Update in Sexually Transmitted Diseases

Peter Kerndt MD, MPH
Director,
Los Angeles County STD Program
## STD Morbidity
### California and United States 2002

<table>
<thead>
<tr>
<th>Condition</th>
<th>California reported cases</th>
<th>US reported cases</th>
<th>US estimated incidence (millions)</th>
<th>US estimated prevalence (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>109,619</td>
<td>754,858</td>
<td>3</td>
<td>NA</td>
</tr>
<tr>
<td>GC</td>
<td>24,282</td>
<td>318,796</td>
<td>0.65</td>
<td>NA</td>
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<tr>
<td>Syphilis</td>
<td>1029</td>
<td>6,240</td>
<td>0.07</td>
<td>NA</td>
</tr>
<tr>
<td>Congenital syphilis</td>
<td>33</td>
<td>349</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>HPV</td>
<td>NA</td>
<td>NA</td>
<td>5.5</td>
<td>20</td>
</tr>
<tr>
<td>HSV</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>45</td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>NA</td>
<td>NA</td>
<td>5</td>
<td>NA</td>
</tr>
<tr>
<td>AIDS</td>
<td>2,973</td>
<td>38,878</td>
<td>0.02</td>
<td>.56</td>
</tr>
<tr>
<td>HIV</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>852</td>
<td>6,660</td>
<td>0.077</td>
<td>.75</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>138,788</strong></td>
<td><strong>1,125,781</strong></td>
<td><strong>15.3</strong></td>
<td></td>
</tr>
</tbody>
</table>
Overview of Complications of Sexually Transmitted Diseases

STDs

- Low Birthweight*
- Upper Tract Infection
- Systemic Infection
- STDs
- Infertility
- Ectopic Pregnancy*
- HIV Infection*
- Cervical Cancer*

* Potentially Fatal
Chlamydia: Epidemiology

- Most common bacterial STD in California and the U.S.
- **AGE:** 70% of infections reported among women are between 15-25.
  - California prevalence of about 7% adolescents 15-19 and 4% among 20-24 year olds.
- **RACE/ETHNICITY:**
  - African Americans>Hispanics>Native Americans>Non-Hispanic Whites and Asian Pacific Islanders.
Genital Chlamydia in Women: Complications

- Untreated genital CT infection: 20-50%
  - Acute PID: 9%
  - Silent PID: 14-20%
  - Infertility: 20-50%

- Ectopic pregnancy: 14-20%
- Chronic pelvic pain: 18%
Chlamydial Cervicitis

- Mucopurulent endocervical discharge
- Edematous cervical ectopy
- Spontaneous or easily induced endocervical bleeding
Chlamydial Urethritis

- Incubation: 5-10 d
- Sx: dysuria, discharge
- Discharge typically thin, clear
- Urethral erythema

Often asymptomatic or very mild symptoms

Website, 2000
Chlamydia — Rates by state: United States and outlying areas, 2001

Note: The total rate of chlamydia for the United States and outlying areas (including Guam, Puerto Rico and Virgin Islands) was 275.5 per 100,000 population.
Chlamydia — Age- and sex-specific rates: United States, 2001

<table>
<thead>
<tr>
<th>Age</th>
<th>Men Rate (per 100,000 population)</th>
<th>Women Rate (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>139.8</td>
<td>2,536.1</td>
</tr>
<tr>
<td>15-19</td>
<td>301.9</td>
<td>2,447.0</td>
</tr>
<tr>
<td>20-24</td>
<td>1,023.1</td>
<td>3,000</td>
</tr>
<tr>
<td>25-29</td>
<td>824.6</td>
<td>2,447.0</td>
</tr>
<tr>
<td>30-34</td>
<td>1,191.6</td>
<td>2,536.1</td>
</tr>
<tr>
<td>35-39</td>
<td>1,191.6</td>
<td>2,536.1</td>
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<tr>
<td>40-44</td>
<td>51.4</td>
<td>119.1</td>
</tr>
<tr>
<td>45-54</td>
<td>18.1</td>
<td>5.1</td>
</tr>
<tr>
<td>55-64</td>
<td>2.9</td>
<td>436.3</td>
</tr>
<tr>
<td>65+</td>
<td>114.2</td>
<td>139.8</td>
</tr>
<tr>
<td>Total</td>
<td>604.9</td>
<td>1,200</td>
</tr>
</tbody>
</table>
Prevalence of Chlamydia Infections in 15-19 Year Old Adolescent Girls by Health Care Setting, California, 1999

Chlamydia Prevalence (% Positive)

Source: California Department of Health Services, STD Control Branch; Los Angeles Infertility Prevention Project; and San Francisco Infertility Prevention Project
Chlamydia Reported Rates by Year
Los Angeles County (LAC), 1998-2002

*Rates per 100,000 population

*Provisional data as of August 5, 2003.
Chlamydia Rates in Los Angeles County, by Gender, 1998-2002

Year | Male | Female
--- | --- | ---
1998 | 115.2 | 412.0
1999 | 132.1 | 489.3
2000 | 170.1 | 489.4
2001 | 184.3 | 526.3
2002 | 218.3 | 547.2
Chlamydia Screening Recommendations

• **Patients are often asymptomatic**
• Screen all sexually active females 25 years of age and under at the first visit and annually thereafter.
• “High-Risk” CT tests, men, and women over age 25.
• Every 3-6 months for HIV positive persons at higher risk
Recommended regimens:
- Azithromycin 1 g p.o. in a single dose (94.9%)
- Doxycycline 100 mg p.o. BID for 7 days (95.9%)

Alternative regimens:
- Ofloxacin 300 mg p.o. BID for 7 days
- Levofloxacin 500 mg p.o. QD for 7 days
- Erythromycin base* 500 mg p.o. QID for 7 days
- Erythromycin ethylsuccinate* 800 mg p.o. QID for 7 days

*Test of cure recommended 3 weeks after treatment with erythromycin because of lower efficacy
Chlamydia Treatment Principles

• DOT therapy optimal

• No presumptive treatment for GC, co-infection occurs in 10% of women in California

• CT re-infection rates 10-38%, a repeat CT test 3-4 months after screen for re-infection is now recommended as standard of care for women.

• Patients should be instructed to abstain from sexual intercourse for 7 days after single dose therapy or until completion of a 7-day regimen.
Management of Sexual Contacts

- All sexual partners within the past 60 days should be evaluated, tested, and treated.
- Physician is required to “endeavor to discover the source of infection, and “to make an effort, through the cooperation of the patient, to bring those cases in for examination and treatment.”
Patient-Delivered Partner Therapy

- **CA H&SC, section 120582:** Allows physicians to prescribe and nurse-practitioners, PAs, and certified nurse-midwives to dispense antibiotic therapy for the male and female sexual partners of male and female individuals infected with genital CT, even if they have not been able to perform an exam of the patient’s partners.
Gonorrhea (GC)

- Dysuria (painful urination)
- Discharge (urethra, cervix, vagina)
- Anorectal mucous
- Penile edema
- Pharyngitis
- Conjunctivitis
- Pelvic pain
- Asymptomatic
Gonococcal Urethritis
Gonoccocal Cervicitis
Untreated Gonorrhea

- Disseminated gonococcal infection
- Pelvic inflammatory disease
- Infertility/sterility
- Meningitis
- Endocarditis
- Perihepatitis
- Perinatal Transmission
  - Neonatorum ophthalmia

Note: The Healthy People 2010 (HP2010) objective for gonorrhea is 19.0 cases per 100,000 population.
Gonorrhea — Rates by state: United States and outlying areas, 2001

Note: The total rate of gonorrhea for the United States and outlying areas (including Guam, Puerto Rico and Virgin Islands) was 126.9 per 100,000 population. The Healthy People year 2010 objective is 19.0 per 100,000 population.

Men Rate (per 100,000 population)

<table>
<thead>
<tr>
<th>Age</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-14</td>
<td>51.8</td>
</tr>
<tr>
<td>15-19</td>
<td>703.2</td>
</tr>
<tr>
<td>20-24</td>
<td>563.6</td>
</tr>
<tr>
<td>25-29</td>
<td>328.4</td>
</tr>
<tr>
<td>30-34</td>
<td>203.9</td>
</tr>
<tr>
<td>35-39</td>
<td>134.3</td>
</tr>
<tr>
<td>40-44</td>
<td>90.5</td>
</tr>
<tr>
<td>45-54</td>
<td>46.8</td>
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<tr>
<td>55-64</td>
<td>17.2</td>
</tr>
<tr>
<td>65+</td>
<td>4.5</td>
</tr>
<tr>
<td>Total</td>
<td>128.6</td>
</tr>
</tbody>
</table>

Women Rate (per 100,000 population)

<table>
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<tr>
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<th>Rate</th>
</tr>
</thead>
<tbody>
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<td>4.5</td>
</tr>
<tr>
<td>Total</td>
<td>128.5</td>
</tr>
</tbody>
</table>
Gonorrhea Prevalence Monitoring, Percent Positive by Gender and Health Care Setting, California, 2001

Percent Positive

0 0.5 1.0 1.4 3.4 4.6 6.0 7.4

Managed Care Organization Family Planning Clinics Juvenile Hall Community Outreach STD Clinics

Female Male
Gonorrhea Reported Rates by Year
Los Angeles County (LAC), 1998-2002

*Provisional data as of August 5, 2003.
Gonorrhea Rates in Los Angeles County, by Gender, 1998-2002

Year
1998
1999
2000
2001
2002
Male
70.7
70.5
90.3
94.7
95.8
Female
61.0
61.9
65.3
75.1
72.8
Gonococcal Isolate Surveillance Project (GISP) — Percent of gonorrhea cases that occurred among MSM, 1988-2001
MSM Prevalence Monitoring Project — Median test positivity by clinic for gonorrhea and chlamydia among MSM attending STD clinics, by HIV status, 2001

Median positivity

- Urethral gonorrhea
- Rectal gonorrhea
- Pharyngeal gonorrhea
- Urethral chlamydia

HIV-positive
HIV-negative or unknown
Screening Females for GC/CT

- **C. trachomatis**
  - NAAT on endocervical swab or urine specimen
  - DNA probe, EIA, or DFA on endocervical swab specimen
  - Culture on endocervical swab specimen

- **N. gonorrhoeae**
  - Culture on endocervical swab specimen
    - If culture unavailable, perform NAAT or DNA probe on endocervical swab
  - NAAT on urine specimen
Screening Males for Urethral Infection

- **C. trachomatis**
  - NAAT on urethral or urine specimen
  - Non-NAAT or culture on urethral specimen

- **N. gonorrhoeae**
  - Culture on urethral swab specimen
  - NAAT or DNA probe on urethral specimen or NAAT on urine specimen
Tests to Screen Women or Men for Rectal or Pharyngeal Infection

- **C. trachomatis**
  - Culture using a *Ct*-MOMP-specific stain.
  - DFA using a *Ct*-MOMP-specific stain.

- **N. gonorrhoeae**
  - Culture with additional testing of presumptively positive (typical morphology, oxidase-positive, Gram negative diplococci) colonies.
Fluoroquinolone Resistant GC (QRNG)

- Widespread in parts of Asia, the Pacific, Hawaii. Many cases reported in CA.
- Culture with antibiotic sensitivities recommended.
- Avoid treatment with fluoroquinolones
Gonococcal Isolate Surveillance Project (GISP) —
Location of participating clinics and regional laboratories: United States, 2001
Gonococcal Isolate Surveillance Project (GISP) — Percent of *Neisseria gonorrhoeae* isolates with decreased susceptibility or resistance to ciprofloxacin, 1990–2000

Note: Resistant isolates have ciprofloxacin MICs $\geq 1$ µg/mL. Isolates with decreased susceptibility have ciprofloxacin MICs of 0.125 - 0.5 µg/mL.
Percent MSM among GISP* Isolates by CA Clinic, 1990-2001 Gonococcal Isolate Surveillance Project

Source: STD Control Branch, DCDC, CA DHS - Provisional 11/2001
Gonococcal Isolate Surveillance Project (GISP), Percent of Neisseria Gonorrhoeae Isolates with Decreased Susceptibility or Resistance to Ciprofloxacin, California Sites, 1991–2001

Note: Resistant isolates have ciprofloxacin Minimum Inhibitory Concentration (MIC) \( \geq 1 \mu g/mL \).
Isolates with decreased susceptibility have ciprofloxacin MIC 0.15 \( \geq 0.6 \mu g/mL \).
STD Clinic Sites: Long Beach, Orange, San Diego, San Francisco.
Source: California Department of Health Services, STD Control Branch and CDC Preliminary 2001 Data.
L.A. Gonococcal Isolate Surveillance Project (GISP)

RESISTANT ISOLATES

ISOLATES RECOVERED  CIPROFLOXACIN RESISTANT ISOLATES
N = 109  N = 12 (11%)

March 13 - July 31, 2003

LAGLC  (67.7%)
South Health Center  (33.3%)
L.A. GISP

TREATMENT OF CIPROFLOXACIN RESISTANT CASES (N = 12)

- Ceftriaxone: 75.0% (9 cases)
- Ofloxacin: 25.0% (3 cases)

March 13 - July 31, 2003
Treatment of Gonorrhea

- Dual therapy for chlamydia is recommended
- Cefixime 400mg PO X 1 dose OR
- Ceftriaxone 125mg IM x 1 dose PLUS
- Azithromycin 1 gm PO x 1 dose OR
- Doxycycline 100mg PO BID x 7d
Oral Alternatives to Cefixime for Treatment of Gonorrhea

- **Pharynx**
  - Azithromycin 2 grams orally in a single dose

- **Cervix, Urethra, Rectum**
  - Azithromycin 2 grams orally in a single dose
  - Cefpodoxime 400mg orally in a single dose
  - Cefuroxime axetil 1 gram orally in a single dose
Pelvic Inflammatory Disease (PID)

- Any infection of the female pelvic cavity
- Cervicitis
- Endometritis
- Salpingitis
- Oophoritis
- Peritonitis
- Abscess formation
Reproductive Anatomy & Spread of Infections
Causative Organisms

- Neisseria Gonorrhoea
- Chlamydia Trachomatis
- Gardnerella Vaginalis
- Streptococcus Agalactiae
- Peptostreptococcus Species
- Bacteroides Species
- Genital Mycoplasma
- Ureaplasma Species
Risk Factors

- IUD Placement
- Multiple Sex Partners
- Gonorrhea or Chlamydia Infections
- Bacterial Vaginosis
- Abortion
- D & C
PID Clinical Presentation

- Fever and chills
- Lower abdominal pain
- Occasional vaginal bleeding
- Local or generalized signs of peritoneal involvement depending on degree of spread of infection
Signs and Symptoms of PID

- Bilateral lower abdominal pain
- Vaginal discharge
- Dysuria
- Fever/chills
- Painful intercourse
- Nausea & vomiting
- Irregular bleeding
- Dysmenorrhea
Symptoms Requiring Hospitalization

- Severe pain in the lower abdomen
- Nausea & vomiting
- Signs of shock (low BP, syncope)
- Fever greater than 101
- Pregnancy
- Surgical emergency cannot be ruled out
Differential Diagnosis of PID

• Ectopic pregnancy
• Acute appendicitis
• Urinary Tract Infection
• Rupture of an Ovarian Cyst
• Septic Abortion
Empiric treatment should be given to women with U/A tenderness or CMT and those with a large number of WBCs on cervical smear

- **Oral/IM Therapy:** Ceftriaxone OR Cefoxitin with Probenicid plus Doxycycline
- **IV Therapy:** Cefotetan+Doxy OR Clindamycin+Gentamicin
Genital Herpes

- Lifelong infection
- HSV-2 seropositivity 20-25% in sexually active population
- Asymptomatic shedding is common, thus many remain undiagnosed
- HSV-1 & HSV-2 may cause genital ulcers
Genital herpes simplex virus type 2 - Percent seroprevalence according to age in NHANES* II (1976-1980) and NHANES III (1988-1994)

Note: Bars indicate 95% confidence intervals.

*National Health and Nutrition Examination Survey
Epidemiology: HSV-2

Review of prevalence in selected populations

- STD clinic attendees (male) 32%
- STD clinic attendees (female) 52%
- Primary care patients, Seattle 23%
- University students, NC .04-4%
- Women aged 18-29 in N.CA 34%
- MSM in San Francisco 27%
- HIV+ MSM in Baltimore 80%

HSV-2 prevalence by sexual partners, United States, NHANES III, 1988-1994

Fleming D et al, NEJM, 1997
Risk Factors for HSV-2 Seropositivity, Gottlieb et al, JID 2002

- 4,128 patients attending STD clinics
- 40.8% seroprevalence
- Independent predictors included:
  - Female sex
  - Black race
  - Older age
  - Less education
  - More lifetime sexual partners
  - Prior diagnosis of syphilis or GC
  - Lack of HSV-1 antibody
Risk of HIV Infection in HSV-2 Seropositive Persons, Wald and Link JID, 2002

- Meta-analysis, 31 studies
- Documented HSV-2 infection prior to HIV, risk estimate = 2.1 (1.4-3.2).
  - Attributable risk percentage = 52%
  - Population attributable risk = 19%-47%
    (varying according to population seroprevalence of SHV-2)
HSV-2 Infection as a Risk Factor for HIV acquisition in MSM, Renzi et al, JID 2003

- Nested case control of 116 HIV seroconverters, 342 controls
- All with HIV infected partner and unprotected anal sex.
- Risk for HIV acquisitions
  - Prior HSV-2 infection OR 1.8 (1.1-2.9)
  - Reporting >12 partners OR 2.9 (1.4-6.3)
  - Reporting fewer herpes outbreaks in the past year OR 0.3 (01.-0.8)
Symptomatology

- Primary disease notable for systemic symptoms of fever, headache, malaise, myalgias
- Painful vesicular lesions in genital regions
- Pain, itching, dysuria, urethral or vaginal d/c
- Inguinal lymphadenopathy
- Pharyngitis with HSV-1 & HSV-2
- Proctitis, cervicitis
Genital Herpes
Spectrum of Presentations

Unrecognized Symptoms 60%
Recognized Symptoms 20%
Asymptomatic 20%
Penile Herpes
Herpes Lesions: Buttocks
Diagnosis of Herpes

• Virologic tests
  – Cell culture from swab of lesions
  – HSV antigen tests
  – PCR, sensitive but not routinely available

• Serologic tests
  – Type specific testing for glycoprotein G
    -Sensitivity 80-98%, specificity 96%
## Performance Profiles of Type Specific Serology Tests

<table>
<thead>
<tr>
<th>Type of test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Time to conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>POCKit HSV-2 (Discontinued)</td>
<td>93-100%</td>
<td>94-97%</td>
<td>Two weeks</td>
</tr>
<tr>
<td>HerpesSelect2 ELISA IgG</td>
<td>96-100%</td>
<td>97-100%</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>HerpesSelect1 &amp; 2 Immunoblot</td>
<td>97-100%</td>
<td>98%</td>
<td>unknown</td>
</tr>
</tbody>
</table>

Wald, 2002
Herpes Treatment

First Clinical Episode

- Acyclovir 400mg TID OR 200mg 5X/day for 7-10 days OR
- Famciclovir 250mg TID for 7-10 days OR
- Valacyclovir 1 gram BID for 7-10 days
Herpes Treatment for Recurrence

**Episodic Therapy for Recurrence**
(Begin within one day of lesion appearance)

- **Acyclovir** 400mg TID x 5d OR 800mg BID x 5d OR
- **Famciclovir** 125mg BID x 5d OR
- **Valacyclovir** 500mg BID x 3-5d OR 1.0 gram QD x 5d.
Herpes Suppressive Treatment

- Reduces recurrences by 70-90%
- Asymptomatic viral shedding continues

- Acyclovir 400mg BID OR
- Famciclovir 250mg BID OR
- Valacyclovir 500mg po QD or 1.0 gram QD

- Genital secretions of 27 HSV-2 positive women
- Genital shedding detected on 28% of days using HSV-PCR
- Shedding is reduced by 80% with daily suppression using acyclovir
Viral Shedding May Occur in the Absence of Lesions

Patterns in Women

| Subject 1: HSV-2 seropositive | Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
|-------------------------------|-----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Cervix                        |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Vulva                         |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Perianal                      |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lesion(s)                     |     | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

| Subject 2: HSV-2 seropositive | Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
|-------------------------------|-----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Cervix                        |     | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Vulva                         |     | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Perianal                      |     | + |   |   | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lesion(s)                     |     |   |   | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

| Subject 3: HSV-1 seropositive | Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
|-------------------------------|-----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Cervix                        |     | + | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Vulva                         |     | + | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Perianal                      |     | + | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lesion(s)                     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

| Subject 4: HSV-2 seropositive | Day | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
|-------------------------------|-----|---|---|---|---|---|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| Cervix                        |     | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Vulva                         |     | + | + | + | + |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Perianal                      |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| Lesion(s)                     |     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |

GSK studies: 2 phase III trials

- **Study 1**: Efficacy trial, double-blinded, randomized, placebo-controlled study on men/women who are seronegative for HSV-1 and -2.

- **Study 2**: Efficacy trial, double-blinded, randomized, placebo-controlled study on men/women of any HSV serologic status.

  Stanberry et al NEJM 2002
Vaccine Efficacy

• Study 1 and Study 2: Overall, both studies showed no significant efficacy
  – Study 1: 38%, p = 0.14
  – Study 2: 18%, p > 0.05

• Efficacy by gender:
  – Study 1: Female 73%, p = 0.01 (double seronegative)
    Male - 11%
  – Study 2: Female 42%, p = 0.19 (HSV-2 negative)
    Male - 10%
Sub-group analysis of Study 2

- Double seronegative female (18-30 years old)
  - Efficacy 74%, p = 0.02

- Attack rate of genital HSV-2
  - For females with HSV-1 positive and HSV-2 negative at baseline versus double seronegative.
    - 1.2% versus 11.9 %, p < 0.001

Note: The Healthy People 2010 (HP2010) objective for primary and secondary syphilis is 0.2 case per 100,000 population.
Primary and secondary syphilis — Rates by state: United States and outlying areas, 2001

Note: The total rate of primary and secondary syphilis for the United States and outlying areas (including Guam, Puerto Rico and Virgin Islands) was 2.2 per 100,000 population. The Healthy People year 2010 objective is 0.2 per 100,000 population.
Primary and secondary syphilis — Counties with rates above and counties with rates below the Healthy People year 2010 objective: United States, 2001

Rate per 100,000 Population

<=0.2  (n=2,533)

>0.2    (n=606)
Primary & Secondary Syphilis, Rates by Gender, California, 1980–2001

Source: California Department of Health Services, STD Control Branch
Primary & Secondary Syphilis, Rates by Gender and Age Group, California, 2002

Source: California Department of Health Services, STD Control Branch
Number of MSM P&S Syphilis Cases by Region and Year

- Northern Region
- Central Region
- Southern Region
- Bay Area Region
- San Francisco
- Los Angeles

1999 2000 2001 2002

3/03 Provisional Data - CA DHS STD Control Branch
Primary & Secondary Syphilis Cases by Gender, California, 1996–2002

P&S Syphilis Rates 1940-2002, California

02/2003 Provisional Data - CA DHS STD Control Branch
Monthly P&S Syphilis Among MSM, California, 1/1999-1/2003

Cases

Jan-99 | Jul-99 | Jan-00 | Jul-00 | Jan-01 | Jul-01 | Jan-02 | Jul-02 | 3-Jan

11/2002 Provisional Data - CA DHS STD Control Branch
Epidemiology of Syphilis in Los Angeles County

Figure 1: Early Syphilis by Sexual Orientation* and Month of Diagnosis, January 1, 2001 Through April 30, 2003 (N = 1250)

- MSM & MSM/W (n=939)
- MSW (n=174)
- All Female (n=137)

Month of Diagnosis:

- JAN01, APR01, JUL01, OCT01, JAN02, APR02, JUL02, OCT02, JAN03, APR03
Early Syphilis Cases By Age & Sexual Orientation, Los Angeles County, 2002

Source: Case Watch, 2002
MSM Early Syphilis Cases by Race/Ethnicity 2002

- White: 48%
- Latino: 36%
- Black: 10%
- API: 3%
- Other/Unknown: 2%
HIV Serostatus of LA County
MSM Early Syphilis Cases
2002 (Provisional), n=520

- HIV+: 59%
- HIV-: 28%
- Unknown: 13%
Syphilis

- Systemic disease caused by Treponema pallidum

- Divided into 4 stages: Primary, secondary, latent, tertiary
Primary/Secondary Syphilis

• **Primary**: Characterized one or more painless chancre or ulcers at the site of infection developing 1-3 weeks after exposure

• **Secondary**: Characterized by skin rash, mucocutaneous lesions, lymphadenopathy, occurring 1-3 months after exposure
Primary Syphilis Chancres
Primary Chancre on Glans
Vaginal Chancre
Labial Chancre “Kissing”
Anal Chancre
Secondary Skin Lesions
Disseminated Syphilitic Rash
Condyloma Lata
Latent Syphilis

- Asymptomatic
- **Early latent** if infection was acquired within the preceding year.
- Late latent (or “unknown latency”) if infection acquired more than one year ago or at an unknown time.
Tertiary Syphilis

- Cardiac abnormalities
- Ophthalmic abnormalities
- Gummatous lesions
- Auditory abnormalities
Non-treponemal Tests (Screen)

RPR and VDRL
- Fourfold change in titer (ie 1:4 to 1:16) indicates a clinical difference or treatment response
- Cannot compare RPR and VDRL
- Can remain positive after treatment
- False positives occur due to other clinical conditions
Treponemal Testing

FTA-ABS and TP-PA

• Required confirmatory test
• Generally remain positive for life (15-25% revert to seronegative)
• Cannot be used to gauge clinical response
Treatment of Primary, Secondary and Early Latent

**Benzathine penicillin G:**

**2.4 million units IM x 1 dose**

- **Alternatives:**
  - Doxycycline 100mg PO BID x 2 weeks OR
  - Tetracycline 500 mg PO QID x 2 weeks OR
  - Ceftriaxone 1 gm IM/IV QD x 8-10 days OR
  - Azithromycin 2 grams PO x 1 dose
Treatment of Late Latent and Unknown Duration

Benzathine Penicillin G:
- 2.4 million units IM x 3 doses spaced one week apart (Total 7.2 million units)
- Alternatives:
  - Doxycycline 100mg PO BID x 4 weeks OR
  - Tetracycline 500mg PO QID x 4 weeks
Jarish Herxheimer Reaction

• Acute febrile reaction occurring after treatment with PCN

• May occur at any stage
  – Most common during early syphilis

• May cause exacerbation of primary & secondary symptoms
Penicillin Allergy

- Important in relation to treatment of pregnant women or HIV infection
- True penicillin allergy is not common
- Allergy skin testing/Desensitization is done only at
  - LAC+USC Medical Center

***Desensitization is not permanent***
Neurosyphilis

• Can occur at any stage
• Meningitis type symptoms common with cranial nerve palsies
• Positive CSF VDRL is diagnostic if non-bloody tap
• CSF leukocyte count is elevated ≥5 WBCs/mm
• Consider FTA-ABS on CSF (high sensitivity)
Indications for Lumbar Puncture

- Any patient with reactive syphilis serology and neurologic symptoms (including visual)
- Late latent (>1 year duration) or syphilis of unknown duration in a patient with HIV
- Treatment failure in non-neurologic syphilis
- Active tertiary syphilis
Clinical and Serologic Indicators Associated with Increased Risk of Neurosyphilis
Marra et al, ISSTDR, 2003

• 326 subjects with syphilis underwent LP
• NS defined as +VDRL and/or WBC ct >20
• 75% male
• 66% late latent
• 72% HIV infected
<table>
<thead>
<tr>
<th>Variable</th>
<th>OR(95%CI)</th>
<th>P value</th>
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<tbody>
<tr>
<td>RPR ≥1:32</td>
<td>10.8 (2.7-43.8)</td>
<td>&lt;0.001</td>
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<td>HIV infected</td>
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<tr>
<td>CD4 &lt;350</td>
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<tr>
<td>RPR ≥ 1:32</td>
<td>6.0 (2.4-14.7)</td>
<td>&lt;0.001</td>
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Predictors of Neurosyphilis
Marra et al, cont
Treatment of Neurosyphilis

- Aqueous crystalline penicillin G 18-24 million units per day administered as 3-4 million units IV every 4 hours OR
- Continuous infusion for 10-14 days
Syphilis and HIV

- Confusing clinical symptomatology
- Genital ulcers facilitate transmission
- Possibly more rapid progression through the stages of syphilis
- Treatment & lab interpretation is the same
- Neurosyphilis may be more common with co-infection of syphilis & HIV
Changes in log10 Viral Load Before-During and During-After

Buchacz et al, HIV Prevention Conf 2003
Changes in Log10 viral load by syphilis stage:

- B-D S1
- B-D S2
- D-A S1
- D-A S2

Category

Before-During and During-After
### Changes in CD4 cell counts by stage

<table>
<thead>
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<th>Category</th>
<th>No.</th>
<th>Mean change</th>
<th>Median change</th>
<th>P value</th>
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<tr>
<td>Overall</td>
<td>31</td>
<td>-61</td>
<td>-16</td>
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<tr>
<td>Primary</td>
<td>12</td>
<td>-36</td>
<td>-12</td>
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<td>Secondary</td>
<td>19</td>
<td>-78</td>
<td>-144</td>
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<tr>
<td><strong>D - A</strong></td>
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<td></td>
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<tr>
<td>Overall</td>
<td>31</td>
<td>+33</td>
<td>+30</td>
<td>0.12</td>
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<tr>
<td>Primary</td>
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<td>+34</td>
<td>0.64</td>
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<tr>
<td>Secondary</td>
<td>20</td>
<td>+38</td>
<td>+30</td>
<td>0.12</td>
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</tbody>
</table>
NGU Causative Organisms

- Chlamydia trachomatis
- Ureaplasma urealyticum
- Mycoplasma genitalium
- Trichomonas vaginalis
- Herpes Simplex
- Adenovirus
- Hemophillus vaginalis
Transmission of NGU

- **Sexual**: via mucous membrane contact (oral, anal, vaginal)
- **Non-sexual**: via UTI, prostatitis, urethral stricture, phimosa, catherization
Symptoms

- Urethral discharge
- Stained underwear
- Dysuria
- Urethral pruritis
- Rectal pruritis
- Asymptomatic
Diagnosis and Treatment of NGU

- Visible urethral discharge
- Negative GC culture
- Presence of PMNs on gram stain of urethral discharge
- Azithromycin 1 gram PO x 1 dose \textbf{OR}
- Doxycycline 100mg PO BID x 7 d
Reportable STDs

- Syphilis (within 24 hours)
- Chlamydia (within 72 hours)
- Gonorrhea (within 72 hours)
- Pelvic Inflammatory Disease (PID)
- Non-gonococcal Urethritis (NGU)
- Chancroid (*H. ducreyi*)
- (Acute Hepatitis A, B, C)