Expedited Partner Therapy in 2022: Updated Guidance and Practical Realities

Lindley Barbee, MD MPH
Associate Professor, Infectious Diseases, University of Washington
Deputy Director, Public Health -- Seattle & King County HIV/STD Program
Medical Director, PHSKC, Sexual Health Clinic
Medical Consultant, CDC, Division of STD Prevention, Clinical Team

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What is Expedited Partner Therapy (EPT)?

Prescription of STI treatment to partners of patient with STI.

Rx written WITHOUT examining sex partner.

Legality varies from state to state.

EPT for gonorrhea and chlamydia has been shown to reduce recurrent STI in patient.*

Evidence for EPT’s effectiveness: a meta-analysis

Effectiveness and cost-effectiveness of traditional and new partner notification technologies for curable sexually transmitted infections: observational study, systematic reviews and mathematical modelling

Effectiveness and cost-effectiveness of EPT with gonorrhea or chlamydia in the index patient by ~40%

- Decreases reinfection of the index patient EPT decreases reinfection with gonorrhea or chlamydia in the index patient by ~40%

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**CLINICAL EFFECTIVENESS OF PARTNER NOTIFICATION**

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>EPT Events</th>
<th>Simple patient ref</th>
<th>RR M-H, random, 95% CI</th>
<th>RR M-H, random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>3.1.1 Chlamydia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cameron 2009</td>
<td>10</td>
<td>110</td>
<td>7</td>
<td>110</td>
</tr>
<tr>
<td>Schillinger 2003</td>
<td>87</td>
<td>887</td>
<td>108</td>
<td>900</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>997</td>
<td>1010</td>
<td>35.6%</td>
<td>0.90 (0.60 to 1.35)</td>
</tr>
<tr>
<td><strong>3.1.2 Gonorrhea or chlamydia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Golden 2005</td>
<td>92</td>
<td>1375</td>
<td>124</td>
<td>1376</td>
</tr>
<tr>
<td>Kissing 2003</td>
<td>39</td>
<td>344</td>
<td>68</td>
<td>285</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>1719</td>
<td>1651</td>
<td>53.2%</td>
<td>0.61 (0.39 to 0.94)</td>
</tr>
</tbody>
</table>

**FIGURE 3** Forest plot of randomised controlled trials of EPT vs. simple patient referral, by infection and overall.

CAVEATS

• Data is from trials from early 2000s. Therefore, before...
  - Azithromycin and cephalosporin reduced susceptibility GC
  - Our understanding about doxy v azithro for rectal CT and rectal CT in cis-
    women

• Only studied in cisgender heterosexuals

• Treatment regimens were
  - Chlamydia: Azithromycin 1g
  - Gonorrhea: Cefixime 400mg plus 1g Azithromycin

• When chlamydia was examined individually, not statistically significant
2021 STI Treatment Guidelines: What’s new for EPT?

• Chlamydia:
  – Use doxycycline 100mg PO BID x 7 days

• Gonorrhea:
  – Use cefixime 800mg PO x 1
  – Add doxy if chlamydia cannot be excluded

• MSM:
  – Use shared decision-making
Why change Chlamydia treatment regimen?

Risk Difference 26%
(95% CI: 16-36%)
p<0.001

N=567

Doxy 100% effective vs. Azithromycin 97%

Azithromycin NOT non-inferior (difference 3.2%)

Doxy TF

0/283

AZM TF

5/284
Why change Chlamydia treatment regimen?

- WHO and CDC guidance suggests removing drug when >5% resistance

- Antimicrobial Stewardship
  - AZM half-life ~68 hours
  - Resistance in many bacterial species
    - Streptococci
    - M. genitalium
    - Shigella
    - Campylobacter

![Graph showing percentage of Neisseria gonorrhoeae isolates with elevated minimum inhibitory concentrations (MICs) to ceftriaxone, cefixime, and azithromycin — Gonococcal Isolate Surveillance Project, United States, 2009–2018.](image)

- AZM-R N. gonorrhoeae ~5% USA
- AZM-R N. gonorrhoeae in MSM ~10%
Why change the Gonorrhea treatment regimen?

- Changes to first-line recommended GC treatment – Ceftriaxone Dose
  - Azithromycin resistance
  - New understanding in PK/PD
  - Mutant prevention concentration

PK/PD: fT>MIC

CHISHOLM (math model): ~20 hours

CONNOLLY (mouse model): ~24 hours

Wide 95% CI
Corresponds to Wide Inter-individual Pharmacokinetics

Dark shading <10 h above MIC, light shading 10–20 h above MIC, no shading >20 h above MIC.
Why change the Gonorrhea EPT treatment regimen?

**PK/PD Criterion: fT>MIC**

<table>
<thead>
<tr>
<th></th>
<th>400mg</th>
<th>800mg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cefixime</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Clinical</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Urogenital</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400mg once dose:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIC 0.008:</td>
<td>96.2% (92.3% - 98.4%) (n=183, MIC ≤0.03)</td>
<td>97.9% (93.9% - 99.6%) (n=141, MIC ≤0.03)</td>
</tr>
<tr>
<td>MIC 0.03:</td>
<td>90.1% (82.2% - 96.3%) (n=77, MIC ≤0.25)</td>
<td>Not enough data</td>
</tr>
<tr>
<td>MIC 0.25:</td>
<td>63.8% (53.3% - 73.5%) (n=94, MIC ≤0.25)</td>
<td>75% (42.8% - 94.5%) (n=12, MIC ≤0.25)</td>
</tr>
<tr>
<td><strong>Rectal</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>400mg once dose:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MIC 0.008:</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>MIC 0.03:</td>
<td>unknown</td>
<td>unknown</td>
</tr>
<tr>
<td>MIC 0.25:</td>
<td>unknown</td>
<td>unknown</td>
</tr>
</tbody>
</table>

**Known fT>MIC**

- **400mg once dose:**
  - MIC 0.008: 32.6 hours
  - MIC 0.03: 25.7 hours
  - MIC 0.25: 15.3 hours

- **800mg once dose:**
  - MIC 0.008: unknown
  - MIC 0.03: unknown
  - MIC 0.25: unknown

**PK/PD**

- **Chisholm (math model):** ~20 hours
- **Connolly (mouse model):** 38.6 hours
What is the evidence for EPT in MSM?

- Evidence remains limited
- One RCT compared EPT to passive partner notification in Peru
  - Not about efficacy based on reinfection
Considerations for 2021 EPT Recommendations

- **Chlamydia regimen**
  - Doxy has more potential side effects compared to Azithro
    - Photosensitivity
    - Pill esophagitis
    - Teratogenic in pregnancy
  - Doxy not studied for EPT
    - Concerns about adherence, inability to assess for pregnancy or counsel etc.

- **Gonorrhea regimen**
  - Limited efficacy at the pharynx
  - New data: Pharyngeal gonorrhea + 20-40%* of heterosexual contacts to GC

- **EPT in MSM**
  - Limited data
  - Pharyngeal GC common
  - Elevated antimicrobial resistance
  - High prevalence of co-infection with syphilis and HIV

*Chow et al STD 2019; McLaughlin et al CDC STD Prevention Conference 2020
PHSKC’s EPT Recommendations

• Chlamydia:
  - For cisgender female partners of cis-men: Use Azithromycin 1g
  - Doxy or azithromycin for male partners

• Gonorrhea:
  - Cefixime 800mg PO PLUS 2g Azithromycin

• MSM:
  - Ideally: Patients notify partners to seek testing (GC/CT/Syph and HIV) & treatment
  - Risk reduction: used shared decision-making
Interviewed pharmacists about EPT knowledge.

About 23% knew what EPT was.

About 14% had received a prescription for EPT.

85% would fill an EPT prescription for someone < 18 years old.

After the call, 97% would fill a prescription for EPT.
Time for Q&A
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