Expedited Partner Therapy (EPT) for Gonorrhea & Chlamydial Infection

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Public Health – Seattle & King County
Overview

- Background on development of EPT
- Overview of data from randomized trials
- Barriers to EPT
- Community-level scale-up
and the Healthy People 2010 target

Note: The Healthy People 2010 target for gonorrhea is 19.0 cases per 100,000 population.
Note: As of January 2000, all 50 states and the District of Columbia had regulations requiring the reporting of chlamydia cases.
Chlamydia in Minnesota
Rate per 100,000 by Year of Diagnosis, 1992-2007
Figure 35. Nonspecific urethritis — Initial visits to physicians’ offices by men: United States, 1966–2000
Adjusted chlamydia prevalence in Infertility Prevention Project (IPP) clinics & gonorrhea incidence, 1988-2005

Adjusted chlamydia prevalence
Gonorrhea incidence

R²=0.95
Chlamydia — Positivity Rates by Age and Gender
MIPPM Clinics, 2002-2007

† The Minnesota Infertility Prevention Project (MIPP) is a project funded by the CDC to provide STD testing and treatment to uninsured men and women ages 15-24. Participating clinics include STD, family planning, adolescent, and community clinics.
Pelvic inflammatory disease — Hospitalizations of women 15 to 44 years of age: United States, 1980–2003
Pelvic inflammatory disease — Initial visits to physicians’ offices by women 15 to 44 years of age: United States, 1980–2004

Visits (in thousands)

Note: The relative standard error for these estimates ranges from 19% to 30%.

SOURCE: National Disease and Therapeutic Index (IMS Health)
Ectopic pregnancy — Hospitalizations of women 15 to 44 years of age: United States, 1980–2003
Racial Disparities in a Probability Sample of American Adolescents

Risk Ratio

- Chlamydia
  - 1.0
  - 5.5
  - 1.8
  - 1.3
  - 5.3

- Gonorrhea
  - 1.0
  - 14.6
  - 1.0
Gonorrhea Rates by Race/Ethnicity
Minnesota, 1997-2007

* Persons of Hispanic ethnicity can be of any race.
Gonorrhea & Chlamydia in the U.S. Circa 2008

- Gonorrhea rates are very low relative to the 1970-80s
- Chlamydia probably dropped with the introduction of screening
- Major morbidity from gonorrhea and chlamydia is way down
- Burden of disease is now probably roughly stable
- Dramatic racial disparities persist
- Additional progress will require new approaches
Strategies to Improve the Control of Bacterial STD

• Primary prevention – behavior change
• Primary & secondary prevention - Case-finding & treatment
  • Increase screening
  • Rescreening – retest those with an STD at 3 months
  • Improve partner treatment
Partner Notification

- Process of notifying the sex partners of persons with an STD and ensuring their treatment
- Public health authorities developed partner notification programs in the 1940s for syphilis
  - Public health advisors interview people with STD and notify their partners
- Growth in the 1960s and 70s and assumed some responsibility for gonorrhea
- Contraction in the 1980s – tentative response to HIV, no response to chlamydia
PN: Data from mathematical models

Source: Am J Epi 2001;153:90
Percentage of Cases of STD/HIV Interviewed for PN in High STD/HIV Morbidity Areas of U.S., 1999-01 & 2006

Could We Provide DIS Services To Everyone with a Reportable STD?

- ~1.5 million cases of HIV, syphilis, gonorrhea, and chlamydia reported annually in U.S.
- ~2800 Disease Intervention Specialists (DIS) to provide services to 75% of cases
- ~$200 million annually for DIS
- CDC STD budget = $108 million in 2007
Chlamydia partner notification practices among private sector providers in King County (n=150)

<table>
<thead>
<tr>
<th>Percent</th>
<th>Told patient to notify partners</th>
<th>Knows all partners treated</th>
<th>Gave patient medication for partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>90</td>
<td></td>
<td>17</td>
<td>4</td>
</tr>
</tbody>
</table>

# Outcomes of partner notification for gonorrhea and chlamydial infection by patient referral

<table>
<thead>
<tr>
<th>City (yr)</th>
<th>Number</th>
<th>STD</th>
<th>% partners evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorado 1977</td>
<td>93</td>
<td>GC</td>
<td>51%</td>
</tr>
<tr>
<td>Colorado 1985</td>
<td>3368</td>
<td>GC</td>
<td>62%</td>
</tr>
<tr>
<td>Canada 1992</td>
<td>37</td>
<td>CT</td>
<td>68%</td>
</tr>
<tr>
<td>London 1994</td>
<td>254</td>
<td>CT</td>
<td>53%</td>
</tr>
<tr>
<td>Amsterdam 1997</td>
<td>440</td>
<td>GC/CT</td>
<td>40%</td>
</tr>
<tr>
<td>Seattle 2001</td>
<td>698</td>
<td>GC/CT</td>
<td>51%</td>
</tr>
<tr>
<td>Indianapolis 2002</td>
<td>241</td>
<td>GC/CT/NGU/TV</td>
<td>65%</td>
</tr>
<tr>
<td>France 2002</td>
<td>145</td>
<td>Any STD</td>
<td>49%</td>
</tr>
</tbody>
</table>
Expedited Partner Therapy (EPT)

- Global term for process of treating partners without their mandatory prior examination
- Patient delivered partner therapy (PDPT) – index patient gives meds to partners
  - Most common form of EPT
Proportion of women “reinfected” with *Chlamydia trachomatis* based on partner notification practices: Swedish observational data

Proportion of patients with chlamydial infection to whom physicians give medications for their sex partners

Source: Sex Trans Dis 2005;32:101

N=2,538 CT  N=1,873 GC
### 3 RCTs of Expedited Partner Therapy (EPT)

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-city CT in ♀¹</td>
<td>1787 Women screened CT+ – mostly FP clinics</td>
<td>Patient-delivered partner therapy (PDPT)</td>
<td>- Partner treated*</td>
<td>90% 1 month</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Infection at 1&amp; 4 months</td>
<td>55% 3-4 months</td>
</tr>
<tr>
<td>Seattle CT/GC²</td>
<td>Population-based</td>
<td>All offered assistance 1) PDPT 2) Partners contacted by hlth. dept. offered direct Rx</td>
<td>- Partner treated*</td>
<td>68% at 10-18 weeks</td>
</tr>
<tr>
<td></td>
<td>2751 Men &amp; Women</td>
<td></td>
<td>- Infection at 3-4 months</td>
<td></td>
</tr>
<tr>
<td>New Orleans urethritis³</td>
<td>977 STD clinic patients</td>
<td>2 Interventions 1) Informational booklet 2) PDPT</td>
<td>- Partner treated*</td>
<td>85% Interview</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Infection at 1-2 months</td>
<td>30% specimen</td>
</tr>
<tr>
<td>Scotland CT</td>
<td>303 Women in STD, FP and Abortion clinics</td>
<td>2 Interventions 1) PDPT 2) Mailed specimen</td>
<td>-Partner treated</td>
<td>65%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>- Infection w/in 12 months</td>
<td></td>
</tr>
</tbody>
</table>

* Partner treatment per participant report in all studies except Scotland

Partner treatment per index patient report

- Talked to partner about STD: 80%
- Partner "very likely" treated: 60%
- All partners treated: 60%
- Sex untreated partner: 10%

Source: NEJM 2005;352:676
Infection during follow-up among 1860 persons completing the randomized trial

Source: NEJM 2005;352:676
Impact of PDPT on Index Patient GC/CT Reinfection in 4 Randomized Controlled Trials
## Impact of PDPT on Index Patient Report that Partner was Treated in 4 Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Study</th>
<th>PDPT</th>
<th>Control</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-city CT in ♀</td>
<td>86%</td>
<td>57%</td>
<td>0.001</td>
</tr>
<tr>
<td>Seattle CT/GC</td>
<td>64%</td>
<td>52%</td>
<td>0.001</td>
</tr>
<tr>
<td>New Orleans urethritis</td>
<td>56%</td>
<td>34%</td>
<td>0.001</td>
</tr>
<tr>
<td>Scottish CT in ♀*</td>
<td>94%</td>
<td>78%</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* Outcome is all partners contacted, not treated
Subgroup Analysis: Reinfection Partner Study

Relative risks associated with receipt of standard care 1-2-1.8

Sources: Golden et al NEJM 1992;352:676² (unpublished data)
Subgroup Analysis: Percentage of Partners Treated

Relative risks associated with receipt of EPT 1-2-1.3

Sources: Golden et al NEJM 1992;352:676^2 (unpublished data)
<table>
<thead>
<tr>
<th>CDC &amp; Professional Activities Related to EPT</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC Dear Colleague Letter</td>
<td>5/05</td>
</tr>
<tr>
<td>Expedited Partner Therapy Review &amp; Guidance Document</td>
<td>2/06</td>
</tr>
<tr>
<td>American Medical Assoc. Statement on EPT</td>
<td>6/06</td>
</tr>
<tr>
<td>Legal Status EPT Evaluation</td>
<td>6/06</td>
</tr>
<tr>
<td>STD Treatment Guidelines</td>
<td>8/06</td>
</tr>
<tr>
<td>CDC EPT Website</td>
<td>10/6</td>
</tr>
<tr>
<td>New Partner Notification Guidelines</td>
<td>2008</td>
</tr>
</tbody>
</table>
Barriers

- Is this legal, and what is my liability?
- Is this an acceptable standard of medical care?
- Will EPT promote antimicrobial resistance?
- Is this ethical?
Legal Status of EPT in the United States

EPT Permissible
EPT Prohibited
EPT newly legal
EPT legal status uncertain
EPT under consideration

Source: Adapted from Hodge JG. AJPH 2008;98:236
Legal Issues in MN

• “Nothing in this chapter prohibits a licensed practitioner from issuing a prescription or dispensing a legend drug in accordance with the Expedited Partner Therapy in the Management of STD guidance document issued by the US CDC.”

• CDC recommends that EPT when other management options are impractical or unsuccessful

Legal Issues

**EPT**

- Name of original patient sufficient in MN
- Information about medications & STD
- Advice about complications and need for care (e.g. PID)
- Where to seek care
• MN Dept Health has information sheets on their website that can be distributed with medications

http://www.health.state.mn.us/divs/idepct/dtopics/stds/ept/ctinstructions.pdf
Liability

- You can always be sued
- Are you acting in a manner that is consistent with standards of care in your community?
- Can you be sued for not providing EPT?
Is EPT a Good Standard of Care?

- A complete evaluation of all partners would be best
- Are we missing concurrent diagnoses?
- Are we placing partners at significant risk of adverse drug reactions?
STD diagnoses in persons presenting as contacts to
gonorrhea, chlamydia or NGU/MPC
Seattle, Baltimore, Birmingham and Denver

<table>
<thead>
<tr>
<th></th>
<th>Women (n=2507)</th>
<th>Heterosexual Men (n=3511)</th>
<th>Men who Have Sex with Men (n=460)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonorrhea*</td>
<td>3.9%</td>
<td>3.1%</td>
<td>6.1%</td>
</tr>
<tr>
<td>PID</td>
<td>3.7%</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>New HIV</td>
<td>0</td>
<td>0.2%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Early Syphilis</td>
<td>&lt;0.1%</td>
<td>0</td>
<td>0.4%</td>
</tr>
</tbody>
</table>

* GC excludes contacts to GC.

Source: CID 2005;40:787
Adverse Drug Reactions

- Anaphylaxis to macrolides is very rare
- PCN
  - Anaphylaxis with cephalosporins is rare (0.1-0.0001%)
  - ~10% of people report having a PCN allergy
  - Cross reactivity to 3rd gen cephalosporins 1-3%
  - Only avertable reactions are those occurring in persons with a known allergy who take meds despite written warnings
- No cases anaphylaxis to date in CA and WA
Antimicrobial Resistance

- No known chlamydial resistance to azithro
- Cephalosporin resistant GC very uncommon is U.S.
  - Some evidence rising MICs in Japan
- Standard of care is to treat contacts to GC & chlamydia without awaiting test results
  - EPT primarily increases antimicrobial use by increasing appropriate treatment of partners
- In 2005, 55 million prescriptions for Azithro; 3 million cases of chlamydia in U.S.
Ethics

Respect for Patient Autonomy
Beneficence
Nonmaleficence
Justice

- Insofar as RCTs show decreased reinfection in index cases given EPT, EPT is a superior standard of care
- Is EPT better for the partner? Can partners make an informed decision?
## EPT Guidelines

<table>
<thead>
<tr>
<th></th>
<th>CDC</th>
<th>CA</th>
<th>MN</th>
<th>WA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heterosexual</strong> GC &amp; CT</td>
<td>“Can be used as an option when other management strategies are impractical or unsuccessful.”</td>
<td>Partners who are “unable or unlikely to seek timely treatment”</td>
<td>Most appropriate for partners who are unable or unlikely to seek prompt clinical services.</td>
<td>Give if partner treatment “not otherwise assured”</td>
</tr>
<tr>
<td><strong>MSM</strong> GC &amp; CT</td>
<td>Should not be considered a routine partner management strategy</td>
<td>No different recommendation – acknowledges potential risk</td>
<td>Not recommended as routine</td>
<td>MSM should be referred to health Dept.</td>
</tr>
<tr>
<td><strong>Trichomonas</strong></td>
<td>Not recommended as routine</td>
<td>Not addressed</td>
<td>Not recommended as routine</td>
<td>Not addressed</td>
</tr>
</tbody>
</table>
California State EPT Program

- Guidelines promulgated and published
  (Sex Transm Dis 2007, epub)

- Paying for EPT
  - Medicare waiver to pay for PDPT denied
  - State bulk purchasing medication for PDPT for Infertility Prevention Program clinics

- CDC funded evaluation in family planning clinics
CA Family Planning Clinic Evaluation: Association of Treatment Outcome with Management Strategy by Relationship Type

Partner Notification Method Employed

- **Patient Referral**: 54%
- **Bring Partner to Clinic (BYOP)**: 20%
- **PDPT**: 14%
- **None**: 10%

Percentage Partners Treated, by Index Case Report

- **Patient Referral**: 40%
- **BYOP**: 79%
- **PDPT**: 77%
- **None**: 12%

Source: Yu. 2007 CDC STD Prevention Conference
## Association of Treatment Outcome with Management Strategy by Relationship Type

<table>
<thead>
<tr>
<th>Partner Management Strategy</th>
<th>Steady Partner (n=551)</th>
<th>Non-steady Partner (n=404)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BYOP</td>
<td>3.6 (1.8-7.4)</td>
<td>3.5 (1.7-7.0)</td>
</tr>
<tr>
<td>PDPT</td>
<td>2.8 (1.4-5.4)</td>
<td>6.0 (3.3-10.8)</td>
</tr>
<tr>
<td>Patient referral</td>
<td>1.4 (0.7-2.6)</td>
<td>2.0 (1.2-3.3)</td>
</tr>
<tr>
<td>None</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*OR adjusted for patient’s age and race/ethnicity

Source: Yu. 2007 CDC STD Prevention Conference
Steps in Developing and Implementing A New Public Health Intervention

1. Evaluate Existing System & Literature on Alternatives
2. Design Intervention
   Consider Feasibility for Wide-Spread Implementation
3. Individual Level Randomized Controlled Trials
4. Cost-Effectiveness Analysis (relative CEA)
5. Re-Design Intervention for Scale-up
7. Community-Level RCT
Scheme of PN Barriers & Interventions

Index patient diagnosed & treated → Partner Notified → Partner Treated

**BARRIERS**
- Doesn’t know partner(s)
- Doesn’t like partner(s)
- Can’t reach partner(s)
- Afraid of partner(s)
- Access to care (clinic hrs, transportation)
- Partner asymptomatic - not concerned

**INTERVENTION**
- DIS
- Pt Delivered Rx
Proportion of Patients with Untreated Partners at Time of Study Interview

Risk factors: > 1 sex partner 60 days or pt does not anticipate sex with partner in future

Source: STD 2001;28:658
**CONFIDENTIAL SEXUALLY TRANSMITTED DISEASE CASE REPORT**

**LAST NAME**

**FIRST NAME**

**INIT**

**TELEPHONE**

**REASON FOR EXAM:**
- Symptomatic
- Routine Exam—No Symptoms
- Exposed to Infection

**ADDRESS**

**CITY/TOWN**

**STATE**

**ZIP CODE**

**DATE OF DIAGNOSIS**

**ETHNICITY**
- H—Hispanic
- N—Non-Hispanic
- U—Unknown

**RACE:**
- W—White
- B—Black
- AI—American Indian
- AN—Alaskan Native
- A—Asian
- NHPI—Native Hawaiian/Other Pacific Islander
- O—Other
- U—Unknown

**PATIENT HAS SEX WITH:**

**SEX**

**DATE OF BIRTH**

**DATE OF DIAGNOSIS**

**MO**

**DAY**

**YR**

**GONORRHEA (lab confirmed)**

**DIAGNOSIS:**
- Asymptomatic
- Symptomatic - Uncomplicated
- Pelvic Inflammatory Disease
- Ophthamia
- Disseminated
- Other Complications:

**SITE(S):**
- Cervix
- Urethra
- Urine
- Rectum
- Pharynx
- Other

**TREATMENT:**
- Cefixime
- Ceftriaxone
- Ciprofloxacin
- Ofloxacin
- Azithromycin
- Doxycycline
- Other

**CHLAMYDIA TRACHOMATIS (lab confirmed)**

**DIAGNOSIS:**
- Asymptomatic
- Symptomatic - Uncomplicated
- Pelvic Inflammatory Disease
- Ophthamia
- Other Complications:

**SITE(S):**
- Cervix
- Urethra
- Urine
- Rectum
- Pharynx
- Ocular
- Other

**TREATMENT:**
- Azithromycin
- Doxycycline
- Erythromycin
- Ofloxacin
- Other

**SYPHILIS**

- Primary (Chancre, etc.)
- Secondary (Rash, etc.)
- Early Latent (<1 yr)
- Late Latent (>1 yr)
- Congenital
- Neurosyphilis
- late

**DATE RX**

**HERPES SIMPLEX**

- Genital (Initial infection only)
- Neonatal
- Laboratory Confirmation
- Yes
- No

**OTHER**

- Chancroid
- Granuloma Inguinale
- Lymphogranuloma Venereum

**DATE RX**

**SUBMITTED BY (PROVIDER)**

**PERSON COMPLETING REPORT**

**ADDRESS**

**CITY**

**STATE**

**TELEPHONE**

**Need Additional Case Report Forms**
Association of PN Plan on Case Report Form with PN Outcomes

- **All partners already treated**
- **Provider to assure PN**
- **Health dept. assistance requested**

### Percentage Distribution

**Percent**

- 100
- 80
- 60
- 40
- 20
- 0

### Categories

1. **% Given PDPT by Clinician Before Health Dept. contact**
   - 32 (32%)
   - 42 (42%)
   - 6 (6%)

2. **% with Untreated Partners**
   - 30 (30%)
   - 40 (40%)
   - 78 (78%)

3. **Given PDPT by Health Dept.**
   - 16 (16%)
   - 22 (22%)
   - 47 (47%)

4. **Increase in Partner Treatment**
   - 13 (13%)
   - 11 (11%)
   - 39 (39%)

**Source:** Golden et al. *Sex Transm Dis* 2007;epub

* Limited to persons contacted >7 days after treatment
Use of PDPT remained significantly greater in the 2004-05 (OR 3.2, 95% CI 2.5-4.1) compared to 1998-2002 after adjusting for diagnosing site, gender, GC vs. CT, and the presence of case report risk factors for PN failure.
Estimated Percentage of Persons Assuring the Treatment of All of their Sex Partners Among All Cases* of Gonorrhea or Chlamydial Infection in King County

* Nonincarcerated heterosexuals
Assessment of Community-Wide EPT: Simulation Model

50% → 60% partners treated

15 realisations, thick line is median.
Includes annual Ct screening of 25% of women aged <26.

10% increase in partner treatment results in a ~25% reduction in CT prevalence at 2 years, and a ~50% reduction in 4 years.
Chlamydia Positivity in Women Tested in IPP Clinics in King County and WA State Outside of King County, 1998-2007
WA State EPT Community-Level Randomized Trial

- Stepped-wedge community-level randomized trial
  - Unit of randomization = health jurisdiction (n=24)
  - Timing of program institution is randomly assigned as “steps”
    - Every ~6 months - 1st step 9/07, 2nd step 5/08, 3rd step 12/08
- Intervention
  - Case-report based triage of cases for assisted partner notification
  - Free PDPT distributed via large clinics & commercial pharmacies
    - Case report form has prescriptions preprinted for faxing
- Outcome = Prevalence of chlamydia in sentinel clinics (IPP), reported incidence of gonorrhea in women
Cases with at Least One Partner Treated via EPT from the Diagnosing Provider, WA State EPT Community-Level Trial Waves 1 and 2
Preliminary Outcomes: Wave 1 Communities, WA State EPT, Proportion of Partners Notified and Treated

Outcomes restricted to persons interviewed >7 days post treatment. Adjusted for demographic factors.
Conclusions

• Expedited partner therapy (EPT) decreases reinfection rates and increases the proportion of partners treated per index patient report

• EPT is legal in MN, but requires that you dispense information for partners

• EPT can be introduced into a diverse large communities and appears to have a population-level effect on the proportion of all partners treated

• The population-level of effect of EPT on the occurrence of STD or STD associated morbidity, like that of other STD interventions, has yet to be proven