for the male** (as noted)
- For men < 35 years – etiology is STD unless proven otherwise



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Epididymitis – Signs and Symptoms

Signs

- Tenderness (can be exquisite) & swelling (subtle to severe) of anterior/posterior lobe of epididymis – in one or both epididymides
 - **With severe swelling – it can be difficult to distinguish scrotal contents**
- May have clinical/laboratory evidence of urethritis
- Need to rule out other causes, **especially testicular torsion**

Symptoms

- Pain in scrotum – mild to severe – usually described by patient as pain in testicle(s)
- Scrotal swelling
- Recent history of urethral burning/discharge
 - **Not always a symptom**

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Epididymitis



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Epididymitis – Diagnostic Criteria

Must meet criteria 1 ~ & ~ either 2 or 3

1. Clinical Sx of pain or Sign of tenderness of at least one epididymis (but could be bilateral)
2. Acute epididymitis in heterosexual men < 35 yr of age is usually
 - Frequently associated with urethritis (≥ 4 pmns/oil immersion field (1000X) on Gram-stained urethral smear
 - Absence of underlying genitourinary pathology
 - Absence of Gram-negative rods on Gram-stained urine

Continued...

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Epididymitis – Clinical Criteria (continued)

3. Acute epididymitis in heterosexual men > 35 years usually not associated with GC &/or CT
 - Infrequently associated with urethritis
 - Commonly associated with underlying genitourinary pathology (including prostate enlargement, “plumbing problems”)
 - Presence of Gram-negative rods on Gram-stained urine (epididymitis in men > 35 is often due to normal flora organisms)
 - Evaluation for underlying urinary tract disease/problem may be indicated

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Epididymitis – Treatment

- Etiology most likely STD

Ceftriaxone 250 mg IM

~ plus ~

Doxycycline 100 mg PO BID x 10 days

- Etiology most likely enteric or Ceftriaxone-allergic patients (& with negative GC test results)

Ofloxacin 300 BID x 10 days

~ or ~

Levofloxacin 500 mg QD x 10 days

