Expeditied Partner Therapy for Sexually Transmitted Diseases

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In this issue of the Clinical Infectious Diseases, Kissinger et al. [1] present the findings of a randomized, controlled trial of patient-delivered partner therapy (PDPT) for male urethritis. This study, the third in a series of 3 randomized, controlled trials conducted in collaboration with the Centers for Disease Control and Prevention (CDC) to evaluate PDPT for bacterial sexually transmitted diseases (STDs), found that men who were provided with medication to give to their sex partners were more likely to report that their partners were treated and less likely to be infected 1 month after receipt of treatment. The trial is the largest study to date of PDPT for men, included a substantial number of persons with gonorrhea, and is the first study conducted among a predominantly African American STD clinic population in the inner city. Thus, the trial extends the findings of previous studies to a new population and substantially increases the available data on PDPT for patients with gonorrhea. Because this is the last of the CDC trials to be published, the time is ripe to assess where we stand with PDPT.

Each year, an estimated 3 million Americans acquire a genital tract infection with Chlamydia trachomatis, and 600,000 are infected with Neisseria gonorrhoeae [2, 3]. Screening programs for these infections are ongoing and have been credited with reducing the burden of disease associated with these STDs [4–6]. However, the incidence of gonorrhea in the United States has now been roughly stable for a decade, and the prevalence of chlamydial infection is either stable or slightly increasing [7]. Whatever the impact of our current public health efforts, it seems unlikely that simply continuing ongoing programs will result in further decreases in the morbidity associated with these infections. So what is to be done?

One option is to improve partner notification. "Partner notification" refers to the process of informing the sex partners of persons with an STD of their exposure and ensuring their treatment. Partner notification was widely adopted as part of syphilis-control efforts in the United States in the 1940s [8]. In some areas of the country, public health partner notification programs were subsequently expanded to include persons with gonorrhea, chlamydial infection, and HIV infection. These programs have traditionally used public health staff, usually Disease Intervention Specialists (DIS), to interview patients with STDs and to ensure that their partners receive treatment. This approach has been shown to increase the proportion of partners treated among male STD clinic patients [9, 10]; however, few data are available on the efficacy of traditional partner intervention efforts for women and for persons who are treated for bacterial STDs outside of STD clinics. Mathematical models suggest that improvements in partner notification could substantially decrease the prevalence of bacterial STDs in the population, but this has never been definitively demonstrated [11, 12]. Thus, although the rationale for improving partner notification programs is strong, the evidence supporting the current approach to partner notification is relatively weak.

Perhaps more importantly, the resources available for partner notification are nowhere near what would be needed to provide traditional public health partner notification services to all persons who receive diagnoses of reportable STDs. In areas of the United States with high STD-related morbidity, <20% of persons with gonorrhea or chlamydial infection reported to health departments were interviewed by public health staff for purposes of partner notification in 1998 [13]. In 2001, only approximately one-third of HIV-infected persons reported to health departments received partner notification services [14]. With increasing numbers of syphilis cases in much of the country, and with clearly inadequate funding and effort devoted to partner notification for HIV infection, it seems unlikely that partner notification programs for gonorrhea and chlamydial infection can be expanded to meet the unmet need for service, partic...
Table 1. Summary of randomized, controlled trials of expedited partner therapy for gonorrhea and chlamydial infection.

<table>
<thead>
<tr>
<th>Ref.</th>
<th>Year</th>
<th>Population</th>
<th>Intervention(s)</th>
<th>Persistent or recurrent STD outcome</th>
<th>NNT to prevent 1 case of reinfection</th>
<th>Outcome for treated partners</th>
<th>NNT to assure treatment of 1 extra sex partner</th>
<th>Comments(s)</th>
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<td>[28]</td>
<td>2003</td>
<td>1787 women treated for chlamydial infection in diverse clinical settings in 5 US cities</td>
<td>Azithromycin PDPT vs. PR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Chlamydial infection was diagnosed in 12% of subjects in PDPT arm vs. 15% in PR arm at 1 or 4 month follow-up&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Chlamydial infection, 33</td>
<td>Not reported</td>
<td>...</td>
<td>Study did not achieve goal enrollment</td>
</tr>
<tr>
<td>[29]</td>
<td>2005</td>
<td>2751 persons (24% were men) reported to have gonorrhea or chlamydial infection in King County, WA</td>
<td>EPT vs. SPR&lt;sup&gt;c&lt;/sup&gt;</td>
<td>At the 10–18-week follow-up, infection was detected in 9.9% of subjects in the EPT arm and in 13% in the SPR arm&lt;sup&gt;d&lt;/sup&gt;</td>
<td>STD, 32; N. gonorrhoeae infection, 12.5; C. trachomatis infection, 50</td>
<td>Partner treatment reported by 64% in the EPT arm and 42% in the SPR arm</td>
<td>PDPT, 8.3</td>
<td>Subgroup analysis showed that EPT was significantly more effective for gonorrhea (RR, 0.32; 95% CI 0.13–0.77) than for chlamydial infection (RR, 0.82; 95% CI, 0.62–1.07)</td>
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<td>[1]</td>
<td>2005</td>
<td>977 men treated for urethritis in New Orleans, LA, STD clinic; 60% had gonorrhea, and 20% had chlamydial infection</td>
<td>3 arms: PDPT with azithromycin plus ciprofloxacin or cefixime, BEPR, and PR&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Infection at follow-up detected in 23% of subjects in the PDPT arm, 14% in the BEPR arm, and 43% in the PR arm&lt;sup&gt;P&lt; .001&lt;/sup&gt;</td>
<td>Gonorrrhea or chlamydial infection, 4.8 (PDPT vs. PR)</td>
<td>Partner treatment reported by 56% of subjects in the PDPT arm, 44% in the BEPR arm, and 34% in the PR arm&lt;sup&gt;P&lt; .001&lt;/sup&gt;</td>
<td>PDPT vs. PR, 5</td>
<td>Follow-up interviews were performed for 79% of men; STD testing was performed for 38% of those men</td>
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NOTE. BEPR, booklet-enhanced patient referral; EPT, expedited partner treatment; NNT, no. of index patients with sexually transmitted infection receiving EPT needed to treat; STD, sexually transmitted disease; PDPT, patient-delivered partner therapy; PR, patient referral; Ref., reference; SPR, standard partner referral.

<sup>a</sup> Patients referred partners for treatment without assistance.

<sup>b</sup> OR, 0.80; 95% CI, 0.62–1.05.

<sup>c</sup> EPT therapy included PDPT with azithromycin for chlamydial infection or azithromycin and cefixime for gonorrhea. Nine percent of partners in the EPT arm were treated after direct contact with study staff. Standard partner referral involved patient referral with an offer of assistance for notifying sex partners.

<sup>d</sup> RR, 0.76; 95% CI, 0.59–0.96.
ularly with use of the current, resource-intensive partner notification model.

Because health departments cannot provide partner notification services to most people with gonorrhea or chlamydial infection, they leave the responsibility for partner notification to diagnosing clinicians and their patients. Most health care professionals do little more than advise patients that their partners need treatment, and <20% of the professionals seem to know whether their patients’ partners have been treated [15, 16]. So, in most instances, patients alone are responsible for partner notification, and probably only approximately one-half of sex partners are treated [15, 17–22]. The inadequacies of this system are glaring, and the 1997 Institute of Medicine report on STDs concluded that the current approach to partner notification employed by US health departments needed to be redesigned [23].

Expedited partner therapy (EPT) should be part of that redesign. EPT is a global term for approaches to treatment of the sex partners of persons with STDs that bypass the requirement that all partners undergo a medical evaluation before therapy. In most instances, EPT has involved patient-delivered partner therapy (PDPT), the practice of dispensing medications to patients to give to their sex partners. Although not traditionally condoned by public health authorities or medical professional organizations, approximately one-half of all STD clinicians in the United States at least occasionally employ PDPT, although relatively few do so consistently [15, 24, 25].

The case for EPT is now strong. The first evidence that EPT might improve partner notification outcomes came from 2 observational studies that found that women treated for chlamydial infections were less likely to have that infection diagnosed again if they were given PDPT [26, 27]. As shown in table 1, the 3 recently completed, randomized, controlled trials support the findings of these observational studies. When the trials are compared, EPT appears to be more effective for prevention of recurrent gonorrhea than for prevention of recurrent chlamydial infection, and the absolute magnitude of benefit associated with EPT is greater when assessing its impact on the percentage of sex partners treated than when evaluating its effect on persistent or recurrent infection. Nonetheless, the finding that EPT reduces the rate of infections seen during follow-up and increases the proportion of partners treated was consistent across studies, was observed in subjects of both sexes, and applied both to patients with gonorrhea and to those with chlamydial infection.

EPT has a downside. Although no published study has reported the occurrence of significant adverse events in partners given PDPT, concern about adverse events persists, and PDPT should be dispensed with instructions and a warning concerning drug allergies. Insofar as partners treated via EPT may elect not to seek medical evaluation, an opportunity to identify concurrent morbidities is lost. However, with the exception of trichomonal infection, for which testing is probably performed inconsistently, relatively few heterosexuals evaluated as sex partners of persons with gonorrhea or chlamydial infection appear to have concurrent STDs that would go untreated with the EPT regimen that is most frequently used. A recent retrospective study conducted in 4 STD clinics in the United States found that only 3.8% of 3503 women evaluated as partners of persons with gonorrhea, chlamydial infection, or nongonococcal urethritis were treated for pelvic inflammatory disease [30]. HIV infection was diagnosed in only 19 (0.4%) of 4716 heterosexual partners, although the prevalence of HIV infection approached 1% among persons seen at the Baltimore, Maryland, STD clinic, and it was >5% among men who have sex with men at this clinic, demonstrating that use of PDPT may be associated with higher opportunity costs in some populations.

It would be best if every sex partner of a patient who received a diagnosis of gonorrhea or chlamydial infection underwent a complete medical evaluation. But that is not happening in the United States; resources are unlikely to exist in the foreseeable future to provide traditional public health partner notification services to the >1,250,000 Americans reported to have an STD or HIV infection annually [7, 31], and syphilis and HIV infection should be prioritized. We need a new approach to partner notification for gonorrhea and chlamydial infection. I believe that most heterosexuals who receive diagnoses of these STDs should be offered medication to give to their sex partner(s), and that public funds should be made available to pay for the medications and to support this activity. At present, the legal status of EPT is uncertain in much of the United States, and it is clearly not legal in some areas [32]. Health departments, professional organizations, and the CDC should work to remove legal barriers to EPT. EPT is not the complete answer to controlling gonorrhea and chlamydial infection. But the data are now sufficiently compelling that EPT should be promoted as a reasonable—and often desirable—standard of care. Future research should focus on establishing cost-effective programs to institute EPT widely, to measure its impact on the prevalence of disease in the population, to minimize and monitor for adverse events associated with the practice, and to develop other means to improve partner notification outcomes, particularly for persons for whom EPT is not effective.

Acknowledgments

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References


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