**Genital Tract Infections: Screening and Treatment**

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www.PolicarLectures.com

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**CDC 2006: Prevention Issues**

- Patients should be advised regarding which STDs they are being tested for… especially HPV on Pap
- Sexual history taking and risk reduction counseling should be routine
- Non-occupational PEP for HIV prevention
- Emergency contraception should be available
- Counseling to avoid douching
- Caution regarding vaginal inflammation from repetitive use of N-9 spermicides

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**Genital Herpes**

- 50 million in U.S. have genital HSV
- 90% of infections unrecognized
- 95% of people with genital HSV-2 have intermittent subclinical shedding
  - Highest in 1st year after infection (25% of days), then declines; 4-6% of days for many years
  - Similar frequency in persons with and without recognized symptoms
  - Accounts for most HSV-2 transmission
  - Uncommon if genital herpes due to HSV-1

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**HSV-2 Serology Tests for Screening**

<table>
<thead>
<tr>
<th>Screening Setting</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screen general population</td>
<td>Should not be offered</td>
</tr>
<tr>
<td>Universal screening in pregnancy</td>
<td>Should not be offered</td>
</tr>
<tr>
<td>Screening in HIV-positive patients</td>
<td>Should generally be offered</td>
</tr>
<tr>
<td>Screening in patients in partnerships with HSV-2 infected people</td>
<td>Should generally be offered</td>
</tr>
<tr>
<td>Screening in patients at risk for STD/HIV</td>
<td>Should be offered to select patients</td>
</tr>
</tbody>
</table>

(Guidelines for the Use of HSV-2 Type-Specific Serologies, CA DHIS 2003)

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**Rates of Transmission of HSV-2 to Susceptible Partners is Reduced with Once-Daily Suppressive Therapy**

RCT of 1,484 hetero couples
- Valacyclovir 500 mg of or placebo QD for 8 months
- Monthly HSV serology for susceptible partners

The valacyclovir group showed
- Decreased transmission
- Lower frequency of shedding
- Fewer copies of HSV-2 DNA when shedding occurred

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**Prevention of Genital Herpes**

- Incident HSV infection reduced by 1.7% over 1 year
  - 96.4% don’t seroconvert in absence of treatment
  - 1.9% seroconvert with treatment
  - Must treat 59 people to prevent one case/ year
- Indications may include
  - Discordant couples (reassess annually)
  - Infected persons with multiple partners
  - MSM
  - HIV-positive
- Counsel regarding condoms, disclosure, abstinence
**CDC 2006: Treatment of Genital Herpes**

<table>
<thead>
<tr>
<th></th>
<th>Acyclovir (generic)</th>
<th>Famciclovir (Famvir)</th>
<th>Valacyclovir (Valtrex)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary (7-10 days)</td>
<td>400 mg TID 200 mg 5 times/d</td>
<td>250 mg TID</td>
<td>1 gram BID</td>
</tr>
<tr>
<td>Recurrent</td>
<td>800 mg TID x2d 800 mg BID x5d 400 mg TID x5d</td>
<td>1 gm BID x1d 125 mg BID x5d</td>
<td>500mg BID x3d 1 gm QD x5d</td>
</tr>
<tr>
<td>Suppression</td>
<td>400 mg BID</td>
<td>250 mg BID</td>
<td>0.5-1.0 gm QD</td>
</tr>
<tr>
<td>Prophylaxis</td>
<td>400 mg BID</td>
<td>250 mg BID</td>
<td>500 mg QD</td>
</tr>
</tbody>
</table>

**Proven to be clinically useful for**
- Primary screening (HPV+Pap), if age 30 and over
- Triage of ASC-US Pap smears
- 12-month follow-up of LSIL in adolescents
- Post-colposcopy and post-treatment follow-up

**No proven benefit for**
- Triage of ASC-H, LSIL, HSIL, AGC Paps
- STD screening in the general population
- Evaluation of sex partners
- Evaluation of genital warts

**Trich Tips: Advice to Clinicians**
- Advise client that Trich could have been transmitted by any partner since sexual debut
- Evaluate NaCl suspensions pronto (< 5 minutes)
- Use fresh NaCl solutions (≤ 1 month old)
- Question the existence of “dead Trich” on micro
- Single dose MTZ still is the treatment of choice
- Tinidazole worth the investment if prior failure or adverse effects (but not urticaria or anaphylaxis)
- Women who are or who may be pregnant can be treated with MTZ

**Nitroimidazole cousin of metronidazole**
- Purported benefits
  - Fewer side effects: nausea, vomiting, dizziness
  - Shorter course of tx for parasitic infections
  - Marginally higher cure rate vs. oral MTZ
- Drawbacks
  - Not an alternative to MTZ if true allergy
  - Much more expensive than generic MTZ
- Use
  - Prior (or recent) oral MTZ failure
  - Prior intolerance of oral MTZ

**CDC 2006: Vaginal Trichomoniasis**

**Recommended regimen**
- Metronidazole 2 grams PO single dose
- Tinidazole (Tindamax) 2 grams x1

**Alternative regimen:**
- Metronidazole 500 mg PO BID x7d

**Cost per dose 2006 AWP**
- Generic MTZ 2 gm $ 1.25
- Flagyl 2 gm $ 15.07
- Tindamax 2 gm $ 12.00

**Drug class extrapolation, based upon suppressive regimen**

**CDC 2006: High Risk HPV Testing**

**Proven to be clinically useful for**
- Tindamax® (Tinidazole) 2 grams x1

**Recommended regimen**
- Metronidazole 2 grams PO single dose
- Tinidazole (Tindamax) 2 grams x1

**Alternative regimen:**
- Metronidazole 500 mg PO BID x7d

**Cost per dose 2006 AWP**
- Generic MTZ 2 gm $ 1.25
- Flagyl 2 gm $ 15.07
- Tindamax 2 gm $ 12.00
**Model of BV Pathogenesis**

- Antibiotics
  - loss of competitive inhibition
- Viral phage
  - Decreased Lactobacillus
  - Increased Anaerobes
- Adhesion to Sperm
  - Increased pH

**BV: Candidates for Treatment**

- Symptomatic non-pregnant women
- Pregnant women, if increased risk of PTB
- Women about to have pelvic surgery
  - Induced abortion
  - Hysterectomy
  - Cervical procedure (e.g., cone biopsy)
- (?) Non-pregnant asymptomatic women with no surgery planned...BV is associated with
  - Acquisition and transmission of HIV
  - PID, urinary tract infections

**CDC 2006: Bacterial Vaginosis**

**Recommended regimens**
- Metronidazole 500 mg PO BID x 7 days
- Metronidazole gel 0.75% 5g per vagina QD x 5 days
- Clindamycin cream 2% 5g per vagina QHS x 7 days

**Alternative regimens**
- Clindamycin 300 mg PO BID x 7 days
- Clindamycin ovules 100 mg per vagina QHS x 3 days

**Recommended regimens in pregnancy**
- Metronidazole 500 mg PO BID x 7 days
- Clindamycin 300 mg PO BID x 7 days

**Counseling Women with Recurrent BV**

- Consider suppression with MTZ vag gel BIW
- Abstain from vaginal sex during treatment
- Don’t douche...with anything!
- Use of condoms (esp in 1st month after treatment) may reduce recurrences
- Clean sex toys (or use condoms) between use by one woman then another
- Avoid vaginal insertion following anal insertion of fingers or penises

**Bacterial Vaginosis Tips**

- Diagnosis
  - “Clue cell positive” if ≥ 20% of epithelial cells are clue cells
  - Amine test with residue on speculum, not slide
  - Vaginal pH between 4.5-6.0
  - “Homogenized milk” vaginal discharge
  - Culture and Pap smear have no role in diagnosis
- Treatment is a trade-off of convenience and cost
  - Oral MTZ: lots of side effects, but cheap
  - Topicals: fewer side effects, but more expensive

**CDC Classification of VVC**

- Uncomplicated VVC (80-90%)
  - Sporadic or infrequent VVC, or AND
  - Mild-to-moderate VVC, or AND
  - Likely to be Candida albicans, or AND
  - Non-immunocompromised women
- Complicated VVC (10-20%)
  - Recurrent VVC, or
  - Severe VVC, or
  - Non-albicans candidiasis, or
  - Uncontrolled DM, immunosuppression, pregnancy
VC: SEVEN DAY Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miconazole</td>
<td>Monistat-7</td>
<td>2% cream, 100 mg sup</td>
</tr>
<tr>
<td>Terconazole</td>
<td>Terazol-7</td>
<td>0.4% cream</td>
</tr>
<tr>
<td>Clotrimazole</td>
<td>Gynelotrimin 7</td>
<td>1% cream, 100 mg tab</td>
</tr>
</tbody>
</table>

- Rx: 1 application at bedtime for 7 days

OTC drugs in italics

VC: THREE DAY Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Butoconazole</td>
<td>Femstat 3</td>
<td>2% cream</td>
</tr>
<tr>
<td>Miconazole</td>
<td>Monistat-3</td>
<td>200 mg supp</td>
</tr>
<tr>
<td>Terconazole</td>
<td>Terazol-3</td>
<td>80 mg supp, 2% cream</td>
</tr>
</tbody>
</table>

- Rx: 1 application at bedtime for 3 days
- Alternative:
  - Miconazole 2% cream
  - Clotrimazole 1% cream
  - Clotrimazole 100 mg tab 2 QHS x 3 days

OTC drugs in italics

VC: ONE DAY Therapy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Brand</th>
<th>Formulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clotrimazole</td>
<td>Mycelx G-500</td>
<td>500 mg suppository</td>
</tr>
<tr>
<td>Tioconazole</td>
<td>Vagistat-1</td>
<td>6.5% ointment</td>
</tr>
<tr>
<td>Miconazole</td>
<td>Monistat 1</td>
<td>1.2 gm suppository</td>
</tr>
<tr>
<td>Butoconazole</td>
<td>Gynazole-1</td>
<td>2% bioadh cream*</td>
</tr>
</tbody>
</table>

Rx: 1 app at bedtime (*anytime)

- Fluconazole | Diflucan 150 mg |

Rx: 1 tablet PO

CDC 2006: Uncomplicated VVC

- Non-pregnant
  - 3, 7 day topicals equal efficacy and price
  - Recommend: 3 day topical or fluconazole PO
- Mild or early case: any 1 or 3 day regimen
- If first course fails
  - Reconfirm microscopic diagnosis
  - Treat with alternate antifungal Rx
  - Candidal culture to speciate
- No role for nystatin, candididin

CDC 2006: Complicated VVC

Severe VVC
- Advanced findings: erythema, excoriation, fissures
- Treat for 7-14 days of topical therapy or fluconazole 150 mg PO repeat in 3 days

Compromised host
- Conventional antimycotic tx for 7-14 days
- Pregnancy
- Topical azoles for 7 days

Recurrence VV (RVVC)
- ≥ 4 episodes of symptomatic VVC per year
- Most women have no predisposing condition
  - Partners are rarely source of infection
- Confirm with candidal culture, since often due to non-albicans species
- Early treatment regimen: self-medication 3 days with onset of symptoms
**CDC 2006: Complicated VVC**

- **Recurrent VVC**
  - Treat for 7-14 days of topical therapy or fluconazole 150 mg PO q 72 h x 3 doses, then
  - Maintenance therapy x 6 months
    - Fluconazole 100-200 mg PO 1-2 per week
    - Itraconazole 100 mg/wk or 400 mg/month
    - Clotrimazole 500 mg suppos 1 per week
    - Boric acid 600 mg suppos QD x 14, then BIW
    - Gentian violet: Q week x2, Q month X 3-6 mo

**Vaginal Candidiasis Tips**

- 2/3 of women who believe that the have chronic or recurrent Candida don’t
  - Verify diagnosis with PCR, fungal culture
- Consider *Candida glabrata*
  - Different presentation, different treatments
- Oral or vaginal yoghurt doesn’t work because
  - Lactobacillus strains don’t adhere to vaginal cells
  - Predominant normal flora is *L. crispatus*, not *L. acidophilus* or *L. bulgaricus*

**ARS Question**

In the lab most commonly used by your practice, which Chlamydia test is used?

- Nucleic acid amplification test (PCR, LCR)
- DNA hybridization test (Genprobe PACE 2)
- Chlamydia culture
- Enzyme immunoassay (Chlamydiazyme)
- Don’t know

**Categories of STI Screening and Testing**

- **Routine screening**
  - Population based risk factors
- **Targeted screening**
  - Personal behavioral risk factors
- **Contact testing**
  - Persons with suspected or known contact (exposure) to another person with a STI

“**Routine” STI Screening**

- **Cervical Chlamydia** (in women)
  - Annually in sexually active women thru 25 yo
- **Cervical gonorrhea** (in women)
  - Annually in sexually active women thru 25 yo
  - Only if practice-site prevalence is at least 1%
- **Pregnant women**
  - Syphilis, HIV, Chlamydia (< 26 years old)
  - Hepatitis B (newborn treatment)
Are We Screening the Wrong Women for Ct?

- Many women in the target age range (25 and younger) are not being screened.
- Yet, in many systems, screening rates for women over age 25 are equal to women 25 and younger.

So what??

- Rates of chlamydia in women over age 25 are <1% and decline with age.
  - Chlamydia infects the columnar epithelium of the cervical ectropion; recedes with aging.
- As prevalence decreases, positive predictive value declines, making incorrect diagnoses more likely.

Targeted Screening: Risk Factors

**GC + Ct screening**
- History of GC, chlamydia, or PID in the past 2 years
- More than 1 sexual partner in the past year
- New sexual partner within 90 days
- Sexual partner who has other partners

**GC screening**
- African American women 26-30 years old, especially in urban areas

**Syphilis, HIV screening**
- Sexual history, partner behaviors, local prevalence

Asymptomatic Non-Pregnant Females

**GC Prevalence < 1%**
- Screen women <26 for Ct
- Repeat Sexual History Annually
- Patient Counseling, Repeat Sexual History and 26th Birthday
- Patient Counseling, Repeat Sexual/Medical History Annually
- Chlamydia Test Annually and 26th Birthday
- Syphilis, HIV screening
- GC + Ct screening

**GC Prevalence ≥ 1%**
- Screen annually for Sexual History
- Patient Counseling
- Repeat Sexual/Medical History Annually
- GC + Ct screening
- Syphilis, HIV screening

CDC, 2005

Female Chlamydia Rates, 2004

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>13-14</td>
<td>2.8%</td>
</tr>
<tr>
<td>15-19</td>
<td>1.79%</td>
</tr>
<tr>
<td>20-24</td>
<td>1.0%</td>
</tr>
<tr>
<td>25-29</td>
<td>0.3%</td>
</tr>
<tr>
<td>30-34</td>
<td>0.2%</td>
</tr>
<tr>
<td>35-39</td>
<td>0.15%</td>
</tr>
<tr>
<td>40-44</td>
<td>0.2%</td>
</tr>
<tr>
<td>45-49</td>
<td>0.2%</td>
</tr>
<tr>
<td>50-54</td>
<td>0.2%</td>
</tr>
<tr>
<td>55-59</td>
<td>0.2%</td>
</tr>
<tr>
<td>60-64</td>
<td>0.2%</td>
</tr>
<tr>
<td>65+</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

35-39 yo: 0.15%
**Anorectal and Oropharyngeal Sampling**

<table>
<thead>
<tr>
<th></th>
<th>Hetero female</th>
<th>Hetero male</th>
<th>MSM</th>
<th>WSW</th>
<th>Symptomatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>GC: oropharynx</td>
<td>NR</td>
<td>NR</td>
<td>Culture, NAAT*</td>
<td>NR</td>
<td>Culture, NAAT*</td>
</tr>
<tr>
<td>GC: anorectal</td>
<td>NR</td>
<td>NR</td>
<td>Culture, NAAT*</td>
<td>NR</td>
<td>Culture, NAAT*</td>
</tr>
<tr>
<td>Cht oropharynx</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>Culture, NAAT*</td>
</tr>
<tr>
<td>Cht: anorectal</td>
<td>NR</td>
<td>NR</td>
<td>Culture, NAAT*</td>
<td>NR</td>
<td>Culture, NAAT*</td>
</tr>
</tbody>
</table>

NR: no recommendation  
* If validated by lab

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**Contact Testing for STIs**

- Test if high risk sexual exposure, based on new or multiple sexual partners, for
  - Gonorrhea
  - Chlamydia
  - Syphilis
  - HIV
- No contact testing for
  - HSV (culture), HPV
  - HBV, HBC (strategy for HBV is vaccination)
- Maybe: HSV-2 serology

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**Testing for STI Co-Infection**

If positive for Test for
- Chlamydia GC, syphilis, HIV
- GC Chlamydia, syphilis, HIV
- Syphilis Chlamydia, GC, HIV
- Primary herpes Chlamydia, GC, syphilis, HIV
- Recurrent herpes (?)… may be long standing
- Trichomoniasis (?)… may be long standing
- Ext genital warts (?)… may be long standing
- BV, candida Not STIs, therefore don’t screen

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**Diagnostic Testing for GC and Ct**

**Women**
- Abnormal vaginal discharge
- Abnormal vaginal bleeding
- Dyspareunia, chronic pelvic pain, PID
- Mucopurulent cervicitis
- Cervical friability
- Unexplained infertility

**Men**
- Dysuria
- Urethral discharge
- Testicular pain

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**Screening and Testing Post-Treatment**

- Test of Cure
  - Long regimen antibiotics with high failure rate
  - *Not* after high efficacy, single dose treatment
- Re-testing: women treated for chlamydia or GC should be re-tested in **3 months**
  - High likelihood of repeat infection
  - Short time to repeat positive test
  - Re-testing identifies highest risk patients

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**Ct + GC Screening Recommendations**

- Nucleic acid amplification test (NAAT) is preferred
  - Preferred to perform test on urine sample
  - Sample endocervix only if pt having pelvic exam
- Second choice: nucleic acid probe
  - Less expensive than amplification tests
  - Less accurate
- Evidentiary exam: chlamydia cell culture
- Other tests considered suboptimal and outdated
  - If done, confirm positive screens
**Gonorrhea (GC) + Chlamydia (Ct) Indications for Treatment**

- Positive GC or Ct screening test
- Sexual partner with known GC or Ct
- Presumptive therapy of mucopurulent cervicitis or urethritis (treat both)
- Pelvic inflammatory disease (treat both)

**CDC 2006: LGT Chlamydia**

- **Preferred treatment**
  - Azithromycin 1 gm orally
    - Dispensed as sachet (powder) or capsules
    - First line treatment in pregnancy
  - Doxycycline 100 mg PO BID for 7 days
    - Avoid prolonged sun exposure (photosensitivity)
- **Alternative treatment**
  - Ofloxacin 300 mg PO BID for 7 days
  - Levofloxacin 500 mg PO QD for 7 days
  - Erythromycin base or EES QID for 7 days

**CDC 2006: GC Treatment Issues**

- Concern over increasing rates of QRNG
  - Rates among heterosexual males outside CA and HI still less than 1% in 2004
- Fluoroquinolones NOT recommended for
  - Acquisition in CA or HI; foreign acquisition
- Oral cephalosporin alternatives
  - ADD cefpodoxime 400 mg PO x 1
  - ADD cefuroxime 1 g PO x 1
- Co-treatment for Ct is recommended, unless negative NAAT

**CDC 2007: LGT Gonorrhea**

**Antibiotic** | **Trade name** | **Dose** | **Adv Eff** | **AWP**
--- | --- | --- | --- | ---
Ceftriaxone | 125 mg IM | + 2 (IM) | 12.98 |
Cefixime | 400 mg PO | + 1 | $6.76 |
Quinolones
- Ciprofloxacin | 500 mg PO | + 3 | 3.62 |
- Ofloxacin | 400 mg PO | + 3 | 4.34 |
- Levofloxacin | 250 mg PO | + 3 | 6.00 |
**Quinolones Co-treat Chlamydia, unless ruled out by NAAT**
- Not commercially available in US
- No longer recommended by CDC

**Update to CDC’s Sexually Transmitted Diseases Treatment Guidelines, 2006:** Fluoroquinolones No Longer Recommended for Treatment of Gonococcal Infections

- 2006 GISP findings of QRNG isolates (5% threshold)
  - Overall population: 13.3% (8.6% no CA, HI)
  - MSM: 38.3% (30.7% no CA, HI)
  - Heterosexual men: 6.7% (5.1% no CA, HI)
  - Philadelphia 26.6%; Miami 15.3%

**CDC 2006: LGT Gonorrhea Alternative Regimens**

- Ceftriaxone 125 mg IM + 2 (IM) 12.98
- Cefixime 400 mg PO + 1 $6.76
- Ciprofloxacin 500 mg PO + 3 3.62
- Ofloxacin 400 mg PO + 3 4.34
- Levofloxacin 250 mg PO + 3 6.00
- Spectinomycin 2 2 gms IM + 3
- Co-treatment for Chlamydia, unless ruled out by NAAT
- Not commercially available in US
- No longer recommended by CDC

**Antibiotic** | **Trade name** | **Dose** | **Adv Eff** | **AWP**
--- | --- | --- | --- | ---
Cefpodoxime | Vantin (b) | 400 mg PO | + 1 |
Cefuroxime | Ceftin (g) | 1 gm PO | + 1 |
Azithromycin | Zithromax (g) | 2 gms PO | + 2 |
Spectinomycin | Trobicin (b) | 2 gms IM | + 3 |
- Single dose IM cephalosporins
- Ceftriaxone 125 mg IM + 2
- Cefotaxime 500 mg IM + 2
- Cefoxitin 2 gm IM + 2

*Legend:*
- g: generic
- b: brand name
**CDC 2006: PID Treatment Principles**

- Better to **over-diagnose** and treat, rather than to under-diagnose
- Early, **aggressive** therapy helps to avoid hospitalization, infertility
- Treatment must address
  - *N. gonorrhoeae*
  - *Chlamydia trachomatis*
  - Anaerobic bacteria
  - (Concomitant) Bacterial vaginosis

**CDC 2006: Outpatient PID**

**Regimen A**
- Levofloxacin 500 mg QD for 14 days OR
- Ofloxacin 400 mg PO BID for 14 days

**Regimen B**
- Ceftriaxone 250 mg IM
  - then doxycycline 100 mg PO BID for 14 days OR
- Cefoxitin 2 grams IM plus probenecid 1 gram PO,
  - then doxycycline 100 mg PO BID for 14 days

*If BV is diagnosed or to improve anaerobe coverage*
- **Add:** Metronidazole 500 mg BID for 14 days

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**QRNG and Treatment of PID**

**Recommended Regimen A**
- Levofloxacin 500 mg orally once daily for 14 days*
- Or
- Ofloxacin 400 mg orally once daily for 14 days*
- With or without
- Metronidazole 500 mg orally twice a day for 14 days

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**CA STD Treatment Guidelines, 2007**

- Quinolones may be used for PID if the risk of GC is low, a NAAT test for GC is performed, and follow-up is likely
- If GC is documented, change to a medication regimen that does not include a quinolone or obtain a test of cure to ensure that the patient does not have a resistant GC infection

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**CDC 2006: Outpatient PID Treatment**

<table>
<thead>
<tr>
<th>Anaerobic coverage</th>
<th>Adverse effects</th>
<th>2006 AWP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefoxitin IM + Doxy + MTZ</td>
<td>Excellent</td>
<td>Poor</td>
</tr>
<tr>
<td>Ceftriaxone IM + Doxy + MTZ</td>
<td>Excellent</td>
<td>Poor</td>
</tr>
<tr>
<td>Ofloxacin + Metronidazole</td>
<td>Excellent</td>
<td>Poor</td>
</tr>
<tr>
<td>Levofloxacin + Metronidazole</td>
<td>Excellent</td>
<td>Poor</td>
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