CD Summary

October 15, 1996
Vol. 45, No. 21

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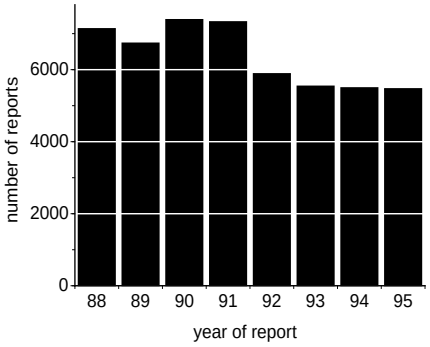
CHLAMYDIAL INFECTIONS: UPDATE AND NEW DIAGNOSTIC TOOLS

CHLAMYDIA TRACHOMATIS is the most common sexually transmitted pathogen in western countries. More than 4 million chlamydial infections are estimated to occur each year in the United States.

Chlamydiosis has been reportable in Oregon since 1987. Infection rates peaked in 1990, and have declined in recent years to less than 200 reported cases per 100,000 persons. In 1995, 5,468 cases were reported (see figure), giving *Chlamydia* infections the pole position on Oregon's list of reportable diseases. The runner up (hepatitis A, with 2,955 cases reported) was a distant second.* This decrease in chlamydiosis cases comes in the wake of stepped-up programs of comprehensive patient screening, treatment, partner notification and education of infected individuals.

Reported Chlamydial Infections, Oregon, 1988-95



DEMOGRAPHIC PATTERNS

In contrast to syphilis, for example, chlamydial infections are most commonly reported among adolescents; in 1995, the rate for 15-19 year olds was five times higher than the overall rate for all ages (see figure). While this difference may be inflated because of screening programs that target this age group, there is no getting around the fact that sexual activity in general and "unsafe" sex in particular are very common among teens and young adults—also putting them at risk for other sexually transmitted diseases and pregnancy.

In general, **reported** *Chlamydia* rates are much lower for males, and this difference is most pronounced among 15-19 year olds (see figure, *verso*). Historically, screening programs have been targeted primarily at young women, who are much more likely to develop symptomatic infections. Although little research has been done to explain why, anecdotal accounts suggest that males are less likely to volunteer for examination.† Confirming that there is no justice in the world of STDs, women are also much more likely to suffer serious sequelae of infection. Lower genital tract infection can progress to endometrial and tubal infection and, in turn, to complications such as infertility, ectopic pregnancy, and chronic pelvic pain.

DIAGNOSTIC CHALLENGES

Early detection and treatment of cervical infections clearly represents an important avenue for the prevention of PID.[1] However, the diagnosis can be difficult because many infected women do not have characteristic signs or symptoms. Early detection relies mainly on screening high risk women using sensitive and specific laboratory tests. Although culture of endocervical swab specimens has been considered the diagnostic gold standard for confirmation of cervical chlamydial infection in women,[3] other screening methods may now be more sensitive.

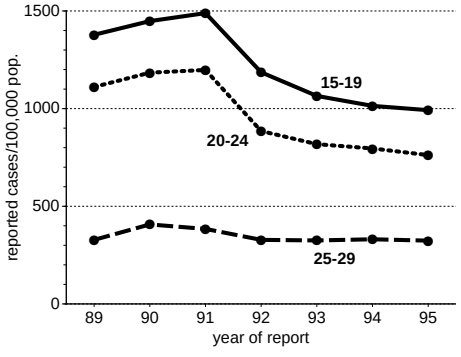
In men, *C. trachomatis* can cause nonspecific urethritis, and is often asymptomatic. Traditional testing methods (e.g., culture, EIA, DFA, and nucleic acid probes) all require the discomfort of a urethral swab. A variety of methods for detecting *Chlamydia* in urine have been tested, but urine cultures have been generally a waste of time. Antigen detection of methods using centrifuged first-void urine have proven moderately successful, but this approach has not been as sensitive as culturing urethral swabs,[5] especially in asymptomatic men.

NEW LCR TEST LICENSED

In December 1995, the FDA licensed a new diagnostic test for *Chlamydia* infections. According to advertising hype, the Ligase Chain Reaction (LCR) test is able to detect the presence of as few as 1-5 organisms through the miracle of DNA replication. In contrast, traditional tests require as many as 100,000 organisms in a clinical specimen for detection.[2] LCR assays can be used with comparable effectiveness on both swab or urine samples. Given the relative ease of collecting the latter, urine may be worth a closer look.

Culture studies indicate that 50-60% of women infected with *C. trachomatis* have infections in both the cervix and the urethra; 30% are infected in the cervix alone; and 5-30% are infected in the urethra alone. Urine samples may contain organisms from the urethra or the cervix, whereas an endocervical swab should not contain organisms from an infected urethra. Thus, given a urine assay that is sufficiently sensitive and specific, urine testing should identify a higher proportion of infected women than testing of endocervical swabs alone. Available evidence suggests that the LCR assay is highly effective for the detection of *C. trachomatis* in urine from women—with or without signs or symptoms of genitourinary tract infection. LCR urine assays pick up some 30% more

Reported Incidence of Chlamydial Infections by Age Group, Oregon, 1989-1995



* Incidentally, hepatitis A rates in Oregon have *plummeted* in 1996. As of October 11, "only" 687 cases had been reported, compared with 2368 by this time last year. Our soap shipment finally arrived, apparently.

† ouch!

CD Summary (ISSN 1058-7888) is published biweekly, free of charge, by the Oregon Health Division, a part of the Dept. of Human Resources. 800 NE Oregon St., Portland, Oregon 97232
Periodicals postage paid at Portland, Oregon.
Postmaster—send address changes to:
CD Summary, 800 NE Oregon St., Suite 730, Portland, OR 97232.

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October 15, 1996
Vol. 45, No. 21

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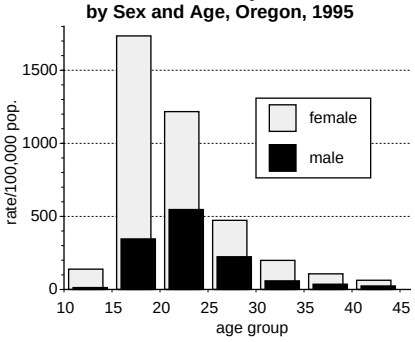
infections than swab cultures. One drawback of only using LCR testing of urine for screening programs is that other disorders that might be diagnosed during a pelvic examination may be missed. The options for evaluating symptom-free women warrant further study.[3]

For men, LCR testing of first-void urine is a most excellent alternative to urethral swabbing for detecting *C. trachomatis* urethral infections.[5] The sensitivity of this test (depending on the study) ranges from 93 to 98% and the specificity approaches 100%. In contrast, urine culture has a sensitivity on the order of 7-9%. Culture or antigen detection from a urethral swab or antigen detection on concentrated urine have a sensitivity of 45-95%, depending on the assay, specimen transport, and other factors.

Lab-Confirmed Chlamydial Infections by Sex and Age, Oregon, 1995



CAVEATS AND CONCLUSIONS

The exceptional performance of this new test suggests that it could become the preferred test for the diagnosis of genitourinary tract infections with *C. trachomatis*. Oregon is one of the few states that have begun using LCR assays in selected health department settings. All is not sweetness and light, however. Urine specimens to be tested by LCR must be kept refrigerated or frozen, and should be received at the lab within 4 days of collection. This poses logistic problems, particularly for remote sites. The main drawback is cost: LCR tests run almost three times the price of EIA assays. Indeed, Oregon currently has only enough money to pay for a limited number of LCR tests. When that pot is empty, we will have to reevaluate our options: go back to EIAs, change screening criteria, etc. While the EIA is still a good test, particularly in higher prevalence populations, cutbacks presumably mean an increase in missed diagnoses. (NB: While most STD clinic patients are treated presumptively, missed diagnoses do limit follow-up activities, including contact tracing efforts.)

Were LCR tests to be widely used, we could see an *increase* in the number of reported cases over the next few years—especially among young males—as a higher proportion of cases are diagnosed. Ultimately, of course, reduction of disease rates will depend not only upon the successful detection and treatment of carriers but our ability to reduce the behaviors that lead to disease transmission.

RECOMMENDED TREATMENT REGIMENS

The recommended* regimens for uncomplicated urethral, endocervical, or rectal chlamydial infections among adults are:

- doxycycline (100 mg p.o. bid x 7 days), *or*
- azithromycin (1 g p.o. in a single dose).

NOTE: Neither doxycycline nor azithromycin is recommended for use during pregnancy. The safety and efficacy of azithromycin for persons ≤15 have not been well established.

Alternative Regimens

Alternative treatment regimens for uncomplicated urethral, endocervical, or rectal chlamydial infections are:

- ofloxacin (300 mg p.o. bid x 7 days), *or*
- erythromycin base (500 mg p.o. qid x 7 days), *or*
- erythromycin ethylsuccinate (800 mg p.o. qid x 7 days), *or*
- sulfisoxazole (500 mg p.o. qid x 10 days).

NOTE: Ofloxacin is not recommended for treating pregnant women or persons <17 years old. Sulfisoxazole is not as effective as other listed regimens.

*CDC, Recommendations for the prevention and management of *Chlamydia trachomatis* infections, 1993. MMWR 1993;42, RR-14:50-55.

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